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ERECTILE DYSFUNCTION AND LOWER ANDROGENICITY IN TYPE 1 DIABETIC PATIENTS

O. ALEXOPOULOU (1), J. JAMART (2), D. MAITER (1), M.P. HERMANS (1), R. DE HERTOGH (1), PH. DE NAYER (3), M. BUYSSCHAERT (1)

SUMMARY - **Objective:** To analyse the clinical characteristics and relevant hormonal profile in type 1 diabetic patients with and without ED.
Material and methods: Fifty one type 1 diabetic patients were studied. ED was assessed by direct interview. Chronic diabetic complications, smoking and alcohol status as well as current use of medications were recorded. Hormonal profile consisted of plasma LH, FSH, prolactin, androstenedione (Δ_4), dehydroepiandrosterone (DHEA), DHEA-sulfate (DHEA-S), free testosterone (FT), estradiol (E_2), sex hormone binding globulin (SHBG), dihydrotestosterone (DHT), cortisol, TSH and free thyroxine (FT_4).
Results: ED was present in 24 patients (47%) (group 1), who were older ($P < 0.001$), had a longer diabetes duration ($P < 0.001$) and a higher systolic blood pressure ($P = 0.017$) when compared to the subjects who did not complain (group 2). ED was positively correlated to all diabetes-related complications ($P < 0.02$). Antidepressive drug(s) were more frequent in group 1 ($P = 0.007$), as well as prokinetics (P=0.043) and ACE-inhibitors (P=0.010). HbA_1c was comparable. Patients with ED had lower levels of Δ_4 ($P = 0.003$), DHEA ($P < 0.001$), DHEA-S ($P = 0.002$), FT ($P = 0.08$) while SHBG ($P = 0.010$) and LH ($P = 0.022$) were higher compared to group 2. Multiple logistic regression analysis showed an independent association of ED with Δ_4 ($P = 0.016$), DHEA-S ($P = 0.037$), SHBG ($P = 0.001$) and insulin dose ($P = 0.025$). There was no significant difference for all other measured hormones.
Conclusion: ED is impressively prevalent in type 1 diabetes and is associated with age, diabetes duration, chronic complications and decreased androgens.

Key-words: diabetes type 1, erectile dysfunction, diabetic complications, adrenal androgens, gonadal androgens.

RÉSUMÉ - **Dysfonction érectile et hypoandrogénicité dans le diabète de type 1.**
Objectif : Nous avons voulu analyser les caractéristiques cliniques et le profil hormonal d'un groupe de diabétiques de type 1 souffrant ou non de dysfonction érectile (DE).
Matériel et méthodes : 51 diabétiques de type 1 ont été inclus dans l'étude. La DE a été identifiée sur la base d'un interrogatoire direct. Outre les paramètres habituels, les complications chroniques du diabète, le tabagisme, la consommation d'alcool et la prise de médicaments ont été systématiquement documentés. Le profil hormonal comportait les dosages plasmatiques de LH, FSH, prolactine, androstènedione (Δ_4), déhydroépiandrostérone (DHEA), DHEA-sulfate (DHEA-S), testostérone libre, estradiol, "sex hormone binding globulin" (SHBG), dihydrotestostérone, cortisol, thyréostimuline et thyroxine.
Résultats : Une DE était notée chez 24 malades (47 %) (groupe 1). Ils étaient plus âgés ($P < 0,001$) et avaient une durée de diabète plus longue ($P < 0,001$) que les malades sans DE (groupe 2). La tension artérielle systolique était aussi plus élevée dans le groupe 1 ($P = 0,017$). Les taux d'HbA_1c étaient comparables. La DE était significativement corrélée aux complications vasculaires et neurologiques du diabète ($P < 0,02$). L'usage d'antidépresseurs, de prokinétiques et d'inhibiteurs de l'enzyme de conversion était significativement plus habituel dans le groupe 1. Nous avons aussi observé que les taux de Δ_4 ($P = 0,003$), DHEA ($P < 0,001$), DHEA-S ($P = 0,002$) et testostérone libre ($P = 0,08$) étaient abaissés chez les patients du groupe 1 par rapport à ceux du groupe 2. En outre, il existait dans le groupe 1 une augmentation de la SHBG ($P = 0,01$) et de la LH ($P = 0,022$). Une analyse de régression multiple a confirmé l'association significative de la DE avec les taux de Δ_4 ($P = 0,016$), DHEA-S ($P = 0,037$) et SHBG ($P = 0,001$) ainsi qu'avec la dose d'insuline ($P = 0,025$). A l'opposé, aucune différence significative entre les deux groupes n'était objectivée pour les autres paramètres hormonaux.
Conclusion : Nous retrouvons une DE chez près de la moitié d'un groupe de patients diabétiques de type 1. Cette DE est corrélée à l'âge, à la durée du diabète, aux complications chroniques et à une hypoandrogénicité.

