

ABSTRACTS



NeuroGASTRO 2019

Biennial Meeting of the European Society of Neurogastroenterology and Motility

September 5th to 7th, 2019

Centro Cultural de Belém Lisbon, Portugal

www.neurogastro2019.org

ORAL ABSTRACT

7 | Xyloglucan for the treatment of diarrhoea predominant irritable bowel syndrome

N. Viazis¹; N. Lolas²; C. Pontas¹; E. Tsoukali¹; G. Karampekos¹; F. Gkeros¹; G. Filippidis¹; M. Vraka¹; C. Chatzievangelinou¹; G. J. Mantzaris¹

¹Evangelismos Hospital, Athens, Greece; ²Private practice, Kalymnos, Greece

Objective: There is a strong rationale for the use of agents with film-forming protective properties, like xyloglucan, for the treatment of acute diarrhoea. However, data for patients with diarrhoea predominant irritable bowel syndrome (IBS) are scarce.

Methods: Retrospective analysis of prospectively collected data in adult patients with diarrhoea-predominant IBS, diagnosed as recurrent abdominal pain or discomfort present at least three days/month in the last three months, associated with two or more points: improvement with defecation, onset associated with a change in frequency of stools, onset associated with a change in form of stool. The consistency of stools was assessed using the 7-point Bristol Stool Scale. Patients with diarrhoea-predominant IBS, were those with loose or watery stools (Bristol scale 6-7) > 25% and hard or lumpy stool <25%, in the absence of anti-diarrhoeal or laxative use. Patients studied received for 28 days a tablet containing Xyloglucan Tamarindus indica seed standardized extract, combined with a pea protein reticulated with grape seed extract and a prebiotic, the xilooligosaccharide (Ibutin-Gelsectan, Galenica s.a. Athens – Greece) twice daily. Patients responding to treatment were those in whom diarrhoea disappeared, i.e. reported two or less non-watery stools emissions per day (stool of type 5 or less on the Bristol scale). The presence and intensity of abdominal pain and flatulence was also measured on a seven-point Likert scale (7 very much better, 6 much better, 5 somewhat better, 4 same, 3 somewhat worse, 2 much worse, 1 very much worse).

Results: From September 2018 till February 2019, 58 patients [males/females = 14/44, mean age (SD) = 45.31 (13.89) years] were studied, from whom 37 (63.7%) responded to treatment, with a mean reduction of stool emission of 0.53 (95% CI: 0.05 to 1.02 stool emissions). A significant improvement in the intensity of abdominal

pain and flatulence was also noted, since 31 (53.4%) and 28 (48.3%) patients reported being much better or very much better regarding the abdominal pain and flatulence respectively. Treatment appeared safe and well tolerated and no serious adverse events were reported.

Conclusions: Treatment with xyloglucan is safe and improves symptoms in patients with diarrhoea-predominant IBS.

8 | Central blockage of nesfatin-1 has anxiolytic effects but does not prevent corticotropin-releasing factor-induced anxiety or depressiveness in male rats

S. G. Kühne¹; M. A. Schalla¹; T. Friedrich¹; P. Kobelt¹; M. Goebel-Stengel²; M. Long³; M. Rivalan³; Y. Winter³; M. Rose¹; A. Stengel²

¹Charité Center for Internal Medicine and Dermatology, Department for Psychosomatic Medicine, Charité-Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany; ²Department of Psychosomatic Medicine and Psychotherapy, University Hospital Tübingen, Tübingen, Germany; ³Cognitive Neurobiology, Berlin Mouse Clinic for Neurology and Psychiatry, Humboldt University, Berlin, Germany

Objective: The anorexigenic peptide nesfatin-1 has not only been described to be involved in food intake regulation but also in the mediation of anxiety and depressive-like behavior in normal weight rats. However, the underlying mechanisms have to be unraveled. Thus, this study aimed to investigate the role of nesfatin-1 in the mediation of anxiety and anhedonia under basal conditions (vehicle) and under corticotropin-releasing factor (CRF)-induced stress.

Methods: Therefore, normal weight male rats received two intracerebroventricular (icv) injections of an anti-nesfatin-1 antibody or IgG control antibody followed by CRF or vehicle before behavioral testing.

Results: In the elevated zero maze (EZM), a test that assesses anxiety and explorative behavior, rats that received the nesfatin-1 antibody followed by vehicle showed significantly increased time spent in and number of entries into the open arms indicating anxiolytic effects of

the nesfatin-1 antibody under basal conditions. Control antibody/CRF-treated animals spent significantly less time in the open arms compared to control antibody/vehicle rats, an effect that was not altered by the application of nesfatin-1 antibody. In the novelty-induced hypophagia test (NIH), a test focusing on depressive-like behavior and anhedonia, no significant effects of the nesfatin-1 antibody could be observed.

Conclusions: These results indicate that central blockage of nesfatin-1 has anxiolytic effects but nesfatin-1 does not participate in CRF downstream mediation of anxiety and depressive-like behavior.

9 | GERD diagnosis by new consensus in clinical practice – The additional value of mean basal impedance

M. Sousa; J. Carvalho; T. Freitas; J. Silva; C. Gomes; E. Afecto

Centro Hospitalar de Vila Nova de Gaia e Espinho, Vila Nova De Gaia, Portugal

Objective: In the last years, there was the need to create a more objective evaluation for gastroesophageal reflux disease (GERD), to better predict treatment outcomes and ROME IV and Lyon consensus were published. However, with classical pH-impedance (pH-I) measures some patients will still have diagnostic uncertainty and new metrics, like mean nocturnal basal impedance (MNBI) have emerged to improve diagnostic yield.

This study aimed to describe prevalence GERD, FH, HE and undetermined using GERD's current consensuses and to evaluate if MNBI could show added value by comparing it in the different groups.

Methods: Patients that performed pH-impedance monitoring (pH-I) for suspected GERD between 2013-2018 were included. GERD was defined as endoscopic evidence of reflux, acid exposure time (AET) > 6% or AET 4-6% and >80 reflux episodes (RE). When there was lack of evidence of reflux on endoscopy and AET < 4%, patients were defined as hypersensitive oesophagus (HE) if positive symptom association and functional heartburn (FH) if negative symptom association. Indeterminate diagnosis was considered in patients with AET = 4-6% and patients without symptoms during 24 hours of measurement.

Results: We included 216 patients – 45% of the patients had typical GERD's symptoms with the remainder referred for atypical symptoms, mainly, chronic cough (25%), laryngitis (21%) and chest pain (14%). The prevalence of GERD, FH, HE was 30%, 24% and 7%, respectively. 31% of the patients had an undetermined diagnosis (8% AET = 4-6%; 31% absence of reported symptoms).

MNBI was correlated with AET and RE ($P < 0.001$) and was lower in patients with AET > 6% and patients with endoscopic evidence of reflux. Although lower in patients with RE > 80 and positive symptom association, it didn't reach statistical significance.

MNBI was lower in patients with GERD compared to FH/HE ($1384 \pm 990\Omega/2507 \pm 891\Omega$; $P < 0.001$) but it did not differ between

patients with FH and EH ($2617 \pm 788\Omega/2580 \pm 1147\Omega$; $P = 0.841$). The cut-off value of MNBI to distinguish GERD from non-GERD was 1747Ω (AUC = 0.820 ± 0.037 ; $P < 0.001$), with a sensitivity of 79% and specificity of 80%.

Conclusions: In our study sample, only 30% of the patients referred for pH-I had confirmed GERD and there was a substantially proportion of patients with an undetermined diagnosis. MNBI can be helpful in differential between GERD and FH/HE.

	MNBI (mean $\pm$ SD)	P
AET	NA	<0.001*
AET > 6%	$1367 \pm 1035\Omega$ vs $4501 \pm 890\Omega$	<0.001*
Number of refluxes	NA	0.01*
Refluxes > 80	$1920 \pm 1185\Omega$ vs $2305 \pm 1048\Omega$	0.06
Positive SI	$1822 \pm 1150\Omega$ vs $2257 \pm 1061\Omega$	0.05
Positive SAP	$1054 \pm 1157\Omega$ vs $2227 \pm 1854\Omega$	0.08
Endoscopic evidence of GERD	$1518 \pm 1047\Omega$ vs $2200 \pm 1047\Omega$	0.013*
GERD vs non-GERD	$1384 \pm 990\Omega$ vs $2507 \pm 891\Omega$	<0.001*
FH vs EH	$2617 \pm 788\Omega$ vs $2580 \pm 1147\Omega$	0.84

Table 1 – Mean nocturnal basal impedance (MNBI) relation to pH-I parameters and in GERD (gastroesophageal reflux disease) vs FH (functional heartburn) and HE (hypersensitive esophagus); SD- Standard deviation, AET – acid exposure time; SI – Symptom index; SAP – Symptom association probability; * $p < 0.05$ was considered statistically significant

10 | DeMeester score in the era of modern diagnosis of GERD

M. Sousa; J. Carvalho; T. Freitas; J. Silva; C. Gomes; E. Afecto

Centro Hospitalar de Vila Nova de Gaia e Espinho, Vila Nova De Gaia, Portugal

Objective: DeMeester Score (DMS) is a composite score first reported in 1974 for the diagnosis of gastroesophageal reflux disease (GERD) in ambulatory pH-impedance monitoring. Recently, Lyon consensus supported a more objective evaluation of patients considering diagnosis only if specific endoscopic findings or when acid exposure time (AET) is greater than 6%. The aim was to compare agreement between DMS and Lyon's criteria for the diagnosis of GERD.

Methods: Included all patients that performed 24 hour pH-impedance monitoring for suspected GERD between 2013-2018. DMS parameters included total number of refluxes, % total time esophageal pH < 4, % upright time esophageal pH < 4, supine time esophageal pH < 4, number of reflux episodes ≥ 5 minutes, and longest reflux episode (minutes). DMS was considered positive for GERD if >14.7. Lyon consensus were considered positive for GERD if AET > 6% or AET 4-6% and number of refluxes >80. Statistical analysis was performed using SPSS. Categorical variables are presented as frequencies and continuous as means $\pm$ standard deviations. Agreement was calculated using Cohen's kappa (κ).

Results: We included 216 patients (64% female, mean age 57 ± 15 years). Most of the patients presented with atypical symptoms (55%) and the majority of pH-impedance monitoring were

performed off therapy (86%). Mean DMS was 21.8 ± 90.6 and mean AET was $5.1 \pm 7.4\%$. Endoscopic evidence of GERD was present in 16 patients (7%). According with DMS, 34% ($n = 74$) of the patients would have a diagnosis of GERD compared to 29% ($n = 63$) with Lyon criteria. There were only 7% discordant results ($n = 15$) between DMS and Lyon criteria, showing an almost perfect agreement ($k = 0.839$; $P < 0.001$).

Conclusions: There are no data that show that Lyon criteria are superior (or inferior) to DMS for the diagnosis of GERD. In our study, the two tests showed almost perfect agreement.

13 | “Anal Tape” a genuine external device for fecal incontinence (FI)

D. M. Livovsky; B. Koslowsky; J. Lysy

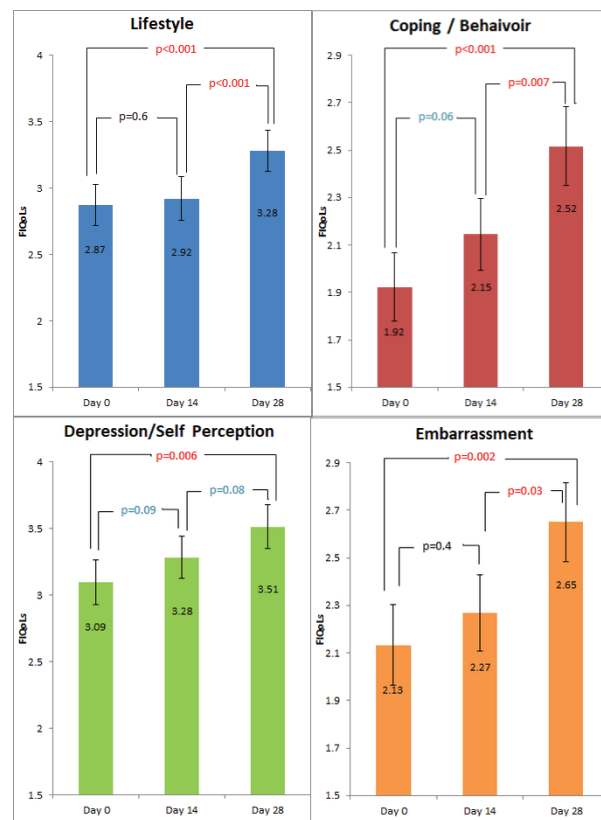
Digestive Diseases Institute, Shaare Zedek Medical Center, Jerusalem, Israel

Objective: FI is a common underreported, debilitating condition with devastating negative impact in quality of life. We developed an “anal tape” and an adjusting applicator to apply it to the skin surrounding the anus. We used a commercially available elastic band with a special adhesive that is approved for use in the skin. We aimed to determine the safety and efficacy of the “anal tape” device in patients with fecal incontinence.

Methods: Four-week prospective, self-controlled open label study of patients with mild to moderate FI. Primary outcome was improvement in any of the 4 domains (lifestyle, coping/behavior, depression/self-perception, embarrassment) in the “FI quality of life scale (FIQOLS)”. Secondary outcomes included improvement in frequency of FI events and safety. Days 0-14 served as self-control period and days 14-28 as study period. Patients were asked to rate their satisfaction and willingness to use the device in the future with a 1-100 points visual analog scale.

Results: Twenty patients were included; median age 64 (Range 27-82), all females. Significant improvement was observed in all domains of the FIQOLS from baseline to day 28 (Lifestyle: 2.8(0.69) to 3.3(0.68) $p < 0.001$; Coping/Behaviour 1.9(0.64) to 2.5(0.73) $p = 0.0002$; Depression/Self-Perception 3.1(0.75) to 3.5 (0.74) $p = 0.006$; Embarrassment 2.13(0.67) to 2.65 (0.76) $p = 0.002$) but not between baseline and day 14 (Lifestyle: 2.8(0.7) to 2.9 (0.7) $p = 0.6$; Coping/Behaviour 1.9(0.64) to 2.1(0.67) $p = 0.06$; Depression/Self-Perception 3.1(0.75) to 3.2 (0.71) $p = 0.09$; Embarrassment 2.13(0.67) to 2.26 (0.89) $p = 0.4$). Quality of life Improved significantly between day 14 and day 28 in all domains except Depression/Self-Perception ($p = 0.08$, in all other comparisons p value was < 0.04) (Figure 1). Out of fifteen completed diaries, 11 had reduced, 2 not changed, and 2 increased FI events. Five patients (25%) had a $> 50\%$ improvement in FI events. Median satisfaction and willingness to use the anal tape in the future was 80 and 90, respectively. Mild difficulty to remove the anal tape was the only adverse event.

Conclusions: The use of the anal tape was safe and effective. The primary outcome of significant improvement in quality of life was achieved.



15 | Validation of GERD diagnosis by the Lyon consensus criteria: Detailed analysis of 4-day PH-studies in patients referred for investigation of reflux symptoms and healthy volunteers with a focus on physiological markers that predict response to therapy in a prospective clinical trial

M. Fox¹; R. Sweis²; E. Tucker³; K. Knowles³; A. Anggiansah⁴; T. Wong⁴

¹Klinik Arlesheim & University of Zürich, Arlesheim, Switzerland; ²Upper Gastroenterology Service, University College London Hospital, London, United Kingdom; ³NIHR Nottingham Digestive Diseases Biomedical Research Unit, Nottingham University Hospitals NHS Trust, University of Nottingham, Nottingham, United Kingdom; ⁴Gastroenterology and Hepatology, Guy's and St. Thomas' Hospital, London, United Kingdom

Objective: The Lyon Classification of gastro-esophageal reflux disease (GERD) is based on clinical, endoscopic and physiological data (Gyawali et al. Gut 2018). Measurements from pH-impedance studies used to discard or support GERD diagnosis include: esophageal acid exposure time (AET $< 4\%$ and $> 6\%$), the association between reflux events and symptoms (symptom index (SI) $> 50\%$) or symptom associated probability (SAP positive; $< 5\%$ probability of a chance association). Intermediate results are considered inconclusive and require support from other measurements or modalities. Current diagnostic cut-offs are based on expert opinion and have not been validated in clinical studies. This analysis of prospectively collected data tested validity of the Lyon Classification in terms of (i) discrimination

between health and disease (ii) diagnostic consistency over 4 consecutive days and (iii) prediction of treatment outcome.

Methods: Clinical, endoscopic and physiological data were analyzed from 136 patients with typical reflux symptoms and 25 healthy volunteers (HVs) that completed 96-hour catheter-free pH-studies (Bravo, Medtronic, Duluth, USA). Prospective clinical validation was performed in 70 patients to assess how candidate biomarkers predict response to twice-daily proton pump inhibitor (PPI).

Results: Endoscopy, AET, Symptom Index (SI) did not discriminate between groups; however, ≥ 3 reflux-associated symptoms per day (nRAS) and positive Symptom Association Probability (SAP) identified patients with high sensitivity and specificity. Diagnostic consistency was high for negative and positive findings at $<2\%$ and $>7\%$ AET, 0 and ≥ 3 nRAS, 0% and $>40\%$ SI and SAP. Prospective validation identified candidate biomarkers that predicted outcome after 2-weeks twice-daily PPI therapy. Endoscopy and AET did not predict PPI response. SI (9.2% vs 30.2%, $P = 0.0023$) and nRAS (1.0 v 2.6, $P = 0.012$) were higher in PPI-responders. Optimal diagnostic cut-offs identified by receiver operating curve analysis were the presence of SI $\geq 25\%$, nRAS ≥ 3 /day and a positive SAP predicted positive outcome.

Conclusions: Thresholds that discriminate HVs from GERD patients and provide a consistent diagnosis can be defined; however, Lyon Classification cut-offs for conclusive GERD diagnosis based on AET and SI should be wider than at present. Clinical validation indicates that the presence of SI $\geq 25\%$, nRAS ≥ 3 /day and a positive SAP predicts a positive response to PPI-therapy.

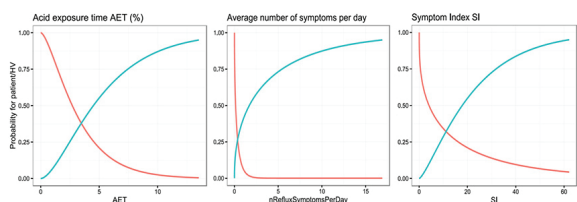


FIGURE. Probability that a record with given Acid Exposure Time (%AET), number of reflux associated symptoms (nRAS) per day or Symptom Index (SI) is from HV or patient. Values are computed from gamma-distribution fits to the data. The difference between the ranges of the confidence intervals was used to discriminate between groups. From these curves one can compute the range where the probability of being a patient is >0.9 , and <0.1 . The range in between is the inconclusive zone.

16 | Microbiological and metabolomic factors predict the clinical outcome of low-FODMAP diet and traditional dietary advice in patients with diarrhea-predominant irritable bowel syndrome: Results of a prospectively planned analysis of data from a randomized controlled trial

L. Zhang¹; M. Fox²; B. Misselwitz³; N. Dai¹

¹Department of Gastroenterology, Zhejiang University School of Medicine Sir Run Run Shaw Hospital, Hangzhou, China; ²Klinik Arlesheim & University of Zürich, Arlesheim, Switzerland; ³University of Zürich, Zürich, Switzerland

Objective: A randomized controlled trial was performed to compare efficacy of low-FODMAP diet (LFD) and traditional dietary advice (TDA) as treatment for irritable bowel syndrome with diarrhea (IBS-D). A prospectively planned analysis was performed to test the hypothesis that dysbiosis in terms of excessive saccharolytic fermentation (i.e. the capability of the colonic microbiota to digest carbohydrates) could predict response to the LFD intervention.

Methods: One hundred and eight IBS-D patients were randomized to LFD or TDA. Primary endpoint was a >50 -point reduction in IBS Severity Scoring System (IBS-SSS) at three weeks. Stool samples collected before and after the dietary intervention were assessed for microbiota (specific taxa and diversity) and metabolomic profile (including short-chain fatty acids and fermentation index described by Valeur and colleagues). Factors associated with outcomes were identified by a logistic regression model analysis.

Results: Among 100 patients (47 women; mean age 44 ± 13 years) that completed the study, the primary endpoint was met in 30/51 (59%) patients with LFD and 26/49 (53%) with TDA ($\Delta 6\%$, 95%-CI: -13% to 24%). In stool samples, LFD increased i-butyric and i-valeric acids, non-saccharolytic taxa and other putative beneficial bacteria, but reduced n-butyric acid ($P = 0.045$) and Bifidobacterium content ($P = 0.019$). Similar effects were not observed for TDA. Saccharolytic fermentation index A at baseline showed a positive associations with outcome in LFD (log odds-ratio = 4.9, 95%-CI: -0.06 to 9.86), conversely, a negative association was found for TDA (log odds-ratio = -6.17 , 95%CI -11.92 to -0.42). Microbiota in responders to LFD and non-responders to TDA had evidence of dysbiosis in terms of reduced microbiota diversity and high saccharolytic capability.

Conclusions: Low-FODMAP diet and traditional dietary advice similarly reduce symptoms in IBS-D patients. LFD but not TDA has effects on microbiota and metabolites. The presence of microbial dysbiosis, in terms of reduced microbial diversity and high saccharolytic capability, predict positive outcome of LFD. These findings suggest that it is possible to identify IBS-D patients likely to respond to LFD based on relatively simple laboratory tests without the need for detailed gene sequencing. This approach would likely improve compliance, efficacy and cost-efficiency of dietary treatment and also avoid any unnecessary risk of adverse events.

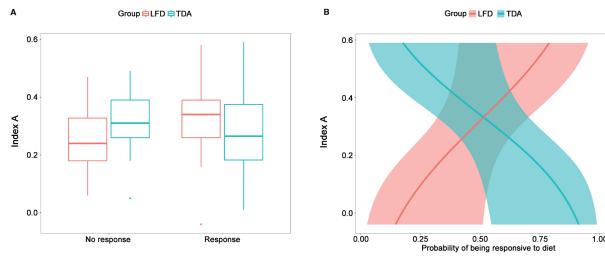


FIGURE. Raw data and model predicted patients' probability of having response to low-FODMAP diet (n=48) or traditional dietary advice (n=39). LFD, low-FODMAP diet; TDA, traditional dietary advice; Index A, indicator of saccharolytic fermentation, is calculated as acetic acid concentrations minus propionic and n-butyric acid concentrations divided by the total concentration of SCFA.

19 | Does intestinal microbiota composition differ between diarrhea-predominant irritable bowel syndrome patients with or without an altered lactulose breath test?

L. B. Fernandez¹; F. Man²; C. Dorribo¹; J. Lasa¹

¹CMBF, Buenos Aires, Argentina; ²GASTRO, Buenos Aires, Argentina

Objective: It has been suggested that the intestinal microbiota is associated with the development of diarrhea-predominant Irritable Bowel Syndrome (IBS-D). A significant proportion of such patients exhibit abnormal hydrogen excretion on lactulose breath tests, which could be associated with small intestinal bacterial overgrowth (SIBO). Patients with IBS-D and an abnormal lactulose breath test may show a different intestinal microbiota profile, which could be associated with such alterations in gas excretion. **AIM:** To compare the bacterial and fungal composition of intestinal microbiota of IBS-D Argentinean patients with or without SIBO.

Methods: Adult patients with IBS-D (Rome III criteria) were consecutively enrolled. One fecal sample per patient was collected for microbiota and mycobiota analyses. Furthermore, patients undertook a lactulose breath test (LHBT). An increase of at least 20 ppm in hydrogen excretion before 100 minutes was considered to be a criterion for SIBO. After genomic DNA extraction and purification, bacterial and fungal composition of fecal samples were analyzed based on 16S rDNA and ITS2 sequencing respectively.

Results: 71 patients were enrolled; mean age was 43.5 ± 14.5 years and 62% were female. 76% were SIBO positive. No significant differences were found in terms of demographic features between SIBO-positive and SIBO-negative patients. 16S rDNA alpha and beta diversity analyses showed comparable microbiota composition between SIBO positive and SIBO negative. However, Akkermansia genus and upper-related taxa were significantly more abundant (+672%, $P = 0.009$) in SIBO negative patients. Furthermore, Turicibacter genus and upper-related taxa were also more abundant (+535%, $P = 0.04$) in SIBO negative patients. Cloacibacillus genus was greatly increased in SIBO negative patients (+8463%, $P = 0.0006$). On the other hand, Ruminococcaceae UCG 003 and Ruminoclostridium 9 genera were decreased in SIBO negative

patients (−70% and −46.6%, $P = 0.003$ and 0.0007 , respectively). Mycobiota analyses showed no major difference.

Conclusions: Differences in terms of bacterial and fungal composition of intestinal microbiota were found between SIBO-positive and SIBO-negative IBS-D patients. Clinical implications of these findings require further investigation.

20 | Impact of saccharomyces boulardii cnm I-745 on microbiota & mycobiota for the treatment of bacterial overgrowth in IBS-D patients

L. B. Fernandez¹; F. Man²; C. Dorribo¹; J. Lasa¹

¹CMBF, Buenos Aires, Argentina; ²GASTRO, Buenos Aires, Argentina

Objective: To compare the efficacy and safety of Sb plus dietary advice vs dietary advice only on small intestinal bacterial overgrowth (SIBO) in IBS-D patients and to describe their impact on intestinal microbiota composition and clinical improvement.

Methods: Adult patients from 2 referral centers in Buenos Aires with IBS-D (Rome III criteria) and SIBO were randomized (1:1) to receive either Sb plus dietary advice (Sb group) or dietary advice only (Control group) for 15 days. At the beginning and at the end of treatment, patients were asked to collect a fecal sample and underwent a lactulose breath test. Severity of symptoms was assessed with the IBS-SSS score and stool consistency was evaluated with the Bristol Stool Scale. Bacterial and fungal composition of fecal samples were analyzed based on 16S rDNA and ITS2 sequencing respectively. Additional qPCR analysis was performed to quantify the abundance of *F. prausnitzii*, *M. smithii*, *B. thetaotomicron* and *P. aeruginosa*.

Results: Fifty-four patients were included and 48 (27 Sb, 21 control) were evaluated for efficacy. Sb treatment led to a significant decrease of hydrogen excretion (difference between groups: −1800, IC95[−3595; −53], $P = 0.04$). Microbiological analyses showed an adequate alpha and beta diversity, which enforced the good quality of samples. With regards to bacterial composition, *c_Coriobacteriia* (−67%), *c_Deltaproteobacteria* (−77.6%) and *g_Hungatella* (−74.9%) were decreased. Interestingly, *F. prausnitzii* was more abundant in patients with marked clinical improvement with Sb: stool consistency normalization (+120%), negative SIBO with improved IBS-related symptoms (+400%), such as reduction of abdominal pain (+76.5%). Mycobiota analyses showed significant modifications in *Saccharomyces* and phylogenetic related lineage (*g_Saccharomyces* (+27%), *g_Debaryomyces* (−88%)) and *g_Filobasidium* (>1000%) and upper related taxa. In addition *g_Penicillium* and upper related lineage were 100 times more abundant in SIBO negative samples after Sb treatment. Five patients in each group reported at least one adverse event (AE). One patient reported 1 serious AE (papillophlebitis) unrelated to the treatment.

Conclusions: Sb CNM I-745 reduced the bacterial overgrowth and improved digestive symptoms in IBS-D patients. These effects were associated with intestinal microbiota modifications. The increased abundance of *F. prausnitzii* observed in *S. boulardii* patients with symptom resolution merits further research.

26 | Mixed method approach investigating patient psychopathology and physician experiences in primary care settings

A. Georgiades¹; A. Accarino²; A. Rodriguez-Urrutia²; F. J. Eiroa Orosa¹

¹University of Barcelona, Barcelona, Spain; ²University Hospital Vall d'Hebron, Universitat Autònoma de Barcelona, Barcelona, Spain

Objective: Functional Gastrointestinal Disorders (FGIDs) are disorders of brain-gut interaction that result from a combination of motility disturbance, visceral hypersensitivity, altered mucosal, immune function, altered gut microbiota and central nervous system processing. The objectives of the present study were to examine the relationship between incongruence, which was defined as a differing perception of the illness between the patient and the physician, and type of diagnosis (functional or organic) with psychopathology.

Methods: The present study involved 1562 patients with gastrointestinal disorders attending primary care centres. Incongruence was calculated as the difference between the clinician-rated functionality (Karnofsky Performance Status Scale) and the subjectively rated quality of life (physical functioning of the SF-36 subscale). Psychopathology was measured by means of scoring the responses given on the Brief Symptom Inventory-18 (BSI-18).

Results: The results indicated that both the presence of incongruent views between the patient and the physician, as well as a functional gastrointestinal diagnosis predict higher levels of psychopathology. Interestingly no interaction was found between the aforementioned variables suggesting that they function independently in psychopathology, thus suggesting that neither of the diagnostic groups had greater levels of incongruence. Whilst both factors contribute to psychopathology, incongruent views between the patient and the physician had a much higher explanatory power on psychopathology than the diagnosis of the patient.

Conclusions: The study has allowed us to identify a psychosocial factor (i.e. incongruence) that may be indicative of lower wellbeing and quality of life.

28 | Early life stress induces type 2 diabetes-like features in ageing mice

H. Ilchmann-Diounou; M. Olier; C. Lencina; A. Riba; S. Barretto; H. Guillou; S. Ellero-Simatos; L. Guzyllakc-Pirou; V. Théodorou; S. Ménard

INRA Toxalim, Toulouse, France

Objective: Early life stress is known to impair intestinal barrier through induction of intestinal hyperpermeability, low-grade inflammation and microbiota dysbiosis in young adult rodents. Interestingly, those features are also observed in metabolic disorders (obesity and type 2 diabetes) that appear with ageing. Based on the concept of

Developmental Origins of Health and Diseases, our study aimed to investigate whether early life stress can trigger metabolic disorders in ageing mice.

Methods: Maternal separation (MS) is an established model of early life stress in rodent. C3H/HeN mice pups were separated from their dam and the rest of the litter 3 hours per day during 10 days starting at post-natal day 2 (PND2). Glucose tolerance and insulin sensitivity were assessed by Oral Glucose Tolerance Test and Insulin Tolerance Test respectively. Fecal microbiota were analyzed by 16S sequencing. Cytokines in supernatant of primary cell culture of small intestine lamina propria (siLP) and spleen were measured by ELISA.

Results: In this study, MS increased fasted blood glycemia, induced glucose intolerance and decreased insulin sensitivity in post-natal day 350 wild type C3H/HeN male mice fed a standard diet without affecting body weight. MS also triggered fecal dysbiosis favoring pathobionts and significantly decreased IL-17 and IL-22 secretion in response to anti-CD3/CD28 stimulation in siLP. Finally, IL-17 secretion in response to anti-CD3/CD28 stimulation was also diminished at systemic level (spleen).

Conclusions: For the first time, we demonstrate that early life stress is a risk factor for metabolic disorders development in ageing wild type mice under normal diet.

30 | Whole genome sequencing analysis of gastroparesis identifies novel risk loci

S. Smieszek; J. Carlin; C. Polymeropoulos; G. Birznieks; M. Polymeropoulos

Vanda Pharmaceuticals, Dc, United States

Objective: Gastroparesis is a disorder characterized by delayed gastric emptying of solid food in the absence of a mechanical obstruction of the stomach, resulting in the cardinal symptoms of early satiety, postprandial fullness, nausea, vomiting, belching and bloating. To ascertain the genetic risk factors for gastroparesis we conducted the first to date whole genome sequencing (WGS) study of gastroparesis cohort.

Methods: We investigated the frequency and effect of rare loss-of-function (LOF) variants in patients with idiopathic and diabetic gastroparesis enrolled in a clinical study, VLY686-2301. The dataset consisted of 119 WGS samples.

Results: Among rare LOF variants, we report an increased frequency of a frameshift mutation within Motilin Receptor (MLNR) gene, variant rs562138828. Motilin is a 22 amino acid peptide hormone expressed throughout the gastrointestinal (GI) tract. The protein encoded by this gene is a motilin receptor which is a member of the G-protein coupled receptor 1 family. We have shown an increased frequency of a frameshift mutation with MAF 0.01 as compared 0.0009 AF in GNOMAD (P-value = 0.01) with Odds Ratio of 21.9. We detect 4/119 gastroparesis patients carry the variant of interest that results in P.Leu202ArgfsTer105. Noteworthy is the fact that

the 4 cases were equally split among idiopathic and diabetic, so this possible GP risk factor appears to be agnostic as to condition. The finding may be of direct relevance to treatment as individuals with the identified mutation may respond differently to gastroparesis treatments especially those targeting MLNR. Among other rare LOF, we identified a case of CHD7 discussed in literature in gastro-related context and a case of CFTR duodenal stenosis pathogenic variant. The CFTR variant has been seen in pancreatitis and is likely causative of Cystic Fibrosis Gut which is characterized by increased mucous viscosity and development of intestinal inflammation, dysbiosis and dysmotility.

Conclusions: Whole genome sequencing of gastroparesis patient samples showed enrichment for rare variants in the MTLR in cases compared with controls. The identified LOF variants within the region can serve as risk factors for disease as well as inform treatments, especially given the knowledge of different response to treatment.

33 | Pancreatic cancer cells access nerves via TGFbeta1-mediated transdifferentiation of perineural epithelial cells into mesenchymal-like cells

I. E. Demir; E. Krohmer; D. Saur; H. Friess; G. Ceyhan

Klinikum rechts der Isar, Technical University of Munich, Muenchen, Germany

Objective: Mechanisms of “neural invasion” in pancreatic cancer are widely unclear. Classically, cancer cells are assumed to actively break or mechanically disrupt the perineural barrier to find access into nerves. Here, we hypothesized an alternative mechanism of cancer cell entry into nerves, i.e. the “transdifferentiation” of perineural epithelial cells of the outermost nerve sheath in the cancer micro-environment.

Methods: Human perineural epithelial cells (HPEC) were cultured within the supernatants of different human pancreatic cancer cell lines and analyzed for markers of epithelial-mesenchymal-transition (EMT). The integrity of the perineural epithelial cell linings was analyzed in human pancreatic cancer tissues by quantitative immunohistochemistry of circumferential perineural GLUT1 staining. Transcriptomic arrays were performed with cancer-conditioned HPEC. Genetically engineered mice with precursors of pancreatic cancer (p48-Cre; LSL-KrasG12D/“KC”) and pancreas-specific TGFbeta1 overexpression (KC; TGFbeta1ov+/) were analyzed for the perineural integrity.

Results: Treatment of HPEC with supernatants of three different human pancreatic cancer cell lines resulted in morphological alterations in the HPEC that were reminiscent of EMT. Accordingly, cancer-conditioned HPEC overexpressed Vimentin and N-Cadherin, and downregulated E-cadherin. The transcriptomic analysis of the cancer-conditioned HPEC revealed expression changes that pointed out towards an EMT signature. Among the

different potential mediators of EMT, the only factor that was specifically enriched in the supernatants of human pancreatic cancer cell lines was TGFbeta1. Accordingly, increasing concentrations of TGFbeta1 in the culture medium of HPEC resulted in prominent EMT-like changes in HPEC. In human pancreatic cancer tissues, GLUT1-expressing HPEC were widely lost as opposed to the intact barrier around nerves in normal pancreas. Moreover, analysis of the perineural integrity in KC; TGFbeta1ov+/ revealed prominent loss of perineural integrity upon TGFbeta1 overexpression when compared to KC mice.

Conclusions: Cancer cell-induced transdifferentiation of perineural epithelial cells seems to be the initial mechanistic event that enables pancreatic cancer cell access into nerves. In this context, TGFbeta1 signaling seems to be of paramount importance in mediating neural invasion in pancreatic cancer and is thus of potential therapeutic relevance.

37 | Distension-evoked nerve-mediated secretion in porcine distal colon

K. Elfers; A. Filzmayer; S. Hoppe; G. Mazzuoli-Weber

Institute for Physiology and Cell Biology, University of Veterinary Medicine Hannover, Foundation, Hannover, Germany

Objective: Distension evoked secretion is mainly studied in rodents models. Due to nutritional and physiological similarities the porcine intestine seems a valuable model for the human one, but little is known about distension evoked secretory functions. Our objective was to investigate porcine colonic secretion in response to mechanical distension.

Methods: Colonic tissue preparations (n = 32) obtained from 8 pigs (~ 28.2 kg, both sexes) were mounted in Ussing chambers and short circuit currents (Isc) were measured. Tissue distension was evoked four times (each 30 minutes apart) by applying a 60 seconds lasting 60 mm Hg pressure with a pump on the serosal side. Amplitude of secretory response and secretion index were calculated and compared in a paired manner in control tissues (n = 4) and tissues bathed with chloride (Cl-) or bicarbonate (HCO3-) free solution (each n = 4) and control tissues and tetrodotoxin (TTX) treated tissues (each n = 8), respectively.

Results: Distension evoked increase in Isc was reduced by trend in tissues after change to Cl- free buffer compared to control conditions (15.29 ± 11.46 vs 19.5 ± 1.05 $\mu\text{As}/\text{cm}^2$) but was not affected by omitted HCO3-. Secretion index was significantly reduced by Cl- free buffer (1846 ± 846.6 vs 238 ± 97.37 $\mu\text{As}/\text{cm}^2$) but not changed by HCO3- compared to control conditions. Tissues pretreated with TTX showed significantly reduced magnitude of secretory response and decreased secretion index compared to responses without TTX (15.41 ± 7.14 vs 9.21 ± 3.62 and 1702 ± 295.7 vs 1294 ± 485.205 $\mu\text{As}/\text{cm}^2$).

Conclusions: In porcine colon distension of the intestinal wall evokes secretion indicated by increase in Isc as it has been shown for other

species. This secretion response is CI- dependent and at least in part nerve mediated as indicated by the effects of CI- free buffer solutions and treatment with TTX. In further experiments we will investigate whether there are effects of age or intestinal localization on the distension evoked secretory response in the porcine colon.

38 | Defining gastrointestinal transit time using video capsule endoscopy: A study of healthy controls

J. O'Grady¹; C. L. Murphy¹; L. Barry²; M. Buckley²

¹University College Cork, Cork, Ireland; ²Mercy University Hospital, Cork, Ireland

Objective: To determine gastric and small bowel transit times, in the fasting state, among ambulatory healthy controls.

Methods: Subjects with no pre-existing gastrointestinal symptoms or conditions were suitable for inclusion. After fasting from midnight the night before, the capsule was swallowed with water and subjects then continued fasting for a further 4 hours. While allowed to leave and carry out usual activities of daily living, the subjects did not engage in strenuous exercise during the eight hour recording period. Endoscopic images were reviewed to determine gastric transit time (GTT), defined as time from first gastric image to first duodenal image, and small bowel transit time (SBTT), defined as time from first duodenal image to first caecal image.

Results: Median, and interquartile range (IQR), gastric transit time was 22 (10- 48) minutes, and median (IQR) small bowel transit time was 198.5 (157-240.5) minutes.

Conclusions: These data, for the first time to our knowledge, provide references for gastrointestinal transit times among healthy ambulatory subjects using capsule endoscopy. This potentially strengthens the clinical use of video capsule endoscopy in the investigation of patients with suspected gastrointestinal motility disorders.

39 | Epidemiology and management of achalasia in Korea based on nationwide 5009 patient dataset: Adoption of high-resolution manometry

K. W. Jung; G. H. Kim

Asan Medical Center, Seoul, South Korea

Objective: The incidence of achalasia has increased since the advent of high-resolution manometry (HRM) in Western countries. However, the precise epidemiology of achalasia in Korea is still unknown. Therefore, we aimed to determine the incidence, epidemiological features, and treatment modalities of achalasia in the entire population of Korea using information from nationwide dataset.

Methods: We evaluated data from the Korean Health Insurance Review and Assessment Service Database for all patients diagnosed with primary achalasia (ICD-10 code: K22.0) between 2008 and 2016. The demographics and treatments were also reviewed.

Results: A total of 5009 achalasia cases (53.6% of whom were females) were identified for the period from 2008 to 2016. The mean incidence per 100 000 individuals over the study period in Korea was 1.1 (95% CI 1.03 to 1.16). We observed a steadily increasing trend in the overall incidence rate from 1.03/100 000 in 2008 to 1.27/100 000 in 2016 (P for the trend 0.014, Figure 1). This increase in incidence coincides with the beginning of the widespread use of HRM in Korea in 2011. The incidence of achalasia increased with age (Spearman rho, 0.77; $P = 0.0003$). During the study period, 1350 patients (26.9%) underwent balloon dilatation and 130 patients (1.9%) underwent surgical myotomy.

Conclusions: Achalasia diagnosis in Korea appears to have increased over the past 10 years similarly to Western countries, possibly due to the improved diagnostic modality of HRM.

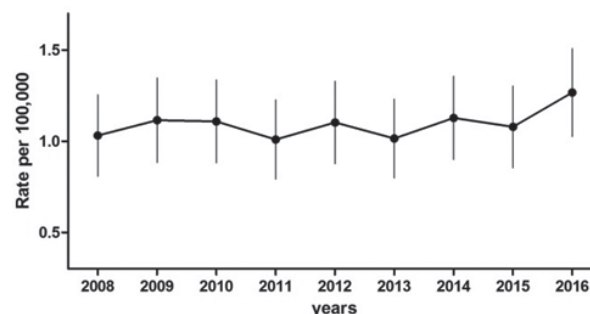


FIGURE 1. The incidence of achalasia in Korea between 2008 and 2016. ($P=0.014$)

40 | Visceral obesity measured by dual X-ray absorptiometry and bioimpedance as the predictor for IBS in obese patients

G. Hauser¹; S. K. Majanovic²; A. Belancic³; S. P. Tonicic²; M. Krpina⁴; M. Tkalcic²

¹Clinical Hospital Centre Rijeka; Faculty of Health Studies, Rijeka, Croatia;

²University of Rijeka, Rijeka, Croatia; ³Clinical Hospital Centre Rijeka; Faculty of Medicine, Rijeka, Croatia; ⁴Faculty of Medicine, Rijeka, Croatia

Objective: The evidence regarding the relationship between visceral abdominal tissue (VAT) and the incidence of irritable bowel syndrome (IBS) are sparse. Moreover, the exact measurement method for VAT is still debatable. Lee. GC et.al reported VAT measurement by CT scan which is an invasive and expensive method and not appropriate in everyday usage. We aimed to measure VAT by dual-energy x-ray absorptiometry (DEXA) and biometric impedance and correlate the values with the presence of IBS symptoms. The primary outcome of this study was to investigate the association between VAT and the risk of IBS. The secondary outcome is to compare two different methods for VAT measurement.

Methods: Totally we enrolled 94 obese patients (76.5% F; mean age M = 47.99; SD = 11.8 years). In this case-control study we compare the VAT, Fatty mass (FM), Free Fatty Mass (FFM), Waist circumference (WC) between subjects with obesity and IBS (IBS group N = 29; 30.9%) and controls (obese patients without IBS, non-IBS group N = 65; 69.1%), who underwent obesity programme at tertiary care centre from January 2018. to January 2019. IBS was diagnosed by using Rome IV criteria questionnaire. The association between IBS and abdominal obesity was evaluated by measuring VAT, FFM, FM and waist circumference (WC) using DEXA and bioimpedance.

Results: The prevalence of IBS in this sample was 30.8%, (OR 0.44; 95% (CI): 0.2645 to 0.7525, $P = 0.0025$) among all enrolled subjects. VAT(L) measured by bioimpedance is significant predictor for IBS in obese patients $t = 2.51$, $df = 63.51$, $p < .05$ ($p = 0.01468$); Cohen's $d = 0.51$ (moderately high) IBS ($M = 4.27$; $SD = 2.35$), non-IBS ($M = 6.09$; $SD = 3.94$). Moreover, there is a significant correlation between VAT measurement with bioimpedance and DEXA. FFM, FM and WC as well are not important predictors for IBS in obese patients. Younger obese patients are more prone to have IBS symptoms than older patients (OR 0.93; 95%(CI): 0.88 to 0.97; $P = 0.007$).

Conclusions: Visceral adiposity measured by the simple and non-invasive method is associated with an increased risk of IBS. Bioimpedance and DEXA are reliable methods for VAT measurement. However, neither FFM, FM, BMI and WC are associated with an increased risk of IBS.

Table 1.

Correlations among obesity measurements measured by DEXA and bioimpedance.

	DEXA	D_FM%	D_FFM%	D_VAT(cm3)
Bioimpedance				
I_FM%		0.89**	-0.89**	0.04
I_FFM%		-0.87**	0.87**	-0.03
I_VAT(L)		-0.32**	0.32**	0.48**

** $p < .01$

Correlations among obesity measurements measured by DEXA and bioimpedance

49 | Activity-based profiling of secreted peptidases in irritable bowel syndrome

L. Decraecker¹; B. De Winter²; V. Cacheux²; K. Augustyns²; A. Denadai-Souza¹; G. Boeckxstaens¹

¹KU Leuven, Leuven, Belgium; ²University of Antwerp, Antwerp, Belgium

Objective: Visceral hypersensitivity, mediated by the sensitization of transient receptor potential (TRP) channels on colorectal nociceptors, is a pivotal mechanism underlying abdominal pain in irritable bowel syndrome (IBS). Among soluble mediators hypothesized to mediate TRP channel sensitization, serine peptidases released by the colonic mucosa are strong candidates. Nevertheless, the identity of dysregulated serine peptidases implicated in IBS remains elusive. We first aim to characterize the subclass of serine peptidases that is overactive in rectal mucosa biopsies from IBS patients compared to healthy volunteers (HV). Additionally, we aim to explore the translational potential of UAMC-00050, a novel

serine peptidase inhibitor with demonstrated efficacy in pre-clinical models of VHS, by assessing its inhibitory activity towards serine peptidases released by the rectal mucosa of IBS patients and HV.

Methods: Rectal mucosa biopsies (HV: $n = 7$, IBS: $n = 24$) were incubated in serum-free cell culture medium for 1 hour at 37°C, after which supernatants were collected and stored at -80°C. Profiling the proteolytic activity of rectal mucosa supernatants was performed with fluorogenic substrates selective for serine peptidase subclasses (trypsin-, chymotrypsin- and elastase-like). Similarly, the inhibitory activity of UAMC-00050 was measured by enzyme kinetics.

Results: Active chymotrypsin-, trypsin- and elastase-like peptidases are secreted by the rectal mucosa of HV and IBS patients. Chymotrypsin- and elastase-like activities were low and did not differ between groups. Conversely, trypsin-like activity was higher, being particularly upregulated in a subpopulation of IBS patients (10/24 of IBS values >95th percentile of HV). Using 100 nM of UAMC 00050 ($IC_{50} = 70$ nM), increased trypsin-like activity present in IBS patient supernatants was normalized to the activity level observed in HV supernatants.

Conclusions: We can conclude that among serine peptidases, trypsin-like peptidases are most likely involved in TRP channel sensitization underlying IBS pathophysiology. Moreover, UAMC-00050, which has demonstrated efficacy in pre-clinical models of IBS, can normalize increased trypsin-like activity released by the rectal mucosa of a subpopulation of IBS patients. To get further insight into the mechanism of action of UAMC-00050, we will assess its impact on TRP channel sensitization triggered by incubation of human cells with supernatants of IBS patients.

53 | Rectal hypersensitivity in IBS: A systematic review and meta-analysis

C. Roberts; A. Albusoda; Q. Aziz

Wingate Institute of Neurogastroenterology, London, United Kingdom

Objective: The aim of this systematic review and meta-analysis is to confirm the presence and determine how common rectal hypersensitivity is in IBS and to see other factors such as IBS criteria, age, gender and IBS subtype affects the presence of rectal hypersensitivity. Secondary aims were to see if rectal hypersensitivity was present in IBD to see if inflammation is driving the rectal hypersensitivity, this was achieving by performing a second meta-analysis.

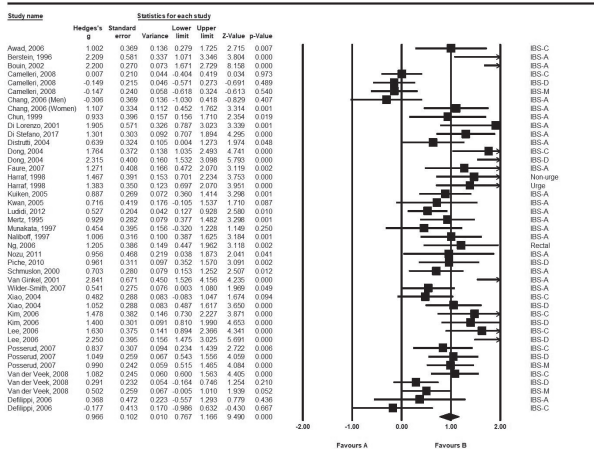
Methods: A systematic review of the literature from MEDLINE and EMBASE databases (1970-Present) was carried out. Prospective studies were included that compared pain or discomfort thresholds to mechanical rectal stimuli in both IBS and control populations. The second review looked at studies assessing pain thresholds to mechanical rectal stimuli in both IBD and control populations. Data were pooled for both meta-analyses and Hedges g effect sizes were calculated with 95% confidence intervals (CIs). This review is registered with PROSPERO (CRD42018095687).

Results: The search strategy identified 684 studies of which 70 were relevant and 31 studies met the inclusion criteria. Rectal sensitivity was greater in an IBS population. The effect size was 0.966

95%CI (0.767-1.166) ($P < 0.0001$). Significant heterogeneity was seen ($I^2 = 77.2\%$). Secondary analysis revealed that gender, IBS subtype and IBS criteria did not significantly affect the presence of rectal hypersensitivity. A significant difference was found between adult and paediatric IBS populations. There was no statistically significant difference between IBD and healthy controls 0.456 95%CI (-0.207-1.119) ($P = 0.178$) ($I^2 = 87.6\%$). Although in active flares there was a significant difference compared to quiescent IBD.

Conclusions: Rectal hypersensitivity is more common in an IBS population compared to controls. Indicating that pain sensation is altered in an IBS population and confirming that an altered rectal pain threshold is a marker of IBS. Rectal hypersensitivity is not present in IBD except during active flares. The mechanisms behind rectal hypersensitivity are not fully understood but are likely due to a combination of peripheral and central factors that require further study to develop mechanism-based management approaches. However, it is unlikely that rectal hypersensitivity that likely occurs in IBS is due to the low-grade inflammatory burden.

Meta Analysis



Meta Analysis

54 | A standardized, valid and unbiased symptom assessment after a carbohydrate challenge: The carbohydrate perception questionnaire (CPQ)

J. Hammer¹; H. F. Hammer²

¹Medizinische Universität Wien, Vienna, Austria; ²Medizinische Universität Graz, Graz, Austria

Objective: Breath tests are extremely popular in clinical practice to determine the presence of carbohydrate malabsorption, however, there is an unmet need for a validated, test-specific symptom questionnaire to evaluate carbohydrate induced perception. Aim: Our aim was to develop and validate a symptom questionnaire for the assessment of carbohydrate related perception.

Methods: After a literature search and initial focus group-style interviews 5 relevant complaints (pain, nausea, meteorism, flatulence,

diarrhea) were identified and a VAS-based questionnaire was constructed. The time frame of symptoms was given as 'current' (for baseline symptom assessment) and 'since filling out the last questionnaire'. Criteria of validity were determined, among others after the implementation of the questionnaire during breath tests in 344 subjects. Correlation between the questionnaire and a medical interview ($n = 338$) was determined; interviews were performed by a physician who was blinded as to the results of the questionnaire.

Results: The scale has good face validity as it is simple, easy to understand and brief. The content validity ratio according to Lawshe equals 1. Intraclass correlation coefficients for test-retest reliability ($n = 159$; 30 minutes interval) demonstrate good repeatability ($P < 0.001$), Cohen's d as a measure of effect size is small (i.e. < 0.40 ; 0.19 or smaller for the five symptoms). Principal component analysis obtained three factors: (A) intestinal gas (three variables: meteorism, flatulence, pain; average loading: 0.83); (B) nausea (one variable: loading 0.94); and (C) diarrhea (one variable; loading: 0.97). The significance according to Bartlett's test of sphericity is < 0.001 . Convergent validity and discriminant validity is supported according to the multitrait-multimethod-matrix method. Moreover, the results given by the questionnaire highly correlate with the result of the medical interview ($p < 0.001$; Fisher exact test). Cronbach's alpha is 0.85 , indicating good internal consistency. Responsiveness to change has been verified during breath tests despite small effect sizes (≤ 0.32).

Conclusions: The adult CarboCeption Questionnaire (aCCQ) is a simple, test-specific questionnaire. It is a valid instrument with excellent psychometric properties to assess gastrointestinal symptoms after carbohydrate ingestion. The aCCQ can replace non-validated symptom assessment during carbohydrate breath tests, e.g. by interview, use of non-validated questionnaires or generic, non-test-specific instruments and allows a standardized diagnosis of carbohydrate intolerance.

57 | An easy quantitative approach to outline neuronal abnormalities in severe gastrointestinal dysmotility

E. Boschetti¹; C. Malagelada²; A. Accarino²; F. Azpiroz²; J. Malagelada²; A. Gori¹; P. Clavensani¹; C. Sternini³; V. Stanghellini¹; R. De Giorgio⁴

¹University of Bologna, Bologna, Italy; ²University-Hospital Vall d'Hebron, Barcelona, Spain; ³UCLA, Los Angeles, United States; ⁴University of Ferrara, Ferrara, Italy

Objective: Current methods to demonstrate enteric neuropathies are mainly based on qualitative histopathological/immunohistochemical evaluation. These methods are hampered by data interpretation and inter-observer variation. This study was designed to establish a quantitative method, to analyze the number of neurons per ganglion in submucosal (SP) and myenteric (MP) plexuses along with the distance between myenteric adjacent ganglia in jejunal full thickness, formalin-fixed, paraffin-embedded biopsies from well characterized severe gut dysmotility (SD) patients.

Methods: Biopsies were collected from 32 SD patients (16-77 years; 22 F); and from $n = 8$ controls (47-73 years 4F). Patients were

subdivided according to a previous qualitative histopathological evaluation: $n = 10$ with an apparently normal (AN) neuro-muscular layer; $n = 14$ with inflammatory (INF) changes throughout the neuromuscular layer; and $n = 8$ with degenerative neuro-muscular alterations (DEG). MP and SP neurons were stained using neuron specific enolase. Neuronal cell bodies/ganglion and the interganglionic distance were counted in at least three sections by 3 independent pathologists. Mann Whitney U test and Kruskal-Wallis test coupled with secondary Dunn's test for multiple comparisons were used for statistical analysis. **Results:** The final discordance among the three operators was only 20%. Compared to controls, MP and SP neurons decreased in SD ($P < 0.001$), as well as in AN ($P < 0.01$), INF ($P < 0.001$) and DEG ($P < 0.001$). Concomitantly the interganglionic distance in SD increased vs. controls ($P < 0.0001$) and in AN ($P < 0.01$), INF ($P < 0.001$) and DEG ($P < 0.001$). **Conclusions:** This method with 80% concordance represents a relatively simple neuronal morphometric approach for paraffin sections from patients with SD. The definition of an increased interganglionic distance may be a criterion to help diagnosis and likely limit the quantitative analysis of neuronal cell bodies per ganglion.

60 | Psychological stress triggers a bystander immune response to food antigens leading to neuronal hyperexcitability and visceral hypersensitivity

J. Aguilera-Lizarraga¹; D. E. Reed²; M. Florens¹; C. Lopez-Lopez²; J. Jaramillo-Polanco²; M. M. Wouters¹; S. J. Vanner²; G. E. Boeckxstaens¹

¹KU Leuven, Leuven, Belgium; ²Queen's University, Kingston, Canada

Objective: Self-limiting infectious gastroenteritis and psychological factors are important risk factors to develop irritable bowel syndrome (IBS). However, the mechanisms underlying the development of visceral hypersensitivity (VHS) remain obscure. We recently showed that mice develop an aberrant immune response to ovalbumin (OVA) during an intestinal infection, with development of mast cell-mediated VHS upon re-exposure to OVA. Here, we evaluated whether, similar to a gastrointestinal infection, psychological stress triggers an aberrant immune response to OVA leading to VHS upon re-exposure.

Methods: BALB/c mice were subjected to repeated water-avoidance-stress (WAS) or sham-stress (shamWAS) for 10 consecutive days and exposed to OVA or saline (OVA-WAS, OVA-shamWAS, saline-WAS). After 5 weeks, mice were re-exposed to OVA. After 8 OVA challenges, OVA-WAS mice were treated with either doxantrazole (mast cell-stabilizer) or vehicle. Visceral pain was evaluated by recording of the visceromotor response upon colorectal distension before and at 2, 4, 6 and 7 weeks post-stress, and after doxantrazole treatment. Next, expression of inflammatory markers was measured in colonic tissue by qPCR. Colonic tissues were also incubated in RPMI medium and supernatant collected. Neuronal excitability was then evaluated using patch-clamp recording in DRG neurons incubated with colonic supernatants. The involvement of H1R was tested using its antagonist pyrilamine.

Results: WAS, but not shamWAS, triggered a short-lasting period of VHS, returning to normal after 4 weeks (Figure 1A). Of note, repeated oral OVA gavage triggered VHS in OVA-WAS mice, but not in OVA-shamWAS or saline-WAS mice (Figure 1A). Doxantrazole treatment normalized VHS in OVA-WAS mice after OVA re-exposure (Figure 1B). OVA-WAS mice displayed increased colonic gene expression of tryptase α/β -1 ($P < 0.05$). Colonic supernatant of OVA-WAS mice reduced neuronal rheobase ($p < 0.02$) and increased the number of action potentials at 2x rheobase ($p < 0.05$) compared to supernatants from normosensitive mice (OVA-shamWAS and saline-WAS), indicating neuronal hyperexcitability. Pyrilamine reversed neuronal hyperexcitability induced by OVA-WAS supernatants ($p = 0.005$), indicating this effect was H1R-mediated. **Conclusions:** Psychological stress can promote the break of oral tolerance to dietary antigens and lead to mast cell-induced VHS upon antigen ingestion. This suggests that, similar to an infectious gastroenteritis, stress may play an important role in the mechanism of food-induced VHS in IBS.

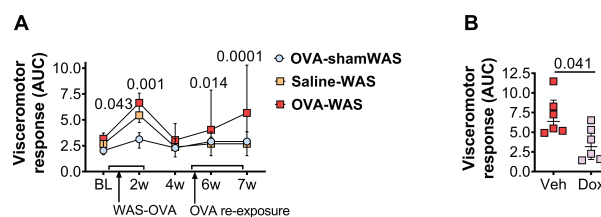


FIGURE 1. (A) Visceromotor response to colorectal distention in OVA-shamWAS (blue circles; $n = 9$), saline-WAS (orange squares; $n = 9$) and OVA-WAS (red squares; $n = 13$) mice at baseline and at 2, 4, 6 and 7 weeks post-stress. (B) Visceromotor response in OVA-WAS mice treated with vehicle (red squares; $n = 6$) or doxantrazole (purple squares; $n = 6$). Data are shown as area under the curve (AUC) normalized to the visceromotor response at maximal distention volume at baseline. Data are reported as median $\pm$ interquartile range (IQR). Two-way RM ANOVA with Sidak's multiple comparisons test was performed for (A) and two-tailed Mann-Whitney test was performed for (B).

64 | Pelvic floor biofeedback is effective treatment for bloating in functional gastrointestinal disorders with outlet dysfunction

P. Iovino¹; M. C. Neri²; L. D'Alba³; F. Cidoni⁴; G. Chiarioni⁴

¹Department of Medicine, Surgery & Dentistry "Scuola Medica Salernitana", University of Salerno, Salerno, Italy; ²Pio Albergo Trivulzio Hospital, Milano, Italy; ³S. Giovanni Addolorata Hospital, Roma, Italy; ⁴Division of Gastroenterology B, AOUI Verona, Verona, Italy

Objective: It has been suggested that biofeedback may improve bloating in constipation due to dyssynergic defecation (DD), but data on different functional gastrointestinal disorders (FGID) are lacking. Aim of our study was to evaluate the efficacy of biofeedback for severe bloating unresponsive to diet advice in FGID patients.

Methods: Sixty-nine consecutive FGID patients consulting for bloating as main complaint were considered for the study. Four refused and were excluded. All the 65 remaining patients reported bloating as

not improved by NICE diet advise augmented by lactose abstinence according to a 5 point Likert scale (worse-major improvement/cure) and rated symptom severity VAS score >24 on a 100-mm scale. All 65 subjects underwent pelvic floor electromyography (EMG) on straining and balloon expulsion test (BET). A biofeedback protocol previously used for constipation due to DD was provided in all patients by a registered nurse who was unaware of the physiology results. Primary study aims were a) subjective report of fair-major improvement from baseline, b) > 50% reduction of bloating VAS score from baseline. Secondary aim was improved BET. Dropouts at 3 months (4 patients) were considered on an intention-to-treat basis. Clinical and physiology follow-up visits were scheduled at 1-3-6 months post-treatment. **Results:** DD was diagnosed in 32 patients (59%), 4 patients (6.3%) were discordant (failed BET, normal EMG), while the remaining 29 patient (43.8%) showed normal defecation pattern. As a whole, 35/65 patients (53.8%) met both primary aims at 1-3-6 months of follow-up (McNemar nonparametric test, p50% reduction of VAS bloating score was observed ($r = 1.00$). In the failed BET group, 30/36 (83.3%) patients learned to evacuate the balloon at all follow-up intervals (Friedman test for non-parametric data $P > 0.001$), while no physiology modifications was observed in the successful BET group. **Conclusions:** Biofeedback aimed to improve defecation effort is effective treatment for severe bloating in FGID with comorbid outlet dysfunction

65 | Tradipitant, a novel NK-1 receptor antagonist, significantly improved nausea and other symptoms of gastroparesis in a phase II trial

J. L. Carlin; V. Rose Lieberman; A. Dahal; M. S. Keefe; C. Xiao; G. Birznieks; M. H. Polymeropoulos

Vanda Pharmaceuticals, Inc., Washington, District Of Columbia, United States

Objective: A phase II multicenter, randomized, double-blind, placebo-controlled trial with gastroparesis subjects demonstrating delayed gastric emptying and moderate to severe nausea were randomized to receive oral 85 mg tradipitant bid or placebo (1:1) for four weeks. Of the 152 patients, 60% of patients had idiopathic and 40% had diabetic gastroparesis. The primary outcome was change in average nausea score from baseline, measured using the 5-point Gastroparesis Core Symptom Daily Diary (GCSDD).

Methods: Overall gastroparesis symptoms were evaluated using the GCSDD, Gastroparesis Cardinal Symptom Index (GCSI), and Patient Assessment of Gastrointestinal Disorders Symptom Severity Index (PAGI-SYM).

Results: A statistically significant and clinically meaningful improvement in nausea and overall gastroparesis symptoms was observed in patients on tradipitant. Subjects receiving tradipitant had a significant decrease in their average nausea score compared to placebo with LS mean difference (95% CI) of -0.53 ($-0.92, -0.13, P = 0.0099$) as well as a significant increase in nausea free days (28.8% increase on tradipitant compared to 15.0% increase on placebo, $P = 0.0160$). A clinically meaningful response of 1-point or more improvement on

the GCSI total score was observed in 46.0% of patients on tradipitant compared to 24.2% of patients on placebo.

Conclusions: Tradipitant treatment resulted in statistically and clinically meaningful improvements in nausea and overall gastroparesis symptoms. Tradipitant was well tolerated with comparable rates of adverse events between tradipitant and placebo groups. These robust efficacy results suggest tradipitant has the potential to become a first line pharmacological treatment for gastroparesis.

71 | Perinatal programming of intestinal homeostasis following exposure to low dose of chlorpyrifos in male rats offspring

M. Guibourdenche¹; H. El Khayat El Sabbouri¹; A. Bouzerara²; N. Djekkoun¹; H. khorsi-Cauet¹; J. Guibourdenche²; V. Bach¹; P. M. Anton³; J. Gay-Quéheillard¹

¹PérisTox, Périnatalité & Risques Toxiques, UMR-I 01, UPJV, Amiens, France;

²Biologie hormonale, CHU Cochin, Université Paris Descartes, AP-HP, Paris, France;

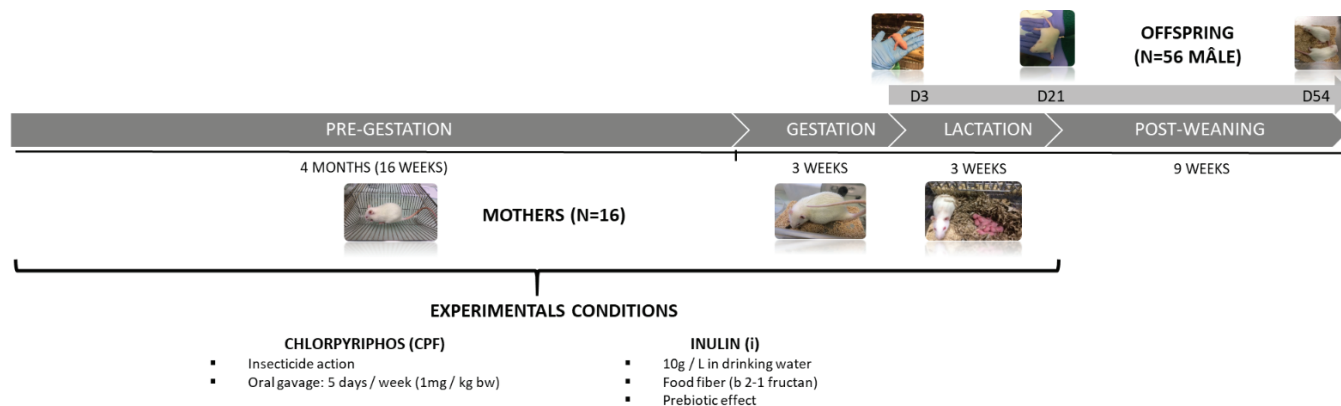
³Equipe PETALES - EA 7519 - Unité Transformations & Agro-Ressources, UniLaSalle, Beauvais, France

Objective: Perinatal period is characterized by phases of development with high sensitivity to environmental factors. Among the risk factors, pesticide exposure are now recognized to program children's metabolism and promote the occurrence of obesity or type 2 diabetes. This study purposes the peri-gestational exposure of mothers (animal model: rat) to a low dose of pesticide (chlorpyrifos, CPF). This exposition might increase the occurrence of obesity, associated with metabolic disorders and disturbances of digestive function in male offsprings.

Methods: 8 female Wistar rats were exposed to CPF, and 8 female rats to its vehicle (controls), supplemented or not with inulin. Female rats were exposed to these experimental conditions during a pre-gestational period of 4 months as well as during the gestation and lactation periods. After weaning, 56 male pups were studied at young adulthood (D60), without any treatment during the experiment. Different segments of the digestive tract were studied for histological analysis, metabolic assays, inflammation and intestinal permeability.

Results: Rats from mothers exposed to CPF have lower birth weights than control pups ($P < 0.05$), but this difference appears to decrease at young adult age (J60). Lipid and glycemic assays did not show significant differences. We noticed a decrease of IGF1 ($p < 0.01$) and leptin plasma levels but not significantly in animals from CPF-exposed mothers. FITC assays didn't show any perturbation of the intestinal permeability. LPS and pro inflammatory cytokines assays (IL6, IL1 β , TNF α) didn't show any tissue inflammation.

Conclusions: Preliminary results reveal that pups from mothers in contact with a pesticide during the peri-gestational period have developmental disabilities characterized by a lower birth weight, but also a decrease in plasma levels of factors involved in growth and metabolism (IGF1 and leptin). We suggest that the pesticide slows down fetal and postnatal development. This hypothesis remains to be confirmed after analysis of tight junction proteins of the intestinal barrier, other inflammatory markers and morphological alterations of the digestive system.



72 | Perinatal programming of intestinal homeostasis following exposure to a high fat diet in male rats offspring

M. Guibourdenche¹; H. El Khayat El Sabbouri¹; A. Bouzerara²; N. Djekkoun¹; H. Khorsi-Cauet¹; J. Guibourdenche²; V. Bach¹; P. M. Anton³; J. Gay-Quéheillard¹

¹PérimTox, Périnatalité & Risques Toxiques, UMR-I 01, UPJV, Amiens, France;

²Biologie hormonale, CHU Cochin, Université Paris Descartes, AP-HP, Paris, France;

³Equipe PETALES – EA 7519 – Unité Transformations & Agro-Ressources, UniLaSalle, Beauvais, France

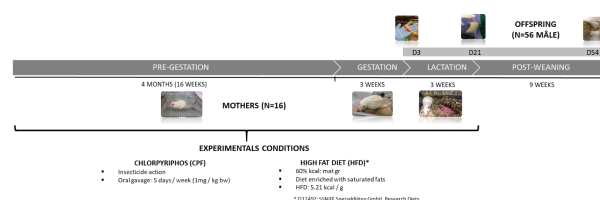
Objective: Perinatal period is characterized by phases of development with high sensitivity to the environmental factors. Among the risk factors, malnutrition or maternal obesity are now recognized to program children's metabolism and promote the occurrence of obesity or type 2 diabetes during postnatal life. This study aims to identify the effects of maternal perigestational exposure to an obesogenic diet in offsprings. This exposure might increase the occurrence of obesity, associated with metabolic disorders, inflammation and disturbances of digestive function in male offsprings.

Methods: Eight female Wistar rats were fed a HFD, and 8 control female rats a standard diet (controls), supplemented or not with inulin. Female rats were exposed to these experimental conditions during a 4-months pre-gestational period as well as during the gestation and lactation periods. After weaning, 50 male pups were studied at young adulthood (D60), without any treatment during the experiment. Different segments of the digestive tract were studied for histological analysis, metabolic assays, inflammation and intestinal permeability.

Results: Rats from mothers fed a HFD have a higher weight than control pups at weaning time ($P < 0.001$), and the inulin appears to limit this weight gain (HFD vs HFDi $p < 0.05$), phenomenon still present at d60 (C vs HFD $p < 0.01$; HFD vs HFDi $p < 0.01$). Lipid and glycemic assays did not show significant differences. FITC assays didn't show any perturbation of the paracellular intestinal permeability. LPS and pro inflammatory cytokines assays (IL6, IL1 β , TNF α) didn't reveal any tissue inflammation.

Conclusions: Our results indicate that pups from mothers fed an obesogenic diet are overweight at both weaning and young adulthood. Interestingly, inulin limits weight gain in these animals. The obesogenic diet of the mother promotes the occurrence of obesity in male offsprings and an inulin-based dietary supplement could help limiting these

deleterious effects. This hypothesis remains to be confirmed after analysis of the intestinal barrier tight junction proteins expression, other inflammatory markers and morphological alterations of the digestive system.



74 | Gut feelings: A randomised, double-blind, placebo-controlled trial of probiotics for depressive symptoms

B. Chahwan¹; S. Kwan²; I. Ashling²; S. V. Hemert³; C. Burke¹; L. Roberts²

¹School of Life Sciences, University of Technology, Sydney, Australia; ²Discipline of Clinical Psychology, Graduate School of Health, University of Technology, Sydney, Australia; ³Winlove Probiotics, Amsterdam, The Netherlands

Objective: Depression is the leading cause of disability worldwide, with evidence suggesting that decreased gut barrier function and inflammation are correlated with depressive symptoms. This study explored whether regular consumption of probiotic supplements (Ecologic® Barrier), led to a reduction in depressive symptoms in participants with a range of symptom severity. The composition of the gut microbiota was additionally monitored to determine any corresponding changes.

Methods: 71 participants with mild to severe depressive symptoms were randomly allocated to two groups, and consumed either a probiotic or placebo supplement daily over eight weeks. Pre- and post-intervention measures of symptoms and vulnerability markers of depression and gut microbiota composition were compared. Participants in the clinical trial were also compared on psychological variables and gut microbiota composition to a non-depressed group ($n = 20$).

Results: Regardless of group allocation, all participants demonstrated improvement in symptoms, suggesting non-specific therapeutic effects associated with weekly monitoring visits. Interestingly, participants with mild and moderate levels of depression who consumed the probiotic demonstrated a significantly greater reduction in cognitive reactivity towards sad mood (a vulnerability factor for depression) compared to the placebo group. However, probiotics did not significantly alter the overall microbiota of depressed individuals after consumption, but the *Lactobacillus* genus showed a significant, but very small increase after probiotic consumption. Additionally, there were only minor differences in the microbiota of depressed individuals pre-intervention when compared to the non-depressed cohort. *Ruminococcus gnavus* was significantly and positively correlated to the DASS depression score.

Conclusions: While microbiota composition was similar between all groups, probiotics did affect a psychological variable associated with susceptibility to depression. Further research is needed to investigate how probiotics can be utilised to modify mental wellbeing, and whether they can act as an adjunct to existing depression treatments.

75 | Does measurement of symptoms during a gastric emptying test improve correlation between symptoms and emptying rate?

F. Carbone; R. de Buysscher; K. Van Den Houte; J. Tack

University of Leuven, Leuven, Belgium

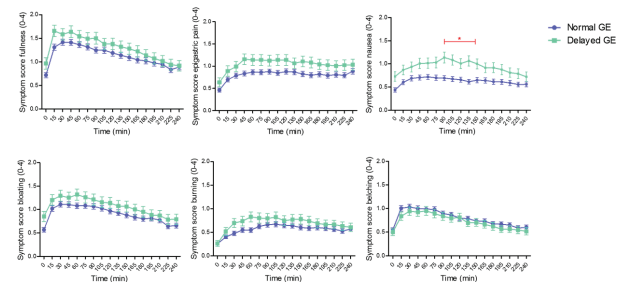
Objective: Functional dyspepsia (FD) and idiopathic gastroparesis (IGP) are characterised by upper gastrointestinal symptoms and a negative endoscopy, and severely delayed emptying in case of gastroparesis. It is argued whether distinguishing these entities is necessary as previous studies showed a poor correlation between delayed gastric emptying (GE) and symptom severity. We aim to evaluate the relationship between symptom severity and GE when simultaneously assessed.

Methods: During a GE test (breath test with ¹³C-octanoic acid labelled 250 Kcal meal), severity (0-4) of 6 symptoms (postprandial fullness (PPF), epigastric pain (EP) and burning (EB), bloating (BL), nausea (N) and belching (B)) was assessed before and every 15 minutes for 4 hours postprandially. The sum of individual symptom scores generates the meal-related symptoms score; the sum of all symptoms generates overall global meal-related symptom severity. Data were compared in patients with normal and delayed GE (cut-off T1/2 ≥ 109 minutes) using non-parametric statistical tests, Mann-Whitney test, 2-Way-Anova with Bonferroni post hoc-test correction and spearman correlation.

Results: Of 504 FD patients (70% females (F), 43.6 ± 0.7 years, 23.3 ± 0.2 kg/m²), 382 patients (67% F, 43.8 ± 0.8 years, 23.3 ± 0.2 kg/m²) had normal and 122 patients (77% F, 42.7 ± 1.5 years, 23.2 ± 0.6 kg/m²) had delayed GE. Global symptom severity tended to be higher in patients with delayed GE (81.9 ± 3.4 vs 99.5 ± 7.1,

$P = 0.06$). Only nausea was significantly increased in patients with delayed GE (10.7 ± 0.8 vs 15.9 ± 1.6, $P = 0.01$). However, no correlations were observed between GE rate and any of the symptoms (global symptom score: $r = 0.06$, $P = 0.2$; nausea: $r = 0.08$, $P = 0.09$). In all analysis, 2-Way-Anova showed significant interactions for increasing symptoms over time, but no significant differences were observed between normal and delayed GE. Only nausea showed partially significant increase in delayed GE 90 minutes after the meal ($P < 0.01$) compared to normal GE.

Conclusions: IGP patients tend to display higher dyspeptic symptoms severity, but only meal-related nausea scores were significantly higher. The severity of symptoms, even when assessed during the meal, was not associated to the GE rate. These findings have important implications for the value of routinely applying GE testing in clinical practice.



76 | Gastroparesis: Outcome of focus groups for the development of a questionnaire for symptom assessment in patients suffering from idiopathic and diabetes gastroparesis

F. Carbone; R. De Buysscher; K. Van Den Houte; L. Holvoet; A. Vandenberghe; J. Tack

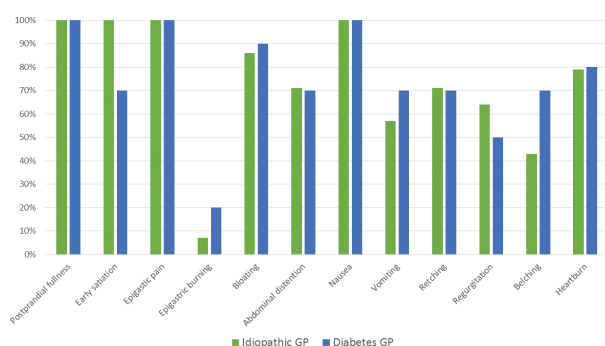
University of Leuven, Leuven, Belgium

Objective: Gastroparesis (GP) is defined as "a combination of symptoms and documented delay in gastric emptying (GE) in the absence of mechanical obstruction". The main causes of GP are Idiopathic gastroparesis (IGP) and Diabetes gastroparesis (DGP). To date, no validated patient reported outcomes (PRO) for evaluation of treatment efficacy in these conditions are available. According to FDA guideline, PRO instrument item generation and selection should be derived from patient focus groups (FGs) and cognitive interviews (CIs). Our aim was to perform FGs and cognitive interviews for the development of a new questionnaire for the assessment of symptom pattern and severity in both IGP and DGP.

Methods: Patients with IGP, a negative endoscopy and a strongly delayed GE rate (T1/2 > 109 minutes, GE breath test) were invited to participate. During the FGs, symptom spectrum of gastroparesis was discussed to determine type of symptoms, triggering by meals or factors, duration, bothersomeness, predictability and impact. A verbal descriptor for each symptom was proposed to the patients after discussion of the symptom. Threshold for selection of symptoms was 50%. From the list of emerged relevant symptoms, Subsequently, FGs for DGP patients were organized using the same framework.

Results: 14 IGP (11 Females, 43.6 ± 3.3 years, $T1/2:155.2 \pm 16.2$) patients participated. All (100%) confirmed experiencing symptoms that were triggered or aggravated by ingestion of a meal. Main symptoms corresponded to postprandial fullness (PPF:100%), epigastric pain (EP:100%), early satiation (ES:100%), nausea (N:100%), retching (RT:71%) and vomiting (V:57%). Other relevant symptoms were bloating (B:86%), abdominal distention (AD:71%), heartburn (H:79%) and regurgitation (RG:64%). In diabetic gastroparesis ($n = 10$, 7 Females, 45.5 ± 3.7 years, $t1/2:156.9 \pm 17.0$ minutes) symptoms were also meal related (100%) and comprised PPF (100%), EP (100%), ES (70%) N (100%), V (70%), RT (70%), RG (50%), B (90%), AD (70%), belching (70%) and H (80%). Following this, pilot instruments were developed and customized through CIs for qualitative and cognitive debriefing to establish content validity.

Conclusions: This study confirm that symptoms corresponding to postprandial fullness, epigastric pain, early satiation, nausea, vomiting, retching regurgitation, bloating and heartburn are the key items for developing a PRO for both idiopathic and diabetic gastroparesis.



78 | Overall safety and tolerability of relamorelin in adults with diabetic gastroparesis: Analysis of phase 2a and phase 2b trial data

M. Camilleri¹; A. Lembo²; R. McCallum³; S. Tourkodimitris⁴; L. Kemps⁴; M. B. Miller⁴; K. Bertelsen⁴; A. Iacob⁴

¹Mayo Clinic, Rochester, Minnesota, United States; ²Harvard Medical School, Boston, Massachusetts, United States; ³Texas Tech University Health Sciences Center, El Paso, Texas, United States; ⁴Allergan plc, Madison, New Jersey, United States

Objective: This study assessed overall safety and tolerability of relamorelin, a pentapeptide ghrelin receptor agonist which accelerated gastric emptying and improved symptoms in patients with diabetic gastroparesis (DG) in Phase 2 clinical trials.

Methods: Randomised, double-blind, placebo-controlled Phase 2 trials (NCT01571297, NCT02357420; results published previously) included DG patients aged 18-75 years over 4 weeks (subcutaneous relamorelin 10 µg once or twice daily [BID] or placebo BID) and 12 weeks (subcutaneous relamorelin 10, 30, or 100 µg or placebo BID) with 1- and 2-week, single-blind placebo run-ins, respectively. Safety assessments included weight, adverse events (AEs), and laboratory tests. Analysis of covariance assessed treatment effect on glycated haemoglobin (HbA1c) and blood glucose post hoc.

Results: Among 204 and 393 Phase 2a and 2b patients, mean ages were 55 and 58 years, 67% and 62% were female, 88% and 89% had type 2 diabetes, respectively. Proportions with ≥ 1 treatment-emergent AE (TEAE) were generally similar across treatment groups (Table). TEAE-related discontinuation was higher in relamorelin groups than placebo. No serious TEAE in Phase 2a was reported in >1 instance; in Phase 2b, worsening gastroparesis, unstable angina, diabetic ketoacidosis and acute renal failure were each reported by two relamorelin-treated patients, and one patient receiving relamorelin 100 µg died from urosepsis, all unrelated to relamorelin. Mean (standard deviation) change from baseline to Week 12 (Phase 2b) HbA1c levels (%) were -0.03 (0.86), 0.48 (1.03), 0.92 (1.53), and 0.81 (1.77) for placebo, relamorelin 10, 30, and 100 µg, respectively. Increased HbA1c and fasting blood glucose levels were dose-related ($P<0.0001$ and $p=0.0043$, respectively).

Conclusions: Relamorelin showed acceptable safety and tolerability in Phase 2 trials. As elevated blood glucose was observed, Phase 3 trials (10 µg BID dose only) will involve proactive glycaemic management. Writing assistance by Complete HealthVizion.

	Phase 2a			Phase 2b			
	Placebo BID (n=88)	Relamorelin 10 µg QD PM (n=87)	Relamorelin 10 µg BID (n=88)	Placebo BID (n=104)	Relamorelin 10 µg BID (n=98)	Relamorelin 30 µg BID (n=109)	Relamorelin 100 µg BID (n=82)
TEAE summary							
Patients with ≥ 1 TEAE, n (%)	30 (43.5)	32 (47.8)	25 (36.8)	49 (47.1)	46 (46.9)	63 (57.8)	45 (54.9)
Serious TEAEs, n (%)	2 (2.9)	1 (1.5)	4 (5.9)	8 (7.7)	7 (7.1)	10 (9.2)	6 (7.3)
TEAEs leading to study drug discontinuation, n (%)	2 (2.9)	5 (7.5)	1 (1.5)	3 (2.9)	3 (3.1)	8 (7.3)	9 (11.0)
TEAEs $\geq 5\%$ in any treatment group, n (%)							
Constipation	4 (5.8)	1 (1.5)	1 (1.5)	3 (2.9)	0 (0.0)	3 (2.8)	0 (0.0)
Diabetes mellitus	2 (2.9)	1 (1.5)	4 (5.9)	0 (0.0)	2 (2.0)	1 (0.9)	3 (3.7)
Diarhoea	2 (2.9)	3 (4.5)	1 (1.5)	0 (0.0)	4 (4.1)	7 (6.4)	6 (7.3)
Dizziness	4 (5.8)	1 (1.5)	1 (1.5)	1 (1.0)	0 (0.0)	1 (0.9)	5 (6.1)
Headache	2 (2.9)	2 (3.0)	5 (7.4)	3 (2.9)	4 (4.1)	6 (5.5)	2 (2.4)
Hyperglycaemia	1 (1.4)	2 (3.0)	0 (0.0)	2 (1.9)	5 (5.1)	10 (9.2)	10 (12.2)
Increased blood glucose	1 (1.4)	0 (0.0)	1 (1.5)	1 (1.0)	3 (3.1)	4 (3.7)	6 (7.3)
Urinary tract infection	4 (5.8)	2 (3.0)	2 (2.9)	7 (6.7)	7 (7.1)	8 (7.3)	7 (8.5)
Fasting blood glucose, mmol/L, mean (SD) CFB*	0.23 (4.5)	0.97 (3.3)	0.81 (2.9)	1.39 (3.4)	1.81 (4.6)	2.40 (4.7)	3.13 (5.1)
Weight, kg, mean (SD) CFB*	-0.01 (1.6)	0.2 (1.6)	0.17 (2.0)	0.25 (2.6)	-0.07 (2.7)	0.59 (3.0)	0.46 (2.2)

*Study duration was 4 weeks for Phase 2a and 12 weeks for Phase 2b. BID, twice daily; CFB, change from baseline; QD, once daily; SD, standard deviation; TEAE, treatment-emergent adverse event

TABLE. Summary of treatment-emergent adverse events in the relamorelin Phase 2a and 2b trials.

83 | Cellular and molecular targets in patients with Parkinson's disease and chronic constipation

F. Giancola¹; F. Torresan¹; G. Nanni²; A. Ioannou³; D. Mandolesi²; F. Bianco²; E. Boschetti²; A. Costanzini⁴; V. Stanghellini²; R. De Giorgio⁴

¹St. Orsola-Malpighi Hospital, Bologna, Italy; ²Dept. Medical and Surgical Sciences, University of Bologna, Bologna, Italy; ³Gastroenterology Unit, 2nd Department of Surgery, Athens, Greece; ⁴Dept. Medical Sciences, University of Ferrara, Ferrara, Italy

Objective: Chronic constipation (CC) in Parkinson's disease (PD/CC) is a severe symptom that impacts on the patient's quality of life. The molecular mechanisms involved in the pathogenesis of CC in PD are only partially understood. This study was aimed to investigate neuropathological and neurochemical features involved in the pathophysiology of PD/CC, focusing on possible abnormalities involving various cellular targets, i.e. enteric neurons, glial and intestinal epithelial barrier (IEB).

Methods: 10 patients with CC/PD, 10 with CC and 14 controls (CTR) were enrolled in the study. Routine biopsies of the colon were obtained during colonoscopy and used for analysis by western blot and immunofluorescence of: 1) vasoactive intestinal peptide (VIP) and its receptors (VIPR1 and VIPR2) that identify vaso-secretomotor submucosal neurons; 2) glial fibrillary acidic protein (GFAP), indicative of glial activation; 3) occludin (OCC) and zonula occludens-1 (ZO-1), two structural proteins of tight junctions which are essential for the IEB integrity.

Results: Both PD/CC and CC patients showed an alteration of VIP, VIPR1 and VIPR2 protein expression vs CTR. The reduction of VIP was more evident in patients with CC vs CTR ($P < 0.05$), while VIPR2 was reduced in patients with PD/CC ($P < 0.01$). GFAP and OCC levels were not altered in the three groups. An increased immunoreactivity (IR) of ZO-1 was observed in PD/CC and CTR vs CC, whereas OCC-IR was more evident in CC vs PD/CC patients. A positive correlation between VIP/GFAP and a negative trend between VIPR2/GFAP45 and between OCC/GFAP35 was identified in CC and PD/CC.

Conclusions: VIP pathway abnormalities could be demonstrated in CC. Notably, neurochemical alterations of the VIP expressing vaso-secretomotor-neurons occurred in association with changes of the integrity of the IEB. Correlations between VIP/VIPR2, GFAP and OCC suggested an interplay of these molecules in the pathogenesis of CC and CC/PD patients.

84 | FEEDMI – Feeding the preterm gut microbiota

J. P. Morais¹; C. Marques¹; D. Teixeira¹; C. Durão¹; A. Faria¹; S. Brito²; M. Cardoso²; I. Macedo²; T. Tomé²; C. Calhau¹

¹NOVA Medical School | Faculdade Ciências Médicas, Universidade NOVA de Lisboa, Lisboa, Portugal; ²Maternidade Dr. Alfredo da Costa, Lisboa, Portugal

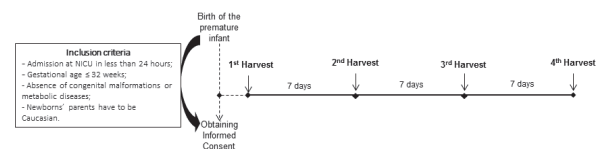
Objective: The aim of this study was to evaluate the influence of different types of infant-feeding (mother own milk-MOM, donor human milk-DHM and formula) on preterm infants' gut microbiota.