Mots-clés : diabète de type 1, dysfonction érectile, complications chroniques, androgènes surrénaliens et gonadiques.

✍ : *M. Buysschaert, Service d'Endocrinologie et Nutrition, Cliniques Universitaires St Luc Avenue Hippocrate 54, UCL 54.74 B-1200 Bruxelles, Belgique.*
E-mail: buysschaert@diab.ucl.ac.be
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(1) Service d'Endocrinologie et Nutrition, Cliniques Universitaires St Luc, Université Catholique de Louvain, B-1200 Bruxelles, Belgique.
(2) Centre de Biostatistique et de Documentation Médicale, Cliniques Universitaires de Mont-Godinne Université Catholique de Louvain B-5530 Yvoir, Belgique
(3) Service de Médecine Nucléaire, Cliniques Universitaires St Luc Université Catholique de Louvain, B-1200 Bruxelles, Belgique.

Erectile dysfunction (ED), although recognized as a common chronic complication of diabetes, is reported with a highly varying prevalence, ranging from 20 to 71% [1-5]. Several studies have investigated the relation between ED and diabetes duration, degree of metabolic control and presence of neurological and/or vascular complications [1, 5-8].

In contrast, there appears to be no recent data dealing with the hormonal profile from both gonadal and adrenal sources with respect to ED in type 1 male diabetic patients.

The aim of this study was therefore to compare the clinical characteristics as well as the relevant comprehensive androgen hormonal profile in type 1 diabetic subjects with and without ED.

PATIENTS AND METHODS

Patients

This prospective study was conducted between November 1999 and March 2000. Fifty-one consecutive Belgian caucasian type 1 male diabetic patients, attending the outpatient diabetes clinic of St Luc University Hospital, were included. Age, weight, height, diabetes-related complications, other medical history and current use of medications were recorded as well as marital status, cigarette smoking and alcohol consumption. Plasma C-peptide, HbA_1c and lipid values were also determined. Subjects with a major illness and/or liver cirrhosis, pelvic disease or other non-diabetic endocrinopathy, in particular primary or secondary hypogonadism or thyroid dysfunction, were excluded from the study as well as subjects with hyperprolactinaemia secondary to different drugs.

The patients' clinical and biological characteristics are shown in *Table I*. Informed consent was obtained from each patient.

The cohort of 51 subjects was divided in two groups, according to the presence or absence of ED. ED was assessed by a direct interview carried out by the medical staff of the diabetes center. The definition of ED used in this investigation was that recommended by the National Institutes of Health Consensus Conference [9]. Thus, patients were asked about their (in)ability to achieve or maintain a sufficient degree of erection allowing for satisfactory sexual intercourse. Group I (with ED) consisted of 24 subjects (47%) while group II (without ED) included 27 patients (53%).

Hormonal profile in both groups (determined on one single occasion) consisted of plasma LH, FSH, prolactin, androstenedione (Δ_4), dehydroepiandrosterone (DHEA), DHEA-sulfate (DHEA-S), free testosterone (FT), estradiol, sex hormone binding globulin (SHBG), dihydrotestosterone (DHT) as well as cortisol, TSH and free thyroxine (FT_4).

TABLE I. *Clinical and biological characteristics of all patients.*

n		**51**
age	(years)	48 ± 14*
duration of diabetes	(years)	20 ± 13
BMI	(kg/m^2)	25.2 ± 3.8
blood pressure	(mmHg)	
systolic		138 ± 15
diastolic		86 ± 9
insulin dose	(U/day)	53 ± 15
C-peptide	(pmol/ml)	0.07 ± 0.08
HbA_1c	(%)	8.8 ± 1.5
marital status1/2/3/4**	(%)	71/6/2/20
no/past/current smoking	(%)	35/29/35
no/past/current alcohol history	(%)	62/2/37

* mean ± SD. ** 1 = married, 2 = separated/divorced, 3 = widow, 4 = never married.

Methods

Assays

C-peptide concentrations were measured by radioimmunoassay. HbA_1c was determined by ion-exchange high performance liquid chromatography. Total cholesterol, LDL-cholesterol, HDL-cholesterol and triglycerides were measured using conventional methods.

LH, FSH and prolactin were measured with the Immulite Automated System, a two-site chemiluminescent enzyme immunometric assay (CDPC, Los Angeles, USA) (detection limits: 0.7 mUI/ml, 0.1 mUI/ml and 0.5 ng/ml for LH, FSH and prolactin respectively). Intra- and interassay CV's were 5-8 and 6-10% respectively for the three measurements. Normal ranges are 1-10 mUI/ml, 1-8 mUI/ml and 2-15 ng/ml for LH, FSH and prolactin respectively.

Δ_4 androstenedione and DHEA were determined by RIA methods after extraction. Specific antibodies against the former were obtained from CER-Hormonology Lab. (Marloie, Belgium) and against the latter from ICN Biomedicals (Ca, USA). The minimal detection limit for both assays was 0.25 nmol/L, with similar intra- and interassays CV's, respectively 5% and 8%. Normal values in men are 5 ± 2.5 nM/L (mean ± 1SD) for Δ_4 and 7-16 nM/L for DHEA.

DHEA sulfate was measured using a solid phase competitive radioimmunoassay obtained from Immu-

notech (France). Intra- and inter CV's were respectively 7% and 10% with an analytical sensitivity at 0.16 µmol/L. Normal range is 2.5-12 µM/L.

Free-testosterone was measured by equilibrium dialysis with labelled testosterone. The concentration was computed from the partition of the labelled and total testosterone. The interassay CV was 6.2%. Normal range is 0.2-0.6 nM/L.

Estradiol and SHBG were measured with two-step radioimmunoassay, using a precipitating second antibody (estradiol: Clinical Assay, Diasorin, Saluggia, Italy; SHBG: Biocade, Liège, Belgium). Intra-and interassay CV's were 4-8 and 6-10% respectively for both assays. Normal ranges are 12-35 pg/ml for estradiol and 10-45 nM/L for SHBG.

DHT was measured by RIA after extraction and chromatography (in-house method). Normal DHT values range from 0.8 to 3 nmol/L with a detection limit of 0.17 nmol/L.

Cortisol was estimated using a solid phase radioimmunoassay (Corti-cote, ICN, Diagnostics Div., Orangeburg, New York, USA). The analytical sensitivity reached 2 nmol/L. Intra- and inter CV's were 4% and 6% respectively.

TSH was measured by solid phase two site immunoradiometric assay (TSH Riabead II, Abbott, Diagnostic Division) with an analytical sensitivity of 0.02 mU/L, intra- and interassay CV's were respectively below 4% and 6%.

Free-T_4 was assessed by a solid phase competitive method (Clinical assays, Gammacoat free-T_4 (two step) Diasorin, Stillwater, Minnesota, USA)). The analytical sensitivity was 0.1 ng/dl, intraassay CV was below 6%, interassay CV below 8%. Normal values are 0.8-2 ng/dl.

Assessment of chronic complications

Retinopathy was diagnosed on the basis of ophthalmoscopy (through dilated pupil) by an experienced ophthalmologist and confirmed by fluorescein angiography. Microalbuminuria was defined as urinary albumin concentration (immunonephelometry (BN II, Behring, USA)) greater than 20 mg/l and less than 200 mg/l, or as urinary albumin excretion between 30 and 300 mg/24h, and proteinuric nephropathy was considered in the presence of gross albuminuria and/or macroproteinuria (Albustix® [Ames] positive). The presence of peripheral neuropathy was based on clinical examination (abnormal knee/ankle reflexes, abnormal Semmes-Weinstein monofilament score) and confirmed by electromyography. Autonomic neuropathy was considered when gastroparesis and/or orthostasis (a fall in systolic BP > 20 mmHg upon standing) was present. Macroangiopathy was considered:

– in subjects who had a history of cardiovascular event and/or in the presence of angina and/or permanent ischaemic electrocardiogram abnormalities at rest, or ischaemic abnormalities in a stress test (usually combined with cardiac non invasive imaging technique),

– in subjects with claudication and/or abolished peripheral pulses and/or foot lesions due to vascular disease demonstrated by echodöppler. Hypertension was defined as a systolic blood pressure ≥ 130 mmHg, a diastolic blood pressure ≥ 85 mmHg (according to JNC-VI recommendations) and/or a history of hypertension with use of antihypertensive drugs.