Methods: This observational study (NCT03663556) included very preterm infants (≤ 32 weeks of gestational age), hospitalized in the neonatal intensive care unit of Maternidade Dr. Alfredo da Costa. Fecal samples were collected from very premature infants every 7 days, for 21 days (figure 1). DNA was extracted from feces samples and different bacterial genus and species have been quantified by RT-PCR.

Results: From 44 first-pass defection (meconium) samples (collected until 72 hours of life), 86% preterm infants had intestinal bacterial colonization. Preliminary results showed an increase in meconium bacterial abundance after vaginal delivery vs C-section ($P = 0.029$). There were no differences in initial intestinal colonization between non-fed infants and fed-infants, highlighting the importance of microbiota transmission from mother-to-child. After 1 week of life, there were no differences in bacterial abundance in infants fed with MOM or DHM. After 3 weeks of life, total bacteria seemed to be decreased in formula fed infants compared to human

milk fed infants, with a significant decrease in Bifidobacterium ($P = 0.037$).

Conclusions: The intestinal colonization of infants without enteric feeding highlights the relevance of vertical microbiota transmission. MOM and DHM seemed to be equally valuable choices for premature infants in respect to microbiota colonization. Long-term feeding with human milk seemed to be advantageous in regard to beneficial bacterial species growth. Acknowledgement: Supported by Milupa DN-ELN2017 grant awarded by the Portuguese Neonatal Society and ERDF through the operation POCI-01-0145-ERDF-007746 funded by the Programa Operacional Competitividade e Internacionalização – COMPETE2020 and by National Funds through FCT – CINTESIS, R&D Unit (UID/IC/4255/2013).



86 | Sevoflurane influences esophagogastric junction distensibility in the absence of esophageal inflammation

A. Benitez¹; D. Jablonka¹; V. Sahu¹; C. Gluckman²; M. Demarshall²; S. Ostapenko¹; G. Falk²; K. Lynch²; C. Menard-Katcher³; A. Muir¹

¹Children's Hospital of Philadelphia, Philadelphia, United States; ²University of Pennsylvania, Philadelphia, United States; ³Children's Hospital Colorado, Aurora, United States

Objective: The functional luminal imaging probe (FLIP) allows for assessment of esophageal morphology and function. FLIP measurements are usually performed during a sedated endoscopy (EGD). However, sedation protocols differ between pediatric and adult populations and between institutions. Sevoflurane is an anesthetic commonly used during pediatric EGDs but its effect on the functional properties measured by FLIP is unknown. We therefore sought to investigate the effect of sevoflurane use on esophageal body diameter, EGJ diameter, and EGJ distensibility index (EGJ-DI) in the absence of esophageal inflammation.

Methods: FLIP was used to measure esophageal body diameter, EGJ diameter, and EGJ-DI in patients ages 15-77 years old undergoing EGD at one pediatric and one adult care site. Patients had no histologic findings of inflammation on EGD. EGJ diameter corresponds to the minimal diameter at an intrabag pressure of 40 mm Hg. EGJ-DI is defined as the minimum cross-sectional area vs intrabag pressure.

Results: Eight patients (ages 15-18 years old) underwent FLIP with a combination of sevoflurane and propofol (S/P) and 11 patients (ages 15-77 years old) with propofol alone (P). Patients receiving sevoflurane were significantly younger, but did not differ in height and weight. Esophageal diameter was not significantly different between groups (S/P median (17.9 mm), S/P range (16.1-19.4 mm);

P median (18.5 mm), P range (13.7–20.2 mm); $P = 0.7$; Figure 1A). However, EGJ diameter was significantly larger in the sevoflurane/propofol cohort compared to propofol alone (S/P median (20.9 mm), S/P range (15.5–22.3 mm); P median (14.1 mm), P range (5.8–20.9 mm); $P = 0.02$; Figure 1B). Similarly, EGJ-DI was significantly different in sevoflurane/propofol subjects when compared to those only on propofol (S/P median ($8.3 \text{ mm}^2/\text{mm Hg}$); P median ($4.5 \text{ mm}^2/\text{mm Hg}$); $P = 0.02$; Figure 1C).

Conclusions: This is the first study to evaluate the effect of anesthesia protocols in the esophageal body and EGJ distensibility using FLIP. Functionality of the EGJ may be altered by the use of anesthetics known to influence muscle tonicity, including sevoflurane. The need for standardized procedural and data analysis methods that take into account anesthesia protocols is of great importance. Further studies will be needed to assess if other anesthetics influence EGJ distensibility or other gastrointestinal sphincters.

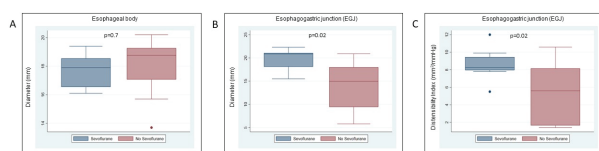


FIGURE 1. Esophageal body diameter (A), esophagogastric junction (EGJ) diameter (B), and EGJ distensibility index (C) in control subjects undergoing endoscopy (EGD) and functional luminal imaging probe (FLIP) measurements under two anesthesia protocols.

89 | Faecal microbiota transplantation (FMT) in IBS using a super-donor: A randomised, double-blind placebo-controlled study

M. El-Salhy¹; T. Hausken²; O. H. Gilja³; A. Kristoffersen⁴; J. G. Hatlebakk³

¹Stord Hospital, Stord, Norway; ²Department of Clinical Medicine, Bergen, Norway; ³University of Bergen, Bergen, Norway; ⁴Department of Clinical Medicine, Oslo, Norway

Objective: FMT has been tried in IBS patients in two double-blind placebo-controlled studies with contradictory results. The present study was conducted to study the effect of FMT using a single donor with a favourable microbiota profile.

Methods: A randomised, double-blind placebo-controlled study was conducted, in which 164 IBS patients were randomised to a either placebo, 30 g or 60 g transplant in ratio 1:1:1. A single well-defined donor was used, which was normobiotic and with a favourable specific microbial signature as recently defined. Abdominal symptoms, fatigue and quality of life were assessed by the IBS-SSS, Birmingham IBS symptom Fatigue Assessment Scale, IBS-QoL and the Short-Form Dyspepsia index Questionnaires. Gut bacterial analysis was done using a commercially available test, GA-map Dysbiosis Test[®]. The primary outcome was a reduction in IBS-SSS score ≥ 50 points

3 months after FMT. The secondary outcome was a change in the intestinal bacterial.

Results: The responses to FMT were 23.6, 75.9 and 87.3% of patients received placebo, 30 g and 60 g transplant, respectively. Symptom remission (SSS ≥ 175 points) occurred in 5.5, 35.2 and 47.3% in placebo, FMT 30 g and FMT 60 g groups, respectively. Similarly, a significant clinical improvement in fatigue (FAS ≥ 4 points) was found in 21.8, 53.7 and 52.7% of patients received placebo, FMT30 g and FMT 60 g, respectively. The corresponding figures for the quality of life (IBS-QoL ≥ 14 points) were 7.3, 61.1 and 58.2%. DI did not decrease in patients received FMT or placebo. However, the intestinal bacterial profiles changed in patients received 30 and 60 g transplant, but not in the placebo group.

Conclusions: FMT is a highly effective treatment for patients with IBS when using well-defined donor with normal DI and a favourable microbial signature and is essential for the clinical success of FMT. Response to FMT increases with increased dose of transplant.

90 | Impacts of perigestational exposure to chlorpyrifos (CPF) and high -fat diet (HFD) on ileum contractility in male rats

H. El Khayat El Sabbouri¹; M. Guibourdenche¹; W. Darwiche¹; N. Djekkoun¹; V. Bach¹; W. H. Joumaa²; W. Ramadan²; J. Gay-Quéheillard¹

¹Peritox laboratory, UMR-I-01, Picardy Jules Verne University, Amiens, France;

²Rammal Hassan Rammal laboratory, Physio-Toxicité Environnementale, EDST, ER 017, Lebanese University, Faculty of sciences, Nabatieh, Lebanon

Objective: Chlorpyrifos (CPF) is an acetylcholinesterase (AChE)-inhibiting organophosphorus insecticide. Exposure to CPF is harmful during the perinatal period. Such developmental perturbations are linked to further disorders at adulthood through fetal programming. These disturbances are related to unbalanced diet and environmental pollutants. This study established the effects of perigestational exposure to CPF and to high-fat diet (HFD) on the contractility of smooth muscle in adult rats.

Methods: 4 groups of 4 female rats were exposed during 4 months before and later during gestation and lactation periods to CPF (1 mg/kg bw/day vs vehicle) with or without HFD. After being sacrificed at the age of 60 postnatal days (PND60), ileal smooth muscle strips were used for *in vitro* contractility measurements in an isolated organ bath system, AChE activity assessment, and genes expression evaluation ($n = 7$ –10 per group).

Results: At PND60, CPF exposure induced an increase in the ileal longitudinal and circular muscles contractility. The circular muscle thickness was also increased. Indeed, CPF exposure was associated with greater expression of the tachykinin (substance P) mRNA and the muscarinic M2 acetylcholine receptor mRNA in the ileum. Furthermore, the expression of tachykinin NK1 receptor mRNA was increased in HFD group compared to controls. The

exposure to either CPF and/or HFD induced a decrease in AchE activity in the ileum.

Conclusions: The perigestational exposure to CPF is associated with increased ileal muscle contractility at adulthood due to lower AchE activity via cholinergic and non-cholinergic mechanisms. Ileal contractility was not affected in the rats of HFD-fed mothers despite elevated NK1 receptor expression and reduced AchE activity levels. Integrating this study helps in preventing chronic gut diseases in adults.

97 | Anhedonia and postprandial distress syndrome in obese patients with and without sleeve gastrectomy: Is there a link?

A. Santonicola; L. Carpinelli; G. Asparago; P. Iovino

Department Of Medicine, Surgery And Dentistry,, Salerno, Italy

Objective: Obese patients (OB) did not show a different prevalence of postprandial distress syndrome (PDS) compared to Healthy Controls (HC). However, PDS is more prevalent in OB after Sleeve Gastrectomy (SG). Hedonic response to a meal is dissociable from satiation in healthy subjects. Anhedonia is the lowered ability to experience pleasure. There are no studies investigated the presence of anhedonia in OB with and without SG and its relationship to PDS symptoms.

Methods: 37 OB without SG and 33 OB with BS were recruited. All patients fulfilled the validated 14 items Snaith-Hamilton Pleasure Scale (SHAPS) to assess Anhedonia as well as the Beck Depression Inventory-II (BDI-II) to screen for depression. All patients underwent a standardized questionnaire investigating the intensity-frequency scores (0-6) of postprandial fullness and early satiation, core symptoms of PDS according to ROME IV criteria.

Results: Table 1. Demographic characteristics, the prevalence and intensity-frequency scores of postprandial fullness and early satiation in OB with and without SG. Data are expressed as percentage (%) or as mean $\pm$ SD.

Mean SHAPS scores were not significantly different in OB with and without SG (1.02 ± 1.16 vs 1.18 ± 1.72 , $P = 0.65$). Patients without SG showed a lower prevalence anhedonia, compared to those with SG (8.1 vs 24.1%) although it did not reach the statistical significance ($P = 0.06$). No correlation was found between presence of anhedonia and PDS ($R = 0.04$; $P = 0.7$).

Conclusions: After SG the prevalence of PDS significantly increased as well as the level of anhedonia. However, no correlation was found between these aspects. Other factors, probably influencing the eating behavior after SG, could play a role.

	OB without SG N=37	OB with SG N=33	<i>p</i>
Males (%)	8(21.6)	8 (24.2)	0.8
Age	36.8 $\pm$ 11.7	36.4 $\pm$ 10.7	0.9
Weight (Kg)	122.9 $\pm$ 20.5	103.2 $\pm$ 34.6	0.03
BMI (Kg/m ²)	45.3 $\pm$ 5.8	36.9 $\pm$ 8.8	0.001
Postprandial fullness intensity-frequency score	1.1 $\pm$ 1.8	2 $\pm$ 2.1	0.03
Early satiation intensity-frequency score	0 $\pm$ 0	2.7 $\pm$ 2.4	<0.001
BDI-II scores	13.3 $\pm$ 12.1	7.6 $\pm$ 7.5	0.009

104 | Exploration of permeability and motility disturbances in a post-inflammatory rat model for irritable bowel syndrome

N. Hanning; A. Smet; H. Van Spaendonck; H. De Schepper; J. De Man; B. De Winter

University of Antwerp, Antwerp, Belgium

Objective: The pathogenesis of Irritable Bowel Syndrome involves different mechanisms including disturbed permeability, sensitivity and motility. We therefore aimed to validate motility and permeability disturbances in a post-inflammatory rat model that is well-known for visceral hypersensitivity.

Methods: A TNBS enema was used to induce acute colitis in male Sprague-Dawley rats; controls received 0.9% NaCl. The post-inflammatory status was confirmed endoscopically before further experiments. To assess gut motility, we determined gastric emptying (GE), distal front and geometric center (GC) of small intestinal transit 30 or 60 minutes after intragastric administration of Evans blue. Small bowel and colonic permeability was assessed *in vivo* at different time points after intragastric and intracolonic administration, respectively, of 4 kDa FITC-dextran. The expression of junctional proteins in jejunum and proximal colon was determined with qPCR. Finally, the inflammatory parameters (colonoscopy, macroscopy, microscopy and myeloperoxidase activity) were scored.

Results: Post-inflammatory rats showed reduced GE compared to control animals after 30 minutes ($41.3 \pm 4.9\%$ vs $57.7 \pm 15.2\%$, $n = 10$ per group, $P < 0.05$; Mann Whitney), but not after 60 minutes. No differences in distal front and GC of small intestinal transit were observed. We did not observe *in vivo* differences in either small bowel or colonic permeability after administration of FITC-dextran. However, the expression of several junctional proteins was significantly disturbed ($P < 0.05$; Mann Whitney) and this effect was more pronounced in jejunum than in colon (fig. 1).

Conclusions: The expression of several junctional proteins was changed in both the jejunum and the proximal colon, indicating that permeability disturbances are present in our post-inflammatory rat model. However, 4 kDa FITC-dextran was not capable of confirming these disturbances *in vivo*. The absence of significant differences in motility after 60 minutes confirms that intragastric administration of

compounds is a valid method to determine *in vivo* permeability changes. Therefore, other marker molecules should be used to assess the *in vivo* intestinal permeability in this animal model.

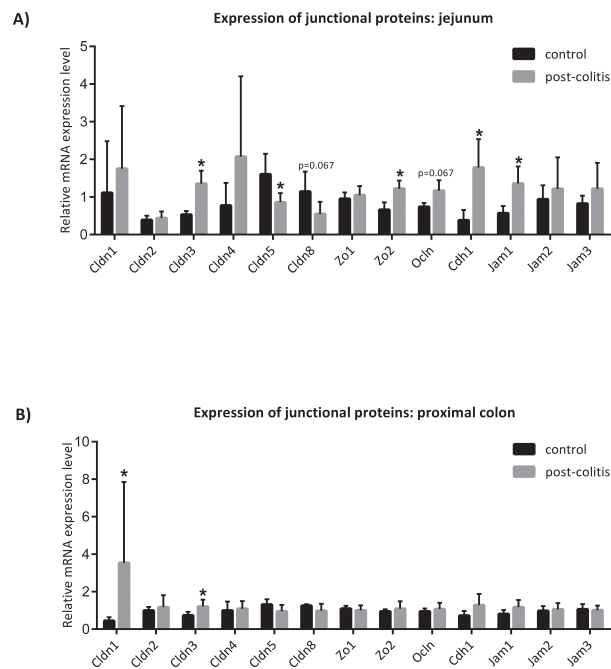


FIGURE 1. Relative mRNA expression of several junctional proteins in the jejunum (A) and proximal colon (B) of the rat (n=10 per group). Data are presented as mean ± SD. Mann-Whitney test; *p<0.05.

108 | Achalasia is a common finding in patients with EoE undergoing high-resolution manometry

M. Ghisa¹; C. Marinelli¹; S. Tolone²; N. De Bortoli³; E. Marabotto⁴; P. Zentili⁴; V. Savarino⁴; B. Barberio¹; F. Zingone¹; E. Savarino¹

¹Division of Gastroenterology, Department of Surgery, Oncology and Gastroenterology, University of Padua, Padua, Italy, Padua, Italy; ²Division of General and Bariatric Surgery, Department of Surgery, Second University of Naples, Naples, Italy, Naples, Italy; ³Division of Gastroenterology, Department of Internal Medicine, University of Pisa, Pisa, Italy, Pisa, Italy; ⁴Division of Gastroenterology, Department of Internal Medicine, University of Genoa, Genoa, Italy, Genoa, Italy

Objective: Eosinophilic Esophagitis (EoE) is a chronic immune/antigen-mediated disorder, characterized by symptoms of esophageal dysfunction (dysphagia and/or food impaction) and, histologically, by eosinophilic-infiltration. EoE has been associated with various esophageal motility disorders, ranging from hypo- to hypercontractile motility abnormalities, and more recently achalasia. The aim of this study was to assess the incidence of achalasia in patients with EoE, and to evaluate the disease course of EoE after achalasia treatment.

Methods: 97 consecutive patients (mean age 39, range 18-75 yo, 20 F), with a diagnosis of EoE assessed in our Unit between 2012 to 2018, were included. The diagnosis was posed according to international criteria (presence of typical symptoms of esophageal

dysfunction; at least 15 eosinophils per high-power field at mid/proximal oesophagus), excluding other causes of eosinophilia. Among 97 patients, in 47 (48%) conventional manometry (CM) or high resolution manometry (HRM) were not performed and were excluded from the study. Patients who accepted to undergo HRM, were studied by suing the standardised international protocol and manometric diagnoses were carried out according to Chicago Classification 3.0.

Results: Among the 50 EoE patients (mean age 41, range 20-75 yo, 8 F), 26 (52%) showed normal manometric pattern. Between patients with abnormal manometric pattern, 16 (67%) had hypocontractile disorders, 8 (33%) hypercontractile abnormalities and 5 (21%) had a diagnosis of achalasia. The figure shows the characteristics of the 5 EoE patients with achalasia and the response to the therapies.

Conclusions: This retrospective study of consecutive patients showed that achalasia, is not uncommon in patients with EoE, affecting about 10% of patients of this cohort. No specific subtype of achalasia is associated with EoE. The high frequency of this association seems to hypothesize a causal link between these two pathologies, whereas all this variability in manometric pattern, epidemiological characteristic and response to therapy, suggests that the relationship is not univocal and that there may be different mechanisms that act independently to determine such association.

Patient n°	1	2	3	4	5
Sex	F	M	F	M	M
History of Allergy	No	Allergic dermatitis and rhinitis	No	Allergic rhinitis	Allergic conjunctivitis
Age at EoE Diagnosis (years)	68	16	73	22	21
EoE Onset (years)	50	6	58	16	16
Diagnostic delay	18	10	22	6	5
Main symptoms	Dysphagia	Dysphagia	Regurgitation	Globus and Dysphagia	Dysphagia and Odynophagia
Endoscopy (EREFS score)	E1R1E1F0S1=4	E1R2E1F1S0=5	E1R0E1F0S1=3	E0R1E1F0S1=3	E1R1E1F0S0=3
HRM	Achalasia type II	Achalasia type III	Achalasia type I	Achalasia type III	Achalasia type II
Esophagogram	Dilation of the esophagus, narrow EGJ	Delayed esophageal emptying	Esophageal stasis, narrow EGJ	Narrow EGJ	Dilation of the esophagus, narrow EGJ
PPI Response	Yes	Yes	No	No	No
Topic Steroid	/	No	No (stop for intolerance)	Yes	Yes
Achalasia therapy	Endoscopic dilation	Not Required	Surgery (Heller+Dor)	Not Required	Endoscopic dilation and then Surgery (Heller+Dor)
EoE outcome after achalasia treatment	PPI responder	PPI responder	Refractory EoE	Steroid responder	Steroid responder

FIGURE. Characteristics of EoE patients with achalasia and response to therapies.

116 | External validation of predictive model for delayed balloon expulsion test based on three-dimensional integrated pressurized volume analysis with high-resolution anorectal manometry

M. Seo¹; S. Joo²; K. W. Jung²; S.-J. Myung²
¹Gangneung Asan Hospital, Gangneung, South Korea; ²Asan Medical Center, Seoul, South Korea

Objective: Anorectal manometry with the push maneuver has a limitation in predicting balloon expulsion (BE) test results. We previously reported that partial least square regression (PLSR) model using integrated pressurized volume (IPV), based on the spatiotemporal plot of high-resolution anorectal manometry (HRAM), was significantly correlated with the success of the BE test results in 26

healthy individuals and 204 constipated patients. The final equation for predicting BE test results could be described with IPV parameters. Here, we aimed to perform external validation study to assess the PLSR model.

Methods: In this study, twenty male patients with chronic constipation were enrolled for external validation. All of the enrolled subjects underwent HRAM and BE tests. Delayed BE was defined as a requirement of more than 1 minutes. HRAM profiles were converted into ASCII files and analyzed using a MATLAB program to calculate the three-dimensional IPV by multiplying the amplitude, distance, and time during simulated evacuation. The PLSR model developed in previous study was applied to this new twenty patients to confirm the model's performance.

Results: In the validation sample of 20 patients, 7 (35%) patients showed delayed BE and the remaining 13 (65%) patients showed early BE based on BE test. The same patients were applied to the PLSR model and it successfully predicted that 5 of 7 patients were in delayed BE group and 11 of 13 patients were in early BE group. In validation set, the PLSR model was able to correctly discriminate delayed BE, with a sensitivity of 71.43% and specificity of 84.62%. The positive predictive value was 71.43% and the negative predictive value was 84.62%. (Table 1)

Conclusions: A previously developed PLSR model for discriminating delayed BE using IPV parameters was externally validated in this study. The validation results have confirmed that the PLSR model has high sensitivity and accuracy for detecting delayed BE as we reported earlier.

Performance characteristics (95% confidence interval)	External validation cohort (n=20)	Previous development cohort (n=230)
Sensitivity, %	71.43 (29.04 - 96.33)	80.65 (72.62-88.67)
Specificity, %	84.62 (54.55 - 98.08)	70.80 (63.19-78.42)
Positive predictive value, %	71.43 (39.13 - 0.67)	65.22 (56.51-73.92)
Negative predictive value, %	84.62 (62.50 - 94.78)	84.35 (77.71-90.99)
Accuracy, %	80.00 (56.34 - 94.27)	74.78 (69.17-80.39)

TABLE 1. Diagnostic performance of the partial least square regression model in the discrimination of delayed balloon expulsion.

117 | Esophageal motility disorders in eosinophilic esophagitis

M. Ghisa¹; C. Marinelli¹; M. D. Coletta¹; F. Zingone¹; S. Tolone²; N. De Bortoli³; E. Marabotto⁴; P. Zentilin⁴; V. Savarino⁴; E. Savarino¹

¹Division of Gastroenterology, Department of Surgery, Oncology and Gastroenterology, University of Padua, Padua, Italy, Padua, Italy; ²Division of General and Bariatric Surgery, Department of Surgery, Second University of Naples, Naples, Italy, Naples, Italy; ³Division of Gastroenterology, Department of Internal Medicine, University of Pisa, Pisa, Italy, Pisa, Italy; ⁴Division of Gastroenterology, Department of Internal Medicine, University of Genoa, Genoa, Italy, Genoa, Italy

Objective: Eosinophilic Esophagitis (EoE) is a chronic disorder, characterize by symptoms of esophageal dysfunction and esophageal eosinophilic-infiltration. It has been often associated with esophageal motility disorders (EMD), ranging from hypo- to hyper- contractile motility disorders. The aim of this study was to evaluate the incidence and clinical characteristics of EMD in EoE.

Methods: 97 consecutive patients (mean age 39, range 18-75yo, 77 M) with a diagnosis of EoE, assessed in our unit between 2012 to 2018, were included. The diagnosis was posed according to the latest international criteria. Among 97 patients, in 47 (48%) high resolution manometry (HRM) was not performed and were excluded from the study. Patients who accepted to undergo HRM, were studied by using the standardised international protocol according to Chicago Classification 3.0. For statistical analysis, Fisher exact test was used.

Results: Among 50 patients included (mean age 41, range 20-75 yo, 42M), 26 (52%) showed normal manometric pattern. Between EoE-patients with EMD, 16 (67%) had hypocontractile disorders, and 8 (33%) had hypercontractile abnormalities. EoE-patients with hypocontractile patterns had frequent failed peristalses (N = 4), ineffective esophageal motility (N = 6), fragmented peristalsis (N = 4), absent peristalsis (N = 2). EoE-patients with hypercontractile patterns had achalasia type III (N = 2), achalasia type II (N = 2), achalasia type I (N = 1), EGJ outflow obstruction (N = 1), Jackhammer esophagus (N = 1), distal esophageal spasm (N = 1). The figure shows the characteristics of age, sex and response to proton pump inhibitor (PPI) of patients in relation to their manometric pattern.

No difference in prevalence of motility abnormalities, nor a predominance of hypo/hyper-contractile pattern, between PPI responsive and PPI non-responsive patients (P 0.49 and P 0.14, respectively) neither between females and males (P 1 and P 0.60, respectively), was shown. Different prevalence of motility abnormalities between younger and older patients (considering mean age) was found, with greater frequency of pathological pattern in young patients (P 0.045) without difference in terms of hypo/hyper-contractile prevalence (P 0.49).

Conclusions: This series shows that EMD are present in about half of EoE patients, especially in young subjects who showed a higher prevalence of hypocontractile disorders. A correlation with patient's gender or response to PPI therapy was not observed.

Patients with normal motility	26 (52%)	Patients with hypercontractile disorders	8 (33%)
Age (mean and median)	43.4yo; 40.5yo	Age (mean and median)	41.9yo; 36.2yo
Age at diagnosis (mean and median)	36.1yo; 33yo	Age at diagnosis (mean and median)	27.2yo; 29.5yo
Sex	22M (84.6%)	Sex	6M (75%)
PPI response	(9 of 17) 52.9%	PPI response	(2 of 9) 22%

Patients with motility disorders	24 (48%)	Patients with hypocontractile disorders	16 (67%)
Age (mean and median)	37.9yo; 33.7yo	Age (mean and median)	36yo; 32yo
Age at diagnosis (mean and median)	29.2yo; 25yo	Age at diagnosis (mean and median)	30.4yo; 24yo
Sex	20M (83.3%)	Sex	14M (87.5%)
PPI response	(7 of 18) 38.3%	PPI response	(5 of 9) 55%

FIGURE. Characteristics of age, sex and response to PPI in relation to manometric pattern.

120 | Smartphone-based symptom assessment using the experience sampling method provides insight into patient specific stress-abdominal pain interaction in irritable bowel syndrome

L. Vork¹; D. Keszthelyi¹; S. Van Kuijk¹; E. Quetglas²; Z. Mujagic¹; C. Leue¹; J. Kruimel¹; A. Masclee¹

¹Maastricht University Medical Center, Maastricht, The Netherlands;

²Grünenthal GmbH, Aachen, Germany

Objective: Gastrointestinal symptoms in irritable bowel syndrome (IBS) have been correlated to psychological factors, such as anxiety, depression and stress. Most studies used retrospective symptom assessment, which hampers considering temporal fluctuations. Real-time symptom assessment might reveal the interplay between abdominal and affective symptoms more reliably in a longitudinal perspective. The aim of this study was to evaluate the association between stress and abdominal pain, using the Experience Sampling Method (ESM) as a real-time and repeated measurement method.

Methods: Thirty-seven Rome-IV IBS patients (IBS; 26 female; mean age 37 years) and 36 healthy subjects (HC; 24 female; mean age 31 years) completed a structured electronic ESM during seven consecutive days. Abdominal pain and stress were scored on an 11-point Numeric Rating Scale by using ESM at a maximum of ten random moments during the day.

Results: Abdominal pain scores were 2.21 points higher in IBS compared to HC ($P < 0.001$), whereas stress levels did not differ significantly ($B: 0.250, P = 0.406$). In IBS, a 1-point increase in stress was associated with, on average, 0.10 points increase in abdominal pain ($P = 0.017$). In HC, this was only 0.02 ($P = 0.002$). Stress levels at $t = -1$ (i.e. lagged scores) were not a significant predictor for abdominal pain at $t = 0$ in both groups, and vice versa.

Conclusions: We demonstrate that real-time stress scores are positively associated with concurrent abdominal pain scores in IBS, but not in HC, whereas abdominal pain scores could not be predicted by preceding stress levels, and vice versa, suggesting an in-the-moment rather than a longitudinal association. Furthermore, our results point towards a difference in response to stress and not a difference in experienced stress per se. This study underlines the importance of considering the individual flow of daily life when evaluating symptom patterns in IBS and supports the use of real-time measurement when interpreting potential influencers of abdominal symptoms.

This study was performed on behalf of the IBS-ESM study group.

121 | Unresponsive dysphagia to proton pump inhibitors in eosinophilic esophagitis patients suggests to start steroid therapy without the need of performing a second upper endoscopy

M. D. Coletta¹; M. Ghisa²; M. Frazzoni³; L. Frazzoni⁴; S. Tolone⁵; N. D. Bortoli⁶; E. Marabotto⁷; M. Furnari⁸; V. Savarino⁹; E. V. Savarino¹⁰

¹Gastroenterology Unit, Padova, Italy; ²Department of Surgery, Padova, Italy; ³Oncology and Gastroenterology, Modena, Italy; ⁴University of Padova, Bologna, Italy; ⁵Gastroenterology Unit, Napoli, Italy; ⁶Department of Surgery, Pisa, Italy; ⁷Oncology and Gastroenterology, Genova, Italy; ⁸University of Padova, Genova, Italy; ⁹Digestive Pathophysiology Unit and Digestive Endoscopy Unit, Genova, Italy; ¹⁰Baggiovara Hospital, Padova, Italy

Objective: Eosinophilic Esophagitis (EoE) is a chronic immune-mediated disorder due to an inflammatory eosinophilic infiltrate (EI) in the esophageal lamina propria. The recognition of at least 15

eosinophils (eos) for high power field (hpf) on esophageal mucosal samples confirm the diagnosis. About 50% of patients with esophageal eosinophilia (EE) responds to a Proton Pump Inhibitor (PPI) therapy twice a day. Histologic sampling during upper endoscopy is mandatory to confirm response. Few data are available on the usefulness of clinical response to predict disease activity and response to PPI treatment. We aimed to evaluate whether symptom remission due to PPI therapy may predict histological remission in patients with PPI-responsive EoE.

Methods: Subjects suspect for EoE were prospectively enrolled in different centers in Italy. At baseline, an esophagogastroduodenoscopy (EGD) with biopsies was performed to diagnose EoE (eos >15 eos/hpf). A PPI b.i.d. was administered for 8 weeks and after an EGD was repeated to assess the endoscopic and histological remission. Symptoms were assessed before and after therapy by a 4-point Likert scale. Remission was considered if less than 15 eos/hpf in mucosal esophageal samples were found. Zero for each symptom after PPI therapy was indicative of clinical response.

Results: Thirty-one (25 Male; Age 18-68) patients with symptoms suggestive of EoE were enrolled. All presented dysphagia, 16 (51%) regurgitation and 19 (61%) heartburn. After 8-week PPI-therapy, 23 (74%) patients responded and 8 (25%) subjects did not. Dysphagia disappeared in all PPI-responsive subjects and only in 4/8 refractory to PPIs. Regurgitation and heartburn resolved in 14/15 (93%) and in 16/17 (94%) of patients responding to PPIs, respectively, and in 1/1 (100%) and 1/1 (100%) of subjects refractory to PPIs, respectively. We calculated, as reported in Table 1, sensitivity, specificity, positive and negative predictive values (PPV and NPV) of dysphagia disappearing in order to segregate PPI-responders from PPI-non responders without performing an EGD.

Conclusions: Response to PPI therapy as assessed by the resolution of dysphagia is useful, but does not suffice to predict histologic response. On the other hand, lack of disappearance of dysphagia after PPIs seems to justify starting steroid therapy without histological confirmation of remission.

Table 1.

Disappearance of dysphagia				
Sensitivity	Specificity	PPV	NPV	p Value
100%	50%	80%	100%	0.002

123 | Enteral nutrition dose-dependently inhibits phasic gastric motility

N. Goelen; G. Doperé; J. Morales; S. Van Huffel; J. Tack; P. Janssen

KU Leuven, Leuven, Belgium

Objective: A neurohumoral feedback loop matches gastric outflow with the processing capacity of the small intestines through regulation of gastric motility. We recently developed the VIPUN Gastric Monitoring System that allows to continuously assess gastric motility using an inflated intragastric balloon mounted on a nasogastric feeding tube. We hypothesised that an increasing flow of enteral nutrition (EN) through the duodenum inhibits gastric motility, exemplifying the neurohumoral feedback loop.

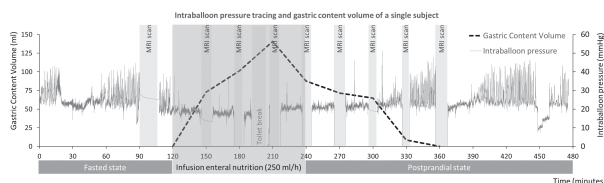
Methods: After an overnight fast, the VIPUN catheter was positioned with the balloon in the stomach. After inflating the balloon with 150 mL air, the catheter was connected to a pressure sensor. A Gastric Balloon Motility Index (GBMI) ranging from 0 (no motility) to 1 (maximum contractile activity) was calculated from the pressure signal. Fasted motility was recorded for 2 hours, thereafter EN (1 kcal/mL) was infused for 2 hours, either at 25, 75 or 250 mL/h. Recording continued for an additional 4 hours. Gastric Content Volume (GCV) was quantified with magnetic resonance imaging every 30 minutes. Data are presented as mean(SD).

Results: Nineteen healthy subjects were enrolled and 12 completed all three visits: 8 women and 4 men aged 31.7(13.6) years with a BMI of 24.4(2.0) kg/m².

Motility decreased during EN infusion at 250 mL/h (Δ GBMI = -0.43, $P < 0.0001$) while no significant changes were observed at 75 mL/h (Δ GBMI = -0.04, $P = 0.31$) and 25 mL/h (Δ GBMI = 0.09, $P = 0.29$). GCV during EN infusion was higher at 250 mL/h (73.3(36.7) mL) vs 75 mL/h (8.0(9.9) mL, $P = 0.0005$).

When EN was present in the stomach (GCV > 0 mL), motility was lower as compared to when the stomach was empty (GCV = 0 mL) (GBMI 0.34(0.24) vs 0.65(0.16), $P < 0.0001$).

Conclusions: Gastric phasic motility was inhibited and GCV was higher with increasing EN infusion rate. Moreover, postprandial motility remained lower until emptying was completed. We conclude that phasic gastric motility is an important driver of gastric emptying which is inhibited through duodenal exposure to relatively large doses of nutrients.



124 | Psychometric evaluation of an esm-based patient-reported outcome measure for symptom assessment in irritable bowel syndrome: A pilot study

L. Vork¹; D. Keszthelyi¹; S. Van Kuijk¹; Z. Mujagic¹; E. Questglas²; C. Leue¹; J. Kruimel¹; A. Masclee¹

¹Maastricht University Medical Center, Maastricht, The Netherlands;

²Grünenthal GmbH, Aachen, Germany

Objective: Currently used end-of-week or end-of-day reports of gastrointestinal (GI) symptoms in irritable bowel syndrome (IBS) are considered suboptimal due to important biases. The experience sampling method (ESM) has been proposed as a more accurate measurement method. The aim of the current pilot study is to evaluate the validity and reliability of a previously developed patient-reported outcome measure (PROM), based on the ESM, for symptom assessment in an IBS population. This measure is hereafter referred to as ESM-IBS-PROM.

Methods: Thirty-seven IBS patients (26 female; mean age 36.7 years) completed the electronic ESM-IBS-PROM at a maximum of ten random moments during the day and an end-of-day symptom diary, both during seven consecutive days. End-of-week questionnaires included the Gastrointestinal Symptom Rating Scale for IBS (GSRS-IBS) and IBS Severity Scoring System (IBS-SSS).

Results: ESM scores for GI symptoms were significantly associated to corresponding end-of-day scores ($P < 0.001$), with moderate-to-good agreement between the methods (Intraclass Correlation Coefficients; ICC > 0.500). However, end-of-day scores were significantly higher than mean ESM scores, and for abdominal pain, end-of-day scores did not differ significantly from the maximum ESM level. The difference between ESM and end-of-week scores was even more pronounced and correlations were weaker. Cronbach's coefficients were good (Cronbach's $\alpha = 0.750$) for lower GI symptoms and moderate-to-good (Cronbach's $\alpha > 0.545$) for four other domains within the ESM-IBS-PROM. Good consistency (ICC > 0.750) was shown between scores of the first half-week and scores of the second-half week (i.e. test-retest reliability).

Conclusions: This pilot study supports the validity and reliability of the previously developed electronic ESM-IBS-PROM for measuring GI symptoms in an IBS population. This PROM has the advantage of providing a more detailed view on individual symptom patterns, with the option to analyze symptom-symptom and symptom-environment interaction. ESM may help to unravel symptom onset, disease course and treatment response in IBS both in clinical practice and research setting. Data are currently being collected in four other centers to confirm and validate these results in IBS populations across centers and countries.

This study was performed on behalf of the IBS-ESM study group.

126 | Duodenal hyperpermeability, eosinophilia and symptoms in functional dyspepsia patients are reduced by proton pump inhibitors

L. Wauters; M. Ceulemans; M. Lambaerts; A. Accarie; R. Farré; J. Tack; T. Vanuytsel

KU Leuven, Leuven, Belgium

Objective: The role of proton pump inhibitors (PPI) in relation to duodenal alterations and symptoms in functional dyspepsia (FD) patients is unclear. We studied permeability, inflammation and symptoms in FD before and after PPI.

Methods: Duodenal biopsies were obtained in healthy volunteers (HV) and FD patients to study transepithelial electrical resistance (TEER) and paracellular passage of fluorescein-labeled dextran (4 kDa) in Ussing chambers before and after pantoprazole 40 mg OD for 4 weeks. Eosinophils were counted on H&E-stained sections per high-power field (HPF; 0.24 mm²). After each endoscopy, a naso-duodenal tube was positioned in the second part of the duodenum with aspiration of fluids after a liquid meal (Fortimel, 300kCal) with pH-measurement. PAGI-SYM and plasma high-sensitivity CRP

(hs-CRP) were measured at each visit. Non-parametric and correlation analyses were performed within- and between-groups.

Results: In total, 25 HV (16 female, median (IQR) age 26 (24;32) years) and 15 FD (13 female, 28 (22;34) years) were included. TEER was similar within- and between-groups. Paracellular passage was higher in FD vs HV off-PPI (25.6 (20.2;31) vs 19 (10.1;23.2) pmol, $P < 0.01$) and decreased in FD on-PPI (delta = -11.2 (-16.2;3.6), $P = 0.02$). Eosinophils were increased in FD vs HV off-PPI (12 (9-18) vs 3 (2-4) /HPF, $P < 0.0001$) and decreased in FD on-PPI (delta = -8 (-13;-5), $P < 0.001$). Duodenal pH increased on-PPI in HV (delta = 0.5 (0.2;1.3), $P < 0.01$) and FD (delta = 0.2 (0.04;0.6), $P < 0.01$). Higher PAGI-SYM ($P < 0.0001$) and a trend for higher hs-CRP was found in FD vs HV off-PPI (2 (0.6;5.5) vs 0.8 (0.3;1.4), $P = 0.06$) with a decrease in PAGI-SYM (delta = -1 (-1.5;-0.2), $P = 0.002$) and trend for decreased hs-CRP (delta = -0.4 (-2.1;0.2), $P = 0.06$) in FD on-PPI. Positive correlations were found between passage and hs-CRP ($r = 0.65$, $P = 0.01$) and eosinophils and PAGI-SYM ($r = 0.57$, $P = 0.02$) in FD off-PPI. Passage also correlated with pH ($r = 0.63$, $P = 0.03$) in FD on-PPI.

Conclusions: Duodenal hyperpermeability, eosinophilia and symptoms in FD patients are reduced by PPI and may be associated with systemic inflammation, which correlates with increased paracellular passage off-PPI. Increased duodenal pH also correlates with, but does not explain the restored permeability in FD on-PPI, suggesting the involvement of other factors such as duodenal eosinophils, which may drive dyspeptic symptoms.

128 | Effect of lactobacillus rhamnosus strain on stress-related intestinal permeability in healthy adults (ProSPer): A randomized, double-blind placebo-controlled trial

L. Wauters¹; T. Smokvina²; K. Geboers¹; Q. Dornic²; A. Accarie¹; K. Verbeke¹; L. Van Oudenhove¹; J. Tack¹; T. Vanuytsel¹

¹KU Leuven, Leuven, Belgium; ²Danone-Nutricia Research, Palaiseau, France

Objective: We aimed to study the effect of *Lactobacillus rhamnosus* CNCM I-3690 on intestinal hyperpermeability, occurring during public speech (Vanuytsel et al., Gut 2014).

Methods: Healthy students were randomized to the *L.rhamnosus* fermented milk or placebo (acidified milk) consumed daily (2 x 125 g) for 4 weeks prior to public speech (exam) and 2 more weeks until NSAID-administration (indomethacin 125 mg; positive control). Small intestinal permeability was quantified by a 2 hours lactulose-mannitol ratio (LMR), fractional excretion of mannitol (FEM) and lactulose (FEL) at baseline and after the exam. Salivary cortisol and State-Trait Anxiety Inventory (STAI) were measured at both visits. Primary outcome was the change during stress vs baseline of LMR between treatment groups. Mixed models with contrasts between groups were applied with correction for multiple testing for secondary endpoints only. Within-group changes were compared to nominal alpha 5%.

Results: In total, 92 students (55 female, mean age 23 ± 1.9 years) were included (46 per group). No differences between groups were found for LMR (delta = 0.003, 95%CI [-0.005;0.01], $P = 0.54$), FEL or FEM. Within-group analyses showed an increase of FEM during exam vs baseline for placebo ($10.6 \pm 3.7\%$ vs $9.3 \pm 2.5\%$, $P = 0.02$) but not *L.rhamnosus* ($10 \pm 4\%$ vs $9.5 \pm 3.9\%$, $P = 0.23$). LMR and FEL increased in both groups after NSAIDs (all $P < 0.001$) but not FEM ($P > 0.07$). Cortisol increased during exam vs baseline in the *L.rhamnosus* (12.6 ± 6.2 vs 4.9 ± 3 ng/ml) and placebo (13.9 ± 7.1 ng/ml vs 5.8 ± 5.4 ng/ml, both $P < 0.0001$) treatment with no difference between groups. STAI increased before the exam vs baseline in the *L.rhamnosus* (41.8 ± 10.7 vs 29.8 ± 5.7) and placebo (45.2 ± 10.4 vs 28.7 ± 6.4 , both $P < 0.0001$) groups with a lower increase in *L.rhamnosus* vs placebo (delta = 4.73, 95%CI [0.62;8.84], $P = 0.02$). No serious adverse events occurred.

Conclusions: Despite the primary endpoint was not reached, *L.rhamnosus* CNCM I-3690 seems to prevent stress-induced hyperpermeability to mannitol, a pathway that differs from NSAID-induced hyperpermeability to lactulose. Subjective but not objective stress-markers were reduced with *L.rhamnosus* vs placebo, suggesting gut-mediated effects potentially via the microbiota.

131 | Types and number of gastroesophageal reflux episodes correlate with nutritional patterns

S. Morozov; V. Kropochev

Federal Research Center of Nutrition and Biotechnology, Moscow, Russia

Objective: The correlation of nutritional patterns with number and types of gastroesophageal refluxes is poorly studied yet.

Aim: To assess the effect of actual nutrition of GERD patients on the number and type of gastroesophageal reflux detected with 24-hours esophageal pH-impedance

Methods: One hundred twenty-four GERD patients (54 men, age (M±m): 46 ± 17.7 y.o., BMI 28.5 ± 0.6 kg/m²) and 41 healthy controls (8 men, age 42 ± 12.4 y.o., BMI 28.3 ± 1.3 kg/m²) were examined with the use of language-specific food frequency questionnaire and 24-hours esophageal pH-impedance (Ohmega, MMS; 2 pH, 6 impedance catheters, Unisensor). The correlation analysis between macro- and micronutrient consumption and the number of gastroesophageal refluxes (GER), their acidity and duration was performed (Statistica 10, StatSoft)

Results: Direct medium-strength correlation was found between esophageal acid exposure time and the energy value of the ration (Spearman rank $R = 0.19$, $P < 0.05$), and the amount of consumed fat ($R = 0.2$, $P < 0.05$).

There was a direct correlation of the total number of GERs with the energy value of the ration ($R = 0.35$, $P < 0.05$), protein ($R = 0.3$, $P < 0.05$), fat ($R = 0.33$, $P < 0.05$), and alcohol consumption ($R = 0.28$,

$P < 0.05$) and the inverse one with the dietary fiber consumption ($R = -0.22$).

Significant direct correlation was found between the number of acid GERs and total energy value of the ration ($R = 0.35$, $P < 0.05$), consumption of fat ($R = 0.32$, $P < 0.05$), protein ($R = 0.25$, $P < 0.05$), carbohydrates ($R = 0.24$, $P < 0.05$) and alcohol ($R = 0.24$, $P < 0.05$).

Number of weak-acid GERs showed direct correlation with the calories intake ($R = 0.22$, $P < 0.05$), fat ($R = 0.21$, $P < 0.05$), protein ($R = 0.22$, $P < 0.05$), alcohol ($R = 0.23$, $P < 0.05$) consumption, and the inverse one with the amount of dietary fiber intake ($R = -0.24$, $P < 0.05$). Number of high GERs correlated directly with the amount of fat ($R = 0.3$, $P < 0.05$), protein ($R = 0.22$, $P < 0.05$), alcohol ($R = 0.25$, $P < 0.05$) consumed, and inversely with the amount of dietary fiber ($R = -0.25$, $P < 0.05$) in the ration.

Paired comparison of the correlation coefficients was performed, but didn't reveal any difference.

Conclusions: High energy value, consumption of fat and alcohol showed direct medium-strength correlation with esophageal acid exposure and number of GERs. Dietary fiber consumption correlated inversely with total number, weak acid and high GERs.

134 | Upper and lower esophageal sphincter resting pressure at the start and at the end of high-resolution esophageal manometry examinations

V. Kropochev¹; S. Morozov¹; A. J. Bredenoord²

¹Federal Research Center of Nutrition and Biotechnology, Moscow, Russia;

²Amsterdam Medical Center, Amsterdam, The Netherlands

Objective: Lower and upper esophageal sphincter resting pressures are not within current classification, though it is recommended to measure them at the beginning of high-resolution esophageal manometry studies. Aim: to evaluate resting pressures of upper and lower esophageal sphincters with high-resolution esophageal manometry.

Methods: Patients referred to the esophageal HRM examination were offered to participate in the trial. HRM examinations were performed in upright (sitting) position using a solid-state 36 channel 10Fr catheter (UniTip, Unisensor AG, USA) inserted transnasally. Patients were allowed not less than 2 minutes (Mean $\pm$ SD 3.0 ± 0.3 minutes) to adapt to the catheter placement. Resting pressures were measured at rest for at least 30 seconds at the beginning of the examination and after 10.5 mL water swallows. Standard software was used to analyze the obtained results (Solar GI, MMS, the Netherlands). Beck depression inventory (BDI-II) was used to assess psychological status as the possible reason of the resting pressure change. The obtained results were compared using non-parametric statistics (Statistica 10, StatSoft, USA).

Results: Eighty-four patients (31 men), age (M $\pm$ m) 48.5 ± 13.2 y.o. were enrolled. Hiatal hernia was present in 37 of them. Mean and minimal upper esophageal sphincter pressures were lower at the

repeated measurement compared to the initial ones. No significant change in LES pressures were found. The results of LES and UES resting pressure measurements are shown in table 1. No correlation of the pressure change was found with age, sex, presence of hiatal hernia and Beck depression inventory rate.

Conclusions: These findings probably should be considered in the future studies aimed to retrieve normal values of the esophageal resting pressure.

	Upper esophageal sphincter		P	Lower esophageal sphincter		P
	initial	repeated		initial	repeated	
Mean resting pressure, mm Hg	123.7 $\pm$ 76.6	87.9 $\pm$ 64.1	<0.0001	30.4 $\pm$ 16.5	23.5 $\pm$ 16.0	0.06
Minimal resting pressure, mm Hg	79.9 $\pm$ 52.4	57.2 $\pm$ 49.1	<0.0001	12.9 $\pm$ 10.7	13.9 $\pm$ 11.8	0.08

TABLE 1. Comparison of mean and minimal UES and LES pressures.

139 | Role of endoflip signal averaging in measuring dynamic pyloric motor function and therapeutic response to G-POEM in refractory gastroparesis

L. Watts; J. R. Baker; A. A. Lee; N. Bowers; R. J. Law; W. L. Hasler

University of Michigan Health System, Ann Arbor, United States

Objective: Pyloric diameters measured by EndoFLIP show significant variability due to phasic and tonic contractions. EndoFLIP measurements of pyloric response to G-POEM in gastroparesis are performed in real time during endoscopy and are influenced by pyloric diameter variations. Impacts of signal filtering to smooth EndoFLIP recordings on measuring pyloric variability and response to G-POEM are unexplored. We hypothesized (i) differences from minimum to maximum pyloric diameter are enhanced by analyzing unfiltered recordings but (ii) detecting increases in pyloric diameter after G-POEM is improved by averaging EndoFLIP readings over 30 seconds.

Methods: G-POEM was performed on 13 patients with refractory gastroparesis. Pre- and post-myotomy EndoFLIP was conducted with inflation to 50 mL. Minimum and maximum pyloric diameters over 60 seconds of recording were measured by FLIP Analytics both with filtering turned off and with filtering to determine average diameter over 30 seconds to smooth the signal.

Results: With EndoFLIP filtering, minimum and maximum pyloric diameters with 50 mL inflation before G-POEM were 15.3 ± 1.5 and 16.2 ± 1.8 mm showing a 0.9 ± 0.6 mm range of diameters (Figure). Removing filters decreased minimum diameters (14.9 ± 1.5 mm) and increased maximum diameters (16.3 ± 1.8 mm), increasing the range of diameters to 1.5 ± 0.7 mm ($P < 0.05$). G-POEM increased minimal diameters on filtered (16.8 ± 2.4 mm, $P = 0.003$) but not unfiltered (15.5 ± 2.7 mm, $P = 0.40$) recordings. G-POEM increased maximum diameters in both filtered (17.7 ± 2.7 mm, $P = 0.02$) and

unfiltered (17.6 ± 2.5 mm, $P = 0.007$) recordings. Ranges from minimum to maximal diameter were less for filtered (0.9 ± 1.1 mm) vs unfiltered (2.1 ± 2.0 mm) recordings after G-POEM ($P = 0.007$). Failure to detect increases in minimum diameter after G-POEM was more common in unfiltered (6 patients) vs filtered (2 patients) recordings; detecting increases in maximum diameter was unaffected by filtering.

Conclusions: Pyloric diameters are highly variable before and after G-POEM and are best detected without EndoFLIP filtering. Variability of minimum diameters measured without filtering can mask detection of responses to G-POEM. Using filtering to average data over 30 seconds smooths signal contours allowing greater discrimination of G-POEM impact on pyloric diameter. Analysis of combined unfiltered and filtered EndoFLIP data permits comprehensive assessment of dynamic and static pyloric function before and after myotomy for refractory gastroparesis.

MEASUREMENT OF VARIABILITY OF PYLORIC DIAMETER WITH AND WITHOUT ENDOFLIP FILTERING

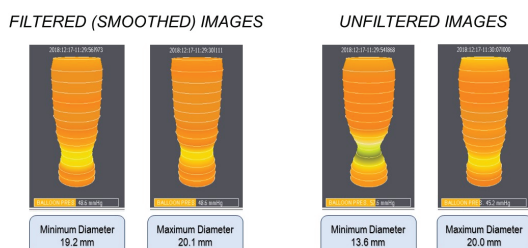


FIGURE. Filtering (left) smooth EndoFLIP signals limiting diameter variation; unfiltered signals (right) permit detection of phasic and tonic pyloric contractility.

140 | Quantified small bowel motility during MRI as a biomarker of Crohn's disease activity: A retrospective study in a paediatric population

A. Menys¹; L. Cococcioni²; S. Kumar¹; F. Kiparissi²; S. A. Taylor¹; T. A. Watson²

¹University College London, London, United Kingdom; ²Great Ormond Street Hospital, London, United Kingdom

Objective: While not considered a disease of dysmotility, hypomotile bowel in Crohn's Disease is associated with inflammatory activity. In adult populations, this relationship has been extensively studied with Magnetic Resonance Enterography (MRE).

This purpose of this retrospective study was to explore the relationship between terminal ileal (TI) motility in children against a symptomatic endpoint.

Methods: A review of a paediatric hospitals imaging database was performed to identify subjects with good quality MRE studies and a clinical appointment ± 1 mo to determine a clinical score for disease activity (PGA, a 4 point score 1 = no disease to 4 = severe). 68 subjects were identified (mean age 13.2, range 6 to 19) with dynamic 'cine' imaging through the terminal ileum. The dynamic imaging was processed, blind to any clinical data, with a previously validated

motility assessment algorithm (GIQuant[®], Motilent, London, UK). A consultant radiologist delineated the TI on each subject within 5 cm of the ileocecal valve and the motility score derived. The TI was used as an repeatedly identifiable reference to enable comparison between subjects. The TI motility score was correlated against the symptom score and the cohort split into clinically active disease PGA > 1 and non-active = 1. The mean difference between groups was assessed with U-Test.

Results: The median TI motility was 0.2 (range 0 to 0.6) and the median PGA symptom score was 1 (range 1 to 4). The correlation between the two measures was $R = -0.32$, $P = 0.011$. The mean motility score of inflamed subjects was 0.18 and 0.26 with a statistically significant difference of 0.08, $P = 0.003$.

Conclusions: This is the first time to our knowledge that quantified small bowel motility has been assessed in the context of Crohn's Disease in a paediatric cohort. Subjects with reduced terminal ileal motility appeared to have a higher symptom load. These results support findings in adult populations but comparison with an endoscopic or histopathological endpoint within the same region of bowel represents an important next step.

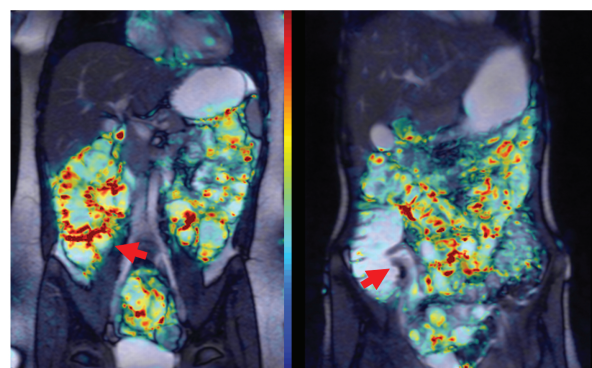


Figure: Motility map (red = high motility, blue = low) overlaid with an anatomical imaging showing the terminal ileum. The terminal ileum (left, red arrow) of a subject with a low symptom score demonstrating good motility. The terminal ileum of a patient with a high symptom score (right, red arrow).

144 | Profiling biomarkers in the gut of a Parkinson's disease mouse model

A. Braun¹; M. Gries¹; S. Rommel¹; S. Schmitteckert²; R. Roeth²; B. Niesler²; K.-H. Schäfer¹

¹University of Applied Science Kaiserslautern, Zweibrücken, Germany;

²University of Heidelberg, Heidelberg, Germany

Objective: With rising life expectancy, Parkinson's disease (PD) is expected to affect an increasing number of people. Clinical symptom development takes several years until PD manifests and unfortunately, there is no curative therapy so far. The patients would highly benefit from an early diagnosis since this would allow timely intervention and prevention. However, it is challenging to obtain biopsies from the brain to monitor the progression of the disease over time. Early pathological signs of PD have been reported within the enteric nervous system of patients generating the hypothesis that the pathology in neurodegenerative disorders might start in the gut and subsequently spreads to the brain. Consequently, pathological analysis of the gastrointestinal

tract seems suitable for staging the diseases. The aim of our study was to identify molecular profiles for early PD pathogenesis.

Methods: Therefore we investigated mRNA and microRNA expression patterns in the gut of a PD animal model (A30P-synuclein over-expressing mouse). Wild type and PD mice with ongoing pathology and in an early stage without motor symptoms were used. The gut mucus layer, myenteric plexus and mesencephalon were investigated separately.

Results: Based on previous results of our group showing protein level alterations in the A30P mice, like synaptobrevin 2, calretinin and superoxide dismutase, corresponding expression analysis on mRNA level was performed by real-time PCR. As microRNAs are relevant in fine tuning of gene expression and have a high potential as non-invasive biomarkers, complementary microRNA profiling is currently performed by n counter nanostring technique.

Conclusions: Our study corroborates data of numerous regulated markers in the gastrointestinal tract of a PD mouse model. Reliable biomarkers for PD in minimal invasive gut biopsies opens up a new perspective to track brain diseases at their early stage in the gut.

145 | Mechanisms underlying propagation of neurogenic motor activity along the smooth muscle of isolated whole mouse colon

N. J. Spencer; M. Costa; T. Hibberd; L. Travis

Flinders University, Bedford Park, South Australia, Australia

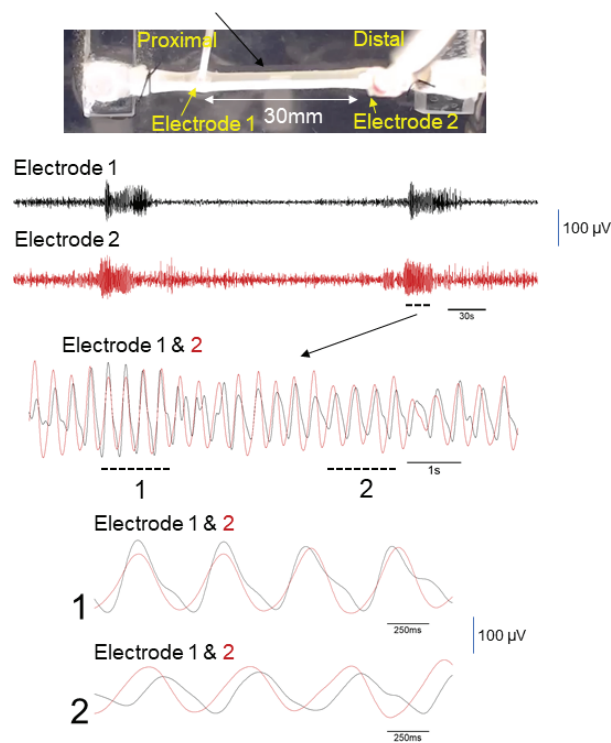
Objective: Our objective was to determine the mechanisms underlying the propagation of smooth muscle contraction, during propulsion of colonic content along isolated intact whole mouse colon.

Methods: We developed a novel imaging system for spatio-temporal mapping of colonic wall movements, whilst at the same time recording simultaneously the electrophysiological activity from the smooth muscle in the proximal and distal colon. This approach allowed us to temporally correlate patterns of electrical activity over large regions of smooth muscle, whilst temporally correlating the propagation of smooth muscle contraction along the colon.

Results: Infusion of fluid into the proximal region of an isolated whole colon generated neurogenic contractions that propagated aborally along the colon every 2-5 minutes at a velocity between 6-11 mm/s (N = 8). The myoelectric activity underlying each propagating contraction consisted of bursts of rhythmic depolarizations at a frequency of 2 Hz (N = 8). Remarkably, during each propagating neurogenic contraction, temporally-coordinated excitatory junction potentials (EJPs) occurred simultaneously in smooth muscle at the proximal and distal colon repetitively at 2 Hz (Figure 1; N = 8). Such coordinated activity in the muscle was abolished by hexamethonium (N = 5), confirming that the ENS was responsible for the temporal synchronization of EJPs at each extreme end of the isolated colon. Action potentials occurred on EJPs in the proximal colon, but synchronized EJPs in the distal colon were suppressed from reaching

action potential threshold, due to descending inhibitory pathways. This was supported by the observation the L-NA (100 micromolar) induced action potentials on each EJP at the distal colon recording site (N = 4).

Conclusions: This is the first observation that rhythmic electrical depolarizations (EJPs) in smooth muscle can occur simultaneously long the entire length of isolated colon, that is generated by rhythmic activity and nicotinic pathways in the ENS. In the colon, the velocity of aborally-propagating neurogenic smooth muscle contraction is determined largely by the extent and rate of withdrawal of descending inhibition, rather than rate of propagation of neural activity in the ENS.



147 | Escherichia coli Nissle 1917 increases intestinal tight junction expression and restores epithelial barrier: Possible implications in irritable bowel syndrome

M. R. Barbaro; D. Fuschi; C. Cremon; E. Capelli; V. Stanghellini; G. Barbara

University of Bologna, Bologna, Italy

Objective: Intestinal epithelial barrier alterations play a key role in the pathogenesis of several gastrointestinal diseases, including Irritable Bowel Syndrome (IBS). Escherichia coli Nissle 1917 (EcN) is a probiotic effective in the maintenance of remission of ulcerative colitis, although the underlying molecular mechanisms remain unclear. The aim of this study was to characterize the potential effect of EcN in reversing the increase of intestinal permeability caused by the mediators spontaneously released by IBS biopsies, by known inflammatory stimuli and to evaluate the molecular mechanisms involved.

Methods: CaCo-2 cells were used as an in vitro model of intestinal epithelial barrier. Paracellular permeability was evaluated using sulfonic-acid-conjugated to fluorescein (FITC). Two concentrations of EcN (10^8 and 10^6) were applied to CaCo-2 with or without inflammatory mediators spontaneously released (SUP) by mucosal biopsies of patients with IBS and healthy controls (HC), SLIGRL (a protease-activated receptor-2 activating peptide), tumor necrosis factor (TNF)- α , interferon (IFN)- γ and. qPCR was used to assess mRNA expression of tight junction proteins, zonula occludens-1 (ZO-1), claudin-1, occluding, junctional adhesion molecule (JAM)-A.

Results: EcN induced a dose-dependent reinforcement of CaCo-2 monolayer compared to untreated CaCo-2 (CTR). SUP of patients with IBS induced a significant increase of paracellular permeability compared to HC SUP ($P < 0.05$). The co-incubation of EcN with IBS-D or -C SUP induced a recovery of permeability rate compared to SUP alone ($P < 0.05$). SLIGRL 50uM and 200uM induced a significant increase in CaCo-2 permeability compared to CTR ($P < 0.05$); the co-incubation of SLIGRL and EcN induced a recovery of epithelial integrity compared to SLIGRL alone. TNF- α and IFN- γ induced an increase in CaCo-2 permeability compared to CTR reverted by EcN. No effect of EcN was observed with IBS-M SUP. qPCR analysis showed EcN induced a significant increase in ZO-1 and occludin expression compared to CTR.

Conclusions: EcN increases the expression of tight junctions, reinforcing intestinal epithelial barrier. EcN reverts the increase of epithelial permeability induced by inflammatory stimuli and IBS SUP. Future studies should explore the potential application on EcN in IBS.

150 | Effects of dietary fibers on the tuft cell population in the mouse colon post radiation

U. Voss¹; D. Malipatlolla²; P. Patel²; S. Devarakonda²; F. Sjöberg²; R. Grandér²; A. Rascón¹; M. Nyman¹; G. Steineck²; C. Bull²

¹Lund University, Lund, Sweden; ²University of Gothenburg, Gothenburg, Sweden

Objective: Pelvic radiation therapy is often associated with gastrointestinal dysfunction. Intestinal tuft cell located within the mucosal epithelium have in the small intestine following full body radiation in mice been shown to be essential for epithelial regeneration. Dietary approaches during and after radiation therapy have also been suggested to aid epithelial health and function. Tuft cells are suggested to be important for translation of chemosensory signals in the lumen. This study investigated the effects of dietary fiber composition on tuft cell numbers in the colon at 1, 6 and 18 weeks post radiation.

Methods: Male mice were divided into high (15% fermentable fiber from oats), low (5% fermentable fiber from oats + 10% non-fermentable fiber) or no fiber in a purified diet with half of each group receiving targeted colonic radiation. Radiation procedure was 4 fractions of 8 Grey at 3.2 Gy/min, with twelve hours between.

Distal colon was collected and tuft cell density per crypt unit calculated using immunocytochemistry.

Results: Results showed that diets containing high percentages of fermentable fibers reduced tuft cell numbers in the colon compared to diets containing no or low percentage of fermentable fibers. One week after radiation no effect on tuft cell numbers in the colon was seen, however at 6 weeks a significant increase of tuft cell number per crypt was observed. This increase was also evident at 18 weeks.

Conclusions: Oat fibers have been shown to decrease epithelial turnover rate which may account for the lower number of tuft cell/crypts in the oat fiber containing diet compared to the no fiber diet. Previously a radiation-induced decrease of tuft cells in the acute radiation response have been observed. Further 7-10 days after radiation tuft cells, like in this study, was found to be present at pre-radiation levels. The 6 and 18-week increase of tuft cells have not previously been shown. The role of this prolonged increase is at present unknown, but may represent a compensatory mechanism to maintain epithelial integrity.

153 | Effect of chronodisruption by chronic jet-lag on gut homeostasis in mice

L. Desmet; T. Thijs; A. Segers; K. Verbeke; I. Depoortere

TARGID, University of Leuven, Leuven, Belgium

Objective: Intestinal microbiota undergo oscillations that are influenced by feeding rhythms. Disruption of the circadian system desynchronizes peripheral clocks and can induce metabolic diseases. We aimed to investigate whether chronodisruption affects metabolic homeostasis and rhythmicity of microbial production of short-chain fatty acids (SCFAs) that feed back to the circadian enteroendocrine clock.

Methods: C57Bl6/5J mice were assigned either to a control group that was housed under a 12-h/12-h light/dark-cycle (Zeitgeber (ZT) 0 lights-on) or to a jet-lag group that was exposed to an 8 hours forward and backward shift 3 days a week during 4 weeks. The expression of clock and metabolic genes were determined by qPCR and fecal SCFA concentrations were analyzed by gas chromatography-flame ionization detector.

Results: Jet-lagged mice gained more weight compared to control mice ($P < 0.05$) and altered their day/night food intake pattern without changing total daily caloric intake.

Distal fecal concentrations of acetate showed no diurnal rhythm, while propionate ($P < 0.05$) and butyrate ($P < 0.01$) concentrations were diurnal, and peaked at ZT5 and ZT3, respectively. In jet-lagged mice diurnal rhythms in propionate and butyrate were delayed with 5 hours ($P < 0.01$) and 3 hours ($P < 0.05$), respectively.

The mRNA expression of BMAL1, CLOCK and REV-ERB α in the colonic mucosa showed diurnal rhythmicity ($P < 0.001$) in both groups, but were delayed with 4, 2 and 5 hours ($P < 0.05$) in jet-lagged mice, respectively. Proglucagon mRNA expression was diurnal ($P < 0.01$) in control mice while rhythmicity was lost in

jet-lagged mice, this was also reflected in blood glucose levels. In both groups, the mRNA levels of ghrelin showed no diurnal rhythms, while plasma levels of ghrelin were diurnally fluctuating in both groups, but were not affected by jet-lag. TNF- α mRNA expression was diurnal ($P < 0.01$) in control mice, while rhythmicity was abolished by jet-lag.

Conclusions: Jet-lag induces changes in food intake pattern thereby delaying the rhythms in fecal SCFA concentrations. Similar delays were observed in clock gene expression that regulate the rhythmicity of metabolic genes like proglucagon and the inflammatory marker TNF- α , possibly contributing to weight gain.

155 | Relevance of central sensitization for gastrointestinal symptoms

I. Midenfjord¹; C. Grinsvall²; P. Koj³; H. Törnblom¹; M. Simrén²

¹Institute of Medicine, Gothenburg, Sweden; ²Sahlgrenska Academy, Gothenburg, Sweden; ³University of Gothenburg, Gothenburg, Sweden

Objective: Central sensitization (CS) has been proposed to be an important mechanism for symptom generation in functional gastrointestinal disorders (FGID). In this study, we explore the association between symptoms and CS in patients with FGID, and in volunteers with no or mild GI symptoms.

Methods: Patients with FGID according to Rome IV and volunteers completed questionnaires on central sensitization (CSI), sensory processing sensitivity (HSP), GI symptoms (GSRS-IBS), psychological distress (HAD) and non-GI symptoms (PHQ-12). The validated cut-off of CSI (≥ 40) distinguished between persons with and without reported CS.

Results: We included 77 FGID patients and 79 volunteers (median age 30 [26-39] vs 25 [22-32] years ($P < 0.001$); females 57 (74%) vs 41 (52%) ($P = 0.007$).

Thirty-three (43%) patients and one (1%) volunteer reported CS. Patients with CS were older (36 [27-47] years vs 28 [24-33] years, $P = 0.02$), had more severe overall GI symptoms (4.0 [3.8-4.5] vs 3.7 [3.2-4.2], $P = 0.03$) and non-GI symptoms (9 [8-10] vs 6 [4-8], $P < 0.001$) than patients without CS, but with no significant differences in psychological distress or sensory processing sensitivity. Linear trend analyses in all study subjects (divided into CS quintiles) demonstrated associations between CS and GI symptoms with large effect sizes (Figure 1). Furthermore, moderate to strong correlations were seen between CS and GI symptoms (total: $\rho = 0.68$; abdominal pain: $\rho = 0.64$; bloating: $\rho = 0.65$; constipation: $\rho = 0.56$; diarrhea: $\rho = 0.58$; satiety: $\rho = 0.55$, all $P < 0.001$).

Conclusions: Central sensitization is common in patients with functional gastrointestinal disorders, and clearly associated with GI symptom severity, indicating that it seems to be an important factor for symptom generation.

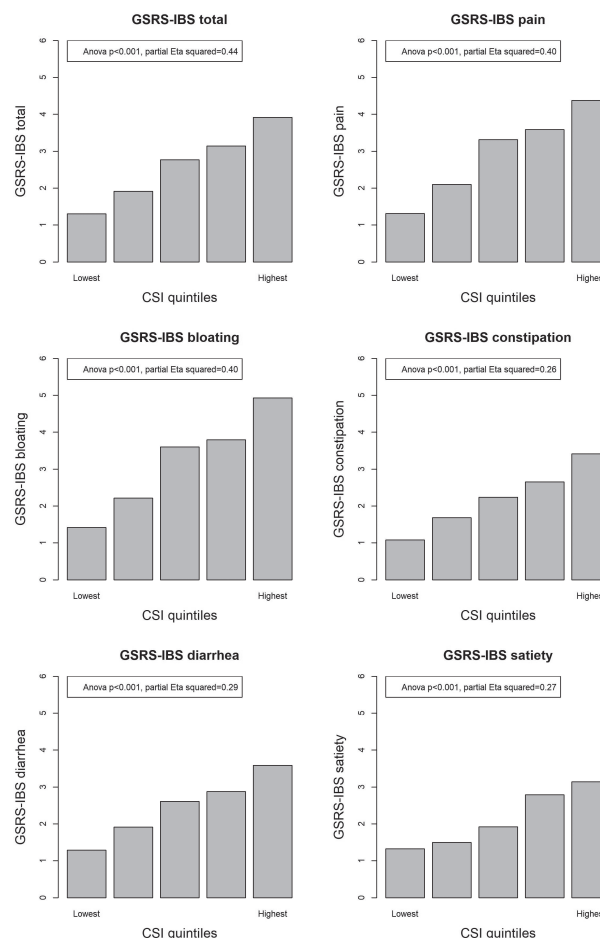


FIGURE 1. Linear relationships between increasing level of central sensitization and gastrointestinal symptoms, all with large effect sizes (partial $\eta^2 > 0.14$). CSI: Central Sensitization Inventory; GSRS-IBS: Gastrointestinal Symptom Rating Scale, IBS version.

156 | Role of the ghrelin receptor in the development of an obese phenotype after maternal malnutrition

S. Sun¹; K. Corbeels²; L. Desmet¹; A. Segers¹; Q. Wang¹; B. Van Der Schueren²; I. Depoortere¹

¹Gut Peptide Research Lab, Targid, Leuven, Belgium; ²Clinical and Experimental Endocrinology, Leuven, Belgium

Objective: The mismatch between undernutrition during pregnancy and adequate nutrition after birth affects the developmental programming of the hypothalamus and increases the risk of developing metabolic diseases. We hypothesize that the high ghrelin levels during maternal undernutrition affect the hypothalamic development and contribute to the conversion to an obesity-prone phenotype when exposed to a high-fat diet (HFD).

Methods: Pregnant C57BL/6J, wild type (WT) and ghrelin receptor (GHSR)^{-/-} mice were assigned to either a normal nourished (NN) group, fed a standard diet (SD) throughout gestation, or an undernutrition (UN) group, fed 70% of the food consumed by the NN group

from 10 days postcoitum. All pups were fostered by NN Swiss mice. After weaning, male pups were fed a SD, followed by a HFD at week 9 (W9).

Results: C57BL/6J UN pups were smaller in body weight ($P < 0.05$) and length ($P < 0.001$) than NN pups at birth and caught-up body weight ($P < 0.05$) and growth ($P < 0.001$) from postnatal day 2 (P2). A steep increase (329%) in plasma octanoyl ghrelin levels was observed between P10 and P15 in both groups. In addition, the hypothalamic mRNA expression of GHSR ($P < 0.05$) was upregulated at P15 in UN pups compared to NN pups.

During lactation, body weight of WT UN pups but not of GHSR^{-/-} UN pups was higher compared to NN littermates. After weaning with a SD between weeks 4 and 8, body weight and food intake remained higher in WT UN pups but lower in GHSR^{-/-} UN pups than in NN controls. After feeding a HFD from W9 for 3 weeks, body weight increased with 17.5% in WT UN mice compared to 14.7% in WT NN mice. No differences in body weight gain were observed between GHSR^{-/-} UN vs GHSR^{-/-} NN mice.

Conclusions: The ghrelin receptor mediates the susceptibility to develop obesity if maternal undernourished mice are exposed to ad libitum feeding after birth.

160 | Efficacy of helicobacter pylori eradication regimens

F. Pereira; R. Azevedo; M. Linhares; D. Ramos; J. Pinto; A. Caldeira; J. Tristan; E. Pereira; R. Sousa; A. Banhudo

Hospital Amato Lusitano, Castelo Branco, Portugal

Objective: *Helicobacter pylori* (Hp) is a major cause of peptic ulcer disease and gastric malignancies. Eradication remains a challenge due to increased antibiotic therapy resistance. We aim to assess the efficacy of the empirical antibiotic regimens prescribed for Hp eradication.

Methods: We conducted a retrospective study between January/2015 and March/2019 including patients with Hp infection. We collected clinical data and antibiotic regimens used, and we evaluated Hp eradication after treatment. Eradication rate was calculated for each treatment regimen.

Results: 206 eradication schemes were included (53.4% female, mean age of 56.4 ± 12.6 years). Main indications for Hp testing were dyspepsia (36%), erosive gastritis/bulbitis (32%) and peptic ulcer disease (21%). The tests more frequently used for diagnosis of Hp infection were histology (55%) and rapid urease test (28%). On the other hand, Hp eradication was mainly confirmed by stool antigen test (46%), histology (24%) and urea breath test (20%). 32% of the patients were treated with triple regimen, 28% with sequential quadruple therapy, 23% with concomitant quadruple treatment, 10% with bismuth-containing quadruple treatment and 7% with levofloxacin-based therapy. Global eradication rate was 78%. Eradication rates according to treatment regimens were the following: triple therapy – 63%, sequential treatment – 88%, concomitant

quadruple treatment – 86%, bismuth-containing quadruple treatment – 95% and levofloxacin-based therapy – 50%.

Conclusions: In our sample, the most frequently antibiotic regimen prescribed was the triple-based therapy, although it showed a poor eradication rate. The most effective regimen was the bismuth-containing treatment. Concomitant and sequential therapies also presented acceptable eradication rates. Therefore, we suggest a quadruple-based therapy with or without bismuth as a first line eradication treatment.

161 | Long term safety and efficacy of a medical device containing xyloglucan, pea protein reticulated with tannins and xylo-oligosaccharides, in patients with diarrhea predominant irritable bowel syndrome

E. Rey¹; B. S. Falcon¹; F. Arguelles²; E. Perez³; C. Ciriza⁴; C. Teruel⁵; F. Geijo⁶

¹Hospital Clinico San Carlos, Madrid, Spain; ²Hospital Virgen Macarena, Sevilla, Spain; ³Hospital Reina Sofia, Cordoba, Spain; ⁴Hospital 12 Octubre, Madrid, Spain; ⁵Hospital Ramon y Cajal, Madrid, Spain; ⁶Hospital Clinico Universitario de Salamanca, Salamanca, Spain

Objective: To evaluate the efficacy and safety of six months treatment with a medical device, containing xyloglucan, pea protein reticulated in tannins and xylo-oligosaccharides, in adult patients with IBS-D.

Methods: This multicenter, open-label, observational study was performed in 100 adult patients with IBS-D (according to Rome IV criteria), having symptoms at inclusion (IBS-SSS > 70). Patients received 4 tablets/day during 6 months.

Baseline characteristics were recorded and patients reported number and type of stool emissions (Bristol scale), bowel habits and fulfilled the IBS symptom severity score (IBS-SSS). Patients were evaluated monthly.

Results: Preliminary results have been obtained to date ($n = 50$). At baseline, mean total IBS-SSS values were 312.2; significant decrease in IBSSS score ($P < 0.001$ compared to baseline) was observed at each month of follow-up (month 1: 210.5; month 2: 214.1; month 3: 216.9; month 4: 210.6; month 5: 209.4; month 6: 200.6) as well as pain, bowel habit, and interference with life subscore. Mean stool frequency was 3.9 and significantly decreased ($P < 0.001$ compared to baseline) at each month of follow-up (2.4; 2.3; 2.4; 2.1; 2.3; 2.4). Mean Bristol stool form scale at baseline was 5.8 and it also decreased significantly ($P < 0.001$ compared to baseline) monthly in the follow-up (4.3; 4.1; 4.6; 4.5; 4.6; 4.6). Ten adverse events were recorded (allergic rhinitis, tonsillitis, vulvar itching, oral aphthae, acute infectious diarrhea, oral ambulatory surgery, otitis, headache, dyspepsia, nausea); relation was the treatment was considered as possible in just one (nausea).

Conclusions: The medical device containing xyloglucan, pea protein reticulated in tannins and xylo-oligosaccharides improves IBS

symptoms in patients with IBS-D at 6-month treatment (tachyphylaxis was not observed) and seems to be safe

162 | Evidence of transcriptional changes in pathways regulating 5-HT release from enterochromaffin cells in irritable bowel syndrome

A. Denadai-Souza¹; J. Aguilera-Lizarraga¹; L. Decraecker¹; N. Fabre¹; A. Beyder²; G. Boeckxstaens¹

¹Department of Chronic Diseases, Metabolism and Ageing; Translational Research Centre for Gastrointestinal Disorders, Laboratory for Intestinal Neuroimmune Interactions, KU Leuven, Leuven, Belgium; ²Enteric Neuroscience Program, Division of Gastroenterology & Hepatology, Departments of Medicine and Physiology & Biomedical Engineering, Mayo Clinic, Rochester, United States

Objective: Antagonists to 5-hydroxytryptamine type 3 receptors (5-HT₃) significantly improve abdominal pain in IBS-D patients. Unfortunately, most of these drugs were withdrawn from the market due to rare yet serious side effects. Herein, we hypothesized that the identification of dysregulated upstream pathways underlying aberrant 5-HT release from EC cells would pave the way to new therapeutic strategies for IBS. Therefore, we designed a proof of concept study to profile transcriptional disturbances to upstream pathways implicated in 5-HT release in IBS.

Methods: Herein, we initially screened for the most stable genes across microarray databases of 347 colorectal human samples of healthy volunteers (HV) and IBS patients (Affymetrix 133 Plus 2 Arrays) by using the RefGenes tool (Nebion; Switzerland). Hence, specific oligonucleotides to reference and target genes from pathways implicated in 5-HT release were designed by using the Real-Time qPCR tool. Stability and disturbances in expression of reference and target genes was investigated by RT-qPCR with cDNA libraries synthesized from total RNA extracted from the colon and rectal mucosa biopsies from HV and IBS patients. The most stable combination of reference genes was validated with the Office Excel Add-in GeNorm v3. Relative expression of genes from 5-HT releasing pathways was calculated by using the DDCT method.

Results: A pair-wise analysis with GeNorm indicated a geometric mean of *RNF2/EDM2* and *RPS11/TMSB10* as the most stable configuration respectively for the colon and rectum of HV and IBS patients. Hence, the analysis of expression relative to reference genes identified an upregulation of multiple genes implicated in 5-HT synthesis, transport and secretion, such as adrenergic, olfactory and mechano-transduction pathways. Furthermore, these changes were particularly enriched in IBS-D.

Conclusions: Herein, we spotlighted that major pathways implicated in 5-HT release from EC cells are upregulated in IBS-D. Follow-up assays based on multiplexed single molecule fluorescence in situ hybridization and immunofluorescence will support these findings with added spatial resolution.

163 | Discriminating non-celiac gluten sensitivity from irritable bowel syndrome: A diagnostic algorithm

M. R. Barbaro¹; C. Cremon¹; A. M. Morselli-Labate¹; A. Di Sabatino²; G. Latella³; C. Ciacci⁴; D. Fuschi¹; V. Stanghellini¹; U. Volta¹; G. Barbara¹

¹University of Bologna, Bologna, Italy; ²University of Pavia, Pavia, Italy; ³University of L'Aquila, L'Aquila, Italy; ⁴University of Salerno, Salerno, Italy

Objective: Non-celiac gluten sensitivity (NCGS) is characterized by intestinal and extra-intestinal symptoms related to the ingestion of gluten-containing foods, in the absence of celiac disease (CD) and wheat allergy. The pathophysiology of NCGS is unclear and no biomarkers are available. The aim of the present work was to investigate the role of serum zonulin as a diagnostic biomarker of NCGS and to develop a diagnostic algorithm.

Methods: Eighty-six patients with NCGS, 59 patients with diarrhoea-predominant irritable bowel syndrome (IBS-D), 15 patients with CD and 25 asymptomatic controls (ACs) were enrolled in a multicenter study. Zonulin serum levels were assessed by immunoenzymatic assay. Clinical and symptomatic data were recorded. The diagnostic power associated to zonulin alone, and to the combination of zonulin and clinical data were calculated.

Results: Compared to ACs, the NCGS and CD patients had significantly increased levels of zonulin ($P < 0.001$, $P < 0.001$), as did both NCGS and CD patients compared to IBS-D participants ($P < 0.001$ and $P < 0.001$, respectively). The diagnostic accuracy of zonulin levels in distinguishing NCGS from IBS-D was 81%, with a sensitivity of 71% and a specificity of 83%. After exclusion of CD, a diagnostic algorithm combining zonulin levels and key symptoms, improved the diagnostic accuracy.

Conclusions: Zonulin serum levels combined with clinical data differentiate NCGS from IBS-D with high accuracy

166 | Diagnosis of rumination syndrome in children with ambulatory impedance-pH monitoring

K. Nikaki¹; A. Rybak²; K. Nakagawa¹; D. Rawat³; P. Woodland¹; O. Borrelli²; D. Sifirm¹

¹Wingate Institute of Neurogastroenterology, QMUL, London, United Kingdom; ²Gastroenterology Department, Great Ormond Street Hospital, London, United Kingdom; ³Paediatric Gastroenterology Department, Royal London Hospital, London, United Kingdom

Objective: According to the Rome IV criteria the diagnosis of rumination in children is based on typical symptoms during clinical evaluation. High resolution manometry/impedance (HRM/Z) can be used to confirm the clinical suspicion of rumination but is rather poorly tolerated in children and only records one postprandial period.

The *aim* of our study was to identify a specific diagnostic pattern of rumination during ambulatory Impedance-pHmetry (MII-pH).

Methods: We retrospectively assessed MII-pH tracings from children with clinical diagnosis of rumination syndrome confirmed by HRM/Z (minimal 2 typical rumination episodes in postprandial evaluation). We then compared the MII-pH parameters of these patients with those from children with GERD and "non-GERD" children (investigated for possible GERD but with normal MII-pH). We established cut-off levels for significant MII-pH parameters and developed a rumination-specific scoring system. We then validated the scoring system on another group of patients who underwent both HRM/Z and MII-pH (traces scored blindly).

Results: We identified 12 children with confirmed diagnosis of rumination based on HRM/Z findings (median age: 13.9 years, 6M:6F). Another 18 children were identified with GERD (median age: 8.1 years, 8M:10F) and 12 children with non-GERD (median age: 12.4 years, 6M:6F). Children with rumination had significantly higher number of total reflux events (RE)/24 h, total number of proximal RE/24 h ($P < 0.0001$) and postprandial non-acid RE/hr ($P = 0.0072$) compared to GERD and non-GERD groups. The SAP for regurgitation/reflux/vomiting was significantly higher in the rumination group ($P = 0.0009$). The scoring system includes: 1) Total proximal RE/24 h > 57.5 , 2) Postprandial non-acid RE/hr > 2 , 3) SAP for regurgitation/reflux/vomiting > 97.5 . Each parameter scores 1 and rumination is diagnosed if the score is < 2 . We validated the scoring system in a group of 18 children who underwent both a HRM/Z and MII-pH (8 diagnosed with rumination – 3M:5F, median age: 13 years – and 10 with a negative HRM/Z – 4M:6F, median age: 8.5 years). The sensitivity and specificity of the score is 75% and 80% respectively.

Conclusions: Children with rumination have many more symptomatic reflux episodes (SI/SAP positive) with high proximal extent, particularly during postprandial periods compared to GERD and controls. Our scoring system allows for early identification of children with rumination syndrome.

167 | Abnormal balloon evacuation in IBS: Relevance for symptoms?

D. Y. Demir; H. Törnblom; M. Simrén

Sahlgrenska University Hospital, Gothenburg, Sweden

Objective: A balloon evacuation test (BET) is used in the diagnostic work-up of patients with suspected functional defecation disorders. The prevalence of abnormal balloon evacuation and the relevance for symptoms in a mixed group of IBS patients is unknown.

Our aim was to assess the proportion of IBS patients with abnormal BET and explore associations to symptoms and rectal sensitivity.

Methods: IBS patients fulfilling the Rome III criteria underwent BET (abnormal if time required to expel the balloon > 2 minutes) and an electronic rectal rapid barostat test. They also kept a 2-week-BSF diary for IBS subtyping, and completed Gastrointestinal Rating Scale

(GSRS) and Rome III questionnaires (focus on symptoms related to disturbed defecation: straining, incomplete bowel emptying or blocked stool, use of manual manoeuvres, difficulties relaxing).

Results: We included 133 IBS patients (mean age $36 \pm \text{SD } 12$) and 82 (61%) were able to evacuate the balloon within 2 minutes. The mean time for balloon evacuation among patients who were able to evacuate the balloon was 28 seconds (range 3–116 seconds). A higher proportion of patients with non-constipated IBS (IBS-D + M + U) demonstrated abnormal balloon evacuation (45%) compared with IBS with constipation (25%) ($P = 0.02$). No differences were seen between patients with normal and abnormal BET regarding severity of IBS symptoms (GSRS-IBS, 13 individual symptoms), symptoms related to disturbed defecation (5 symptoms), or rectal discomfort thresholds (barostat test).

Conclusions: A substantial proportion of IBS patients have abnormal balloon evacuation test results. However, the relevance for symptoms remain unclear, as no obvious association with symptom pattern or severity were noted, except for a surprising association with IBS without constipation. Future analyses should focus on the association with other tests of anorectal function.

168 | Frizzled-4 – A new player in the identification of human ENS progenitor cells

P. Neckel; M. Scharr; K. Seid; L. Just

Institute of Clinical Anatomy and Cell Analysis, Tübingen, Germany

Objective: Neural progenitor cells from the enteric nervous system are a potential source for future cell replacement therapies. Yet, we know little about the molecular mechanisms regulating this cell pool, let alone specific markers to identify neural progenitors in the ENS, especially in the human intestine. Here, we hypothesize that the canonical Wnt pathway plays a central role in ENS progenitor proliferation and that the Wnt-receptor Frizzled-4 is expressed by human ENS progenitor cells.

Methods: We investigated the influence of Wnt signaling on the proliferation of isolated postnatal ENS progenitors from murine and human intestine using gene-chip analysis, BrdU-incorporation assays, immunohistochemistry, western blot, and RT-PCR experiments. We used FACS analysis, immunohistochemistry, and patch clamping to isolate and characterize Frizzled-4 expressing cells from human intestine.

Results: Here we present sound evidence that the activation of the canonical Wnt pathway increases the proliferation of enteric neural progenitors and leads to a higher yield of differentiated neurons in vitro, both in humans and mouse models. We used this knowledge to identify the Wnt-receptor Frizzled-4 as a potential novel marker expressed on human postnatal ENS progenitor cells. Frizzled-4^{positive} cells gave rise to neurosphere-like bodies and ultimately differentiated into neurons. These new-born neurons also expressed Na_v , K_v and BK channels and, hence, suggest functional differentiation into neurons. In Frizzled-4^{negative} cultures, we did not detect any neural cells.

Conclusions: Canonical Wnt signaling has stimulating effects on the proliferation of neural progenitors of the murine and human ENS. The

Wnt-receptor Frizzled-4 is expressed by human neural progenitor cells and can be used for their isolation and purification. Frizzled-4^{positive} cells are capable of proliferation and functional neuronal differentiation in vitro. Therefore, Wnt signaling and its molecular pathway components are likely to be an important part of ENS progenitor regulation.

169 | Sub-segmental motility patterns identified by high-resolution jejunal manometry

C. Malagelada; C. Galan; A. Nieto; A. Accarino; J.-R. Malagelada; A. Fernando

Vall d'Hebron University Hospital, Barcelona, Spain

Objective: The manometric diagnosis of severe intestinal dysmotility is performed at most institutions via conventional multi-lumen catheters with sensors 5 to 10 cm apart. The recent application of high-resolution manometry catheters with closely spaced sensors to other gut segments has been highly successful. The objective of the present study was to develop a standard procedure for jejunal high resolution manometry to characterize normal sub-segmental motility patterns.

Methods: A 36-channel high-resolution manometry catheter (MMS-Laborie, Enschede, The Netherlands) was orally placed under radiological guidance in the jejunum of 15 healthy subjects (8 men, 7 women; 20-38 age range). Intestinal motility was recorded during 5 hours, 3 during fasting and 2 after a 450 kcal solid-liquid meal. Analysis of motility patterns was supported by computerized tools.

Results: All healthy subjects showed at least one complete migrating motor complex during the three hour fasting period. Phase III activity lasted 5.2 ± 0.6 minutes and migrated aborally at a velocity of 10 ± 2 cm/min. High-resolution spatial analysis showed that during phase III each individual contraction propagated rapidly (1 cm/s) over a 20-25 cm segment of the jejunum. Phase II activity was mainly composed of propagated high-amplitude contractions (8 ± 1 contractions/hour) which progressed uninterruptedly down the jejunum. After meal ingestion, intestinal motility comprised numerous isolated, non-propagated contractions, but also high-amplitude propagated contractions (6 ± 2 contractions/hour) similar to those detected during phase II.

Conclusions: Sub-segmental jejunal motility analysis with high-resolution manometry identifies contractile patterns which are not apparent with conventional manometric catheters.

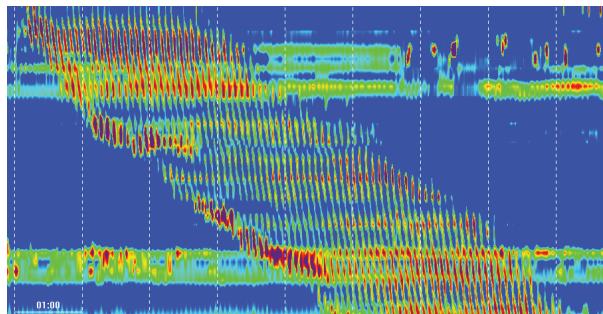


FIGURE. Phase III of the MMC by high-resolution jejunal manometry.

170 | Treatment of functional gastrointestinal diseases in children: Are herbals an option? A systematic review

J. Möller¹; O. Kelber²; E. Raskopf³; K. Nieber⁴

¹Research & Development, Darmstadt, Germany; ²Phytomedicines Supply and Development Center, Darmstadt, Germany; ³ClinNovis GmbH, Cologne, Germany; ⁴Kooperation Phytopharmaka GbR, Bonn, Germany

Objective: Functional gastrointestinal diseases, which include functional dyspepsia (FD) and irritable bowel syndrome (IBS), are characterised by symptoms like abdominal pain, nausea and fullness, leading to a severely impaired quality of life.

Given the high medical need in these indications especially in children, the question for effective and well-tolerated treatment options in this age group arises.

Methods: A PubMed-Medline search for clinical studies and reviews regarding FD and IBS in children in compliance with the PRISMA statement was conducted and complemented by hand searching and cross-referencing.

Results: The search gained 79 hits for FD in children, thereof 13 on pharmacological treatment options, of which 2 were herbals. For IBS, it gained 321 hits, 23 of which were pharmacological treatments, thereof 5 herbals. These were Psyllium, Peppermint oil and STW 5 (Iberogast) as well as Turmeric, Cannabis, Aloe vera and Ginger, with clinical studies in children mentioned only for Psyllium, STW 5 and Peppermint oil. For FD, Hippophae rhamnoides and STW 5 were identified, with clinical evidence on both. Only Iberogast was mentioned for both diseases. A closer look into the evidence for this preparation showed a number of studies supporting therapeutic usefulness in children of all ages, retrospectively as well as prospectively. These included 44.488 children, showing an excellent safety profile in this age group and a convincing rating of the therapeutic usefulness.

Conclusions: Functional GI diseases are an important indication especially in children, where herbal preparations provide effective treatment options with a low risk profile and therefore play a prominent role in their management. Grades of evidence are different and most convincing for Iberogast likewise in FD and IBS, while Psyllium and Peppermint oil as well as Hippophae rhamnoides show evidence only for IBS or FD, respectively.

References: [1] Malfertheiner, DigDis. 2017;35(Suppl 1):25-29.

[2] Shulman, ClinGastroenterolHepatol 2017;15:712-719.

[3] Charrois, PediatrRev 2006;27:49-51.

[4] Grigoleit, Phytomedicine 2005;12:601-6.

[5] Fifi, Nutrients 2018;10:E1715.

[6] Xiao, HelvNuclMed 2013;16:3843.

[7] Kelber, ZPhytother 2010;31:40-47.

[8] Gundermann, Päd 2004;10:408.

[9] Vinson, Gastroenterol. 2011;140:102.

[10] Nazarenko, Med.novosti 2008;10:79-83.

[11] Aryaev, ModPed. 2009;5:151-4

[12] Shadrin, ModPed. 2012;6:161-5.

[13] Bovbel, Med.novosti 2009;4:51-54.

[14] Ermakova, Med.novosti 2009;8:72-78.

172 | Fecal impaction in the colon may induce obstructive patterns in intestinal manometry

C. Malagelada; H. Monrroy; M. Mego; L. Alcalá; A. Accarino; J.-R. Malagelada; F. Azpiroz

Vall d'Hebron University Hospital, Barcelona, Spain

Objective: Intestinal manometry may detect phasic pressure patterns that suggest small bowel obstruction. The most common is the "clustered contractions pattern", characterized by repetitive short spouts of intestinal contractions in the postprandial period. When encountered in patients with chronic unexplained digestive symptoms, an exhaustive radiological evaluation of the gut should be performed to exclude partial mechanical obstruction. If no luminal compromise is identified by the imaging studies, an underlying neuropathic disorder of the bowel may be the probable diagnosis. The objective of this study was to determine the clinical significance of this pattern in patients evaluated for a possible intestinal motility disorder.

Methods: Between 2010 and 2018, 526 patients with chronic digestive symptoms were evaluated by intestinal manometry at our centre and 62 of them showed the postprandial clustered contractions pattern. In the present study we retrospectively analyzed the clinical diagnosis and outcome of these 62 patients.

Results: In 36 patients (58%) the postprandial clustered contractions pattern was diagnosed as secondary to either mechanical intestinal sub-occlusion ($n = 15$) or to a systemic disorder causing intestinal neuropathy ($n = 21$). In the remaining 26 patients, the cause of the clustered contractions manometric pattern was undetermined. Eight of these 26 patients had a history of severe constipation, and in 6 of them substantial fecal retention by abdominal x-ray or CT scan was detected on the day of the manometric procedure. In this subgroup, a second intestinal manometry was performed within a range of 39 ± 30 days, preceded by bowel preparation with a combination of oral laxatives and enemas. Proper elimination of fecal retention was confirmed by a subsequent abdominal x-ray. In all 6 patients, colonic cleansing completely normalized intestinal motility and resolved the obstructive pattern detected in the previous manometric evaluation.

Conclusions: Obstructive motility patterns of the small bowel may occur as a response to colonic fecal retention in patients with severe constipation. This observation is potentially relevant to the clinical diagnosis of intestinal neuropathy.

173 | Small intestinal bacterial overgrowth and glucose hydrogen breath test characteristics differ in patients taking versus not taking opioids

K. N. Harer; J. R. Baker; L. Watts; W. D. Chey; A. Lee; W. L. Hasler

University of Michigan, Ann Arbor, United States

Objective: Opiates delay gut transit, thus we postulated that opioid users exhibited increased prevalence of small intestinal

bacterial overgrowth (SIBO) vs non-users. We aimed to compare (i) SIBO prevalence measured by glucose breath tests (GBT) using accepted hydrogen (H_2) production criteria and temporal H_2 excretion profiles in patients with active opioid prescriptions vs those without active opioid prescriptions and (ii) symptom profiles of patients using vs not using opioids who had positive GBT suggestive of SIBO.

Methods: Retrospective analysis was conducted of adults undergoing GBT at a tertiary medical center from 1989-2018. GBT positivity was defined as $H_2 \geq 12$ ppm above basal within 120 minutes after 50 gm glucose (before June 2017) or ≥ 20 ppm above basal within 90 minutes after 75 gm glucose (after June 2017). Upper and lower GI symptoms were recorded in dichotomous fashion.

Results: Of 3602 patients with a positive GBT and complete data, 535 (14.9%) were opioid users and 3067 (85.1%) were opioid non-users. Opioid users were older (53.0 vs 50.4 years, $P < 0.001$) with higher BMI (29.4 vs 27.8 kg/m², $P < 0.001$) vs non-users. Opioid users (311/535, 58.1%) were more likely to have GBT positivity by H_2 criteria than non-users (1365/3067, 44.5%) (OR 1.723, $P < 0.001$). Breath H_2 levels were higher at baseline and each time point after glucose ingestion in opioid users vs non-users (all $P < 0.003$; Figure). Among patients with positive GBT, time to peak H_2 trended faster in opioid users vs non-users (67.2 vs 71.1 minutes, $P = 0.06$). Of those with positive GBT, heartburn, regurgitation, chest pain, nausea, vomiting, abdominal pain, and diarrhea were more often reported by opioid users vs non-users whereas bloating, gas, and constipation were not more prevalent.

Conclusions: Opioid users more often satisfied diagnostic criteria for SIBO compared to non-users based on hydrogen excretion parameters on glucose breath testing. Opioid users also exhibited temporal differences in hydrogen production vs non-users. The prevalence of many upper and lower GI symptoms was higher among opioid users vs non-users with SIBO. SIBO in opioid users may be a consequence of gut transit delays and should be a diagnostic consideration in patients taking this medication class presenting with unexplained GI symptoms.

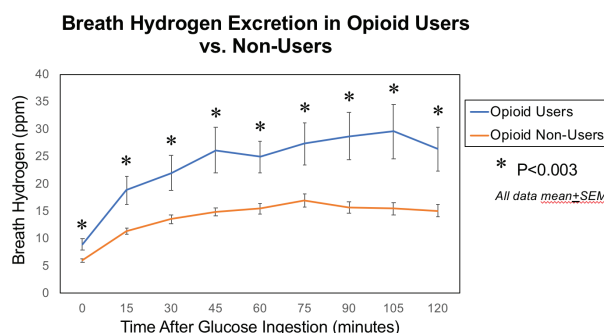


FIGURE. Breath hydrogen excretion in opioid users vs. non-users. Breath hydrogen levels were higher at baseline and each time point after glucose ingestion in opioid users vs. non-users (all $P < 0.003$).

174 | Functional gastrointestinal diseases: Epidemiological data from 1515 patients under an herbal therapy

J. Möller¹; E. Raskopf²; O. Greinert³; G. Zadoyan⁴; S. Schleicher³; K. Sha-Hosseini⁴; O. Kelber⁵; J. Singh⁴; R. Mösges⁶; K. Nieber⁷

¹Universitätsklinikum Köln, Darmstadt, Germany; ²ClinNovis GmbH, Cologne, Germany; ³Institut für Medizinische Statistik und Bioinformatik, Cologne, Germany; ⁴Universitätsklinikum Köln, Cologne, Germany; ⁵Institut für Medizinische Statistik und Bioinformatik, Darmstadt, Germany; ⁶Consulting HMP, Cologne, Germany; ⁷Kooperation Phytopharmaka GbR, Bonn, Germany

Objective: Data on patients with functional GI diseases from unselected patient cohorts can improve the understanding of patients' needs in daily practice. Therefore data on patients treated with a herbal medicinal product for this indication, STW 5, were selected from the PhytoVIS study, a non-interventional study in 20 870 patients who had used a herbal product within the last 8 weeks before the survey [1].

The aim was to describe the epidemiology, medical needs, and the perceived usefulness of the therapy in this patient group.

Methods: The database contained 24 056 patient questionnaires, documented in physicians' practices and pharmacies by trained students of human medicine or pharmacy who acted as interviewers, in compliance to the ENCePP Code of Conduct [2]. Questionnaires related to STW 5 were evaluated regarding epidemiological data as well as on the use of the medicine and its perception.

Results: Of all datasets, 1515 could be retrieved containing STW 5, with the main patient group being females aged 18 to 31. Of all patients 94% reported the therapeutic effect to be moderate or better, 63% stated it to be very good. Only 2% felt the condition to be unchanged or worsened. The tolerability of STW 5 was convincing, 95% of patients had no adverse events at all, only 0.6% felt an impairment after taking the product. These findings are in accordance with the published data from more than 50 000 patients treated with this herbal medicine [3].

Conclusions: PhytoVIS turned out to be a suitable tool to study the epidemiology of patients with functional GI diseases treated with the herbal medicinal product STW 5. STW 5 proved to be a fast-acting and effective therapeutic option not only in a vast variety of gastrointestinal complaints, but also regardless of factors like the age of the patients, thus making it an interesting option for vulnerable patient groups like children and the elderly and for patients suffering from often multi-causal gastrointestinal diseases with different symptoms.

Acknowledgment: The study is supported by Kooperation Phytopharmaka GbR, Bonn, Germany.

References: [1] Raskopf, ZPhytother2017;38(Suppl 1):44.

[2] ENCePP2018, EMA/929209/2011.

[3] Storr, Pharmacon 2016;4:356-364.

178 | Combination of neural crest derived stem cells (NCSCs) and adipose tissue-derived microvascular fragments (Ad-MVF): Are Prevascularized Neurospheres A Better Approach For The Treatment Of hirschsprung's disease?

M. Weyland¹; T. Später²; M. Martin¹; M. W. Laschke²; K.-H. Schäfer¹

¹University of Applied Sciences Kaiserslautern, Working Group Enteric Nervous System, Zweibrücken, Germany; ²Saarland University, Institute for Clinical & Experimental Surgery, Homburg, Germany

Objective: Transplantation of neural crest derived stem cells (NCSCs) from the enteric nervous system (ENS) as a cell therapy of dysganglionosis is one of the major goals for the treatment of Hirschsprung's disease patients. Transplantation of spheroids brings the advantage of having a kind of long-term delivery of cells within the tissue. Adding endothelial cells to these spheres might lead to a kind of stem cell niche situation within the neurosphere that could be of advantage for the transplantation.

Methods: In this study we combined adipose tissue derived-microvascular fragments (ad-MVFs) and isolated cells of the ENS to form prevascularized neurospheres. The formation of these spheres *in vitro* was characterized by immunohistochemistry and immunofluorescence.

Results: We could demonstrate that the inclusion of ad-MVFs into the neurospheres does not influence cell growth, proliferation (Ki67) or cell death (cleaved caspase-3), but establishes a well-defined endothelial network within the sphere.

Furthermore, we were able to show that the distribution of neurons and glial cells after differentiation is similar with and without ad-MVFs. To assess the function of the preformed microvascular network we transplanted the spheres into a dorsal skinfold chamber to verify the formation of blood vessels and the interconnection between those and existing blood vessels of the host tissue.

Conclusions: A better blood supply of transplanted neurospheres into a diseased gut would support the chances of survival and differentiating into functional ganglion-like structures.

179 | Changes of the enteric nervous system in a Parkinson's disease mouse model before clinical onset

M. Gries¹; A. Braun¹; S. Schulte¹; M. Weyland¹; M. Laschke²; M. Baller¹; Y. Liu³; M. Schroda⁴

¹University of Applied Sciences Kaiserslautern, Zweibrücken, Germany;

²Saarland University, Institute for Clinical & Experimental Surgery, Homburg,

Germany; ³Saarland University, Department of Neurology, Homburg, Germany;

⁴University of Kaiserslautern, Kaiserslautern, Germany

Objective: Parkinson's disease (PD) is the most common neurodegenerative disorder with motor and non-motor symptoms, including gastrointestinal dysfunction. Many studies have considered the

enteric nervous system (ENS) as part or even starting point of the disease, so that it could be used as a reliable source for biomarkers in PD. To understand and study the pathogenesis of PD, mouse models have been developed, such as the murine A30P model. Like PD, this mouse model shows the characteristic α -synucleinopathy resulting in a loss of dopaminergic neurons, accumulation of intraneuronal inclusions with misfolded α -synuclein peptides, the so-called Lewy bodies and neurites, and finally, motor and coordination impairments from the age of 8-10 months onwards. Here we aim to identify ENS changes in an early stage of a Parkinson's disease model.

Methods: In this study we evaluated clinical parameters of different aged A30P mice by gait analysis using the CatWalk method. Pre-clinical mice were further analyzed using mass spectroscopy and whole-mount immunofluorescence to estimate protein expression profile in myenteric plexus. Moreover, gastrointestinal motility was measured before clinical manifestation by *ex vivo* perfusion experiments.

Results: Gait parameters collected by CatWalk System showed no motor deficits for 8-12-week-old A30P mice, while 12- to 13-month-old PD mice were clinically impaired. Proteomic data revealed a significant altered expression profile in A30P mice before clinical onset of disease compared to corresponding wild-type mice, which could also be confirmed by whole-mount immunostainings, e.g. calretinin, neurofilament-L and synaptobrevin-2. Assessment of colonic gastrointestinal motility exhibited significant prolonged motility intervals and a significant decrease of contraction numbers in Parkinson mice at this early stage.

Conclusions: Thus, our results indicate that the ENS may serve as a pre-diagnostic marker for PD.

180 | TRPM8 and TRPA1 mRNA expression in colonic biopsies of patients with irritable bowel syndrome and healthy controls

Z. Z. Weerts¹; M. Peiris²; P. Xu¹; L. Vork¹; E. Wilms¹; M. Elizalde¹; D. Jonkers¹; A. Blackshaw²; A. Masclee¹; D. Keszthelyi¹

¹Division of Gastroenterology and Hepatology, Department of Internal Medicine, Maastricht University Medical Center, Maastricht, The Netherlands; ²Wingate Institute of Neurogastroenterology, Blizard Institute, Barts and The London School of Medicine and Dentistry, Queen Mary, University of London, London, United Kingdom

Objective: Transient Receptor Potential (TRP) channels are involved in peripheral nociceptive mechanisms and neuroimmune interactions contributing to visceral hypersensitivity – a hallmark of irritable bowel syndrome (IBS). TRP Ankyrin 1 (TRPA1) has pronociceptive properties and is sensitized by inflammatory mediators. TRP Melastatin 8 (TRPM8) activation, is likely protective against nociception and inflammation. In a cohort of IBS patients and controls, our aims were to: 1) measure TRPM8 and TRPA1 mRNA transcript expression, 2) correlate expression levels with GI symptoms, and 3) explore regional differences in colonic expression.

Methods: Sigmoid biopsies were collected from 30 IBS patients (Rome III) and 23 healthy controls. Additional proximal colon biopsies were obtained in 24 of the 30 patients. TRPM8 and TRPA1 mRNA levels were analyzed in duplicate by quantitative reverse-transcriptase-polymerase-chain-reaction (Bio-Rad), using primers from Biolegio and normalized to GAPDH. Symptoms were assessed using the gastrointestinal-symptom-rating-scale and a 14-day diary. Data were analyzed by linear regression and Wilcoxon signed-rank tests. mRNA results are expressed as relative mRNA values using the $-2^{\Delta Ct}$ method.

Results: Sigmoid expressions of both TRPM8 and TRPA1 were significantly upregulated in IBS patients vs controls (Figure 1), $P < 0.0005$ and $P < 0.0001$, respectively, corrected for age and gender. Interestingly, TRPM8 expression in the proximal IBS colon was significantly higher compared to the sigmoid, whereas TRPA1 expression in the IBS sigmoid was significantly higher than in the proximal colon, both $P < 0.0001$. In IBS patients, expression did not correlate with symptom severity.

Conclusions: These results demonstrate for the first time that sigmoid TRPM8 and TRPA1 mRNA levels are significantly higher in IBS patients compared to healthy subjects. These findings are important because TRPM8 up-regulation can play a role in anti-inflammatory mechanisms and TRPA1 is implicated in preclinical models of visceral pain. Further investigation is warranted to ascertain the functional relevance of these findings. *Trial registration:* NCT00775060.

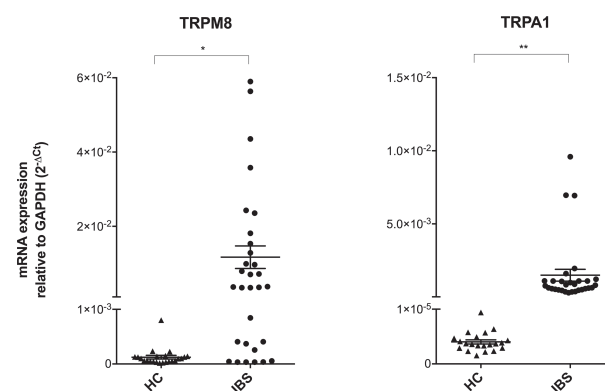


FIGURE 1. Relative mRNA expression of TRPM8 and TRPA1 in sigmoid biopsies in healthy controls (HC) and IBS patients. Triangles and dots represent relative mRNA values ($-2^{\Delta Ct}$), lines represent means and standard errors. TRPM8 and TRPA1 were significantly upregulated in IBS vs. HC, * $p < 0.0005$ and ** $p < 0.0001$, respectively, obtained by linear regression with correction for age and gender.

182 | STW 5 in patients with irritable bowel syndrome and other functional gastrointestinal diseases: Results of a surveillance study

B. Vinson¹; S. Skeib¹; O. Kelber²; E. Raskopf³; K. Nieber⁴

¹Bayer Consumer Health, Medical and Clinical Affairs Phytomedicines, Phytomedicines Supply and Development Center, Steigerwald Arzneimittelwerk GmbH, Darmstadt, Germany; ²Bayer Consumer Health, Innovation and Development, Phytomedicines Supply and Development Center, Steigerwald Arzneimittelwerk GmbH, Darmstadt, Germany; ³ClinNovis GmbH, Cologne, Germany; ⁴Institute of Pharmacy, University of Leipzig, Leipzig, Germany

Objective: Pharmacy-based surveys on everyday life therapeutic use and patient satisfaction are tools to gain real life evidence on patient needs for over-the-counter medicinal products [1].

The herbal preparation STW 5 has been available in the German market for more than 58 years [2]. Its scientific evidence for treatment of functional gastrointestinal diseases like irritable bowel syndrome and functional dyspepsia includes a multitude of clinical, pharmacological and toxicological studies [3]. Up to now, few data on self-assessed usage behavior, perception of effectiveness and tolerability for STW 5 are available.

Methods: Therefore, pharmacy customers with product desire or recommendation for STW 5 were asked to participate in a survey on the product. Patients received a questionnaire regarding demographic data, gastrointestinal complaints, effectiveness, tolerability and satisfaction with the product. They were asked to answer it during the next few days and send it back to a contract research institute within a week.

Results: Data from 843 patients were evaluated. 29.4% were male, 70.6% female. The majority was 30-49 years old. In 384 patients, complaints were related to the upper, in 139 to the lower abdomen, in 311 patients to both regions. In 7.3% of the 384 patients a functional dyspepsia had been diagnosed, in 16.9% of the 139 patients an irritable bowel syndrome. Up to 64% of the patients specified a good or very good improvement of the respectively predominant symptom with treatment of STW 5. Symptom relief was perceived as fast and covered the comprehensive spectrum of complaints. Tolerability was rated good to very good in 97.4% of all patients and did not differ between patient groups. Correspondingly 93.2% of the users were „very satisfied” or „satisfied”. 91% of the customers would recommend STW 5 to others for treating their complaints.

Conclusions: Overall, it can be concluded that this pharmacy based survey gives a reliable picture of the behavior of users of STW 5, with high satisfaction values in irritable stomach, irritable bowel syndrome and single symptoms. The favorable tolerability ratings confirm the ratings from the clinical studies on the product.

References: [1] Nieber, Med.Wochenschr.f.Pharmazeuten2009 (8):301-6.

[2] Storr, Pharmakon. 2016;4:356-364

[3] Abdel-Aziz, Planta Med. 2017;83:1130-1140

183 | A single gut microbe bacteroides thetaiotaomicron alters epithelial expression of claudin-3 and TLR-2

R. Aktar¹; R. Stentz²; A. Parkar²; A. Brion²; A. Goldson²; S. Carding²; A. Blackshaw¹; M. Peiris¹

¹Wingate Institute of Neurogastroenterology, Queen Mary, London, United Kingdom; ²Quadram Institute of Bioscience, Norwich, United Kingdom

Objective: We have demonstrated that epithelial cells such as enteroendocrine cells (EECs) dynamically respond to the microbial environment [1]. The aim of this study was to understand how microbes

interact with the epithelium and influence cellular phenotypes. *Bacteroides Thetaiotaomicron* (Bt) - a stable human gut resident [2] was used to recolonise germ-free mice to establish if this microbe alters tight junction proteins, Toll-like receptors (TLRs) and epithelial proliferation.

Methods: Proximal colonic tissue from germ-free (GF), conventional (CONV) and germ-free mice conventionalized (3-days) with Bt (Bt-RECOL) was used to assess relative expression of tight junction proteins, intestinal stem cell markers and TLRs using qPCR with Quantitect PCR Primer Assays. All graphs show individual values $\pm$ SEM and t-test were performed ($P < 0.05$).

Results: RNA expression of claudin-7, occludin-1, junctional adhesion molecule (F11R) and tight junction protein (TJP) were unchanged across all three groups. However, Bt-RECOL mice had significantly lower claudin-3 expression compared to CONV ($P = 0.0285$). Expression of intestinal transcription factor (ATOH-1), a regulator of intestinal secretory cell differentiation [3], was significantly reduced in GF ($P = 0.0097$) and Bt-RECOL ($P = 0.0073$) compared to CONV. Expression of intestinal stem cell marker, LGR5 [4] significantly decreased in GF ($P = <0.0001$) and Bt-RECOL ($P < 0.0001$) compared to CONV. RNA expression of TLR-1, -4, -5 and -9 were unchanged across all groups. TLR-2 expression significantly reduced in GF mice ($P < 0.0001$), however, Bt-RECOL returned expression ($P < 0.0001$) to CONV (Figure 1).

Conclusions: Our data suggest Bt does not have direct effects on epithelial cell proliferation, however, it can specifically alter expression of claudin-3 and TLR-2 in the gut epithelium. This is likely to be an effect specific to gram negative bacteria like Bt as supernatants from this family of bacteria activate TLR-2 [5] and increase secretion by altering claudin-3 expression [5]. This suggests gram negative microbes such as Bt preferentially interact with TLR-2 and claudin-3 to influence epithelial activity.

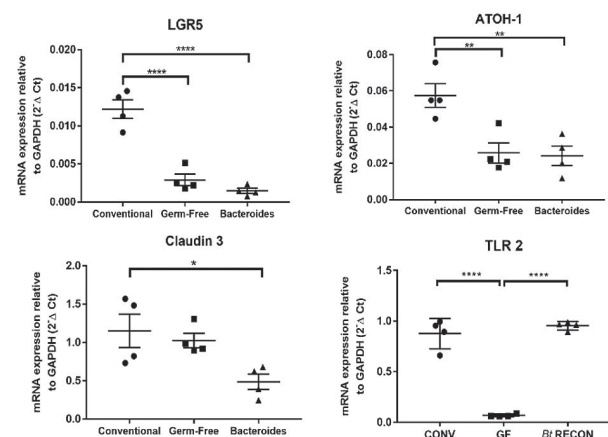


FIGURE 1. *Bacteroides thetaiotaomicron* (Bt) specifically increases TLR-2 and decreases claudin 3 expression but does not influence cell proliferation/differentiation mechanisms.

187 | Conventionalisation of germ free mice with bacteriodes thetaiotaomicron induces proliferation of inhibitory motor neurones and specifically alters proximal colonic motility

R. Aktar¹; N. Parker¹; R. Stentz²; A. Parker²; A. Brion²; A. Goldson²; S. Carding²; A. Blackshaw¹; M. Peiris¹

¹Wingate Institute of Neurogastroenterology, London, United Kingdom;

²Quadram Institute of Bioscience, Norwich, United Kingdom

Objective: Vagal-afferent endings are attuned to the microbial environment as evidenced by decreased neuronal innervation in germ-free (GF) conditions, a deficit restored by *Bacteriodes thetaiotaomicron* (Bt) [1]. To delineate the influence Bt exerts on neuronal populations, expression of motor neurons (nitric oxide synthase (NOS) and Substance P (SP), neuronal proliferation (S100 β via NGF release) [2] and neuronal budding (GAP43) markers were assessed. Colonic motility function was measured using manometry.

Methods: Proximal colonic tissue from GF, conventional (CONV) and germ-free mice conventionalised (3-days) with Bt (Bt-RECOL) was used to perform immunohistochemistry. Immunoreactive pixels were quantified using ImageJ. Colonic manometry was performed using a water-perfused multi-lumen catheter [3]. All values are $\pm$ SEM, *t*-test was used to assess significance ($P < 0.05$).

Results: GF conditions significantly decreased NOS expression in myenteric plexus (MYP) compared to CONV ($P = 0.0056$) but was restored in Bt-RECOL (Bt-RECOL vs GF, $P = 0.0387$). Bt-RECOL increased SP expression in MYP ($P = 0.0287$) and mucosa ($P < 0.0001$) compared to CONV and GF mice. MYP expression of S100 β and GAP43 was unaltered in GF conditions but mucosal S100 β was reduced ($P = 0.0004$). Bt-RECOL increased mucosal ($P < 0.0001$) and MYP ($P = 0.0002$) S100 β compared to CONV. Similarly, mucosal ($P = 0.0349$) and MYP GAP43 ($P = 0.0075$) expression increased compared to GF and CONV, respectively (Figure 1). In functional experiments, colonic migrating motor complexes (CMMCs) increased in GF, and was not normalised by Bt-RECOL (Figure 1). Bt-RECOL mice had increased proximal colonic contractions compared to CONV and GF, while, amplitude was unaltered.

Conclusions: The proliferative effect of Bt on inhibitory motor neurons (NOS and SP) as evidenced by increased neuropeptide staining and GAP43 expression, is likely to be driven by glial cells-known to be upregulated by the presence of gut microbiota [5]. Functionally, Bt enhances region specific contractions, thus this specific microbe may preferentially influence proximal colonic neurons which have complex neuronal wiring and variable neuronal innervation compared to other regions [6]. Bt-RECOL does not normalise CMMC pattern suggesting complex motor functions require a bacterial quorum to be present [7].

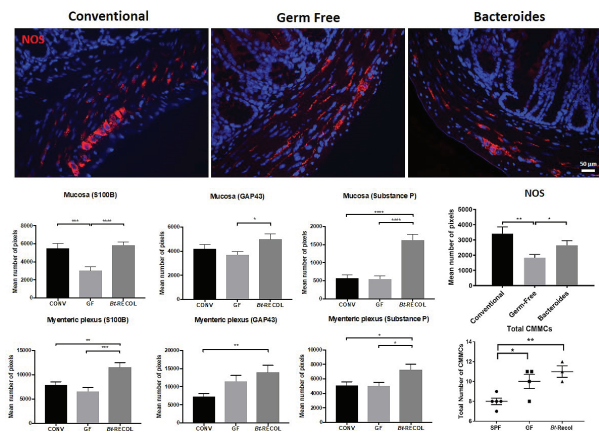


FIGURE 1. Bt has a proliferative effect on inhibitory motor neurones and neuronal growth. Colonic migrating motor complex (CMMC) is increased in Bt.

191 | Isolation and culture of primary myenteric neurons and glial cells from human colon: The effects of different concentrations of nerve growth factor

A. Palmer¹; M. Straface¹; J. Chin-Aleong²; C. Knowles²; G. J. Sanger¹

¹QMUL Blizard Institute, London, United Kingdom; ²Royal London Hospital, London, United Kingdom

Objective: Physiological functions of the human myenteric plexus can be studied using intact tissues. To study cellular functions of live human myenteric cells we aim to develop a simple, reproducible method of primary human neuronal and glial cell co-culture and demonstrate its use experimentally.

Methods: Human non-inflamed GI tissue was obtained from surgical resections, with informed consent. For patients with bowel cancer, macroscopically-normal tissue was used at least 5-10 cm from the tumour.

After removing the mucosa, the tissue was cleaned, finely minced and digested in collagenase and trypsin. The digestate was filtered, and cells plated on laminin and poly-d-lysine in selective media. The media had a base of Neurobasal-A, and contained nerve growth factor (NGF), glial-derived neurotrophic factor, Supplement B-27, L-glutamine and antibiotic-antimycotic. The media encouraged adherence and development of enteric and glial cells, discouraging survival of other cell types in the digestate¹.

¹Smith et al. J Vis Exp 2013;78:50688

Results: To optimise for use with human tissue the submucosa was removed, and washes in dithiothreitol and 70% ethanol removed contaminants (a problem for surgical specimens). Digestion duration was optimised to 4 hours for maximum live cell yield; 1.7 g human stomach tissue yielded 14 million live cells with 82% viability (determined using Trypan blue) with 4 hours collagenase digestion at 37°C.

Cells were routinely cultured for 14 days. Immunostaining against S100 and β III-tubulin showed the presence of neurons and glial cells in culture, both developing numerous extensions.

Cells from different colon samples were each cultured in NGF 0, 10, 50 and 200 ng/ml. The cells showed increased neurite growth patterns in an approximately concentration-dependent manner, demonstrating effective experimental use.

Conclusions: This technique provides a routine method of myenteric neuronal and glial cell co-culture from human surgical resections for real-time study of cellular mechanisms. Culture with different concentrations of NGF altered neurite extension, demonstrating utility of the method.

193 | TAK-954 (TD-8954) has anti-inflammatory properties and improves postoperative ileus in mice

N. Stakenborg¹; I. Appeltans¹; N. Fabre¹; P. R. Wade²; G. E. Boeckxstaens¹

¹Translational Research Center for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium; ²Gastrointestinal Drug Discovery Unit, Takeda Pharmaceuticals, Cambridge, United States

Objective: We previously showed in a model of postoperative ileus (POI) that activation of the anti-inflammatory pathway by vagus nerve stimulation or administration of the 5-HT₄ receptor agonist prucalopride before surgery inhibits surgery-induced intestinal inflammation and improves gastrointestinal transit, an effect mediated by inhibition of resident *muscularis* macrophages. TAK-954 is a novel, highly selective 5-HT₄ receptor agonist in early clinical development for the prophylaxis and treatment of POI. In this study, we evaluated the actions of TAK-954 to determine whether parenteral administration prior to surgery has anti-inflammatory properties and improves POI.

Methods: The effect of a single pre-operative administration of TAK-954 (0.003, 0.01, 0.03, 0.1 or 1 mg/kg s.c.) or vehicle (VEH) was studied in a model of intestinal manipulation-induced POI (n = 8-24 wild-type mice/group). The degree of POI was quantified 24 hours postoperatively by assessment of fluorescently labeled dextran distribution in the gastrointestinal tract expressed as the geometric center (GC). The anti-inflammatory effect was measured by the influx of myeloperoxidase (MPO) positive cells and pro-inflammatory cytokine expression (i.e. *Il1 α* , *Il1 β* , *Il6*, *Tnf- α* , *Ccl2* and *Cxcl2*) in *muscularis externa* tissue. For these experiments, a single pre-operative dose of 5 mg/kg prucalopride was given to a separate set of mice as a selective 5-HT₄ agonist positive control.

Results: Intestinal manipulation resulted in an impairment of intestinal transit (i.e. POI) as shown by a reduction in the geometrical center (GC) in the vehicle-treated mice (VEH: GC = 4.7 ± 0.3). Pre-operative treatment with TAK-954 potently improved small intestinal transit 24 hours after surgery (Figure 1) with a maximal effect of 0.01 mg/kg, comparable to prucalopride. In line, 0.01 mg/kg TAK-954 significantly reduced the influx of MPO-positive cells (VEH:

143 ± 13 vs TAK-954: 92 ± 19 MPO-positive cells/field; $P < 0.05$) and the expression of the pro-inflammatory cytokines *Il1 β* (VEH: 0.0016 ± 0.0002 vs TAK-954: 0.0007 ± 0.0001 ; $P < 0.05$) and *Cxcl2* (VEH: 0.014 ± 0.002 vs TAK-954: 0.0076 ± 0.0014 ; $P < 0.01$) in the *muscularis externa* compared to vehicle-treated animals.

Conclusions: Similar to prucalopride, pre-operative administration of TAK-954 prevents manipulation-induced inflammation and thus improves intestinal transit in a murine model of POI. These data indicate that pre-operative administration of TAK-954 should be further investigated as a possible prophylaxis and therapeutic treatment for POI in humans.

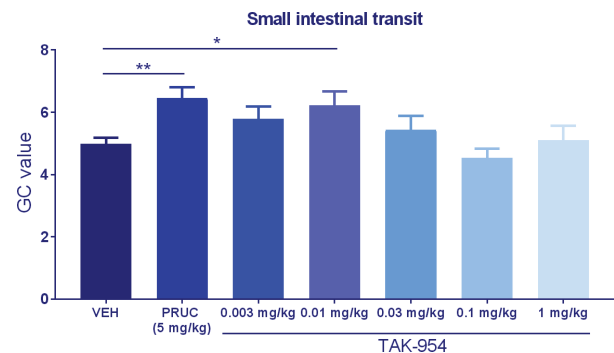


FIGURE 1. Recovery of intestinal transit after single subcutaneous administration of TAK-954 in murine model of postoperative ileus. Data are shown as geometrical center (GC) of dextran distribution through the gastrointestinal tract and are expressed as mean $\pm$ SEM from n=8-24 mice/group. * $p < 0.05$, ** $p < 0.01$, One-way ANOVA with Bonferroni post-hoc test. VEH=vehicle, PRUC= prucalopride.

194 | Gastrointestinal dysfunction in autism: Altered motility and achalasia in *Foxp1*^{+/-} mice

H. Fröhlich¹; M. L. Kollmeyer¹; V. C. Linz¹; M. Stuhlinger¹; D. Groneberg²; A. Reigl²; E. Zizer³; A. Friebe²; B. Niesler¹; G. Rappold¹

¹Department of Human Molecular Genetics, Heidelberg, Germany; ²Institute of Physiology, Würzburg, Germany; ³Department of Internal Medicine I, University of Ulm, Ulm, Germany

Objective: Dysfunction of motor, social, sensory, and cognitive aspects play a major role in autism spectrum disorder (ASD). Frequently, the associated gastrointestinal dysfunction is overlooked, and it is not clear how it relates to the core features of ASD. FOXP1 syndrome is characterized by autistic traits, social deficits, and intellectual disability and has already been studied in some detail. Feeding difficulties and constipation, together with other gastrointestinal problems were also reported in these patients. Whether these symptoms are due to primary gastrointestinal impairment or an epiphenomenon caused by altered behaviour or side effects of psychotropic medication has remained unclear until now. To address this, we investigated the gastrointestinal tract of *Foxp1*^{+/-} mice, which reflect FOXP1 haploinsufficiency in patients.

Methods: Our approach involves a histological examination of the gastrointestinal tract, organ bath experiments, oesophageal manometry and behavioural testing.

Results: Expression of *Foxp1* was detected in all segments of the gastrointestinal tract, and was reduced in *Foxp1*^{+/-} mice. *Foxp1*^{+/-} tissue showed a marked atrophy of the tunica muscularis in the oesophagus and colon. Moreover *Foxp1*^{+/-} animals have a lower body weight than wild type mice and display altered feeding behaviour with decreased food and water intake. We detected a pronounced defect in nitric oxide-induced relaxation of the lower oesophagus sphincter which was subsequently confirmed by manometry. In addition to achalasia, total gut transit was significantly prolonged most likely due to impaired colonic contractility and peristalsis.

Conclusions: Overall, our findings indicate for the first time that the observed gastrointestinal disturbances in patients with FOXP1 syndrome may be caused by impaired motility, specifically in the oesophagus and colon. Furthermore, this is the first report of achalasia attributed to a heterozygous gene deletion.

196 | Impact of high-fat diet and toll-like receptor 4 signaling on the integrity of mouse enteric and central nervous systems

I. Marsilio¹; V. Caputi¹; S. Cerantola¹; M. Bistoletti²; C. Giaroni²; M. Zusso¹; M. C. Giron¹

¹University of Padova, Padova, Italy; ²University of Insubria, Varese, Italy

Objective: Toll-like receptor 4 (TLR4) is involved in controlling neuroplasticity of both enteric and central nervous systems (ENS and CNS). Our aim was to investigate the role of TLR4 in the neuroglial rearrangements of ENS and CNS in a mouse model of high-fat diet-induced obesity.

Methods: TLR4^{-/-} (N = 16) and wild-type (WT; N = 16) C57BL/6J male mice (age = 6 ± 2 weeks) were fed with standard-diet (SD; fat: 18% kcal) or high-fat diet (HFD, fat: 60% kcal) for 8 weeks. Ileal longitudinal muscle-myenteric plexus whole-mounts and hippocampus frozen-sections were analyzed to evaluate the distribution of neuronal marker HuC/D, astroglial markers S100β and GFAP, and macrophage/microglia marker Iba1.

Results: In the ENS of TLR4^{-/-} mice, SD determined a reduction of the total number of HuC/D⁺ neurons (-11%, N = 4, P < 0.05) together with increased S100β immunoreactivity (+80%, N = 4, P < 0.01) and higher number of Iba1⁺ muscularis macrophages (+33%, N = 4, P < 0.05), with no changes in GFAP⁺ gliofilament length. In both genotypes, HFD determined a significant increase in the total number of myenteric HuC/D⁺ neurons (+13% in WT mice and +27% in TLR4^{-/-} mice, N = 4, P < 0.05) and enteric gliosis together with a marked reduction of Iba1 immunofluorescence (-50% in WT mice, -68% in TLR4^{-/-} mice, N = 4, P < 0.05).

In the hippocampus of TLR4^{-/-} mice fed with SD, a marked loss of HuC/D⁺ neurons (-30%, N = 4, P < 0.01) was accompanied with a

significant GFAP⁺ density index enhancement (+27%, N = 4, P < 0.05) and GFAP⁺ gliofilament length (+70%, N = 4, P < 0.05) with no difference in S100β density index. In WT hippocampus, HFD caused a marked reduction in the total number of HuC/D⁺ neurons (-34%, N = 4, P < 0.05) and microglia activation, evidenced by increased Iba1 immunofluorescence (+33%, N = 4, P < 0.05).

Conclusions: These findings highlight that TLR4 is involved in high-fat diet neuro-glial plasticity in both ENS and CNS.

197 | Comparison of MRI assessed small bowel dysmotility in irritable bowel syndrome (IBS) and healthy controls

R. Gollifer¹; A. Menys¹; S. Månsson²; P. Leander²; O. Ekberg²; S. A. Taylor¹; D. Atkinson¹; B. Ohlsson²

¹UCL, London, United Kingdom; ²Lund University, Malmö, Sweden

Objective: Irritable bowel syndrome (IBS) is characterised by gastrointestinal symptoms, subclassified into constipation-predominant IBS (IBS-C), diarrhoea-predominant IBS (IBS-D) and mixed IBS (IBS-M) [Drossman, D. A., 2016]. Abnormal motility patterns have been hypothesised as a key cause of symptoms. Quantitative measures of motility can be derived from routine clinical small bowel Magnetic Resonance Enterography (MRE) using advances in medical imaging post-processing [Odille, F. et al., 2012]. In this study, we investigate whether there are differences in motility patterns between IBS subgroups and healthy controls.

Methods: 34 IBS patients and 20 healthy controls (HCs) underwent MRE at SUS, Sweden, after ingesting 1 L of macrogol 3350 solution 45 minutes prior the scan. The MRE protocol included a free breathing (minimum 50 seconds) cine motility sequence, repeated to encompass the whole small bowel volume. Visual Analogue Scale for IBS (VAS-IBS) to assess current abdominal symptoms was available [Bengtsson M, Hammar O, Mandl T, Ohlsson B., 2011]. A total of 5 motility analysis metrics were developed to assess 1) mean motility, 2) spatial motility variability, 3) temporal motility variability, 4) area of active bowel and 5) distension (figure 1A). For each metric, Kruskal-Wallis was performed to see if there were differences between IBS subgroups (IBS-M, IBS-C, IBS-D) and HCs, followed by Mann-Whitney U to determine which 2 groups showed differences.

Results: Differences were found between IBS-M and IBS-C for mean motility, temporal variation and area of active bowel (all P < 0.005) (figure 1B). Specifically, values were significantly lower in IBS-C. No significant differences were found between IBS overall or IBS subgroups and HCs (figure 1B).

Conclusions: This preliminary study suggests that there are potential small bowel motility differences between IBS-C patients, and other subtypes, notably IBS-M. Motility metrics are highly variable in health and not significantly different to IBS patients overall. However this normal variability appears to be reduced in IBS-M and IBS-C subtypes.

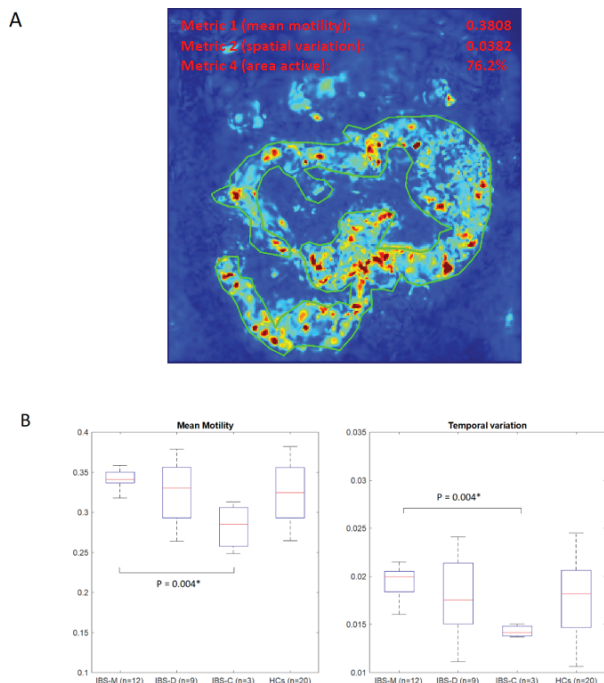


FIGURE 1. Motility map with associated algorithm derived metrics for mean motility (metric 1), spatial motility variability (metric 2) and area of activity (metric 4) displayed (A). Boxplots comparing the subgroups of IBS vs Healthy Controls for mean motility and temporal variation of motility (B).

198 | Evaluating the correlation between cancer progression and mast-cell mediated distress in pancreatic cancer: The PancStress study

P. L. Pfitzinger¹; E. Salvo-Romero²; H. Friess¹; I. E. Demir¹

¹Department of Surgery, Klinikum rechts der Isar, Technical University of Munich, School of Medicine, Munich, Germany; ²Universitat Autònoma de Barcelona, Barcelona, Spain

Objective: Pancreatic cancer (PCa) is one of the deadliest malignancies worldwide. Besides pain, factors such as impairment of self-determination and -containment and psychological distress count as important comorbidities of PCa. Over 50% of PCa patients show depression-like distress symptoms, which, when quantified, showed the highest scores compared to other human malignancies. Also, inflammatory processes in PCa play an important role in tumor initiation, progression and invasion. Recent studies showed that mast cell (MC) activity directly correlates with pain intensity in patients suffering from neuropathic pain in PCa.

Methods: With this study we would like to evaluate for the first time the correlation between MC activity in PCa patients and their distress-levels. The suggested study protocol will be presented for discussion.

Results: The PancStress study is a multicentric prospective study (Department of Surgery, Klinikum rechts der Isar, Technical University of Munich, Germany, and Universitat Autònoma de Barcelona, Spain) including PCa patients who will undergo primary surgical resection for suspected PCa. Pain will be evaluated by the means of

a standardized questionnaire, and preoperative distress-level will be assessed by 4 different questionnaires: Distress Thermometer, Hospital Anxiety and depression scale – Depression (HADS-D), Perceived Stress Questionnaire 20 (PSQ-20) and Short Form 36 (SF-36). During the surgical resection of the tumor, the PCa specimens are collected for further histopathological analysis focusing on MC activation. Another part of the PCa specimen will be kept in a buffer solution for Transmission Electron Microscopy analysis. Here, piecemeal degranulation (loss of intragranular electro-density without signs of intergranular or granule-to-cell membrane fusion) will be analyzed in MC as a marker for their activated state. Simultaneously in vitro essays for PCa cell growth with supernatants from activated MC will determine the direct effect MC have on PCa growth.

Conclusions: The prospective PancStress study will further elucidate the interactions of psychological distress and its immunological response in the human PCa, giving us a deeper insight into new potential methods for controlling cancer progression, pain and depression in PCa. The study has been selected the winner of the NeuroGASTRO TANDEM Young Investigator Meeting 2017 (Cork, Ireland).

202 | Assessment of small bowel motility in chronic intestinal pseudo-obstruction using caloric stimulation and dynamic MRI

K. L. Van Rijn¹; C. S. De Jonge¹; G. Bouma²; K. Horsthuis³; A. J. P. M. Smout⁴; A. J. Bredenoord⁴; J. Stoker¹

¹Amsterdam UMC, location AMC, dept. of Radiology and Nuclear Medicine, Amsterdam, The Netherlands; ²Amsterdam UMC, location VUMC, dept. of Gastroenterology and Hepatology, Amsterdam, The Netherlands; ³Amsterdam UMC, location VUMC, dept. of Radiology, Amsterdam, The Netherlands; ⁴Amsterdam UMC, location AMC, dept. of Gastroenterology and Hepatology, Amsterdam, The Netherlands

Objective: Chronic intestinal pseudo-obstruction (CIPO) is a rare disorder, characterized by failure of intestinal motility. Magnetic Resonance Imaging (MRI) has emerged as a non-invasive method for evaluating bowel motility. This study aimed to gain insight in small bowel motility in CIPO patients, by measuring in the fasted and fed state using an MRI protocol with caloric stimulation.

Methods: Seven CIPO patients were included, diagnosed based on symptoms of intestinal obstruction and abnormal findings at antroduodenal manometry. All subjects underwent a dynamic MRI protocol comprising of two fasting state scans and subsequently three postprandial scans after orally taking in a small-volume, high-caloric-density, test meal (Nutridrink, 300 kcal). At every time-point, three slices at different locations in the abdomen were scanned. Global disturbances in intestinal motility were assessed visually by an experienced abdominal radiologist. Small bowel motility was quantified using a validated post-processing technique (GIQuant, Motilent, London UK) with the use of a new edge detection technique to account for dilated bowel. Analysis resulted in an intestinal wall-specific motility score in arbitrary units (AU).

Results: In four out of seven CIPO patients, visual MRI assessment showed air-distended intestinal loops and hyperactive intestinal motility in both the fasted and postprandial state. The remaining three patients, of whom two with scleroderma, showed no obvious visual alterations. Motility quantitation demonstrated varying intestinal motility between and within subjects, the latter mainly dependent of slice location. Averaged intestinal motility ranged from 0.11 to 0.27 AU in the fasted state (medians 0.15 and 0.16 AU) and from 0.11 to 0.31 AU in the postprandial state (medians 0.16, 0.16 and 0.16) (figure 1).

Conclusions: Surprisingly, we found hyperactive small bowel motility in four out of seven CIPO patients, which could be a sign of uncoordinated intestinal motility. Median quantitated motility was comparable in the fasted and fed state. Going forward, quantitated data, extensive visual assessment and advanced imaging analysis tools will be further explored to gain insight in the pathophysiology of CIPO.

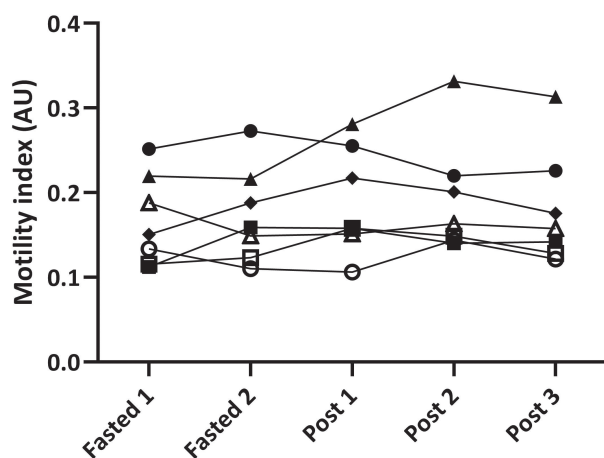


FIGURE 1. Small bowel motility scores in individual subjects over time. Fasted 1 and 2 were scanned in the fasted state with 10 minutes in between. Post 1, 2 and 3 were scanned within a time-frame of 30 minutes, after ingestion of a test meal.

203 | Small intestine neuromuscular dysfunctions in a mouse model of high-fat diet-induced obesity: Involvement of toll-like receptor 4 and serotonin

S. Cerantola¹; I. Marsilio¹; V. Caputi¹; M. Bistoletti²; A. Bertazzo¹; C. Giaroni²; M. C. Giron¹

¹University of Padova, Padova, Italy; ²University of Insubria, Varese, Italy

Objective: Obesity is associated to enteric dysfunctions (e.g. gut dysbiosis, neuroplasticity). In this study, we assessed the role of Toll-like receptor 4 (TLR4) in enteric serotonergic system in a mouse model of high-fat diet-induced obesity.

Methods: TLR4^{-/-} (N = 16) and wild-type (WT, N = 16) C57BL/6J male mice, aged 6 ± 2 weeks, were fed with 2-month standard-diet (SD; fat: 18% kcal) or high-fat diet (HFD; fat: 60% kcal). Distribution of neuronal (HuC/D, nNOS) and glial (S100β) markers

was determined by immunofluorescence in longitudinal-muscle-myenteric plexus whole-mounts. Gastrointestinal transit was measured by nonabsorbable-FITC-labeled dextran distribution. Ileal contractility was evaluated following 30 μM serotonin (5-HT) addition with or without 0.1 μM ondansetron (5-HT3R antagonist). Ileal levels of 5-HT, tryptophan (TRP) and kynurenine (KYN) were measured by HPLC with fluorescence detection.

Results: TLR4 absence protected against body-weight gain after HFD (+21 ± 0.8% in TLR4^{-/-} mice vs + 33 ± 1.4% in WT mice, N = 16, P < 0.05). In TLR4^{-/-} mice, SD determined a delayed gastrointestinal transit, a 3.8-fold increase in 5-HT-mediated contraction, sensitive to ondansetron (N = 8, P < 0.01), a reduced number of nNOS⁺ neurons (-25 ± 0.9%, N = 5, P < 0.05) and an increase of S100β immunoreactivity (79 ± 2%, N = 5, P < 0.01). In WT mice, HFD caused a delayed gastrointestinal transit, a 2.8-fold increase in 5-HT-mediated contraction, sensitive to ondansetron, enteric reactive gliosis and lower nNOS⁺ neurons (-23 ± 2%, N = 8, P < 0.05) whereas, in TLR4^{-/-} mice, HFD induced only a 1.3-fold increase in 5-HT-response. In TLR4^{-/-} mice, SD determined a significant increase in TRP (+27%), 5-HT (+55%) and KYN (+66%) tissue levels. In WT mice, HFD caused a marked increase in TRP (+152%), 5-HT (+148%) and KYN (+300%) tissue levels whereas in TLR4^{-/-} mice HFD induced a 2-fold increment of both TRP and KYN.

Conclusions: Our study suggests that TLR4 and the serotonergic system are potential mediators of gastrointestinal pathophysiological changes associated with obesity.

205 | Hirschsprung's disease: Unravelling molecular pathomechanisms by the assessment of patients' material on complementary levels

S. Schmitteckert¹; T. Mederer¹; R. Röth¹; S. Holland-Cunz²; V. Benes³; N. Paramasivam⁴; F. Lasitschka⁵; G. Rappold¹; P. Romero⁶; B. Niesler¹

¹Department of Human Molecular Genetics, University Hospital Heidelberg, Heidelberg, Germany; ²Hirschsprung Research Initiative Basel-Heidelberg-Mannheim, Basel, Switzerland; ³Genomics Core Facility, EMBL, Heidelberg, Heidelberg, Germany; ⁴Medical Faculty Heidelberg, Heidelberg University, Heidelberg, Germany; ⁵Institute of Pathology, University Hospital Heidelberg, Heidelberg, Germany; ⁶Pediatric Surgery Division, University Hospital Heidelberg, Heidelberg, Germany

Objective: Hirschsprung's disease (HSCR) is a congenital neurogastrointestinal disorder, characterized by the absence of enteric neurons (aganglionosis) mainly in the rectosigmoid section of the colon. It has an oligogenic origin and is caused by functional impairment of neural crest and progenitor cells during embryonic development. Underlying molecular and functional disturbances are still not clarified, hampering patient-specific therapeutic interventions. A complete resection of the aganglionic part represents the only treatment option so far. As a consequence, patients often suffer lifelong from postoperative complications like enterocolitis. To explore molecular pathomechanisms in more detail, we

analyzed patient material on complementary levels by combining Next Generation Sequencing with multiplexed expression analyses on transcript and protein level.

Methods: Trio Whole Exome Sequencing (WES) was initially started with four patients and their non-affected parents and will be expanded to 20 trios. To assess and subsequently combine expression with WES data, molecular profiles of 800 genes in corresponding archived paraffin-embedded ganglionic and aganglionic specimens will be investigated by the multiplexed nCounter target gene approach. To validate our findings, complementing protein determination will be performed.

Results: WES of initial patients was followed by bioinformatic filtering and revealed genetic variants in 3 to 9 novel candidate genes per patient, which were confirmed by Sanger-sequencing. To verify this data and to combine them with comparative expression data from archived ganglionic and aganglionic specimens, nCounter expression as well as immunofluorescence analyses are carried out. Data generation is ongoing and final results will be presented.

Conclusions: In summary, our complementing approach combining Next Generation Sequencing with multiplexed expression analyses of archived specimens has the potential to fundamentally contribute to unravelling HSCR-associated molecular pathomechanisms.

207 | Poor correlation between endoscopic findings, eosinophilic infiltration and reflux burden in patients with eosinophilic esophagitis

M. D. Coletta¹; M. Ghisa¹; M. Frazzoni²; L. Frazzoni³; S. Tolone⁴; N. De Bortoli⁵; E. Marabotto⁶; M. Furnari⁶; V. Savarino⁶; E. V. Savarino⁷

¹Gastroenterology Unit, Department of Surgery, Oncology and Gastroenterology, Padova, Italy; ²Digestive Pathophysiology Unit and Digestive Endoscopy Unit, Baggiovara Hospital, Modena, Italy; ³Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy; ⁴General and Bariatric Surgery Unit, Department of Surgery, University of Campania Luigi Vanvitelli, Napoli, Italy; ⁵Department of Translational Research and New Technology in Medicine and Surgery, University of Pisa, Pisa, Italy; ⁶Gastroenterology Unit, Department of Internal Medicine, University of Genova, Genova, Italy; ⁷Gastroenterology Unit, Department of Surgery, Oncology and Gastroenterology, University of Padova, Padova, Italy

Objective: Eosinophilic Esophagitis (EoE) is a chronic immune-mediated disorder due to an inflammatory eosinophilic infiltrate (EI) in the esophageal lamina propria. The Endoscopic Reference Score (EREFS) define the endoscopic appearance, whereas esophageal EI is used to diagnose EoE (>15eos/ high power field) and to estimate disease severity. The relationship between EoE and gastroesophageal reflux disease (GERD) has been demonstrated, although the magnitude of it is unknown. No sufficient data exist about the correlation of eosinophilic infiltrate with clinical presentation, endoscopic findings and reflux burden. We aimed to correlate EI with clinical presentation, endoscopic findings (expressed by the EREFS) and reflux burden (assessed by impedance-pH studies).

Methods: Patients with suspected EoE were prospectively enrolled in Italian different centers. An esophagogastroduodenoscopy (EGD) was performed to confirm the presence and entity of inflammatory EI in the proximal and distal esophagus. Endoscopic findings were expressed by EREFS (presence of edema, rings, exudates, furrows and stricture,) whereas esophageal symptoms (dysphagia, bolus impaction, heartburn and regurgitation) were assessed by mean of a 4-point Likert scale, from 0 (absent symptom) to 3 (severe symptom). Moreover, each patient underwent 24-hour pH-impedance testing off-medication. We measured the acid exposure time (AET; abnormal >4.2%), number of total reflux episodes (TRE; abnormal >54) and post-reflux swallow-induced peristaltic wave (PSPW) index and of mean nocturnal baseline impedance (MNBI).

Results: Forty-one (34 males, mean age 38, mean BMI 24) EoE patients were enrolled. Patients complained of dysphagia (mean score 2, range 1-3), heartburn (mean score 1, range 0-3) and regurgitation (mean score 1, range 0-2). The mean EREFS score was 2 (range 0-4), while the mean number of eosinophils was 33 (range 15-78). Impedance-pH feature is reported in the Table. Correlation was assessed by means of linear regression analysis and no statistically significant correlation was found between pick of eosinophils or EREFS score and pH-impedance testing parameters ($P = ns$). Neither a correlation between pick of eosinophils count and value of EREFS was observed ($P = ns$).

Conclusions: Eosinophils pick count in the esophageal mucosa of patients with EoE does not correlate with the severity of disease in term of endoscopic findings, symptomatic presentation and reflux burden.

Impedance-pH Features	Patients with EoE N=41
Acid Exposure Time (AET), %	2 (0-8)
Total Reflux Episodes (TRE), n	41 (2-92)
Acid Reflux Episodes, n	31 (1-69)
Weakly Acidic Reflux Episodes, n	9 (0-37)
Proximal Reflux Episodes, n	21 (0-65)
Bolus Exposure, sec	1 (0.1-3.6)
Median Bolus Clearance Time, sec	14 (4-35)
Post-reflux swallow-induced peristaltic wave (PSPW) index	30 (0-70)
Mean nocturnal baseline impedance (MNBI)	1001 (237-3349)
Data are expressed as mean (range)	

208 | Sequential versus concomitant non-bismuth quadruple therapy as first-line eradication for helicobacter pylori

F. Pereira; R. Azevedo; M. Linhares; D. Ramos; J. Pinto; A. Caldeira; J. Tristan; E. Pereira; R. Sousa; A. Banhudo

Hospital Amato Lusitano, Castelo Branco, Portugal

Objective: *Helicobacter pylori* (Hp) is a major cause of peptic ulcer disease and gastric malignancies. Hp eradication rate has reduced, in part because of increased antibiotic therapy resistance. Recent international guidelines have shown preference towards Concomitant non-bismuth quadruple therapy as first-line empirical option, instead of sequential treatment, when choosing a non-bismuth regimen. We aim to compare the efficacy of the Sequential and Concomitant therapies as first line empirical antibiotic regimens in terms of Hp eradication rate.

Methods: We conducted a retrospective study between January/2015 and March/2019 including patients with Hp infection. Patients were treated as first-line eradication therapy with the Sequential quadruple treatment (comprising 5 days of proton-pump inhibitor and amoxicillin, followed by 5 days of proton-pump inhibitor, clarithromycin and metronidazole) or the Concomitant non-bismuth quadruple therapy (comprising 14 days of proton-pump inhibitor, amoxicillin, metronidazole and clarithromycin). Eradication of Hp was confirmed after treatment. Eradication rate was calculated for each treatment regimen.

Results: 101 patients were included (52.5% female, mean age of 55.4 ± 13.4 years). Main indications for Hp testing were dyspepsia (33%), peptic ulcer disease (31%) and erosive gastritis/bulbitis (27%). The tests more frequently used for diagnosis of Hp infection were histology (56%) and rapid urease test (35%). 55 (54.5%) and 46 (45.5%) patients were treated with Sequential and Concomitant therapies, respectively. Hp eradication was mainly confirmed by stool antigen test (53%), histology (20%) and urea breath test (18%). Global eradication rate was 88%. Hp eradication rate achieved 89% with Sequential therapy and 87% with Concomitant treatment, with no statistical difference ($P > 0.05$).

Conclusions: Global eradication rate with non-bismuth quadruple regimens was good (88%), with no statistical difference between Sequential and Concomitant treatments. Therefore, we suggest that both the protocols may be used in current clinical practice as first line empirical eradication treatment.

210 | Eosinophilic esophagitis quality of life questionnaire well correlates with disease activity and response to therapy in active eosinophilic esophagitis patients

M. Ghisa¹; B. Barberio¹; M. D. Coletta¹; M. Inferrera¹; C. Marinelli¹; S. Tolone²; N. De Bortoli³; P. Zentilin⁴; V. Savarino⁴; E. Savarino¹

¹Division of Gastroenterology, Department of Surgery, Oncology and Gastroenterology, University of Padua, Padua, Italy, Padua, Italy; ²Division of General and Bariatric Surgery, Department of Surgery, Second University of Naples, Naples, Italy; ³Division of Gastroenterology, Department of Internal Medicine, University of Pisa, Pisa, Italy, Pisa, Italy; ⁴Division of Gastroenterology, Department of Internal Medicine, University of Genoa, Genoa, Italy, Genoa, Italy

Objective: Eosinophilic Esophagitis (EoE) is a chronic disease characterised by significant impairing of quality of life (QoL). The EoE-QoL-A (EQA) is a 5- scale 30-item, self-reported, validated questionnaire for the assessment of QoL in these patients. Data on the usefulness of this questionnaire in clinical practice are lacking. Thus, we decided to apply the EQA in a consecutive population of EoE patients, in order to evaluate whether the EQA changes on the basis of histological disease activity and therapeutic response to drug administration.

Methods: Thirty patients (7 Female, mean age 33-yo, range 18-75-yo) with a definite diagnosis of EoE, referred to our Unit, were included. The diagnosis was done according to the latest international criteria. Patients were enrolled at outpatient level, at first admission or follow-up, between January 2018 to February 2019. Patients, were evaluated clinically and histologically before (baseline) and after medical therapy (proton pump inhibitors or topical steroid for 8 weeks). At both time points, EoE patients completed the EQA. Histological activity was described as dichotomous parameter: 0 for less than 15eos/hpf and 1 for more than 15 eos/hpf. Pearson correlation coefficient and paired t test were used for the analysis.

Results: At baseline, all patients were histologically active, with a mean value of EQA of $45.07 \pm SD32.69$. After 8 weeks of medical treatment, EQA mean value was $37.63 \pm SD28.37$. A strong significant decrease of EQA score was therefore observed ($P = 0.021$). After 8 weeks of medical treatment, 21 patients (70%) achieved histological response. However, no difference in terms of EQA values between histological responders/non-responders, was shown ($P = 0.296$). Moreover, no significant EQA changes occurred in non-responder patients before and after treatment ($P = 0.878$). In contrast, EQA significantly improved in histologically responder patients before and after treatment ($P = 0.0113$).

Conclusions: EQA is a valid, reliable disease-specific tool for the measurement of QoL in adult EoE Italian population. It can facilitate the assessment of therapeutic response and histological remission. Our data confirmed that therapy significantly improves QoL in EoE, mainly when histological remission is achieved. Developing multiple national-language versions of EQA is an important step in standardization of research protocols and ambulatory management of this disease.

211 | Can we predict clinical phenotypes in esophagogastric junction outflow obstruction using high-resolution manometry

J. Carvão¹; A. Peixoto²; G. Macedo²

¹Hospital Central do Funchal, Funchal, Portugal; ²Hospital São João, Porto, Portugal

Objective: The Chicago Classification (CC) defines esophagogastric junction outflow obstruction (EGJOO) as an elevated integrated residual pressure (IRP) associated with preserved peristalsis. However, is not uncommon to encounter patients with EGJOO who fulfill CC criteria for abnormal peristalsis, which could lead to a definition of EGJOO subtypes. We aimed to find a possible association between EGJOO subtypes and clinical presentation.

Methods: We conducted a retrospective study of patients diagnosed with EGJOO in a tertiary centre during a 13-month period (1 January 2018-31 January 2019). Patients with EGJOO were sub-classified as distal esophageal spasm (DES), hypercontractile esophagus (HE) or ineffective esophageal motility (IEM), according to the CC classification. Clinical, endoscopic, and imaging studies were also analysed.

Statistical analysis was performed using the SPSS (v.23). A significance level was set at <0.05 .

Results: Of the 35 patients included in the study, 71.4% were females and the median age was 55 years (21-78). The median IRP was 22.2 mm Hg (15.30-48.30). 14% patients had a diagnosis of systemic sclerosis. Most of the patients presented with dysphagia (60%), followed by heartburn/regurgitation (25.7%) and chest pain (14.3%). 14.3%, 11.4% and 5.7% of patients meet additional criteria for DES, IEM, EIC, respectively. No association between symptom presentation and EGJOO subtypes (DES, IEM, EIC) was found. In addition, there was no difference between EGJOO subtypes and manometric findings. Follow-up data were available in 22 patients, of which 11 were submitted to some therapeutic intervention (5 pharmacological, 6 botulinum toxin injection), with variable responses.

Conclusions: Our data suggest that, irrespective of the high frequency of associated abnormalities of the esophageal body peristalsis, it seems that no clinical phenotypes can be distinguished from manometric findings. However, further studies are still needed to clarify if these abnormalities could have a clinical impact in deciding the best therapeutic approach to these patients.

214 | Multiple rapid swallow discriminates functional from anatomical esophago-gastric junction outflow obstruction

M. D. Coletta¹; M. Ghisa¹; A. Gubbiotti¹; M. Frazzoni²; L. Frazzoni³; S. Tolone⁴; N. De Bortoli⁵; F. Zingone¹; V. Savarino⁶; E. V. Savarino¹

¹Gastroenterology Unit, Department of Surgery, Oncology and Gastroenterology, University of Padova, Padova, Italy; ²Digestive Pathophysiology Unit and Digestive Endoscopy Unit, Baggiovara Hospital, Modena, Italy; ³Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy; ⁴Department of Medical and Surgical Sciences, University of Bologna, Napoli, Italy; ⁵Department of Translational Research and New Technology in Medicine and Surgery, University of Pisa, Pisa, Italy; ⁶Gastroenterology Unit, Department of Internal Medicine, University of Genova, Genova, Italy

Objective: Esophago-Gastric Junction Outflow Obstruction (EGJ-OO), is a major oesophageal motor disorder characterized by an elevated IRP (>15 mm Hg*s*cm with Medtronic device) and preserved peristalsis. In case of EGJ-OO, an evaluation by using Computer tomography (CT) or ultrasound endoscopy (EUS) has been suggested in order to rule out presence of organic disease. Indeed, at least 50% of EGJ-OO is associated with anatomical abnormalities (i.e. hiatal hernia, peptic stricture, previous foregut surgery or EGJ cancer). We aimed to evaluate whether additional high-resolution manometry (HRM) tests such as multiple rapid swallow (MRS) and rapid drinking challenge (RDC) can discriminate between functional and anatomical EGJ-OO in order to further select which patients should undergo radiology or EUS

Methods: Consecutive patients complaining of oesophageal symptoms were enrolled. Each patient underwent to upper endoscopy and esophagogram with barium and an oesophageal HRM. In case

of IRP > 15 mm Hg*s*cm without a pattern of achalasia, a diagnosis of EGJ-OO was established. Anatomical EGJ-OO (A-EGJ-OO) was defined by the presence of: hiatal hernia, previous foregut surgery, peptic strictures, mucosal or submucosal lesions, and eosinophilic esophagitis. In absence of any of these diagnoses, a functional EGJ-OO (F-EGJ-OO) was defined.

Results: Forty-nine patients with EGJ-OO were enrolled [24 Male, mean age 49 (10-83)]. Fourteen (29%) presented an A-EGJ-OO and thirty-five (71%) had a F-EGJ-OO. MRS test was available in thirty-seven patients and was abnormal in 8/9 of A-EGJ-OO and in 13/28 of F-EGJ-OO. Using Fisher's test, the difference in percentage of abnormal MRS test in the two group was statistically significant ($P < 0.05$). Mean DEA and peak-DCI were higher in F-EGJ-OO as compared to A-EGJ-OO (68 ± 28 vs 108 ± 49 and 2409 ± 1702 vs 4763 ± 3701 , respectively). In contrast, the mean DCI was higher in F-EGJ-OO compared to A-EGJ-OO (1379 ± 1050 vs 2752 ± 2535 ; $P = 0.07 = \text{n.s.}$) and RDC was not different between the two groups ($P = \text{ns}$).

Conclusions: Abnormal MRS test in patients with EGJ-OO could be a useful tool to segregate anatomical from functional EGJ-OO patients. Among F-EGJ-OO patients, a major contractile force seems to be present, suggesting that this could be correlated with inadequate adaptation of the esophageal body motility to the appearance of a recent flow obstruction.

218 | Role of esophageal manometry in the staging of multiorganic dysfunction in patients with systemic sclerosis

P. Costa-Moreira; A. Peixoto; R. Ramalho; G. Macedo

Centro Hospitalar e Universitário São João, Porto, Portugal

Objective: Systemic sclerosis (SSc) is a complex disorder of the connective tissue with multiple systemic manifestations. Esophageal impairment shares the same pathophysiological mechanisms of other organ damage in SSc.

We aimed to evaluate the relationship between extradiagnostic clinical and laboratory data with the manometric findings in a cohort of patients with SSc.

Methods: Retrospective analysis of conventional (CEM) and high resolution (HRM) esophageal manometry data during a 10-year period (2008-2018). For each case, the clinical course, autoantibody profile and respiratory function tests were evaluated.

Results: Fifty-two patients with SSc (mean age 52.8 ± 13.7 years, 90.4% female) were submitted to esophageal manometry (HRM in 35% of cases).

According to LeRoy classification, the predominantly observed disease subtypes were limited cutaneous form/CREST (37%) and overlap syndromes (46%).

At the date of manometry, esophageal symptoms were present in 82.7% of the cases. Abnormal manometry findings were found in 57.7% of patients; the most frequent disorder was ineffective motility ($n = 35$).

Raynaud's phenomenon was associated with the presence of pathological findings in esophageal manometry (OR 16.7; $P = 0.01$).

Autoantibody positivity (Anti-centromere, Anti-SL70, Anti-RNP, and Antinuclear antibodies) was not associated with the presence of abnormal manometry findings.

Carbon monoxide diffusing capacity was significantly lower in patients with ineffective motility ($54.1 \pm 22.8\%$ vs $73.8 \pm 19.5\%$, $P = 0.03$).

Patients who underwent HRM had a significant proportion of pathological findings when compared to CEM (77.8% vs 47.1%, $P = 0.03$).

Conclusions: Raynaud's phenomenon and abnormal respiratory function tests were associated with the presence of pathological manometric findings. Esophageal manometry may be considered in SSc patients as a tool for multiorgan dysfunction stratification.

221 | Eosinophilic esophagitis – Visual score: A novel pictorial self-administered tool to assess quality of life in patients with eosinophilic esophagitis

M. Ghisa¹; C. Marinelli¹; B. Barberio¹; M. Infrerra¹; M. D. Coletta¹; S. Tolone²; N. De Bortoli³; V. Savarino⁴; P. Zentilin⁴; E. Savarino¹

¹Division of Gastroenterology, Department of Surgery, Oncology and Gastroenterology, University of Padua, Padua, Italy, Padua, Italy; ²Division of General and Bariatric Surgery, Department of Surgery, Second University of Naples, Naples, Italy, Naples, Italy; ³Division of Gastroenterology, Department of Internal Medicine, University of Pisa, Pisa, Italy, Genoa, Italy; ⁴Division of Gastroenterology, Department of Internal Medicine, University of Genoa, Genoa, Italy, Genoa, Italy

Objective: Eosinophilic Esophagitis (EoE) is a chronic disease characterised by significant impairing of quality of life (QoL). Current methods for measure QoL are almost tricky and not easy to use routinely. Starting from the validated EoE-QoL-A questionnaire (EQA), we elaborated the EoE Visual Score (EVS), an easy and quick, self-administered questionnaire for daily clinical practice. The aim of this pilot study was to evaluate EVS and its correlation with clinical response to therapy, histological disease activity and EQA.

Methods: Thirty patients (7 Female, mean age 33-yo, range 18-75-yo), who received diagnosis of EoE according to International Criteria at our unit, were included. Patients were enrolled at outpatient level, at first admission or follow-up, between January 2018 to February 2019. The EVS is a 10-scale, 11-areas, pictogram depicting the different areas QoL associated (eating/diet-impact, social-impact, emotional-impact, disease-anxiety, choking-anxiety). Patients were evaluated clinically and histologically before and after medical therapy. At both time points, all patients completed the EQA and EVS. Histologic activity was described as dichotomous parameter: 0 for less than 15eos/hpf and 1 for more than 15eos/hpf. Pearson correlation coefficient and paired t-test were used for the analysis.

Results: At baseline, patients were all histologically active, with a mean value of EQA and EVS of $45.07 \pm SD32.69$ and $26.37 \pm SD20.43$.

After 8 weeks of medical treatment, mean value of EQA and EVS were $37.63 \pm SD28.37$ and $21.43 \pm SD20.92$, respectively. A strong significant correlation between EQA and EVS at both time points ($r = 0.784$ $P < 0.001$ and $r = 0.816$ $P < 0.001$) was observed. EVS had a significant mean value difference before and after treatment ($P = 0.032$). After 8 weeks of medical treatment, 21 patients (70%) achieved histological response, but no difference in EVS mean values was found between histological responders vs non-responders ($P = 0.222$). Moreover, no significant difference for EVS mean values was observed before and after treatment in both histological non-responder ($P = 0.064$) and responders ($P = 0.105$).

Conclusions: The EVS is an effective and quick tool for daily clinical practice, able to depict patients QoL and to facilitate the assessment of therapeutic response. It well correlates with the already validated EQA. Nevertheless, further larger studies are required to evaluate the usefulness of EVS in clinical practice.

223 | Evaluation of IBS symptom severity and stool parameters in primary care

K. Van Den Houte; F. Carbone; J. Tack

TARGID, Leuven, Belgium

Objective: Irritable bowel syndrome (IBS), characterized by abdominal pain related to the stool pattern in the absence of an underlying organic disease, is highly prevalent. However, the characteristics of IBS patients in primary care and their stool parameters are largely unknown. The aim of this study was to identify predictors of IBS symptom severity based on selected stool parameters of IBS patients.

Methods: Patients, diagnosed with IBS by 62 general practitioners, filled out questionnaires concerning demographics, Rome IV criteria, IBS subtypes, and symptom severity (IBS-SSS). Patients were subdivided based on their IBS-SSS score (normal <75, mild 75-175, moderate 175-300, severe ≥ 300). In addition, they collected a stool sample to assess gut inflammation by calprotectin (≥ 250 $\mu\text{g/g}$ abnormal), secretory immunoglobulin-A (sIgA), β -defensin-2; and pancreatic exocrine insufficiency by elastase (mild 200-500, moderate 100-200, severe <100 $\mu\text{g/g}$).

Results: Questionnaires and stool samples of 273 IBS patients (74% female, mean age 42 ± 0.9 , BMI 24 ± 0.3) were analyzed. Seventy percent fulfilled the Rome IV criteria (Rome+). The following IBS-SSS distribution was found: 4, 16, 41, 39% for normal, mild, moderate, and severe IBS-SSS. Five percent of all patients had an abnormal calprotectin of which 62% had a mixed stool type. Severe elastase deficient values occurred in 2%, but this was not associated with predominant diarrhea. Patients with an abnormal calprotectin and severe elastase were excluded for further analysis.

Calprotectin (26 ± 3 vs 23 ± 3 mg/kg), sIgA (3104 ± 426 vs 2122 ± 727 $\mu\text{g/ml}$), β -defensin-2 (55 ± 6 vs 71 ± 12 ng/ml), and elastase (414 ± 7 vs 396 ± 12 $\mu\text{g/g}$) did not differ significantly between Rome+ and Rome- patients respectively and stool types, and were not correlated to IBS-SSS. Within Rome+, there were trends towards a higher sIgA ($P = 0.09$) in patients with constipation compared

to normal (4200 ± 814 vs 2540 ± 577 $\mu\text{g/ml}$) and a higher calprotectin ($P = 0.07$) to mixed (32 ± 8 vs 20 ± 3 mg/kg). Calprotectin tended to be lower in patients with mild IBS-SSS (17 ± 3 mg/kg) compared to moderate IBS-SSS (27 ± 3 mg/kg) ($P = 0.06$).

Conclusions: In primary care IBS, abnormal calprotectin and severely decreased elastase were found in 5 and 2% respectively. No significant differences in stool calprotectin, elastase, sIgA, and β -defensin-2 occurred between Rome+ and Rome-, stool pattern based subgroups, but tendencies were observed that deserve further analysis on a larger sample.

226 | Development of Olorinab, a cannabinoid type 2 receptor agonist, for the management of chronic abdominal pain disorders

P. D. R. Higgins¹; B. Cash²; K. Gilder³; B. Lindstrom³; B. A. English³; S. Turner³; L. Chang⁴

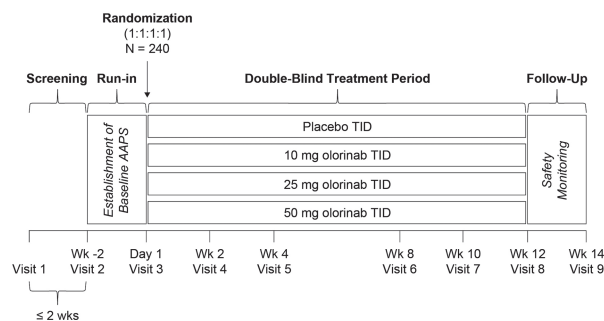
¹University of Michigan, Ann Arbor, United States; ²McGovern Medical School, Houston, United States; ³Arena Pharmaceuticals, Inc, San Diego, United States; ⁴David Geffen School of Medicine at UCLA, Los Angeles, United States

Objective: Non-habit-forming therapies with acceptable adverse event (AE) profiles are needed for conditions with persistent abdominal pain. Although non-selective agonists of the cannabinoid type 2 receptor (CB_2) exhibit analgesia, their utility is limited by psychoactive effects likely from off-target CB_1 activation in the brain. Olorinab (APD371) is a peripherally restricted, selective CB_2 agonist in development for abdominal pain in inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS). Olorinab demonstrated no psychoactive effects in healthy volunteers and was evaluated in a small phase 2a study of abdominal pain in Crohn's disease (CD).

Methods: The open-label phase 2a study enrolled adults with quiescent CD experiencing abdominal pain; subjects were randomly assigned 1:1 to 25 or 100 mg oral olorinab 3 times daily (TID) for up to 8 weeks. The primary outcome was safety; exploratory endpoints included change in average abdominal pain score (AAPS; scale 0 [no pain] to 10 [worst pain]) and pain-free days/week.

Results: In the phase 2a study ($N = 14$), AAPS was significantly improved in evaluable subjects ($n = 11$) at week 8 and was reduced from Baseline (BL) by -4.6 ($P < 0.001$; mean BL, 6.0). Mean pain-free days/week increased from 0 at BL to 2 at week 8 ($n = 11$). AEs were reported in 67% who received 25 mg and 75% who received 100 mg (mostly mild/moderate, none serious; most common: drug hypersensitivity, pain in extremity, hypomagnesaemia). No subjects discontinued because of AEs, and no psychoactive effects were reported.

Conclusions: The phase 2a olorinab study provided evidence for visceral analgesia without psychoactive effects in subjects with quiescent CD and abdominal pain. Based on these promising results, a double-blind, placebo-controlled phase 2 study will evaluate the efficacy pharmacokinetics, and safety of olorinab for abdominal pain in adult patients with IBS with constipation or diarrhoea (IBS-C/D; up to 12 weeks of treatment) (Figure).



AAPS, average abdominal pain scale; TID, 3 times per day; Wk, week
Notes: The Screening Period may be extended to up to a total of 4 weeks for subjects who consent to colonic biopsy. On Day 1, subjects will arrive at the study site in the morning and will stay for an overnight observation period.

FIGURE. Phase 2 study design of olorinab for abdominal pain in IBS.

227 | Agreement between tests of anorectal function for presumed dyssynergia in patients with unexplained constipation

J. Baker; W. D. Chey; L. Watts; M. Armstrong; K. Collins; M. Thibault; W. Hasler

University of Michigan, Ann Arbor, United States

Objective: Dyssynergic defecation is common among chronically constipated patients. Rome IV criteria for dyssynergia require patients to exhibit 2 of 3 impaired evacuation features on anorectal function testing: Balloon Expulsion Test (BET), evacuation pattern on Anorectal Manometry (ARM), and/or rectal evacuation on Defecography (DEF). Little is known about agreement between these tests in a large data set. We aimed to (i) determine agreement between anorectal function test results in patients with suspected dyssynergia and (ii) compute positive and negative predictive factors (PPV, NPV) for BET and ARM results in comparison to abnormal and normal DEF, respectively.

Methods: Retrospective analysis of 649 chronically constipated patients who underwent BET, ARM, and DEF at a tertiary care center (2007-19). Abnormal BET was defined as inability to expel a 50 mL water-filled balloon in <60 seconds. Abnormal ARM was defined as $<20\%$ anal relaxation during simulated defecation. Abnormal DEF was defined as inadequate anorectal angle, poor anal relaxation, and/or incomplete contrast evacuation. Statistical analyses included Cohen's kappa (k) and binary classification tests (PPV, NPV).

Results: Patients were 84% female, 88% Caucasian, with mean age of 52.8 ± 16.1 years (range: 18-88) and mean BMI of 27.8 ± 6.7 kg/m^2 (range: 12.3-57.9). Abnormal evacuation features were found for 35.7% by BET, 45.2% by ARM, and 38.8% by DEF. Kappa correlation statistics showed poor agreement of evacuation results between tests: BET vs DEF ($k = -0.08$), ARM vs DEF ($k = -0.03$), and BET plus ARM vs DEF ($k = 0.17$). Among those with abnormal DEF, 54.9% (95% CI: 48.1-61.6%) had abnormal BET, 44.2% (95% CI: 38.4-50.1%) had abnormal ARM, and 56.7% (95% CI: 47.9-65.2%) had abnormal BET plus ARM. PPV for abnormal BET, ARM, and BET plus ARM to predict abnormal DEF was poor (Table). NPV for normal BET, ARM, and BET plus ARM to predict normal DEF was moderate.

Conclusions: Standard anorectal function testing, ARM and BET, are poorly correlated with DEF acknowledging the challenges using DEF as a gold standard. Reasonably high NPV of BET suggests BET may be acceptable screening test for dyssynergia or an evacuation disorder.