Statistical analysis

Frequencies were compared between both groups by chi-square or Fisher exact test as appropriate. Numerical variables are expressed as mean ± SD and were compared by Wilcoxon rank sum test. The independent influence of various parameters on ED was tested by a multivariate logistic regression with backward selection of variables by likelihood ratio test. As the number of variables (9) seems high with respect to the number of subjects, the robustness of the result was studied by a cross-validation procedure (10 random partitions of the cohort between a training set to estimate the coefficients of the regression equation and a validation set to verify the prediction) and a jackknife procedure (*n* equations estimated on (*n*–1) subjects and applied for verification to the remaining patient). All statistical tests are two-tailed. A P value < 0.05 is considered as statistically significant.

■ RESULTS

Table II shows the clinical and biological characteristics of diabetic patients according to whether they presented ED or not. The group suffering from ED (Group I) was older, had longer diabetes duration and higher systolic blood pressure (BP), when compared to the group without ED (Group II). There was no significative difference for BMI, daily insulin dose, number of insulin injections and diastolic BP. HbA_1c and lipid profile were also comparable.

Univariate analysis shows that plasma adrenal androgens such as Δ_4, DHEA, DHEA-S were significantly decreased in patients with ED when compared with patients without ED *(Table III)*. Overt abnormalities (below normal range values) were present for Δ_4, DHEA and DHEA-S in 4 and 1, 15 and 5 and 6 and 0 patients with and without ED, respectively. We also observed in group I a trend for decreased plasma FT and significantly increased SHBG levels. Higher LH values were also recorded in the ED group, whereas an observed increase of FSH levels was not statistically significant *(Table III)*.

Multiple logistic regression analysis to determine whether androgens predict ED independently of other factors was performed using a model including age, duration of diabetes, daily insulin dose, FT, SHBG,

TABLE II. *Clinical and biological characteristics of patients with and without erectile dysfunction (ED).*

		Group I (ED present)	Group II (no ED)	*P*
n		24	27	–
age	(years)	56 ± 11	41 ± 13*	< 0.001
duration of diabetes	(years)	26 ± 10	14 ± 13	< 0.001
BMI	(kg/m^2)	26.0 ± 3.6	24.5 ± 3.9	0.017
blood pressure	(mm/Hg)			
systolic		143 ± 15	134 ± 13	*NS*
diastolic		86 ± 9	85 ± 9	*NS*
insulin dose	(U/day)	54 ± 17	52 ± 14	*NS*
scheme	1/2/3/4/CSII** (*n*)	1/2/2/16/3	0/3/5/17/2	*NS*
HbA_1c	(%)	9.0 ± 1.7	8.7 ± 1.2	*NS*
cholesterol	(mg/dl)	220 ± 49	207 ± 36	*NS*
LDL-cholesterol	(mg/dl)	131 ± 40	122 ± 41	*NS*
HDL-cholesterol	(mg/dl)	61 ± 18	62 ± 12	*NS*
triglycerides	(mg/dl)	137 ± 61	115 ± 63	*NS*
marital status	1/2/3/4*** (%)	71/12/4/12	74/0/0/26	*NS*
no/past/current smoking	(%)	25/33/42	44/26/30	*NS*
no/past/current alcohol history	(%)	54/4/42	67/0/33	*NS*

* mean ± SD. ** number of daily insulin injections or continuous subcutaneous insulin infusion. *** 1 = married, 2 = separated/divorced, 3 = widow, 4 = never married.

Δ_4, DHEA, DHEA-S and LH. The results show an independent association of ED with daily insulin dose (P=0.025) as well as with Δ_4 (P = 0.016), DHEA-S (P = 0.037), SHBG (P = 0.001), the robustness of the logistic regression equation being satisfactory with both cross-validation and jackknife procedures. Therefore, patients with ED present a decrease of Δ_4 and DHEA-S independently of age and duration of diabetes. Plasma DHT, estradiol, cortisol and prolactin levels were comparable in both groups. Thyroid function evaluated by TSH and FT_4 was also normal and similar in both groups.

As shown in *Table IV*, ED was significantly associated with a higher prevalence of other chronic diabetic complications such as retinopathy (P = 0.002), nephropathy (microalbuminuria and macroproteinuria) (P = 0.008) and neuropathy (P < 0.001). The ED group also had a higher prevalence of macroangiopathy (P = 0.001), ischaemic heart disease (P = 0.019), peripheral vascular disease (P = 0.004) and hypertension (P < 0.001).

As indicated in *Table V*, cardiovascular drugs were not more frequently used by ED patients, except ACE-inhibitors (P = 0.010). A significantly increased use in group I was evidenced for digestive tract prokinetics (P = 0.043), vitamins (P = 0.018) as well as antidepressant drugs (P = 0.007). It is however of interest to mention that in a subgroup with ED, after having excluded patients on antidepressants (n = 6), the androgen profile remained identical (data not shown). No significant correlation was evidenced between ED and smoking or alcohol consumption, nor was there any association with marital status.