Evacuation Test in Comparison to DEF	Positive Predictive Value (95% Confidence Interval)	Negative Predictive Value (95% Confidence Interval)
BET	51.3% (46.4% - 56.1%)	74.0% (70.8% - 76.9%)
ARM	51.6% (46.8% - 56.4%)	58.8% (55.7% - 61.9%)
BET and ARM	30.2% (26.3% - 34.3%)	85.4% (82.7% - 87.8%)

228 | Characterization of symptom severity and quality of life in ibs patients diagnosed in primary care

K. Van Den Houte; F. Carbone; J. Tack

TARGID, Leuven, Belgium

Objective: Irritable bowel syndrome (IBS) is highly prevalent in primary care, although characteristics of patients diagnosed with IBS by general practitioners, still remain to be studied. Therefore, the objective of this study was to evaluate IBS symptom severity, quality of life, and work productivity in IBS patients diagnosed by general practitioners.

Methods: IBS patients, included by 62 general practitioners, completed questionnaires evaluating demographics, stool types, Rome IV criteria, IBS symptom severity (IBS-SSS), quality of life (IBS-QoL), anxiety (GAD), depression (PHQ9), somatization (PHQ15), and work productivity and activity impairment (WPAI). Patients were subdivided into severity categories based on their IBS-SSS scores: normal <75, mild 75-175, moderate 175-300, severe ≥ 300 .

Results: Two hundred ninety-nine primary care IBS patients (75% females, mean age 42 ± 0.9 years, mean BMI 24 ± 0.3) were included and characterized by the following stool types: constipation (22%), diarrhea (26%), mixed stool type (40%), and normal (11%). Normal, mild, moderate, and severe IBS-SSS were represented in 3, 17, 40, and 40% of all patients respectively. Patients with severe IBS-SSS differed significantly from the other IBS-SSS subgroups in QoL, GAD, PHQ9, PHQ15, and WPAI with all *P*-values lower than 0.05. Symptom severity scores were positively correlated with IBS-QoL ($R = 0.55$), GAD ($R = 0.35$), PHQ9 ($R = 0.38$), PHQ15 ($R = 0.60$), and WPAI ($R = 0.46$).

The Rome IV criteria were fulfilled by 70 percent of all patients (Rome+). Rome+ patients were characterized by a significantly higher IBS-SSS score (290 ± 6 vs 194 ± 10 , $P < 0.0001$), IBS-QoL (35 ± 1.2 vs 23 ± 1.5 , $P < 0.0001$), GAD (7 ± 0.4 vs 5 ± 0.4 , $P = 0.0002$), PHQ9 (7 ± 0.3 vs 5 ± 0.5 , $P = 0.005$), and PHQ15 (13 ± 0.3 vs 10 ± 0.5 , $P < 0.0001$) compared to Rome-. In addition, the work productivity was more affected in the Rome+ group (3.1 ± 0.2) compared to Rome- (1.7 ± 0.3 , $P = 0.0004$).

Conclusions: In IBS patients, diagnosed by general practitioners, more than two thirds fulfill the Rome IV criteria. Symptom severity,

quality of life, anxiety, depression, somatization, and work productivity were significantly different between the Rome + and Rome - group and the group with severe IBS-SSS compared to normal, mild, and moderate IBS-SSS.

229 | Fecal eosinophil cationic protein as potential marker of disease activity in patients with eosinophilic esophagitis

M. Ghisa¹; D. Basso²; M. Inferrera¹; C. Cosma²; C. Marinelli¹; S. Tolone³; N. De Bortoli⁴; V. Savarino⁵; P. Zentilin⁵; E. Savarino¹

¹Division of Gastroenterology, Department of Surgery, Oncology and Gastroenterology, University of Padua, Padua, Italy, Padua, Italy; ²Division of Laboratory Medicine, Department of Medicine-DIMED, University of Padua, Padua, Italy, Padua, Italy; ³Division of General and Bariatric Surgery, Department of Surgery, Second University of Naples, Naples, Italy, Naples, Italy; ⁴Division of Gastroenterology, Department of Internal Medicine, University of Pisa, Pisa, Italy, Pisa, Italy; ⁵Division of Gastroenterology, Department of Internal Medicine, University of Genoa, Genoa, Italy, Genoa, Italy

Objective: Eosinophilic Esophagitis (EoE) is a chronic disorder, characterized by symptoms of esophageal dysfunction and, histologically, by eosinophilic-infiltration. Endoscopic and histological examination is required both at diagnosis and follow-up, since a reliable non-invasive marker has not been identified yet. Eosinophil cationic protein (ECP) is released during eosinophils degranulation and it can be assessed in human faeces. We evaluated the potential use of ECP in EoE patients' faeces (F-ECP) as a potential marker of disease activity.

Methods: 29 consecutive EoE-patients assessed at our Unit between January 2018 to January 2019 for endoscopic follow-up, were included. Faecal and histological specimen were collected on the same day. Histological activity was staged considering the number of eosinophils for high-power field (Eos/HPF). A control-group of 71 patients (mean age 52-yo, range 35-64, 38 Male), in whom EoE had been excluded according to International criteria, was included. F-ECP was evaluated with a fluorescence-enzyme immunoassay (PHADIA, Thermo Fisher Scientific). Spearman's rank correlation was applied and F-ECP predictive positive and negative values (PPV, NPV) were calculated.

Results: EoE-study-population consisted of 29 patients affected by EoE (mean age 32-yo, range 18-62yo, 24 M), showing F-ECP values ranging from 0 to 172 $\mu\text{g/L}$ (mean value 17.3 $\mu\text{g/L}$), compared to values ranging from 0 to 32 $\mu\text{g/L}$ (mean value 8.1 $\mu\text{g/L}$) in the control-group. A statistically significant relationship between F-ECP and Eos/HPF was observed ($r_s = 0.4172$, P (2-tailed) = 0.02438). PPV and NPV of F-ECP were evaluated using two cut-off values, F-ECP < 2 $\mu\text{g/L}$ (as negative) and F-ECP < 8.1 $\mu\text{g/L}$ (as mean value in the control group). Among the study group, 21 patients (72%) showed histological remission, but only 8 (38%) had F-ECP negative values. Setting a cut-off value of 8.1 $\mu\text{g/L}$, F-ECP NPV and PPV for histological remission were 86% and 40%, respectively, while they were 100% and 38% with cut-off value of 2 $\mu\text{g/L}$.

Conclusions: Our preliminary data show a good correlation of F-ECP values with histology activity and a clear difference in terms of levels between EoE patients and controls. However, the wide variability of our ECP levels evaluated, requires further cases and more histologically-active patients, in order to assess its usefulness in clinical practice.

230 | High resolution manometry traditional parameters are not useful to predict response to endoscopic treatment in patients with esophago-gastric junction outflow obstruction

M. D. Coletta¹; M. Ghisa¹; A. Gubbiotti¹; M. Frazzoni²; L. Frazzoni³; S. Tolone⁴; N. De Bortoli⁵; F. Zingone⁶; V. Savarino⁷; E. V. Savarino⁶

¹Gastroenterology Unit, Department of Surgery, Oncology and Gastroenterology, University of Padova, Padova, Italy; ²Digestive Pathophysiology Unit and Digestive Endoscopy Unit, Baggiovara Hospital, Modena, Italy; ³Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy; ⁴General and Bariatric Surgery Unit, Department of Surgery, University of Campania Luigi Vanvitelli, Napoli, Italy; ⁵Department of Translational Research and New Technology in Medicine and Surgery, University of Pisa, Pisa, Italy; ⁶Gastroenterology Unit, Department of Surgery, Oncology and Gastroenterology, University of Padova, Padova, Italy; ⁷Gastroenterology Unit, Department of Internal Medicine, University of Genova, Genova, Italy

Objective: Esophago-Gastric Junction Outflow Obstruction (EGJ-OO), is a major oesophageal motor disorder characterized by an elevated IRP (>15 mm Hg*s*cm with Medtronic device) and preserved peristalsis. Pathogenesis and treatment of this high-resolution manometry (HRM) diagnosis is unknown, although the majority of the experts agree on using endoscopic dilation or botox injection, particularly in patients reporting dysphagia and weight loss. We aimed to investigate whether HRM features could be useful to predict the therapeutic outcome in EGJ-OO patients undergoing endoscopic therapy

Methods: Patients with symptoms of esophageal dysfunction (e.g. dysphagia, chest pain, and regurgitation) underwent upper endoscopy to rule out organic disease, and thereafter HRM. Symptoms severity was assessed by a 4-point Likert type scale from 0 (absent symptom) to 3 (severe symptom). A manometric diagnosis of EGJ-OO was made according to CC ver. 3.0. and in case of drugs-unresponsive (i.e. calcium channel blockers or phosphodiesterase 5 inhibitors) symptoms after six months, an endoscopic treatment [pneumatic dilation (PD) or botox injection (BT)] was proposed to the patients. We opted for using BT in elderly subjects (> 75 years) or in case of relevant comorbidities. Clinical response was defined by a symptom score of 0 or 1 for the main symptom (i.e. the leading one requiring outpatient visit and further investigations). Only patients with a follow-up of at least 6 months were considered.

Results: Thirteen [8M, mean age 64 (50-83)] patients with EGJ-OO underwent endoscopic treatment (11 PD and 2 BT). In the group treated by PD, 9/11 (82%) had a good response and 2 failed the

treatment. Among the two patients who underwent BT, 2/2 (100%) had a good response. The difference in efficacy of the two treatments was found to be not statistically significant by Fisher's test ($P = ns$) analysis. By using uni- and multivariate regression analysis, a monometric parameter predictive of response to treatment was not observed ($P = ns$).

Conclusions: Traditional HRM parameters are not useful to predict the response of EGJ-OO patients to endoscopic treatment. Further metrics should be developed in order to understand which patients may benefit of endoscopic treatment in case of EGJ-OO diagnosis.

233 | Multielectrode arrays as tools for the investigation of pathological changes in the enteric nervous system

S. Schulte; E. Loris; A. Braun; M. Gries; H. Rabe; K.-H. Schäfer

University of Applied Sciences Kaiserslautern, Zweibrücken, Germany

Objective: Multielectrode Arrays (MEAs) are biomedical chips that are used for deduction of electrical potentials of excitable cells, like neurons and cardiac cells. MEAs consist of a defined number of planar electrodes, arranged in an array on which cells are cultivated. These devices enable the investigation of the impact of pharmacologically active substances, e.g. possibly toxic peptides such as Amyloid- β (A- β) or α -Synuclein (α -Syn) on neuronal activity. However, isolated primary cells need time to restore their set of receptors, prolonging the duration of experiments and usage of MEA-chips. Also, long-term deduction of electrical signals is confined due to corrosive and conditioning effects of culture media and cells on the surface of the devices.

Methods: We therefore used an alternative approach in cultivating cells on coverslips, measuring them upside-down on MEAs. This extends the useful life of chips and increases the number of experiments per time. In addition, we aim to develop a microfluidic system for MEA-chips for a constant exchange of culture medium. This enables deduction of electrical activity in long-term experiments.

Results: Since neurodegenerative diseases (Alzheimer's and Parkinson's disease) might start in the gut, we studied the effect of disease-related peptides (A- β and α -Syn) on the ENS. Analysis of electrical signals indicated changes in activity of enteric neurons, suggesting a direct effect of the tested peptides on the ENS *in vitro*. Extending our analysis to *ex vivo*, we assessed electrical activity of the gut wall using modified MEA-chips, that allow the suction of tissue onto an array of electrodes. We were able to deduct electrical signals directly from the gut wall, which may be used *in vivo* in the future.

Conclusions: Overall, our results indicate that the described modifications of MEA-technology offer an effective method for studying the impact of neurodegenerative diseases on the enteric nervous system *in vitro* and *ex vivo*.

234 | Morphovolumetric analysis of the abdomino-thoracic cavity in patients with functional abdominal distention during basal conditions and during episodes of abdominal distention....talking of 101 patients

E. B. Orozco¹; E. Burri²; A. Accarino³; F. Azpiroz³

¹Digestive System Research Unit, University Hospital Vall d'Hebron, Barcelona, Spain, Barcelona, Spain; ²Gastroenterologie und Hepatologie Medizinische Universitätsklinik, Liestal, Switzerland; ³Digestive System Research Unit, University Hospital Vall d'Hebron, Barcelona, Spain

Objective: Verify the usefulness of CT scan in patients with functional abdominal distention and abdominophrenic dyssynergy

Background: In a series of studies over the past 10 years we investigated the mechanisms of visible abdominal distention in the absence of organic cause. We have now analysed a pool of 101 patients who participated in these prospective studies following the same experimental procedure.

Methods: Only patients with discrete episodes of abdominal distention were included in these studies after ruling out organic disease. Patients were evaluated during basal conditions (without or minimum abdominal distention) and during episodes of severe abdominal distention by abdominal (n = 68) or abdomino-thoracic (n = 43). CT scans; hence, abdominal data of 101 patients and thoracic data of 43 of them were available.

Results: During episodes of self perceived abdominal distention all patients but one exhibited an increase in girth. Distention was associated with a descent of the diaphragm with relatively modest increase in intestinal gas (66 ± 9 mL) and total abdominal contents (520 ± 210 mL). Of the 43 patients with thoracic evaluation, 38 of them exhibited thoracic insufflation (by 342 ± 184 mL volume increment) with increased anteroposterior diameter of the thorax (8 ± 3 mm).

Conclusions: Abdominal distention is a somatic expression produced by the walls rather than by its content.

Basal condition



Bloating condition



Functional Bloating

236 | Low-cost strategies in the evaluation of defecation disorders

A. C. Caetano¹; D. Costa¹; R. Gonçalves²; J. C. Pinto¹; C. Rolanda¹

¹Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho; Braga Hospital, Braga, Portugal; ²Braga Hospital, Braga, Portugal

Objective: Rome IV criteria establish the diagnosis of the defecation disorders (DD) requiring the presence of clinical criteria and the presence of abnormal physiological findings. However, this physiological evaluation can be extensive, inaccessible and costly. After an extensive review of the literature, we found 3 potential "low-cost" tools – a clinical DD score, the balloon expulsion test (BET) and the digital rectal examination (DRE) score published by Tantiplachiva. Our aim was to evaluate their performance as separate or combined tests in the diagnostic algorithm of DD.

Methods: This prospective study occurred between September 2017 and March 2019 in the Gastroenterology Department in a tertiary hospital. All patients that fulfilled clinical criteria for chronic constipation were invited to participate. Besides the gold standard physiological tests (in our Department – anorectal manometry and defecation imaging), the patients answered the clinical DD score and were evaluated by DRE and BET. Multivariate binary logistic regression, ROC curves and the DeLong test were performed.

Results: From 90 patients with the clinical criteria of chronic constipation, 37 (41.1%) were diagnosed with DD, mainly female (n = 31, 83.8%) with a median age of 62 years old. The clinical DD score revealed an AUC of 0.539 (SE = 0.069, P = 0.574) and the DRE displayed an AUC of 0.573 (SE = 0.058, P = 0.210). The BET displayed a sensitivity of 78.38% and specificity of 55.77%. At multivariate analysis, age (OR 1.04, 95% CI 1.03-1.07, P = 0.031) and abnormal BET (OR 4.63, 95% CI 1.72-12.39, P = 0.002) were significant predictors of DD. The predictive power of the model obtained was 73.8% (SE = 0.054, P < 0.0001), significantly superior to the clinical DD score (P = 0.034) and the DRE (P = 0.037). Following the categorization of both variables, the predictive power of the model improved to 76.8% (SE = 0.047, P < 0.0001), with a sensitivity of 58.33% and specificity of 86.54% when both TEB abnormal and age ≥ 55 are present.

Conclusions: The clinical DD score and the DRE did not reveal discriminative power to identified patients with DD. Our predictive model (using age and the abnormal BET) performed significantly better than the former tools and improved BET specificity to exclude DD.

237 | The role of esophageal high-resolution manometry in approach of gastroesophageal reflux disease

A. L. Santos; A. Peixoto; J. Silva; R. Ramalho; G. Macedo

Gastroenterology Department. Centro Hospitalar de São João. WGO Oporto Training Center. Porto Medical School, University of Porto, Porto, Portugal

Objective: Recent studies have demonstrated the important role of high-resolution manometry (HRM) in assessment of patients with gastroesophageal reflux disease (GERD) and it is now formally recommended by The Lyon Consensus. We intended to relate the findings in HRM with those of 24 hours pHmetry in patients with GERD.

Methods: Retrospective study, with inclusion of patients who were referred to perform 24 hours pHmetry and submitted to HRM, in a tertiary referral center, between March 2018 and July 2019. Chicago Classification v3.0 and The Lyon Consensus were used for the interpretation of data from the procedures.

Results: A total of 49 patients were included, 53% females, with a mean age of 50 ± 14 years. In pHmetry assessment, 38% of patients had findings compatible with GERD and 9% with reflux hypersensitivity. Among the referenced patients, 71% presented changes in HRM: 38% esophagogastric junction obstruction (EGJ), 15% hypotonicity of the LES and 5% ineffective esophageal motility (IEM). The presence of IEM was associated with an abnormal pHmetry ($P = 0.040$) as well as with the positive symptom association probability (SAP). The median acid exposure times (AET) was 0.7% (IQR 0.2-5.5%) and the median DeMeester score (DmS) was 3.8 (IQR 1.2-10). HRM was performed after a median of 5 years (IQR 2-8) after the symptoms' onset. The most prevalent symptom was the heartburn (67%) but regurgitation and chronic cough were those more often associated reflux in the pHmetry ($P = 0.002$ and $P = 0.014$, respectively). In 75% of cases there was a previous therapeutic trial with proton pump inhibitor, mostly without clinical improvement (57%); this fact was related with a LES hypotonicity in HRM ($P = 0.018$). In 71% of patients, the HRM's findings had an impact in the subsequent patients' therapeutical strategy.

Conclusions: The routine performance of a manometric study in patients submitted to a pHmetry allows the identification of motor findings in approximately three-quarters of patients, facilitating the subsequent therapeutic approach.

238 | Esophageal manometry in gastroesophageal reflux disease: Is there superiority of the high resolution over conventional?

A. L. Santos; A. Peixoto; J. Silva; R. Ramalho; G. Macedo

Gastroenterology Department. Centro Hospitalar de São João. WGO Oporto Training Center. Porto Medical School, University of Porto, Porto, Portugal, Porto, Portugal

Objective: Conventional esophageal manometry (CM) presents a controversial role in assessment of patients with gastroesophageal reflux disease (GERD). High-resolution manometry (HRM) seems to add information in the assessment of these patients, although its role remains uncertain. We intended to compare the findings of CM and HRM in patients with GERD as well as its impact in patient's approach.

Methods: Historical retrospective cohort study, including patients who were referred to perform CM or HRM previous to pHmetry. Demographic characterization, with assessment of manometric findings in each group and determination of the impact of these findings in terms of therapeutic strategy.

Results: A total of 95 patients were included, 46 with CM (63% female, mean age of 46 ± 17 years) e 49 with HRM (53% female, mean age of 50 ± 14 years). The median time between the onset of symptoms and manometry was higher in HRM [5 years (IQR 2-8) vs 4 years (IQR 2-8). Manometric changes were seen in 50% of cases of MC [39% of LES hypotonicity, 15% of ineffective esophageal motility (IEM),] and 71% in HRM (38% of esophagogastric junction obstruction, 15% of LES hypotonicity and 15% of IEM). Heartburn was the main symptom in both groups (74% in CM and 67% in HRM). A previous therapeutic trial with proton pump inhibitor occurred in 65% of cases of MC and 67% of HRM, with effective response in 14% and 43%, respectively. In both groups, the most frequent finding was esophagitis (40% and 35%, respectively). The impact of manometry in patient's follow-up (in terms of therapeutic) was higher in HRM (71% vs 44%).

Conclusions: HRM allows an increment of pathologic findings in the approach of patients with GERD when compared to CM, including major motor disorders, with consequent changing in therapeutic approach of these patients.

239 | Low-dose penicillin exposure in adolescent mice has long-term effects on gut function

K.-A. M. Neufeld; S. Farhin; T. Delungahawatta; B. Tomar; W. Kunze; J. Bienenstock

McMaster Brain-Body Institute, Hamilton, Canada

Objective: Previous work has shown that low-dose penicillin treatment in dams during the perinatal period has long-term consequences for offspring's microbiota-gut-brain axis (LeClercq et al 2017), some of which are prevented by concurrent treatment with probiotic. Here, we examine the potential impact of low-dose antibiotic treatment during a later critical period of development – adolescence – on intestinal motility, gene expression in the gut and fecal microbiome.

Methods: 3-week-old BALB/c male and female mice were weaned and randomized into treatment groups of water (control), low-dose penicillin (AB), or AB/*Lactobacillus rhamnosus* JB-1™ (AB/JB-1). AB treated animals received 31 mg/kg penicillin V in drinking water

from 18:00-9:00/day. AB/JB-1 treated animals received the same but with the addition of JB-1 (10^9 c.f.u/day) in drinking water from 9:00-18:00. Treatments continued from 3w to 6w of age. At 12w of age intestines were harvested and motility of both colonic and jejunal segments was video recorded in a perfusion organ bath, producing spatiotemporal maps of diameter changes. Intestinal tissue and fecal pellets from a separate cohort were collected for respective mRNA gene expression and microbiome analyses.

Results: There were no sex differences in the effects of low-dose penicillin treatment on intestinal motility. AB treated mice showed increases in frequency of neuronally dependent propagating contractile clusters in the jejunum, which was attenuated with AB/JB1 co-treatment. In addition, AB/JB1 treatment significantly reduced the amplitude of colonic contractions in both control and AB treated mice.

Conclusions: Low-dose penicillin treatment during adolescence has long-term, sex-independent effects on intestinal motility in mice which are ameliorated with co-treatment of probiotic JB-1. Continued work examining mRNA expression of relevant genes in gut tissue and microbiome is ongoing.

241 | Psychomotor development in relation to the severity of stunting and paediatric environmental enteropathy (PEE) – AFRIBIOTA project

M. Doria¹; P. Vonaesch¹; A. S. Ferreira²; V. Guillemot¹; T. Rajaonarivo³; V. Rambolamanana³; P. Sansonetti¹

¹Institute Pasteur, Paris, France; ²Universidade de Lisboa, Lisboa, Portugal;

³Institute Pasteur, Antananarivo, Madagascar

Objective: Solid evidence can be gathered from the literature to support the role of stunting, particularly in the context of recurrent/chronic enteric infections and/or PEE, in causing retardation of psychomotor development, particularly cognitive functions in young children. This eventually leads to delays in school acquisitions, thus programming increased social fragility in their future life. PEE seems to start early in life at a period when brain development, particularly synaptogenesis, is extremely active and thus very fragile and susceptible to environmental cues.

Methods: AFRIBIOTA is a case-control study for stunting recruiting 460 children in Madagascar aged 2-5 years with no overt signs of gastrointestinal disease are recruited (260 with no growth delay, 100 moderately stunted and 100 severely stunted). A team of clinical psychologists performed an in depth psychomotor analysis for all enrolled children in five main domains: gross motor, fine motor, communication, cognition and social competences.

Results: The psychomotor development of children with stunting and/or PEE was compared to non-stunted children. Results suggest significant differences between the two nutritional groups (non-nutrit children and severely malnourished children) on mobility,

cognitive functions, sociability, with the exception of communication. Moreover, as expected, family socio-economic status seems to have a negative impact on the child developmental score.

Conclusions: The association between nutrition and brain-related development functions was assessed. Stunting negatively affects mobility, cognitive and personal/social competences in early childhood. Potential intervention points will be pinpointed for future prevention strategies.

242 | Analysis of enteric nervous system and intestinal epithelial barrier to predict complications in hirschsprung's disease

A. Dariel¹; L. Grynberg²; M. Auger²; T. Durand²; P. Aubert²; A. Venara²; P. Derkinderen²; H. Boudin²; C. Brochard²; M. Neunlist²

¹Assistance Publique des Hôpitaux de Marseille, Marseille, France; ²Inserm U1235, Nantes, France

Objective: In Hirschsprung's disease (HD), the postoperative course remains unpredictable. The aim was to define predictive factors of the main postoperative complications: obstructive symptoms (OS) and Hirschsprung-associated enterocolitis (HAEC).

Methods: In this prospective multicentre translational cohort study, samples of resected bowel were collected at time of surgery in 18 neonates with short-segment HD in tertiary care hospitals. OS and HAEC were noted during the postoperative follow-up. We assessed the enteric nervous system and the intestinal epithelial barrier (IEB) in ganglionated segments by combining immunohistochemical, proteomic and transcriptomic approaches, with functional ex vivo analysis of motility and para/transcellular permeability.

Results: Ten HD patients presented postoperative complications (median follow-up 23.5 months): 6 OS and 4 HAEC. Immunohistochemical analysis showed significant 41% and 60% decreases in the median number of nNOS-IR myenteric neurons per ganglion in HD with OS, as compared to HD with complications without OS, and HD without complications ($P = 0.0095$, $P = 0.002$, respectively). Paracellular and transcellular permeabilities were significantly increased in HD with HAEC, as compared to HD with complications without HAEC ($P = 0.016$, $P = 0.009$, respectively), and HD without complications ($P = 0.029$, $P = 0.017$, respectively). No statistical difference was found concerning tight junctions and inflammatory markers expression, nevertheless significant positive correlations were found between the expression of TLR2/4 and the number of nNOS-IR neurons per ganglion.

Conclusions: Our study is the first to provide predictive factors of postoperative complications in HD patients. Novel drugs able to modulate neuronal phenotype and enhance the IEB permeability could be of great interest for preventing/treating not only postoperative complications in HD but also other intestinal motility disorders.

244 | *Faecalibacterium prausnitzii* effects on radiation-induced colonic injuries: Application for the management of pelvic radiotherapy complications

A. Lapiere¹; V. Robert²; C. Demarquay¹; J.-M. Chatel²; A. Semont¹

¹IRSN, Fontenay Aux Roses, France; ²INRA, Jouy En Josas, France

Objective: Cancers in the pelvic area are mostly treated by radiotherapy. Radiation of healthy tissues surrounding tumor leads to side effects years after the end of the treatment. Late onset of specific symptoms led to the definition of a new pathology, called Pelvic Radiation Disease (PRD), in 2010. Gastrointestinal dysfunctions observed in PRD considerably affect patient's quality of life. These dysfunctions could be the consequence of a high inflammatory process induced in radiosensitive organs, as colon and rectum, after the rupture of intestinal barrier. It has been also showed changes in the intestinal microbiota diversity after radiotherapy. Indeed, *Faecalibacterium prausnitzii* (*Fp*), which plays physiological key role in the colonic homeostasis, is decreased. Our assumption is that *Fp* could be used as radio-protective agent for patients undergoing a pelvic radiotherapy, by preventing important colonic injuries occurrence.

Methods: To show this last point, we studied the effect of daily 10⁹ CFU *Fp* administration, 72 hours after a 29 Gy colorectal irradiation. Treatment began 3 days before irradiation and continued until the day before euthanasia. We focused our analysis on structural, functional alterations of colonic barrier and inflammatory responses.

Results: *Fp* treatment reduces radiation-induced colonic toxicity. Indeed, we reported a reduction of crypt epithelial atypia associated with increased crypt height. Moreover, we showed an increase of SOX9, DCLK1, and PCNA immunostaining of epithelial cells, corresponding respectively to progenitor/stem cells, tuft cells and proliferative cells in colonic epithelium. *Fp* administration also reduces radiation-induced para-cellular permeability and inflammatory cell infiltration.

Conclusions: These results demonstrate that *Fp* administration may have radio-protective potential by maintaining colonic barrier integrity. In order to maximize therapeutic efficiency, co-administrations of *Fp* with mesenchymal stromal cells are undergoing.

249 | The RoLe of irritable bowel syndrome in LactOse INTolerance (LION Trial): Protocol of a multicentre randomized controlled clinical trial

N. Zádori¹; P. Varjú¹; Á. Vincze²; F. Izbéki³; A. Rosztóczy⁴; R. Róka⁴; P. Hegyi¹; J. Czimmer²

¹Institute for Translational Medicine, University of Pécs Medical School, Pécs, Hungary; ²Division of Gastroenterology, First Department of Internal Medicine, University of Pécs Medical School, Pécs, Hungary; ³Division of Gastroenterology, Fejér County Saint George Teaching Hospital of University of Pécs, Székesfehérvár, Hungary; ⁴1st Department of Medicine, Albert Szent-Györgyi Health Center, University of Szeged, Szeged, Hungary

Objective: Irritable bowel syndrome (IBS) is a common functional gastrointestinal disorder, with no specific pharmacological treatment. IBS can lead to significant impairment of quality of life (e.g. social isolation or stigmatization), decreased work productivity and an increase of health care and societal costs. Intolerance to dairy products and other foods is more frequent among patients with IBS than healthy subjects. There are quite a few clinical studies published investigating the relationship between lactose intolerance (LI) and IBS. Although there are overlapping symptoms, it is not yet clear whether IBS has a role in developing of LI. In addition to that there is no high-quality evidence to support the idea of the effectiveness of lactose restriction in patients with IBS.

Methods: LION is a prospective, double blind, four armed randomized controlled, multicentre trial. As both IBS and lactose intolerance present frequently in our population and their symptoms highly overlap, the aim of this study is to provide evidence on the role of IBS in lactose intolerance and on the efficacy of lactose-free diet and lactase enzyme substitution. The trial protocol was structured following the recommendations of the SPIRIT 2013 Statement. Patients meeting all inclusion and no exclusion criteria will be randomized into one of the four possible treatment arms: 1. lactase with lactose restricted diet (LD); 2. lactase without diet (LND); 3. placebo with diet (PD); 4. placebo without diet (PND). The study will be performed with the adaptive "therapy switching" design: if patient's condition is the same within 2 weeks after randomization or getting worse, then the patient will be transferred to another therapeutic arm of the study. The primary endpoint will be the amount of subjects with significant improvement in each treatment arm.

Results: The study organization and the data collection will be carried out between July 2019- September 2021.

Conclusions: LION study would provide the first direct correlation between IBS and lactose intolerance. We would like to provide important epidemiological data on the prevalence of IBS and lactose intolerance and malabsorption.

250 | Increased oesophageal symptoms and manometric abnormal patterns in opioids users: Experience of a large tertiary referral centre

K. Nikaki; P. Woodland; S. Gabieta-Sonmez; E. Yazaki; D. Sifrim

Wingate Institute of Neurogastroenterology, Barts and the London School of Medicine and Dentistry, Queen Mary University London, London, United Kingdom

Objective: Opioid induced oesophageal dysfunction is increasingly recognized. The inability to discontinue opioids pauses a challenge in the management of these patients. Opioids mainly affect organization of peristalsis and relaxation of the lower oesophageal sphincter. The relationship between type of opioids intake, symptoms and manometric pattern is still unclear.

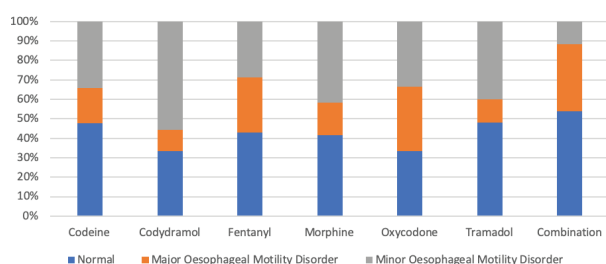
Aim: To record the prevalence of major and minor oesophageal disorders in patients using opioids and compare this to non-users.

Methods: We identified 155 patients on opioids registered on our HRM database between October 2013 and March 2019. Type of opioids, symptoms and manometric features were reviewed and compared between opioids users and non-users ($n = 6465$). Patients with an incomplete test, studied following fundoplication or with a known major motility disorder were excluded.

Results: The prevalence of opioid use in our patient population was 2.3%. Opioids used included Tramadol ($n = 50$), Codeine ($n = 45$), Morphine Sulphate ($n = 12$), Co-dydramol ($n = 9$), Fentanyl ($n = 7$), Oxycodone ($n = 6$) and Combination therapy ($n = 26$). The commonest reason for opioid use was a musculoskeletal disorder (55%). The main complaint was dysphagia in 21%, chest pain in 10%, heartburn and regurgitation in 35%, cough in 8% and other (abdominal pain, vomiting, belching, globus) in 26%. Another 42.5% reported dysphagia as secondary symptom. Compared to non-users of opioids, dysphagia was the main complaint in 13.5% and chest pain in 4.8%, whilst another 21% reported dysphagia as secondary symptom. There was a significant difference in the prevalence of all major and minor manometric abnormalities between opioid users and non-users ($P < 0.0001$). The incidence of GOJ obstruction was 11.6% vs 1.6% respectively, Jackhammer oesophagus and Distal Oesophageal Spasm 4.5% vs 1.2%, Achalasia type 3 1.9% vs 0.18%, Absent peristalsis 1.3% vs 0.09%, Nutcracker oesophagus 3.9% vs 0.17%, IEM 29.6% vs 10%. Amongst opioid users whose main complaint was dysphagia or chest pain, Achalasia type 3 was present in 6% and GOJ obstruction in 19%. Although numbers are relatively small, more potent opiates (Fentanyl, Oxycodone) and combinations of opiates appeared associated with a greater risk of major motility disorders.

Conclusions: The prevalence of symptoms and oesophageal dysmotility was higher in opioids users, highlighting the level of awareness required for this problem.

Opioid induced oesophageal dysfunction based on type of opioid used



252 | The yield of combined multichannel intraluminal impedance pH monitoring (MII-PH monitoring) among Filipino patients with suspected refractory gastroesophageal reflux disease: A St. Luke's medical center experience

M. J. H. Navarro; S. I. Q. De Ocampo

St. Luke's Medical Center, Institute of Digestive and Liver Diseases, Quezon City, Philippines

Objective: The main objective of the study is to determine the yield of combined multichannel intraluminal impedance-pH monitoring (MII-pH monitoring) among Filipino patients with suspected refractory GERD at St. Luke's Medical Center

Methods: *Study Design:* Retrospective, cross-sectional

Study Population: Suspected refractory GERD patients who underwent MII-pH Monitoring

Outcome Measures: Proportions of patients with persistent acid reflux, hypersensitive esophagus and functional heartburn

Statistical Analysis: Descriptive statistics

Results: There are total of 50 subjects included in the study. Majority of the patients was in their 4th to 5th decade of life. Most of the patient presented with typical symptoms of reflux, specifically heartburn (44.00%) and regurgitation (40.00%). In this study, most common indication for referral involved patients that were non-responsive to proton-pump inhibitors (86.00%). The manometric findings most commonly revealed normal esophageal motor function (52.00%).

It can be noted that patients with phenotypic group of *persistent acid reflux* (i.e. patients with abnormal acid exposure with positive symptom association), revealed overall prevalence of 20.00% (10 out of 50 patients). Majority were males (60.00%), around 40.00% presented with esophagitis on EGD, alongside with normal manometric findings (60%), and positive SI (60.00%) / positive SAP (100%).

Where as those patients under the phenotypic group of *hypersensitive esophagus* (i.e. normal acid exposure with positive symptom association), revealed overall prevalence of 18.00% (9 out of 50 patients). Patients involved were mostly females (77.78%), all presented without esophagitis on EGD (100.00%), 55.56% with normal esophageal motor function on manometry, and all patients have positive SAP (100%) / negative SI (100%).

On the other hand, in patients labeled under the group of *functional heartburn* (i.e. normal acid exposure with negative symptom association), revealed overall prevalence of 62.00% (31 out of 50 patients). Majority were females (52.94%), presented with normal manometric findings (48.39%). All patients presented without esophagitis on EGD (100.00%) with negative SAP (100%) / negative SI (100%).

Conclusions: Among suspected refractory GERD patients, MII-pH study diagnosed (see figure 1) majority of them with *functional heart burn* (62.00%) followed by *persistent acid reflux* (20.00%) and *hypersensitive esophagus* (18.00%). Hence, MII-pH monitoring is helpful in the work-up of patients with suspected refractory GERD as it will redirect course of management.

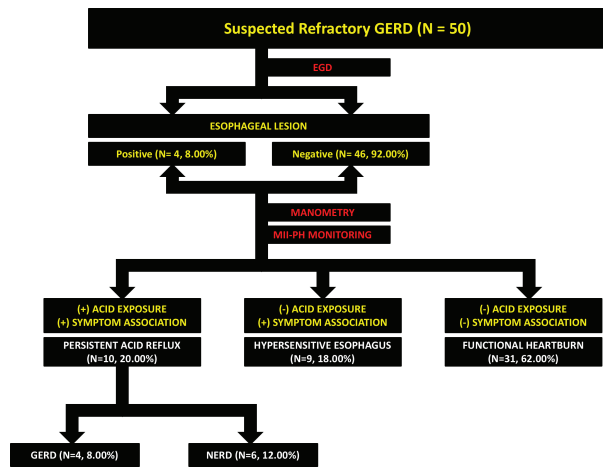


FIGURE 1. Proportion of patients according to phenotypic group.

254 | Duodenal hyperpermeability and markers of inflammation are linked with gastric emptying and symptoms in functional dyspepsia patients

L. Wauters; M. Lambaerts; D. Frings; A. Accarie; R. Farré; J. Tack; T. Vanuytsel

KU Leuven, Leuven, Belgium

Objective: The role of duodenal alterations in relation to gastric emptying and symptoms in functional dyspepsia (FD) patients is unclear.

Methods: FD patients with postprandial distress (PDS) according to Rome IV were recruited. Gastric emptying for liquids and solids was determined using the calculated half emptying time of the ¹³C-glycine (significantly delayed >75 minutes) and ¹⁴C-octanoic acid (> 110 minutes) breath tests, respectively. Duodenal biopsies were collected to measure the transepithelial electrical resistance (TEER) and paracellular passage of a fluorescein-labeled dextran (4 kDa) in Ussing chambers. After the endoscopy, a naso-duodenal tube was positioned in the second part of the duodenum with aspiration of fluids before and after a liquid meal (Fortimel, 300kCal) with measurement of pH. High-sensitivity C-reactive protein (hs-CRP) was measured in plasma and Patient Assessment of Gastrointestinal Disorders Symptom Severity Index (PAGI-SYM) was collected. Descriptive and correlation analyses were performed to determine markers of gastric emptying and FD symptoms.

Results: In total, 17 FD patients (15 females, median (IQR) age 28 (22-34) years) were recruited with 15 (88%) belonging to the pure PDS group and 2 (12%) the overlap group. The median gastric half emptying time was 68 (41-76) min for liquids and 66 (57-80) min for solids. Significantly delayed gastric emptying was present in 4 patients (24%) for liquids and 1 patient (6%) for solids. Median TEER was 22.1 (19.2-27) $\Omega \cdot \text{cm}^2$ and paracellular passage 25.2 (20-30.3) pmol. Fasting and fed pH were similar (7 (5.2-7.3) vs 6.5 (6.2-6.8), $P = 0.72$) and hs-CRP was 2 (0.6-5.5) mg/L. Fasting duodenal pH correlated with gastric emptying for liquids ($r = 0.59$, $P = 0.02$). Gastric

emptying for solids correlated with both duodenal paracellular passage ($r = 0.62$, $P = 0.03$) and plasma hs-CRP ($r = 0.57$, $P = 0.03$). In addition, gastric emptying for solids was negatively correlated with the intensity of bloating ($r = -0.53$, $P = 0.04$).

Conclusions: Although delayed gastric emptying for solids is uncommon, duodenal alterations with increased permeability and low-grade systemic inflammation are linked with gastric emptying in FD patients with PDS-symptoms. These data provide further substance for the potential central role of the duodenum in symptom generation and gastric motor abnormalities.

256 | Non-food allergies in functional gastrointestinal disorders

R. Cogliandro¹; V. Stanghellini²; A. M. Morselli-Labate³; S. Del Vecchio¹; C. Chiara²; L. Bellacosa³; C. Cremon⁴; G. Barbara¹

¹Department of Digestive Diseases, Bologna, Italy; ²University of Bologna-St Orsola Hospital, Bologna, Italy; ³Italy, Bologna, Italy; ⁴University of Bologna, Bologna, Italy

Objective: Aim: To evaluate prevalence of food and non-food allergies in functional gastrointestinal disorders (FGIDs)

Materials and Methods: Clinical features and allergies were prospectively investigated in outpatients referred for digestive symptoms. Each patient answered validated questionnaires and underwent both serum and cutaneous allergic tests: IgE and skin prick testing to food and inhalant allergens; patch testing (SIDAPA 40 aptens). FGIDs, were diagnosed according to the Rome III criteria.

Results: Between 2011 and 2014, 1050 patients were consecutively enrolled: 970 with FGIDs ($F = 75.1\%$; 42.8 ± 14.6 years, $m \pm SD$) and 80 with organic diseases ($F = 51.3\%$, 48.7 ± 16.7 years). 718 FGIDs patients (74.0%; $F = 76.7\%$; 41.82 ± 14.3 years) vs 42 organic patients (52.5%; $F = 52.4\%$; 43.7 ± 14.9 years; $P = 0.001$) presented ≥ 1 positive allergic tests. Specifically, 35.3% vs 20.3% for foods ($P = 0.014$); 62.2% vs 44.2% for inhalants ($P = 0.002$); 38.4% vs 23.5% for chemicals ($P = 0.014$); 72.2% vs 49.4% for non-food allergies in general ($P = 0.001$). Only non-food allergies were significantly more frequent in patients with than in those without GERD, functional pain, nausea and vomiting syndromes, and IBS. 78.7% patients with and 69.9% without GERD had ≥ 1 positive allergic tests ($P = 0.002$): 43.1% vs 34.2% for chemicals ($P = 0.004$), 65.8% vs 59.1% for inhalants ($P = 0.046$), 76.7% vs 68.2% for non-food allergies ($P = 0.004$). 82.9% patients with and 71.0% without functional pain had ≥ 1 positive allergic tests ($P = 0.001$): 46.4% vs 35.8% for chemicals ($P = 0.007$), 73.7% vs 58.2% for inhalants ($P = 0.001$), 82.6% vs 68.6% for non-food allergies ($P = 0.001$). A higher frequency of chemical allergies was found in patients with than in those without nausea and vomiting syndromes (53.3% vs 37.3%, $P = 0.019$) and IBS (42.2% vs 31.3%, $P = 0.002$).

Conclusions: Non-food allergies are twice as common as food allergies in FGIDs. Allergies against non-food allergens, unlike those against food allergens are particularly frequent in GERD, IBS, functional abdominal pain, nausea and vomiting syndromes. Cross-reactivity between pollens and vegetal foods and chemical contamination of foods may play a role in the determinism of FGIDs.

257 | Association between gastroesophageal reflux disease (GORD) symptoms and erosive tooth wear (ETW): A prospective cross-sectional case control study

R. Alharthi¹; R. Moazzez¹; D. Bartlett¹; J. Jafari²

¹King's College London, London, United Kingdom; ²Guy's & St. Thomas Hospital, London, United Kingdom

Objective: The most common oral manifestations of patients with GORD symptoms is ETW. The aim of this study is to assess the risk factors associated with developing ETW in patients with GORD symptoms, and to identify the predictive factors for ETW.

Methods: Series of patients assessed for GORD at the Oesophageal-Lab, Guy's Hospital selected who: 1) consented, 2) completed Reflux Symptom Questionnaire 7-day recall (RESQ-7) (frequency and intensity of symptoms); 3) done 24 hour-impedance-pH testing; acid exposure times calculated.

4) ETW assessed using Basic Erosive Tooth Wear Examination (BEWE) (an index dividing mouth into 6 areas, scored 0-3 (0 = no ETW, 1 = initial erosion, 2 = loss of hard tissue <50% of surface area, 3 = loss of hard tissue =>50% of surface area). Those with a cumulative score of >11 and at least 1 oral area scoring 3 were included in ETW group (ETW), the rest in the NETW group (No ETW).

Data analysed using STATA software, mean (SD), t-test analysis and ROC curve analysis were applied. $P < 0.05$ was considered significant.

Results: 121 patients recruited: ETW (n = 64), NETW (n = 57). (Mean±SD) of intensity and frequency of individual symptoms of heartburn, hoarseness and coughing were significantly higher in ETW group: Heartburn intensity(ETW:12.7 ± 0.9 vs NETW:9.7 ± 0.9; $P = 0.03$), frequency(ETW:14.3 ± 1.0 vs NETW:10.3 ± 1.0; $P = 0.007$). Hoarseness intensity(ETW:2.25 ± 0.2 vs NETW:1.32 ± 0.2; $P = 0.004$), frequency(ETW:2.8 ± 0.2 vs NETW:1.5 ± 0.2; $P = 0.0004$). Coughing intensity(ETW:3.0 ± 0.2 vs NETW:1.6 ± 0.2; $P = 0.004$), frequency(ETW:3.5 ± 0.2 vs NETW:1.98 ± 0.2; $P = 0.0001$).

ROC curve analysis of all symptoms: patients with total frequency of >25 and/or total intensity of >36 have more chance of ETW amongst GORD patients.

119/121 patients completed impedance-pH testing, total acid exposure time was significantly higher in ETW(1.48 ± 0.06) patients vs NETW(1.28 ± 0.06); $P = 0.02$.

Conclusions: This study demonstrates three predictive values of developing ETW in GORD patients:

1) Heartburn, hoarseness and coughing as opposed to other reflux symptoms, which may indicate progression of reflux to proximal oesophagus and oral cavity.

2) Abnormal total acid exposure time, regardless of the body position or diurnal changes.

3) Total frequency >25 and/or intensity >36 of all symptoms on RESQ-7.

258 | The diagnostic outcome of high-resolution esophageal manometry (HREM) among Filipino patients with esophageal symptoms from a multicenter, tertiary level hospitals in the philippines

M. J. H. Navarro; S. I. Q. De Ocampo

St. Luke's Medical Center, Institute of Digestive and Liver Diseases, Quezon City, Philippines

Objective: To determine the diagnostic outcome of HREM among Filipino patients presented with esophageal symptoms

Methods: Study Design: Retrospective, cross-sectional

Study Population: Patients referred for evaluation of esophageal motility

Intervention: High-resolution esophageal manometry (HREM)

Results: In this study, total of 103 patients was evaluated using high-resolution esophageal manometry (HREM). Majority of the patients included were females (60.20%) and the mean age was 45.71 years. Most of the patients were referred for HREM because of persistent reflux symptoms despite PPI (59.22%), followed by dysphagia (34.95%).

In relation to the distribution of HREM findings, grouped according to indication for the study. For the entire population, the most common HREM finding was abnormal (64.08%). Majority of patients referred for HREM because of gastroesophageal reflux related disease revealed normal results (53.73%), on the other hand majority of patients referred for HREM because of dysphagia revealed abnormal results (97.22%).

With regards to the proportion and number of the studies that were abnormal, grouped accordingly to each motility disorder. Overall, an abnormal motility occurred in 64.08%. The most common motility abnormality was weak peristaltic disorders in 50.00% followed by EGJ disorder in 45.45%.

Involving patients with abnormal HREM based on study indication. The most common motility disorders based on symptom category were as follows: Dysphagia, Achalasia Type I in 17 out of 35 patients (48.57%) followed by Achalasia Type II in 12 out of 35 patients (34.29%); GERD, Ineffective Peristalsis in 22 out of 31 patients (70.97%) followed by Fragmented Peristalsis in 5 out of 31 patients (16.13%)

Conclusions: This study characterizes the diagnostic outcome of HREM in a five-year experience from a tertiary hospital in the Philippines. Findings in this study suggest most patients referred for

HREM are those with GERD symptoms. This study confirms the overall high prevalence of weak peristaltic disorders and underscores the need to further study the pathophysiology and management of this ubiquitous disorder. The finding of achalasia in 83.33% of our patients with dysphagia is consistent with recent reports regarding the rising incidence of this disorder and underscores the need of prompt motility testing in this population.

	WEAK PERISTALTIC DISORDER			EGJ DISORDER				HYPERTENSIVE PERISTALTIC DISORDER	
	Fragmented Peristalsis	Ineffective Peristalsis	Absent Peristalsis	Outflow Tract Obstruction	Achalasia, Type I	Achalasia, Type II	Achalasia, Type III	JE	DES
Dysphagia n=30 (53.03%)	0 (0.00)	3 (8.57)	2 (5.71)	0 (0.00)	17 (48.57)	12 (34.29)	1 (2.86)	0 (0.00)	0 (0.00)
GERD n=31 (46.97%)	5 (16.13)	22 (70.97)	1 (3.23)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	3 (9.68)
Total N= 66 (100%)	5 (7.58)	25 (37.88)	3 (4.55)	0 (0.00)	17 (25.76)	12 (18.18)	1 (1.52)	0 (0.00)	3 (4.55)

FIGURE. JE, Jackhammer Esophagus; DES, Diffuse Esophageal Spasm.

260 | Opioids consumption in patients referred for functional gastro-intestinal disorders

C. Melchior¹; C. Desprez¹; F. Wuestenberghs²; A.-M. Leroi¹; A. Lemaire³; G. Gourcerol¹

¹Rouen University Hospital, Rouen, France; ²CHU UCL Namur, Yvoir, Belgium;

³Valenciennes Hospital, Valenciennes, France

Objective: Opioids consumption is increasing worldwide. Opioids intake may impact on gastro-intestinal (GI) symptoms, although this has never been studied in patients referred for functional GI disorders (FIGD). We aimed to determine the impact of opioids intake in a FIGD cohort.

Methods: All patients diagnosed with FIGD and referred for GI motility tests in our hospital were evaluated from 2013 to 2019. Irritable bowel syndrome (IBS) and functional dyspepsia (FD) were determined according to Rome criteria. GI symptoms were quantified using a 5 point Likert scale, and constipation severity was specifically measured using the KESS score. Quality of life was quantified by the Quality of Life Index (GIQLI). Anxiety and depression were evaluated using the Hospital (HAD) scale. Patients were categorized as being treated on a chronic basis with either tramadol, step II opioids, step III opioids or as being opioids-free.

Results: 2933 consecutive patients were included. Patients suffered from IBS, FD or both in 37.3%, 64.2% and 24.8%. Among them, consumption of tramadol, step II and step III opioids were 1.8, 1.3 and 0.3% in 2013 and increased to 4.3, 3.4 and 1.9% in 2018 ($P < 0.03$ for each). Tramadol intake was associated with increased vomiting, KESS and IBS-SSS scores. Step III opioids intake was also associated with increased vomiting (table 1), but not with severe constipation compared with patients opioids free.

Conclusions: In FIGD, opioids intake has more than tripled over a 5 year period, and was associated with more severe vomiting scores. Tramadol intake, but not step III opioids, was associated with more severe constipation scores. This may suggests that tramadol-associated constipation is inadequately relieved in our cohort.

	Tramadol (n=124)	Step II opioids (n=63)	Step III opioids (n=37)	Association (n=20)	Controls without opioids (n=2689)	p
Age	53 ± 16	50 ± 13	51 ± 12	55 ± 9	49 ± 17	0.0322
BMI	26 ± 5	28 ± 6*	26 ± 7	28 ± 7	26 ± 57	<0.0001
Female	79%	84%	86%	80%	72%	<0.0001
Functional disorders						0.96
-IBS	-27%	-31%	-26%	-42%	-30%	
-FD	-50%	-48%	-56%	-33%	-51%	
-Both	-23%	-21%	-17%	-25%	-19%	
Vomiting score	0.6 ± 1*	0.6 ± 1.1	1.0 ± 1.1*	0.4 ± 1.0	0.3 ± 0.8	<0.0001
Kess score	15 ± 7*	12 ± 7	14 ± 8	14 ± 6	12 ± 7	0.0355
IBS-SSS	314 ± 98 *	268 ± 110	295 ± 98	247 ± 140	262 ± 105	0.0250
GIQLI	73 ± 19*	77 ± 28	70 ± 22	77 ± 24	84 ± 22	0.0005
HAD anxiety	10 ± 4	10 ± 4	10 ± 5	10 ± 5	10 ± 4	0.74
HAD depression	7 ± 5	7 ± 5	8 ± 4	8 ± 5	6 ± 4	0.03

TABLE 1. Patients' characteristics according to opioids consumption.

262 | High resolution impedance manometry (HRIM) using yogurt (viscosity matched to barium) for bolus clearance after therapy in achalasia

S. Bhatia; A. Karad; S. Sundaram; M. Meshram; L. Sawant; D. Suryawanshi

Seth GS Medical College, Mumbai, India

Objective: Timed barium esophagogram (TBE) is established test for assessing bolus clearance in achalasia post-treatment. However, radiation exposure is an important disadvantage. Esophageal bolus transit can be evaluated by HRIM. Previous studies comparing Impedance bolus height (IBH) using saline and TBE showed fair correlation. We compared bolus clearance by TBE vs HRIM using yogurt (viscosity matched to barium – calculated using Ostwald viscometer) in patients treated for achalasia.

Methods: HRIM was performed using solid-state system (MMS, Netherlands). Twenty patients (age 45.1 y; 8 men) treated with pneumatic dilatation (Rigiflex, Boston Scientific) were evaluated with TBE (200 mL Barium) and HRIM (200 mL yoghurt) two weeks after dilatation. Both tests were performed in upright position. Barium column height and impedance bolus height (IBH) were measured at 0, 1 and 5 minutes. Analysis of IBH was performed with spatial impedance variation plot overlayed on esophageal pressure topography. All patients gave consent, and protocol was approved by the IRB.

Results: At baseline, 5, 11 and 4 patients had type I, II and III achalasia, respectively. Eckardt score showed an improvement of 5 (range 1-9) points. The mean column height as measured by IBH and TBE at 5 minutes was similar (4.6 [range 0-12.5] cm vs 4.25 [0-16] cm). Pearson correlation between the TBE column and IBH was 0.665, 0.759 and 0.729 at 0, 1 and 5 minutes, respectively. Bland Altman plot (Figure 1) for bolus clearance as measured by TBE and HRIM showed good agreement between the modalities.

Conclusions: There is good agreement between HRIM (performed using yoghurt) and TBE for evaluation of bolus clearance after therapy in achalasia patients. Single HRIM study done with viscosity matched liquid to barium can give information about bolus clearance and motor function in treated achalasia patients, avoiding radiation exposure.

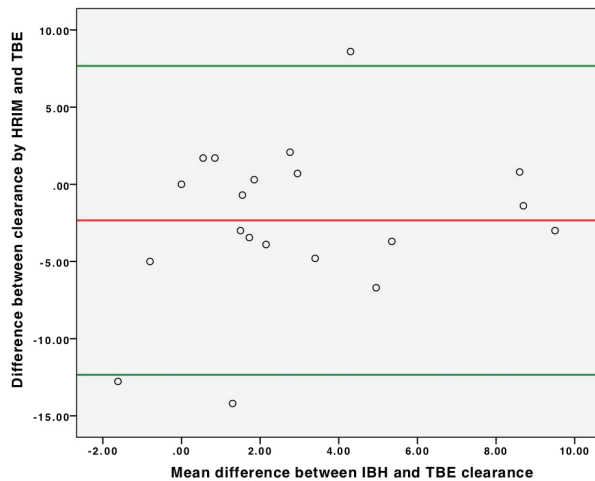


FIGURE 1. Bland Altman plot comparing bolus clearance by HRIM and TBE at 5 minutes.

263 | Effects of astressin 2B and nesfatin-1 on food and water intake in *Suncus murinus*

S. W. Chan¹; Z. Lu¹; I. Sakata²; T. Sakai²; G. Lin³; J. A. Rudd³

¹Caritas Institute of Higher Education, Hong Kong, Hong Kong SAR; ²Saitama University, Saitama, Japan; ³The Chinese University of Hong Kong, Hong Kong, Hong Kong SAR

Objective: Nesfatin-1 induces emesis and reduces feeding in *Suncus murinus* (house musk shrew). In the present studies, we examine if the action of nesfatin-1 to induce emesis and inhibit feeding can be prevented by the corticotropin-releasing factor receptor 2 (CRF₂) antagonist, astressin 2B.

Methods: *Shrews* were anaesthetised with sodium pentobarbitone (40 mg/kg, i.p.) and then stereotactically implanted with a guide cannula into the lateral ventricle. They were allowed 7-days recovery before being fasted overnight and administered astressin 2B (3 nmol, i.c.v.), or saline (5 μ l i.c.v.), 15 minutes prior to nesfatin-1 (5 pmol, i.c.v.), or saline (5 μ l, i.c.v.). Emesis and spontaneous behaviour were measured every h for 6 hours.

Results: Nesfatin-1 predictably reduced food intake, but it failed to emesis ($P < 0.05$, $N = 6-8$). Surprisingly, astressin 2B alone also reduced food intake ($P < 0.05$, $N = 6-8$). As a pretreatment, astressin 2B did not affect the action of nesfatin-1 to suppress feeding ($P > 0.05$, $N = 6-8$). Neither astressin 2B nor nesfatin-1 affected water consumption during the 6 hours assessment period.

Conclusions: Nesfatin-1 can inhibit food intake in the absence of emesis. The action of astressin 2B suggests that CRF₂ is involved in mechanisms of feeding control, but the pathway may be independent of nesfatin-1 receptor systems. The studies were fully supported by a grant from the Research Grants Council of the Hong Kong SAR, China (Project no. UGC/FDS11/M02/16).

264 | Mast cell stabilizers can serve as “co-analgesics” in acute and chronic pancreatitis

H. Steenfadt; S. Klauss; S. Schorn; H. Friess; Güralp. O. Ceyhan; I. E. Demir

Department of Surgery, Klinikum rechts der Isar, Technical University of Munich, Munich, Germany

Objective: Severe abdominal pain is the leading symptom of acute (AP) and chronic pancreatitis (CP). We could recently show that neuropathic pain in CP is linked to perineural accumulation of activated mast cells. Therefore, we now hypothesized that inhibition/stabilization of mast cells may lead to improvement of pancreatitis-associated pain and tested mast cell stabilizers (i.e., ketotifen and cromoglycate) as potential “co-analgesics” in AP and CP.

Methods: Repetitive i.p. injections of cerulein were applied to C57BL/6 mice for inducing AP or CP, and mice were randomized into six different groups receiving either 1) vehicle, 2) ketotifen, 3) cromoglycate, 4) ketotifen+metamizole, 5) cromoglycate+metamizole or 6) metamizole alone. All drugs were applied s.c. and orally in combination with metamizol either prior to pancreatitis induction (prophylactically) or from the second week of pancreatitis induction (therapeutically). To assess pain, abdominal mechanosensitivity at the abdominal area was assessed via von Frey filaments.

Results: In the dosage finding study, the effective analgesic dosages were identified (metamizol: 500 mg/kg KG; ketotifen: 10 mg/kg KG; cromoglycate: 500 mg/kg KG). Importantly, AP- and CP-mice treated with ketotifen or cromoglycate *alone* displayed only a slight reduction of pain scores. A moderate analgesic effect was detectable in AP- and CP-mice treated with metamizol. Strikingly, the combined administration of ketotifen or cromoglycate with metamizol led to prominent reduction in the von Frey scores at the abdominal area in both AP and CP, with more increasing effect during the later phase of disease progression.

Conclusions: Mast cell stabilizers may be considered as novel „co-analgesics“ in the treatment of pancreatitis-associated pain. Further

prospective, randomized controlled trials with patients with CP were urgently needed to check a possible translation of this effect from murine to human CP.

265 | Irritable bowel syndrome and bladder pain syndrome comorbidities are associated with altered quality of life, anxiety, depression and sleep in patients with functional dyspepsia

F. Wuestenberghs¹; M. Baron²; C. Melchior³; C. Desprez⁴; J.-N. Cornu²; A.-M. Leroi⁵; G. Gourcerol⁴

¹Department of Hepato-Gastroenterology, CHU UCL Namur, Godinne University Hospital, UCLouvain, 5530 Yvoir, Belgium; ²Department of Urology, Rouen University Hospital, UNIROUEN, Normandie University, F-76000 Rouen, France; ³Department of Gastroenterology, Rouen University Hospital, INSERM Unit 1073, UNIROUEN, Normandie University, F-76000 Rouen, France; ⁴Department of Physiology, Rouen University Hospital, INSERM Unit 1073, UNIROUEN, Normandie University, F-76000 Rouen, France; ⁵Department of Physiology, INSERM CIC-CRB 1404, Rouen University Hospital, INSERM Unit 1073, UNIROUEN, Normandie University, F-76000 Rouen, France

Objective: Functional dyspepsia (FD) and irritable bowel syndrome (IBS) are known to overlap. However, the impact of overlap between bladder pain syndrome (BPS) and FD remains unknown. Our aim was to evaluate the presence and the impact of IBS and/or BPS in FD patients.

Methods: 1598 consecutive patients with investigated dyspeptic symptoms were studied. FD and IBS were diagnosed according to Rome criteria. Presence of BPS was assessed using NIDDK 2006 criteria. Quality of life was quantified by the Gastrointestinal Quality of Life Index (GIQLI). Anxiety and depression were evaluated using the Hospital Anxiety and Depression (HAD) scale. Sleep was assessed using the Pittsburgh Sleep Quality Index (PSQI) and the Insomnia Severity Index (ISI).

Results: Among all dyspeptic patients, 892 patients fit Rome criteria for FD. 476 fit only criteria for FD (FD-only), 200 fit both FD and IBS criteria (FD+IBS) and 122 fit both FD and BPS criteria (FD+BPS). 94 fit all criteria for FD, IBS and BPS (FD+IBS+BPS). 430 patients were free of diagnostic criteria for FD, IBS and BPS and served as a control group. Age differed among the groups ($P = 0.0002$), patients with IBS being younger. Female predominance increased with increasing comorbidities ($P < 0.0001$). QIQLI score in the control group was 95.6 and was decreased in FD-only patients (84.1; $P < 0.0001$), in FD+IBS (74.4; $P < 0.0001$) and FD+BPS patients (75.5; $P < 0.0001$) compared to FD-only patients and was further decreased in patients with FD+IBS+BPS patients (63.7; $P < 0.0001$) (Figure 1). The HAD scale increased with the number of diagnostics (13.6 in the control group; 15.2 in FD-only patients; 16.5 and 16.9 in FD+IBS and FD+BPS patients respectively; 19.7 in FD+IBS+BPS patients; $P < 0.0001$). PSQI and ISI scores also increased with the number of diagnostics, with the poorest quality of sleep observed in patients with FD+IBS+BPS.

Conclusions: Overlaps between FD and IBS and/or BPS are frequent, since IBS was present in 33% and BPS in 24% of FD patients

respectively. Associated diagnosis of IBS and BPS decreased quality of life, altered anxiety-depression scale and were associated with altered sleep in patients with FD.

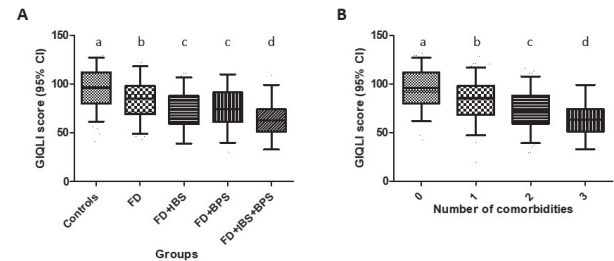


FIGURE 1. Comparisons of the mean GIQLI score (whiskers with 95% CI) between different diagnostic groups (A) and between groups of increasing number of comorbidities (none, FD, IBS and BPS) (B). Groups without common letters significantly differ ($p < 0.0001$). BPS: Bladder Pain Syndrome; CI: Confidence Interval; FD: Functional Dyspepsia; GIQLI: Gastrointestinal Quality of Life Index; IBS: Irritable Bowel Syndrome.

267 | Early life experiences and development of irritable bowel syndrome: A systematic review

K. T. H. Siah; S. Low

National University Hospital, Singapore, Singapore

Objective: Early-life experiences can have lifelong consequences on health and disease. Childhood experiences had been associated with the development of Irritable bowel syndrome. We aimed to systematically review the risk factors and protective factors associated with IBS development.

Methods: A computer-assisted search of the PubMed database from 1966 to 2018 was performed. Using medical subject heading (MeSH) and title words for the "Irritable Bowel Syndrome"[Mesh] OR "Colonic Diseases, Functional"[Mesh] AND "risk" OR "risk factors," AND "Infant"[Mesh] OR "Perinatal Care"[Mesh] OR "Prenatal Care"[Mesh] OR "Mothers"[Mesh] OR "Maternal Exposure"[Mesh] OR "Maternal-Child Nursing"[Mesh] OR "Maternal-Fetal Exchange"[Mesh] OR "Maternal Behavior"[Mesh] OR "Maternal Health"[Mesh] OR "Mother-Child Relations"[Mesh] OR "Maternal-Fetal Relations"[Mesh] OR "Child"[Mesh] OR "Child Care"[Mesh]. Reference lists of relevant articles were reviewed for additional citations. The selection criteria were: (a) studies conducted in adolescents or adults with IBS that (b) investigate premorbid factors occurring specifically during the perinatal and childhood period as well as parental factors and are (c) associated with the development of IBS.

Results: The initial search of the PubMed database yielded 77 articles. Thirty-three articles met the inclusion criteria. The studies were categorized into 3 categories: Parental, Perinatal and Childhood. There were 3 protective factors identified: parental emotional warmth, old maternal age at delivery and high protein foods during childhood. Parental risk factors for IBS included young maternal age,

parental history of IBS, psychological traits like anxiety or depression, parental history of mental illness or substance abuse and childhood parental deprivation. Perinatal risk factors for IBS included low birth weight, gastric suction at birth and birth by Caesarian section. Childhood risk factors of IBS included 1) History of gastroenteritis: Salmonella infection, antibiotic use, lasting more than 7 days or weight loss more than 10 pounds. 2) History of abuse: emotional, sexual or physical. 3) Psychological traits: anxiety, depression 4) Affluent childhood environment 5) Poor sleep 6) Antecedent allergic diseases.

Conclusions: More studies need to explore the parental and perinatal influence on the development of IBS. A prospective birth cohort will provide valuable insight into the role of early life experiences in IBS.

270 | Intestinal resident macrophages refine connectivity in the enteric nervous system

M. F. Viola; S. De Schepper; S. Verheijden; P. V. Berghe; G. Boeckxstaens

KU Leuven, Leuven, Belgium

Objective: CX3CR1^{high} macrophages in the muscularis externa (MMØ) are closely associated to neurons in the myenteric plexus, regulate peristalsis through BMP-2 secretion and have been shown to clear apoptotic neurons. This study aims to elucidate whether MMØ also participate in neuronal network refinement.

Methods: *Wnt1.Cre^{+/-} Tomato^{LSL/wt}Cx3cr1^{GFP/wt}* transgenic mice were used to live-image the interaction between CX3CR1^{high} MMØ and WNT1⁺ neurons in the enteric nervous system (ENS). Developmental pruning of synapses was analysed by quantification of pre-synaptic machinery (Synapsin I+) engulfed by MMØ, using Imaris-based image analysis. Neuronal phagocytosis by MMØ in the myenteric plexus was evaluated during development (2 weeks) and adulthood (8-12 weeks) in *Wnt1.Cre^{+/-} Tomato^{LSL/wt}Cx3cr1^{GFP/wt}* mice using flow cytometry. Finally, MMØ were selectively depleted using anti-CSF1R during early development, weaning and adulthood and the effect of depletion on the ENS was evaluated through immunohistochemistry.

Results: Using ex-vivo live-imaging we demonstrated transient and dynamic filopodial contacts between MMØ and neurons in the myenteric plexus. During postnatal development, synaptic pruning by MMØ was shown to be significantly higher at P21 and at 8 weeks of age ($P < 0.0001$, $n = 3$). In the small intestine, phagocytosis of neurons by MMØ was found to be significantly higher during development ($18 \pm 2\%$ tdTomato+ MMØ, $n = 3$) compared to adulthood ($9 \pm 2\%$; $P = 0.01$, $n = 3$). In line, depletion of MMØ during development led to a significant increase in neurons ($17 \pm 6\%$; $P = 0.005$, $n = 3$) in α CSF1R-treated mice compared to controls as evaluated at P21. In contrast, depletion in adulthood significantly reduced the number of enteric neurons.

Conclusions: MMØ shape neuronal connectivity and ENS maturation during postnatal development through synaptic refinement and neuronal phagocytosis while in adulthood MMØ protect and support enteric neurons. These findings demonstrate the plasticity of MMØ to adapt their function according to the environmental and developmental needs and illustrate their crucial role in the maintenance of the ENS.

271 | Infantile achalasia: Spontaneous resolution case report

C. R. Bingham; M. Mutalib

Evelina London Children's Hospital, London, United Kingdom

Objective: Achalasia is a rare disorder in infants and can be mistaken for other conditions such as gastro-oesophageal reflux. Case reports available in literature mainly cover cases where the patient has been treated surgically with myotomy and there is no literature on spontaneously resolving cases in infants or children. A single case of surgically induced Type III achalasia in an adult patient that resolved without treatment has been reported.

Methods: A patient presented at 8 months of age to their local hospital with vomiting of all liquids and solids following weaning, resulting in significant weight loss and failure to thrive. A barium swallow test showed distal narrowing and a distended oesophagus so the patient was transferred to a tertiary centre. An oesophageal manometry at 14 months of age revealed aperistalsis and an increased lower oesophageal sphincter pressure, leading to a diagnosis of Type I achalasia. Endoscopy, histology and basic metabolic workup were negative. Regular gastroscopies with three oesophageal dilations followed, providing immediate, but not long-term relief from vomiting. Vomiting continued to be reported whenever thicker textures than a puree were introduced.

Results: Following parental reports of a reduction in symptoms despite eight months having elapsed since the patient's last dilatation and improved tolerance for lumpier and thicker textures, a second oesophageal manometry was undertaken at 28 months of age. The oesophageal manometry clearly showed evidence of intact oesophageal motor activity and an appropriately relaxed lower oesophageal sphincter (normal IRP). A comparison of the oesophageal manometries performed at 14 and 28 months can be found in Figure 1.

Conclusions: To the best of our knowledge, this is the first reported case of spontaneously resolving infantile achalasia. Increasing use of high resolution manometry may yield a greater number of infantile achalasia diagnoses and it is clear that these investigations should be repeated where possible to ensure that spontaneous resolutions are not missed in cases that are conservatively managed.

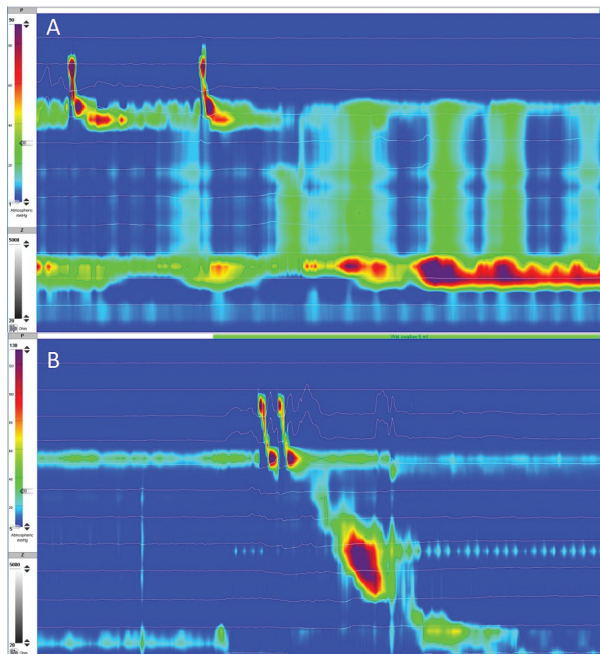


FIGURE 1. High resolution manometry images taken at 14 months (A) and 28 months (B) of age.

273 | Clinical utility of high-resolution-esophageal-manometry with a solid test meal. A cross sectional study

J. Arguero¹; K. G. Zermeno²; M. A. Balmori²; O. R. Aguilera²; A. M. Conejo²; M. Marcolongo¹; J. M. R. Troche²

¹Hospital Italiano de Buenos Aires, Buenos Aires City, Argentina; ²Instituto de Investigaciones Médico Biológicas, Veracruz, Mexico

Objective: Esophageal motility disorders are diagnosed based on the Chicago Classification (CC v3.0) which protocol uses 10 (5 mL) single water swallows (SWS). Provocative tests have been used to increase the diagnostic yield. Recently, Fox M. et al have proposed

the use of a solid test meal (STM) to assess esophageal physiology better during eating. Using this protocol, new parameters are also proposed: IRP > 25 mm Hg to diagnose OGJ-obstruction, DCI > 1000 mm Hg.cm.sec for diagnose ineffective esophageal motility (IEM). This new classification is known as Chicago adapted for solids (CC-S).

The objective of this study is to establish normal values (NV) of the STM as well to evaluate its clinical utility in a group of hispanic patients with esophageal disorders.

Methods: Twenty five healthy controls (HC) (60% men, mean age 25 ± 5) and 118 patients (61% women, mean age 52.4 ± 5) who were referred to Gastrointestinal Motility Units (Mexico and Argentina). All patients underwent HRM following the conventional protocol and then, incorporated a STM (200 g of rice). During the STM we evaluated: #of swallows, amount of rice consumed, time of consumption, number of effective swallows, effective contractions per minute, percentage of effective swallows, #of TLESRs, and #of belches. Diagnoses established with CCv3.0 were compared with diagnoses according to the CC-S.

Results: Ninety percent of HC completed the STM and NV are shown in the Table. Diagnoses in patients were: normal 43% (n = 51), IEM 41% (n = 48), achalasia 8% (n = 9), OGJ-obstruction 3% (n = 4), absent peristalsis 2.5% (n = 3), 2% (n = 2) distal esophageal spasm and 1% (n = 1) jackhammer.

Rice consumption by swallow was lower in patients with aperistalsis < IEM < OGJ-obstruction < achalasia < hypercontractile disorders < HC ($P < 0.05$). STM diagnosed more major motility disorders than SWS (20% vs. 15%, $P = 0.45$) and changes the manometric diagnosis in 42% of the cases. In 50% (n = 24) of the cases with IEM diagnoses, the STM reveal a normal peristalsis. STM diagnoses more Jackhammer esophagus compare to SWS.

Conclusions: Our results support the use of a STM for the detection of major motility disorders. Many individuals with IEM on SWS had normal motility on STM. These findings provide strong evidence that the STM can increase diagnostic yield.

TABLE. Solid test meals in healthy controls and esophageal diseases

	Healthy controls n=25	Achalasia n=9	IEM n=48	EGJ obstruction n=4	Absent peristalsis n=3	Hipercontractile disorders n=3	p Value
Number of subjects completing SMT in 8 minutes	90%	22%	17%	25%	0%	33%	0.02
Time of consumption (minutes)	7.1 ± 1.29	8.8 ± 0.6	8.8 ± 2.2	9.5 ± 2.3	8.0 ± 1	7.6 ± 0.5	0.10
Rice consumption(g)	166 ± 45	109 ± 72	115 ± 58	130 ± 47	34 ± 7	161 ± 3	0.02
Rice consumption by time (g per minute)	25.3 ± 11	21.4 ± 30	13.6 ± 7.8	14 ± 6	4.2 ± 0.9	22 ± 5.9	0.001
Rice consumption by swallow (g per swallow)	9.1 ± 3.7	10.3 ± 12	10.6 ± 8	7.3 ± 1.9	1.9 ± 0.4	10.4 ± 2	0.018

275 | Small intestine neuromuscular dysfunction in a mouse model of dextran sulfate sodium-induced colitis: Involvement of toll-like receptor-4

S. Cerantola¹; I. Marsilio¹; V. Caputi¹; E. Salviato¹; M. Ridolfi¹; S. Zuanetti¹; M. Bistoletti²; C. Giaroni²; A. Bertazzo¹; M. C. Giron¹

¹University of Padova, Padova, Italy; ²University of Insubria, Varese, Italy

Objective: Enteric commensal bacteria play a crucial role in the pathogenesis of inflammatory bowel disease (IBD), a group of recurring debilitating inflammatory conditions, triggered by inappropriate activation of the immune system by gut microbiota. IBD-associated specific mutations include genes involved in microbial recognition, such as mutations in the Toll-like receptor 4 (TLR4). In this study, we aimed to assess the impact of TLR4 signaling on the structural and functional integrity of enteric nervous system (ENS) in a model of dextran sulfate sodium (DSS)-induced colitis.

Methods: Male TLR4^{-/-} mice (8 ± 1 weeks old; N = 32 mice) received 1.5% DSS in their drinking water for 5 days, then switched to regular drinking water for 3 days. Inflammation was measured using the disease activity index and by histologic analysis of intestinal tissues. Changes in ileal muscle tension were isometrically recorded following: i) electric field stimulation (EFS, 10 Hz); ii) addition of 30 μM serotonin (5-HT) with or without 0.1 μM ondansetron (5-HT3R antagonist). Plasma levels of 5-HT were measured by HPLC with fluorescence detection. Distribution of neuronal (HuC/D and nNOS), glial (GFAP) and 5-HT3R markers was determined by immunofluorescence in longitudinal-muscle-myenteric plexus whole-mounts (LMMPs).

Results: In vitro contractility studies in TLR4^{-/-} mice showed a significant reduction in 5-HT-induced excitatory response (~50%, N = 8, *P* < 0.001), sensitive to ondansetron (N = 8, *P* < 0.001), and a 1.9-fold increase of neuronal cholinergic transmission (at 10 Hz; N = 8, *P* < 0.01) after DSS treatment. Changes in ENS neurochemical coding were evidenced by the reduction of nNOS⁺ neurons (~32%, N = 5; *P* < 0.05) with a proportional increase of HuCD⁺ neurons, together with a slight but not significant reduction of 5-HT3R and GFAP immunofluorescence in DSS-treated TLR4^{-/-} LMMPs. A marked increase in 5-HT plasma levels (15 ± 5%, N = 5; *P* < 0.05) was found after DSS treatment.

Conclusions: In mice, TLR4 signaling influences the severity of small intestine inflammation as well as ENS structure and neurochemical coding, affecting cholinergic- and serotonergic-mediated neuromuscular function.

276 | Intraintestinal delivery of tastants using a naso-duodenal-ileal catheter does not influence food intake or satiety

T. Klaassen; A. M. E. Alleleyn; M. Van Avesaat; F. J. Troost; D. Keszthelyi; A. A. M. Masclee

Maastricht University, Maastricht, The Netherlands

Objective: Intraduodenal activation of taste receptors has been shown to increase satiety and reduce food intake. Taste receptors are expressed throughout the whole gastrointestinal (GI) tract. Currently it is unknown, whether the effect of taste receptor activation to influence satiety and food intake is more pronounced in the proximal or distal GI tract.

The aim of the present study was to investigate the effects of intra-duodenal- vs intraileal infusion of a tastant mixture (sweet, bitter, and umami) on food intake and satiety feelings.

Methods: Fourteen healthy volunteers (11 female, age 25.6 ± 10.5 years, mean BMI 22.3 ± 1.7 Kg/m²) were intubated with a naso-duodenal-ileal catheter. In a single-blind randomized controlled trial, participants received four regimens on consecutive test days: duodenal placebo and ileal placebo (DPIP), duodenal tastants and ileal placebo (DTIP), duodenal placebo and ileal tastants (DPIT), duodenal tastants and ileal tastants (DTIT). On test days, 150 minutes after a standardized breakfast, mixtures were infused for 60 minutes. Fifteen min after cessation of infusion, participants received an *ad libitum* pasta meal and food intake was measured. Visual analogue scales (VAS) scores for satiety feelings and GI symptoms were collected over the course of the test day.

Results: Intraintestinal infusion of the tastant mixture did not alter food intake compared with intraintestinal infusion of placebo (DPIP: 786.6 ± 79.2 kcal, DTIP: 803.3 ± 69.0 kcal, DPIT: 814.7 ± 77.3 kcal, DTIT: 834.8 ± 59.2 kcal, *P* 0.59). No differences in VAS scores for satiety feelings and GI symptoms were observed.

Conclusions: Within the setting of the present study, infusion of a tastant mixture into the duodenum and/or the ileum using a naso-duodenal-ileal catheter did not influence food intake or satiety feelings. It is possible that the burden of the four-day naso-duodenal-ileal intubation masked a small effect that tastants might have on food intake and satiety.

278 | Prevalence and impact of self-reported constipation in the general population

J. Pannemans¹; K. Van Den Houte¹; B. Fischler²; H. Piessevaux³; F. Carbone¹; J. Tack¹

¹KU Leuven, Leuven, Belgium; ²CHU Saint-Pierre, Brussels, Belgium; ³Cliniques Universitaires Saint-Luc, Sint-Lambrechts-Woluwe, Belgium

Objective: Chronic constipation (CC), as defined by the Rome IV criteria, is a highly prevalent functional bowel disorder. However, as the criteria impose strict diagnostic thresholds, the prevalence of self-reported constipation is considerably higher, and there is major overlap

with other bowel disorders, especially irritable bowel syndrome. We therefore conducted a pooled-analysis to evaluate the presence of self-reported constipation in the general population, its association with other bowel symptoms and its health-economic impact.

Methods: We used an internet survey (Medistrat internet panel, representative of the adult population) to collect information on bowel symptoms' prevalence and their impact. In this analysis, we focused on patients who reported constipation symptoms over the last 12 months. First, we compared participants who experienced constipation to those who reported other bowel symptoms. Second, subjects reporting constipation were subdivided in painful constipation (PC), and those who did not experience abdominal pain (NPC).

Results: 1012 subjects (mean age 45.2 ± 0.5 years, 62% females), of whom 217 (21%) reported constipation, completed the survey. Subjects reporting constipation experienced more other bowel symptoms than those without constipation [3 (2-6) vs 2 (1-4), $P < 0.0001$]. The constipation group reported higher prevalence of abdominal pain, altered stool frequency, alternating bowel habits and bloating (all $P < 0.05$). Further, constipated subjects reported higher symptom occurrence ≥ 3 days per month (65.9% vs 52.9%; $P < 0.01$). Of those with constipation, 134 patients reported NPC compared to 83 patients with PC. More patients with NPC compared to PC marked constipation as their most bothersome symptom (75% vs 44%, $P = 0.014$). In addition, excessive gas was experienced more frequently in the NPC compared to the PC group (64% vs 39%, $P = 0.044$). PC patients also reported more consultations with a medical doctor (40.24% vs 14.29%, $P < 0.0001$), and more visits to specialists (50% vs 10%, 95% CI 1.8-44.9), but not to general practitioners or other doctors in the past 12 months.

Conclusions: Self-reported constipation, often associated with other bowel symptoms, is a highly prevalent condition in the general population. Especially when abdominal pain is present, this generates major healthcare costs.

279 | Naloxegol partly restores changes in the postprandial cyclic meal response of the colon in a randomized three-way crossover high-resolution colon manometry study in healthy volunteers

J. Pannemans¹; I. Demedts²; H. Geysen¹; A. Pauwels¹; T. Vanuytsel¹; J. Tack¹

¹KU Leuven, Leuven, Belgium; ²UZ Leuven, Leuven, Belgium

Objective: Opioid induced constipation (OIC) is a highly prevalent condition amongst patients treated with opioids for chronic pain. Constipation and other gastrointestinal side effects can be as prevalent as 40-90% resulting in non-compliance and quality of life reduction. The effects of opioids on colonic motor function and their reversal by opioid antagonists have been poorly studied. We therefore conducted a crossover trial to study effects of codeine and the peripheral μ -opioid receptor antagonist naloxegol on colonic manometry patterns in healthy volunteers (HV).

Methods: On each of three study visits, participants underwent a colonoscopy (conscious sedation with midazolam) after half-standard PEG preparation for colonic manometry catheter (40-sensor high-resolution manometry catheter 2.5 cm spacing, Laborie) placement. Colonic motility was evaluated during 2 hours after a standardized bread meal (645 kcal). After waking up, HV received naloxegol (25 mg)/placebo, placebo/codeine (60 mg followed by 30 mg one hour postprandial) or naloxegol/codeine by oral administration in a randomized, double-blind crossover fashion. The data were analysed using mixed-models analysis in SAS with post-hoc analysis after correction for multiple testing.

Results: Ten HV [3 male, aged 26.5 (range 20-63) years] finalized all three study visits.

Data on motor pattern prevalence are presented in Table 1 [data are reported as median (interquartile range). (a) $P < 0.01$ vs placebo/codeine, (b) $P < 0.05$ vs placebo/codeine, (c) $P < 0.05$ vs naloxegol/placebo]. Long antegrade propagating waves (PW) were significantly decreased in the codeine/placebo compared to codeine/naloxegol condition. No significant differences were found for short antegrade PW or short retrograde PW. The postprandial cyclic patterns were significantly altered by the treatment condition. First, the cyclic antegrade PW were lower in the placebo/codeine compared to the naloxegol/placebo and naloxegol/codeine treatment. Second, the cyclic retrograde were significantly more frequent in placebo/codeine compared to the two other treatment groups. Finally, significantly less cyclic simultaneous PW were present in the naloxegol/placebo vs placebo/codeine condition.

Conclusions: Codeine administration increased cyclic retrograde activity and decreased cyclic antegrade activity in the postprandial period and this effect was reversed by naloxegol. These observations enhance our understanding of the mechanism of OIC and its treatment with peripheral μ -opioid receptor antagonists.

	Naloxegol/ Placebo	Placebo/ Codeine	Naloxegol/ Codeine	p-value main effect
Short antegrade	3.0 (2.00-5.50)	2.5 (1.00-4.50)	4.0 (2.00-7.00)	0.307
Short retrograde	6.0 (2.75-15.00)	3.5 (2.00-4.00)	4.0 (3.25-7.75)	0.544
Long antegrade PW	2.0 (0.75-7.00)	1.5 (0-3.00)	3.5 (2.00-12.00) ^a	0.005
Cyclic antegrade PW	14.5 (7.25-21.75) ^b	7.0 (3.75-13.50)	15.0 (5.25-23.00) ^b	0.013
Cyclic retrograde PW	43.5 (20.75-65.00) ^b	78.0 (43.50-84.50)	37.5 (17.75-52.75) ^{a,c}	0.003
Cyclic simultaneous PW	7.0 (2.25-16.25) ^a	17.5 (6.25-50)	10.0 (5.25-13.00)	0.006
Simultaneous PW	3.0 (0.75-6.50)	2.0 (0.75-3.25)	2.5 (2.00-7.25)	0.361

PW: pressure wave

FIGURE. Overview of colonic motor pattern prevalence in the postprandial period after codeine and naloxegol administration. Data are reported as median (interquartile range). [a] $p < 0.01$ vs. placebo/codeine [b] $p < 0.05$ vs. placebo/codeine [c] $p < 0.05$ vs. naloxegol/placebo.

281 | Peroral endoscopic myotomy effect on esophageal motility – Experience of a tertiary portuguese center

R. Mendo¹; C. Félix¹; J. P. Rodrigues¹; P. Barreiro¹; E. Pires²; C. Chagas¹

¹Centro Hospitalar Lisboa Ocidental, Hospital de Egas Moniz, Lisboa, Portugal;

²Hospital da Luz, Lisboa, Portugal

Objective: Peroral endoscopic myotomy (POEM) is a novel endoscopic therapy recently introduced for the treatment of achalasia. The aim of this work is to evaluate the changes occurred in esophageal motility after POEM in patients with achalasia.

Methods: Eighteen patients with achalasia (4 patients with subtype I; 12 patients with subtype II; and 2 patients with subtype 3) from a tertiary Portuguese center underwent POEM from May of 2017 until December 2018. Esophageal motility of all patients was evaluated preoperatively and 3 months after POEM using high-resolution manometry, which was performed with a measurement of the lower esophageal sphincter (LES) resting pressure followed by ten water swallows. Eckardt score was used to assess symptoms severity, being measured preoperatively, 1 month and 3 months after POEM. Statistical analysis was performed using SPSS.

Results: In liquid swallows all the parameters of LES resting pressure, integrated relaxation pressure (IRP), and intra-bolus pressure (IBP) decreased between pre- and post-POEM patients ($P < 0.05$). IRP decreased significantly from 31.6 ± 8.2 mm Hg before POEM to 14.4 ± 2.9 mm Hg after POEM ($P < 0.05$). Panesophageal pressurization after POEM was present in 8.3% ($n = 1$) of patients with subtype II achalasia. Symptom improvement was demonstrated by a preoperatively, 1 month post-POEM and 3 months post-POEM Eckardt score $\pm$ standard deviation of 7 ± 2.4 ; 0.4 ± 0.7 and 0.6 ± 0.98 respectively.

Conclusions: POEM significantly reduced LES resting pressure and symptom severity assessed by the Eckardt score. The changes occurred in IRP correlated with the decreases of the Eckardt score.

282 | Microbiome analysis of small intestinal bacterial overgrowth patients including post helicobacter pylori eradication treatment

T. T. Perets¹; O. Ashorov¹; D. Hamouda¹; S. B. Simon²; D. Boltin¹; I. Dotan¹; O. Koren²; R. Dickman¹

¹Gastroenterology Laboratory, the Division of Gastroenterology RMC and Sackler Faculty of Medicine TAU, Petah Tikva, Israel; ²Microbiome Research Lab BIU, Zefat, Israel

Objective: The gastrointestinal (GI) tracts of humans are among some of the most densely populated environments for microbes. These microbial populations play an important role in maintaining normal GI function and preventing GI disorders. Although not much is known about the involvement of the GI microbiota in inducing small intestinal bacterial overgrowth (SIBO), it is believed that a dysbiotic flora may increase the likelihood of the syndrome. Our

objective was to investigate and describe the microbiota population of SIBO positive vs SIBO negative patients.

Methods: We enrolled 55 patients with SIBO symptoms including abdominal bloating and gas, 39 female and 16 male, of mean age 53 ± 17 years and of mean BMI 25 ± 4 . All patients performed SIBO hydrogen breath test and stool was collected from them for microbiome analysis.

Results: Out of the 55 patients, 42 [76.4% (13 male and 29 female)] were diagnosed as SIBO positive and 13 [23.6% (3 male and 10 female)] as SIBO negative. Microbiome analysis revealed mild differences ($q = 0.025$) between positive and negative patients presented by one strictly anaerobic genus *Methanobrevibacter* of the *Methanobacteriaceae* present in the SIBO negative patients. Further evaluation revealed a subgroup of 7 [12.7%] patients (2 SIBO+ and 5 SIBO-) who were treated previously for *Helicobacter pylori* (1st line successful treatment). Analysis of their microbiome demonstrated a completely different diversity ($q = 0.001$) of phyla in two levels when compared to the other 48 patients.

Conclusions: It is apparent that SIBO positive patients differ from SIBO negative in their diversity of microbiome. Previous studies confirm that antibiotic administration can result altering composition of GI taxa and function. Our results agree with this evidence in that first line treatment for *Helicobacter pylori* eradication triggers dysbiosis.

283 | When can you treat gord by loosening los?

I. Miah¹; S. Alavi²; G. Sui¹; T. Wong¹; S. Zeki¹; J. Jafari¹

¹Guy's Hospital London, London, United Kingdom; ²Kingston University London, London, United Kingdom

Objective: Introduction: A group of patients with gastro-oesophageal reflux disease (GORD) coexist with oesophagogastric outflow obstruction (OGJOO). Treatment of GORD in these patients may require a different approach as opposed to other patients.

Aim of this study is to investigate the mechanism of GORD in OGJOO.

Methods: Patients undergone 24 hour impedance-pH monitoring and high-resolution manometry between 2015-2018 screened. Patients diagnosed with GORD selected and categorised into: 1) GORD-O with concurrent OGJOO, 2) GORD-N with normal oesophageal body motility as defined by the Chicago classification[1].

Results: In total, 66 patients were recruited: 28 patients in GORD-O (F:M = 21:7; age 45-80 years) and 38 patients in GORD-N (F:M = 27:11; 21-78 years).

Ratio of acid exposure time per acid reflux episode was significantly higher in GORD-O (8.0 mins/episode vs 3.1 mins/episode, $P = 0.0215$). GORD-N showed significantly higher acid reflux count (47.2 vs 32.1, $P = 0.0036$).

There was no statistically significant difference between GORD-O and GORD-N for: total acid exposure time, Clearance Time Percent on pH (9.3% vs 10.2%, $P = 0.2372$) and; acid exposure time (121.1mins vs 139.24, $P = 0.1536$) subsequently.

Conclusions: Since both in GORD-O and GORD-N total acid exposure time was not significantly different, having significantly lower number of reflux events in GORD-O indicates that the dominant cause for GORD here is indeed prolonged acid exposure. Treatment of reflux in GORD-O would therefore be by facilitating oesophageal clearance ie reducing LOS pressure rather than conventional antireflux surgeries. A further study to follow-up both objective and subjective improvement of GORD after reduction of LOS pressure in GORD-O patients can further confirm the findings of this study. Small sample size is one limitation of this study.

284 | Is there any link between oesophageal hypomotility small intestinal bacterial overgrowth?

M. De Silva¹; A. Wolak¹; S. Zekin¹; S. Alavi²; J. Jafari¹

¹Guy's Hospital London, London, United Kingdom; ²Kingston University London, London, United Kingdom

Objective: It is known that Small Intestinal Bacterial Overgrowth (SIBO) is linked with gut hypomotility as well as long term use of acid suppressants. However, due to difficulties for investigating small intestinal motility, identifying the underlying cause for SIBO in patients remains mainly unknown and speculative.

The aim of this study is to investigate the relation of oesophageal motility findings with SIBO, as an indicator of gut hypomotility.

Methods: Patients who completed: oesophageal high resolution manometry, lactulose test (for SIBO) and 24 hour impedance-pH reflux monitoring from June 2017 to Dec. 2018 selected. Diagnoses were made based on: Chicago classification for oesophageal motility disorders v3 [1], the North American consensus guideline for Hydrogen and Methane breath testing 2017 [2], and the Lyon consensus on reflux monitoring 2017 [3]. Statistical analysis tool: GraphPad Prism: ROC-analysis, two tailed Fisher's exact test and demographic analysis. Significant *P* value: < 0.05.

Results: 71 patients completed both HRM and SIBO testing (F:M = 46:25, median age 49, 25-70 years old). 25/71 patients were diagnosed with SIBO out of whom 17 (68%) had also ineffective oesophageal motility, 6 (24%) normal oesophageal motility and 2 (8%) oesophagogastric outflow obstruction.

57 patients completed both 24 hour reflux monitoring and SIBO test. 20/57 diagnosed with SIBO; GORD in 5/20 confirmed (20%). ROC curve analysis: distal contractile integral (DCI) < 450 mm Hg.cm.s has a sensitivity of 63.64% and specificity of 52% in predicting SIBO (95% CI: 47%-77%).

SIBO was significantly associated with IOM than with normal motility (*P* < 0.004). Majority of SIBO patients were not suffering from GORD (GORD vs no GORD: *P* < 0.008). Lower oesophageal sphincter basal pressure and DCI were not significantly different between patients with and without SIBO.

Gender on SIBO: female 39%, male 24% had SIBO. Age on SIBO: highest prevalence of SIBO was 50-60 years old (50%); dramatic reduction >60 years (18%).

Conclusions: SIBO is significantly associated with poor oesophageal body motility. This can be due to underlying poor small intestinal motility in a group of patients with IOM. Oesophageal body motility can be a surrogate for small intestinal motility (requires further research).

POSTER ABSTRACT

11 | Rectal compliance is affected by enteric nervous system and interstitial cells of Cajal in gastrointestinal smooth muscle

H. Kim¹; S.-B. Ryoo²; T. S. Sung³; J. Lee³; S. D. Koh³

¹Yonsei University Wonju College of Medicine, Wonju, South Korea; ²Seoul National University College of Medicine, Seoul, South Korea; ³University of Nevada Reno, Reno, United States

Objective: Rectal compliance is different from the colonic propulsive movement. Abnormal rectal compliance is presented in many functional gastrointestinal motility disorders, such as constipation and fecal incontinence. This study aimed to explore the electromechanical characteristics of rectal compliance in the murine rectum and to investigate the contribution of intrinsic inhibitory neurotransmission and interstitial cells to rectal compliance.

Methods: Male C57BL/6 mice, aged 8 weeks were used. For in vivo experiments, the mice were anesthetized with isoflurane, and anorectal manometry was applied to measure rectal compliance. In ex vivo with using murine rectum, intra-rectal pressure was measured in organ bath. The colonic migrating motor complex (CMMC) measurements and electrophysiological microelectrode recordings for membrane potential were performed using smooth muscle strips and segments. Calcium imaging was used to measure the calcium transients in the interstitial cells and smooth muscle cells within the rectum of the mice expressing a genetically encoded calcium indicator (GCaMP). Drugs affecting inhibitory neurotransmission including L-NNA and apamin were applied.

Results: The rectal compliance was significantly decreased after in vitro intraperitoneal injection and ex vivo infusion into organ bath of L-NNA and apamin, respectively (*P* = 0.002 vs 0.005; *P* = 0.016 vs 0.015). In ex vivo experiments, rectum did not have CMMC, and after treatment of the L-NNA or apamin in the organ bath, the rectal contractions were increased, not CMMC (6.19 ± 3.98 vs 20.35 ± 15.78 mN·min, *P* = 0.031), and propagation of contractions from the distal colon increased (7.20 ± 3.32 vs 29.12 ± 20.75 mN·min, *P* = 0.046). In membrane potential with electric field stimulation, inhibitory junction potential significantly increased after L-NNA and apamin, respectively (17 ± 2.9 vs 16 ± 1.6 mV, *P* = 0.04; 24 ± 2.5 vs 13 ± 3.6 mV, *P* = 0.02). In calcium transient of smooth muscle, AUC in rectum was smaller than that of colon (9.36 ± 4.57 vs 3.49 ± 2.58 IU·min, *P* = 0.03), and AUC in rectum increased after L-NNA and apamin, respectively (3.79 ± 1.93 vs 9.71 ± 4.52 IU·min, *P* = 0.001; 3.26 ± 1.92 vs 8.31 ± 4.12 IU·min, *P* = 0.021). In calcium transient of ICC of rectal circular muscle, AUC significantly increased after L-NNA (7.39 ± 2.52 vs 10.98 ± 3.71 IU·min, *P* = 0.012).

Conclusions: Murine rectal compliance was identified, and enteric inhibitory neurotransmissions were related to the rectal compliance. ICC could control the rectal smooth muscle activities.

14 | Gastroesophageal reflux disease and paroxysmal non-valvular atrial fibrillation – A case-control study

O.-B. Barboi; M. Floria; I. Ciortescu; V. Drug

Saint Spyridon Hospital, Iasi, Romania

Objective: There is still a controversy regarding the relationship between gastroesophageal reflux disease (GERD) and paroxysmal non-valvular atrial fibrillation (AF). Having the same predisposing factors as well as the adjacent anatomical positioning and nerve innervations between esophagus and atria can explain this relationship. The aim of this study was to evaluate the association between GERD and AF.

Methods: A prospective case-control study was conducted at a tertiary care centre from North-East of Romania over a period of 13 months (July 1, 2014–July 31 2015). We included 135 patients divided in four groups: patients with GERD and paroxysmal non-valvular AF (GERD+AF group), patients with GERD and sinus rhythm (GERD+non-AF group), patients with AF and non-GERD (AF+non-GERD group) and patients without GERD and AF (non-GERD+non-AF group). All patients underwent upper endoscopy, echocardiography, 24-hour electrocardiographic Holter monitoring and lab tests.

Results: The 135 patients were divided as follow: 36 GERD+AF patients, 25 GERD+non-AF patients, 39 AF+non-GERD patients and 35 non-GERD+non-AF patients. All groups were homogenous regarding sex distribution and age. Esophagitis increased the relative risk of the association of AF and GERD by 2.5 times ($P < 0.005$). Heart rate variability in terms of time-domain parameter (SDNN) was lower in GERD+AF group patients than the other three groups (69.60 vs 109.33 vs 123.56 vs 12.1, $p < 0.005$). Regarding cardiac ultrasound parameters, median value of left atrial area in the group with GERD and AF patients was statistically higher comparatively with GERD+non-AF group (25.79 ± 5.13 cm² vs 23.88 ± 5.10 cm², $p < 0.005$). Hypertriglyceridemia was statistically significantly higher in GERD+AF group than in the other groups ($p = 0.005$).

Conclusions: These results suggest the association of GERD and AF, which is sustained by both the theory of inflammation and of the autonomic nervous system imbalance.

17 | POEM in patients with achalasia of normal IRP

E. Kim; I. Yoo; D. H. Jung; J. Y. Cho; S. P. Hong

CHA University, Seongnam, South Korea

Objective: Integrated relaxation pressure (IRP) is an important diagnostic criteria to define the achalasia. However, there are some

cases with typical symptoms and signs of achalasia with normal IRP. The aim of this study was to evaluate the clinical characteristics and outcomes after peroral endoscopic myotomy (POEM) in patients with achalasia of normal IRP.

Methods: The cases of achalasia were collected those were performed POEM from November 2014 to April 2018 at CHA Bundang Medical Center. Achalasia of normal IRP was defined by Eckardt score, EGD, high-resolution manometry (HRM) and endoluminal functional lumen imaging probe (EndoFlip®), and timed esophagogram.

Results: POEM was done in 129 patients with achalasia and among them, 31 patients were achalasia with normal IRP. Achalasia patients with normal IRP were older, had longer symptom duration, and more tortuous esophagus. In EndoFlip, distensibility index (DI) and cross-sectional areas (CSA) were higher in patients with normal IRP. Therapeutic outcomes showed no statically significant differences. With correlation analysis, IRP and age, disease duration, or DI had negative correlation with statistical significance.

Conclusions: Achalasia patients with normal IRP were older, had longer disease duration and higher DI and CSA than patients with elevated IRP. In two groups, therapeutic outcomes were not different.

18 | Metagenomic analysis of intestinal microbiota and mycobiota among diarrhea-predominant irritable bowel syndrome patients from Argentina

L. B. Fernandez¹; F. Man²; C. Dorribo¹

¹CMBF, Buenos Aires, Argentina; ²GASTRO, Buenos Aires, Argentina

Objective: It has been suggested intestinal microbiota is associated with the development of diarrhea-predominant Irritable Bowel Syndrome (IBS-D). There is scarce evidence regarding this aspect among IBS-D patients from a South American population. Additionally, intestinal mycobiota has not been exhaustively studied on this patients AIM: To describe bacterial and fungal composition of intestinal microbiota among Argentinean patients with IBS-D

Methods: Adult patients with IBS-D (Rome III criteria) from Buenos Aires, Argentina were consecutively enrolled. One fecal sample per patient was collected for microbiota and mycobiota analyses. Patients completed the IBS Symptom Severity Scale (IBS-SSS). Demographic features were assessed as well as stool consistency via the Bristol Stool Scale. After genomic DNA extraction and purification, bacterial and fungal composition of fecal samples were analyzed based on 16S rDNA and ITS2 sequencing respectively. Correlation between microbial and fungal abundance and the clinical features was assessed by Pearson correlation test.

Results: 71 patients fulfilling inclusion criteria were enrolled. Firmicutes was the predominant phyla (73.61%), followed by Bacteroidetes (13%). A relatively elevated proportion of Proteobacteria (8%) was identified. Alistipes was the most represented genus. When analyzing correlations between microbiota composition and different clinical features, we found a negative

correlation ($r = -0.5$, $P 0.003$) between stool consistency score and butyrate-producing microorganisms, such as *Butyrivibrio* and *Lachnospiraceae* UCG010 genera. Symptom severity assessed by IBS-SSS was positively correlated with the abundance of *Victivallaceae* uncultured organisms, *Synergistes* and *Ruminococcus gnavus* groups genera ($r = 0.42$, 0.33 and 0.32 respectively, $P 0.05$). ITS2 DNA sequences analysis showed that the predominant fungal phyla were Ascomycota (89.12%), followed by Basidiomycota (2.78%); *Saccharomyces*, *Debaryomyces* and *Candida* were the dominant genera. No significant correlation between mycobiota components and clinical features was found.

Conclusions: We describe the bacterial and fungal composition of intestinal microbiota in IBS-D patients from Argentina. Although certain significant correlations were identified between microbiota composition and clinical features such as symptom severity, the clinical implications of such findings deserve further research.

21 | Impact of the herbal medicinal preparation stw 5 on the gut microbiome and metabolomic changes of stw 5 induced by gut bacteria in human fecal samples in-vitro

T. Thumann¹; E. M. Pferschy-Wenzig¹; C. Moissl-Eichinger²; S. Duller²; C. Hoegenauer³; H. Aziz-Kalbhenn⁴; R. M. Ammar⁴; S. Rabin⁴; R. Bauer⁵

¹Institute of Pharmaceutical Sciences, Department of Pharmacognosy, University of Graz, Universitätsplatz 4, 8010 Graz, Austria, Graz, Austria; ²Center for Medical Research, Medical University of Graz, Graz, Austria; ³Medical University of Graz, Stiftingtalstraße 24, Graz, Austria; ⁴Bayer Consumer Health, Darmstadt, Germany; ⁵Institute of Pharmaceutical Sciences, Department of Pharmacognosy, University of Graz, Universitätsplatz 4, Graz, Austria

Objective: STW 5 is an orally administered herbal medicinal liquid preparation for the treatment of functional disorders of the gastrointestinal (GI) tract, such as functional dyspepsia (FD) and irritable bowel syndrome (IBS). STW 5 is the only herbal product listed in ROME IV guidelines for the treatment of functional dyspepsia. The digestion of this plant extract by stomach and pancreatic enzymes and metabolism by the gut microbiome may lead to the formation of new bioactive metabolites. This study aims to investigate the bidirectional impact of both gut bacteria and STW 5 constituents vice versa.

Methods: STW 5 was pre-digested using the static in-vitro digestion model InfoGest. The pre-digested suspension was incubated with human fecal samples under anaerobic conditions to mimic the intestinal fermentation by the gut microbiome. After 30 minutes, 4 hours and 24 hours, samples were taken to investigate both the metabolomic and microbiome changes. The peak areas detected by UHPLC-HRMS were compared to the respective STW 5 dilutions without any human faeces. In addition, shifts in the gut microbiome caused by STW 5 were assessed by Illumina Next Generation Sequencing.

Results: In-vitro digestion by the InfoGest model had no significant impact on the constituents of STW 5. However, triterpene glycosides

and polyphenols, major compounds of STW 5, were subsequently metabolized very fast by the fecal bacteria. New small molecule metabolites were detected. In addition, a significant change in the gut microbiome composition was observed.

Conclusions: Investigations of STW 5 in the in-vitro digestion model InfoGest indicate that the constituents of STW are hardly changed in the upper intestinal tract. However, incubation of STW 5 with human fecal samples led to extensive metabolism of major STW 5 constituents and to production of small molecules that may contribute to its activity. Also, the observed changes in the gut microbiome composition may be relevant for the mechanism of action of STW 5.

22 | Efficacy of the herbal combination stw 5 in FD patients meet rome IV criteria: Meta-analysis

R. M. Ammar¹; M. Wargenau²; V. Stanghellini³

¹Bayer Consumer Health, Darmstadt, Germany; ²M.A.R.C.O. Institute for Clinical Research and Statistics, Dusseldorf, Germany; ³Università degli Studi di Bologna, Bologna, Italy

Objective: Functional dyspepsia (FD) is a chronic gastroduodenal syndrome with a high prevalence worldwide. FD diagnostic criteria have substantially changed over the last decades, since ROME I in 1991 up to the current ROME IV proposal. STW 5 is a herbal combination used for treating functional gastrointestinal disorders, including FD and IBS. STW 5's efficacy was evaluated in seven different randomized, controlled clinical trials (RCTs) in FD patients. This meta-analysis aims to re-analyze available RCTs to assess the efficacy of STW 5 in FD patients who meet ROME IV criteria.

Methods: MEDLINE, EMBASE, BIOSIS Preview, Derwent Drug File, Current Contents, and the Cochrane Controlled Trials Register were searched for RCTs recruiting adults with FD comparing STW 5 with placebo. Analysis of the selected studies was performed in accordance with the diagnostic criteria for FD according to Rome IV criteria. Changes in symptom scores (from baseline to Day 28) were submitted to analysis-of-covariance (ANCOVA) with baseline score and treatment as fixed effects separately for each study. Meta-analysis was then applied on study-specific ANCOVA results to obtain common ("pooled") estimates for the mean differences with 95% confidence intervals (CI) between STW 5 and placebo concerning the improvement after therapy. Improvements were evaluated for each single symptom, FD subtypes, and FD global symptoms. In addition, responder rates were evaluated where patients with a symptomatic improvement concerning severity from "at least moderate" at baseline to "none or mild" after 28 days of treatment were defined as responder.

Results: Five RCTs were eligible providing 551 patients. The MD for improvement of bothersome fullness, early satiety, epigastric pain/burning symptoms with STW 5 vs placebo were 0.26 (95% CI 0.12-0.41), 0.23 (95% CI 0.10-0.36), 0.27 (95% CI 0.12-0.42), respectively.

The MD for improvement of postprandial distress syndrome (PDS), global symptoms were 0.32 (95% CI 0.17-0.47) and 0.30 (95% CI 0.16-0.45), respectively. The combined analysis of this data set showed a significant benefit of STW 5 over placebo in improving global FD symptoms, with a number needed to treat (NNT) of 8.

Conclusions: From the current evidence, STW 5 is an effective treatment for all subtypes of FD.

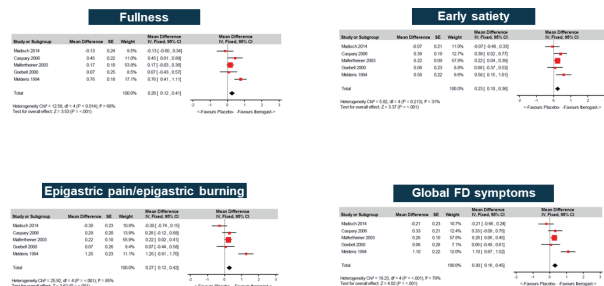


FIGURE Forest Plot of Efficacy of STW 5 versus Placebo in Randomized Controlled Trials in Functional Dyspepsia.

23 | Long non-coding RNA THRIL controls TNF-A related inflammatory process in stomach

S. K. Lee; J.-H. Yoon

Yonsei University College of Medicine, Seoul, South Korea

Objective: Recently, long non-coding RNAs (lncRNAs) have emerged in association with regulation of the mucosal immunology. We investigated the roles of lncRNA THRIL (TNF- α and heterogeneous nuclear ribonucleoprotein L [hnRNPL] related immunoregulatory lncRNA) in TNF- α related inflammation in stomach.

Methods: 1. Cell lines: Human gastric normal epithelial cell line GES-1, and 4 different gastric cancer cell lines including MNK28, MKN74, MKN45, AGS and KATOIII 2. Infectious agents and bacteria: Escherichia coli lipopolysaccharides (LPS), H. pylori strains 8822 (cytotoxin-associated gene A [CagA]-) and 60190 (ATCC 49503, CagA+), and Δ CagA (an isogenic mutant of 60190 lacking CagA) 3. Total RNA extraction, reverse transcription and quantitative real-time PCR (qRT-PCR): The expression level THRIL, hnRNPL, NF- κ B1 (p50), TNF- α and IL-8 was determined by qPCR using iQ SYBR Green Supermix (Applied Biosystems) and normalized to glyceraldehyde-3-phosphate dehydrogenase (GAPDH). 4. Enzyme-linked immunosorbent assay (ELISA), Western blot for secreted TNF- α , IL-8 5. Knock-down of THRIL by two different siRNAs and shRNA 6. Immunofluorescence and Western blot for NF- κ B cascade including NF- κ B p65, I κ B α , phospho-I κ B α , IKK α , IKK β , and phospho-IKK α /IKK β 7. Results: The amount of THRIL expression in the GES-1 cells was relatively smaller than that in the gastric cancer cell lines. siRNAs and shRNA for THRIL not only significantly reduced TNF- α basal excretion but also attenuated TNF- α secretion by H. pylori 60190 and Δ CagA strains. NF- κ B1 (p50) mRNA level in the GES-1 cells was upregulated by H. pylori 60190 infection, however shRNA for THRIL block

induction of NF- κ B1. The phosphorylation of IKK α /IKK β was reduced by shRNA for THRIL in contrast to that with control. Finally knockdown of THRIL attenuated NF- κ B nuclear translocation by H. pylori 60190.

Conclusions: We found that THRIL modulates H. pylori-induced inflammation in stomach. This finding also implies the importance of lncRNA as a regulatory factor involved in the pathogenesis of inflammations or infectious diseases in humans stomach.

24 | The associations between gastroesophageal reflux disease and the central obesity of the elderly

J. H. Kim¹; B. G. Kim²

¹Dongguk University College of Medicine, Dongguk University Ilsan Hospital, Goyang, South Korea; ²Ulsan University College of Medicine, Ulsan University Hospital, Ulsan, South Korea

Objective: Central adipose tissue not only has metabolic effects but also increase intra-abdominal pressure, which is associated with the development of gastroesophageal reflux disease (GERD). Abdominal visceral adipose tissue volume is associated with an increased risk of GERD. The aim of this study was to investigate the associations between erosive esophagitis (ERD) and minimal change esophagitis (MCD) in terms of central obesity.

Methods: The subjects aged over 65 years who underwent abdominal computerized tomography and upper endoscopy for routine checkup at the same day were collected from Feb 2007 to October 2016. 24 subjects with ERD and 18 subjects with MCD were enrolled. The abdominal obesity was evaluated by measuring visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT), ratio of VAT to SAT, total adipose tissue (TAT), body mass index (BMI).

Results: Male was significantly frequent in ERD than MCD (83.3% vs 50.0%, $P = 0.04$). No significant differences were observed between groups in terms of H. pylori infection and presence of hiatal hernia. BMI (24.4 ± 2.7 vs 24.7 ± 2.2 , $P = 0.78$), VAT (64.8 ± 26.1 vs 69.7 ± 26.1 , $P = 0.55$), SAT (75.7 ± 26.5 vs 90.6 ± 36.0 , $P = 0.13$), ratio of VAT to SAT (0.90 ± 0.42 vs 0.85 ± 0.41 , $P = 0.71$), and TAT (140.5 ± 40.1 vs 160.3 ± 50.9 , $P = 0.17$) were not significantly different between two groups.

Conclusions: In elderly, male sex was more affected ERD. However, central obesity was not different between ERD and MCD.

25 | The impact of a prebiotic mix, FOS-inulin, on hepatic drug-metabolising enzymes and drug efflux transporter

J. Walsh; M. Boehme; John. F. Cryan; Timothy. G. Dinan; Brendan. T. Griffin; G. Clarke; Niall. P. Hyland

University College Cork, Cork, Ireland

Objective: Our aim was to investigate whether fructooligosaccharide (FOS)-inulin could alter hepatic CYP and MDR expression and whether this treatment effect was age-dependant.

Methods: Mice (2 and 10 months old) were fed FOS-Inulin (92%-8%) supplemented chow for 14 weeks. Control mice received standard chow (n = 9-10). Mice were euthanised by decapitation and total RNA was isolated from harvested liver tissue. Reverse-transcriptase PCR was employed to compare the mRNA expression of CYPs and MDR1. Data were analysed by two-way ANOVA and Bonferroni's multiple comparisons test.

Results: Age affected the response to prebiotics on CYP2a4 gene expression which was significantly up-regulated in young vs middle-aged mice ($P < 0.01$). A significant prebiotic effect on CYP3a13 was only observed in young mice characterised by decreased gene expression ($P < 0.05$). Interestingly, the age-related impact on MDR1a was opposite to the treatment-induced effect; significantly decreased expression of MDR1a in young versus middle-aged mice was accompanied with a FOS-inulin induced significant upregulation in young mice ($P < 0.05$). A significant down-regulation of MDR1b gene expression was observed with increasing age ($P < 0.05$) whilst the expression of CYP2b10 and CYP3a11 were not affected by either age or prebiotic.

Conclusions: Our data illustrates that both age and prebiotics may differentially affect the expression of hepatic CYP genes and MDR1. This study highlights that prebiotics can indirectly impact the expression of hepatic enzymes important for the metabolism of a range of commonly used drugs and provides the impetus to consider prebiotics as a potential source of variation in drug response in patients of specific age groups.

27 | Initial experience and clinical outcomes of peroral endoscopic myotomy for the treatment of esophageal achalasia and esophageal motility disorders

K. Jung; S. E. Kim; M. I. Park; S. J. Park; W. Moon; J. H. Kim

Department of Internal Medicine, Kosin University College of Medicine, Busan, South Korea

Objective: Recently, peroral endoscopic myotomy (POEM) has been performed as an initial method in place of laparoscopic myotomy or balloon dilatation as a treatment for achalasia and other major motility disorder. We describe our initial experience and clinical outcome with the twelve POEM procedures performed at our institution.

Methods: Twelve patients (mean age 47 ± 15.1 years) with achalasia and major esophageal motility disorders were performed POEM. This completely endoscopic procedure involved an opening with mid-esophageal mucosal incision, a submucosal tunneling to cardia portion of stomach, and selective myotomy of circular muscle layer including the lower esophageal sphincter. The mucosal incision site was closed by endoscopic clips. Clinical data including

manometry, esophagogram, symptom and procedure was analyzed retrospectively.

Results: Before POEM, mean Integrated Relaxation Pressure (IRP) of manometry was 24.78 ± 9.86 and balloon dilatation was performed on seven patients previously. All twelve patients successfully treated by POEM procedure, and the myotomy had a median length of 13 cm (range 10 to 16 cm). After the procedure, passage disturbance of endoscope was improved in all patients. Operative time ranged from 62 to 170 minutes. No leaks were detected in the postoperative esophagogram and mean hospital admission days was 11.17 ± 4.2 . No clinical complications were observed, and there was significant clinical improvement on Eckardt score (7.0 ± 2.3 vs 1.2 ± 0.8 , P

Conclusions: Based on the clinical results of our institution, POEM is a safe and clinically effective treatment for symptomatic achalasia. Long-term data for sustained symptom improvement maintenance will be needed in the future.

29 | Sex and gender specific differences of prevalence and risk factors of gastro-esophageal reflux disease

S. G. Yoo; S. Y. Kim; H.-K. Jung

Ewha Womans University Mokdong Hospital, Seoul, South Korea

Objective: Sex and gender related factors might play a major role in the development of reflux esophagitis (RE) and symptomatic gastro-esophageal reflux disease (GERD). We aimed to evaluate the prevalence and risk factors of RE and symptomatic GERD, and determine whether sex and gender specific differences exist.

Methods: The study was conducted on a health cohort consisting of 10 158 subjects who underwent comprehensive health screening including endoscopy, radiologic examination and blood test. Demography, lifestyles and gastrointestinal symptoms were investigated using self-reported structured questionnaire. Women added questionnaires about menstrual status and menopause.

Results: The prevalence of RE was significantly higher in male than in female (10.6% vs 2.0%, $P < 0.001$) in women, however, that remained similar regardless of age in men. Apart from the common risk factors of obesity and current smoking for RE, the aged over 70 (OR = 2.90, 95% CI 1.19-7.04, $P = 0.019$) in female and hiatal hernia (odds ratio [OR], 2.54; 95% confidence interval [CI], 1.81-3.62; $P < 0.001$) and hypertriglyceridemia (OR, 1.28; 95% CI, 1.06-1.55; $P = 0.012$) in male were significant risk factors. In symptomatic GERD, high somatization was a common risk factor.

Conclusions: This study showed a male predominance of RE, but a female predominance of symptomatic GERD. In female, the dynamic increase in the prevalence of GERD is closely related to the menopause conditions and its duration. There were special risk factors for RE and symptomatic GERD according to sex and gender differences.

31 | Altered enteric neuro-inflammatory signature in patients with Parkinson's disease – A pilot study

J. Zimmermann¹; E. Schäffer²; S. Heinzel²; B. Niesler; N. C. Facility³; A. Scharf¹; D. Zorenkov²; M. Ellrichmann⁴; D. Berg²; T. Wedel¹; F. Cossais¹

¹Institute of Anatomy, University of Kiel, Kiel, Germany; ²Department of Neurology, University of Kiel, Kiel, Germany; ³Department of Human Molecular Genetics, University of Heidelberg, Heidelberg, Germany; ⁴Experimental Endoscopy Department of Internal Medicine, University of Kiel, Kiel, Germany

Objective: Neuroinflammation is a key process in the pathogenesis of Parkinson's disease (PD). However, characterization of neuroinflammatory pathways is limited by the impossibility to study biopsies from central nervous system in living patients. Accumulating data report that the enteric nervous system (ENS) is also affected in PD. An analysis of intestinal biopsies obtained from PD patients indicates that enteric neuroinflammation is also taking place in PD. However, a detailed analysis of the enteric neuroinflammation pathways occurring in PD is still missing.

Methods: Deep colonic biopsies, containing mucosal and submucosal nerve tissue, were obtained from 12 PD patients and 12 controls. Digital multiplexed mRNA expression analysis was used to quantify the expression levels of a panel of 429 genes involved in neuroinflammation and neuropathological disorders.

Results: Expression of 7 genes was altered in PD patients in comparison to controls (FDR adjusted P -value ≤ 0.05) and differential correlation based on the expression of these genes was altered in PD. Global expression of 5 of these genes defined a robust neuroinflammatory signature that was observed in 9 out of 12 PD patients.

Conclusions: These results confirm that enteric neuropathological pathways are altered in PD and suggest that the altered gene expression pattern may be specific for this disease. Further characterization of this neuroinflammatory signature might help to identify novel biomarkers for PD and potential new therapeutic targets.

32 | Association between gerd with extradiigestive symptoms in two channel ambulatory phmetry

M. G. Hernandez; C. M. G. Caparros; M. J. B. Lopez

Hospital Universitario Son Espases, Palma De Mallorca, Spain

Objective: Manifestations of gastroesophageal reflux disease (GERD) are classified as esophageal and extraesophageal symptoms. We rely on anamnesis, questionnaires and the response to treatment with PPI, however, they are insufficient to make a conclusive diagnosis of GERD. Ambulatory double-channel pHmetry is considered the gold standard and has modified the diagnostic approach of the typical and atypical manifestations of GERD. In our research, we want to investigate the association between extradiigestive symptoms and two channel pHmetry results

Methods: Descriptive research of extradiigestive symptoms and associated factors: personal history, tobacco and referring services. Retrospective analysis of the cohort of patients with two channel pHmetry studied at the University Hospital Son Espases.

Results: Forty-five patients with extraesophageal symptoms studied with two channel pHmetry were included: 32 women (71.1%) and 13 men (28.9%). The referral services by clinic attributable to extraesophageal GERD are Otorhinolaryngology (ENT), 26 patients, Pneumology (NML) 10 and Gastroenterology (DIG) 8. The personal history of the patients was heterogeneous and unrelated to the manifestations of GERD. We didn't find an apparent relationship or attributable to the symptoms in our smokers patients. The most frequent symptoms are: Cough (20 occasions), Dysphonia (9), strange body sensation (13), Asthma difficult to control (5), Chest pain (2), Pharyngeal itch (2). Patients previously diagnosed with GERD were also studied with an overlap of symptoms: Cough (7 occasions), Dysphonia (1) and strange body (2). Only a pathological DeMeester value is obtained in the proximal canal in one patient referred by NML, however, the patient presents a normal DeMeester in the distal canal and does not present symptoms during the period explored. A pathological DeMeester was obtained in the distal canal in 9 of the patients referred by ENT, 4 referred by NML, and 3 referred by DIG. During the test 22 patients (Burning). Of these, we studied those with Symptomatic Association Index (SAP) when over than 0%: 2 patients with a positive SAP only in the proximal canal, 7 only in the distal canal and 5 who presented positivity simultaneously in both channels.

Conclusions: The association between extradiigestive symptoms and the results of dual channel pHmetry seems weak in our cohort

34 | Psychological characteristics of patients visited brain-gut stress clinic: Focus on depression, anxiety, childhood trauma and resilience

S. C. Choi¹; Y. S. Kim¹; H. S. Ryu¹; S.-Y. Lee²; S.-H. Jang²

¹Division of Gastroenterology, Department of Internal Medicine, Wonkwang University Hospital, Digestive Disease Research Institute, Iksan, South Korea;

²Department of Psychiatry, Wonkwang University Hospital, Digestive Disease Research Institute, Iksan, South Korea

Objective: This study aimed to compare the psychosocial characteristics among groups [group 1: patients diagnosed with functional gastrointestinal disorders (FGID), group 2: adults complaining functional gastrointestinal symptoms, group 3: normal control group], and investigate the factors related to therapeutic needs for FGID.

Methods: Total 99 patients diagnosed with FGID in Brain-Gut Stress Clinic of Wonkwang University Hospital were selected as a FGID patient group, 87 adults who complained functional gastrointestinal symptoms were selected as a FGID-positive group and 79 adults were selected as a normal control group based on the Rome IV diagnostic criteria. Demographic factors were investigated and psychosocial factors were evaluated using the Korean-Beck Depression

Inventory-II, Korean-Beck Anxiety Inventory, Korean-Childhood Trauma Questionnaire (CTQ) and Connor-Davidson Resilience Scale (CD-RISC). Student *t*-test, one-way ANOVA and logistic regression analysis were used to compare differences among groups.

Results: In comparison of the FGID group (FGID patient + FGID-positive group) to the normal control group, the odd ratio (OR) of the FGID group was 8.047 in the high risk of anxiety group (95% CI: 2.37-27.28). In childhood trauma, there were differences in the sum of CTQ ($t = -2.366$, $P = 0.019$) and sexual abuse ($t = -2.103$, $P = 0.036$). In the high risk of emotional neglect of CTQ subscale, the OR of FGID was 2.023 (95% CI: 1.09-3.72). In resilience, there were differences in the sum of CD-RISC ($t = 2.613$, $P = 0.031$) and optimism ($t = 3.209$, $P < 0.01$). In comparison of the FGID patient to the FGID-positive group, the OR of the FGID patient group was 3.944 in the depression high risk group (95% CI: 1.68-9.20). Childhood trauma differed in the sum of CTQ ($t = -2.366$, $p = 0.019$) and physical neglect ($t = -4.086$, $p < 0.001$). In the high risk of emotional neglect of CTQ subscale, the OR of FGID patient group was 3.27 (95% CI: 1.75-6.08). In resilience, there were differences in the sum of CD-RISC ($t = 4.333$, $p < 0.001$), hardiness ($t = 2.881$, $p < 0.01$), persistence ($t = 4.196$, $p < 0.001$), optimism ($t = 6.071$, $p < 0.001$), support ($t = 2.726$, $p < 0.01$), and spiritual in nature ($t = 3.039$, $p < 0.01$).

Conclusions: The FGID patients have distinctive psychosocial factors compared to the both FGID-positive and normal control group. Therefore, the active interventions for psychosocial factors are required in the treatment of patients with FGID.

35 | The effect of neuromedin B on motility in isolated, vascularly perfused rat colon

S. J. Youn¹; K. B. Kim²; H. W. Kim²; J.-H. Han¹; S. M. Yoon¹; H. B. Chae¹; S. M. Park¹; B.-S. Ko³

¹Chungbuk National University, Cheongju, South Korea; ²Chungbuk National University Hospital, Cheongju, South Korea; ³Cheongju St. Mary's Hospital, Cheongju, South Korea

Objective: Neuromedin B (NMB) has been shown to stimulate contractions of various smooth muscle preparation from isolated gut.

Methods: The aim of this study was to investigate the effect of NMB on the isolated rat colon and to clarify whether the action of NMB on colonic motility is mediated via the influence of autonomic nervous system. Effect of NMB on colonic motility was studied in totally isolated rat colon vascularly perfused with Krebs solution containing 0.1% BSA and 3% Dextran at 1.2 mL/min via SMA. Luminal pressure was monitored via microtip catheter pressure transducers from proximal and distal colon. After control, NMB was administered at 12, 24, 119, 238 pM in a stepwise increase fashion. Motility index was calculated for the last 5 minutes of each 15 minutes period and expressed as %change over basal level.

Results: NMB increased distal colonic motility in rats. The stimulating effect of NMB on distal colon was almost completely abolished by atropine, hexamethonium, tetrodotoxin, propranolol,

respectively. But the stimulating action of NMB on distal colon was not inhibited by phentolamine.

Conclusions: Neuromedin B increase distal colonic motility in rats. The stimulatory action of NMB on distal colon requires local cholinergic input or local adrenergic input via β -receptor.

The effect of Neuromedin B on colonic motility

NMB Dose (pM)	MI of Proximal colon (mean $\pm$ SE %, n=6)	MI of Distal colon (mean $\pm$ SE %, n=6)
0	0	0
12	17.7 $\pm$ 11.8	111.7 $\pm$ 45.7*
24	86.2 $\pm$ 86.2	392.0 $\pm$ 122.1*
119	37.0 $\pm$ 17.7	432.6 $\pm$ 123.7*
238	38.6 $\pm$ 25.1	255.7 $\pm$ 126.8*
238(P), 119(D) + Hexamethonium	50.5 $\pm$ 22.7	16.8 $\pm$ 16.7**
238(P), 119(D) + Phentolamine	38.0 $\pm$ 30.8	157.1 $\pm$ 92.5
238(P), 119(D) + Atropine	21.3 $\pm$ 7.6	0.76 $\pm$ 0.76**
238(P), 119(D) + Tetrodotoxin	61.3 $\pm$ 22.7	57.5 $\pm$ 5.9**
238(P), 119(D) + Propranolol	60.9 $\pm$ 37.3	60.8 $\pm$ 54.7**

MI: Motility index, (P): Proximal colon, (D): Distal colon, * $P < 0.05$ vs. basal, ** $P < 0.05$ vs. 119 pM(D)

36 | Anti-inflammatory and epithelial protective effects of herbal preparation STW5-II on mouse intestinal organoids

M. Elbadawi¹; R. M. Ammar²; H. Abdel-Kalbhenn²; S. Rabini²; T. Efferth¹

¹Department of Pharmaceutical Biology, Johannes Gutenberg University, Mainz, Germany; ²Bayer Consumer Health, Darmstadt, Germany

Objective: Background: Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder (FGID) characterized by recurring abdominal pain associated with alterations in the form and frequency of the stool. Low-grade inflammation and altered epithelial barrier play an important role in the pathogenesis of IBS. STW5-II is a multi-herbal preparation marketed in Germany for the treatment of FGID including FD and IBS. Aim: This study aims to establish organoids based IBS model and to investigate the anti-inflammatory effect of STW5-II in addition to its protective effect on the intestinal epithelial barriers.

Methods: Mouse intestinal organoids were cultured in Matrigel domes. Organoids were treated with STW5-II for 24 hours followed by inflammation induction. A cocktail of pro-inflammatory cytokines (IFN- γ , TNF- α , IL-1 β , IL-6) and bacterial components (lipopolysaccharide LPS-B5, flagellin) were used to simulate IBS associated inflammation and to disrupt the intestinal epithelial integrity. The effects of STW5-II on intestinal organoids were investigated by western blotting and immunohistochemistry. We have investigated the expression of pSTAT1, pNF κ B, iNOS, aquaporin 3 and Claudin-1.

Results: The model was successfully established. Our immunoblotting analysis revealed that STW5-II was effective in reducing the levels of pSTAT1, pNF κ B and iNOS. These findings were further confirmed by immunohistochemistry. In addition, immunohistochemical analysis highlighted that STW5-II counteracts cytokines mediated deregulation of aquaporin 3 and claudin 1 resulting in epithelial protective effect. This effect could be attributed to the ability of STW5-II to downregulate pSTAT1 and pNF κ B.

Conclusions: STW5-II possesses a multi-target anti-inflammatory action via inhibition of both pSTAT1 and pNF κ B. It is effective

in reducing oxidative stress via inhibition of iNOS. Furthermore, STW5-II maintains intestinal epithelial integrity and structure via modulating tight junction proteins. Adding this to its previously documented MoA in modulating intestinal motility and visceral pain could explain the multi-symptomatic efficacy of STW5-II in IBS patients.

41 | Is there a link between IBS and stuttering? – Preliminary results gastrointestinal manifestation of systemic disease

G. Hauser¹; T. N. Herceg²; S. P. Tonic³; I. Benjak⁴; D. Novosel²; M. Tkalcic³

¹Department of Internal Medicine, Division of Gastroenterology, Clinical Hospital Centre Rijeka, Rijeka, Croatia, University of Rijeka, Faculty of Health Studies, Rijeka, Croatia, Rijeka, Croatia; ²VaLMod Centre, SLP, Varazdin, Croatia, Varazdin, Croatia; ³Department of Psychology, Faculty of Humanities and Social Sciences, University of Rijeka, Croatia, Rijeka, Croatia; ⁴Department of internal medicine, County hospital Varazdin, Croatia, Varazdin, Croatia

Objective: Theories of stuttering have described the role of anxiety in several ways, from treating it as the main cause of the disorder to a mere by-product of stuttering. Most studies have detected a positive correlation between anxiety and stuttering severity, with higher levels of anxiety in the stuttering population compared to healthy persons. The aim of this study was to examine the prevalence of IBS in a sample of people who stutter and to explore the relationship between several anxiety measures and IBS symptom frequency among people who stutter.

Methods: A total of 57 people who stutter (73.6% M, M age = 32.4 years) and were treated for stuttering at VaLMod rehabilitation centre were recruited. During their regular holistic multidimensional logopaedic treatment they completed the Rome IV diagnostic questionnaire, a short questionnaire on the frequency of 6 IBS symptoms, State-Trait Anxiety Inventory (STAI-T), Visceral Anxiety Inventory (VSI) and Anxiety Sensitivity Index ASI.

Results: Only 8 participants (4F, 4M) fit the IBS criteria (Rome IV), which is a somewhat lower prevalence rate compared to the general population. People who stutter, but do not fit the IBS criteria, have higher STAI scores (M=44.53; SD=9.34) than a normative age group of healthy persons (M=35.55; SD=9.76). People who stutter and fit the IBS criteria have even higher (t=2.59; df=9.62; p<.05) STAI scores (M=53.99; SD=9.41). Their STAI score seems to be higher than the score obtained for the regular, non-stuttering IBS population, previously published in our other studies (M=46.30; SD=9.63). People who stutter and fit the IBS criteria have higher scores in VSI scores (t=2.26; df=8.34; p<.05), ASI scores (t=2.76; df=8.34; p<.05) and the frequency of IBS symptoms (t=4.67; df=8.18; p<.01) than those who don't fit the IBS criteria

Conclusions: It seems IBS is not more frequent in people who stutter. However, it seems that stuttering aggravates anxiety in IBS. Patients who stutter and have IBS seem to have more pronounced anxiety than people who stutter but don't have IBS and people who have IBS but don't stutter.

42 | Affective determinants of symptom severity in IBS patients

S. P. Tonic¹; M. Tkalcic¹; F. Blazic²; R. T. Peric³; A. Radovan²; G. Hauser^{2,4}

¹Department of Psychology, Faculty of Humanities and Social Sciences, University of Rijeka, Croatia, Rijeka, Croatia; ²Department of Internal Medicine, Division of Gastroenterology, Clinical Hospital Centre Rijeka, 51000 Rijeka, Croatia, Rijeka, Croatia; ³University Hospital Sveti Duh, Department of Hepatology and Gastroenterology, 10000 Zagreb, Croatia; J.J. Strossmayer University of Osijek, Medical school, 31000 Osijek, Croatia; University of Rijeka, Faculty of Health Studies, 51000 Rijeka, Croatia, Rijeka, Croatia; ⁴University of Rijeka, Faculty of Health Studies, 51000 Rijeka, Croatia, Rijeka, Croatia

Objective: Irritable Bowel Syndrome (IBS) is one of the most common and challenging disorder confronting gastroenterologist. Symptoms include abdominal pain associated with altered bowel habits. The disorder is characterized by heightened anxiety and depression. Even IBS patients with no comorbidities have higher, although still subclinical levels of anxiety and depression. There are many aspects of anxiety that can possibly contribute to IBS symptom perpetuation, but perhaps the most illness specific one is visceral anxiety. The aim of this study was to test the predictive value of trait anxiety, depression and visceral anxiety in the prediction of IBS symptom severity.

Methods: A total of 39 Rome IV-diagnosed IBS outpatients at tertiary care centre (79.4% F, M age = 49.4 years) were recruited. They completed a set of questionnaires, including State-Trait Anxiety Inventory (STAI-T), Beck Depression Inventory (BDI-II) and Visceral Anxiety Inventory (VSI). They also kept a diary for 14 days which, among other aspects, involved completing a short symptom intensity scale. The total symptom intensity was calculated for each day and a final average of 14 days was used for each participant.

Results: Symptom severity was positively correlated with trait anxiety (r = .37*), depression (r = .35*) and visceral anxiety (r = .58**). Hierarchical regression analysis showed that in the final model only visceral anxiety was a significant predictor ($\beta = 0.51^{**}$) of symptom severity and the model explained a total of 35.8% of symptom severity variance. Considering that trait anxiety significantly predicts symptom severity ($\beta = 0.37^{*}$) when entered in the model alone and that adding depression ($\beta = 0.17$) in the second step reduces that effect to non-significant ($\beta = 0.24$), and finally adding visceral anxiety in the third step completely nullifies that effect ($\beta = 0.08$) there are indications that depression partially and visceral anxiety fully mediates the trait anxiety – symptom severity relationship.

Conclusions: The obtained results indicate that trait anxiety and depression might be related to symptom severity via visceral anxiety, which emphasizes the importance of using this simple, yet very informative measure of illness-specific anxiety in IBS patients.

43 | Dietary intakes in patients with functional dyspepsia: Compared with data from Korean national health and nutrition examination survey (KNHANES VII-1)

H. S. Lee¹; K. J. Lee²; J. K. Kang²

¹Inje University Busan Paik Hospital, Busan, South Korea; ²Ajou University School of Medicine, Suwon, South Korea

Objective: Patients with Functional dyspepsia (FD) have a tendency to avoid specific food because their symptoms tend to be induced by their food consumption. However, few studies have investigated the association between FD and food consumption. This study aimed to investigate the dietary intakes in patients with FD, compared with general population.

Methods: Thirteen patients with FD (5 postprandial distress syndrome, 6 epigastric pain syndrome, 2 overlap) participated in the study. Their dietary patterns consisted of 115 food items were compared, with general population data from Korean National Health and Nutrition Examination Survey (KNHANES VII-1). Survey data were used to calculate food consumption per week.

Results: Food consumption of ramen (0.32 ± 0.813 vs 1.08 ± 1.222 ; $P = 0.006$), black-bean-sauce noodle (0.14 ± 0.118 vs 0.33 ± 0.454 ; $P < 0.001$), pear (0.26 ± 0.097 vs 0.38 ± 0.767 ; $P = 0.001$), snack (0.22 ± 0.323 vs 0.77 ± 1.297 ; $P < 0.001$) in FD patients were significantly lower, compared with general population. Food consumption of soybean paste soup (4.50 ± 3.837 vs 0.85 ± 1.151 ; $P = 0.005$), soybean paste stew (4.10 ± 3.837 vs 1.02 ± 1.161 ; $P = 0.022$), tofu (2.41 ± 2.641 vs 0.66 ± 1.026 ; $P = 0.034$), stewed beans (2.18 ± 2.715 vs 0.35 ± 1.162 ; $P = 0.032$), steamed egg (3.21 ± 3.201 vs 0.86 ± 1.388 ; $P = 0.021$), hair-tail (0.60 ± 0.774 vs 0.26 ± 0.503 ; $P = 0.014$), bean sprout (3.75 ± 3.880 vs 0.85 ± 1.035 ; $P = 0.020$), seasoned pumpkins (2.22 ± 2.368 vs 0.38 ± 0.663 ; $P = 0.016$), boiled potato (1.45 ± 1.972 vs 0.14 ± 0.376 ; $P = 0.034$), and chestnut (1.17 ± 1.636 vs 0.12 ± 0.382 ; $P = 0.004$) in patients with FD were significantly higher than those of general population.

Conclusions: This study suggested that dietary intake of FD patients differs from that of general population. This dietary change of FD patients may be due to postprandial symptoms.

44 | Characteristics of fecal metabolic profiles in irritable bowel syndrome with predominant diarrhea investigated by 1H-NMR coupled with multivariate statistical analysis

S. Y. Shin¹; C. H. Choi¹; W. S. Kim¹; H.-K. Choi²

¹Chung-Ang University College of Medicine, Seoul, South Korea; ²Chung-Ang University College of Pharmacy, Seoul, South Korea

Objective: Gut microbiota and its metabolites are known to be closely related to various diseases. The aim of this study was to identify fecal metabolites of patients with irritable bowel syndrome with predominant diarrhea (IBS-D) and compare with those of healthy controls (HC) using 1H-nuclear magnetic resonance spectrometry (1H-NMR).

Methods: A total of 29 IBS-D patients diagnosed according to the ROME IV criteria, and 16 HC without other specific disease were enrolled. With their usual diet maintained, the fecal samples were collected, and analyzed by nuclear magnetic resonance spectrometry (NMR)-based global metabolic profiling coupled with multivariate statistical analysis. Identified fecal metabolites were compared between the two groups.

Results: We detected 55 metabolites by averaged 600 MHz 1H-NMR spectra of fecal samples, based on Chenomx NMR suite database and the human metabolome database (HMDB; <http://www.hmdb.ca/>): 16 amino acids, 16 organic acids, 4 amines, 4 phenols, 3 sugars and 12 other compounds (Fig 1). Further confirmation of these metabolites was performed by 1H-1H COSY and 1H-13C HSQC, as shown in Fig 2. Orthogonal partial least square-discriminate analysis (OPLS-DA) score plots showed clear separation between the HC group and the IBS-D group, which suggests that the levels of certain metabolites in fecal samples were different (Fig 3). From the 55 identified metabolites, we found 15 characteristic fecal metabolites with a variable influences on projection values (VIP) cutoff value >1 from OPLS-DA, which distinguish between HC group and IBS-D group: succinate, methanol, isobutyrate, lactate, cadaverine, putrescine, glutamate, arginine, leucine, glycerol, valine, proline, serine, methionine, and threonine.

Conclusions: Our study provides characteristic fecal metabolites in Korean patients with IBS-D by 1H-NMR coupled with multivariate statistical analysis. There are significantly different fecal metabolites between IBS-D and HC. These data can be used as a basis for identifying the causes of disease and developing treatments.

47 | What is appropriate upper endoscopic interval among dyspeptic patients with previously normal endoscopy? A Korean multicenter study with bayesian change point analysis

J. W. Kim¹; K. W. Jung²; J. G. Kwon³; J. B. Lee²; J. K. Park⁴; K. B. Bang⁵; C. H. Tae⁶; J. H. Oh⁷

¹Inje University Ilsan Paik Hospital, Goyang, South Korea; ²Asan Medical Center, Seoul, South Korea; ³Daegu Catholic University School of Medicine, Daegu, South Korea; ⁴Gangneung Asan Hospital, Gangneung, South Korea; ⁵Dankook University College of Medicine, Cheonan, South Korea; ⁶Ewha Womans University Hospital, Seoul, South Korea; ⁷The Catholic University of Korea, Seoul, South Korea

Objective: Appropriate interval for performing follow-up endoscopy among dyspeptic patients to detect upper gastrointestinal (UGI) tract dysplasia without abnormal findings on previous endoscopy is unclear. We analyzed the multicenter-collected data from the Korean Society of Neurogastroenterology and Motility.

Methods: We collected clinical data of dyspeptic patients who visited the gastroenterology department and underwent two or more sessions of upper endoscopy during 2012-2017 at seven university hospitals in Korea. Patients with endoscopic interval between 90 days and 760 days were included. For those with multiple endoscopic sessions, only the first two were analyzed. Positive outcome

was defined as adenoma or cancer in upper gastrointestinal tract. To identify the point of change and estimate the properties of the stochastic process before and after the change, we used Bayesian regression with Metropolis-Hastings algorithm.

Results: There were 1595 patients. Mean age was 58.8 years (standard deviation [SD], 12.8). Median interval of endoscopy was 437 days (SD, 153). On follow-up endoscopy, there were 12 patients (0.75%) who had UGI dysplasia (four with gastric cancer and eight with gastric/duodenal adenoma). As the prior hypothesis, we presumed the change point (CP) of increase in frequency of organic lesion as 360 days. After random-walk Metropolis-Hastings sampling with Markov Chain Monte Carlo (MCMC) iterations of 5000, the CP was 560 days (95% credible interval [CI] 139-724). There was an increase in frequency of dysplastic lesions from an estimated average of 0.007 (95% CI, 0.002-0.021) cases per day before day 560, to 0.024 (95% CI, 0.006-0.073) cases per day after day 560. After day 560, the mean frequency increased by a factor of 4.4 (95% CI, 0.4-13.8).

Conclusions: To rule out dysplastic lesions among dyspeptic patients who had previously normal endoscopy, a 1.5 to 2-year interval could be offered as follow-up interval for repeat upper endoscopy.

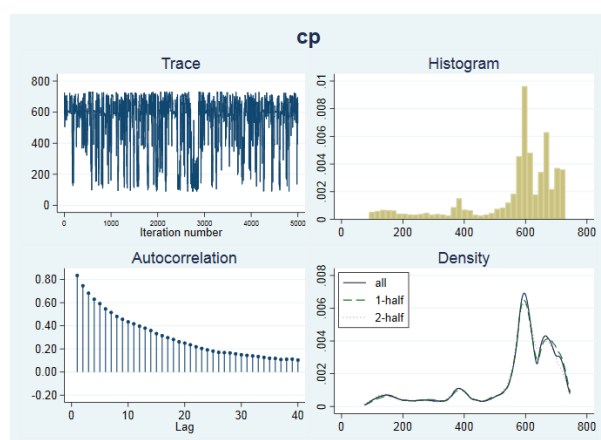


FIGURE Diagnostic plots of change point analysis to estimate the time point with increase in dysplasia on follow-up endoscopy. Change point (CP) analysis using random-walk Metropolis-Hastings sampling with Markov Chain Monte Carlo (MCMC) iterations of 5,000, the CP was 560 days. The trace plot is shown at upper left, with decreasing autocorrelation between the iterations shown at lower left. Overall estimated histogram for frequency of upper gastrointestinal neoplasia is shown at upper right. The density plots between the first and the second halves of the trace (lower right) show similar results.

48 | Prevalence of opioid therapy in patients with functional gastrointestinal disorders reviewed at a tertiary centre

A. Mari¹; M. Pesce²; A. Emmanuel²; N. Z. Lopez²

¹Nazareth Hospital EMMS, Nazareth, Israel; ²UCLH, London, UK

Objective: The appropriateness of chronic opioid use in patients with non-cancer pain is increasingly challenged due to limited evidence of its

efficacy and the risk of problematic use and dependence. The side effects of opioids on gut function suggest this therapy should be particularly avoided in patients with functional gastrointestinal (GI) disorders. Data on the prevalence of opioid use in patients with functional GI disorders is unknown. We aimed to evaluate the prevalence of opioid use in functional GI patients referred to a tertiary Neurogastroenterology clinic and to determine the risk factors for their initiation

Methods: 100 consecutive outpatients (85 females, 37 ± 15 years) with functional GI disorders referred for a specialist opinion at our tertiary referral centre were retrospectively reviewed. Two independent researchers (AM and FL) carried out a detailed chart evaluation of the presence and type of comorbidities and concomitant pharmacotherapy. Patients were also specifically asked about opioid use, the duration of therapy and the clinical indication for starting the opioids.

Results: Twenty-one patients (20F, 38 ± 12 years) were taking chronic opioid therapy. The main reason for opioid initiation was chronic musculoskeletal pain (12 patients, 57%), chronic abdominal pain (5 patients, 24%) and chronic pelvic pain (1, 5%). The mean duration of the opioid treatment was 2.7 ± 1 years. The risk factors associated with opioids use are depicted in table 1. In terms of management, patients under opioid were offered naloxegol (20%), psychology-based interventions (29%), and referral to pain specialists to rationalize opioid use (38%). The majority of the patients in the opioid group (80%) were referred for tertiary opinion from other areas of the UK, as compared to the 60% of patients without chronic opioid use.

Conclusions: Female patients with chronic functional GI disorders with associated extra-intestinal functional pain syndromes and psychological comorbidity are prescribed opioid therapy more frequently. These patients are at increased risk of developing eating difficulties requiring advanced nutritional support, which is known to be more complicated in opioid users. Access to multidisciplinary coordinated therapy including pain management and psychological therapy is required early in these patients to avoid these adverse outcomes.

50 | Efficacy of dolichos lablab L. on irritable bowel syndrome: Open-label prospective pilot trial

J. G. Kwon¹; J. T. Jung¹; E. Y. Kim¹; K. S. Park²; C. H. Yang³

¹Daegu Catholic University School of Medicine, Daegu, South Korea; ²Keimyung University School of Medicine, Daegu, South Korea; ³Dongguk University School of Medicine, Gyeongju, South Korea

Objective: Pathophysiology of irritable bowel syndrome (IBS) is poorly understood and management of IBS remains a challenge. Dolichos lablab L. (DL), a bean species, has traditionally been used for treating gastrointestinal disorders in China and Korea. However, no studies have investigated its use for treating IBS. The aim of this study is to examine the efficacy of DL on the symptom relief of IBS.

Methods: Twenty adult patients with IBS were enrolled. Eligible patients satisfied Rome IV criteria for diagnosis of IBS. After a 2-week observation period, all participants received DL extract capsules

for 8 weeks. Primary endpoint was the mean change of abdominal pain from baseline assessed by visual analogue scales (VAS) score for 8 weeks of treatment. Secondary endpoints were the changes in abdominal pain from baseline as week 4, patient-reported symptom improvement including stool frequency and consistency, and IBS-quality of life (IBS-QoL) at week 8.

Results: The VAS scores of abdominal pain at week 8, were significantly decreased. ($P < 0.0001$) Overall symptomatic improvement was observed in 13 (65%) participants at week 4 and 17 (85%) participants at week 8. Compared to baseline, the participant's IBS-QoL and frequency of defecation were significantly lower at 8 weeks after the administration of DL. Adverse events were observed in 2 participants and no drug-related severe adverse event was observed.

Conclusions: Treatment with DL was associated with relief of abdominal pain, overall symptomatic improvement and decreased frequency of defecation. The results showed the potential therapeutic application of DL in the treatment of IBS. Future studies with greater statistical power are needed to clarify the possible effects of DL in the treatment of IBS patients.

51 | Water avoidance stress alters colonic microbiota and short chain fatty acids in the rat

Y. S. Kim¹; M. S. Kim²; M. Y. Lee²; T. Unno³; H.-S. Ryu¹; S. C. Choi¹; M.-S. Park⁴

¹Digestive Disease Research Institute Wonkwang University, Iksan, South Korea; ²Department of Physiology Wonkwang University, Iksan, South Korea; ³Faculty of Biotechnology, School of Life Sciences Jeju National University, Jeju, South Korea; ⁴Institute of Metabolic diseases Wonkwang University, Iksan, South Korea

Objective: Water avoidance stress (WAS) in rat commonly used in the study for the effect of mental stress on the gastrointestinal tract. We aimed to investigate the effect of WAS on gut microbiota and short chain fatty acid (SCFA). We also investigate whether the administration of *Lactobacillus brevis* (LB) strains can decrease WAS effect.

Methods: Twenty-four female Wistar rat was divided into four experimental groups (Sham WAS, WAS, WAS with LB199, WAS with LB377). All rats exposed to 10 days WAS or sham WAS, and probiotics were administered by oral gavage once daily. Body weight, food intake, and fecal pellet output (FPO) were measured daily. After ten days, the cecum was harvested, and cecal SCFA was analyzed by gas chromatography. Fecal pellet was collected, and fecal microbiota was analysed by 16S rRNA NGS using MiSeq.

Results: WAS significantly increased FPO, but probiotic could not prevent increased defecation. The food intake in the WAS group was slightly decreased, but it was not significant. Cecal propionate and acetate level were not different among groups. In NGS analysis, there was no definite compositional change in gut microbiota. In WAS group, *Roseburia* (butyrate producer) was decreased, and *Akkermansia* and *Ruminococcus* were increased compared with Sham WAS group. In WAS with LB 199 group, *Lactobacillus reuteri*, *Roseburia*, and S24-7 (family) OTU 017 were increased, and S24-7 OTU 005, *Runimococcaceae_unclassified* OTU 224 were decreased comparing

with WAS group. In WAS with LB 377 group, S24-7 (family, OUT 017, OUT 122, OUT 274) were increased, and *Runimococcaceae_unclassified* and S24-7 (OTU 006) were decreased compared with WAS group. The butyrate level was decreased in WAS group though it was not significant ($P = 0.065$) and it was increased in WAS with LB 377 group but not in WAS with LB 199 group.

Conclusions: Psychological stress alters some gut microbiota including butyrate producers and decreases colonic butyrate level in the rat. *Lactobacillus brevis* administration can reduce the effect of psychological stress, but it was strain specific.

Differential abundance test: WAS vs Sham



52 | Diarrhoea-predominant irritable bowel syndrome colonic biopsies exhibit tuft cell hyperplasia

M. Connolly; J. Aigbologa; R. O'Brien; M. M. Buckley; J. M. Buckley; D. O'Malley

University College Cork, Cork, Ireland

Objective: Tuft cells are a rare subtype of gastrointestinal epithelial cell, which are thought to be activated by parasites and allergic reactions. Luminal stimulation causes release of pro-inflammatory cytokines, which can modulate gastrointestinal function. Irritable bowel syndrome (IBS), a heterogeneous functional bowel disorder, characterised by abdominal pain and altered bowel habit, exhibits altered circulating cytokine profiles. The aim of this study was to investigate if the number of colonic tuft cells was altered in human IBS or in a stress-sensitive animal model of IBS.

Methods: The number of DCLK1 immuno-labelled tuft cells with a strong cytoskeleton labelled with Phalloidin-iFluor 488 was compared between mucosal biopsies from diarrhoea- and constipation-predominant IBS patients and healthy controls ($n = 6$ per group). The number of tuft cells was also compared in colonic cross-sections from stress-sensitive Wistar Kyoto rats and the control Sprague Dawley comparators ($n = 3$ per group).

Results: As compared to healthy controls, colonic tuft cell hyperplasia was detected in diarrhoea-predominant IBS mucosal biopsies ($P < 0.05$). Increased numbers of tuft cells were also detected in the colonic mucosa of Wistar Kyoto rats ($p < 0.05$) as compared to Sprague Dawley controls.

Conclusions: These findings illustrate a previously unreported change in IBS colonic morphology. Gastroenteritis, which could stimulate tuft cell hyperplasia, is a strong predictor of developing IBS. However, none of this patient cohort was diagnosed with post-infectious IBS. Moreover, clean rodent housing indicates that a catalyst other than the known stimuli of protozoans and helminths caused the increase in tuft cells in Wistar Kyoto rats. Activation

of the stress response and its capacity to exacerbate and prolong symptom flares is an accepted contributing factor in human IBS pathophysiology, and as such, is worthy of further investigation as an underlying cause of colonic tuft cell hyperplasia in IBS.

55 | Diagnostic yield and agreement of balloon expulsion test, high resolution anorectal manometry, and defecography in patients with intractable symptoms of chronic constipation

K. J. Lee¹; H. S. Lee²; J. W. Park¹

¹Ajou University Hospital, Suwon, South Korea; ²Inje University Hospital, Busan, South Korea

Objective: The balloon expulsion test (BET), anorectal manometry (ARM), and defecography represent the three main diagnostic modalities for evacuatory function. However, evidence has shown considerable disagreement between the three diagnostic modalities. The aim of the study was to compare the diagnostic yield and agreement between the tests in patients with intractable symptoms of chronic constipation.

Methods: Fifty four consecutive adult patients (M:F=16:38, median age 62 years) with intractable symptoms of chronic constipation were studied in a prospective manner. All patients met the criteria of Rome IV for functional constipation. All patients underwent high resolution ARM using a water-perfused catheter (Solar GI, MMS, Enschede, the Netherlands) with BET, and defecography. Abnormal BET was defined as >60 s. Abnormal ARM was defined as impaired anal relaxation (<20%) or an insufficient increase in rectal pressure (<45 mmHg) on the push maneuver. Functional abnormalities on defecography included impaired evacuation (<35%) or no increase of anorectal angle on defecation. Structural abnormalities included rectocele >4 cm in depth, recto-anal intussusception, or rectal prolapse.

Results: Abnormal BET was observed in 14 patients (25.9%). Sixteen patients (29.6%) showed abnormal ARM findings. Abnormal BET and/or ARM findings were observed in 24 (44.4%) patients. Ten patients, whose BET was negative, showed abnormal ARM findings (18.5% more diagnostic yield). Functional and structural abnormalities on defecography were found in 25 (46.3%) and 12 (22.2%) patients, respectively. Thirty one patients (57.4%) showed at least one abnormal finding on defecography. Twenty-four patients, whose BET was negative, showed abnormal findings on defecography (44.4% more diagnostic yield). Fifteen patients, whose BET and ARM findings were normal, showed abnormalities on defecography (27.8% more diagnostic yield). Agreement was slight between BET and ARM ($\kappa = 0.171$). There was poor agreement between BET and defecography ($\kappa = -0.072$). Agreement was moderate between ARM and functional findings on defecography ($\kappa = 0.504$), and between ARM and defecography ($\kappa = 0.336$).

Conclusions: There is considerable disagreement between BET and the results of ARM and defecography. BET does not seem to be appropriate as a screening test for evacuation disorders, and addition of ARM and defecography can increase the diagnostic yield of evacuation disorders.

56 | Trimebutine – Intestinal microflora modulator in experimental dysbiosis

N. Tropskaya; I. Vilkova; E. Kislyakova; T. Chernenkaya; T. Popova

Skifosovsky Research Institute for Emergency Medicine, Moscow, Russia

Objective: This study investigates the intestinal microflora species composition in rats with dysbiosis after the course administration of a non-selective opiate receptor agonist – trimebutine.

Methods: 21 male Wistar rats weighing 250-300 g were used. The control group consisted of 7 healthy rats. Antibiotics – amoxicilline (28.5 mg/kg) and metronidazole (22.8 mg/kg) were administered orally daily for 7 days in the “dysbiosis” group ($n = 7$). Trimebutine prokinetic drug (2.86 mg/kg) was administered once daily for 7 days after 7 daily administration of antibiotics in the group “dysbiosis + trimebutine” ($n = 7$). Cecum samples were collected for bacterial studies.

Results: Administration of antibiotics for 7 days significantly changed the qualitative and quantitative composition of the rat's intestinal microflora in the dysbiosis group compared with the control group. Thus, the numbers of *E.coli* and *Klebsiella* spp. significantly increased (up to 108 CFU/ml and 106 CFU/ml, respectively). The disappearance of *Staphylococcus* spp. and the appearance of *Candida* spp. were shown. The number of *Lactobacillus* sp. and *Bifidobacterium* sp. species was slightly increased. The disappearance of *Klebsiella* spp., as well as the restoration of the number of *Staphylococcus* spp. to the normal values was found after the administration of prokinetic drug trimebutine (group “dysbiosis + trimebutine”). In addition, there were a significant increase of *Lactobacillus* spp. (109 CFU/ml) and *Bifidobacterium* spp. (108 CFU/ml) in cecum.

Conclusions: Course administration of trimebutine in experimental dysbiosis led to the restoration of conditionally pathogenic microflora in the cecum and a significant increase in the number of normal eobionts. This may indicate a modulating effect of a non-selective opiate receptor agonist on the intestinal microflora.

58 | Quality of the internet information for Korean patients with functional constipation

K. S. Park¹; Y. J. Lee¹; H. S. Ryu²; Y. S. Cho³; J. W. Kim⁴; S.-Y. Park⁵; T. H. Lee⁶; S.-E. Kim⁷; J. E. Shin⁸

¹Keimyung University School of Medicine, Daegu, South Korea; ²Wonkwang University School of Medicine, Iksan, South Korea; ³Soonchunhyang University College of Medicine, Cheonan, South Korea; ⁴Kyung Hee University School of Medicine, Seoul, South Korea; ⁵Chonnam National University Hospital, Gwangju, South Korea; ⁶Soonchunhyang University College of Medicine, Seoul, South Korea; ⁷Ewha Womans University College of Medicine, Seoul, South Korea; ⁸Dankook University College of Medicine, Cheonan, South Korea

Objective: The internet is one of the most frequently used tool for patients to obtain information about their disease. Despite of increasing use of internet, little is known about the quality of the web sites especially on functional constipation (FC). We aimed to evaluate the quality of the internet information for the Korean patients with FC.

Methods: Members of Constipation Study Group in the Korean Society of Neurogastroenterology and Motility developed Quality Evaluation Instrument (QEI) based on the recent guidelines of FC in Korea. Through searching of the terms 'constipation' and 'functional constipation' in the three most renowned search engines in South Korea, 50 websites were selected in this study. Two gastroenterologists rated these web sites according to QEI that awarded sites points (0-68), 5-point global quality score (GQS) and the validated DISCERN instrument (15-75).

Results: The median QEI score was 7 ([min-max] 0-47; [IQR] 4.0-14.25) and the median GQS was 1 ([min-max] 0-4; [IQR] 1-2). When evaluated by DISCERN, 14% (7/50) were rated as excellent to good and 86% (43/50) as fair to very poor. In spearman correlation analysis, QEI score showed good correlation not only DISCERN instrument ($r = 0.82$, $P < 0.001$) but also GQS ($r = 0.75$, $P < 0.001$). Based on analysis using DISCERN instrument, the institutional sites scored best, whereas alternative medicine, mess media and support sites scored significantly lower than other sites. There was no significant difference among search engines in regards to mean DISCERN score, QEI and GQS.

Conclusions: The quality of the Korean web sites providing health information on FC showed substantial variation. In order to provide adequate health information to patients with FC, it is necessary to establish an assurance system to control quality of health information.

59 | Wireless motility capsule compared with gastric emptying scintigraphy in the assessment of diabetic gastroparesis

D. A. Sangnes¹; M. Bekkelund²; E. Søfteland¹; G. Dimceviski³

¹Haukeland University Hospital, Bergen, Norway; ²University of Oslo, Oslo, Norway; ³University of Bergen, Bergen, Norway

Objective: Gastroparesis is a serious late complication of diabetes mellitus. It can lead to nausea, vomiting, postprandial distress, abdominal pain and difficulties in blood sugar regulation. Delayed gastric emptying is mandatory for establishing the diagnosis. In this study, we compared wireless motility capsule (WMC) with gastric emptying scintigraphy (GES).

Methods: Seventy-two patients (49 women) with diabetes mellitus types 1 and 2 (59 / 13) and symptoms compatible with gastroparesis, were prospectively included between 2014 and 2018. Patients were admitted to Haukeland University Hospital during examinations. After a minimum of 8-hours fast, they were simultaneously examined with WMC and 4-hour GES. All patients were on intravenous glucose-insulin infusion during testing.

Results: At standard cutoff-value (300 minutes), WMC found delayed gastric emptying in 52% of patients. Compared to GES, the method had a sensitivity of 0.92 and a specificity of 0.73. Correlation was $r = 0.74$, Kappa measure of agreement 0.61, both $P < 0.001$. By Receiver Operating Characteristics (ROC), the area under the curve was 0.95 ($p < 0.001$, 95 % CI 0.89 – 1.00). Using ROC curve coordinates, we calculated a new cut off value of 385

minutes for delayed gastric emptying with WMC. This gave sensitivity 0.92, specificity 0.85 and agreement 0.72 ($p < 0.001$) in comparison with GES. Inter-rater reliability for gastric emptying time with WMC was $r = 0.996$ ($p < 0.001$).

Conclusions: In patients with suspected diabetic gastroparesis, WMC showed substantial agreement with GES for determining gastric emptying. By elevating the cut-off value for delayed emptying from 300 to 385 minutes, we found an even higher specificity without reducing sensitivity. Inter-rater reliability for WMC was very strong.

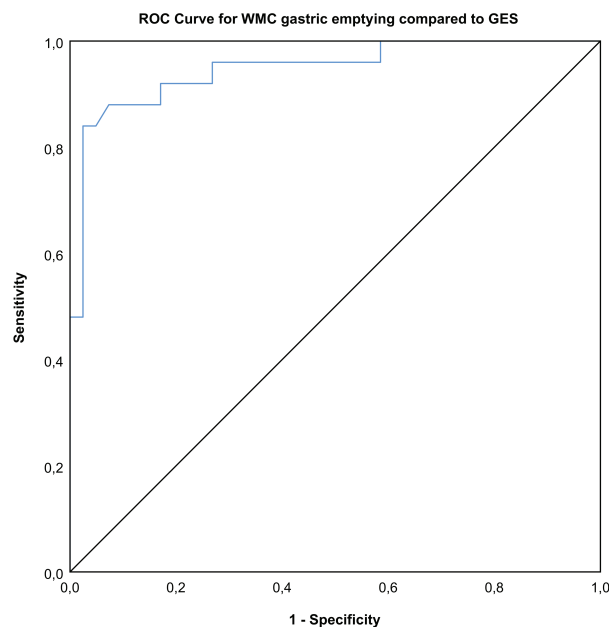


FIGURE. ROC curve for WMC gastric emptying compared to 4-hour GES. AUC for the ROC was 0.95 ($p < 0.001$, 95 % CI 0.89 – 1.00).

Abbreviations: ROC, Receiver Operating Characteristics; WMC, Wireless Motility Capsule; GES, Gastric Emptying Scintigraphy; AUC, Area under Curve.

61 | The clinical application of esophageal functional luminal imaging probe (FILP) panometry in Korean achalasia patients who underwent peroral endoscopic myotomy: Based on a single center database

L.-C. Hsing¹; K. M. Choi²; K. W. Jung¹; S. Joo²; M. Seo³; H.-Y. Jung¹

¹Departments of Gastroenterology, University of Ulsan College of Medicine, Asan Medical Center, Seoul, South Korea; ²Departments of Biomedical Engineering, University of Ulsan College of Medicine, Asan Medical Center, Seoul, South Korea; ³Gangneung Asan Medical Center, Gangneung, South Korea

Objective: Esophageal functional luminal imaging probe (FILP) panometry has been used to evaluate clinical characteristics of esophageal motor disorders. However, its clinical application and usefulness are not fully validated. We investigated the clinical usefulness of

FLIP panometry using a single tertiary center database of achalasia patients who underwent peroral endoscopic myotomy (POEM).

Methods: From October 2017 to December 2018, achalasia patients who underwent FLIP panometry before POEM were enrolled. Follow-up included esophageal manometry and symptoms questionnaires. FLIP data were analyzed after interpolating with the cubic spine method using MATLAB software.

Results: Records of 33 patients (M:F = 17:16, age = 51.09 ± 16.03) were included. Manometric diagnoses were achalasia type I (N = 8), type 2 (N = 19), type 3 (N = 5), and esophagogastric junction (EGJ) outflow obstruction (N = 1). FLIP panometric diagnoses were spastic achalasia (N = 16), achalasia without contractility (N = 5), EGJ outflow obstruction (N = 1), spastic motor disorder (N = 8), and absent contractility (N = 3). Eckardt symptom scores showed significant improvement after POEM (from 5.61 ± 2.61 to 1.52 ± 1.28 , $P < 0.01$). Achalasia subtype did not predict the responsibility to POEM; however, patients with spastic motor disorder or absent contractility identified by FLIP panometry showed marginal symptomatic improvement after POEM ($P = 0.04$).

Conclusions: The FLIP provides an alternative and complementary method in HRM for evaluation of esophageal motility disease. The FLIP panometry showed a potential in the prediction of clinical course after POEM. However, It still needs more data to validate its clinical meaning.

62 | Complex ultrasound assessment of gut function in metabolic syndrome: Role of colonic wall thickness, motility, inflammatory and vascular markers

R. V. Bubnov¹; M. Y. Spivak²

¹Clinical Hospital Pheophania, Kyiv, Ukraine; ²Zabolotny Institute of Microbiology and Virology NAS of Ukraine, Kyiv, Ukraine

Objective: Metabolic syndrome (MetS) is associated with alteration gut motility. The mucosal and submucosal layers of colonic wall are the place of interaction with gut microbiota triggering mucosal immunology pathways. Ultrasound (US) can help detect gut motility, evaluate colonic wall thickness and other parameters like metabolic (NAFLD, liver size and stiffness), vascular (mesenteric blood flow) and inflammatory (visceral fat/spleen size) markers for stratification of patients with MetS. The Aim was to evaluate the relevance of ultrasound measurements of colon wall thickness, inflammatory and vascular markers in obese patients.

Methods: We included 120 overweight subjects (age 24-76 years; 65 females), BMI > 30, waist circumference (WC) > 110. 30 healthy volunteers were controls. All patients underwent general clinical, lab tests; abdominal ultrasonography using multiparameter US of liver, shear wave elastography (SWE); measured bile ducts (CBD, choledochus and segmental bile ducts diameters), spleen size, abdominal and visceral fat (FV). Colonic wall thickness has been evaluated on ultrasound imaging of anterior wall in transverse, ascending and descending colon and in

small intestine, also M-mode was used to analyze peristaltic waves. We did standardized Doppler spectral analysis of mesenteric blood flow evaluation velocity criteria in superior & inferior mesenteric arteries.

Results: Constipation, colon hyperpneumatosis, hypomotility was in 68% patients; higher incidence of hypertension (in 62%); hypercholesterolemia (in 45%); hyperuricemia (in 28%); hyperglycemia (in 32%); nephropathy (in 37%), portal hypertension (in 32%) was in obese individuals ($P < 0.05$). Microbiota alteration was in 86 patients (78 patients demonstrated cholestasis). We observed decreased colonic wall thickness to 2-3.5 mm in obese individuals (up to 1-3 mm in DMT2 patients) vs 3-5.5 mm in controls. Mesenteric blood flow Doppler detected increasing PSV in superior & inferior mesenteric artery in obese individuals (up to 135-170 cm / sec vs 105-143 cm/s in controls, $P < 0.05$), abdominal aorta atherosclerosis, aneurisms. Microsplenia and increased VF correlated with thinning colonic wall ($r > 0.7$).

Conclusions: Decreasing colonic wall thickness is associated with constipation symptoms, metabolic syndrome, diabetes and altered mesenteric blood flow. Microsplenia and increased visceral fat are promising imaging markers of MetS.

63 | Functional gastrointestinal differences in gastric bypass patients using the wireless motility capsule

L. Ladebo¹; P. V. Pedersen¹; C. Brock¹; A. M. Drewes¹; L. L. Christrup²; A. E. Olesen³

¹Mech-Sense, Department of Gastroenterology and Hepatology, Aalborg University Hospital and Department of Clinical Medicine, Aalborg University, Aalborg, Denmark; ²Department of Drug Design and Pharmacology Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark; ³Department of Clinical Medicine, Aalborg University, and Department of Clinical Pharmacology, Aalborg University Hospital, Aalborg, Denmark

Objective: A Roux-en-Y gastric bypass (RYGB) alters the anatomy and physiology of the gastrointestinal tract by minimizing the stomach with 80% and bypassing the duodenum. Thus, the aim of this study was to determine the differences in gastrointestinal transit times and pH profiles in RYGB patients compared to healthy controls, using the wireless motility capsule (WMC).

Methods: 19 RYGB patients and 14 healthy controls underwent a standardized WMC assessment. Gastric emptying time (GET), small intestine transit time (SBTT), orocecal transit times (OCTT), colonic transit time (CTT), whole gut transit time (WGTT). Additionally, pH profiles for each segment were determined. Data were assessed by two independent investigators. Based on distribution of data a Student's t-test or Mann-Whitney U test was performed.

Results: Preliminary results showed that GET ($P < 0.0001$) and OCTT ($P = 0.001$) were significantly shorter in RYGB patients compared to healthy controls. No difference in SBTT ($P = 0.494$), CTT ($P = 0.145$) and WGTT ($P = 0.585$) was found. Furthermore, the median gastric ($P < 0.0001$) and orocecal pH ($P = 0.001$) were significantly higher in patients.

Conclusions: Gastric transit times were shorter and gastric pH profiles were more alkaline in RYGB patients compared to healthy

controls. Consequently, OCTT showed the same significant results. Results can be used for physiologically based pharmacokinetic modelling, which can help optimize drug therapy for this patient group with altered gastrointestinal physiology.

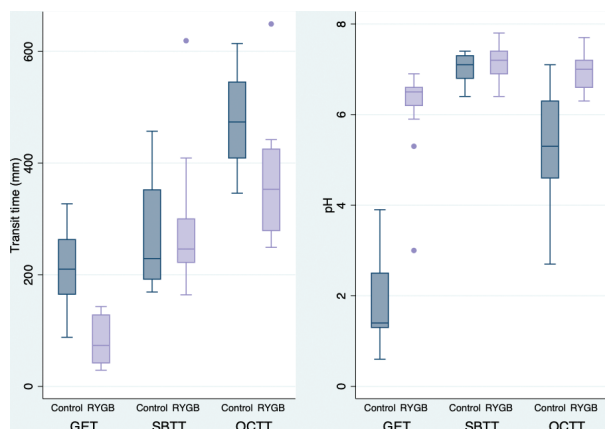


FIGURE. Boxplots of transit time and median pH in healthy controls versus RYGB patients for GET, SBTT and OCTT. Significant differences between GET and OCTT were found for both transit time and pH.

66 | Self-reported non-celiac gluten sensitivity in Korean population: Demographic and clinical characteristics

H. J. Kim; R. Cha

Department of Internal Medicine, Gyeongsang National University School of Medicine, Changwon, South Korea

Objective: Non-Celiac Gluten Sensitivity (NCGS) is a syndrome characterized by intestinal and extra-intestinal symptoms related to the ingestion of gluten-containing food. As no biomarkers of this disease exist, its frequency has been estimated based on self-reported symptoms, but no data are available about self-reported NCGS in Korean population. To explore the prevalence of self-reported NCGS in Korean population and to study their demographic and clinical characteristics. **Methods:** This study was performed among Korean participants between 18 and 80 years of age who visited gastroenterology outpatient clinics at nine tertiary hospitals in South Korea from January 2016 until February 2017. Asymptomatic adults were also recruited through a public advertisement. A total of 393 population completed a modified validated questionnaire for self-reported NCGS. Symptoms and quality of life were evaluated by means of 10-cm VAS. **Results:** Eighty subjects (20.7%) self-reported that they suffered from NCGS; The NCGS self-reporters very often had in IBS group (33.6%) compare than control group (5.8%) and symptomatic non-IBS group (23.4%). Multiple symptoms were recorded; the most frequent gastrointestinal symptoms being bloating (75%), abdominal discomfort (71.3%), and belching (45%); among the extra-intestinal symptoms, the most frequent were fatigue and headache. Over half

of the self-reported NCGS patients (66.3%) had symptoms after whet ingestion within less than 1 hour. Location of the symptoms after flour contained food ingestion with self-reported NCGS subjects are upper abdomen (38.7%), whole abdomen (30%), lower abdomen (20%) and middle abdomen (12.5%).

Conclusions: We showed that NCGS is quite Korean people, with a reported frequency of 20.7%. NCGS is associated with high symptom burden in IBS patients. Further study of self-reported gluten-induced symptoms are needed.

67 | Pneumatic dilatation without fluoroscopy for achalasia treatment

S. Kim; C. Choi; H. Kim; D. H. Kang; S. Park; H. Nam; D. Ryu

Pusan National University Yangsan Hospital, Yangsan, South Korea

Objective: Pneumatic balloon dilation under fluoroscopy is a relatively safe and effective nonsurgical treatment for achalasia patients. Access to fluoroscopic equipment is limited in some endoscopic unit, which leads to delays in treatment or to transfer to other centers for balloon dilation under fluoroscopy. This observation study describes a clinical outcome of pneumatic balloon dilation without fluoroscopy for achalasia patients.

Methods: The single center observational case study was conducted at a tertiary care hospital during 5 years included 5 patients (5 female, mean age 45 years, age range 32-57 years) with achalasia (diagnosed by endoscopy, clinical presentation, barium esophagogram, and conventional manometry). Remission was assessed by a structured interview and a previous symptoms score.

Results: Symptoms were dysphagia (n = 5, 100%), regurgitation (n = 3, 60%), chest pain (n = 2, 40%), and weight loss (n = 1, 20%). Four patients (80%) underwent a first dilation, one patient (20%) was a second dilation. One patient was required an additional balloon dilatation after 24 months from first balloon dilatation within a median of 20.7 months (range 16-48 months). The mean duration of symptoms prior to treatment was 13.0 ± 13 months. Relief of dysphagia was obtained for all patients and symptom score decreased from 2.4 before dilation to 0.1 at 1 month. Major complication (perforation, bleeding) after dilation was not occurred.

Conclusions: Pneumatic dilatation without fluoroscopy can be effectively and safely underwent for treatment of achalasia.

68 | Clinical outcome of pneumatic dilatation for pediatric patients with achalasia

S. Kim; S. Park; H. Nam; D. Ryu

Pusan National University Yangsan Hospital, Yangsan, South Korea

Objective: Pneumatic balloon dilation under fluoroscopy is a relatively safe and effective nonsurgical treatment for adults with achalasia. The clinical outcome of pediatric patients with achalasia is

limited. This observation study describes a clinical outcome of pneumatic balloon dilation for pediatric patients with achalasia.

Methods: The single center observational case study was conducted at a tertiary care hospital during a 10 years included 4 patients (2 female, mean age 14.3 years, age range 6-17 years) with achalasia (diagnosed by endoscopy, clinical presentation, barium esophagogram, and conventional manometry).

Results: Symptoms were dysphagia ($n = 4$, 100%), regurgitation ($n = 3$, 75%), chest pain ($n = 0$), and weight loss ($n = 1$, 25%). All patients underwent a first dilation. All patients were required an additional balloon dilatations. The success rate was 75%. Two patients needed second balloon dilatation during 3 years. One patient received 7 times pneumatic dilatation during 10 years. One patient received the esophagectomy because of perforation during second pneumatic dilatation.

Conclusions: The efficacy of pneumatic dilatation for pediatric patients with achalasia is limited. Alternative treatment such as endoscopic or surgical myotomy may be considered earlier.

69 | The role of glucose breath test for small intestinal bacterial overgrowth in children with functional abdominal pain disorders

C.-N. Paik¹; D. B. Kim¹; J. M. Lee¹; Y.-J. Kim¹; J. Lee²

¹Department of Internal Medicine, College of Medicine, St. Vincent's Hospital, Suwon, South Korea; ²Department of Pediatrics, Hanil General Hospital, Seoul, South Korea

Objective: Small intestinal bacterial overgrowth (SIBO) is expected in children with functional gastrointestinal disorders (FGID). This study was to estimate the prevalence of SIBO and investigate the clinical role of SIBO in children with FGID.

Methods: This prospective study involved children with functional abdominal pain disorder (FAPD) fulfilling the Rome IV. An hydrogen (H₂) – methane (CH₄) glucose breath test (GBT) using the EasySampler™ Breath Test Kit with symptom questionnaire, birth history, and types of feeding the presence of allergy. The diagnosis of SIBO was considered when there was an increase in the breath H₂ or CH₄ concentration of at least 12 ppm over the baseline value within 60 minutes after ingestion of the glucose solution.

Results: Fifty five children (range; 6-18 years, median; 12 years) were enrolled. SIBO was detected in 10 patients (18.2%). Irritable bowel syndrome ($P = 0.09$), loose stool ($P = 0.08$), and urgency ($P = 0.10$) were tend to be more common in children with SIBO than in children without SIBO. Whereas the history of allergy ($P = 0.10$) was less tend to be found in children with SIBO compared to those without SIBO. No significant differences were observed in other demographic findings.

Conclusions: In the presence of SIBO, the prevalence of IBS or functional intestinal symptoms appear to be common, but the history of allergy was less prevalent.

70 | Trust in the gastroenterologist and trust in the internet: Do they go against each other in irritable bowel patients?

T.-S. Rotaru¹; C. Anton²; O. Barboi²; C. Mihai²; G. Stefanescu²; V. Drug²

¹University of Medicine and Pharmacy Gr. T. Popa Iasi, Iasi, Romania; ²University of Medicine and Pharmacy Gr. T. Popa Iasi, University Hospital St Spiridon, Institute of Gastroenterology and Hepatology, Iasi, Romania

Objective: A patient's trust in their doctor is essential for his/her compliance to treatment. However, many patients with Irritable Bowel Syndrome (IBS) prefer to look up over the Internet for information in order to diagnose and treat themselves. Our first objective was to develop scales measuring the IBS patients' trust in their doctor as well as their trust in the information provided by the Internet. We also hypothesized a significant difference between those who look up for information over the Internet and those who don't with respect to the measure of trust in their gastroenterologist.

Methods: A small size sample with IBS ($N = 27$) completed a questionnaire of trust in their gastroenterologist which was elaborated based on current literature and on previous qualitative research. Some of these patients ($N = 16$) reported to have consulted the Internet regarding their diagnosis and possible treatments. Therefore, they also completed a questionnaire regarding their trust in the information about IBS, which they looked up over the Internet.

Results: Despite the small sample of patients, we operated reliability statistical computations for both scales. In both cases, the average inter-item correlation fit the interval 0.15-0.50. In the inter-item correlation matrix, we suppressed most of the items responsible for deviations from the 0.15-0.50 interval. The Alpha Cronbach coefficient was 0.83 for the trust in the gastroenterologist scale (ten items left). There was a statistically significant difference between those who looked up for information over Internet and those who didn't with respect to their trust in the gastroenterologist $t(25) = -4.6$, $P < 0.01$. Effect size calculated with G*Power Statistics was large (Cohen's $d = 1.65$).

Conclusions: The results for the scale of trust in the gastroenterologist is promising for the development of a stable self-report tool. Those who use Internet for information about IBS might have lower trust in their gastroenterologist due to their general lack of tolerance towards uncertainty and their hypochondriac tendencies. These results confirm some insights in our previous qualitative research about IBS patients' trust in their doctor.

73 | Gender difference in lactulose breath test

J. O. Chung; S.-Y. Park; H. A. Cho; J. W. Kim; J.-S. Rew

Chonnam national university hospital, Gwangju, South Korea

Objective: There are conflicting reports on the effect of host factors on the results of hydrogen breath test. The objective of this study was to investigate the association between clinical factors and lactulose breath tests.

Methods: Among a total of 307 consecutive patients with functional gastrointestinal symptoms over 7 years who had undergone lactulose hydrogen breath test, 268 patients were enrolled in this study. We analyzed the demographic and clinical factors for positive lactulose breath test.

Results: Of 268 patients included in this study, 143 (53.4%) were females. The median age and BMI of all patients was 58.0 years (range, 18.0–80.0 years) and 22.5 kg/m² (range, 14.4–34.3). There was a weak positive correlation between body mass index and baseline hydrogen level ($\rho = 0.134$, $P = 0.031$). There were significant differences 'H₂ > 20 ppm within 90 minutes' ($P = 0.013$), '≥20 ppm rise in H₂ within 90 minutes' ($P = 0.049$), CH₄ > 10 ppm within 90 minutes' ($P = 0.024$) and '≥10 ppm rise in CH₄ within 90 minutes' ($P = 0.001$) between men and women. After adjusting for age and BMI, women were significantly associated with positive results for 'H₂ > 20 ppm within 90 minutes' and '≥20 ppm rise in H₂ within 90 minutes'. Furthermore, positive results of methane parameters except 'baseline CH₄ > 10 ppm' were still more frequently observed in women. Patients with '≥20 ppm rise in H₂ within 90 minutes' (28/64, 43.8%) had more positive results for early methane rise than patients without early hydrogen rise (0/204, 0%, $P < 0.001$).

Conclusions: Hydrogen and methane breath tests were associated with gender. Hydrogen production was also correlated with methane production.

77 | Health-related quality of life, work productivity, and indirect costs among patients with diabetic gastroparesis

J. L. Abel¹; K. Burslem¹; J. A. Doshi²; L. Lee³

¹Allergan plc, Madison, New Jersey, United States; ²University of Pennsylvania, Philadelphia, Pennsylvania, United States; ³Kantar Health, San Mateo, California, United States

Objective: Diabetic gastroparesis (DG) is a complication of long-standing diabetes mellitus (DM). This study assessed the impact of DG on health-related quality of life (HRQoL), work productivity, activity impairment, and indirect costs among a sample of the US population.

Methods: Adult respondents were identified from the self-administered, internet-based, 2017 National Health and Wellness Survey. DG patients self-reported a diagnosis of DM (type 1 or 2) and gastroparesis. Controls had no reported diagnosis of DM or gastroparesis. 5 level EuroQoL 5 dimensions (EQ-5D-5L) index, Medical Outcomes Study 36-Item Short Form Health Survey Instrument version 2 mental and physical component summary (MCS, PCS) [range: 0–100], and Short Form-6 Dimensions (SF-6D) [health utility; range: 0–1] assessed HRQoL. Work Productivity and Activity Impairment Questionnaire: General Health (WPAI:GH) evaluated absenteeism, presenteeism, and daily activity impairment (higher percentages = greater impairment). Mean annualised indirect costs were estimated based on overall work productivity loss (absenteeism +

presenteeism). A propensity scoring approach matched DG patients and controls 1:1. Generalised linear models compared DG patients to matched controls, adjusting for unbalanced variables between groups post-match (ie age, ethnicity, exercise, alcohol consumption, income, body mass index, geographic region).

Results: 236 respondents were included (118 DG patients and matched controls). After regression adjustment, DG patients had significantly lower HRQoL versus controls based on EQ-5D-5L index (0.65 versus 0.71; $p = 0.010$), MCS (40.75 versus 43.66; $p = 0.045$), PCS (37.58 versus 43.64; $p < 0.001$), and SF-6D (0.59 versus 0.65; $p = 0.001$) mean scores. DG patients reported 2.02 times greater presenteeism (mean: 31.02% versus 15.37%; $p = 0.029$), 2.14 times greater overall work impairment (mean: 38.29% versus 17.92%; $p = 0.023$), and 1.29 times greater activity impairment (mean: 50.34% versus 39.04%; $p = 0.006$) versus controls. Estimated total indirect costs were nearly 6 times higher for DG patients versus controls (mean: \$15,330.09 versus \$2573.97; $p = 0.002$).

Conclusions: DG patients have significantly lower HRQoL, greater impairments in work and daily activities, and higher indirect costs vs matched controls, imposing a considerable burden on patients and employers. Writing assistance by Complete HealthVizion.

79 | Prevalence of gastroesophageal disease in Korea

K. Y. Tae¹; O. Y. Lee¹; S. Y. Woon²; K. N. Lee¹; J. H. Yoon¹; D. W. Jun¹; H. L. Lee¹; H. S. Choi¹; B. C. Yoon¹

¹Hanyang University Hospital, Seoul, South Korea; ²Inha University Hospital, Incheon, South Korea

Objective: GERD affects greatly on the life quality of the patients, accounting for a high healthcare cost in worldwide. GERD is one of the most frequent gastroesophageal disorders found in Western populations, and its prevalence in Asia is relatively low but increasing prevalence has been reported over time. There have been a few studies that investigated the domestic prevalence of GERD, but they used endoscopy or symptom frequency of heartburn or regurgitation as diagnostic tools. To our best knowledge, there has been no study that used GERD-Q to calculate prevalence. Therefore, this study aims to investigate prevalence and risk factors of GERD using GERD-Q tool.

Methods: The survey was carried out from September 6th to 13th in 2018 targeting general male and female adults living in South Korea. The subjects were selected randomly through quota sampling, according to the population ratio (sex, age, region). GERD-Q is composed of 6 items (heartburn, regurgitation, epigastric pain, nausea, sleep disturbance, use of medication) and cut-value was 8. Additionally, heartburn and regurgitation frequency over last year were used.

Results: Prevalence of GERD in Korea was 7.5% using GERD-Q and 6.2% with at least once a week of heartburn and/or regurgitation. There were no association with any of the risk factors (sex, age, education level, occupation, income, marital status). GERD negatively affect quality of life.

Conclusions: Prevalence of GERD in Korea was 7.5% using GERD-Q and GERD negatively affect quality of life.

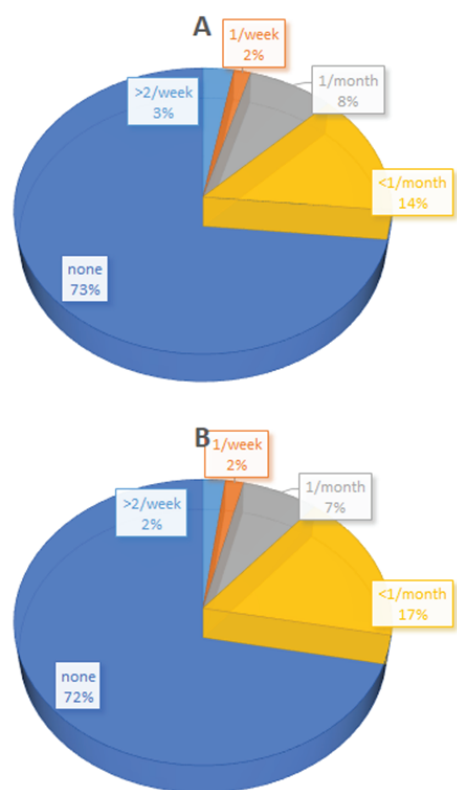


Fig. 1 Prevalence of GERD symptom: (A) Heartburn (B) Regurgitation

80 | Low concentrations of arginine vasopressin (AVP) act at V1A receptors in human stomach to increase frequency and amplitude of spontaneous rhythmic contractions: Role in nausea

R. Makwana¹; S. Elahi¹; M. Adebibe²; J. Loy²; G. J. Sanger¹

¹Queen Mary University of London, London, UK; ²Homerton Hospital, London, UK

Objective: Nausea is associated with electrical tachygastric and an elevated blood concentration of AVP. Exogenously-administered AVP causes nausea and tachygastric or bradygastric^{1,2}. We investigated if these changes were secondary to nausea or if AVP or the associated peptide, copeptin, could directly cause tachygastric in human stomach.

Methods: Isometric contractions of the circular muscle from gastric fundus and corpus-antrum (sleeve gastrectomy; 5 males, 9 females) were recorded in response to AVP (10^{-12} – 10^{-5} M), electrical field stimulation (EFS; 5 Hz, 0.5 ms, 10 s/min, 110% maximal voltage) or copeptin (10^{-9} – 10^{-7} M; peptide derived from the precursor of AVP). AVP was also examined after 30 minutes incubation with relcovaptan (V_{1A} antagonist; 10^{-9} – 10^{-6} M), L371257 (OT antagonist; 10^{-7} M) or atropine (10^{-6} M) with tetrodotoxin (10^{-6} M) and L-NAME

(3×10^{-4} M). Changes in muscle tension were expressed as % maximal contraction to carbachol (CCh; 10^{-3} M). Increases in spontaneous contractions were compared relative to basal values. Data are mean $\pm$ s.e.m (n = donors).

Results: The fundus and corpus-antrum spontaneously contracted rhythmically (respectively, 1.1 ± 0.1 mN and 4.7 ± 0.3 mN amplitude) at similar frequency (~ 2.6 /min; n = 14). In both regions CCh elicited contractions of equal magnitude (~ 90.5 mN). AVP concentration-dependently increased muscle tension, amplitude and frequency of spontaneous contractions in both regions with similar potency (pEC_{50} 9.0–9.5) and threshold concentration (10^{-11} – 10^{-10} M); changes in amplitude were greatest in the fundus. Relcovaptan alone had no effects, but competitively antagonised each action of AVP (pK_B 9.3–9.5), which were refractory to L371257, tetrodotoxin, atropine and L-NAME. EFS evoked contractions in both stomach regions of similar amplitude ($\sim 25.4\%$ of CCh; n = 4), which were abolished by tetrodotoxin or atropine, but unaffected by AVP. Copeptin was not pharmacologically active.

Conclusions: In both stomach regions AVP acted at V_{1A} receptors to equi-potently and directly augment the frequency and amplitude of spontaneous contractions at concentrations measured during nausea, most likely by acting at pacemaker cells, suggesting a role in the aetiology of nausea.

References: [1] Caras et al. *Neurogastroenterol Motil* 1997;9:151–156. [2] Kim et al. *Am Physiol* 1997;272:G853–G862.

81 | Association between interstitial cells of Cajal and anti-vinculin antibody in human stomach

J. H. Kim; S.-J. Nam; S. H. Lee; T. S. Kim; M. Lee; J. M. Park; D. H. Choi; C. D. Kang; S. J. Lee; S. C. Park

Kangwon National University Hospital, Chuncheon, South Korea

Objective: Interstitial cells of Cajal (ICC) are known as the pacemaker cells of gastrointestinal tract, which regulate gastrointestinal motility. It has been reported that acute gastroenteritis induces intestinal dysmotility through antibody to vinculin, a cytoskeletal protein in gut, resulting in small intestinal bacterial overgrowth, so that anti-vinculin antibody can be used as a biomarker for irritable bowel syndrome. However, there are limited data on relationship between ICC and anti-vinculin antibody in human stomach. Thus, this study aimed to determine correlation between levels of circulating anti-vinculin antibody and ICC density in inner muscular layer and myenteric plexus of human stomach.

Methods: Paraffin-embedded gastric specimens from 45 patients (median age 66 years, male 80.0%, female 20.0%, Diabetes Mellitus 20.0%), with gastric cancer who received gastric surgery at Kangwon National University Hospital from 2013 to 2017 were used for immunohistochemistry. Each specimen was stained with DOG-1 specific antibodies, then number of positive cells in inner circular muscle, and myenteric plexus were counted. Corresponding patient's blood samples were used to determine the amount of anti-vinculin antibody by enzyme-linked immunosorbent assay (ELISA).

Results: The median concentration of anti-vinculin antibody was 121.7 ng/mL (IQR 44.6–450.6), the median number of ICC in inner circular muscle with positive DOG-1 stain was 151 per 2.5 mm² (IQR 24.5–319.0), and the number of ICC in myenteric plexus with positive DOG-1 stain was 28 per 2.5 mm² (IQR 5.5–83.0). Increased level of circulating anti-vinculin antibodies were significantly associated with reduced number of ICC in myenteric plexus ($P = 0.01$; Spearman correlation), but not inner circular muscle.

Conclusions: Increased level of circulating anti-vinculin antibody was significantly correlated with decreased density of ICC in myenteric plexus of human stomach, which suggest regulation of ICC expression by anti-vinculin antibody in patients with gastrointestinal dysmotility. Further studies are needed to determine such relationship in functional dyspepsia.

82 | How does meal composition influence the evaluation of gastrointestinal motility measured by the wireless motility capsule?

M. M. Christensen¹; H. Pedersen¹; K. K. B. Clemmensen¹; A.-M. L. Wegeberg²; J. S. Quist¹; K. Færch¹; C. Brock²

¹Steno Diabetes Center Copenhagen, Gentofte, Denmark; ²Aalborg University Hospital, Aalborg, Denmark

Objective: Gastrointestinal motility is important in appetite regulation and glucose homeostasis and can be studied with the wireless motility capsule (WMC) technique. The WMC is usually administered together with a SmartBar which, however, has a nutrient composition that differs substantially from a standard western meal. The aim of the study is to compare gastrointestinal transit times and postprandial metabolite- and hormonal responses to a SmartBar and a western breakfast meal.

Methods: 15 healthy, normal weight participants attend a randomised two-day cross-over study at which they ingest the WMC with either a SmartBar (260 kcal, 7E% fat, 74E% carbohydrate, and 19E% protein) or a standard breakfast meal (498 kcal, 34E% fat, 49E% carbohydrate, and 17E% protein). Gastric emptying time (GET) is the primary end-point. Blood samples are drawn in the fasted state and at 8 timepoints until 240 minutes after ingestion. Total (tAUC) and incremental (iAUC) areas under the curve are calculated by the trapezoidal rule.

Results: The study is ongoing and preliminary results of the first 6 completed participants are summarized in Table 1. Data of all 15 participants will be presented at the conference. GET tended to be longer after the breakfast meal compared to the Smartbar (Δ GET = 110 minutes, $P = 0.06$). Small bowel- (SBTT), colonic- (CTT) and whole gut (WGTT) transit times did not differ between test days. There were no differences in tAUCs of either plasma glucose, insulin, or triglyceride; however, iAUC of triglyceride was higher after the breakfast meal ($P = 0.01$).

Conclusions: Preliminary results suggest that GET increase with meal size, while SBTT, CTT and WGTT are unaffected by meal size and composition. As expected, plasma triglyceride iAUC was higher after the breakfast meal, due to the higher fat content of the breakfast meal.

	Breakfast meal (n=6)	SmartBar (n=6)	Delta value	P-value
Gastrointestinal transit times				
GET (min)	308 [286, 320]	204 [179, 229]	110 [60, 123]	0.06
SBTT (min)	274 [238, 305]	262 [243, 282]	23 [-2, 46]	0.52
CTT (min)	762 [593, 1778]	1039 [899, 1923]	-244 [-343, -152]	0.15
WGTT (min)	1269 [1150, 2384]	1525 [1362, 2465]	-141 [-182, -82]	0.26
Plasma glucose				
tAUC (mmol/l x min)	1438 [1313, 1485]	1289 [1276, 1318]	89 [-66, 218]	0.42
iAUC (mmol/l x min)	165 [68, 200]	117 [43, 163]	50 [-6, 131]	0.34
Peak (mmol/l)	7.2 [6.9, 7.9]	8.0 [7.8, 8.5]	-1.0 [-1.8, 0.2]	0.09
Nadir (mmol/l)	4.6 [4.6, 5.0]	4.3 [3.4, 4.6]	0.7 [0.2, 1.5]	0.01
Plasma insulin				
tAUC (pmol/l x min)	33799 [29571, 39619]	36600 [33743, 39979]	-4755 [-10245, 4899]	0.52
iAUC (pmol/l x min)	26798 [22592, 32871]	29491 [24900, 34564]	-4035 [-8865, 4005]	0.63
Peak (pmol/l)	370 [314, 400]	470 [384, 526]	-103 [-127, -71]	0.08
Nadir (pmol/l)	25 [19, 30]	20 [13, 23]	7.5 [6.5, 8.8]	0.33
Plasma triglyceride				
tAUC (mmol/l x min)	154 [149, 239]	136 [118, 158]	32 [27, 89]	0.20
iAUC (mmol/l x min)	16 [2.5, 25]	-30 [-33, -21]	29 [27, 52]	0.01
Peak (mmol/l)	0.8 [0.7, 1.3]	0.7 [0.6, 0.8]	0.1 [0.0, 0.5]	0.26
Nadir (mmol/l)	0.6 [0.6, 0.9]	0.5 [0.4, 0.6]	0.2 [0.1, 0.4]	0.11

TABLE 1. Gastrointestinal transit times and postprandial plasma responses measured after ingestion of the wireless motility capsule with either a breakfast meal or a SmartBar and delta values (breakfast meal – SmartBar). Data are presented as median [Q1, Q3]. Differences between the two test days were determined using Wilcoxon signed-rank test. GET, gastric emptying time; SBTT, small bowel transit time; CTT, colonic transit time; WGTT, whole gut transit time; tAUC, total area under the curve; iAUC, incremental area under the curve.

85 | How do patients treat abdominal pain and cramping and what do pharmacists recommend?

A. Lampert; S. Landes; T. Schüett

Medical Affairs Consumer Healthcare, Sanofi-Aventis Deutschland GmbH, Frankfurt, Germany

Objective: Abdominal pain and cramping is a common condition that impairs quality of life and thus, patients are looking for rapid solutions to relieve their symptoms. Treatment habits and source of decision for treatments are yet described in literature. In this Sanofi-sponsored study, we aimed to evaluate how patients treat abdominal pain and cramping and investigated the recommendation habits of community pharmacies for this symptom.

Methods: We asked 938 patients with abdominal pain and cramping in Germany which products they used during the last 12 months to treat their symptoms (Feb. 2015). An online survey amongst 100 pharmacists and 100 pharmacy technicians was conducted to determine their recommendation behavior for patients with abdominal pain and cramping in German community pharmacies (Sep. 2018). Descriptive statistics were used for analyzing the data.

Results: Most patients (81%) reported to use OTC-products to alleviate symptoms. Almost half used NSAIDs (47%) to reduce symptoms and one fifth used antispasmodics (22%) or herbal medicinal products (20%). In addition, more than half (61%) applied home remedies, such as hot water bottle, to support symptom relief. In contrast, pharmacists and pharmacy technicians primarily recommended antispasmodics (58%), such as hyoscine butylbromide, or herbal medicinal products (40.5%), such as STW-5 or peppermint oil, while NSAIDs (1%) or probiotics (0.5%) were rarely recommended as first choice treatment.

Conclusions: Patients self-treat abdominal pain and cramping primarily with OTC-products suggesting they're primarily looking for easily accessible solutions. Abdominal pain is often caused by spasms of visceral smooth muscle. Due to their mechanism of action, antispasmodics are considered most appropriate to alleviate symptoms. Although antispasmodics are primarily recommended by community pharmacists, patients rather used NSAIDs. Since antispasmodics directly alleviate abdominal cramping and subsequently pain and are generally better tolerated than most analgesics, patients should be informed about more targeted treatment options to relieve abdominal pain and cramping.

87 | Assessing needs of IBS patients with regard to healthcare delivery – A focus group study in Dutch patients

J. Snijkers; A. Masclee; J. Kruimel; D. Keszthelyi

MaastrichtUMC+, Maastricht, The Netherlands

Objective: Irritable Bowel Syndrome (IBS) is a highly prevalent gastrointestinal disorder and is associated with reduced quality of life and high healthcare utilization. There is increasing need for improving healthcare outcomes for IBS patients. Therefore, a focus group study was initiated to evaluate the needs of IBS patients in order to improve healthcare delivery.

Methods: An initial draft was constructed based on the input of national experts in the field of neurogastroenterology & motility. Focus group interviews with IBS patients ($n = 23$, mean age 43 years, 91.3% female) meeting the Rome III criteria were performed. Interviews were conducted in four separate locations in the Netherlands to ensure geographic diversity. The first part consisted of an open discussion in which participants were questioned about their previous experiences and aspects they considered to be essential to improve care for IBS patients. In the second part, participants were asked to criticize the draft based on the input of experts.

Results: Participants emphasized the need of clear communication; patients felt there was a lack of knowledge about the impact of IBS among healthcare providers and therefore limited useful advice is given. Participants were satisfied about the following suggestions in the initial draft: dedicated (multidisciplinary) team, experts in the field of IBS, focus on research, standardized guidelines for diagnosis and treatment. An addition in response to the focus groups is a website with information about IBS, new developments and participation in scientific trials. Besides, cooperation between the gastroenterologist and general practitioner needs attention.

Conclusions: There is need for improvement of IBS patients care, in particular providing sound and up-to-date information on IBS including novel insights using interactive tools and enhancing cooperation between different healthcare providers. Based on input of experts and focus groups, a protocol was developed which is to be

implemented in the secondary healthcare setting to increase patients' outcomes and quality of life. This is currently being tested in a multicenter feasibility study.

88 | Association of abdominal obesity and Barrett's esophagus

S. J. Noh¹; O. Y. Lee¹; C.-H. Yang²; B. C. Yoon¹; H. S. Choi¹; H. L. Lee¹; D. W. Jun¹; K. N. Lee¹; J. H. Yoon¹

¹Hanyang University, Seoul, South Korea; ²Dong Guk University, Gyeongju, South Korea

Objective: Barrett's esophagus (BE) is known as a precursor to esophageal adenocarcinoma, and has been well-recognized in the Western countries due to its prevalence. In comparison, its relatively low incidence in Asia has led to only a handful of studies looking into the significance of this condition in the Asian population. However, westernization of life style has contributed to change in the prevalent disease types and patterns in Korea. Thus, the prevalence of BE and esophageal adenocarcinoma in Korea is expected to increase. This study aimed to identify associations between BE and abdominal obesity by assessing patients' body mass index (BMI) and the distribution of visceral, subcutaneous, and gastro-esophageal junctional fat on their CT images.

Methods: 472 patients with an established diagnosis of BE on esophagogastroduodenoscopy at Hanyang University hospital between January 2014 and June 2017 were identified. After those with other underlying diseases were excluded, 20 patients who had had abdominal CT within 3 years pre- or post-diagnosis were included in BE cases. The control group consisted of those without underlying disease or abnormal findings on endoscopy and/or abdominal CT. BE cases and the control were matched 1:1 in terms of their gender and age (± 3 years). Retrospective assessment of the variables of interest were undertaken. The variables included total abdominal fat, subcutaneous, visceral, and gastro-esophageal junctional fat mass on CT images, abdominal circumference, and BMI of the patients. Independent sample *t*-test analysis was used.

Results: No statistically significant differences regarding total abdominal fat ($P = .313$), subcutaneous fat ($P = .756$), visceral fat ($P = .057$), and BMI ($P = .667$) were identified between the BE cases and the control. Patients with BE were found to have significantly higher gastro-esophageal junctional fat mass ($P = .031$) and greater abdominal circumference ($P = .048$) when compared to those measured in the control.

Conclusions: The significant differences in the gastro-esophageal junctional fat and abdominal circumference between the BE cases and the control suggest that these factors likely play an important role in the pathogenesis of BE.

91 | Does motilin regulate gastrointestinal (GI) motility of bullfrog (*Lithobates catesbeiana*)? In vitro study using isolated GI strips

T. Kitazawa¹; S. Zhang¹; H. Teraoka¹; Y. Okuhara¹; H. Kaiya²

¹Rakuno Gakuen University, Ebetsu, Japan; ²National Cerebral and Cardiovascular Center Research Institute, Suita, Japan

Objective: Motilin (MLN) is a 22 amino-acid gut peptide, located in the mucosa of upper small intestine and stimulates the gastrointestinal (GI) motility of mammals and birds. Presence of MLN-like peptide in fish has been reported but presence and function of MLN in amphibian GI tract have not been well examined. Aim of present study is to clarify the functional roles of MLN in the bullfrog GI motility.

Methods: The effects of human MLN and erythromycin on contractility of isolated bullfrog GI strips were examined. The bullfrog GI tract was divided into stomach, upper, middle and lower intestines, and both longitudinal and circular muscles were prepared at each region. Immunohistochemical study using anti-human MLN serum was also performed.

Results: Each GI preparation responded to high-K⁺, a muscarinic agonist and substance P. Human MLN caused a concentration-dependent contraction in the upper intestinal preparations (10⁻⁹ M–10⁻⁶ M) but other preparations were insensitive to MLN. Circular muscles were more sensitive to human MLN than longitudinal muscles. Chicken MLN, similar structure with human MLN but not erythromycin caused the contraction of the upper intestine. Neither tetrodotoxin nor GM109 (a MLN receptor antagonist) decreased the contraction by human MLN. Immunohistochemical study using anti-human MLN antibody was not able to detect the MLN-positive cells in the mucosa of bullfrog intestine.

Conclusions: Human MLN causes the contraction of bullfrog GI tract in a region-dependent manner through direct action on smooth muscle cells. Therefore although bullfrog MLN is unknown at present, MLN peptide is possible to regulate GI motility in amphibians like mammals. However, failure of detection of MLN immunoreactivity suggests the different structure of bullfrog MLN if it is expressed in the intestine. In addition, the lack of agonist action of erythromycin and the lack of antagonist action of GM109 suggests the different structure of bullfrog MLN receptor from that of mammals.

92 | Identification of ghrelin and motilin in the pheasant, and their mechanical actions in isolated gastrointestinal tract

S. Zhang¹; I. Sakata²; H. Kaiya³; H. Teraoka¹; Y. Okuhara¹; T. Kitazawa¹

¹Rakuno Gakuen University, Ebetsu, Japan; ²Saitama University, Saitama, Japan; ³National Cerebral and Cardiovascular Center Research Institute, Suita, Japan

Objective: Although motilin (MLN) and ghrelin (GHRL) are family peptides derived from the same ancestor gene, the action of GHRL in the chicken and quail GI tract differs despite MLN causes GI

contraction in both species. Aim of the present study is to identify MLN and GHRL in different avian species, pheasant (*Phasianus colchicus versicolor*) and to characterize the actions of both peptides on GI motility.

Methods: Structure of MLN and GHRL was identified in the pheasant by molecular cloning. The actions of both peptides on the contractility of GI strips were examined *in vitro*.

Results: Molecular cloning indicated that pheasant MLN structure was FVPFFTQSDIQKMQEKERIKGQ. MLN-immunoreactive cells were located in the mucosa of duodenum. Structure of the pheasant GHRL was GSSFLSPAYKNIQQQKDKTRKPTGRLH, and the immunoreactive cells were located in the mucosa of proventriculus. Chicken MLN caused contraction of the proventriculus and small intestine of pheasant. The crop and colon were quite insensitive to MLN. Mechanisms of chicken MLN-induced contraction were different between proventriculus (neurogenic) and small intestine (myogenic). Mammalian MLN receptor antagonists, GM109 and MA2029 did not decrease the responses of chicken MLN in the pheasant GI tract. Human MLN but not erythromycin caused contraction. On the other hand, rat, chicken and quail GHRLs did not cause any mechanical changes in every GI strip. In addition, GHRL did not interact the MLN-induced responses.

Conclusions: Both MLN system and GHRL system are present in the pheasant GI tract as similar with other birds. MLN caused the contraction of the proventriculus and small intestine by different mechanisms but GHRL was ineffective causing contraction and interaction with MLN. Therefore, MLN-related mechanism but not GHRL-related mechanism is common in the regulation of GI motility in avian species.

93 | Changes of macrophage phenotype and gastrointestinal motility in mice with vancomycin induced dysbiosis

Y. Inoue; H. Fukui; Y. Ran; T. Kondo; T. Kono; S. Fukushima; K. Tozawa; T. Tomita; T. Oshima; H. Miwa

Hyogo college of medicine, Nishinomiya, Japan

Objective: The gut microbiota plays an important role in various host physiology including immune system, metabolism, hormone secretion and gastrointestinal (GI) motility. The use of antibiotics causes the imbalance of gut flora profiles and it's resultant dysbiosis is known to cause obesity, insulin resistance and functional gastrointestinal disorders. However, it is unclear how dysbiosis cause such disorders in the host. In the present study, focusing the alteration of macrophage phenotype, we investigated the relationship among colonic macrophage phenotype, metabolism and GI motility in antibiotics-induced dysbiosis.

Methods: Mice (Specific pathogen-free ICR, 6 weeks old, female) were orally administered vancomycin (0.2 mg/ml) in drinking water for five weeks. Pathophysiological features (body weight, food intake and intestinal pathology) were observed. The gastrointestinal

transit time (GITT) was measured by administration of carmine red (6% w/v) solution. The expression of CD80 (M1 macrophage marker) and CD163 (M2 macrophage marker) was examined by immunohistochemistry, and the expression cytokines mRNA was evaluated by realtime RT-PCR in colonic tissues.

Results: The amount of food intake, the gain of body weight and the weight of cecum were significantly greater in vancomycin treated group than in control. GITT was significantly prolonged in the vancomycin treated group than in control. The number of M1 macrophages was significantly increased in the colonic mucosa of vancomycin treated mice, whereas the number of M2 macrophages was decreased in both mucosal and muscle layers of the colon in those mice. The expression of IFN- γ and IL-12 were significantly increased in the vancomycin treated group than in control. GITT showed a positive correlation with the number of M1 macrophages. Conversely, GITT showed a negative correlation with the number of M2 macrophages in the colonic mucosa and muscle layer.

Conclusions: Vancomycin treatment affects GI motility with the alteration of macrophage phenotype in the colon.

94 | Circadian rhythm seems intact in patients with type 1 diabetes and autonomic dysfunction and enteropathy

A.-M. L. Wegeberg¹; T. Meldgaard²; I. M. N. Wigh²; P. S. Sørensen²; S. L. Jensen²; V. S. Zaugg²; N. Ejlskjær³; A. M. Drewes²; C. Brock¹

¹Mech-Sense, Aalborg University Hospital & Clinical Institute, Aalborg University, Aalborg, Denmark; ²Mech-Sense, Aalborg University Hospital, Aalborg, Denmark; ³Steno Diabetes Centre North Jutland, Aalborg, Denmark

Objective: The autonomic nervous system regulates gastrointestinal activity through physiological stimuli and modulatory reflexes. Diabetic autonomic neuropathy (DAN), can lead to dysmotility and concomitant debilitating symptoms. However, it is unknown if the circadian rhythm reflected in gut motility is afflicted. Therefore, we investigated circadian differences in colonic contractility in healthy participants (HP), and people with type 1 diabetes (T1D) presented with or without DAN. Furthermore, we investigated if the circadian rhythm was associated to known dysmotility.

Methods: 21 HP, 41 T1D, and 34 T1D/DAN, were included. All underwent a standardized wireless motility capsule assessment. Recordings were analyzed with MotiliGI by two independent groups, with disagreements decided by consensus. 60 minutes colonic motility index was measured at: 1) morning (after waking up), 2) day (eight hours after waking up), 3) evening (before going to bed), and 4) night (at lowest temperature during night), in all three groups and compared with a repeated measures mixed model. A Spearman's correlation between night/morning ratio and colonic transit time was performed.

Results: There were no within-day interaction effect on motility index, between the three groups. However, as expected, significant circadian differences in motility index was shown ($P > 0.001$), see figure. Transit times were non-significantly prolonged in T1D (27 hours 33 minutes (17 hours 39 minutes-41 hours 49 minutes)) and T1D/DAN (38 hours 36 minutes (20 hours 3 minutes-50 hours 45 minutes)) compared to HP (16 hours 24 minutes (12 hours-25 hours 49 minutes)). However, the ratio was not associated to the transit time in any of the groups.

Conclusions: These findings indicate that assessment of physiological circadian rhythm, reflected in the dynamic motility index, is intact in T1D with/without DAN. Colonic dysmotility was present in diabetes but not associated to circadian differences, and therefore it is plausible that the centrally regulated "gut-clock" is not part of the pathogenesis leading to enteropathy and prolonged transit times.

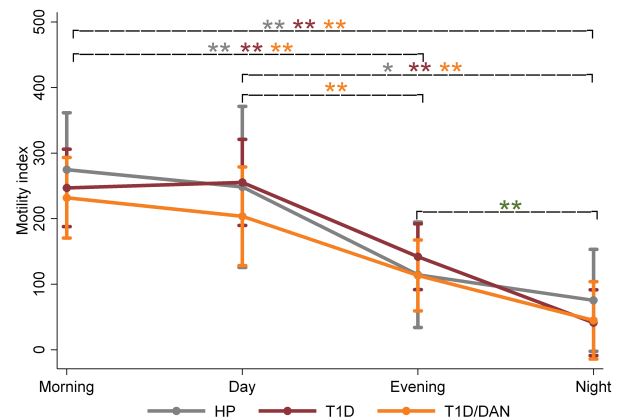


FIGURE. Motility index in healthy participants (HP), and people with type 1 diabetes presented with (T1DM/DAN) or without (T1D) neuropathy for 60 minutes readings in 1) morning (after waking up), 2) day (eight hours after waking up), 3) evening (before going to bed), and 4) night (at lowest temperature during night). Graph shows intact circadian rhythm in T1D and T1D/DAN.

95 | Development of micro wired PH electrode for real-time monitoring for gastroesophageal reflux disease

J. H. Park¹; J.-I. Sohn¹; N. H. Kim¹; E.-B. Kim²

¹Kangbuk Samsung Hospital, Seoul, South Korea; ²Departments of Electronics and Control Engineering, Hanbat National University, Daejeon, South Korea

Objective: Diagnostic device for gastroesophageal reflux disease brings many discomforts such as restriction of daily living and pain and in the nasal cavity and pharynx. In this study, we tried to develop a wireless measurement method and a micro-sized pH electrode for human body insertion

Methods: Commercial glass packaged pH meter is formed by a sensing and a reference electrodes in a KCl solution. For the prevention of leakage of the solution, breakage of the glass package, injury of the body elements, micro-sized noble metal wire, which has

a characteristic of biocompatibility, should be solidified using a solution and after solidified wire fabrication, the designed meter was tested for feasibility of measurement

Results: The values of this new device was consistent with pH values of commercial pH meter. Potentials in pH 1 to 12 solution was measured to obtain the sensitivity of the sensor with linearity. And a simulation test was designed for acid reflux with different frequency, interval, and duration time in pH 2 solution. The proposed sensor was capable of getting the same potential for 24 measurements in 3 days, and it had sensed same pH values of 2 for one hour with every 10 minutes. Furthermore, The sensor was able to continuously measure the pH change for up to 48 hours.

Conclusions: The newly developed wireless pH monitoring equipment will be helpful for the diagnosis of patients with reflux esophagitis because of low inconvenience and reliable test results for a long time.

96 | Analysis of postreflux swallow-induced peristaltic wave index is consider as a method for evaluating the effectiveness of esophageal clearance and the criterion for phenotyping of gastroesophageal reflux disease

O. Storonova; A. Makushina; A. Paraskevova; A. Trukhmanov; V. Ivashkin

Sechenov University, Moscow, Russia

Objective: absent contractility and minor motility disorders of esophagus cause poor clearance and aggravate the course of GERD. The impedance metric postreflux swallow-induced peristaltic wave (PSPW) index was proposed to evaluate esophageal clearance, motility efficiency as well as motility abnormalities. Our aim was to determine correlation between PSPW-index and parameters of high-resolution manometry (HRM) characterizing esophageal clearance. To evaluate PSPW-index* as a criterion for phenotyping of GERD.

Methods: 60 GERD mean age 44.7(19-71)years (30 ERD, 30 NERD) and 20 healthy volunteers (45.2(26-65)years)) underwent HRM with 22-channel water-perfused catheter (Solar GI MMS, The Netherlands) and 24-hour multichannel intraluminal impedance-pH monitoring. We analyzed PSPW-index, distal contractile integral (DCI), peristaltic break. The statistical analysis was done using Statistica for Windows10.0 (StatSoft Inc.).

Results: PSPW-index and DCI values decrease with more severe course of GERD ($r = -0.4$; $P = 0.0002$; $r = -0.49$; $P = 0.000$ respectively). Statistically significant difference between PSPW-index ($P = 0.02$), DCI ($P = 0.001$), PSPW-index and peristaltic break ($P = 0.028$) medians among ERD, NERD and control were observed. In the whole GERD group significant correlations between PSPW-index and DCI, and peristaltic break ($r = 0.337$; $P = 0.0091$, $r = -0.269$; $P = 0.038$ respectively) were determined. In NERD

correlation was revealed between PSPW-index and DCI ($r = 0.378$; $P = 0.04$). In ERD group correlations didn't achieve a statistically significant level.

In NERD PSPW-index, DCI, peristaltic break medians were 0.56 [0.51;0.75], 565 [346.0;816.0] mm Hg*s*cm, 2.95 [1.7; 5.0] cm respectively. In ERD: 0.23 [0.17;0.33], 249 [109.0;676.0], 4.8 [1.8;5.9]. In control group: 0.42 [0.3;0.5], 1040.5 [650.0;1722.0], 1.9 [0.85;3.55].

Conclusions: correlations between PSPW-index and HRM-parameters characterizing impaired esophageal clearance (DCI, peristaltic break) allows to consider that PSPW-index can be used as a criterion for evaluating the effectiveness of esophageal clearance. Decreasing level of these parameters reflects the likelihood of a more severe course of the disease and can be used as additional criteria in phenotyping of GERD.

*Abnormal value: PSPW-index <61% [Frazzoni M et al.Clin Gastroenterol Hepatol.2016] or 0.61 in absolute

98 | Short-term probiotic treatment improve gut function, increase bowel wall thickness and alleviate abdominal signs of metabolic syndrome

R. V. Bubnov¹; M. Y. Spivak²

¹Clinical Hospital Pheophania, Kyiv, Ukraine; ²Zabolotny Institute of Microbiology and Virology National Academy of Sciences of Ukraine, Kyiv, Ukraine

Objective: Metabolic syndrome (MetS) is associated with alteration of gut function. Intestinal wall barrier is a place of interaction with microbiome promoting adaptive immune responses associated with MetS. Ultrasound (US) can detect gut motility, decreasing colonic wall thickness, metabolic, inflammatory and vascular markers for stratification patients with MetS. Modulating gut microbiome and aerobic exercises can improve abdominal and gut health.

The Aim: was to study the efficacy of lifestyle-modifying interventions on gut function, colonic wall thickness, inflammatory and vascular markers of MetS evaluated on ultrasound.

Methods: We included twenty overweight patients (age 37-65 years), BMI > 30, waist circumference (WC) > 110. Six patients underwent lifestyle modification – increased physical activity and aerobic exercises (yoga, plank and walking 10K steps daily); six patients were given probiotics (L. casei IMV B-7280 / B. animalis VKB / B. animalis VKL strains (10^8 CFU/d, 10 days); eight remained controls. All patients preserved unchanged diet and underwent general clinical, lab tests; multiparameter abdominal US, measuring liver, bile ducts, spleen size, abdominal and visceral fat (FV), colonic wall thickness (transversal colon), visualizing colon (anti) peristalsis; Doppler evaluation of mesenteric blood flow; dynamic US of postural stability.

Results: We detected increasing visceral fat (to 26 ± 6 mm), liver size and stiffness in all obese patients. Liver size decreased in right lobe

from 176 mm to 154 mm after probiotic treatment and to 166 mm after physical activity. Weight, BMI, WC and VF decreased after probiotic administration. Constipation, colon hyperpneumosis, hypomotility detected in all obese, improved after both interventions; colonic wall thickness was decreased to 2–3.5 mm in obese individuals (3–5.5 mm in controls); restored to 4–5 mm after probiotic treatment. After probiotic treatment mesenteric blood flow restored (PSV from 140–170 cm/s to 123 cm/s, $P < 0.05$), gut microbiota improved in increasing microbial diversity, LAB, decreasing pathogens. Spleen size restored to normal values (length to 100–110 mm) in cases with microsplenitis. Aerobic physical activity improved postural parameters, decreased BMI, WC and did not improve VF, colonic wall, microbiota.

Conclusions: Short-term probiotic therapy is effective to treat visceral obesity and constipation, restore bowel wall, mesenteric blood flow, alleviate signs of MetS in overweight patients superior vs aerobic exercises.

99 | The effect of ilaprazole in patients with non-erosive reflux disease

S. K. Lee

Yonsei University College of Medicine, Seoul, South Korea

Objective: Patients with gastroesophageal reflux disease without esophagitis show varying responses to proton pump inhibitors (PPIs). The aim of this study was to objectively evaluate the effect of a new PPI, ilaprazole, on patients with heartburn but without reflux esophagitis.

Methods: This prospective study was performed on 20 patients with heartburn but without reflux esophagitis. All patients underwent upper endoscopy and 24-hr combined multichannel intraluminal impedance and pH esophageal monitoring (MII-pH). They were then treated with ilaprazole (20 mg) once daily for 4 weeks. The GerdQ questionnaire, histologic findings, and inflammatory biomarkers were used for assessment before and after ilaprazole.

Results: Among the 20 patients, 13 (65%) showed GerdQ score ≥ 8 . Based on MII-pH results, patients were classified as true nonerosive reflux disease ($n = 2$), hypersensitive esophagus ($n = 10$), and functional heartburn ($n = 8$). After treatment, patients showed a statistically significant improvement in GerdQ score ($P < 0.001$). Among histopathologic findings, basal cell hyperplasia, papillary elongation, and infiltration of intraepithelial T lymphocytes improved significantly ($P = 0.008$, $P = 0.021$, and $P = 0.008$; respectively). Expression of TNF- α , IL-8, TRPV1, and MCP-1 decreased marginally after treatment ($P = 0.049$, $P = 0.046$, $P = 0.045$, and $P = 0.042$; respectively).

Conclusions: Daily ilaprazole (20 mg) is efficacious in improving symptom scores, histopathologic findings, and inflammatory biomarkers in patients with heartburn but no reflux esophagitis.

100 | A population-based study of associations between functional gastrointestinal disorders and life style in Xi'an, China

J. Xu¹; L. Hei¹; S. Ma¹; H. Zhao¹; L. Shang²

¹Department of Gastroenterology, The affiliated hospital of Northwest University, Xi'an No.3 hospital, Xi'an, China; ²Department of Health Statistics, Air Force Medical University, Xi'an, China

Objective: To investigate the incidence and risk factors of functional gastrointestinal disorders (FGIDs) in the resident population of Xi'an, and to clarify the relationship between life style and FGIDs.

Methods: Of 920 recruited residents in Xi'an, 830 were selected for an epidemiological survey using a cluster sampling method. All subjects were interviewed face-to-face to complete the Chinese version of ROME IV FGIDs questionnaire, Chinese version of international physical activity questionnaire, Pittsburgh sleep quality index, food frequency questionnaire, self-rating anxiety scale and self-rating depression scale. The prevalence of FGIDs and associations between FGIDs and diet habit, sleep disturbance, physical activity and psychological factors were determined using EpiData Software. Logistic regression analysis was performed to identify the potential risk factors for FGIDs.

Results: The prevalence of FGIDs in this sample population was 18.7% (155/830). There were 25 (3%) cases of overlap of different FGIDs. No significant difference in the prevalence of FGIDs was observed between men and women ($P > 0.05$). The sleep score (PSQI) of patients with FGIDs (5.4 ± 3.0) was significantly higher than that of non-FGIDs (3.6 ± 2.5) ($P < 0.01$). The anxiety score of patients with FGIDs (44.9 ± 8.4) was significantly higher than that of non-FGIDs (41.5 ± 6.9) ($P < 0.01$). In this survey, it was found that there was no statistically significance in dietary patterns between FGIDs and non-FGIDs patients, but dietary habits might be related to the pathogenesis of FGIDs. Compared with non-FGIDs, FGIDs patients preferred to eat grilled food, sour food, sweet food, spicy food, high-fat food, cold food and fast food ($P < 0.05$). There was no statistically significant difference in exercise status between patients with FGIDs and those without FGIDs. Multivariate logistic regression analysis showed that Body Mass Index, education level, alcohol consumption, anxiety, sleep, hot food, eating fast and snack food were associated with the incidence of FGIDs ($P < 0.05$).

Conclusions: The prevalence of FGIDs and overlap syndrome in Xi'an, China was lower than that reported in other countries. There was a strong correlation between specific lifestyle habits and psychosocial characteristics and the presence of FGIDs.

101 | Perceptions and practices on the management of constipation: results from the Korean national survey

J.-W. Kim¹; S.-Y. Park²; Y. S. Cho³; J. E. Shin⁴; Y. J. Lee⁵; H. S. Ryu⁶; T. H. Lee⁷; S.-E. Kim⁸; K. S. Park⁹; S. J. Kang¹⁰

¹Kyung Hee University Hospital, Seoul, South Korea; ²Chonnam National University Hospital, Gwangju, South Korea; ³Soonchunhyang University College of Medicine, Cheonan, South Korea; ⁴Cheonan Hospital, Cheonan, South Korea; ⁵Dankook University College of Medicine, Daegu, South Korea; ⁶Keimyung University School of Medicine, Iksan, South Korea; ⁷Wonkwang University School of Medicine, Seoul, South Korea; ⁸Soonchunhyang University Seoul Hospital, Seoul, South Korea; ⁹Ewha Womans University College of Medicine, Daegu, South Korea; ¹⁰Keimyung University School of Medicine, Seoul, South Korea

Objective: Constipation is a gastrointestinal disorder that is frequently seen in clinical practice. Although guidelines have been published for the evaluation and treatment of constipation in Korea, little is known about the treatment strategies and satisfaction of various therapeutic options. Therefore, this study aimed to evaluate the practice patterns for constipated patients and compare management strategies among gastroenterologists and non-gastroenterologists in Korea.

Methods: An internet survey was conducted nationwide, randomly targeting gastroenterologists and non-gastroenterologists. A 20-item questionnaire was used to evaluate physicians' perceptions and practices with respect to the management options available in Korea for the treatment of constipation.

Results: Study participants were 193 physicians involved in the clinical practice of constipation. Of the participants, 86 (44.6%) were gastroenterologists and 107 (55.4%) were non-gastroenterologists. The most important symptom was considered to be infrequency (48.7%), followed by incomplete evacuation (16.6%), hard stool (15%) and straining (10.9%). In the diagnosis of constipation, the use of Rome criteria, colonoscopy, and Bristol form scale were more frequent in the gastroenterologist group. Among the participants, magnesium salts (78.8%) were the most preferred drug for constipation treatment, followed by non-absorbable carbohydrate (59.1%) and bulking laxative (42%). There was no difference in drug choice between gastroenterologist and non-gastroenterologist.

Conclusions: The management strategies for constipation which are used by gastroenterologists and non-gastroenterologist are fairly similar. However, there were some differences between the two groups in symptom perception and diagnostic approach in constipation patients. This study may provide several educational ideas to improve the diagnostic and therapeutic approach to constipation.

102 | Balloon inflation velocity and sensory thresholds in high-resolution anorectal manometry

C. Pehl¹; H. Foerster²; W. Koczi¹

¹Hospital Vilsbiburg, Vilsbiburg, Germany; ²Center for Neurogastroenterology, Vilsbiburg, Germany

Objective: Sensory dysfunction can lead to obstructed defecation (ODD) and fecal incontinence (FI; Dis Colon Rectum 2003; 46: 238-46). Therefore, evaluation of rectal sensory thresholds (balloon distension) is integral part of high-resolution anorectal manometry (HRAM; Z Gastroenterol 2007; 45: 397-417). However, standardisation of velocity of balloon inflation is lacking (Neurogastroenterol Motil 2017; 29: e13016).

Aim: Comparison of sensory thresholds of rectal balloon distension inflated by hand-hold syringe, rapid, and slow acting pump.

Methods: 24 consecutive patients seen in our lab were included (6 ODD, 18 FI). HRAM was performed according to the German recommendations (Z Gastroenterol 2007; 45: 397-417) using a hand-hold 50 mL syringe for balloon inflation (SI) with evaluation of balloon volume at perception threshold (BVP), (constant) urge threshold (BVU), and maximum tolerable volume (MTV). Thereafter, the thresholds were determined by inflating the balloon by electrical pump in randomised order rapidly (50 mL/s; RP) and slowly (2 mL/s; SP).

Results: Pearson correlation was higher between SI and RP (BVP 0.82, BVU 0.91, MTV 0.90) than between SI and SP (0.54, 0.69, 0.81) or RP and SP (0.67, 0.74, 0.96). Significant higher thresholds (Tab. 1) for perception and urge were seen by SP compared to RP (BVP $P = 0.04$, BVU $P = 0.04$) and SI (0.01, 0.01). Yet, the absolute differences between SI, RP, and SP were small.

Table 1: Median sensory thresholds for perception (BVP) and urge (BVU) and maximum tolerable volume (MTV) for rectal balloon distension with hand-hold syringe (SI), rapid (RP), and slow (SP) automated pump inflation.

	SI	RP	SP
BVP	30 mL	30 mL	35 mL
BVU	80 mL	80 mL	100 mL
MTV	170 mL	160 mL	170 mL

Conclusions: Automated pump balloon inflation is feasible and allows standardised inflation velocities. Sensory thresholds are dependent on inflation velocity. However, the differences are small and it has to be demonstrated whether these differences are clinically meaningful.

103 | Alterations of mucosal impedance values in the duodenum and antrum of patients with functional dyspepsia

K. J. Lee¹; J. G. Kang¹; S. T. Lee²

¹Ajou University Hospital, Suwon, South Korea; ²Chonbuk National University Hospital, Chonju, South Korea

Objective: Mucosal impedance values can reflect mucosal permeability or resistance. Recently, alterations of duodenal mucosal permeability is suggested to be involved in the pathogenesis of functional dyspepsia (FD). The aim of the study was to measure the mucosal impedance values in the duodenum and antrum of patients with FD and compare those values with controls.

Methods: Sixteen adult patients (M:F = 5:11, median age 58 years) with FD diagnosed by the Rome IV criteria and 12 healthy controls without organic diseases and any abdominal symptoms (M:F = 2:8, median age 59 years) were studied in a prospective manner. Patients with FD were subclassified into postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS), using the criteria of Rome IV. Mucosal impedance was measured during esophagogastroduodenoscopy (EGD) at the duodenum first portion (D), distal antrum (A), and distal esophagus near the EG junction (E). Subjects in whom organic lesions including erosions, ulcers, and tumors were found on EGD were excluded. Basal impedance values were selected.

Results: Age and sex ratio did not significantly differ between patients with FD and controls. Mucosal impedance values at D was significantly lower in patients with FD ($606.2 \pm 118.1 \Omega$; $P < 0.001$), in patients with PDS alone ($585.7 \pm 89.9 \Omega$; $P = 0.002$), and in patients with PDS and EPS ($660.0 \pm 114.0 \Omega$; $P = 0.013$), compared with controls ($1150.0 \pm 392.3 \Omega$). Those values tended to be lower in patients with EPS alone ($575.0 \pm 170.8 \Omega$; $P = 0.056$). Mucosal impedance values at A was significantly lower in patients with PDS alone ($671.4 \pm 160.4 \Omega$; $P = 0.049$) and tended to be lower in patients with PDS and EPS ($560.0 \pm 167.3 \Omega$; $P = 0.070$), compared with controls ($960.0 \pm 206.5 \Omega$). Those values did not significantly altered in patients with EPS alone ($575.0 \pm 206.1 \Omega$; $P = 0.499$). Mucosal impedance values at E were not significantly altered, compared with controls, irrespective of the presence of heartburn or chest pain with a frequency of at least once a week.

Conclusions: Mucosal impedance values on the duodenum and distal antrum are decreased in a subgroup of FD, particularly in patients with PDS. The role of altered mucosal permeability in the duodenum and distal antrum in the pathogenesis of FD needs to be further investigated.

105 | A randomized, double-blind, placebo-controlled study for the effect of machihyeon in patients with constipation

J. E. Shin¹; J. H. Choi²; K. B. Bang¹

¹Dankook University College of Medicine, Cheonan, South Korea; ²Research Institute R&D Center, Korea Drug Co., Ltd., Seoul, South Korea

Objective: In the experimental mouse model, Machihyeon (70% ethanol dried extract of *Portulaca oleracea*) was associated with an increase in fecal volume and improvement in fecal evacuation by enhanced intestinal motility. This study aimed to investigate the efficacy and safety of Machihyeon for the treatment of patients with constipation.

Methods: A total of 60 patients with functional constipation as defined by ROME IV criteria were enrolled in this randomized, double-blind, placebo-controlled study. Patients were randomly assigned to Machihyeon group or placebo group. The primary outcome was the change of complete spontaneous bowel movements (CSBM) and improvement in constipation related symptoms over 8 weeks. Patient Assessment of Constipation Quality of Life (PAC-QOL) and

Symptoms (PAC-SYM) scores were evaluated. Secondary outcome was the change of colonic transit time (CTT) measured using radio-paque markers.

Results: A total of 48 patient consisted of treatment group ($n = 25$) and control group ($n = 23$) were analyzed. 38 patients (79%) were female. Baseline characteristics including age, body mass index, were not significantly different between the two groups except for sex. CSBM was improved significantly in Machihyeon group compared with placebo over 8 weeks treatment ($P = 0.005$). Machihyeon was significantly associated with sustained symptoms relief in flatulence, gas, bloating, feeling of incomplete evacuation, straining, and hard stool during 4-8 weeks treatment (all $P < 0.001$). The overall PAC-QOL score improvement was observed in Machihyeon group ($P = 0.02$). Improvement in PAC-SYM scores was observed with no statistical significance. CTT was decreased from 41.8 ± 18.2 hours to 31.9 ± 20.2 hours after 7 weeks of treatment (P interaction = 0.01). Prominent decrease in CTT was observed in the left side colon. There were no significant differences in adverse events between the groups.

Conclusions: The use of Machihyeon significantly improved CSBM, the severity of symptoms in patients with constipation and associated with reduced bowel transit time. Further large studies are required to assess the benefits of Machihyeon for the treatment of constipation.

106 | Non-obese non-alcoholic fatty liver disease is associated with erosive esophagitis

K. B. Bang¹; H. D. Shin¹; K. W. Nam¹; J. E. Shin¹; J. H. park²; S. W. Kim¹

¹Dankook University College of Medicine, Cheonan, South Korea; ²Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, South Korea

Objective: Obesity has been registered as a risk factor for GERD. Although non-alcoholic fatty liver disease (NAFLD) shares common features such as insulin resistance or metabolic syndrome with obesity, data regarding the association between the NAFLD and GERD is scarce. This study aimed to investigate the relationship between the NAFLD and erosive esophagitis in non-obese, non-diabetic Korean adults

Methods: A cross-section study was performed to assess the association between the erosive esophagitis and NAFLD in non-obese, non-diabetic participants. A total of 17445 subjects who underwent health check-up and upper endoscopy were enrolled. Fatty liver disease was diagnosed using ultrasonography. The presence and odds ratio (OR) of erosive esophagitis was accessed in patients with NAFLD

Results: Participants with erosive esophagitis were associated with NAFLD. The prevalence of erosive esophagitis was higher in subjects with NAFLD than those without NAFLD (6.7% vs 3.6%, $P < 0.001$). The risk of erosive esophagitis was significantly high in subjects with NAFLD (OR 1.93, 95% confidence interval [CI] 1.62-2.30). After adjustment with multiple variables including metabolic component,

abdominal obesity and smoking, the association between the erosive esophagitis and NAFLD remained significance (OR 1.29, 95% CI 1.06-1.56, $P < 0.001$).

Conclusions: Erosive esophagitis is highly prevalent in non-obese, non-diabetic NAFLD patients. NAFLD is independently associated with erosive esophagitis regardless of obesity. Our result might represent another putative cause of erosive esophagitis such as hormonal factors besides obesity.

107 | Prevalence of functional gastrointestinal disorder by Rome III criteria in Korean obese subjects

J. Lee; M.-J. Cho; S. Hwang; H.-J. Hwang; Y. Kim; C.-H. Lim; J. H. Oh

The Catholic University of Korea, Seoul, South Korea

Objective: There is insufficient evidence for a functional gastrointestinal disorder (FGID) in obese patients. The purpose of this study was to investigate the difference in the prevalence of symptoms in FGID between non-obese and obese subjects. In addition, obstructive sleep apnea syndrome (OSA) patients proven by polysomnography would be related to FGID by Rome III.

Methods: A total of 164 subjects were evaluated in Eunpyeong St. Mary's Hospital, Korea, between July 2017 and February 2019. Nocturnal polysomnography (PSG) was conducted and an FGID questionnaire was asked. The apnea-hypopnea index (AHI) ≥ 30 by PSG was defined as severe OSA subjects. Rome III criteria were used for diagnosis of FGID. The subjects with body mass index (BMI) ≥ 30 was defined as obesity.

Results: Among 164 subjects who underwent polysomnography, 49 were obese and 115 were non-obese. The BMI (kg/m^2) was 34.9 ± 5.6 in obese subjects, and 25.2 ± 2.7 in non-obese subjects ($P < 0.001$). There was no difference between groups in age, sex, smoking, and alcohol. There was no difference in the prevalence of functional esophageal disorders in obese and non-obese subjects (16.3% vs 8.7%, $P = 0.304$). There was no difference in both groups regarding the prevalence of functional dyspepsia (8.2% vs 6.1%, $P = 0.724$), irritable bowel syndrome-constipation (30.6% vs 24.3%, $P = 0.481$), and irritable bowel syndrome-diarrhea (24.5% vs 20.9%, $P = 0.759$). There was no difference in the prevalence of FGID symptoms between the subjects with severe OSA and mild-moderate OSA.

Conclusions: There is no difference in the prevalence of FGID symptoms in obese patients and non-obese patients in Korea, however, obese subjects tend to have a higher prevalence of FGID symptoms than non-obese subjects.

109 | The changes of colonic contractility in 5FU induced mucositis in mice

M. S. Kim¹; J. Myung¹; Y. S. Kim²; H.-S. Ryu²; S. C. Choi²; W. C. Park³; K. Y. Kim³; J. M. Oh³; M. Y. Lee¹

¹Department of Physiology, Digestive Disease Research Institute, School of Medicine, Wonkwang University, Iksan, South Korea; ²Department of Gastroenterology, Digestive Disease Research Institute, School of Medicine, Wonkwang University, Iksan, South Korea; ³Department of Surgery, Digestive Disease Research Institute, School of Medicine, Wonkwang University, Iksan, South Korea

Objective: 5-FU, one of the drugs commonly used for cancer treatment, has been known to induce mucosal inflammation in the gastrointestinal tract including stomach and small bowel when using long-term or high dose, and it causes not only inflammation induced pain, but also change in gastrointestinal motility.

Although 5-FU-induced mucositis is known to be common in upper GI tract including small intestine, there is little research into the prevalence of mucositis and functional changes in the colon. Thus, the objective of this study was to investigate the effect of 5FU on the changes of contractility and inflammatory cytokines in colon.

Methods: Twenty male C57/BL6 mice were received 5-FU (50 mg/kg, i.p.) or saline as a control group. In order to study the changes of contractility, on the 5th to 7th day after 5-FU treatment, mice were sacrificed and removed entire colon. The colon was divided into proximal and distal segments and each segment was mounted in a longitudinal or circular muscle direction in a 10-mL organ bath. We determined the intergroup differences of the area under the curve (AUC) as percentage changes in contractility after applying electrical field stimulation (EFS) at 2 Hz, 5 Hz, 20 Hz over basal period with or without sympathetic (propranolol and phentolamine) or nitric oxide inhibitor (LNAME 10⁻⁶) pretreatment.

Results: 5FU treated mice showed exaggerated relaxation response to EFS in proximal longitudinal and circular muscle without inhibitor pretreatment. Even though there is no significant statistical difference in distal segments, contraction and relaxation in response to EFS in 5FU treated mice was apparently changed into sawtooth like contractility pattern. The response to EFS did not change significantly and showed the maintenance of the exaggerated relaxation response in 5FU treated mice under the presence of nitric oxide inhibitor, L-NAME or adrenergic blocker, phentolamine and propranolol.

Conclusions: These results suggest that 5 FU have an influence in the exaggerated relaxation response in the proximal colon and it might be caused by inducible nitric oxide due to the 5 FU induced colonic inflammation. This study may provide a direction to minimize side effects related to the colonic function caused by 5-FU treatment.

110 | Development and validity evaluation of a self-evaluated questionnaire for functional dyspepsia

K. Jung¹; H.-K. Jung²; J. G. Kwon³; C. H. Tae⁴; K. B. Bang⁵; J. K. Park⁶; J. Y. Lee⁷; C. M. Shin⁸; K. C. Huh⁹; S. T. Lee¹⁰

¹Department of Internal Medicine, Kosin University College of Medicine, Busan, South Korea; ²Department of Internal Medicine, Ewha Womans University College of Medicine, Ewha Womans University Mokdong Hospital, Seoul, South Korea; ³Department of Internal Medicine, Daegu Catholic University School of Medicine, Daegu, South Korea; ⁴Department of Internal medicine, Ewha Womans University College of Medicine, Ewha Seoul Hospital, Seoul, South Korea; ⁵Department of Internal Medicine, Dankook University College of Medicine, Cheonan, South Korea; ⁶Department of internal Medicine, Gangneung Asan Hospital, University of Ulsan College of Medicine, Gangneung, South Korea; ⁷Department of Internal Medicine, Keimyung University School of Medicine, Daegu, South Korea; ⁸Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, South Korea; ⁹Department of Internal Medicine, Konyang University College of Medicine, Daejeon, South Korea; ¹⁰Department of Internal Medicine, Chonbuk National University Medical School, Jeonju, South Korea

Objective: There is uncertainty about how to measure patient self-reported outcomes in functional dyspepsia (FD). The aim of this study was to development of instruments and to determine of the respondent definition for patient reported outcomes to evaluate the efficacy of therapeutic agents in FD patients.

Methods: Self-reported questionnaire for upper gastrointestinal symptoms (SEQ-UGIS) was developed through structural processes and translation with cultural validation. Two-week reproducibility was evaluated and construct validity was assessed by correlating subscale scores with SEQ-UGIS, Patient-Assessment of Gastrointestinal Disorders (PAGI-SYM), Nepean dyspepsia index-Korean version (NDI-K) and validated NDI-K quality of life (QOL) questionnaires. Finally, discriminative validity was performed by comparing the changes of SEQ-UGIS score after four weeks' treatment with proton pump inhibitor and prokinetic drug.

Results: A total of 121 Korean patients were included (mean age 48.8 ± 13.3 years, female 67.8%). Internal consistency of 11 item SEQ-UGIS was good (Cronbach's alpha = 0.53-0.85); test-retest reliability was acceptable (intra-class correlation coefficient = 0.70-0.74). The SEQ-UGIS score was expected to be highly correlated with the subscale of dyspepsia domain of the PAGI-SYM (Pearson correlation coefficient $r^2=0.651$, $P < 0.001$), NDI-K dyspepsia subscale ($r^2=0.784$, $P < 0.001$) and NDI-K QOL subgroups ($r^2=-0.324$ to -0.431 , all $P < 0.001$). Both drug responder and non-responder showed significant decrease in SEQ-UGIS scores after treatment, and significant difference in changes of mean difference between the two groups (-9.17 ± 9.15 vs -4.58 ± 7.79 , $P = 0.030$).

Conclusions: This study support that SEQ-UGIS for functional dyspepsia has the reliability, validity and can be useful tool to evaluate therapeutic response in patient with FD.

	Responders n=29	Non-responders n=38	<i>p</i> value
SEQ_Typical FD (Q1-3)			
Baseline	12.97 ± 4.76	14.05 ± 5.75	0.412
At 4 weeks	8.86 ± 3.34	11.74 ± 5.48	0.010
difference	"-4.10 ± 5.50"	"-2.32 ± 4.83"	0.162
SEQ_Major UGIS (Q1-6)			
Baseline	26.52 ± 8.53	27.53 ± 8.73	0.637
At 4 weeks	17.34 ± 5.51	22.95 ± 9.22	0.003
difference	"-9.17 ± 9.15"	"-4.58 ± 7.79"	0.030

TABLE. Validation of the self-evaluated questionnaire for functional dyspepsia.

111 | The different characteristics Of symptomatic belching between belching disorder and GERD with belching

J. S. Lee¹; S. O. Jeong¹; T. H. Lee¹; S. J. Hong²; Y. S. Cho³; J. S. Park¹; S. R. Jeon¹; H. G. Kim¹

¹Institute for Digestive Research, Digestive Disease Center, Soonchunhyang University College of Medicine, Seoul, South Korea; ²Digestive Disease Center and Research Institute, Soonchunhyang University College of Medicine, Bucheon, South Korea; ³Division of Gastroenterology, Department of Internal Medicine, Soonchunhyang University Cheonan Hospital, Soonchunhyang University College of Medicine, Cheonan, South Korea

Objective: To compare the characteristics of belching [supragastric belching(SGB) and gastric belching (GB)] in association with reflux between the patients with BD and GERD patients with belching.

Methods: Twenty-four hour impedance pH monitoring data were retrospectively analyzed from 10 BD (5 female, median age 40.5 y) and 10 GERD patients with belching who has main symptom as heartburn and/or regurgitation (6 female, median age 58.5 y). Total 3101 symptomatic SGB/GB from BD and 720 symptomatic SGB/GB from GERD group were manually classified as isolated, reflux related (preceding, during, and following reflux) and undefined, and also acidic and non-acidic according to the individual patients. We compared reflux parameters, parameters of high resolution manometry including hyper-dynamic UES, number of total/SGB/GB, ratio of SGB/GB, ratio of reflux related/isolated SGB, ratio of reflux related/isolated GB, and acidic/nonacidic SGB/GB between BD and GERD with belching.

Results: Reflux parameters were significantly increased in GERD group. Total number of symptomatic belching was significantly higher in BD than GERD group (median 112.5 vs 56, $P < 0.05$). SGB/GB ratio were not different between two groups. In SGB, reflux related SGB was significantly higher in GERD group than BD group (75.5% vs 41.9%, $P < 0.001$). In SGB, ratio of acidic belching was significantly higher in GERD group than BD (Median 38.1% vs 8.9%, $P < 0.05$) and nonacidic belching was significantly higher in BD. In GB, ratio of acidic belching was also significantly higher in GERD group than BD (49.2% vs 16.9%, $P < 0.05$). Of the total 2790 symptomatic SGB from BDs, the most common type was 'isolated' followed by 'during', 'preceding' and

'following' (62.9%, 33.3%, 3.6%, 0.3%) but, of the 659 symptomatic belching from GERDs, the most common type was 'during' followed by 'isolated', and 'preceding' (65.4%, 24.3%, 9.4%).

Conclusions: BD showed higher number of belching than GERD group, but, SGB/GB ratio did not different. SGB was frequently related to reflux in GERD than BD, and acidic belching regardless of GB or SGB might be related to GERD. Therefore SGB and acidity may have a role in the pathogenic mechanism of GERD. However, in BD, SGB is usually non-acidic and does not related to reflux.

112 | Secretion of THBS4 is induced by increased PDGFR β -associated Ca²⁺ signaling in colorectal cancer

M. S. Kim¹; J. Myung¹; Y. S. Kim²; H.-S. Ryu²; S. C. Choi²; W. C. Park³; K. Y. Kim³; M. G. Kim³; M. Y. Lee¹

¹Department of Physiology, Digestive Disease Research Institute, School of Medicine, Wonkwang University, Iksan, South Korea; ²Department of Gastroenterology, Digestive Disease Research Institute, School of Medicine, Wonkwang University, Iksan, South Korea; ³Department of Surgery, Digestive Disease Research Institute, School of Medicine, Wonkwang University, Iksan, South Korea

Objective: Thrombospondin-4 (THBS4), which is formed a pentamer as an extracellular matrix protein, is known to play essential roles in wound healing by contributing to the fibrosis and tissue remodeling through cell migration, attachment and proliferation as well as angiogenesis during tumor development. Platelet-derived growth factor receptor β (PDGFR β) is a membrane protein and a receptor tyrosine kinase that not only activates proteins such as SRC and PI3K to function in cell proliferation and angiogenesis but also show correlated increase with invasion and metastasis in colorectal cancer. Remodeling of intracellular Ca²⁺ has been found in colorectal cancer (CRC). We hypothesized that the secretion of THBS4 in colorectal cancer has a significant correlation with PDGFR β . Thus, the purpose of this study was to identify that PDGFR β -associated Ca²⁺ signaling induced by the secretion of THBS4.

Methods: For the purpose of the study, the colorectal adenocarcinoma tissues were collected from the patients in Wonkwang University with the informed consent and DLD1, adenocarcinoma human cell lines were cultured. Immunofluorescence staining, TCA precipitation and Western blotting were conducted to the adenocarcinoma tissues and DLD1 cell lines.

Results: The expression of THBS4 and PDGFR β was significantly increased in the colorectal adenocarcinoma tissues compared to the normal tissues in immunofluorescence and Western blot. Especially, the expression of THBS4 was highly increased in the extracellular area of tumor cells in contrast to the highly expression in the cytoplasm in normal tissues. The secretion of THBS4 was significantly decreased after the application of PDGFR inhibitor to the cultured

cell lines overexpressing PDGFR β and THBS4 in Western blot. Additionally, the secretion of THBS4 was also significantly decreased after the application of IP3R inhibitor, 2-APB and STIM1 inhibitor, ML-9 in a dose-dependent manner as well as after knockdown using IP3R or STIM1 siRNA to the cultured cell lines in Western blot.

Conclusions: These results suggest that over-expressed PDGFR β in tumor tissues induces Ca²⁺ signaling and increase THBS4 secretion and then promote tumor development via proliferation and angiogenesis.

113 | Prevalence of rapid gastric emptying in patients with PDS type functional dyspepsia

K. Nakamura; T. Tomita; K. Tozawa; T. Oshima; H. Fukui; H. Miwa

Division of Gastroenterology, Department of Internal Medicine, Hyogo College of Medicine, Nishinomiya, Japan

Objective: Gastric motility abnormalities have been considered to be pathophysiological features of functional dyspepsia (FD). It is reported that gastric motility abnormalities are associated with dyspepsia symptoms. Delayed gastric emptying provoke dyspepsia symptoms such as fullness or bloating. However, it has been reported that some FD patients had rapid gastric emptying recently. It is unclear how many FD patients with rapid gastric emptying in Japan and the association of emptying rate with clinical symptoms. The aims of this study were to (i) investigate the prevalence of rapid gastric emptying and (ii) evaluate the association between rapid gastric emptying and dyspeptic symptoms using gastric scintigraphy in the PDS type of FD.

Methods: 40 healthy subjects and 94 PDS type of FD patients were enrolled in the study. The volunteers and patients ingested a radiolabeled (99mTc) solid test meal, and scintigraphic images were recorded. Gastric accommodation and emptying were assessed by scintigraphic imaging. The patients' dyspeptic symptoms were also explored using self-completed symptom questionnaires with 10 variables (4 scales, 0-3 points) at the same time.

Results: 40 healthy subjects (age 44.7 $\pm$ 18.0 years, M/F:27/13) and 94 PDS type of FD patients (age 54.3 $\pm$ 17.3 years, M/F:29/65) were enrolled. In 40 healthy subject, average of gastric emptying was 53.0 $\pm$ 14.7 minute. Based on this result, we defined less than 38.3% as rapid gastric emptying. In 94 FD patients, the prevalence of rapid gastric emptying was 11.7% (11/94) and 7 patients of those had impaired gastric accommodation. There was no association between rapid gastric emptying and dyspeptic symptoms.

Conclusions: Rapid gastric emptying was seen in 11.7% of Japanese PDS type FD patients. There was no association between rapid gastric emptying and dyspeptic symptoms on gastric scintigraphy.

114 | Supragastric belching induce re-reflux during reflux period are frequent phenomenon in GERD patients with belching

J. S. S. Lee¹; T. H. Lee¹; J. S. Park¹; S. R. Jeon¹; H. G. Kim¹; J.-O. Kim¹; S. J. Hong²; Y. S. Cho³; K. C. Huh⁴

¹Institute for Digestive Research, Digestive Disease Center, Soonchunhyang University College of Medicine, Seoul, South Korea; ²Digestive Disease Center and Research Institute, Department of Internal Medicine, Soonchunhyang University College of Medicine, Bucheon, South Korea; ³Division of Gastroenterology, Department of Internal Medicine, Soonchunhyang University Cheonan Hospital, Soonchunhyang University College of Medicine, Cheonan, South Korea; ⁴Division of Gastroenterology, Department of Internal Medicine, Soonchunhyang University Cheonan Hospital, Soonchunhyang University College of Medicine, Daejeon, South Korea

Objective: Two different reflux association patterns of supragastric belching (SGB) were described as 1) SGB occurred immediately prior (<1 s) to the onset of the reflux episode (SGB preceding GER), and 2) SGB occurred during the reflux episode (SGB during GER). However, SGB during GER may elicits reflux or not (innocent bystander).

Our aims are to evaluate the proportion of gastric belching (GB) and SGB, SGB patterns and also discriminate how many SGB preceding GER occur during reflux period in patients with gastroesophageal reflux disease.

Methods: Total 24 patients (16 female, median age 53 year, range 28-69) was retrospectively selected using recent 2 years medical records and 24 hour impedance pH monitoring data. Inclusion criteria were patients with typical reflux symptoms and recorded belching symptoms during 24 hour impedance pH monitoring and exclude previous GI surgery and on drug study. We analyzed manually the number of GB, SGB, SGB preceding GER, SGB during GER including number of SGB preceding GER during reflux events. We compared total number of GB and SGB, number of GB and SGB during reflux periods, and SGB preceding GER and SGB preceding GER during reflux periods. We also measure correlations between GB or SGB and reflux parameters.

Results: Total 1423 symptomatic belching were observed (median number 42, range 6-240). Of these 1191 were SGB. SGB were more common than GB in all patients except 2 (median number 35 vs 6 respectively, $P < 0.001$). The number of SGB were significantly correlated with esophageal acid exposure % time, bolus total acid % time, bolus total all reflux % time, and all reflux episode ($P < 0.05$), however the number of GB were not correlated with these reflux parameters. During reflux periods, SGB frequently occurred than GB (median number 20 vs 3 respectively, $P < 0.001$). SGB preceding GER frequently occurred during reflux period than non-reflux period (median number 8 vs 3 respectively, $P < 0.05$).

Conclusions: SGB are frequently occur than GB in GERD patients with belching. SGB also well correlated with gastroesophageal reflux and may elicit reflux especially during reflux periods. It may induced re-reflux, which affect reflux duration.

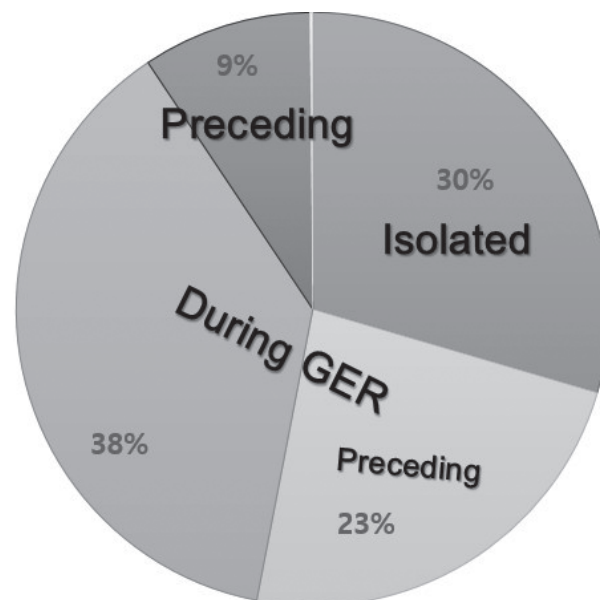


FIGURE. Distribution of SGB patterns. Preceding SGB during GER (23%) were more common than preceding SGB (9%).

115 | Differential effects of oxidative stress on mouse jejunal and colonic mechanosensitive afferent

A. Almuhammadi¹; D. Grundy²

¹Department of bioscience, King Abdulaziz University, Jeddah, Saudi Arabia;

²Department of biomedical science, University of Sheffield, Sheffield, UK

Objective: Oxidative stress is implicated in the pathogenesis of many gastrointestinal conditions, such as inflammatory bowel disease (IBD), ischemia and colon cancer. How diverse regions of the gut react to, and handle, elevated levels of reactive oxygen species (ROS) is unclear. Here, we investigated the effect of oxidative stress on sensory signalling in the small intestine and colon

Methods: sensory afferent nerve firing in response to distension was recorded in-vitro from jejunum and colon of male C57BL/6J. Data are presented as mean±SEM with $n = 5-6$. Statistical analysis was performed using Student's *t*-test and ANOVA (two way) as appropriate. $P < 0.05$ was considered as significant. Epithelial cells were isolated from each region and RNA were extracted for expression analysis, $n = 3$. RNA was used to determine differential gene expression in jejunum and colon by microarray analysis

Results: Ramp distension of segments of intestine evoked a biphasic increase in afferent discharge, which represents the activation of low threshold (LT), wide dynamic range (WDR) and high threshold (HT) mechanosensitive afferent fibres. To examine the regional difference in response to oxidative stress, H_2O_2 (100 & 500 μM) and mitochondrial inhibitor antimycin A (20 μM) were bath applied to the jejunum and colonic segments. In the jejunum, the response to H_2O_2 (100 & 500 μM) was observed as an increase in spontaneous nerve firing while antimycin A (20 μM) had no effect. Neither had

any effect on mechanosensitive responses. However, in the colon, nerve firing in response to distension was significantly enhanced by both H_2O_2 (100 & 500 μM) and antimycin A (20 μM), mainly in the WDR & HT component ($P = 0.02$). Moreover, baseline nerve activity increased from $14.43 \pm 4.3 \text{ spike s}^{-1}$ to $23.08 \pm 5.7 \text{ spike s}^{-1}$, $P = 0.02$. Microarray analysis showed that mucosal genes encoding antioxidant mechanism were significantly higher in the jejunum than colon.

Conclusions: our result suggests differential sensitivity to oxidative stress by jejunum and colonic afferents. Difference in response could be due to variance in expression of genes involved in ROS generation and antioxidant mechanism.

118 | Non-diabetic patients with gastroparesis-like symptoms assessed with gastric emptying scintigraphy and wireless motility capsule

M. Bekkelund¹; D. A. Sangnes²; L. Aabakken³; G. Dimcevski⁴; J. G. Hatlebakk²

¹Department of Clinical Medicine, University of Oslo and National Centre for Functional Gastrointestinal Disorders, Department of Medicine, Haukeland University Hospital, Oslo, Norway; ²National Centre for Functional Gastrointestinal Disorders, Department of Medicine, Haukeland University Hospital and Department of Clinical Medicine, University of Bergen, Bergen, Norway; ³Department of Clinical Medicine, University of Oslo and Department of Transplantation Medicine, Section for Gastroenterology, Oslo University Hospital, Oslo, Norway; ⁴Department of Clinical Medicine, University of Bergen, Bergen, Norway

Objective: In non-diabetic gastroparesis, most studies find no association between symptom severity and gastric emptying. Few studies have examined what generates symptoms in patients with suspected gastroparesis, but normal gastric emptying. In this study, we investigated if symptoms of gastroparesis could originate from other parts of the gastrointestinal tract by correlating symptom data with transit times and manometrical data obtained with a wireless motility capsule (WMC).

Methods: Thirty-five non-diabetic patients (73.4% women) with symptoms compatible with gastroparesis, were prospectively included. Twenty-three were idiopathic, four post-operative, three rheumatic, three neurologic, and two were of miscellaneous origin. Patients were examined with simultaneous WMC and gastric emptying scintigraphy (GES) of a solid meal. We measured gastric emptying, regional transit times and motility parameters, including Motility Index (MI) of the stomach and intestines. Symptom severity was assessed with the Patient Assessment of Upper Gastrointestinal Symptom Severity Index (PAGI-SYM).

Results: With GES, we found delayed gastric emptying in 35%, whereas WMC gastric emptying time was delayed in 54%. WMC detected delayed small bowel transit time in 43% of patients, while inability to generate normal maximum pressure in the small bowel were detected in 34%. WMC MI of the stomach correlated $R = -0.599$ ($P < 0.01$) with nausea, and MI of the small bowel correlated $R = -.689$ ($P < 0.01$) with nausea.

Conclusions: In patients with symptoms compatible with gastroparesis, we found a strong negative correlation between nausea and small bowel MI, and a moderate negative correlation with gastric MI. Based on these results, we recommend investigating both stomach and small bowel motility when examining patients with suspected gastroparesis.

119 | Clinical outcome after singular EsoFLIP dilation in patients with esophagogastric junction outflow obstruction

L. Schnurre; F. Murray; V. Schindler; D. Pohl

University Hospital Zurich, Zurich, Switzerland

Objective: Esophagogastric junction outflow obstruction (EGJO) is characterized by an impaired EGJ- relaxation but remaining esophageal peristalsis. Balloon dilation has been shown an effective therapy option in EGJO. A new advanced hydraulic dilation technology, the esophageal functional luminal imaging probe (EsoFLIP), facilitates dynamic monitoring with measurements of intraluminal values during intervention. The aim of our study was to evaluate treatment response after single EsoFLIP dilation in patients with EGJO and evaluate the safety profile.

Methods: Dilation was performed under endoscopic control with the EsoFLIP device using a self-developed dilation algorithm starting with an initial balloon volume of 30 mL, followed by stepwise volume additions of 5 mL until a maximum of 50 mL. Further volume increases were tailored individually at 1-3 mL intervals in accordance to previously measured values, intraballoon pressure and clinical impression. Symptom scores were assessed by the Eckardt score (ES) before and earliest 1 week after intervention. Esophageal emptying before and after intervention was recorded with timed barium esophagogram (TBE).

Results: We studied 24 consecutive patients with EGJO (median age 64, 11 females) undergoing their first hydraulic dilation performed with EsoFLIP. Diagnosis based on high-resolution manometry findings according Chicago Classification 3.0. Total ES was significantly reduced from median 6.5 cm at baseline to 3 cm, postinterventionally ($P < 0.001$). The median height of the barium column was significantly reduced from 6.5 cm to 2 cm at 1 minute in the TBE ($P < 0.02$) and from 3 cm to 0 cm at 5 minutes ($P < 0.05$). No major complications like hospitalization, perforation or severe bleeding occurred. Three of the included patients developed reflux symptoms caused by dilation.

Conclusions: We found good efficacy in both subjective and objective treatment outcome after singular, individualized EsoFLIP dilation in patients with EGJO with favorable side effect profile. We are currently collecting further data from our cohort including additional tailored EsoFLIP dilations. Providing procedural real-world measurements, we believe EsoFLIP may be the dilation technology of choice in the future.

122 | A 2019 perspective on health and celiac disease regarding complete mucosal recovery

R. Nemteanu¹; A. Plesa¹; I. Girleanu¹; L. Gheorghe²; I. Ciortescu¹; M. Danciu³; C. Stanciu¹; A. Trifan¹

¹University of Medicine and Pharmacy "Grigore T. Popa", Institute of Gastroenterology and Hepatology, "St. Spiridon" Hospital", Iasi, Romania;

²Department of Radiology, University of Medicine and Pharmacy "Gr. T. Popa", Iasi, Romania; ³Department of Pathology, University of Medicine and Pharmacy Gr. T. Popa, Iasi, Romania

Objective: Documentation of mucosal recovery after treatment with a gluten free diet (GFD) may be clinically relevant because persistent mucosal damage appears to increase the risk of severe complications in patients with celiac disease (CD), even in the absence of symptoms. The aim of this study was to assess the serological response and mucosal recovery rate among a cohort of adult patients diagnosed with CD under a GFD.

Methods: The study included adult patients with biopsy proven CD evaluated at a tertiary referral center. All patients included in the study had duodenal biopsies at diagnosis and at least one follow-up intestinal biopsy to assess mucosal recovery after at least 6 months after diagnosis and initiation of GFD.

Results: Of the 102 patients who were enrolled, 80 (78.4%) were females, mean age 40.36 ± 12.31 years. The initial histopathology showed complete VA (Marsh 3c) in 34 (33.3%), subtotal (Marsh 3b) in 18 (17.6%) cases, while the remainder had mild enteropathy in 23 (22.5%) cases. Ninety-three (91.2%) patients underwent a follow-up appointment. Among them, 68 (66.7%) had at least one follow-up biopsy. Mucosal recovery was identified in 42 (41.2%) cases, whilst 25 (59.5%) had some degree of intestinal VA (Marsh type 3). Mucosal healing was confirmed in only one case (Marsh 0). Follow-up biopsy demonstrated persistent VA in 14 (56%) patients. Patients with partial VA on the initial diagnostic biopsy were less likely to have persistent VA on follow-up biopsy than those who originally had total/subtotal VA ($P = 0.003$).

At follow-up, the mean antibody titer was 28.14 ± 60.19 U, and serological response was documented in 79 (76.7%) cases. Among the 79 cases who had negative tTG levels, different degrees of VA were documented ($n = 15$, 19%).

Conclusions: It is currently unknown whether mucosal recovery or complete mucosal healing is actually linked to survival among patients with CD. Intact mucosa has remained a desirable goal of the therapy.

125 | Bifidobacterium infantis 35624 improves symptoms in non-responders to a low FODMAP diet

V. Passananti; L. Martin; N. Z. Lopez; A. Emmanuel

University College of London Hospital, London, UK

Objective: The low FODMAP diet (LFD) has become increasingly used as first line therapy for irritable bowel syndrome (IBS).

However, at least 30% of patients are non-responders and it is unclear what the next therapeutic step should be in this large cohort. Furthermore, the reduction of dietary prebiotics with the LFD can result in reduced diversity of the gut microbiota. In placebo-controlled trials, Alflorex, Bifidobacterium infantis 35624, has been shown to significantly improve IBS symptoms and restore diversity of the microbiota. Our objective is to determine the effect of the probiotic Bifidobacterium infantis 35624 in patients with IBS who did not respond to the LFD.

Methods: 43 consecutive patients (40 female, mean age 41 years [range 21-59] with diarrhoea-predominant IBS for 8.1 years [range 0.6-23]) who had did not respond to the LFD at our institution were treated with 35624 probiotic 1 capsule per day for 12 weeks. The IBS-symptom severity score (IBS-SSS), hospital anxiety and depression (HAD) and visual analogue scales (VAS) of frequency, consistency, straining and urgency was determined in all patients baseline and post-treatment.

Results: There was no change in IBS-SSS scores before and after LFD, confirming absence of response to diet (mean total 246.5 to 238.6, $P = 0.67$). Following treatment with 35624 there was significant improvement in total IBS-SSS ($P < 0.04$), especially for severity and frequency of pain and abdominal distension ($P < 0.01$ and $P < 0.05$). The number of severe cases of IBS was reduced from 10 to 5 (24 to 12%). Significant reduction in anxiety and depression were scores following treatment ($P < 0.005$ and $P < 0.006$). VAS demonstrated a significant improvement in bowel frequency ($P < 0.02$) and urgency ($P < 0.04$) but not bowel consistency ($P < 0.13$) or straining ($P < 0.21$).

Conclusions: Probiotic treatment with Bifidobacterium infantis 35624 results in significant improvement in symptom severity, stool frequency and urgency in patients with diarrhoea-predominant IBS who are non-responsive to a LFD. This improvement is accompanied by improved psychological state and points to the importance of bacteria in the brain-gut axis.

127 | Randomised controlled trial: Face to face vs audio-visual education programme in IBS patients

V. Passananti; N. Zarate-Lopez; C. Perrin; J. Storrie; A. Raeburn; A. Emmanuel

University College of London Hospital, London, UK

Objective: Self-management in patients with irritable bowel syndrome allows better understanding of the condition in order to improve symptoms. Although it is recommended in most guidelines, there is little data on how best to deliver this in practice. We present the results of a randomised controlled trial of short- and medium-term follow-up following a face-to-face educational programme (FEP) vs an audio-visual education (AVE) provided online.

Methods: The educational programme involved five consecutive weekly sessions and follow-up after a 5-week break. Eighty-one

patients (63 f, mean age 35, range 19-91) were studied. All had baseline, immediate post treatment and follow-up at 12-month HAD score, IBS-SSS, VSI and EDL-5 to assess anxiety/depression, bowel symptoms severity and quality of life, respectively.

Results: Fifty-four patients completed the educational programme (67%); 54% patients completed the online education and 78% the live group sessions. There were 18 patients with IBS-C, 23 IBS-D and 13 IBS-M. Thirty-two (59%) had improved IBS-SSS after treatment; 65% of FEP patients and 90% of AVE patients. HAD scores at baseline demonstrated 67 patients (83%) with anxiety and 36 (44%) with both anxiety and depression. No statistical difference in state anxiety or depression was observed at baseline between the two groups. At the end of treatment, anxiety was statistically improved in both groups. Mean anxiety scores fell from 11 at baseline to 7.7 ($P < 0.001$). There was an excellent correlation between increase VAS score (general health) and reduction in IBS-SSS scores ($P = 0.26$).

Conclusions: We confirm that educational programs are an effective treatment for IBS patients. Both programs reduced anxiety and improved symptom severity effectively.

No statistical difference was found between the two-different programs, online and face to face. Taking into account costs and potential accessibility the online education could be an attractive therapeutic option in the management of patients with IBS.

129 | Clinical and manometric factors that influence the severity of fecal incontinence

C. Ciriza De Los Ríos; I. Castel; F. Canga

Hospital Universitario 12 de Octubre, Madrid, Spain

Objective: Fecal incontinence (FI) is defined as the involuntary and recurrent loss of feces. It represents a clinical condition that may significantly alter the quality of life of the patients and its etiology is often multifactorial. High resolution anorectal manometry (HRAM) is more intuitive and reproducible with better inter-observer agreement when compared to the conventional procedure.

The aim of the study is to identify demographic, clinical and HRAM results that can influence FI severity.

Methods: Observational cross-sectional study carried out with 437 prospective patients studied for FI. Demographic and clinical data were obtained and HRAM (Manoscan[®], Medtronic) was performed in all of them. The anal canal pressures were referred to the atmospheric pressure. Severity of FI was quantified using the Wexner score, considering FI as mild when the score was <9 and moderate-severe when this score was ≥ 9 . Logistic regression models were used to calculate odd ratios (OR).

Results: Of 437 patients, 358 (81.9%) were female. 238 (54.5%) patients had a Wexner score ≥ 9 . There were no differences in FI severity according to gender: 38 (16%) male and 200 (84%) female, Wexner score ≥ 9 vs 41 (21%) male and 158 (79%) female, Wexner

score <9 ; $P = 0.209$). The factors that influence FI severity and OR were:

Factor	OR	95% CI
Squeeze (≤ 125)	2.5	1.5-3.9
Surgery (YES vs NO)	2.4	1.5-3.9
Comorbidities	1.9	1.6-3.3
Diarrhoea	1.7	1-2.7
Age (40- 59) vs (18-39)	2.6	1.3-5.3
Age (≥ 60) vs (18-39)	3.8	1.8-7.9
Frequency (daily vs monthly)	4.5	2.7-9.1
Frequency (daily vs weekly)	2.7	1.4-5.2

The model has a concordance of 77.6%. ROC analysis is represented in the figure.

Conclusions: Main factors that influence FI severity were age, squeeze pressure lower than 125 mm Hg, daily frequency of episodes, abdominal and anorectal surgery, associated comorbidities and the presence of diarrhoea.

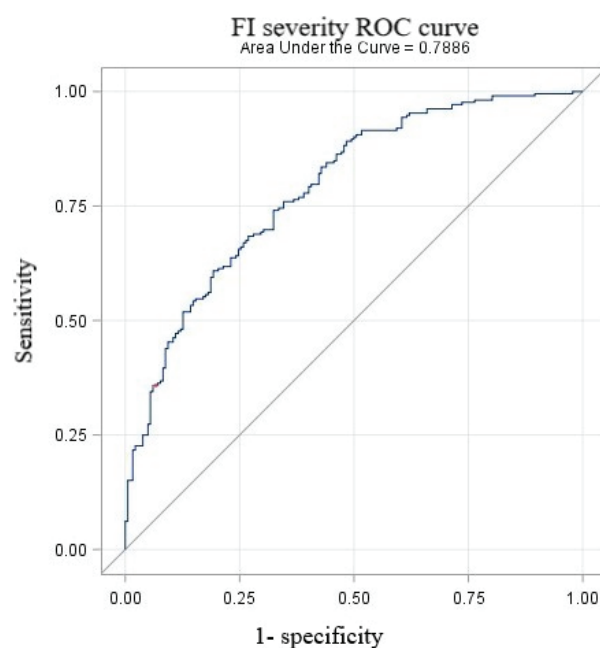


FIGURE. Factors for FI severity ROC curve.

130 | Decreased esophageal wall compliance and longitudinal muscle dysfunction in esophagogastric junction outflow obstruction

J. H. Kim

Inje University Busan Paik Hospital, Busan, South Korea

Objective: The aim of the study was to evaluate the esophageal wall compliance in patients with esophagogastric junction outflow obstruction (EGJOO) with high resolution esophageal manometry.

Methods: 15 patients diagnosed as EGJOO with HRM were classified into two groups; EGJOO with intact body peristalsis (group A)

and EGJOO with ineffective body peristalsis (group B). Ineffective body peristalsis was defined as $\geq 50\%$ of failed or weak peristalsis ($\text{DCI} < 450 \text{ mm Hg}\cdot\text{s}\cdot\text{cm}$). Baseline esophageal muscle thickness, cross-sectional area (CSA) at peak dilatation, frequency of failed esophageal body contraction using intraluminal ultrasound (ILUS), and LES contractile integral were analyzed compared to normal control ($n = 8$).

Results: 4 patients were classified as group B, whereas 11 patients classified as group A. Baseline muscle thickness and LES contractile integral were significantly increased in group A than that of normal control and group B. In contrary, CSA at peak distension was significantly decreased in group A than that of group B and normal control. There was no significant difference in baseline esophageal wall thickness, CSA at peak distension and LES contractile integral between group B and normal control. Failed esophageal contraction with ILUS during swallow was more frequently found in group B than normal control.

Conclusions: Decreased esophageal body compliance and defect of longitudinal muscle contraction might be the main pathophysiology for EGJOO.

132 | The effect of exercise and psychological comorbidity on gut microbiota in young males

T. Unno¹; S. K. Byun²; C. Sohn³; S. C. Choi⁴; M.-S. Park⁵; Y. S. Kim⁴

¹Faculty of Biotechnology, School of Life Sciences Jeju National University, Jeju, South Korea; ²Division of Sports Science Wonkwang University, Iksan, South Korea; ³Dept of Food & Nutrition Wonkwang University, Iksan, South Korea; ⁴Digestive Disease Research Institute Wonkwang University, Iksan, South Korea; ⁵Institute of Metabolic diseases Wonkwang University, Iksan, South Korea

Objective: The gut microbiota has an essential role in maintaining homeostasis and metabolism. Physical exercise is a possible modifier. We investigated the effect of exercise on intestinal microbiota in young male adults.

Methods: Twenty-five bowling players, 26 soccer players, and 29 non-athlete healthy male were recruited. Various factors were assessed by the international physical activity questionnaire (IPAQ), food frequency questionnaire (FFQ), Hospital Anxiety/Depression scale (HADS). Blood and stool samples were collected, and sequencing for fecal microbiome analysis was performed by the MiSeq system.

Results: The blowing and soccer players were younger than non-athlete healthy controls (21.5 ± 0.8 , 21.3 ± 1.2 and 23.0 ± 2.8 years, respectively, $P < 0.005$). Body mass index (BMI) was higher in bowling players, and Waist-Hip ratio (WHR) was lower in soccer players compared to other groups. Anxiety score was higher in athletes group than non-athlete controls, and depression score was higher in bowling players compared with other groups. The level of physical activity was high in the order of soccer players, bowling players, and non-athlete controls. The FFQ showed that there was no difference in total energy intake and nutrient composition

among groups. The α -diversity did not significantly differ among the three groups, and PCoA based analysis did not show a clear clustering of the microbial population of each group. All fecal samples were divided into two clusters. NMDS at the genus level shows that Cluster I is more with *Bacteroides*, whereas Cluster II is more with *Prevotella*. Athlete group tends to have more cluster II type microbiota although it is not significant. In the athlete group, *Prevotella copri*, *Bilophila*, and *Faecalibacterium* were significantly increased regardless of their HDAS score, BMI, and WHR. *Prevotella copri* positively correlated to the level of physical activity ($P < 0.01$). *Bilophila* and *Faecalibacterium* correlated to duration of athletic career ($P < 0.01$). According to PICRUST results, the module of carbohydrate metabolism is increased in Type I enterotype, and module of glycan biosynthesis and metabolism was increased in Type II enterotype.

Conclusions: These results showed that exercise increases several species and showed different metabolic activity regardless of psychological status. The *Prevotella copri* correlates to physical activity.

133 | The change of intestinal barrier as aging and irritable bowel syndrome, preliminary study

Y. H. Kwon; J. Y. Hwang; J. H. Park

Kyungpook National University Hospital, Daegu, South Korea

Objective: The pathophysiological mechanisms of the irritable bowel syndrome (IBS) are complex and have not been fully elucidated. Tight junction (TJ) have important role for construction of a constitutive barrier of epithelial cells, and regulate the permeability of the barrier. However, there was little known the change of TJ as aging. The present study aimed to investigate the molecular and cellular mechanisms of TJ changes in IBS as aging.

Methods: Colonic mucosal biopsies were acquired at right colon from old (≥ 65 years old) and young (20-40 years old) human, old and young IBS patients (each group $n = 8$). The change of inflammation ($\text{TNF-}\alpha$, $\text{IL-1}\beta$, and IL-10) and tight junction (claudin 1, 2, 5, occludin, and ZO-1) were measured by real-time PCR.

Results: $\text{TNF-}\alpha$, $\text{IL-1}\beta$, IL-10 and claudin 2 mRNA were increased and claudin 1, 5, occludin and ZO-1 mRNA were decreased in whole IBS group ($n = 19$) compared to control group ($n = 10$). Comparing young ($n = 12$) and old IBS group ($n = 7$), inflammatory cytokine-related factors ($\text{TNF-}\alpha$, $\text{IL-1}\beta$, IL-10) were increased and claudin 1 and 5 also increased in old IBS group, however, claudin 2, occludin and ZO-1 mRNA were decreased in old IBS group. However, there were no significant statistical differences between two groups. The inflammatory cytokine-related mRNA showed increased pattern and occluding and ZO-1 showed decreased pattern in IBS group and aging. Claudin 2 showed decreased pattern as aging, however, this factor showed increased pattern in IBS group. However, all factor did not showed any statistical difference except IL-10 between young control and old IBS group ($P < 0.05$) (Fig-1).

Conclusions: In conclusion, compromised intestinal barrier function has been associated with inflammation in the gut mucosa as aging in IBS patients.

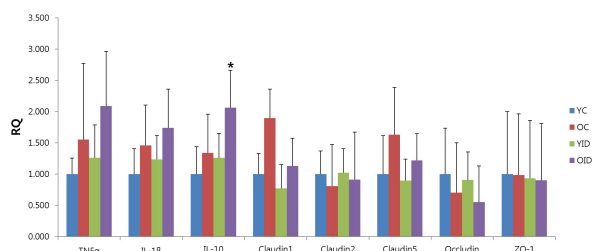


Fig . Relative transcript level of Inflammatory cytokine-related genes and Epithelial gut tight junction-related genes according to age in two tissue groups.

Transcript levels were normalized to *GAPDH*. Bars represent the mean $\pm$ SE, $n \leq 11$, * $P < 0.05$

YC, young control, $n \leq 4$;

OC, old control, $n \leq 6$;

YID, Young irritable bowel syndrome patient, $n \leq 12$;

OID, old irritable bowel syndrome patient, $n \leq 7$

135 | Efficacy and safety of GQ-lab daily in patients with irritable bowel syndrome: A randomized, double-blind, placebo-controlled, parallel-group study

C. M. Shin; Y. J. Choi; H. Yoon; Y. S. Park; N. Kim; D. H. Lee

Seoul National University Bundang Hospital, Seongnam-Si, South Korea

Objective: To evaluate the symptomatic efficacy of gQ-lab daily (a probiotic preparation of 10 species: *Lactobacillus rhamnosus* IDCC3201, *L. acidophilus* IDCC3302, *L. casei* IDCC3451, *L. plantarum* IDCC3501, *L. helveticus* IDCC3801, *Enterococcus faecium* IDCC2102, *Bifidobacterium longum* IDCC4101, *B. bifidum* IDCC4201, *B. lactis* IDCC4301 and *B. breve* IDCC4401) for the relief of abdominal symptoms and the improvement in quality of life (QoL) in IBS patients.

Methods: One hundred subjects with IBS by Rome III criteria (49 diarrhea predominant IBS, 28 constipation predominant IBS, and 23 mixed-type IBS patients) were consecutively enrolled. They were randomized into either gQ-lab administration group or placebo group. All subjects visited the clinic to assess compliance, symptoms, and safety at 0, 2 and 4 weeks; fecal and urine samples were collected at 0, 4 weeks. Primary endpoint was the improvement of overall symptoms at week 4. Quantitative polymerase chain reaction (qPCR) method was used to determine the changes in the probiotics in the feces. In addition, we analyzed and compared the bacteria-derived extracellular vesicles (EVs) of the study subjects by using 16S ribosomal RNA gene sequencing of their stool and urine samples, which allowed us to identify over 3200 operational taxonomic units corresponding to gut microbiota reported in previous studies.

Results: Ninety-five subjects (49 and 46 in gQ-lab and placebo group, respectively) completed the study protocol with no adverse effect. At week 4, there was a significantly higher relief of overall IBS

symptoms in the gQ-lab group than in the placebo group ($P < 0.01$). Especially, gQ-lab significantly improved psychological stress and anxiety ($P = 0.013$) and diet-related symptoms ($P = 0.031$). Although bacteria-derived EVs in feces and urine showed insignificant results, the quantitative changes of the probiotics in the feces from baseline to week 4 by qPCR method showed that *L. plantarum*, *L. acidophilus*, *L. helveticus*, *B. longum* and *B. breve* were significantly increased in gQ-lab group ($P < 0.05$ by repeated measure ANOVA).

Conclusions: gQ-lab daily may be effective in IBS patients. After administration of gQ-lab, some strains in *Lactobacillus* and *Bifidobacterium* species appear to be successfully colonized in the gut.

136 | Treatment response of high dose and standard dose rabeprazole for gastroesophageal reflux disease with extraesophageal manifestations: A single center, randomized, open-label trial

J. H. Cho; C. M. Shin; H. Yoon; Y. S. Park; N. Kim; D. H. Lee

Seoul National University Bundang Hospital, Seongnam-Si, South Korea

Objective: The extraesophageal manifestations (atypical symptoms) of gastroesophageal reflux disease (GERD) are more difficult to treat than the typical symptoms. However, a comparison of the efficacy of high dose and standard dose rabeprazole on the atypical symptoms is not well known.

Methods: This single center, randomized, open-label study included patients with GERD who were randomly assigned to 8 weeks treatment with rabeprazole 20 mg once daily (standard dose group) or 20 mg twice daily (high dose group). Patients were assessed before treatment and at weeks 4 and 8 with a 5-graded scale questionnaire consisting of 2 typical symptoms (heartburn and acid regurgitation) and 8 atypical symptoms (chest pain, cough, globus, wheezing, hoarseness, belching and dysphagia). Sufficient improvement of reflux symptom was defined as $\geq 50\%$ reduction from the initial questionnaire score.

Results: Final analyses included 35 patients in the standard dose group and 38 patients in the high dose group. The rate of sufficient improvement for typical symptoms was significantly higher in the high dose group than in the standard dose group (100.0% vs 84.0%, $P = 0.040$). For atypical symptoms, the rate of sufficient improvement tended to higher in the high dose group than in the standard dose group (82.4% vs 63.0%, $P = 0.087$). Typical and atypical symptom scores were significantly improved at 8 weeks in both groups, with significant intergroup differences in time course changes.

Conclusions: Twice daily treatment with rabeprazole is more effective than standard dose in patients with atypical symptoms of GERD as well as typical symptoms.

137 | Predictors for positive hydrogen breath test in the patients with abdominal symptoms

S.-J. Kim; C.-H. Lim; B.-I. Lee; Y.-S. Cho; Y. K. Cho; M.-G. Choi

Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, South Korea

Objective: Chronic post-operative abdominal pain/discomfort after bowel reposition is a common feature after abdominal surgery. Bowel reposition abdominal surgery may affect intestinal microbiome and cause symptoms. We investigated the prevalence and characteristics of small intestinal bacterial overgrowth (SIBO) after bowel repositioning condition.

Methods: Data were collected from tertiary medical institution (Seoul St. Mary's hospital, Korea) from December 2010 to January 2019. We reviewed patients who underwent the hydrogen breath test (HBT; using glucose or lactulose) with abdominal symptoms (e.g. pain, bloating, diarrhea). There were 37 patients with bowel reposition (gastrectomy 25, colectomy 5, small bowel resection 4, pancreatoduodenectomy 3) and 264 patients with suspicious functional gastrointestinal disease (FGID).

Results: A total of 301 patients (mean age 54.1 years; 53.0% female) were evaluated in this study. Sixty-five (24.6%) of patients with FGID and 22 (59.5%) of patients with bowel reposition had a positive HBT result. A positive HBT result was more likely in older patients (OR, 1.03; 95% CI, 1.01-1.05). And patients with bowel reposition were also more likely to have a positive HBT result (OR, 3.38; 95% CI, 1.61-7.11). There was no significant correlation between the presence of HBT and body mass index.

Conclusions: Bowel repositioning condition as well as older age was predictors of positive HBT in patients with abdominal symptoms. Further investigations of symptom correlation and treatment outcomes of patients with bowel repositioning condition are required.

138 | 'Esophageal remodeling' after peroral endoscopic myotomy (POEM) in sigmoid-type achalasia

Y. H. Youn¹; H. J. Yoon¹; D. H. Jung¹; J. C. Park²; H. Park¹

¹Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, South Korea; ²Yonsei University College of Medicine, Seoul, South Korea

Objective: The sigmoid-shaped esophagus is considered as the most advanced stage of achalasia. The peroral endoscopic myotomy (POEM) showed excellent outcomes for the treatment of achalasia, even in sigmoid type. However, the 'esophageal remodeling' after POEM for the treatment of sigmoid-type achalasia has not been known well. So, we aimed to investigate the 'esophageal remodeling' after POEM for advanced achalasia with sigmoid-shaped esophagus.

Methods: We analyzed data from a prospectively collected database of POEM subjects. Among 98 patients with achalasia who underwent POEM at Yonsei University Health System between July 2013 and December 2018, we recruited 13 patients with sigmoid-type

achalasia (7 male; mean age: 53.3 years) whose preoperative and postoperative barium esophagogram (BE) results were available. Sigmoid-type achalasia is subdivided into sigmoid-type (Sg) and advanced sigmoid-type (aSg) according to 'Descriptive Rules for Achalasia of the Esophagus'. (Sg: the lines obtained along with long axes of the esophagus cross at an angle of 90°-135°, aSg: an angle of <90°). We compared the morphological changes, including changes in angle of tortuosity of esophagus, HRM parameters and Eckardt score after POEM for sigmoid-type achalasia.

Results: Eight patients were Sg type and five patients were aSg type. During follow-up period, clinical treatment success (Eckardt score ≤ 3) was achieved in all of cases (13/13). Mean pre-treatment symptom score was 7.0 (range 4-10) compared with a mean post-treatment score of 0.5 (range 0-1, $P < 0.001$). When comparing the postoperative BE, morphological improvement was observed in 84% (11/13), including curvature straighten. The flexural angle on BE was more obtuse after POEM (91.45 vs 114.6°, $P = 0.046$). Two patients did not show morphological change. Their symptom duration was longer than the group with morphological improvements ($P < 0.001$).

Conclusions: POEM provided not only excellent clinical symptom relief, but also 'esophageal remodeling' in terms of obtuse flexural angle of esophagus on BE in sigmoid-type achalasia.

141 | Effects of deoxycholic acid on the human colon contractility

Y. W. Min; E.-J. Ko; P.-L. Rhee

Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea

Objective: Bile acid malabsorption accounts for approximately 30% of cases of diarrhea-predominant irritable bowel syndrome.

Methods: This study focused on investigating the effects of bile acid on the human colon muscle contraction, and elucidating its mechanism of action. Sigmoid colon longitudinal muscle strips were obtained from subjects who underwent colectomy for colon cancer. Isometric force measurements were calculated in response to electrical field stimulation (EFS, 0.3 ms in trains of 10 Hz for 20 s, 150 V). Peak and AUC during and after EFS, were measured in a basal state, and after sequential addition of deoxycholic acid (DCA, 1 mM), atropine (1 μM), MRS2500 (1 μM), and N-nitro-L-arginine.

Results: Peak contraction and AUC during EFS significantly decreased after addition of DCA, decreased further after addition of atropine, and persisted after sequential addition of MRS2500 and L-NNA. Peak contraction and AUC off EFS significantly decreased after addition of DCA, and persisted after sequential addition of atropine, MRS2500, and L-NNA. Pretreatment with L-NNA decreased the inhibitory effect of DCA on peak contraction and AUC during EFS.

Conclusions: DCA inhibits the contraction of longitudinal muscle in the human sigmoid colon. Nitric pathway partly involves the mechanism of action.

142 | Cardiovascular safety of domperidone use: Population based cohort and self-controlled case series study

B. G. Song; Y. C. Lee; Y. W. Min; K. Kim; P.-L. Rhee

Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea

Objective: Epidemiologic studies suggested the association between domperidone use and serious ventricular arrhythmia (VA) including sudden cardiac death (SCD). However, multiple randomized controlled efficacy studies failed to detect such adverse events. Because of inconsistent results, there has been controversy over the cardiovascular safety of domperidone. Our study was aimed to examine the risk of VA/SCD associated with domperidone use vs itopride, mosapride or non-use of all three medications in general population.

Methods: This was a large population-based cohort study and self-controlled case series in a cohort in the National Health Insurance Service-National Sample Cohort (NHIS-NSC) with a recorded VA/SCD and at least one prescription for any prokinetics from 2003 to 2013. A total of 3202 subjects were identified and included in the final analysis. Rate ratio for VA/SCD in periods of time exposed to prokinetics compared with unexposed periods, and exposed periods to itopride which is known having no-proarrhythmic effect, as a control.

Results: Conditional Poisson regression models showed that the use of domperidone, itopride, or mosapride was significantly associated with an increased risk of VA/SCD compared with non-use (adjusted RR 1.321 (95% CI 1.076-1.620), adjusted RR 1.465 (95% CI 1.176-1.826), and adjusted RR 1.359 (95% CI 1.111-1.662), respectively). However, risk of VA/SCD was not higher in domperidone use compared with itopride use (adjusted RR 0.527 (95% CI 0.331-0.840)).

Conclusions: Our study suggests that the increased risk of VA/SCD attributed to domperidone use is not higher than that for itopride use.

143 | Clinical application of the gastroesophageal reflux disease questionnaire in patients with suspected laryngopharyngeal reflux symptoms

Y. D. Kim¹; C. M. Shin¹; W.-J. Jeong¹; N. Kim¹; Y. S. Park¹; D. H. Lee¹; K. C. Huh²

¹Seoul National University Bundang Hospital, Seongnam-Si, South Korea;

²Konyang university Hospital, Daejeon, South Korea

Objective: To evaluate the usefulness of Gastroesophageal Reflux Disease Questionnaire (GerdQ) in patients with suspected laryngopharyngeal reflux (LPR) symptoms (globus, cough, hoarseness and throat pain)

Methods: A total of 111 patients with suspected LPR symptoms were incorporated from either otorhinolaryngology or gastroenterology clinic. Patient's laryngoscopic findings were graded by reflux finding score (RFS, n = 98), and RFS ≥ 7 was considered as positive

LPR. Patient's LPR symptoms were evaluated using reflux symptom index (RSI). Erosive esophagitis by endoscopy (n = 111) or abnormal results on 24-hr multichannel intraluminal impedance-pH (MII-pH) testing (n = 111) were used as diagnostic references for gastroesophageal reflux disease (GERD). Esophageal motor function was evaluated using high resolution esophageal manometry (HREM, n = 111); distal contractile integral (DCI) < 450 mm Hg-cm-s or fragmented peristalsis (defect > 5 cm) or absent peristalsis was considered as esophageal hypomotility.

Results: Ninety-one of 98 (92.9%) subjects were diagnosed as LPR but only 17 of 111 (15.3%) had GERD. For GerdQ, the cutoff value of 9 showed the highest area under curve (AUC) by receiver operating curve (ROC) analysis (AUC = 0.616); the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were 52.9%, 70.2%, 24.3% and 89.2%, respectively. For RSI, the cutoff value of 13 showed the highest diagnostic yield (AUC = 0.654); the sensitivity, specificity, PPV and NPV were 75.3%, 40.0%, 95.9% and 8.0%, respectively. In patients with GERD (n = 17), both distal and proximal baseline impedance levels (3 cm and 15 cm above esophagogastric junction, respectively) were decreased ($P < 0.05$) and proximal extent of reflux were increased ($P < 0.001$). However, there was no difference in esophageal body motor function between patients with or without GERD ($P > 0.05$).

Conclusions: GERD is infrequent among patients with suspected LPR symptoms. In this population, the sensitivity of GerdQ is low thus GerdQ has a limited role in GERD diagnosis.

146 | Efficacy of DA-5204 (Stillen 2X[®]) for patients with gastroesophageal reflux disease: A randomized, double-blind, placebo-controlled pilot study

J. H. Cho; C. M. Shin; Y. D. Kim; H. Yoon; Y. S. Park; N. Kim; D. H. Lee

Seoul National University Bundang Hospital, Seongnam-Si, South Korea

Objective: Proton pump inhibitor (PPI) alone is not satisfactory for the treatment of gastroesophageal reflux disease (GERD). Therefore, we investigated the efficacy of DA-5204 (Stillen 2X[®], 90 mg of *Artemisia asiatica* 95% ethanol extract per tablet) and PPI combination therapy on GERD in comparison to PPI alone.

Methods: This randomized, double-blind, placebo-controlled study randomly assigned 70 patients with endoscopically proven esophageal mucosal injury (Los Angeles classification A or B) into 2 groups: pantoprazole 40 mg once daily with DA-5204 twice daily (DA-5204 group) or pantoprazole 40 mg once daily with placebo twice daily (placebo group) for 4 weeks. The primary endpoints were endoscopically effective (normal mucosa or minimal change) or complete healing (normal mucosa) rates, and secondary endpoint was sufficient relief ($\geq 50\%$ reduction) of reflux symptoms using Gastroesophageal Reflux Disease Questionnaire (GerdQ) questionnaire.

Results: Final analyses included 29 patients with the DA-5204 group and 30 patients with the placebo group. At weeks 4, there was a significant difference of the endoscopically effective healing rate between the two groups (DA-5204 group vs placebo group; 93.1% vs 56.7%; $P = 0.001$) as well as the complete healing rate (DA-5204 group vs placebo group; 82.8% vs 33.3%; $P < 0.000$). The rates of sufficient relief for reflux symptoms according to GerdQ tended to be higher in the DA-5204 group than in the placebo group, with no significant difference.

Conclusions: Our findings suggest that combined therapy with PPI and DA-5204 is more effective in treating GERD than PPI alone.

148 | The effect of experimentally-induced oesophageal hypersensitivity on conditioned pain modulation

A. Albusoda; R. Idrees; A. Farmer; Q. Aziz

The Wingate Institute for Neurogastroenterology, QMUL, Barts and the London SMD, London, UK

Objective: Functional gastrointestinal disorders are common and characterised by chronic unexplained pain. Visceral hypersensitivity is a key feature in many of these cases. Conditioned pain modulation (CPM) is a natural bulbar reflex permitting “pain to inhibit pain” by descending inhibition, and is a validated measure that interrogates the brain-gut axis. CPM appears to be reduced in people with functional gastrointestinal disorders. Our aim was to determine the relationship between experimental visceral hypersensitivity and CPM in healthy humans, to better understand the pathophysiology of functional gastrointestinal disorders. We also aimed to investigate if the development of experimental oesophageal hypersensitivity is associated with a reduction in the magnitude of CPM.

Methods: In this pilot single-armed correlational study, we measured both electrical pain tolerance thresholds and CPM prior to, and following, a 30-minute distal oesophageal infusion of 0.15 M hydrochloric acid. Following acid infusion, the pain threshold is expected to drop due to sensitisation. Conditioned Pain Modulation was measured by testing their pain threshold in the proximal oesophagus while the participant had a foot immersed in cold water at 2°C to 4°C. When the CPM is higher, the pain threshold rises due to stronger descending inhibition. We applied a linear regression model (IBM SPSS 25, USA). Psychological data such as anxiety and autonomic data were also recorded.

Results: 17 participants were included (mean age 26.53 ± 1.468). The percentage changes in their CPM following acid infusion ranged from -23.08% to 29.17%. There is a positive correlation between the baseline CPM and the drop in pain threshold following acid infusion (Pearson correlation 0.596, significance 0.012, 95% CI 0.154 to 1.038). There is a negative association between the degree of pain hypersensitivity and the percentage change in CPM (Pearson correlation -0.552, significance 0.022, 95% CI -0.965 to -0.089).

Conclusions: Baseline CPM predicts the degree of development of pain hypersensitivity in healthy humans. Moreover, the stronger the

CPM reflex, the less they sensitise to acid infusion. Further studies are required to confirm findings and establish why this reflex is reduced in functional gastrointestinal disorders and whether there are various clinical measures that can modulate this reflex for therapeutic benefit.

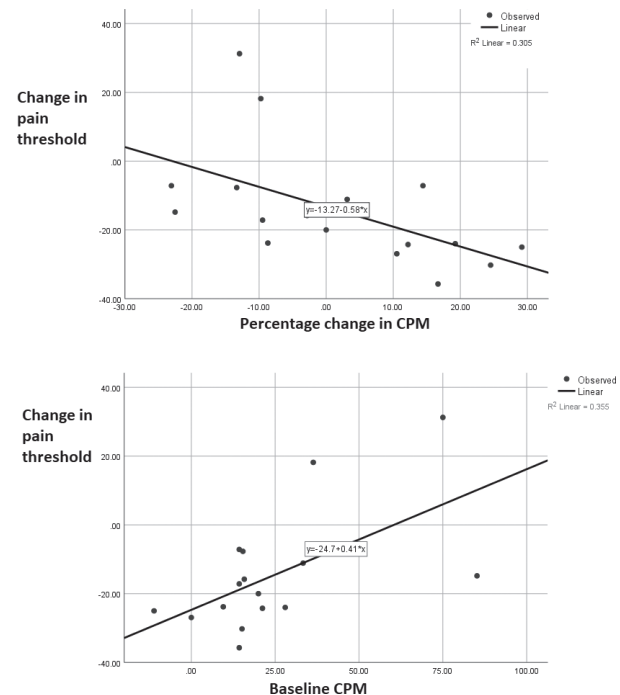


FIGURE. Scatter plots showing the relationship between baseline CPM and change in pain threshold, and change in CPM and change in pain threshold before and after acid infusion.

149 | Analgesic and anti-inflammatory effects of the FXR-FGF19 axis activation in ulcerative colitis

M. Panek-Jeziorna; A. Mulak

Department of Gastroenterology and Hepatology, Wroclaw Medical University, Wroclaw, Poland

Objective: Fibroblast growth factor 19 (FGF19) is a key target of the farnesoid X receptor (FXR) regulating bile acid homeostasis. The FXR activation inhibits intestinal inflammation in inflammatory bowel disease. The aim of the study was to evaluate serum FGF19 level and its correlation with abdominal pain intensity and serum CRP and fecal calprotectin levels in patients with ulcerative colitis (UC).

Methods: Fasting serum FGF19 level was measured using ELISA test in 16 patients with active UC (7 F, 9 M; mean age 38), 15 patients with non-active UC (8 F, 7 M; mean age 46), and 19 healthy controls (11 F, 8 M; mean age 39). The disease activity was assessed based on the clinical and endoscopic evaluations, measurement of abdominal pain intensity by visual analog scale (VAS), as well as serum CRP and fecal calprotectin levels. Non-parametric statistics were used and results are expressed as median and the lower and upper quartiles [25Q-75Q].

Results: Median serum FGF19 level was higher in patients with non-active UC: 175.3 pg/ml [108.7-342.3] than in patients with active UC:

114.3 pg/ml [68.9-155.3], $P = 0.093$. Median FGF19 level in healthy controls amounted to 151.6 pg/ml [90.6-224.2] and there were no statistically significant differences between the patients with active and non-active UC compared to healthy controls. Median serum CRP and fecal calprotectin levels were significantly higher in active UC compared to non-active UC: 19.4 vs 2.2 mg/L and 1974.3 vs 87.1 $\mu\text{g/g}$, respectively ($P < 0.001$). Median VAS scores for abdominal pain during the week preceding the examination amounted to 0 [0-4] in patients with non-active UC vs 4.5 [2-6.5] in patients with active UC ($P = 0.028$). An inverse correlation was observed between FGF19 and CRP levels ($R = -0.38$, $P = 0.036$), FGF19 and fecal calprotectin levels ($R = -0.36$, $P = 0.045$), as well as FGF19 level and abdominal pain intensity ($R = -0.48$, $P = 0.007$). Serum FGF19 level was not correlated with disease activity indices.

Conclusions: The inverse correlations between FGF19 level and abdominal pain and inflammatory markers in UC may imply its potential analgesic and anti-inflammatory effects – direct or due to the FXR-FGF19 axis activation.

151 | Constipation and gut motility is associated with posture instability: Role of muscle trigger points and potential to treat by targeted dry needling

R. V. Bubnov¹; L. Kalika²; M. Y. Spivak³

¹Clinical Hospital Pheophania, Kyiv, Ukraine; ²NY Dynamic Neuromuscular Rehabilitation & Physical Therapy <https://nydnrehab.com/> Kyiv, Ukraine;

³Zabolotny Institute of Microbiology and Virology, Kyiv, Ukraine

Objective: Intestinal motility depends on nerve impulses from CNS, enteric nervous system (ENS), has strong linkage with posture, cholestasis. Dry needling (DN) of myofascial trigger points (MTrP) under ultrasound (US) guidance is a prioritized method for treatment myofascial pain, restoring posture. Hypothesis: Posture imbalance can be associated with visceral dysfunction, pain and constipation; correcting posture via MTrP DN can improve abdominal symptoms.

The aim was to test the hypothesis of linkage of posture and gut motility and evaluate potential to alleviate constipation via restoring posture.

Methods: We included 24 patients (17 females, aged 33-62 y.o.) with mild and moderate constipation, muscle pain (low back, visceral pain), altered posture, clinically diagnosed reduced motility in spine, pelvis and lower extremity levels. Another healthy 20 individuals (aged 18-50 y.o.) were controls. All patients underwent general clinical, lab tests; precise physical tests, general multiparameter abdominal US, liver, bile ducts (common bile duct, CPD), visualizing colon (anti) peristalsis; dynamic US of postural stability; functional neuromuscular US in shoulder, intervertebral spaces, sacroiliac joint (SIJ), legs, abdominal wall, diaphragm and pelvic floor motility, central and peripheral trigger points identification. Then patients received DN of detected MTrP under US guidance.

Results: We detected different patterns of decreasing motility, contractility on M-mode during functional tests in all levels in group 1 ($P < 0.05$); posture parameter were altered (organ ptosis, weakness of abdominal wall, pelvic floor hypermobility, diaphragm elevation and motion restriction); local areas of spasticity (trigger points) were successfully detected on shoulders, pelvis and spine for precise guidance of deep DN. After DN of detected MTrP the signs of inactivation trigger points, motion recovery in all areas. US patterns of colon hyperpneumatosis, hypomotility, signs of reflux, nephroptosis were detected and improved after DN. We registered increasing of CPD diameter to 9.6 mm (segmental bile ducts to 1.3 mm) in all patients with constipation; and decreasing after DN to 7.3 mm. Microbiota alteration was in 18 patients with constipation and cholestasis (expansion of CBD over 11 mm).

Conclusions: Posture imbalance is associated with visceral dysfunction and constipation; correcting posture via trigger points DN is effective to improve both posture and abdominal symptoms.

152 | Characteristics of the duodenal microbiota composition in patients with functional abdominal bloating: A pilot study

M.-G. Choi; Y.-K. Cho; S. B. Yoon; C.-H. Lim; S. W. Han

The Catholic University of Korea, Seoul, South Korea

Objective: Functional abdominal bloating is a common and troublesome symptom, but its pathogenic mechanisms have not been fully understood to date. In this study, we characterized the mucosa-associated microbiota in the duodenum of patients with bloating and compared with healthy-controls.

Methods: Males and females, 20-70 years old, with a diagnosis of functional abdominal bloating (Rome IV) and the absence of any relevant structural disease by endoscopy were recruited. The duodenal biopsy samples were obtained by aseptic technique from 10 patients with bloating and 10 control subjects. Microbiota compositions were analyzed by the 16S ribosomal RNA gene sequencing.

Results: Proteobacteria and Firmicutes were the first and second most predominant phyla in the duodenal mucosa of both bloating-patients and healthy-controls. Proteobacteria and Firmicutes accounted for 58.8 and 25.2% of microbial counts in the bloating-group and 60.0% and 15.9% in the control-group, respectively. The third most common microbacterium was Bacteroidetes in the bloating-group and Actinobacteria in the control-group. Acidobacteria were observed in more proportion in bloating patients (1.6%) than in healthy controls (0.6%). There was no difference in the Shannon's index between bloating-patients (3.22 ± 0.71) and healthy-controls (2.53 ± 1.03).

Conclusions: In this pilot study, the composition of duodenal microbiota in bloating patients was slightly different from the controls. More studies are needed to determine the role of duodenal microbiota in functional abdominal bloating.

154 | Bergamot essential oil and its constituent linalool, inhibit cholinergically-mediated contractions of human and rat isolated colon

M. Straface¹; R. Makwana¹; L. Rombola²; J. Chinaleong³; L. A. Morrone²; G. J. Sanger¹

¹Queen Mary University of London, London, UK; ²University of Calabria, Rende, Italy; ³Royal London Hospital, London, UK

Objective: Bergamot essential oil (BEO) is a phytocomplex used in complementary and alternative medicine, and to promote a citrus flavour in food and drink. In rats, BEO can modulate anxiety-like behaviours and synaptic functions within the CNS¹. We have examined the ability of BEO and its major constituents to modulate enteric nerve functions in human and rat isolated colon.

Methods: Human colon was obtained at surgery for bowel cancer following informed consent; mucosa-free strips were cut parallel to the circular muscle. Rat colon (Sprague-Dawley) was cut as circular muscle preparations. Strips were suspended between platinum wire electrodes in tissue baths for isometric recording (Krebs solution; 5% CO₂ in O₂; 37°C; 1 or 2 g tension for rat and human). Electrical Field Stimulation (EFS) was used to evoke cholinergically-mediated contractions (pulse trains of 5 Hz, pulse width 0.5 ms, for 10 s every 1 minute, at 110% maximal voltage)². Cumulative concentration-response curves were obtained for BEO (10⁻⁶-10⁻³%v/v) and its main constituents: (-)-linalool, (R)-(+)-limonene and linalyl-acetate (10⁻⁹-10⁻⁴ M). Changes in contraction amplitudes were expressed as mean ± s.e.m % inhibition; n = numbers of patients or animals.

Results: BEO and its constituents caused concentration-dependent inhibition of EFS-evoked contractions. In human colon, the E_{max} for BEO was 55.8 ± 4.2% and the pEC₅₀ 3.8 ± 0.3; n = 5. For its constituents the rank-order of activity was (-)-linalool (E_{max} 76.8 ± 6.9%; pEC₅₀ 6.7 ± 0.2; n = 4) > > linalyl acetate (E_{max} 53.4 ± 2.9%; pEC₅₀ 5.9 ± 0.5; n = 4) > > (R)-(+)-limonene (E_{max} 27.5 ± 4.3%; pEC₅₀ 4.8 ± 0.2; n = 3); time-matched vehicle control was without effect (E_{max} 1 ± 3.7%; n = 3). Similar but less potent activity was obtained in rat colon (eg. linalool pEC₅₀ 5.8 ± 0.2%; E_{max} 72.5 ± 2.1%; n = 4).

Conclusions: The results indicate that BEO, largely via the actions of linalool, inhibits human and less potently, rat enteric neurotransmission, providing a potential mechanism for use as a complementary treatment of gastrointestinal diseases.

References: [1] Rombola et al. *Molecules*, 2017; <https://doi.org/10.3390/molecules22040614>.

[2] Celtek et al. *Neurogastroenterol Motil* 2006;18:853-61.

157 | Dysphagia in patients with severe brain damage

I. Pichugina; N. Pryanikova; A. Yakovlev; A. Shajbak

Federal Research and Clinical Center of Intensive Care Medicine and Rehabilitology, Moscow, Russia

Objective: To study the characteristics of dysphagia in patients with brain damage.

Methods: The study included 10 patients (6 men, 4 women; middle age 55.5 ± 10.4 years) with dysphagia after severe brain damage, who are on treatment in intensive care. All patients underwent routine examinations, speech therapist examination, esophagogastroduodenoscopy, endoscopic evaluation of swallowing function, video fluoroscopy of swallowing act and high-resolution manometry

Results: In the survey all patients (100%) diagnosed a violation of faringal phase of swallowing. The study of the esophageal phase of swallowing by a high-resolution manometry apparatus revealed that 1 patient had normal esophageal motility (10%), ineffective esophageal motility was present in 4 patients (40%), distal esophageal spasm – in 4 patients (40%), and 1 patient had absent contractility (10%). In addition, high-resolution manometry made it possible to adjust speech therapy sessions for each individual patient

Conclusions: Evaluation of all three phases of swallowing is necessary to assess swallowing disorders. Conducting high-resolution manometry during sessions with a speech therapist allows to choose an individual rehabilitation program, taking into account the characteristics of this particular patient

158 | The influence of bisphenol a on co-localization of neuregulin 1 and vasoactive intestinal polypeptide in the myenteric neurons of the porcine ascending colon

K. Szymanska

Department of Clinical Physiology, Faculty of Veterinary Medicine, University of Warmia and Mazury, Olsztyn, Poland

Objective: Neuregulin-1 (NRG-1) belongs to epidermal growth factor family and participates in development of the heart and nervous system. Bisphenol A (BPA) is primarily used in the plastics production and may affect living organisms. Myenteric plexus (MP) is the part of the enteric nervous system (ENS), which mainly regulates intestinal motility. The aim of the present study was to investigate the influence of BPA on co-localization of NRG-1 and vasoactive intestinal polypeptide (VIP – main inhibitory factor in the ENS) in the neurons of the MP within the ascending colon in domestic pig, which seems to be an appropriate biomedical model for processes occurring in human ENS.

Methods: Fragments of the ascending colon were collected from 10 immature gilts divided into two groups: group A (n = 5) – receiving empty gelatin capsules and group B (n = 5) – receiving capsules with BPA in dose 0.05 mg/kg b.w./d for 28 days. These fragments were subjected to routine double-staining immunofluorescence method using antibodies against NRG-1 and VIP. To determine the percentage of neurons showing the co-localization, NRG-1 – positive neurons (considered as 100%) were assessed with regard to the presence of VIP – positive neurons.

Results: Administration of BPA caused an increase in the percentage of co-localization of NRG-1 – and VIP – positive neurons (from about 24% to about 30%).

Conclusions: Even short-term BPA administration modifies the neurochemical characterization of the enteric neurons and the degree of co-localization of NRG-1 and VIP and it is not neutral for the organism. Observed changes may suggest neuroprotective roles of NRG-1 and VIP in the ENS but the explanation of exact functions of these substances requires further studies.

Publication supported by National Science Centre (Grant No. 2018/29/N/NZ7/00183)

Publication supported by KNOW (Leading National Research Centre) Scientific Consortium "Healthy Animal – Safe Food", decision of Ministry of Science and Higher Education No. 05-1/KNOW2/2015.

159 | Rapid drink challenge test (RDC) during high resolution impedance manometry (HRIM) for evaluation of the responses to peroral endoscopic myotomy (POEM) in patients with achalasia

I. Marin¹; C. Guarner-Argente²; M. Rodriguez¹; B. Benslaiman¹; J. Serra¹

¹Motility and Functional Gut Disorders Unit. University Hospital Germans Trias i Pujol, Badalona, Spain; ²Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

Objective: Introduction: Pressure responses to a RDC and the height of the retained column after timed barium esophagogram correlate with treatment success in patients with achalasia. However, responses after POEM, which means a larger myotomy, have not been studied.

Aim: To evaluate pressure responses and the height of the water column retained during the RDC, before and after POEM, in patients with achalasia using HRIM.

Methods: We prospective studied 15 consecutive patients (7M, 8F, mean age 56 years) diagnosed with achalasia and treated with POEM. In each patient, a 200-mL RDC was performed before and 2-12 months after treatment. Pressure responses and bolus clearance were measured using HRIM. Symptoms were scored by the Eckardt Scale.

Results: Before treatment, all patients showed an obstructive pattern of pressure responses characterized by pressurization of the esophageal body ($37 \pm 7\%$ of time with pressure >20 mm Hg, pressure gradient across the EGJ 20 ± 4 mm Hg) and a retention of the ingested water column (12 ± 2 cm at 1 minute, and 10 ± 2 cm at 5 minutes after the RDC). Treatment with POEM reverted this situation, producing a reduction of the pressurization of the esophageal body ($3 \pm 1\%$ of time with pressure >20 mm Hg, pressure gradient across the EGJ 2 ± 2 mm Hg; $P < 0.05$ vs before treatment for both) and a reduction of the retained water column 1 minute after the end of the RDC (5 ± 1 cm; $P < 0.05$ vs before treatment), that was associated to clinical improvement (Eckardt score 8.0 ± 0.6 vs 0.9 ± 0.2

before vs after treatment, respectively; $P < 0.05$). However, during the following minutes, 6 of 15 patients had some reflux episode, leading to an increment in the registered water column at 5 minutes after the RDC (7 ± 1 cm; NS vs before treatment).

Conclusions: Combined measurement of pressure and impedance responses to a RDC using HRIM confirm normalization of esophageal function in patients successfully treated with POEM and could be a useful tool to objectively assess treatment responses in patients with achalasia. However, reflux is common after POEM, and the height of the water column 5-min after the test needs to be evaluated carefully

164 | Oesophageal reflux hypersensitivity – Prevalence based on Rome IV criteria at a UK tertiary hospital: A retrospective study with a prospective component

G. Amarasinghe; Q. Aziz; D. Sifrim

Queen Mary University of London, London, UK

Objective: Retrospective cohort study with a prospective component to phenotype our population of patients with reflux hypersensitivity (RH), comparing them with patients with gastro oesophageal reflux disease (GORD) and functional reflux disorders.

Oesophageal RH, defined by ROME IV is a condition of typical reflux symptoms associated with physiological reflux events in the absence of GORD, eosinophilic oesophagitis and major motility disorders.

Methods: 3000 patients were identified (January 2010-December 2015). All patients with RH, and a representative group with GORD, functional heartburn (FH) and functional chest pain (FCP) were evaluated.

Results: Of 1869 patients with typical symptoms of GORD, 211 with RH (65% female, median age 44y, range 19- 82) were included. Of 995 patients with GORD, 32 (33% female, median age 54y, range 29-77), and of 276 patients with FH/FCP, 31 (67% female, median age 47y, range 18-73) were included.

65% of RH patients were female (FH/FCP 65%, GORD 33%). RH patients were significantly younger than GORD patients ($P = 0.0089$). There was no significant difference in age between RH and FH/FCP ($P = 0.4955$).

Heartburn was the commonest symptom (154/211), (23/32), (20/31) followed by regurgitation (153/211), (19/32) (10/31). Chest pain (32/211), (4/32), (16/31) and epigastric pain (25/211), (5/32), (11/31) were less common.

Median number of total reflux episodes during the recording period was 38 [25-58] with RH. This was lower than GORD (54 [43-75]) ($P = <0.0001$) and higher than FH/FCP (28 [12-35]) ($P = 0.0004$).

Bloating (RH 66%, GORD 63%, FH/FCP 84%) and belching (RH 62%, GORD 79% and FH/FCP 77%) were prominent symptoms. Nausea and vomiting was seen more with FH/FCP (35%) compared to RH (32%), but significantly less with GORD (21%) ($P = 0.0269$).

Conclusions: In the literature, a few limited studies show a female preponderance in RH. Our study echoes these findings, albeit in a larger cohort.

We have shown that heartburn and regurgitation are more prominent symptoms in RH. Median number of total reflux events was greater than FH/FCP but less than GORD. These findings have not been evaluated previously.

Our study adds to the further understanding of RH.

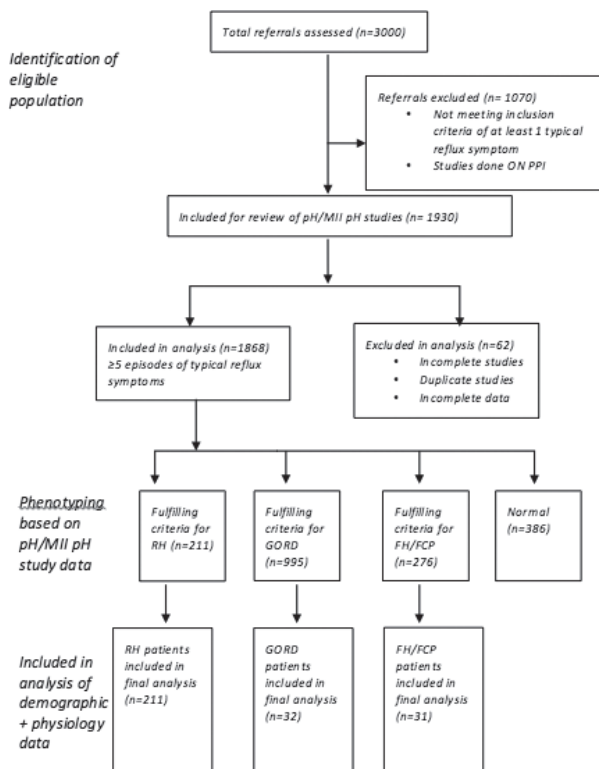


Figure 1: Schematic of study design.

165 | Complementary study pipeline to analyse the complex genetics of Hirschsprung's disease

T. Bernardo¹; International Hirschsprung's Disease Consortium²

¹Jointogether Group, SL, Lisboa, Portugal; ²safsf, Asg, Samoa

Objective: Hirschsprung's disease (HSCR) is characterized by a lack of enteric neurons (aganglionosis) in distinct segments of the colon causing megacolon formation. Its pathomechanisms originate in early embryonic development due to dysfunctions of neural crest cells (NCCs). During enteric nervous system (ENS) development, proliferation, migration, differentiation and cell survival of NCC-derived progenitor cells are impaired. Surgical resection of the aganglionic part is the only treatment option. Patients often suffer lifelong from gut dysfunctions. HSCR is classified as oligogenic disorder, however, identified risk loci only account for a minority of patients. These facts underline the need to gain better insight into its molecular pathogenesis. This study aims to identify and characterize novel candidate genes for HSCR by taking genetic, bioinformatics, molecular and functional data into account.

Methods: Whole exome sequencing was performed on the DNA of two sporadic long-segment HSCR cases and their non-affected relatives. Identified genetic variants were bioinformatically filtered to identify putative candidate genes and further narrowed down to four candidates based on literature and network analyses. The candidates were further investigated in a genome-engineered neuronal cell culture model. Gene-specific knockout clones were generated using the CRISPR/Cas9 technology in SHSY5Y cells and investigated on morphological and functional level. Gene-specific knockout clones were generated using the CRISPR/Cas9 technology in SHSY5Y cells and investigated on morphological and functional level. Gene-specific knockout clones were generated using the CRISPR/Cas9 technology in SHSY5Y cells and investigated on morphological and functional level. Gene-specific knockout clones were generated using the CRISPR/Cas9 technology in SHSY5Y cells and investigated on morphological and functional level.

Results: All four genes are expressed in murine gastrointestinal tissue of different developmental stages. In comparative analyses, gene-specific knockout clones showed differences in their differentiation behaviour, proliferation and migration capacity as well as cell survival during neuronal differentiation.

Conclusions: Further evidence accumulated that the candidates might play a role in the HSCR pathoetiology which underscores that our study pipeline represents an excellent tool to gain insight into HSCR.

171 | Co-stimulating influence of R-Spondin 1 on the proliferation of enteric progenitor cells derived from mice and human patients in vitro

M. Scharf¹; P. Neckel¹; K. Seid¹; S. Scherer²; L. Just¹

¹Institute of Clinical Anatomy and Cell Analysis, Tübingen, Germany;

²Department of Pediatric Surgery, University Children's Hospital Tübingen, Tübingen, Germany

Objective: In the Wnt dependent stem cell compartment of the intestinal crypt, R-Spondin1 has a strong mitogenic activity on LGR5 expressing cells. Here we tested the hypothesis, that R-Spondin1 has a similar co-stimulating influence on progenitor cells derived from the enteric nervous system (ENS).

Methods: We systematically evaluated the influence of R-Spondin1 stimulation during proliferation and differentiation of cultured enteric neural progenitor cells. Isolated ENS progenitors from *Tunica muscularis* of the small intestine of newborn and adult wild-type C57BL/6 mice as well as from Wnt1-Cre2 reporter mice were used. We also obtained intestinal tissue samples from patients and isolated ENS cells. Influence of R-Spondin1 was analyzed by proliferation assays, qRT-PCR, and immunocytochemistry.

Results: Gene expression analysis of proliferating enterospheres verified gene expression of known Wnt target genes, e.g. axin2 and lef1. Our cell culture experiments revealed that the total cell mass of proliferating enterospheres enlarged after R-Spondin 1 treatment. Furthermore, total number of isolated neurons (HuC/D⁺) as well as

the amount of BrdU co-labeled neurons increased in comparison to respective control groups after R-Spondin1 treatment.

Conclusions: Our results shed a light on the influence of R-Spondin1 on the proliferative capacity of enteric neural progenitors, thereby confirming our working hypothesis. Further experiments will verify the intrinsic Wnt regulation of the enteric progenitor niche.

175 | Different expression of neurotrophic factors in the subtypes of irritable bowel syndrome

J. Y. Lee; K. S. Park; Y. J. Lee

Keimyung University School of Medicine, Daegu, South Korea

Objective: Emerging evidence show that the mechanism of irritable bowel syndrome (IBS) is associated with neurotrophic factors. The aim of the present study was to investigate the expression of neurotrophic factors according to the IBS type.

Methods: From 30 IBS patients (15 IBS-constipation, 15 IBS-diarrhea) and 24 controls, mRNA expression of transient receptor potential vanilloid-1 (TRPV1), nerve growth factor (NGF), glial cell-derived neurotrophic factor (GDNF) were assessed by RT-PCR.

Results: Significant increases in the mRNA levels of TRPV1 ($P < 0.05$, IBS-C vs control), GDNF and NGF (both $P < 0.05$, IBS-C vs control) were detected, but no difference were detected in IBS-D. The expression of TRPV1 was correlated with that of GDNF ($P < 0.001$) and NGF ($P < 0.001$).

Conclusions: Different expressions of neurotrophic factors were observed according to subtypes of the IBS, especially colonic mucosal TRPV1, NGF, and GDNF levels were higher in IBS-C.

176 | Increased resting state functional connectivity between regions of reduced brain volume in irritable bowel syndrome

R. Simon; N. Barazanj; O. Bednarska; S. Walter

Linköping University, Linköping, Sweden

Objective: Differences in both brain volume and functional connectivity have been reported in irritable bowel syndrome (IBS) though the relationship between volume and functional connectivity remains unclear. Based on renewed interest in identifying the role of the cerebellum in IBS(1), and it's potential role in interoception(2), our group has used volumetric-based morphometry to identify regions of significantly reduced brain volume in IBS patients in both the cerebellum and the insula. Here we aim to investigate resting state functional connectivity (rs-FC) between these two interoceptive regions, and associations with psychological measures.

Methods: Magnetic resonance data were acquired on 34 female healthy controls (HCs) and 63 female IBS patients using a 3T MRI scanner. Ten minutes of eyes-closed resting state-fMRI data were

acquired with a single-shot, gradient-echo EPI sequence that effectively covered the whole brain.

Resting state-fMRI data were preprocessed and analyzed using the standard pipeline in CONN-functional connectivity toolbox and SPM 12. ROI-to-ROI statistical analyses were performed using ROIs from the r-pINS and both the posterior and anterior cerebellum. Psychological measures included the following: CSQ-Coping strategy questionnaire, BPI-Brief pain inventory.

Results: IBS patients had significantly higher resting state functional connectivity between the R-pINS and anterior cerebellum than HCs (Fig. 1A). There were weak-to-moderate correlations with psychological measures previously shown to be associated with brain volume measurements in these same regions(Fig. 1B).

Conclusion: Our preliminary findings indicate that in regions of reduced brain volume in IBS patients, there is higher functional connectivity than in HCs. These findings also provide evidence for a potential insular-cerebellar association in IBS.

References: [1] Claassen J, Labrenz F, Ernst TM, Icenhour A, Langhorst J, Forsting M, et al. Altered cerebellar activity in visceral pain-related fear conditioning in irritable bowel syndrome. The Cerebellum. 2017;16(2):508-17.

[2] Kuehn E, Mueller K, Lohmann G, Schuetz-Bosbach S. Interoceptive awareness changes the posterior insula functional connectivity profile. Brain Struct Funct. 2016;221(3):1555-71.

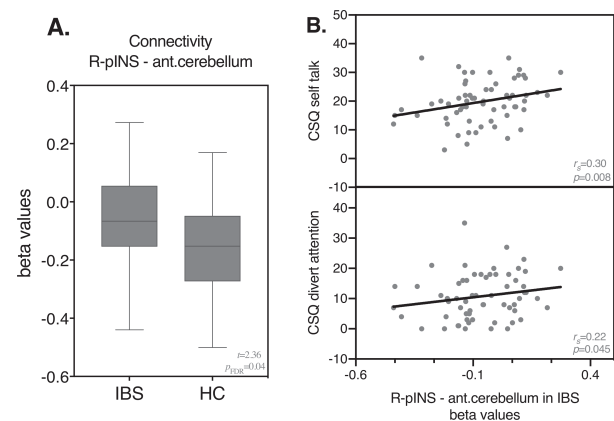


FIGURE 1. A. Between group differences in resting state fMRI connectivity between the right posterior insula and the anterior cerebellum (bars represent max-min values) B. Weak-moderate correlations between coping strategy questionnaires (CSQ) and resting state fMRI connectivity.

177 | Cases of hyperinflation injury during esophagogastrroduodenoscopy

K. B. Kim¹; H. W. Kim¹; J.-H. Han²; S. M. Yoon²; H. B. Chae²; S. M. Park²; S. J. Youn²; B.-S. Ko³

¹Chungbuk National University Hospital, Cheongju, South Korea; ²Chungbuk National University, Cheongju, South Korea; ³Cheongju St. Mary's Hospital, Cheongju, South Korea

Objective: Hyperinflation injury caused by inadvertent air-inflation can occur during upper endoscopy. But the cases were seldom reported in the literatures.

Methods: The medical records of esophagogastroduodenoscopy in our hospital for the past 5 years were reviewed retrospectively. The information of patients' age, sex, use of anticoagulant, and measured gastric injury site, endoscopic appearance such as atrophic gastritis, therapeutic modality, use of sedative agents during endoscopy, and purpose of endoscopy were collected.

Results: 56 627 cases (33 072 patients) have undergone upper endoscopy from Apr, 2011 to Sep, 2016. in our hospital. 14 patients (0.042%) were suffered from hyperinflation injury during upper endoscopy. There were 8 female and 6 male patients, and 6 patients have used either antiplatelet agents or anticoagulants. 12 patients (85.7%) were sedated either midazolam, propofol or both agents during endoscopy. 10 patients (71.4%) had atrophic gastritis in endoscopic appearance. Most of the injuries were caused by less experienced endoscopists. It had not occurred during the therapeutic procedure. 6 cases were confined to cardia, 1 case was arisen at fundus, 7 cases were extended from high body to mid body. Hemoclipping or band ligation was applied to 4 patients (28.6%) to prevent further bleeding or mucosal injuries.

Conclusions: Hyperinflation injuries during upper endoscopy were mostly arisen at cardia and high body/lesser curvature side. Putative causal factors were less experience or attention of endoscopist, atrophic gastritis, sedative state, patient's age, use of anticoagulant or antiplatelet agents. Mild mucosal injuries were self-limited, and moderate to severe bleeding or injuries was effectively treated with endoscopic hemoclipping or band ligation. However, we should pay attention to avoiding inadvertent hyperinflation injury during upper endoscopy.

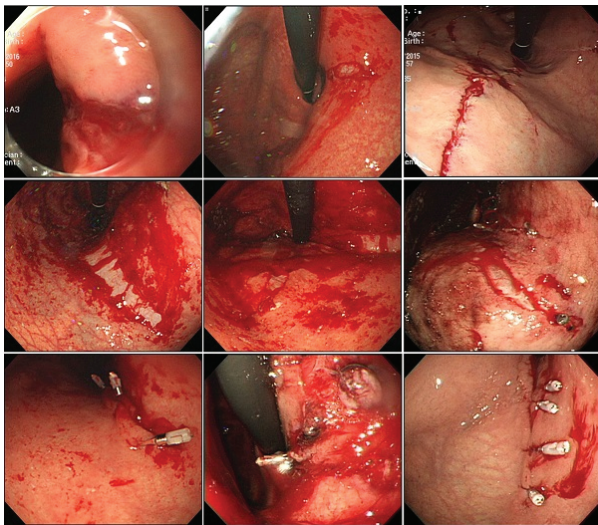


FIGURE. Cases of hyperinflation injury with mucosal tear during upper endoscopy.

181 | Insufficient rome criteria to diagnose pure functional abdominal pain and epigastric pain syndrome: The need of ruling out chronic abdominal wall pain

K. H. Song; K. C. Huh; H. S. Koo; S. M. Kim

Konyang University Hospital, Daejeon, South Korea

Objective: There is firm evidence that chronic abdominal wall pain (CAWP) is one of the major cause of chronic abdominal pain. CAWP has been easily ignored and the physician may misdiagnose CAWP as functional abdominal pain syndrome (FAPS) or even as epigastric pain syndrome (EPS). We investigated whether there is a difference between clinical response for local anesthetic injection or a somatic nerve block (a major therapeutic option for CAWP) in CAWP alone and in CAWP-FAPS overlap.

Methods: From January 2012 to April 2017, patients complaining of abdominal pain were undergone relevant studies. CAWP with negative screening exams were enrolled. Greenbaum's criteria were adopted to diagnose CAWP while FAPS was diagnosed according to the Rome III criteria. For eligible patients, Rome IV criteria of EPS were surveyed also, if they were Rome III-based EPS. CAWP alone group and CAWP-FAPS overlap group were treated by tap block. Baseline and post-treatment pain score were recorded by 10-Likert scale. The 0.1% lidocaine mixture was used for the local anesthetic injection. After the local treatment, the responsiveness was assessed and 1 or 2 sessions of additional injection were performed if it is warranted. Clinical responsiveness was defined by over 50% degree reduction in symptom score.

Results: A total of 595 Patients complained with chronic abdominal pain were underwent EGD, colonoscopy, blood exam and imaging study (US or CT scan). Among them, 49 participants without obvious abnormal result to explain the pain were enrolled (11 of overlap, 38 of CAWP only). Mean age was 49.5 ± 11.2 and female was predominant by 1.45 fold. The most frequently affected area was epigastrium followed by right iliac in both groups. Kaplan-Meier analysis of unresponsiveness after the local treatment revealed no significant difference between the two groups ($P = 0.781$). The responsiveness at 3 months after the treatment also was not significantly different. When we diagnosed with Rome III criteria, EPS-CAWP overlap was less common ($P = 0.035$, McNemar test).

Conclusions: Clinical responsiveness to the local anesthetic injection was not different between CAWP-FAPS overlap and CAWP alone. Rome III criteria of EPS is more suitable to discriminate EPS from CAWP than Rome IV criteria.

184 | Cerebellar grey matter volume reduction in IBS is correlated to pain and adaptive behavior

N. Barazani¹; O. Bednarska¹; R. Simon²; S. Walter¹

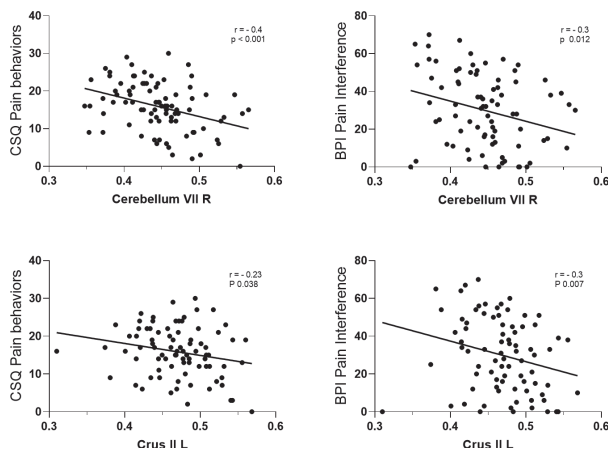
¹Department of Clinical and Experimental Medicine, Linköping University, Linköping, Sweden, Linköping, Sweden; ²Department of Medical and Health Sciences, Linköping University, Linköping, Sweden, Linköping, Sweden

Objective: IBS is a symptom-based disorder with heterogeneous pathophysiology, where disturbances in the brain-gut axis play a major role in causation and maintenance. Little is known about the cerebellar role in IBS, in several MRI studies the cerebellum is masked to reduce noise. There are reports of functional and structural cerebellar changes in other chronic pain studies. Changes in cerebellar functional connectivity correlate to self-efficacy and pain management. In IBS, an increase in cerebellum activity was shown during visceral pain acquisition. Less is known about grey matter volume (GMV) changes in the cerebellum. Our aim is to compare the cerebellum GMV in IBS and healthy controls, and correlate those to IBS symptoms.

Methods: 87 IBS patients and 47 age-matched healthy control. All underwent structural brain MRI. The images were all Pre-processed using SPM 12 and the CAT 12 toolbox. Region of interest analysis of cerebellar sub-regions using automated anatomical labelling atlas on the segmented grey matter of each group using Mango image processing system. The cerebellum being a major perception-action hub we used the Brief Pain Inventory (BPI) scale and coping strategies questionnaire (CSQ) questionnaire to assess pain and coping behaviours.

Results: We found a significant between group difference for BPI and CSQ subscales. Using age and total grey matter volume used as covariates, general linear model analysis for between group comparisons showed less grey matter volume in cerebellar regions VII right, bilateral VIII and Crus II among IBS. Spearman bivariate analysis show a negative correlation for grey matter volume of these regions with pain reinterpretation and pain behavior CSQ subscales, and for all regions except Crus II right with BPI pain interference.

Conclusions: Several cerebellar regions in IBS patients show negative correlation with pain interference of daily activities and coping behavior. We postulate that this cluster of regions are involved in pain stimuli interpretation and adaptive reactions in IBS.



185 | Real-world insights on gender differences on the impact of constipation to daily life

R. Lange¹; A. Trasy²; P. Kamman¹

¹Consumer HealthCare, Medical Affairs, SANOFI, Frankfurt, Germany;

²Consumer HealthCare, Medical Affairs, SANOFI, Bridgewater, New-Jersey, United States

Objective: Constipation has an impact on the emotional and social well-being of patients (1) and gender differences have been reported (2). The impact of constipation symptoms on the daily life of patients has been in the focus of a real-world investigation in a self-medication setting (3). To further understand the gender differences regarding constipation symptoms and well-being an additional analysis has been carried out.

Methods: A Sanofi-sponsored large convenience survey has been conducted in USA to measure patient-reported outcomes (PROs) related to constipation and symptom management strategies. Respondents were members of an online platform who self-reported constipation in the past 6 months.

Results: Of the 5725 participants recruited, 5323 completed the survey (3023 female, 2266 male, 34 other). With regard to the 3 most frequent symptoms (N = 5582), female patients reported a more frequent occurrence vs males: "Straining" (N = 2272 [71.5%]) vs N = 1430 [60.3%]), "bloating" (N = 2006 [63.2%]) vs N = 1005 [42.4%], and "long period between bowel movement" (N = 1760 [55.4%]) vs N = 965 [40.7%]). Also the average number of symptoms (4.2 vs 3.4), the average severity (4.3 vs 3.9 [0 to 10 scale]) and the duration of constipation symptoms (82.2% vs 68.0% longer than 1 day) were higher for females.

"I usually feel physical discomfort" was the aspect noted most frequently by both sexes (females: 75.5%; males 65.5%) to describe how constipation impacts their daily life. A difference between genders became most obvious for aspects related to the self-perception, 29.7% (67.1% vs 37.4%) more females reported "I feel and look bloated", 20.9% (35.4% vs 14.5%) "I need to wear looser clothing" and 18.7% (36.2% vs 17.4%) "I don't feel attractive" compared to men (Figure 1).

Conclusions: Constipation in a self-medication setting seems to have more pronounced impact on female patients as constipation episodes manifest with more symptoms, are more intense and longer lasting. In daily life female patients seem to be stronger impacted emotionally, specifically with regard to their self-perception.

References: [1] Wald A, et al. *Aliment Pharmacol Ther.* 2007

[2] L'Heureux-Bouron D, et al. *Ther Adv Gastroenterol.* 2018

[3] Lange R, et al. *Constipation Management Strategies: Consumer Preferences and Activity Tracker-based Behavior.* DDW 2019.

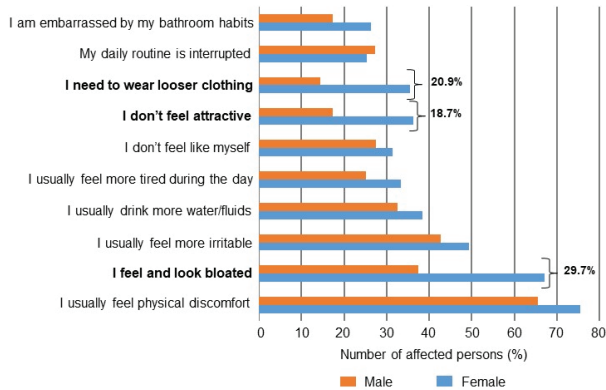


FIGURE 1. Impact of constipation symptoms on daily life by gender.

186 | Psychodynamic differences in Crohn's disease, ulcerative colitis and healthy controls, a cross-sectional study

F. Engel¹; S. Berens¹; D. Baumeister¹; A. Gausz²; R. Schaefer³; J. Tesarz¹

¹Department of General Internal Medicine and Psychosomatics, University Hospital Heidelberg, Heidelberg, Germany; ²Department of Gastroenterology and Hepatology, University Hospital Heidelberg, Heidelberg, Germany; ³Division of Internal Medicine, Department of Psychosomatic Medicine, University Hospital Basel, Heidelberg, Germany

Objective: The most common inflammatory bowel diseases are Crohn's disease (CD) and ulcerative colitis (UC). For both diseases perceived stress seems to play an important role in activity and exacerbation of the disease. Differences in the physiological stress response can be explained by psychodynamic factors. The objective of this study was (1) to compare CD, UC and healthy controls regarding to psychodynamic structure, attachment and mentalization (2) to investigate if there are differences concerning anxiety and depression. **Methods:** Patients were recruited in the primary, secondary and tertiary care. Patients with an endoscopic ensured CD/UC without remission were selected. Healthy controls (HC, without any somatic or psychiatric disease) were recruited via an online-survey. The three groups (CD, UC, HC) were individually matched ($n = 93$ in 3 groups). Psychodynamic structure (OPD-SQ), attachment (ECR-R), mentalization (MZQ), depression (PHQ-9) and anxiety (GAD-7) were compared.

Results: There were no significant differences between CD and UC in the cases examined. No differences between attachment and mentalization have been found. The psychodynamic structure differed between CD/UC and HC with a small/medium effect size (0.35/0.56), while the structure in CD/UC still seemed in the range of healthy controls of other studies. Symptoms of anxiety and depression were mild in CD/UC in the average and were significantly higher compared to HC.

Conclusions: In the average psychodynamic deficits and complaints were small in CD/UC and the groups didn't differ. Further research should focus on subgroups with higher burden.

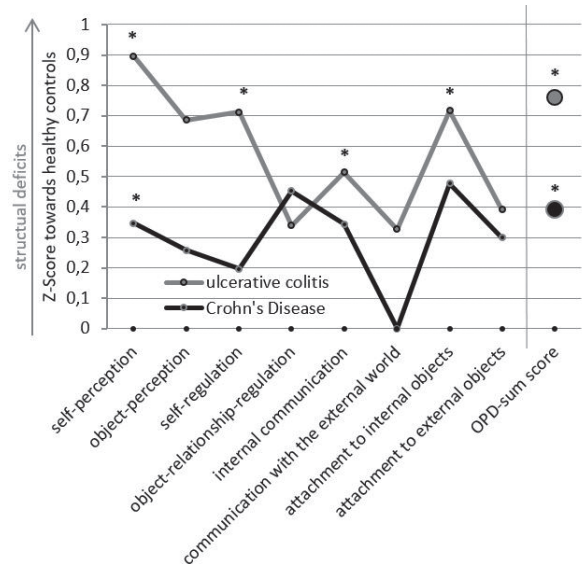


FIGURE. Structural deficits (OPD), CD/UC standardized towards healthy controls. M-W-U test towards healthy controls, * $p=0.05$

188 | Complementary study pipeline to analyse the complex genetics of Hirschsprung's disease

T. Mederer¹; S. Schmitteckert¹; J. Volz¹; F. Lasitschka²; P. Günther³; G. Rappold¹; P. Romero³; B. Niesler¹; S. Holland-Cunz⁴; R. Hofstra⁵

¹Department of Human Molecular Genetics, University Hospital, Heidelberg, Germany; ²Institute of Pathology, University Hospital, Heidelberg, Germany; ³Pediatric Surgery Division, University Hospital, Heidelberg, Germany; ⁴Hirschsprung Research Initiative Basel-Heidelberg-Mannheim, Basel, Switzerland; ⁵International Hirschsprung's Disease Consortium, Rotterdam, The Netherlands

Objective: Hirschsprung's disease (HSCR) is characterized by a lack of enteric neurons (aganglionosis) in distinct segments of the colon causing megacolon formation. Its pathomechanisms originate in early embryonic development due to dysfunctions of neural crest cells (NCCs). During enteric nervous system (ENS) development, proliferation, migration, differentiation and cell survival of NCC-derived progenitor cells are impaired. Surgical resection of the aganglionic part is the only treatment option. Patients often suffer lifelong from gut dysfunctions. HSCR is classified as oligogenic disorder, however, identified risk loci only account for a minority of patients. These facts underline the need to gain better insight into its molecular pathogenesis. This study aims to identify and characterize novel candidate genes for HSCR by taking genetic, bioinformatics, molecular and functional data into account.

Methods: Whole exome sequencing was performed on the DNA of two sporadic long-segment HSCR cases and their non-affected relatives. Identified genetic variants were bioinformatically filtered to identify putative candidate genes and further narrowed down to four candidates based on literature and network analyses. The candidates were further investigated in a genome-engineered neuronal cell culture model. Gene-specific knockout clones were generated

using the CRISPR/Cas9 technology in SHSY5Y cells and investigated on morphological and functional level.

Results: All four genes are expressed in murine gastrointestinal tissue of different developmental stages. In comparative analyses, gene-specific knockout clones showed differences in their differentiation behaviour, proliferation and migration capacity as well as cell survival during neuronal differentiation.

Conclusions: Further evidence accumulated that the candidates might play a role in the *HSCR* pathoetiology which underscores that our study pipeline represents an excellent tool to gain insight into *HSCR*.

189 | Localization of cannabinoid receptors in the canine and feline gastrointestinal tract

R. Chiocchetti¹; G. Galiazzo¹; A. Stanzani¹; F. Giancola²; C. Tagliavia¹; M. De Silva¹; F. Fracassi¹; M. Pietra¹

¹Department of Veterinary Medical Sciences – University of Bologna, Bologna, Italy; ²St. Orsola-Malpighi Hospital, Bologna, Italy

Objective: The endocannabinoid system (ECS) is involved in the control of gastrointestinal inflammation and visceral pain. The present ex vivo study was aimed to investigate the distribution of the canonical [CB₁ (CB1R) and CB₂ (CB2R)], and putative cannabinoid receptors [G protein-coupled receptor 55 (GPR55), nuclear peroxisome proliferator-activated receptors alpha (PPARα), transient receptor potential ankyrin 1 (TRPA1), and serotonin receptor 5-HT1a (5-HT1aR)] in the gastrointestinal tract of the dog and the cat.

Methods: Gastrointestinal tissues (pylorus, duodenum, ileum and distal colon) from four dogs and four cats were collected after spontaneous death or after euthanasia, following owners consent. Specimens were processed by immunohistochemistry using species-specific primary antibodies. Antibodies targeting enteric neurons, glial cells (EGCs), enteroendocrine cells (EECs), mast cells (MCs), macrophages, and plasma cells were employed in co-localization experiments to identify the different cell types expressing cannabinoid receptors.

Results: CB1R-immunoreactivity (CB1R-IR) was observed in epithelial and lamina propria (LP) cells, and in myenteric plexus (MP) neurons in both the species.

CB2R-IR was expressed by LP MCs and immunocytes, blood vessels and smooth muscle cells in the dog. In the cat it was expressed by EECs, intestinal epithelial cells, and macrophages.

GPR55-IR was expressed by LP macrophages and smooth muscle cells in the dog; in the cat it was expressed by EECs, immunocytes and MP neurons.

PPARα-IR was expressed by smooth muscle cells and EGCs in both the species. In the cat PPARα-IR was also expressed by immunocytes and gastric parietal cells.

TRPA1-IR was expressed by globet cells in both the species and enteric neurons only in the cat.

5-HT1aR-IR was expressed by epithelial cells in the cat and by globet cells, LP cells and MP neurons in the dog.

Conclusions: The present research provides an anatomical basis supporting the therapeutic use of cannabinoid receptor agonists in relieving motility disorders and visceral hypersensitivity in acute or chronic enteropathies.

190 | Effects of probiotics in patients with bloating and abdominal pain

D. B. Vera; A. Pinto; E. P. De Arce; A. Sandoval; A. M. Madrid

Division of Gastroenterology, Clinical Hospital University of Chile, Santiago, Chile

Objective: There are few reports about the effect of probiotics in patients with abdominal pain and bloating. Our aim is to compare the efficacy of two types of probiotics formulated with a single species vs multispecies in the management of abdominal pain and bloating in patients without small intestinal bacterial overgrowth (SIBO).

Methods: Prospective, double-blind, longitudinal study. 73 patients with bloating, abdominal pain and without SIBO according lactulose H₂ breath test; age 51 (18-74) years, 67 women. Patients were randomized in two probiotics, A: single species (Vintix®; *S. boulardii* CNCM I-745) with 36 patients and B: multispecies (Multiflora Plus®; *L. casei*, *L. rhamnosus*, *L. bulgaricus*, *L. acidophilus*, *S. thermophilus*, *B. breve*, *B. longum*) 37 patients, one capsule twice a day for one month. The patients were consulted during breath test for baseline symptoms, 15 and 30 days post-treatment, were registered intensity (visual scale 0-10), frequency of symptoms (1-3) and total score with intensity and frequency (0-30). Analysis with Kruskal-Wallis and post-hoc test.

Results: 53 patients (73%) completed therapy and control at 15 days (29 and 24 patients respectively) and 35 patients (48%) attended to control at 30 days (21 and 14 respectively). Group A presented a decrease in bloating score from 19.4 to 9.1 and abdominal pain from 12.8 to 5.3; group B from 17 to 7.5 for bloating and pain from 12 to 2.3 ($P < 0.0001$), group A had a greater decrease in bloating compared to baseline than group B. Abdominal pain decreased more in group B compared to baseline than group A ($P < 0.0001$). Without adverse events.

Conclusions: Both probiotics were useful in reducing abdominal pain and bloating and could be used in treatment for symptomatic patients without SIBO. Probiotic single species for bloating and multispecies for abdominal pain. Studies with a greater number of patients should be considered.

Groups (double-blind randomized)	Bloating			Abdominal Pain		
	1	2	3	1	2	3
Groups (started/finished)						
A: 29/29/21 <i>Saccharomyces boulardii</i> (CNCM I-745) lyophilized 250 mg	19,4	9,7	9,1	12,8	7,4	5,3
B: 24/24/14 <i>Lactobacillus casei</i> , <i>Lactobacillus rhamnosus</i> ; <i>Lactobacillus acidophilus</i> ; <i>Lactobacillus bulgaricus</i> <i>Streptococcus thermophilus</i> ; <i>Bifidobacterium breve</i> ; <i>Bifidobacterium longum</i>	17	11	7,5	12	4,6	2,3

1: baseline; 2: 15 days after treatment and 3: 30 days after treatment.

FIGURE. Bloating and Abdominal pain in patients. At baseline, 15 and 30 days after treatment with probiotics.

192 | Differentiation of neurons from cultured human primary enteric glial cells

A. Palmer¹; S.-H. Chng²; J. Chin-Aleong³; C. Knowles³; V. Pachnis²; G. Sanger¹

¹QMUL Blizard Institute, London, UK; ²Francis Crick Institute, London, UK;

³Royal London Hospital, London, UK

Objective: Studies in mice demonstrate that enteric glial cells can differentiate into neurons in vivo following tissue injury¹. We aim to demonstrate glial-derived neurogenesis in vitro using human gastrointestinal surgical resection samples.

¹Laranjeira et al. J Clin Invest. 2011;121(9):3412-24.

Methods: Human colon was obtained, with informed consent, from surgical resections for bowel cancer. Macroscopically-normal tissue was used at least 5-10 cm from the tumour.

After removal of the mucosa the tissue was cleaned, finely minced, and digested in collagenase and trypsin. The unfiltered digestate was initially cultured in high concentrations of fetal bovine serum to encourage cell survival and adherence. After 24 hour the media was replaced by pro-glial media, containing nerve growth factor (NGF), supplement N-2 and supplement G-5 to encourage proliferation of glial cells. Finally, the filtered, passaged cells were cultured in pro-neuronal media, which contains NGF, glial-derived neurotrophic factor, brain-derived neurotrophic factor, neurotrophin-3 and other supplements, to support neuronal differentiation from glial cells.

Results: Steps were taken to reduce contamination (a problem for surgical specimens) through removal of the submucosa, washing in dithiothreitol and 70% ethanol and filtration of media. Collagenase digestion duration was optimised to 4 hours for maximum live cell yield; 1.7 g human stomach tissue yielded 14 million live cells with 82% viability (as determined using Trypan blue) with 4 hours digestion at 37°C. Immunostaining against β III-tubulin demonstrated neurons in culture following the differentiation stage of the protocol.

Conclusions: We have demonstrated that neuronal differentiation from primary human glial cells is possible in vitro, using human surgical specimens. The density of cells seeded into culture is currently undergoing optimisation to increase survival and proliferation of glial cells, and future experiments will test functionality and glial lineage of the neurons. In the future this technique may find utility in treatment of conditions with reduced enteric neurons, such as Hirschsprung's disease and diabetes.

195 | Does hydrogen and methane based-breath test with lactulose allow to determine orocecal transit time in patients with small intestinal bacterial overgrowth?

D. B. Vera; A. Sandoval; A. M. Madrid

Division of Gastroenterology, Clinical Hospital University of Chile, Santiago, Chile

Objective: The hydrogen test and methane based-breath test with lactulose (HMBT) is used as an indirect study of with small intestinal bacterial overgrowth (SIBO), its usefulness and ability to determine the orocecal transit time (OCTT) was permanent discussion. Our aim is to characterize the different curves obtained with this method to diagnose SIBO, and according to diagnosis to establish OCTT in symptomatic patients.

Methods: Retrospective study of 3.482 HMBT performed in symptomatic adults between 2012 and 2018, with standardized technique. SIBO was defined in all curves as the elevation of H₂ above 20 ppm of the basal in twice or more measurements in the first 60 minutes (min). Curve A, considers the OCTT to the second pick of elevation of the curve, curve B does not allow to determine OCTT by sustained elevation of the curve from at least twice before 60 minutes. Curve C, second elevation after 60 minutes where the figure that is measured is twice the figure that precedes it, that time is considered OCTT. Analysis with Mann-Whitney test.

Results: 130 patients (3.7%) did not produce hydrogen, they were not considered in the study, 3.352 HMBT were evaluated. Without SIBO 54% with OCTT 100.6 $\pm$ 26.4 minutes. SIBO curve A in 18%, with OCTT 96.8 $\pm$ 17 minutes, curve B 10% it is not possible to determine OCTT, curve C 16% OCTT 82.7 $\pm$ 14 minutes, lower than without SIBO ($P < 0, 0001$).

Conclusions: HMBT would predict the arrival of lactulose in the colon in patients with SIBO, allowing this technique to determine OCTT. SIBO is observed in a high percentage of symptomatic subjects.

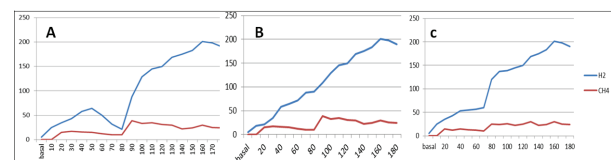


FIGURE. Types of curves (A,B and C) of hydrogen (H2) and methane (CH4).

199 | Intake of dairy products in patients with irritable bowel syndrome

G. Carrasco¹; D. B. Vera²; M. Gotteland¹; A. M. Madrid²

¹Department of Nutrition, Faculty of Medicine, University of Chile., Santiago, Chile; ²Division of Gastroenterology, Clinical Hospital University of Chile, Santiago, Chile

Objective: Irritable Bowel Syndrome (IBS), is a digestive disorder of multifactorial origin and characterized by abdominal pain, which can affect food intake, and therefore, nutritional adequacy. One of the food groups that are intuitively eliminated from intake is dairy products, the main sources of calcium (Ca²⁺) in the diet. The general Chilean population consumes 419 and 518 mg / day of Ca²⁺ in women and men respectively. Our aim is to describe the ingestion of dairy products and the adequacy of calcium in patients with IBS.

Methods: Cross-sectional study in 33 patients with IBS (subtypes constipation, diarrhea and mixed). 88% women. Age 35.6 ± 12.1 years; Body Mass Index 24.7 ± 3.6 kg/m². Food intake was evaluated through a modified consumption trend survey (foods high in *Fermentable, Oligosaccharides, Disaccharides, Monosaccharides and Polyols*, FODMAPs). The questionnaires were analyzed with The Food Processor SQL software.

Results: The energy intake of the intake was 1.652 ± 562 kcal (15% protein, 50% carbohydrates and 35% lipids). 78% of the subjects consume mature cheeses; 9% fresh cheese; 50% yogurt with lactose and 31% yogurt lactose-free; 38% consume milk with lactose and without lactose 22%. A contribution of 303.8 ± 272 mg/Ca⁺² was observed.

Conclusions: The intake of dairy products in patients with IBS is low and they have a lower Ca⁺² intake than the Chilean general population. This could mean long-term complications in these patients that should be evaluated. The most consumed dairy products correspond to mature cheeses, high-fat foods.

200 | Acute colitis following chronic traumatic brain injury in mice induces persistent neurobehavioral deficits

M. Hanscom; D. J. Loane; T. Shea-Donohue; A. Faden

University of Maryland, Baltimore, United States

Objective: Disruptions in the bidirectional communications of the brain-gut axis are increasingly implicated in the onset and progression of a variety of neurological disorders. We previously reported that following experimental traumatic brain injury (TBI) in mice, pathogenic bacterial infection in the colon exacerbated the cortical lesion. The aim of this study was to determine the effects of acute experimental colitis (gut inflammation) on chronic neurological function following TBI.

Methods: Male C57BL/6 mice were placed in either naïve (anesthetic), sham (craniotomy), or controlled cortical impact (CCI) groups. Twenty-eight days after injury, cohorts of mice in all groups were administered regular drinking water (N = 6-9/group) or 3% DSS (N = 7-8/group) in drinking water for 7 days to induce colitis (injury), followed by replacement with regular water in all groups for an additional 28 days (recovery). Mice were tested on beam walk (BW), novel object recognition (NOR) and Morris water maze (MWM) to assess motor and cognitive function. Changes in social and anxiety-like behavior were assessed during the recovery stage using social approach (SA), light-dark box (LDB) and marble burying (MB).

Results: Acute colitis resulted in and exacerbated, respectively, deficits in spatial memory (MWM), declarative memory (NOR) and motor function (BW) in Sham- and CCI-injured mice up to four weeks following DSS-treatment. Deficits in social behavior (SA) and increased anxiety-like (LBD, MB) behavior in Sham+DSS and CCI+DSS mice were also observed. These changes were not observed in either

Sham+H₂O or Naïve+DSS mice. Stereological analyses of the brain revealed that although there was no worsening of CCI-injury lesion volume, there were significant decreases in hippocampal CA1 and DG neuronal cell densities in Sham+DSS and CCI+DSS groups.

Conclusions: This pre-clinical gut-brain interaction study demonstrates that in contrast to water-administered groups, acute colitis persistently induced and exacerbated neurobehavioral deficits in sham- and CCI-injured mice. Notably, neurobehavioral deficits were associated with hippocampal neurodegeneration in DSS-treated sham and CCI mice. These data demonstrate that a delayed bout of colitis (gut inflammation) can dramatically exacerbate neurological outcomes after TBI, and that sham-injury (craniotomy only) primes the brain for persistent neurological deficits.

201 | Low-FODMAP diet improve symptoms and quality of life in patients with irritable bowel syndrome?

G. Carrasco¹; D. B. Vera²; M. Gotteland¹; A. M. Madrid²

¹Department of Nutrition, Faculty of Medicine, University of Chile, Santiago, Chile; ²Division of Gastroenterology, Clinical Hospital University of Chile, Santiago, Chile

Objective: The diet FODMAPs (Fermentable Oligosaccharides Disaccharides Monosaccharides and Polyols) (DF) excludes foods short-chain carbohydrate, highly fermentable. The literature supports DF as an alternative treatment in patients with irritable bowel syndrome (IBS). There are few reports about impact of DF in IBS patients. Our aim is to evaluate improvement of abdominal pain, bloating, intestinal habit and quality of life in patients with IBS with DF and unrestricted diet (UD).

Methods: Prospective, longitudinal study, 33 patients with IBS age 36 ± 12 years, 88% female sex, randomized in DF (17) and 16 UD for 6 weeks. Weekly severity of abdominal pain, bloating, bowel habit with IBSSS questionnaire (Irritable Bowel Syndrome Severity Score) and quality of life with baseline SF-36 questionnaire and 6 weeks was evaluated. IBSSS score 0-500; <75 healthy; 75-175 mild IBS; 175-300 moderate IBS and >300 severe IBS. Analysis with ANOVA repeated measures and t-test.

Results: Patients with DF decreased severity of all symptoms of IBS, from moderate to mild at the end of the intervention 260 ± 17 to 148 ± 17 ($P < 0.0001$), UD patients decreased 254 ± 19 to 185 ± 20 ($P < 0.007$), maintaining moderate IBS. Abdominal distention between basal and week 3 and 6 decreased with respect to the SII group with UD ($P < 0.006$). Patient with both diets does not improve quality of life.

Conclusions: The FODMAPs diet was useful in reducing the symptoms in patients with IBS, reducing the severity of the symptoms. Without changes in quality of life

204 | Patients with gastro-oesophageal reflux disease have sparse transient receptor potential melastatin 8 expression in the oesophageal mucosa

A. Ustaoglu; P. Woodland; M. Peiris; D. Sifrim

Queen Mary University of London, London, UK

Objective: Transient receptor potential melastatin 8 (TRPM8) is a non-selective cationic channel of the TRP family. Peripherally, it is known to have a role in cold and menthol-induced sensory transduction. Animal histological studies, and observations in humans (cold water can induce oesophageal pain, infusion of menthol into the oesophagus of reflux patients can induce heartburn) have suggested that there may be a visceral nociceptive role of TRPM8 in the oesophagus. However, there are currently no studies of TRPM8 in the human oesophageal mucosa. We recently published a study describing the mucosal afferent neuronal anatomy in gastroesophageal reflux disease (GORD) phenotypes. We hypothesised that TRPM8 is highly expressed on these afferent nerves and/or epithelial cells of the human oesophageal mucosa. In this study, we aim to characterise TRPM8 expression in the oesophageal mucosa of GORD patients.

Methods: We conducted immunofluorescence-immunohistochemistry studies to investigate expression of TRPM8 and the neuronal marker calcitonin gene-related peptide (CGRP) in the oesophageal mucosa of 16 GORD patients. Of these, 7 had oesophagitis, 2 had erosive reflux disease, while 3 were NERD patients, 2 were functional heartburn patients, and 2 patients awaiting definite physiology testing. Distal oesophageal biopsies were taken at endoscopy, and 10 µm sections cut. These were co-stained with CGRP (Thermo Fisher Scientific, PA1-30927, 1:400) and TRPM8 (Alomone, ACC-049, 1:400) antibodies. Efficacy of TRPM8 antibody staining was confirmed using positive (IBD colon biopsies) and negative controls.

Results: TRPM8 did not co-label on nerve fibres immunoreactive for CGRP, a marker of sensory neurons. Limited expression of TRPM8 was observed on oesophageal epithelial cells (1 out of 16 patient biopsies). In biopsies where submucosa was present, TRPM8 was found to be expressed prominently in the submucosa.

Conclusions: In contrast to expected findings, TRPM8 expression is very limited in the human oesophageal epithelium of patients with heartburn. Therefore, it is unlikely to be a candidate target for future therapy. We are further characterising the sensory phenotype of the oesophageal mucosa to identify such targets.

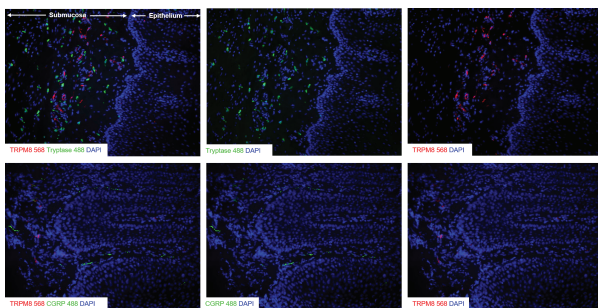


FIGURE. Showing IF-IHC staining for TRPM8 (Red) with neuronal and immune cell markers (Green) in the oesophageal submucosa and epithelium.

206 | A pilot study of the effect of mindfulness-based stress reduction on clinical symptoms and immune response of patients with diarrhoea-predominant Irritable Bowel Syndrome (IBS-D)

C. J. Beltrán¹; J. Galimany¹; C. Olea¹; C. Iribarne²; F. Valenzuela¹; A. Cortes¹; V. Torres¹; L. Valenzuela¹; E. P. D. Arce¹; A. M. Madrid¹

¹Hospital Clínico Universidad de Chile, Santiago, Chile; ²Clínica Las Condes, Santiago, Chile

Objective: Irritable Bowel Syndrome (IBS) patients are characterized by a high prevalence of psychiatric comorbidity. The Mindfulness Based-Stress Reduction (MBSR) program has demonstrated that reduce the severity of symptoms of IBS patients. Studies in Chile are scarce as well as those that address the impact of MBSR on the immune response of patients. The aim was to evaluate the effect of the MBSR program on the clinical symptoms and the inflammatory response of IBS-D patients.

Methods: The authors performed a pilot longitudinal study in women with IBS-D (ROMA IV) recruited from HCUC (n = 17). Questionnaires to evaluate severity of symptoms (IBS-SSS) as well as psychological status (perceived stress scale [PSS-4], coping strategy indicator [CSI], general self-efficacy [GSI], Five Facet Mindfulness Questionnaire (FFMQ), quality of life (QOL) by short form-36 questionnaire [SF-36], Hospital Anxiety and Depression Scale (HADS), were assessed before and after MBSR program. The IL-6 and C-reactive protein (CRP) serum level were determined by ELISA.

Results: Most patients report experiences of early life stress associated to the onset of clinical symptoms. MBSR significantly improves FFMQ (pre: 117.6 ± 16.70; post: 142.5 ± 14.64, $P = 0.0002$); QOL: physical component (pre: 65.05 ± 17.75, post: 76.37 ± 13.92, $P = 0.0004$); anxiety (pre: 10.35 ± 4.28, post: 7.17 ± 4.01, $P = 0.0056$) and depression symptoms (pre: 6.47 ± 3.69, post: 4.00 ± 3.46, $P = 0.0068$); PSS (pre: 26.41 ± 9.42, post: 20.18 ± 7.69, $P = 0.0419$); CSI subscales: Problem Solving (pre: 65.29 ± 23.28, post: 78.24 ± 19.76, $P = 0.0497$); Express Emotions (pre: 45.00 ± 23.65, post: 57.94 ± 21.00, $P = 0.0119$); Cognitive Restructuring (pre: 57.94 ± 20.54, post: 75.29 ± 16.63, $P = 0.0102$); Problem Avoidance (pre: 32.65 ± 21.30, post: 52.65 ± 19.77, $P = 0.0029$); IBS-SSS: satisfaction with bowel habits (pre: 39.71 ± 21.76, post: 55.88 ± 28.68, $P = 0.0442$); tending to decrease severity (pre: 45.59 ± 15.90, post: 35.29 ± 21.76, $P = 0.0688$) and frequency of abdominal pain (pre: 4.52 ± 1.87, post: 2.80 ± 2.83, $P = 0.0839$). Serum CRP level increased significantly after MBSR (pre: 1.31 ± 1.3, post: 3.21 ± 4.09, $P = 0.0416$), with no changes in IL-6 levels.

Conclusions: The results show that MBSR improves clinical and psychological symptoms of IBS-D patients through the induction of mindfulness, affecting the inflammatory response. The replication of these results with a larger number of patients will allow strengthening the benefits of MBSR in the treatment of IBS. OAIC HCUC, FONDECYT 1181699.

209 | Altered GI motility in mouse models of multiple sclerosis

F. Uhlig; B. Lavoie; D. N. Kremontsov; C. Teuscher; G. M. Mawe

University of Vermont, Burlington, United States

Objective: Multiple Sclerosis (MS) is an autoimmune disease involving CNS neuron and glia cell degeneration. In addition to the well-recognized somatic deficits, MS frequently involves autonomic dysfunction, including constipation. We and others have recently shown *in-vivo* and *in-vitro* that features of enteric nervous system (ENS) dysfunction can be detected in the animal model of MS, experimental autoimmune encephalomyelitis (EAE). In order to perform mechanistic studies involving genetically encoded GCaMP5, we conducted studies to better understand the time course of GI symptomatology in EAE, and its relationship with clinical symptoms in mice with a C57Bl/6J background.

Methods: EAE was induced in male C57Bl/6J or B6SJL.F1 mice and GI motility was assessed by bead expulsion, faecal water content and whole GI transit time at multiple time points after EAE induction.

Results: Induction using mouse spinal cord homogenate (MSCH) combined with intraperitoneal injection of pertussis toxin (PTX) produced profound clinical symptoms starting at day 12 that were associated with delayed colonic transit, decreased faecal water content and pellet counts. However, control animals that only received PTX also displayed GI symptomatology. PTX-independent models were therefore evaluated. B6 mice that were induced with MSCH did not present either clinical or GI symptoms in the absence of PTX treatment. Injection of myelin oligodendrocyte glycoprotein (MOG) induced clinical disease around day 16. GI symptomatology was present at day 20 but not at later time points. This transient presentation of GI symptoms would be disadvantageous for future mechanistic studies. Hence, we introduced SJL/J mice into our studies as they are more susceptible to EAE. B6SJL.F1 hybrid mice induced with proteolipid protein (PLP-1) displayed clinical symptoms starting at day 16. GI symptomatology was present from day 19 and was sustained until the day of euthanasia (day 49). Induction of F1's with MSCH induced disease in 50 % of animals, some of which also displayed GI symptoms close to the day of onset.

Conclusions: In summary, GI dysfunction, linked to clinical symptoms, was detected in several EAE models. PLP induction induces sustained GI symptomatology in B6SJL.F1, and appears to be the best for performing mechanistic studies using calcium imaging.

Supported by NIH grant DK113800.

212 | Activated enteric glial cells in the colon of patients with irritable bowel syndrome: Influence on bacterial passage

F. M. De-Faria¹; M. Jones²; S. Walter¹; Å. V. Keita¹

¹Linköping University, Linköping, Sweden; ²Macquarie University, Sydney, Australia

Objective: The pathogenesis of irritable bowel syndrome (IBS) includes abnormalities in motility, visceral sensation, brain-gut interaction, psychosocial distress, gut immune activation, intestinal microbiome and intestinal permeability. Formed by enteric neurons and enteric glial cells (EGC), the enteric nervous system (ENS) orchestrate several gastrointestinal functions. EGC are essential to ENS homeostasis and, consequently, to gut functions. We aimed to evaluate EGC phenotype and passage of live *Escherichia coli* HS and *Salmonella typhimurium* in colonic biopsies from IBS patients and healthy controls (HC) to verify whether changes occurred in IBS could be linked to EGC.

Methods: Sigmoid biopsies were collected from 30 female patients with IBS meeting Rome III criteria and 15 age-matched female HC. We employed Ussing chambers to address intestinal permeability to live bacteria. EGC phenotype was characterized by immunofluorescence and western blotting using antibodies to glial fibrillary acidic protein (GFAP) and S100 calcium binding protein B (S100B).

Results: Our findings showed activation of EGC in IBS patients based on GFAP protein expression ($P = 0.0003$), but not S100B ($P = 0.59$), suggesting that EGC were partially activated in this group of patients. GFAP and S100B expression positively correlated both in IBS and HC groups. We did not find significant correlations between EGC phenotype and symptoms, perhaps due to the collaborative nature of EGC as enhancers of ENS communication rather than main active players. Ussing chamber experiments revealed, however, potential influence of EGC status on bacterial translocation. Intercorrelations between IBS and HC on GFAP vs *E. coli* HS and GFAP vs *S. typhimurium* suggested that mucosal EGC participate in the translocation of live bacteria across the colonic mucosa in IBS, but not in HC.

Conclusions: EGC are important players in gastrointestinal functions as part of complex network, but not as independent actors. Our data reinforces this concept, suggesting that EGC might indicate the physiological (pathological) status of the ENS. We showed that EGC are phenotypically altered in IBS which could may facilitate bacteria passage at the mucosal layer.

213 | Mas-related G protein-coupled receptor C11 (Mrgprc11) induces visceral hypersensitivity in the mouse colon: A novel target in gut nociception?

S. Van Remoortel¹; H. Ceuleers²; J. G. De Man²; R. Buckinx¹; B. Y. De Winter²; J.-P. Timmermans¹

¹Lab of Cell Biology and Histology, University of Antwerp, Wilrijk, Belgium; ²Lab of Experimental Medicine and Pediatrics, Division of Gastroenterology, University of Antwerp, Wilrijk, Belgium

Objective: Visceral hypersensitivity, an important cause of abdominal pain in bowel disorders such as IBD and IBS, presents with a poorly understood pathophysiology and limited treatment options. The Mas-related G protein-coupled receptor C11 (Mrgprc11), a member of the family of Mas-related G protein-coupled receptors

(Mrgprs), has become a promising target in pain research, but its role in gut nociception is currently uninvestigated. Therefore, we explored the expression and functional role of Mrgprc11 in the gut nociceptive innervation.

Methods: Mrgprc11 expression was evaluated in colonic DRG neurons (T11-L1 and L6-S1) using *in situ* hybridization (ISH) and immunohistochemistry (IHC). Visceromotor responses (VMRs) to colorectal distension (CRD) assessed the effect of the Mrgprc11 agonist (BAM8-22) on colonic pain sensitivity in healthy mice. Moreover, we determined pERK1/2-immunoreactivity in the thoracolumbar spinal cord after noxious CRD. Finally, from a translational point of view, we looked for expression of the human counterpart of Mrgprc11, MRGPRX1, in human thoracolumbar dorsal root ganglia (DRG).

Results: ISH and IHC confirmed Mrgprc11 expression in mouse colonic DRG neurons. Intracolonic administration of BAM(8-22) significantly increased colonic pain sensitivity in an Mrgprc11-dependent manner, and led to a significantly increased degree of neuronal activation in the thoracolumbar spinal cord upon noxious stimulation. Furthermore, MRGPRX1 expression was also detected in a proportion of human thoracolumbar DRG neurons.

Conclusions: We established a novel function for Mrgprc11 in the gut nociceptive innervation and propose the receptor as a new player in visceral hypersensitivity. Overall, these findings warrant further research on evaluating the therapeutic potential of Mrgprc11 and MRGPRX1 in abdominal pain disorders, especially given the recent discovery that these receptors are linked to protease-mediated signaling.

215 | Jackhammer esophagus: Clinical and manometrical characterization in two portuguese centers

J. Chivia¹; J. Rodrigues²; E. Pires³; C. Chagas⁴

¹Gastroenterology department, Lisboa, Portugal; ²Hospital de Egas Moniz, Lisboa, Portugal; ³Gastroenterology department, Hospital da Luz, Lisbon., Lisboa, Portugal; ⁴Gastroenterology department, Hospital de Egas Moniz, Lisbon, Lisboa, Portugal

Objective:

Introduction: The Jackhammer esophagus is classified by the most recent Chicago classification (CCv.3, 2015) as a major disorder of peristalsis characterized by normal relaxation of the esophagogastric junction, and sequential peristaltic contractions of excessive amplitude and duration. It is usually accompanied by esophageal symptoms, such as dysphagia, chest pain, and heartburn. The pathophysiology and clinical impact of this condition are not completely understood, and the most effective therapeutic approach has not yet been established.

Aims: Clinical and manometric characterization of patients diagnosed with Jackhammer esophagus by CCv.3 in two Portuguese Centers with competence in high-resolution manometry.

Methods: Retrospective analysis of all patients diagnosed with Jackhammer esophagus in two Portuguese Centers, from February 2016 to February 2019. The data collected consisted of demographic information (age, gender), clinical symptoms (dysphagia, chest pain, typical or atypical symptoms of gastroesophageal reflux disease – GERD) and manometric variables (distal contractile integral, distal latency, peristalsis integrity, integrated relation pressure, lower esophageal sphincter morphology, and resting pressure). The results are presented by means and standard deviation.

Results: A total of 39 patients were diagnosed with Jackhammer's esophagus. The mean age was 62 ± 11 years with female predominance (69%). Among the symptoms reported, 44% (n = 17) of the patients had GERD (n = 17), followed by dysphagia 36%, n = 14) and chest pain (23%, n = 9). A mean of 4 hypercontractile contractions per patient and an average DCI of 7817 ± 3347 mm Hg cm sec, DL of 6 ± 1.6 sec and IRP of 14.7 ± 7.6 mm Hg were recorded. The esophageal hernia was identified in 40% of the patients (n = 16) and 78% had a normal bolus transit.

Conclusions: Jackhammer esophagus was diagnosed mainly in patients with symptoms of GERD, which is in concordance with the association between the two conditions already described in the literature. This corroborates the need for investigation of underlying GERD due to potential therapeutic implications.

220 | Analysis of gender specific responses to laxative treatment

S. Landes

Medical Affairs CHC, SANOFI, Frankfurt, Germany

Objective: Constipation is gender-biased, it is more frequent in women than men, and has a stronger impact on the health-related quality-of-life (HRQoL) of women [1]. Bisacodyl (BIS) and sodium picosulfate (SPS) are well recognised to relieve constipation-related symptoms leading to an improvement in the HRQoL of constipated subjects. A post-hoc analysis was performed to explore whether laxative treatment impact genders differently.

Methods: A pooled analysis of two recent clinical trials EudraCT No. 2007-001991-34 and EudraCT No. 2007-002087-10 included 718 patients, treated with SPS or BIS (468 [342 females/126 males]), or placebo (250 [206 females/44 males]).

Results: Over the four weeks of treatment, the mean ($\pm$ SE) of weekly complete spontaneous bowel movements (wCSBM) increased from 1.0 ($\pm$ 1.27) to 4.5 ($\pm$ 0.20) [weeks 1-4] in female, and from 1.0 ($\pm$ 1.35) to 3.8 ($\pm$ 0.30) in male subjects; the mean ($\pm$ SE) of weekly

spontaneous bowel movements (wSBM increased from 3.7 (± 3.41) to 8.8 (± 0.24) [weeks 1-4] in female and from 4.1 (± 3.25) to 7.6 (± 0.35) in male subjects treated with laxatives.

The difference in the adjusted means between the treatment and placebo groups [wCSBM [weeks 1-4]: women 2.8 (± 0.25) & men 1.8 (± 0.51); wSBM [weeks 1-4]: women 4.3 (± 0.29) & men 2.8 (± 0.59)] were statistically significant in the two gender groups ($P < 0.0005$ for all vs placebo).

In both genders, the laxative treatment improves the HRQoL measured by Patient Assessment of Constipation (PAC)-QoL questionnaire. Compared to the placebo group, a statistically significant improvement from baseline was demonstrated in the "overall score" and almost in all subdomains (except "psychosocial discomfort" in men) (Figure 1). The beneficial effect of laxative treatment was stronger in women when compared to men in such subdomains as "satisfaction" and "physical discomfort".

Conclusions: Laxative treatment improved bowel functioning in both genders. The treatment response, however, appeared to be more pronounced in female subjects based on the objective (bowel movement frequency) and subjective (HRQoL) parameters. Overall, women seem to benefit more from the treatment with bisacodyl or sodium picosulfate, respectively.

References: [1] Wald *et al.* Aliment Pharmacol Ther 2007.

222 | Assessment of diabetic enteropathy using wireless motility capsule

J. Frey¹; D. A. Sangnes¹; G. Dimcevski²; E. Søfteland¹

¹Haukeland University Hospital, Bergen, Norway; ²Dept. of Clinical Medicine, Bergen University, Bergen, Norway

Objective: To investigate intestinal motility in patients with DM and suspected gastroparesis using wireless motility capsule (WMC).

Methods: Sixty-five DM patients (45 women, 53 type 1 DM) referred to Haukeland University Hospital for evaluation of suspected gastroparesis, were prospectively included. Patients filled out the Gastrointestinal Symptom Rating Scale (GSRS)-questionnaire and underwent GI motility testing with WMC. Based on GSRS we identified individuals with diarrhea syndrome (comprised of diarrhea, loose stools and urgent need for defecation) and constipation syndrome (constipation, hard stools and feeling of incomplete evacuation). Using a GSRS cutoff ≥ 4 (moderate, severe and very severe symptoms), motility parameters and intraluminal pH were compared between the groups displaying each of the syndromes and the rest of the study population.

Results: Seventeen patients (26%) had diarrhea syndrome (GSRS ≥ 4). This group had shorter small bowel transit time than the rest of the patients (207 minutes vs 284 minutes, $P = 0.029$), shorter colonic transit time (1117 minutes vs 3265 minutes, $P < 0.001$), higher colonic pH (7.1 vs 6.7, $P = 0.047$) and lesser change in pH over the ileocecal junction (0.7 vs 1.0 $P = 0.033$). Seventeen patients (26%)

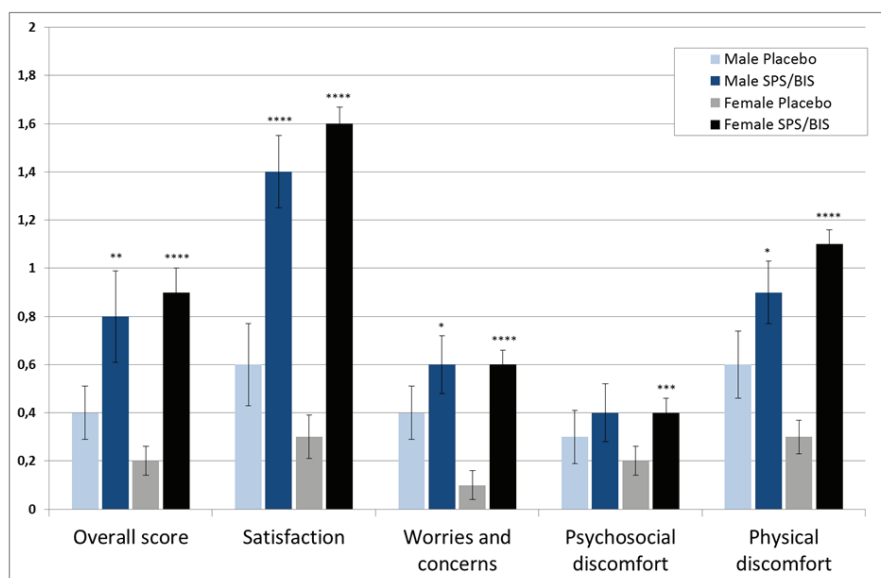


Figure 1: Treatment related improvement in PAC-QoL scores per gender after 4 weeks of treatment

Adjusted means ($\pm$ SE) for the improvement in the subscale scores of the Patient Assessment of Constipation Quality of Life (PAC-QoL) questionnaire from baseline per gender and treatment (SPS/BIS or placebo) after 4 weeks of treatment.

**** $p < 0.0001$ vs. Placebo; *** $p < 0.001$ vs. Placebo; ** $p < 0.005$ vs. Placebo; * $p < 0.05$ vs. Placebo

had constipation syndrome (GSRS ≥ 4). No significant differences in the investigated parameters were found between these and the rest of the study population.

Conclusions: >50% of patients with DM and suspected gastroparesis also had bothersome diarrhea or constipation. Using WMC, we found differences in bowel transit times and intraluminal pH between patients with diarrhea syndrome and the rest of the study population. No differences were found between patients with constipation syndrome and the rest of the study group. These findings contribute to better understanding of the pathophysiology of diabetic enteropathy.

224 | Fatigue in irritable bowel syndrome: Association with both mesocorticolimbic connectivity and insular neurotransmitter concentrations

A.-K. Norlin¹; S. Walter¹; O. Bednarska¹; S. Tapper¹; P. Lundberg¹; A. Tisel¹; S. Elsenbruch²; A. Icenhour²; R. Simon¹; M. Engström¹

¹Linköping University, Linköping, Sweden; ²University Hospital Essen, University of Duisburg-Essen, Essen, Germany

Objective: Fatigue is a common and debilitating symptom in Irritable Bowel Syndrome (IBS). We investigated if fatigue impact on daily life in IBS patients is mediated by the same central neural systems as in primarily neurological disorders such as multiple sclerosis. In those the reward pathway of the mesocorticolimbic circuit seems to hold a prominent role alongside insula, which likely is of importance for the awareness of fatigue.

Methods: 88 IBS patients from the Gastroenterology Department, University Hospital in Linköping and 47 healthy age and gender matched controls (HC) were administered the validated modified fatigue impact scale (mFIS). For the assessment of resting-state functional connectivity of the mesocorticolimbic network, most participants underwent functional magnetic resonance imaging (fMRI). To evaluate concentrations of the inhibitory neurotransmitter γ -aminobutyric acid (GABA+) and the excitatory glutamate and glutamine (Glu + Gln = Glx) of the anterior mid-insula (aINS), magnetic resonance spectroscopy (MRS) was performed in about half of the participants.

Results: IBS patients perceived higher fatigue impact than HC ($P < 0.001$). In IBS patients, higher impact of fatigue was associated with lower connectivity between the nucleus accumbens and the prefrontal cortex of the left hemisphere ($T = -3.05$, $p_{FDR} = 0.038$). In HC, fatigue impact was associated with increased connectivity between the right nucleus accumbens and aINS bilaterally ($T_{RaINS} = 3.38$, $p_{FDR} = 0.019$, $T_{LaINS} = 3.09$, $p_{FDR} = 0.021$). In IBS, but not in HC, fatigue impact was positively correlated to GABA+ ($r = 0.39$, $P = 0.011$) and negatively correlated to Glx ($r = -0.30$, $P = 0.049$) concentrations in the right aINS.

Conclusions: Fatigue impact on daily life in IBS patients seems to be mediated by similar central neural systems as fatigue of primarily neurological disorders.

225 | The introduction of Rome IV criteria decreased dramatically the prevalence of irritable bowel syndrome (IBS) in south-east Hungarian blood donors

K. Helle¹; L. Bálint¹; V. Szekeres²; O. Incze¹; G. Ollé¹; K. Vadász¹; R. Róka¹; A. Rosztóczy¹

¹First Department of Medicine, University of Szeged, Szeged, Hungary;

²Hungarian National Blood Transfusion Service, Szeged, Hungary

Objective: Irritable Bowel Syndrome (IBS) is a common disease in the general population, but its prevalence among the apparently healthy population is much less known.

Therefore the *aim* of our study was to obtain data about the incidence of IBS-related symptoms considering a healthy population and to draw general conclusions.

Methods: Healthy blood donor volunteers were enrolled ($n = 1293$, M/F: 699/540, mean age: 39 (17-66) years). Symptoms of functional bowel disorders were assessed by questionnaires according to the different Rome criteria (IV, III, II and I). The general well-being – quality of life (QoL) – of the subjects was also established.

Results: Only 0.73% of the studied subjects fulfilled the Rome IV diagnostic criteria of IBS, while 7.6, 7.0 and 9.8% completed the previous Rome III, II and I criteria respectively. Compared to the non-IBS subjects the QoL was significantly worse in patients with IBS (VAS score: 80.9 vs 75.4 $P < 0.0004$). Subjects who fulfilled the criteria of IBS were predominantly female ($\chi^2 = 9.32$, $P = 0.0022$) and were more probably intellectual workers ($\chi^2 = 14.91$, $P = 0.00058$). Other studied parameters (smoking, coffee and alcohol consumption, age, BMI) did not show association with the presence of IBS.

Conclusions: In the South-East Hungarian blood donor volunteers IBS related symptoms seem to be less common compared to other countries. The introduction of the most recent Rome IV criteria resulted a dramatic decrease in the prevalence of IBS in otherwise healthy subjects. IBS related symptoms impaired significantly the QoL of the subjects.

231 | Manometric diagnosis of achalasia and its subtypes: are chicao classification 3 (CC3) criteria really better than the conventional?

G. Ollé; K. Helle; O. Incze; L. Bálint; K. Vadász; R. Róka; A. Rosztóczy

First Department of Medicine, University of Szeged, Szeged, Hungary

Objective: The conventional manometric diagnosis of achalasia was based on the presence of complete esophageal aperistalsis with at least intermittent failure of lower esophageal sphincter relaxation. These were generally associated by increased intraesophageal pressure resulted by esophageal outflow obstruction. More recently the CC3 classification introduced new parameters to simplify the diagnosis.

The aim of our study was to compare the diagnostic yield of the conventional and the CC3 criteria in patients with clinical suspicion of achalasia.

Methods: Fifty-eight consecutive patients [M/F: 26/32, mean age: 52 (8-87) ys.] with clinical suspicion of achalasia (symptoms, Barium swallow test, upper gastrointestinal endoscopy) were submitted to water perfusion, high resolution esophageal manometric (Solar GI HRM, MMS, Netherlands) examination with a 22 channel silicon catheter. During manometry, patients were in supine position, and had at least 10 good quality wet swallows (5 cm³ water). Manometric tracings were evaluated according to the conventional and the CC3 criteria.

Results: High resolution esophageal manometry was completed in 53/58 (91%) of the studied patients. In the remaining 5 subjects, the catheter could not be passed to the stomach, and only the esophageal body motility had been evaluated. Despite the strong clinical suspicion 19 patients could not be diagnosed to have achalasia due to the low (<15Hgmm) IRP4 value. Of the remaining 39 patients 17 had "type 1", 21 had "type 2" and 1 had "type 3" achalasia. In the 19 patients with low IRP4, 9 had more than 20% PP which is the criterion of type 2 achalasia, while the remaining 10 patients can only be classified as "acontractile esophagus" since they had only very low amplitude simultaneous waves after swallowing. In contrast, 49 patients had "classic", 8 "vigorous", and 1 "spastic" achalasia according to the conventional criteria.

Conclusions: In the everyday practice CC3 system seems to be less accurate for the diagnosis of achalasia. Major problems are the high IRP4 cut off value for esophageal outflow obstruction and the low cut-off value for PP. Former important parameters such as percentage of LES relaxation and intraesophageal pressure may need to be reintroduced in the future.

232 | *Holdemanella* Spp. improves glucose tolerance and benefits endogenous GLP-1 system in diet-induced obese mice

M. R. Perez¹; I. L. Almela¹; C. B. Vilarrubias¹; M. C. Cenit Laguna¹; E. M. Gómez Del Pulgar Villanueva¹; A. B. Pérez¹; L. R. Ruzafa²; J. A. Lamas²; Y. Sanz¹

¹Instituto de Agroquímica y Tecnología de Alimentos (IATA-CSIC), Paterna, Spain;
²Cinbio (The Biomedical Research Centre)-University of Vigo, Vigo, Spain

Objective: Obesity represents a major health challenge worldwide due to its high prevalence and associated comorbidities such as type 2 diabetes. Associated peripheral low-grade inflammation impairs insulin signaling which, in turn, aggravates the obese phenotype. Insulin sensitivity might be ameliorated through the reduction of peripheral inflammation but also enhancing the effects of endocrine signals, such as the gut hormone glucagon-like peptide 1 (GLP-1), which contributes to maintaining glucose homeostasis. Gut microbiome-based strategies may help to combat obesity through the modulation of both intestinal immune and enteroendocrine

systems. With the aim of identifying next generation of probiotics against obesity we selected a bacterial strain of *Holdemanella* spp. for its in vitro anti-inflammatory properties to explore in vivo its anti-obesity effects as well as its underlying mode of action.

Methods: Mice, fed with control or high fat high sugar (HFHSD) diet, daily received the potential probiotic (1×10^9 cfu/mice) or vehicle by oral gavage for 14 weeks. Body weight (BW) was monitored weekly and an oral glucose tolerance test (OGTT) was performed at week 12. In the liver, we examined glucose uptake and metabolic routes while in the gut we analysed immune and neuro-endocrine markers.

Results: The probiotic did not prevent BW gain induced by HFHSD although reduced basal glycemia and improved OGTT. Additionally, the bacterium ameliorated the insulin dependent glucose uptake and reduced gluconeogenesis in the liver of obese mice. The anti-diabetic effects of the bacteria were not associated with benefits on intestinal immunity, but with significantly increase of GLP-1 in plasma and changes in GLP-1 receptor expression in ileum. We also found an increased expression of the neurofilament peripherin, a peripheral nervous system marker, in intestinal vagal afferents where GLP-1 receptor is mainly expressed. Neuroactive properties of the bacteria were further explored in GLP-1-sensitive vagal sensory neurons isolated from nodose ganglion. Perforated patch clamp recordings revealed depolarization of the resting membrane potential induced by *Holdemanella* spp.

Conclusions: Herein, we demonstrated for the first time that this bacterial strain beneficially influences the intestinal GLP-1 system which might contribute to prevent glucose intolerance in obesity through endocrine- or intestinal afferents-mediated paracrine routes.

235 | Food antigen-specific IgE antibodies in the development of visceral hypersensitivity

P. Jain; M. V. Florens; J. Aguilera-Lizarraga; M. F. Viola; G. Boeckxstaens

Department of Chronic Diseases, Metabolism and Ageing; Translational Research Center for Gastrointestinal Disorders, Laboratory for Intestinal Neuroimmune Interactions, KU Leuven, Leuven, Belgium, Leuven, Belgium

Objective: Irritable bowel syndrome (IBS) is characterized by altered bowel habit and abdominal pain in the absence of an organic cause. Abnormal pain signaling or visceral hypersensitivity (VHS) is a major disease mechanism that results from mast cell (MC) activation. Here, we tested the hypothesis that MC activation results from IgE-mediated crosslinking in a mouse model post infectious (PI)-VHS and in IBS patients.

Methods: Mice (Balb/C) were infected with *C. rodentium* in the presence of ovalbumin (OVA) and re-exposed to OVA, 5-7 weeks post-infection. OVA-specific IgE levels were evaluated in serum and colon of the mice.

Mice were treated with anti-IgE or its isotype (control) monoclonal antibody (1 mg/kg/week, i.p.) before OVA re-exposure. Visceromotor pain to colorectal distension was assessed by abdominal muscle

electromyography before infection and after the 8th OVA gavage. Colonic permeability was assessed by using Ussing chambers. IBS patients (11 females and 2 males, 31 years, IQR [22-43]) who met the Rome III criteria and healthy volunteers (6 females, 38 years, IQR[25-52]) were recruited and symptoms were assessed by visual analogue scale (abdominal pain, abdominal discomfort and bloating). Rectal biopsies were collected and immunostained to quantify IgE on MCs by confocal imaging.

Results: Infection with *C. rodentium* and OVA re-exposure induced VHS and increased colonic permeability in mice. OVA-specific IgE levels were present in the colon of hypersensitive, but not in normo-sensitive mice or in serum. Treatment with an anti-IgE antibody, but not with control antibody prevented the development of VHS and increased colonic permeability upon re-exposure to OVA (Figure 1). Increased IgE immunofluorescence on MCs was detected in 7 of 13 IBS patients. Of interest, levels of IgE immunofluorescence positively correlated ($r = 0.6$, $P = 0.045$) with abdominal pain severity in patients.

Conclusions: These data suggest a role for food antigen-specific IgE in the development of VHS in a murine model of PI-VHS providing a novel potential mechanism by which food ingestion leads to abdominal pain in a subgroup of IBS patients.

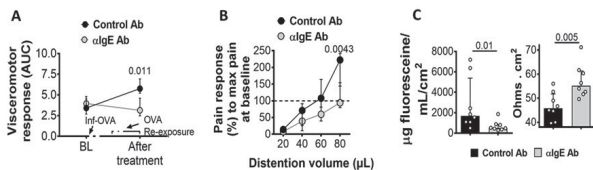


FIGURE 1. (A-B) VMR to colorectal distention in VHS mice ($n=8$ /group). Two-way RM ANOVA with Sidak's multiple comparisons (C) Colonic permeability expressed as passage of fluorescein sodium (left) and transepithelial resistance (right) of VHS mice ($n=8$ /group). Unpaired t-test. Data are shown as median $\pm$ IQR.

240 | Role of psychiatric co-morbidities in gastrointestinal clinico-pathological features in IBS-D

A. Henao¹; X. Serra¹; M. Puigcerver¹; A. Rodriguez²; M. Pigrau³; I. Paracuellos³; C. Alonso-Cotoner³; M. Vicario³; J. Santos³; B. Lobo³

¹Gastroenterology Department. Hospital General Vall d'Hebron, Barcelona, Spain; ²Psychiatry Department. Hospital General Vall d'Hebron, Barcelona, Spain; ³Gastroenterology Department. Digestive Diseases Research Unit. Hospital General Vall d'Hebron, Barcelona, Spain

Objective: To evaluate the prevalence of psychiatric co-morbidities in a cohort of patients of IBS-D in a tertiary referral hospital and its association with gastrointestinal clinico-pathological features.

Methods: We reviewed medical records of a cohort of patients diagnosed of IBS-D who underwent to a jejunal biopsy by Watson capsule between 2008 and 2016. We collected the following variables: IBS symptom severity, psychological background profile, diagnosis

of mood disorders, and mucosal jejunal lymphocyte and mast cell counts.

Results: AA cohort of 176 patients with IBS diagnosed based on Rome II and Rome III criteria were studied. The patients had an average age of 36 ± 10.5 years old; of these patients 67.6% (119/176) were female, a suitable mucosal jejunal biopsy was obtain in 159 patients. Half of the patients (85/169) reported moderate severe IBS symptoms based on IBS-SSS, the median intensity of abdominal pain was 4.2 (IQR 1.9-6.5), bowel movements 3.0 (IQR 2.2-4.0) and stool consistency (BSFS) 5.0 (IQR 5.0-6.0). The proportion of patients who had overlapping symptoms of dyspepsia was 54.5% (96/176). Median background levels of stress based on Holmes-Rahe and the Perceived Stress Scale (14-items) were 142.5(IQR 75.3-227.0) and 23.4 (95% IC 22.0-24.7), respectively, indicative of moderate stress. In addition, Beck's inventory of depression revealed median score of 8 (IQR 3.8-14.0) not indicative of state depression. In this cohort the proportion of patients who had anxiety disorders or depression was 39.2% (69/176) and 15.3% (27/176), respectively. Out of all, 56.1% of the cases were diagnosed by general practitioner. Patients with depression exhibited higher background stress and Beck's Inventory scores. Interestingly, patients with anxiety disorders exhibited lower number of intraepithelial lymphocytes in the jejunal mucosa (Table 1). Surprisingly, we did not find an association between IBS severity and the presence of psychiatric co-morbidities, though this may be a selection bias as the diagnosis was not established by a psychiatric interview in most cases.

Conclusions: Psychiatric co-morbidities do not seem to play a role in the severity of common gastrointestinal complaints in a cohort of IBS-D followed in a tertiary referral hospital.

	Depression	No Depression	<i>p</i>	Anxiety	No Anxiety	<i>p</i>
Gender (M:F)	8;19	48;97	0.893	20;49	36;67	0.679
Age(yo) (median;95% IC)	38 (36.0-44.9)	34 (33.2-36.4)	0.013	37.0 (34.1-38.4)	34.0 (33.1-37.5)	0.256
IBS-SSS (mean;95%IC)	296.4 (258.1-334.6)	250.7 (235.2-266.3)	0.778	263.5 (240.4-286.7)	254.1 (235.3-273.0)	0.801
Abdominal pain score (median;95%IC)	5.0 (3.3-6.1)	3.8 (3.7-4.6)	0.185	4.1 (3.5-4.9)	3.7 (3.6-4.7)	0.287
Stool consistency (BSFS)	6.0 (5.3-6.2)	5.5 (5.3-5.6)	0.130	6.0 (5.2-5.8)	5.5 (5.3-5.7)	0.589
Bowel movements (median; 95%IC)	3.0 (2.3-4.3)	3.0 (2.9-3.7)	0.813	3.0 (2.7-3.8)	3.0 (3.8-3.1)	0.774
Dyspepsia (%)	74/145	20/27	0.268	39/89	55/155	0.988
Holmes-Rahe Scale (median; 95%IC)	240.0 (181.9-378.2)	133.0 (130.7-169.8)	0.016	159.0 (153.8-221.0)	136.0 (126.6-186.6)	0.155
Perceived stress Cohen scale (median; 95%IC)	26.0 (22.9-30.8)	23.0 (20.8-23.9)	0.314	23.0 (21.3-26.3)	24.0 (20.6-24.2)	0.761
Beck's Inventory (median; 95%IC)	13.0 (10.3-15.9)	7.0 (6.9-9.4)	0.004	8.0 (8.2-12.8)	7.0 (6.5-8.9)	0.324
Intraepithelial lymphocytes /100 enterocytes	17.0 (12.9-21.3)	17.0 (14.5-21.3)	0.956	15.0 (14.8-18.8)	19.0 (18.0-23.1)	0.036
Mucosal Mast cells count	26.0 (18.8-30.1)	24.0 (22.7-27.1)	0.886	25.0 (22.0-28.8)	24.0 (22.0-27.3)	0.958

243 | Relationship between stool form and quality of life in patients with chronic constipation: An internet questionnaire survey

H. Ohkubo; T. Takatsu; N. Misawa; T. Yoshihara; K. Ashikari; T. Matsuura; A. Fuyuki; T. Higurashi; A. Nakajima

Yokohama City University Hospital, Yokohama, Japan

Objective: Chronic constipation (CC) is a functional bowel disorder with a high prevalence worldwide; however, treatment satisfaction and quality of life (QOL) is low. In this study, we aimed to elucidate the relationship between stool form and QOL in patients with CC.

Methods: We conducted an online questionnaire survey in September 2018 targeting adult patients in Japan who had been diagnosed with CC and were taking prescribed drugs. Assessments included the type of drug treatment, treatment duration, frequency of drug use, Bristol Stool Form Scale (BSFS) score, and Japanese version of the Patient Assessment of Constipation Quality of Life (PAC-QOL) scores. The relationship between BSFS and Japanese PAC-QOL scores was analyzed statistically.

Results: A total of 614 subjects (306 males and 308 females, 20–79 years old) were enrolled. Of these, 398 (64.8%) regularly used magnesium oxide and 162 (26.4%) did stimulant laxative in Japan, especially 81 (50.0%) used stimulant laxative 'everyday'. Mean score of the Japanese version of the PAC-QOL was 1.28 and the lowest score (highest QOL) of 0.94 was observed in BSFS type 4. Significant difference was seen between BSFS type 4 and all the other types except type 7. In patients with BSFS type 6–7, 36% had an experience of self-discontinuation of prescribed drugs and 53% had an experience of self-reduction because of the excessive effect and side effect (diarrhea).

Conclusions: Normalization of the stool form (BSFS type 4) is important for improving the QOL in patients with constipation. Given that about one-third to half of patients have an experience of self-discontinuation or self-reduction of drugs, physicians should reconsider the prescription in BSFS type 6–7 patients because of the possibility that they may keep prescribing unnecessary laxatives.

245 | Relationship among food hypersensitivity, serum cytokine and mucosa-associated intestinal microbiota in patients with diarrhea predominant irritable bowel syndrome

R. Katsumata; Y. Handa; S. Fukushima; K. Gouda; H. Matsumoto; A. Shiotani

Kawasaki Medical School, Kurashiki, Japan

Objective: Microbiota in the GI tract exists not only in the lumen but also in the mucosal epithelium. Only small number of studies was reported examining the gut microbiota attached to intestinal mucosa and mucus, in other words mucosa-associated microbiota (MAM). The population of fecal microbiota and MAM was reported to be different. So far, MAM of diarrhea predominant irritable bowel syndrome (IBS-D) was scarcely evaluated. In addition to that, relationship among food hypersensitivity, serum cytokine and MAM was not clear. The aims are to clarify the diversity and characteristics of the MAM in the patients with IBS-D comparing to the controls and to evaluate relationship among food hypersensitivity, serum cytokine and MAM in patients with IBS-D.

Methods: IBS-D was diagnosed using Rome 4 criteria. Subjects who received colonoscopy because of fecal occult blood and showed no

organic disorder were enrolled as healthy controls. After preparation by 2 L polyethylene glycol, mucosal brushing samples were taken from end of ileum. The samples were profiled by the Illumina MiSeq platform. The V3–V4 regions of the gene encoding 16S rDNA (460 bp) were tailed PCR amplified. Diversity was evaluated by Shannon–Wiener Index, Observed species, chao 1. Peripheral venous blood samples were obtained to assess serum cytokine and IgE-mediated food hyper sensitivity. Relationship among food hypersensitivity, serum cytokine and MAM were calculated.

Results: Seven IBS-D (including 2 positive food hypersensitivity patients) and five healthy controls were analyzed. α -diversity of MAM was not significantly different between IBS-D and MAM. Composition of MAM in IBS-D was similar to healthy controls at phylum level. *Lachnospiraceae* was lower in IBS-D than controls at genus level. *Lachnospiraceae* was not strongly associated with inflammatory cytokines. The abundance of *Anaerostipes* was higher and that of *Erysipelotrichaceae* was lower in food hypersensitivity positive IBS-D patients.

Conclusions: MAM of IBS-D was slightly different compared to that of healthy controls. IgE-mediated food hypersensitivity was associated to alteration of MAM in IBS-D patients.

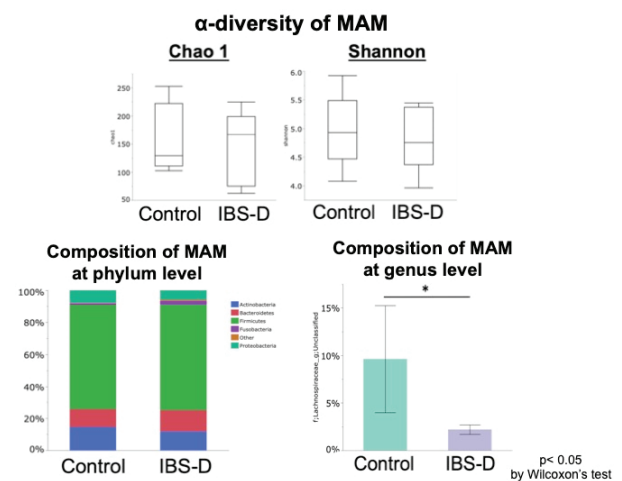


FIGURE. Comparison of α -diversity and composition in mucosa-associated microbiota between IBS-D and Controls.

246 | The benefits of inulin, choline and silymarin combined treatment in patients with constipation-predominant irritable bowel syndrome – a randomized case-control study

O. B. Barboi; I. Chirila; I. Ciortescu; C. Anton; C. Mihai; V. Drug

UMF Grigore T Popa Iasi, Iasi, Romania

Objective: Irritable bowel syndrome (IBS) is a common medical problem all over the world that implies an important social burden. Only a few therapies demonstrated beneficial effects in IBS patients. The intake of inulin has been linked to the regulation of bowel peristalsis, stool consistency and frequency.

The aim of this study is to assess the benefit of a combined therapy with inulin, choline and silymarin in patients with constipation-predominant IBS (IBS-C).

Methods: We conducted a randomized case-control study at a tertiary center of North-East of Romania that included 21 patients (15 females, 6 males, mean age 52.42 years) diagnosed with IBS-C according to ROME IV criteria. The patients were assigned into two groups: group A included 12 patients that received a specific constipation-diet and group B with 9 patients that received both the diet and the medicine containing inulin, choline and silymarin (Stoptoxin[®], Fiterman Pharma, Iasi, Romania). After 4 weeks we performed the crossover of the two groups: group A received Stoptoxin and group B continued to follow the dietary regimen alone. All the patients were evaluated after 28 and 56 days for assessing the severity of IBS symptoms.

Results: The two groups were homogenous in terms of demographic features and initial IBS symptoms. Administration of Stoptoxin was followed by the improvement of all IBS symptoms, with the best outcome being obtained for bloating, frequency and consistency of stools. The global improvement of IBS symptoms (100%) was statistically more significant after 28 days (70%) comparative to 56 days (30%) irrespective of the regimen used first ($P < 0.01$). Group B patients had a greater improvement in IBS symptoms than group A patients (79.2% vs 62.4%) after the first 28 days. An improvement of IBS symptoms was also noted in group A, but not so significant. After 56 days, the group B patients had a slightly improvement compared to group A regarding all the symptoms.

Conclusions: The combination therapy with inulin, choline and silymarin associated with constipation-specific diet showed a better effect in patients with IBS-C than diet alone.

247 | Effects of sildenafil on esophageal peristaltic characteristics and reserve in humans

C.-L. Chen; C.-H. Yi; T.-T. Liu; W.-Y. Lei; J.-S. Hung; M.-W. Wong

Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation and Tzu Chi University, Hualien, Taiwan

Objective: Sildenafil induced smooth muscle relaxation of the esophagus by blocking type 5 phosphodiesterase that degrades cyclic guanine monophosphate. The aim of our study is to investigate the effect of sildenafil on esophageal motility and peristaltic reserve in healthy adults by water perfused HRM.

Methods: Fifteen healthy adults (12 men, age 21-39, mean 27 years) participated in a randomized double blind study on 2 separate days with oral intake of either sildenafil 50 mg or placebo. All subjects underwent HRM with ten water swallows and 5 multiple rapid swallows 1 hour after oral intake of sildenafil or the placebo. The HRM parameters included esophagogastric junction contractile integral (EGJ-CI), resting lower esophageal sphincter (LES) pressure, 4-second integrated relaxation pressure (4-s IRP), distal contractile

integral (DCI), resting upper esophageal sphincter pressure (UESP), and the response to MRS.

Results: Sildenafil significantly reduced ECJ-CI ($P < 0.001$), LES pressure ($P < 0.001$), 4-s IRP ($P = 0.002$), and DCI ($P < 0.001$). There was no difference in UESP ($P = 0.87$) between sildenafil and the placebo. Sildenafil induced a significant decrease in peristaltic vigor including absent peristalsis in 12 subjects and ineffective esophageal motility in 3 subjects. Peristaltic response and augmentation following MRS was significantly inhibited with sildenafil (7% vs 100%, $P < 0.001$, and none vs 73%, $P < 0.001$).

Conclusions: By using HRM, we have demonstrated that sildenafil inhibits EGJ barrier function, resting LES pressure, and the relaxation of LES. Sildenafil appears to inhibit esophageal contractility as well as peristaltic reserve in healthy adults, but has no effects on resting UESP. Despite no effects on UES pressure, sildenafil induces esophageal hypomotility in healthy volunteers without prior esophageal dysmotility.

248 | Mindfulness based cognitive therapy in patients with functional dyspepsia in a tertiary referral centre in Singapore

Y. K. Ng; Y. Hao; A. M. L. Ong; Y. T. Wang; K. Doshi

Singapore General Hospital, Singapore, Singapore

Objective: Functional dyspepsia (FD) is a disorder of the brain-gut axis characterised by symptoms of abdominal discomfort. Mindfulness-based therapies use meditation and relaxation to achieve a state of consciousness, mindfulness, during which one consciously attends to his or her moment-to-moment experience. We aim to determine the effectiveness of group mindfulness based intervention in improving the symptoms and quality of life in patients with functional dyspepsia.

Methods: We performed an assessor-blinded randomised treatment-as-usual waitlist controlled trial. We recruited patients prospectively from the gastroenterology specialist outpatient clinic who have Rome-3 FD. Short Form Nepean Dyspepsia Index (NDI-SF) and EuroQOL VAS scale were administered by blinded assessors pre and post treatment. They were randomised to undergo Mindfulness Based Cognitive Therapy (MBCT) or to Treatment-as-Usual (TAU). The questionnaires were repeated at the end of the MBCT. Subjects in the MBCT arm undergo weekly 2-hour-long standardised MBCT sessions for 8 weeks with 1 half-day retreat conducted by 2 accredited psychologists.

Results: A significant difference in improvement of NDI-SF scores was found between MBCT ($n = 14$) and TAU ($n = 13$) groups at post treatment assessment (see table) indicating that participants in the MBCT arm experienced a greater improvement as compared to those in the TAU arm. There were no significant differences between baseline and post-treatment assessment and between baseline and 3-month follow-up on the VAS scales.

Conclusions: Participants in the MBCT arm experienced a greater improvement in their symptoms as compared to those in the TAU arm. A study with larger recruitment would be needed to further investigate this trend.

		Mean Baseline (SD)	Mean End of MBCT (SD)	Mean change baseline to end (SD)	Mean difference between MBCT and TAU	p
NDI-SF	MBCT	28.14 (9.54)	16.81 (4.75)	-11.33 (7.53)	6.19 (8.38)	<0.01
	TAU	25.00 (8.72)	23.00 (9.58)	-2.0 (9.16)		
EuroQoL-VAS	MBCT	57.79 (21.43)	61.45 (15.34)	3.66 (18.64)	1.8 (18.45)	0.53
	TAU	62.69 (16.91)	63.25 (19.50)	0.56 (18.25)		

251 | A molecular-based regenerative medicine approach for the treatment of hirschsprung disease

R. Soret¹; S. Schneider²; G. Bernas¹; O. souchkova¹; B. Charrier¹; F. Righini-Grunder³; A. Aspirot³; C. Faure³; R. Heuckeroth²; P. Nicolas⁴

¹University of Quebec at Montreal, Montreal, Canada; ²The Children's Hospital of Philadelphia Research Institute, Philadelphia, United States; ³Centre hospitalier universitaire Sainte-Justine, Montreal, Canada; ⁴Montreal, Canada

Objective: Hirschsprung disease (HSCR) is a potentially fatal human birth defect where the enteric nervous system (ENS) is missing from the end of the bowel. In all affected children, the region without enteric neurons (aganglionic bowel) tonically contracts causing functional distal obstruction (megacolon). For 70 years, children with HSCR have had their life saved by surgical removal of the aganglionic bowel. However, many of these children continue to have problems after surgery, warranting the need for alternative treatments.

Methods: Using mouse models of HSCR Holstein (a model for Trisomy 21; overproduction of collagen VI), TashT (a model for male-biased HSCR; dysregulation of both RET and EDNRB signaling pathways) and Piebald-lethal (Ednrb^{l/l}; s-l; a model for EDNRB mutation-associated HSCR) we discovered that postnatal administration of GDNF via rectal enema prevents death by megacolon in about half of homozygous mice. This treatment induces the formation of new enteric ganglia in the otherwise aganglionic bowel, and these ganglia are very similar to those found in the native ENS.

Results: Current data indicate that exogenous GDNF penetrates the aganglionic region from the luminal side, thereby turning on an endogenous GDNF-RET autoregulatory loop in the colon wall. Both exogenous and endogenous GDNF then appear to trigger the formation of enteric neurons and glia from Schwann cells at the surface of extrinsic nerve fibers, which are especially abundant in the longitudinal muscle layer of aganglionic bowel. Importantly, we also validated that our approach could work with human tissue. When human aganglionic bowel is cultured for 7 days in presence of GDNF, we are able to stimulate the proliferation of Schwann cells, and to induce neurogenesis.

Conclusions: Our data strongly suggest that a regenerative approach might be envisaged for treating at least a subset of HSCR cases, without any need for surgery.

255 | Identifying a biological signature of vulnerability to prenatal maternal stress: Implications for infant neurodevelopment

J. M. Keane¹; G. Clarke¹; F. P. M. Carthy²; A. S. Khashan²; L. C. Kenny³; J. F. Cryan¹; T. G. Dinan¹; S. M. O. Mahony¹

¹University College Cork, Cork, Ireland; ²Irish Centre for Fetal and Neonatal Translational Research, Cork, Ireland; ³University of Liverpool, Liverpool, UK

Objective: Stress during pregnancy can negatively influence birth outcomes and incur adverse neurodevelopmental consequences in the offspring. Psychological stress can increase gastrointestinal (GI) permeability leading to bacterial components entering circulation, induction of a low-grade inflammatory state as well as alterations in tryptophan metabolism. All of which can impact negatively on neurodevelopment. We aim to investigate whether psychological stress during pregnancy elicits a measurable biological signature.

Methods: Plasma samples collected at 15 and 20 weeks of gestation from a healthy cohort of nulliparous female participants with singleton pregnancies (N = 102) were analysed. Participants also complete the Perceived Stress Scale (PSS), State-Trait Anxiety Inventory (STAI) and Edinburgh Postnatal Depression Scale (EPDS) at each visit. Median scores, derived from Screening for Pregnancy Endpoints study (N = 1774), were used to dichotomize low and high scoring groups. Surrogate markers of GI permeability, pro-inflammatory cytokines and chemokines were measured by Enzyme-linked Immunosorbent Assay.

Results: Lipopolysaccharide binding protein, a surrogate marker of translocation of cell wall components from Gram-negative bacteria, was found to be increased across time-points in the high stress groups (16.028 ± 0.715; 16.975 ± 0.826; 15.433 ± 0.795 vs 11.997 ± 0.715; 12.724 ± 0.665; 13.129 ± 0.729, P = 0.000; 0.000; 0.035 – PSS; STAI; EPDS respectively). Tumour Necrosis Factor Alpha concentrations were also found to be influenced by high levels of stress and anxiety but not depression across time-points (1.126 ± 0.116; 0.726 ± 0.082; 0.596 ± 0.80 vs 0.546 ± 0.114; 0.511 ± 0.066; 0.595 ± 0.070, P = 0.001; 0.045; 0.996 – PSS; STAI; EPDS respectively).

Conclusions: The present study identifies two biomarkers which demonstrate the potential to form the core of a maternal biological signature of vulnerability to prenatal stress. It is envisaged that such a biological signature could be used to inform suitable intervention strategies aimed at counteracting the effects of prenatal maternal stress either via stress reduction techniques or microbiota targeted nutritional approaches to improve epithelial barrier function of the GI tract.

259 | Non-invasive assessment of gastric accommodation and motility with magnetic resonance imaging: A feasibility study in healthy lean females

H. E. Fitzke¹; J. Broad¹; A. Menys²; Q. Aziz¹; S. A. Taylor³

¹Queen Mary University London, London, UK; ²Motilent Ltd, London, UK;

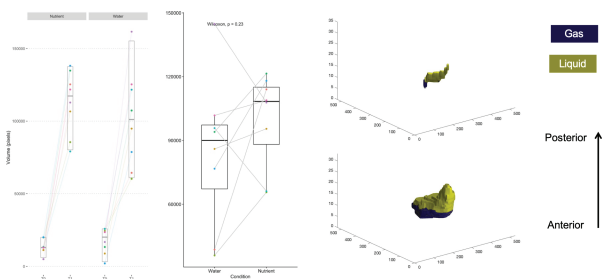
³University College London, London, UK

Objective: Impaired gastric accommodation (GA) and motility are implicated in a number of disorders including functional dyspepsia and gastroparesis but there are few non-invasive methods available to assess them simultaneously. Our objective was to test the feasibility of using magnetic resonance imaging (MRI) to assess gastric physiology, post-prandial GA and motility.

Methods: Eight healthy lean females (median age 27.4 [range 24–33]) were scanned before and after 300 mL nutrient drink (ND, Ensure 1 kcal per ml) or tap water. Internal and gas volumes were manually segmented on T2-weighted coronal images and GA quantified as the change in proximal gastric volume. Dynamic 2D imaging was processed using GIQuant© to quantify antral motility. Non-parametric paired statistical analyses were used to compare baseline internal and gas volumes and response to each challenge.

Results: All subjects completed the scan protocol without any adverse events. Baseline gas fraction was 35% [range 18–63%] and there was no difference in baseline gastric volumes ($P = 0.9$) or gas fraction ($P = 0.99$) between visits. At the group level, GA was observed as a 5.7 and 8.5-fold increase in proximal gastric volume following water and ND respectively ($P = 0.008$). The median increase in proximal volume was greater following the ND compared to water but the difference between conditions was not significant ($P = 0.23$, Figure 1). Pooling of gastric contents was observed in the fundus at baseline and post-drink resulting in poor visualisation of the antrum. Due to this and excessive through-plane motion from respiration, it was not possible to quantify motility based on registration of 2D dynamic coronal imaging.

Conclusions: This non-invasive method for assessing GA is an attractive alternative to more invasive probes such as gastric barostat or manometry. However, further optimisation and validation is required to correlate changes in volume with intragastric pressure. Although the supine position has been preferred for anatomical gastric MRI, the distribution of gas in the antrum and liquid in the fundus is not 'physiological' and precluded semi-automated analysis of motility. Future investigations utilising MRI to assess both anatomical and dynamic responses should consider prone or upright scanning and 3D or multi-slice acquisition.



261 | Rumination versus GERD-related postprandial regurgitation: A different postprandial gastric PH profile

K. Nakagawa¹; A. Sawada¹; Y. Hoshikawa¹; K. Nikaki¹; P. Woodland¹; E. Yazaki¹; A. Masamune²; D. Sifrim¹

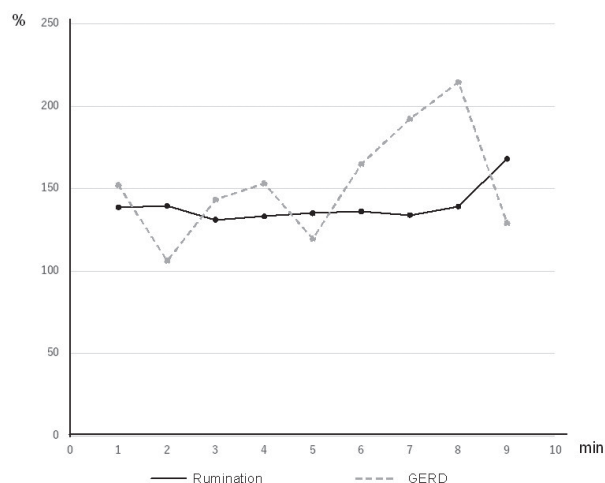
¹Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, UK; ²Division of Gastroenterology, Tohoku University Graduate School of Medicine, Sendai, Japan

Objective: We have recently reported that patients with persistent GERD related regurgitation have a different postprandial pattern of gastro-esophageal reflux compared to ruminators i.e. ruminators have many more postprandial non acid reflux events. The reason for such difference is unknown. It is possible that gastric contents composition or distribution differs between both groups. The aim of this study was to compare postprandial oesophageal and gastric pH profiles in ruminators and patients with GERD related regurgitation.

Methods: We assessed MII-pH and HRM/Z tracings ("off" PPI) from 28 consecutive patients with clinical diagnosis of rumination syndrome confirmed by HRM/Z (25 females; mean age 33.4 ± 9.8 years). We compared the MII-pH tracings of rumination patients with MII-pH tracings of 30 patients with refractory GERD symptoms (but no clinical suspicion of rumination) consisting of 10 patients with AET $\geq 6\%$ (True NERD), 10 patients with Reflux Hypersensitivity and 10 patients with Functional Heartburn (13 females; mean age 41.3 ± 11.7 years). In order to assess pH profiles of the postprandial periods, we measured mean nadir oesophageal and gastric pH (measured 15 cm below LES) during 10 minutes intervals during 90 minute-postprandial periods.

Results: The oesophageal pH of refluxates over the postprandial period was significantly less acidic in ruminators than in GERD (MANOVA, $P < 0.001$). The pattern of gastric pH was similar between both groups. The ratio of oesophageal pH / gastric pH (%) presented high consistency over time in ruminators, but showed high variability in GERD (Figure).

Conclusions: Patients with rumination have less acidic reflux episodes than GERD patients. However, both groups showed a similar gastric corpus postprandial pH profile. We hypothesize that origin of non acidic refluxate in rumination is the buffered mid stomach content backward propelled by abdominal straining whereas acidic refluxates in GERD patients with regurgitation comes from a more proximal gastric acid pocket.



266 | Anti-inflammatory and barrier stabilizing effects of a herbal combination medicine of myrrh, coffee charcoal and chamomile flower extract in a multi-component cell model of the inflamed intestinal mucosa

L. Weber¹; K.-H. Goos²; K. Nieber¹; J. Arnhold¹; C. Vissienon¹

¹University of Leipzig, Leipzig, Germany; ²Repha GmbH Biologische Arzneimittel, Langenhagen, Germany

Objective: Myrrhinil-Intest[®], a herbal medicinal product of myrrh (*Commiphora molmol* E.), coffee charcoal (*Coffea Arabica* L.) and chamomile flower dry extract (*Matricaria chamomilla* L.), has been used for decades to treat various gastrointestinal diseases. A randomized clinical trial supports the use of the preparation for the treatment of IBD [1]. However, the underlying pharmacological mechanisms have not yet been fully elucidated.

The aim of the present study was to assess the influence of the individual components of Myrrhinil-Intest[®] on inflammatory cross-talk between immune and intestinal epithelial cells as well as intestinal barrier impairments observed in the pathophysiology in IBD using a complex co-culture cell model.

Methods: To model the intestinal mucosa, Caco-2 and HT29-MTX cells were differentiated on transwell inserts and inflammatory stimulation was realized by co-cultivation with LPS-activated human macrophages for 48 hours. At the same time treatment with different concentrations of the plant extracts was performed. The barrier function was evaluated by measurements of transepithelial electrical resistance (TEER) and the secretion of cytokines (IL6, TNF) and chemokines (IL8, MCP-1) was quantified by ELISA.

Results: Myrrh and coffee charcoal exhibited concentration-dependent barrier-stabilizing effects. All three plant extracts inhibited the release of proinflammatory cytokines from macrophages and chemokines from epithelial cells in varying concentrations. Table 1 summarizes the observed mean inhibitory and effective concentrations.

Conclusions: Thus, the individual components of Myrrhinil-Intest[®] inhibited the inflammatory communication between immune and

intestinal epithelial cells. In addition, myrrh and coffee charcoal counteracted an intestinal barrier impairment, which confirms the use of the herbal combination in IBD therapy.

References: [1] Langhorst J et al. Alimentar Pharmacol Ther. 2013; 38(5):490-500.

	EC50 – barrier stabilization (TEER)	IC50 – Inhibition of cytokine-/chemokine release			
		IL6	TNF	IL8	MCP-1
Myrrh extract (<i>Commiphora molmol</i> ; 0.1 – 100 µg/ml)	67 µg/ml	9 µg/ml	13 µg/ml	34 µg/ml	36 µg/ml
Coffee charcoal extract (<i>Coffea Arabica</i> ; 1 – 500 µg/ml)	108 µg/ml	129 µg/ml	-	62 µg/ml	132 µg/ml
Chamomile flower extract (<i>Matricaria chamomilla</i> ; 0.1 – 200 µg/ml)	-	-	35 µg/ml	62 µg/ml	-

TABLE 1. Overview of the mean effective and inhibitory concentrations (EC50 / IC50).

268 | Mucosal IgG production and plasma cells-nerves interaction: Potential mechanisms of gut-brain axis dysfunction in diarrhoea-prone irritable bowel syndrome

E. Melón-Ardanaz¹; C. Pardo-Camacho¹; M. Albert-Bayo¹; A. M. González-Castro¹; M. P. Pastor¹; A. Nieto¹; F. Azpiroz²; J. Santos²; M. Vicario²

¹Vall d'Hebron Institut de Recerca. Gastroenterology Department. Hospital Universitari Vall d'Hebron, Barcelona, Spain; ²CIBER-EHD, Madrid, Spain. Vall d'Hebron Institut de Recerca. Gastroenterology Department. Hospital Universitari Vall d'Hebron, Barcelona, Spain

Objective: Enhanced humoral immunity has been identified in the intestinal mucosa and we aim to characterize the antibody-mediated response and its association with IBS pathophysiology.

Methods: Mucosal jejunal biopsies and stool samples were obtained from diarrhoea-IBS (IBS-D; n = 18) patients meeting Rome III criteria and age-matched healthy volunteers (H; n = 18). Bowel movements, stool consistency and abdominal pain were monitored. Psychological stress, anxiety and depression symptoms, were assessed by validated self-administered questionnaires. The number and the activation of mucosal plasma cells were determined by transmission electron microscopy. Luminal immunoglobulins (Ig) were determined in faecal content by ELISA.

Results: Mucosal plasma cells were located in proximity to nerve endings. This distance was significantly lower in samples from IBS-D compared to H (IBS-D: 1.26 (0.21-4.25); H: 2.13 (0.26-7.06) micrometers; $P < 0.05$). Individual plasma cells were observed scattered in control group, whereas clusters of long-lived activated plasma cells featured the jejunal mucosa of IBS-D. The number of plasma significantly correlated with proximity to nerve endings ($r^2 = -0.63$, $P < 0.01$). Stool Ig quantification showed significantly higher concentration of total IgG (IBS-D: 11.38 (1.5-45.82); H: 3.68 (0.61-35.34) ng/mg protein; $P < 0.05$) and IgG2 (IBS-D: 0.71 ± 0.53 ; H: 0.40 ± 0.29 ng/mg protein; $P < 0.05$) in IBS-D. No statistically significant differences were observed in sIgA, IgM, IgE, IgG1, IgG3 and IgG4 concentration between groups. Notably,

luminal IgG positively correlated with abdominal pain ($r^2 = 0.50$; $P < 0.05$) and distance of plasma cells to nerves negatively correlated with psychological stress ($r^2 = -0.55$; $P < 0.05$) and depression ($r^2 = -0.46$; $P < 0.05$).

Conclusions: Mucosal humoral immunity and its interaction with nerves are identified as potential factors associated with brain-gut axis dysfunction in IBS-D. Studies aimed at determining the underlying mechanisms warrant further investigation.

269 | Neurohumoral mechanisms of decreased food intake and body weight gain after neuromodulation of vagus nerve in rats fed a high-fat diet

K. Gil; M. Kurnik-Lucka; A. Furgala

Jagiellonian University Medical College – Department of Pathophysiology, Krakow, Poland

Objective: There is growing evidence that vagus nerve stimulation (VNS) exerts a suppressive effect on both short- and long-term feeding in animal models. We previously showed that VNS with high-frequency (10 Hz) electrical impulses decreased food intake and body weight in rats. In the present study, we investigated the effect of chronic VNS on the levels of appetite-regulating peptides, vagal neurons, serum lipid concentrations, feeding behavior and appetite in rats fed a high-fat diet and vagus-related neurons activation.

Methods: Adult male rats were implanted with a microstimulator (MS) and fed a high-fat diet (42 days, 10 Hz). The left vagus nerve was stimulated subdiaphragmatically with electrical pulses generated by the MS. Daily food intake and body weight, as well as total serum cholesterol, triglycerides, LDL and HDL lipoproteins levels were measured. Adipose tissue content was evaluated by weighing epididymal fat pads, while aortic and hepatic fragments were taken for routine histological examination. Specimens from nodose ganglions, nucleus of the solitary tract and arcuate nucleus were immunostained for c-FOS. Neuropeptide Y (NPY), secretin, glucose-dependent insulinotropic peptide (GIP), glucagon-like peptide-1 (GLP-1) and corticotropin-releasing factor (CRF) serum concentrations were measured by ELISA method.

Results: Chronic VNS significantly decreased food intake, body weight gain and epididymal fat pad weight. VNS also lowered the total serum cholesterol and triglyceride levels. Furthermore, hepatic steatosis and discrete changes evoked by high-fat diet in aortic wall were reduced following VNS. The serum concentrations of CRF, secretin and GIP were elevated, NPY levels were decreased and GLP-1 levels remained unchanged after VNS. C-Fos-positive neurons count in nodose ganglions, nucleus of the solitary tract and arcuate nucleus were elevated in VNS group.

Conclusions: The study demonstrates that chronic electrical VNS exerts anorexigenic effects on food intake and body weight gain, reducing body fat accumulation and lowering the blood concentration of lipids, thus may be potentially useful for diet-induced obesity

management. Numerous appetite-related peptides influencing regulatory circuits concerned with metabolic processes may contribute to these effects.

272 | Is 3D-high resolution esophageal manometry useful in diagnosis of achalasia?

L. A. Novais

LNMD Laboratório de Neurogastroenterologia e Motilidade Digestiva. Nova Medical School FCM CEDOC -UNL, Lisbon, Portugal

Objective: Achalasia is an esophageal disorder of unknown cause characterized by aperistalsis of esophagus body and impaired relaxation of lower esophageal sphincter (LES). High resolution esophageal manometry (HRM) has improved the sensitivity of manometry for detecting achalasia, greatly helped in making the diagnosis. Inability to traverse the EGJ or diaphragm is a technical limitation of HRM

To evaluate whether 3D-HRM would be useful whenever it was not possible to study it by HRM, since the diagnosis of achalasia hinges on the manometric identification of defective deglutitive LES relaxation

Methods: We prospectively evaluated 10 patients (at ages 46-94 years; 60% female patients) whenever it was not possible to study it by HRM

The 3D-HRM assembly (ManoScan 3D, Given Imaging/ Metronic, Los Angeles, CA) is a 128-channel solid-state manometric recording device incorporating a 9-cm 3D-HRM segment of 12 rings spaced 7.5 mm apart.

In the use of 3D-HRM in patients with larger hiatal hernia, we found a higher success rate in the evaluation of the esophagogastric junction (EGJ), which seemed to have reduced the flexibility of the probe tip. The informed consent was obtained from each subject if inability to traverse the EGJ with HRM, to do 3D-HRM in the same manometry evaluation.

Results: Of the 10 patients evaluated in that with the HRM in which it was not possible to study SLE, in 8 with 3D-HRM this evaluation was achieved. The integrated pressure relaxation (IRP): Mean 28.86 mm Hg (16.8 to 37.5 mm Hg). Chicago classification sub-types (type I-1; type II-5, type III-2)

Conclusions: We described a subset of aperistalsis patients with probable diagnosis of achalasia, in which HRM was ineffective in the esophago-gastric junction study and in the determination of IRP.

The 3D-HRM was useful in confirming the diagnosis of achalasia. A HRM less flexible catheter tip of the probe, would obviate inability to study the EGJ in the evaluation of this subset patients with achalasia.

274 | The effect of kisspeptin on the brain – Gut axis elements in the activity-based anorexia (ABA) rats

K. Skowron¹; P. Stach¹; K. Jasinski²; M. Kurnik-Lucka¹; A. Gil¹; V. Aleksandrovych¹; A. Baranowska¹; M. Jurczyk¹; W. Weglarz²; K. Gil¹

¹Jagiellonian University Medical College – Department of Pathophysiology, Krakow, Poland; ²Institute of Nuclear Physics Polish Academy of Sciences, Krakow, Poland

Objective: Anorexia nervosa is a severe condition affecting 1% of adult females. It essentially consists of a restriction of energy intake, intense fear of gaining weight and distortion of the body image. Hypothalamus plays a major role in the regulation of our metabolism sensing peripheral and central signals and activating orexigenic/anorexigenic neuronal responses, mainly mediated by excitatory neurotransmitters (e.g. glutamate) or inhibitory (GABA). It has been reported, that kisspeptin, a neuropeptide that promotes cooperation of the neurons in hypothalamus region, plays a role in the regulation of the hypothalamic–pituitary–gonadal axis and influences the reproductive functions of the body. Thus, we hypothesized that kisspeptin may form a crucial link between the energy balance of the body and the normal function of gonads in anorectic patients.

Methods: We adopted an animal model of AN induced by voluntary physical activity and restricted feeding schedule in female Wistar rats and assessed daily body weight gain and food intake. Based on the role of hypothalamus in processes that are believed to be crucial in the development of ABA, we focused our research on the metabolic status of this particular region in anorectic rats and established so-called 'neurochemical profile' of hypothalamus in controls and ABA rats using magnetic resonance spectroscopy methods. We also investigated enteric regulatory cells: interstitial cells of Cajal, telocytes, autonomic cholinergic and nitrergic neurons in the gut by immunofluorescence methods. We then investigated the effects of subcutaneous administration of kisspeptin (20 nmol/rat) on the selected parameters.

Results: ABA rats showed a significant weight loss from the first day. Despite the progressive weight loss, anorectic rats consumed gradually more food each day, but their total food intake reached half of the level of the control group. Anorexia impaired hypothalamic glutamatergic neurotransmission, leading to a decrease in glutamate and GABA levels. Kisspeptin administration partially reinstated these effects. No morphological differences between enteric cells in ABA rats after kisspeptin were observed.

Conclusions: Kisspeptin seems to partially restore glutamate and GABA signaling influencing the feeding control mechanisms in ABA rats. These results support our hypothesis that the reduced concentration of kisspeptin participates in the multifactorial pathogenesis of anorexia nervosa.

277 | High resolution anorectal manometry performed on patients with fecal incontinence after low anterior resection surgery for rectal cancer

L. L. Couceiro; I. Castel; F. Canga; C. Ciriza De Los Ríos

Hospital Universitario 12 de Octubre, Madrid, Spain

Objective: Low anterior resection syndrome (LARS) after sphincter-preserving surgery is a common problem related to the surgical treatment of rectal cancer. The etiology is multifactorial and the clinical outcomes are widely heterogeneous including fecal incontinence (FI), however the manometric patterns of LARS are unclear as the literature is not very extensive.

Our aim was to evaluate anorectal function after LAR using HRAM and describe the anorectal manometric alterations in these patients.

Methods: 11 patients studied for FI after low anterior resection (LAR) were included. Epidemiological, clinical and high-resolution anorectal manometry (HRAM) data were obtained from all of them. Severity of FI was quantified using the Wexner score, considering FI as moderate-severe when this score was ≥ 9 . Solid state HRAM (Manoscan[®], Medtronic[®]) was used.

Results: 11 patients with FI were included, 8 (72.7%) were male, mean age 64.7 (56.1-73.5). Most of them 8 (72.7%) had comorbidities. Bowel habit was more than 3 times/d in 8 (72.7%) patients. Fecal consistency (Bristol scale) was: normal (type 3 and 4): 5 (45.5%) patients; type 5: 2 (18.2%) patients; diarrhea (type 6 and 7): 4 (36.4%) patients. FI was predominantly passive and with daily frequency in 8 (72.7%) patients. Wexner score was ≥ 9 in 9 (90.9%) of patients.

Manometry results were:

Parameter	Mean value	CI 95%
Mean Resting pressure (mm Hg)	59	47.2-70.1
Maximum Resting pressure (mm Hg)	77.5	62.5-92.5
Maximum Squeeze pressure (mm Hg)	144.2	107.8-180.5
% Increase during squeeze	83.1	44.7-121.6
Squeeze duration	13.5	10.7-16.3
Anal canal length	3.1	2.7-3.5

Internal anal sphincter (IAS) was hypotensive in 8 (72.7%) patients and anal canal spontaneous relaxations were observed in 8 (72.7%) patients (figure). External anal sphincter (EAS) was considered hypotensive in 6 (54.6%) patients and squeeze duration was lower than normal in 5 (45.5%) patients. Cough maneuver was abnormal in 6 (54.5%). Simulated defecation was normal in all of them.

Conclusions: FI after LAR is severe, its predominantly passive with daily frequency. HRAM most frequent pattern is hypotensive IAS with spontaneous relaxation of the anal canal.

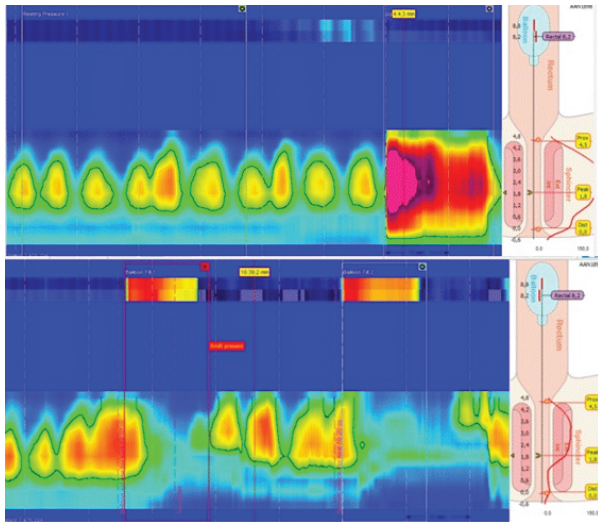


FIGURE. Manometric pattern of LARS.

280 | Irritable bowel syndrome and serum tryptase: Correlation with subtype and severity of IBS

I. Castel De Lucas; C. Ciriza De Los Ríos; F. C. Rodríguez-Valcárcel; G. C. Tortajada

University Hospital 12 de Octubre, Madrid, Spain

Objective: The irritable bowel syndrome (IBS) is a functional disorder defined by abdominal pain with bowel movement alteration. Mast cells are part of the inflammatory infiltrate in the intestinal mucosa. Recent studies have linked mast cells tryptase degranulation with more abdominal pain in patients with IBS. Thus tryptase could be a serological marker of inflammation in IBS and identify patients that may improve with mast-cell stabilizers.

Assess the level of tryptase in patients with IBS compared with a control group. Determine if there are differences in tryptase concentration depending on the subtype and severity of IBS and if it correlates with quality of life in these patients.

Methods: Prospective case-control study carried out in a single center. Recruitment between January 2017 and November 2018. Inclusion criteria: Patients of both genders older than 18 year diagnosed with IBS according to Roma IV criteria. Control group with healthy subjects with no pathological history and a negative questionnaire for intestinal symptoms. 32 patients are included divided in IBS-C and IBS-D and 51 controls.

Results: 32 patients (30 women, 93.75% and 2 men, 6.25%) and 51 controls were included. 21 patients (65.62%) had IBS-D and 11 (34.38%) IBS-C. The tryptase media in the patient group was 4.84 IC95% [3.92-5.76] and in the control group 3.64 IC 95% [3.23-4.04], finding a statistically significant difference ($P = 0.0397$). There was no statistically significant difference in tryptase levels between IBS subtypes (5.01 [IC 95% 3.95-6.07] in the IBS-C and 4.73 IC 95% [3.42-6.04] in the IBS-D group), $P = 0.3156$. There was a statistically significant between the level of tryptase and the score on quality of life (IBS-QOL questionnaire), $P = 0.0004$, and the patient health status (PHQ-9), ($P < 0.0001$). We didn't find statistical correlation between tryptase levels and IBS severity ($P = 0.662$).

Conclusions: A statistically significant higher level of tryptase was found in patients than in controls. There was a negative correlation between tryptase and quality of life and health status. Tryptase seems to have an involvement in the pathogenesis of IBS as well as in various aspects of the disorder. We consider increasing the sample size to continue to study the implications of tryptase in various aspects of IBS.