■ DISCUSSION

Erectile dysfunction is a frequent complication in type 1 diabetes [1]. In our own survey, an impres-

TABLE III. *Hormonal profile in patients with and without erectile dysfunction.*

		Group I (ED present)	Group II (no ED)	*P*
n		24	27	–
Δ_4	(nM/L)	2.9 ± 0.5	3.8 ± 1.1	0.003
DHEA	(nM/L)	6.6 ± 3.4	11.4 ± 5.0	< 0.001
DHEA-S	(µM/L)	3.8 ± 2.2	5.8 ± 2.3	0.002
free testosterone	(nM/L)	0.23 ± 0.07	0.28 ± 0.10	*NS*
SHBG	(nM/L)	74.5 ± 25.2	56.9 ± 20.8	0.010
dihydrotestosterone	(nM/L)	0.83 ± 0.28	0.84 ± 0.35	*NS*
estradiol	(pg/ml)	22.4 ± 8.3	20.4 ± 4.5	*NS*
FSH	(mUI/ml)	13.6 ± 15.7	6.8 ± 5.2	*NS*
LH	(mUI/ml)	6.0 ± 4.6	3.5 ± 3.0	0.022
prolactin	(ng/ml)	8.0 ± 3.8	6.6 ± 4.6	*NS*
cortisol	(nM/L)	308 ± 117	297 ± 120	*NS*
TSH	(µU/ml)	1.3 ± 0.8	1.3 ± 1.0	*NS*
FT_4	(ng/dl)	1.26 ± 0.23	1.29 ± 0.22	*NS*

sively high prevalence of self-reported ED at 47% was observed, a figure close to that reported in 1995 by Brunner *et al.* in Austria [3]. Our diabetic subjects suffering from ED were older and had a longer duration of diabetes than those without ED. This is in agreement with previous observations, in particular the data of Klein *et al.* [1]. The role of poor glycaemic control as a potential determinant of risk for ED has been highlighted by various authors [1, 5, 7, 10], but was not observed in our patients on the basis of a single measurement of HbA_1c.

No relation was evidenced with smoking nor with alcohol consumption. The latter finding is in agreement with the data of Klein *et al.* [1]. Although con-

TABLE IV. *Chronic complications in diabetic patients with and without erectile dysfunction.*

		Group I (ED present)	Group II (no ED)	*P*
n		24	27	–
retinopathy	(%)	79	37	0.002
neuropathy	(%)	92	30	< 0.001
nephropathy	(%)	58	22	0.008
macroangiopathy	(%)	46	4	0.001
ischaemic heart disease	(%)	29	4	0.019
peripheral vascular disease	(%)	38	4	0.004
hypertension	(%)	79	22	< 0.001

TABLE V. *Pharmacological profile in patients with and without erectile dysfunction.*

	Group I (ED present)	Group II (no ED)	*P*
n	24	27	
β-blockers	5	2	*NS*
diuretics	3	2	*NS*
ACE-inhibitors	13	5	0.010
Ca-antagonists	7	3	*NS*
centrally acting antihypertensive	1	0	*NS*
hypolipidemic drug	5	1	*NS*
antiaggregants	6	2	*NS*
nitrates	3	1	*NS*
anticoagulants	1	0	*NS*
gastroprokinetics	4	0	0.043
anxiolytics/hypnotics	5	2	*NS*
antidepressants	6	0	0.007
vitamins	5	0	0.018

trary to previous reports, we found no significant difference in marital status between subjects with and without ED [1].

To date, very scarce information is available regarding the adrenal and gonadal hormonal profiles in type 1 diabetic males, in relation to ED. Our survey is, to the best of our knowledge, the first report where hormones or prohormones, from both gonadal and adrenal sources, were simultaneously recorded. For practical reasons, they were measured on a single occasion. Thomas *et al.* reported small intra- and intersubject variability for DHEA-S [11]. Our data show that minor androgen levels are decreased in type 1 diabetic subjects when ED is present. Indeed, when compared with diabetic patients without dyserection, men with ED had significantly lower concentrations of Δ_4, DHEA, DHEA-S as well as a tendency for reduced values of gonadal FT. The lower FT values in these patients were also associated with significantly higher SHBG concentrations, reflecting lower androgen exposure. These results could account for the higher plasma gonadotropins, in particular LH, that we observed in the presence of ED. On the other hand, DHT, estradiol and cortisol were comparable in both groups, as were prolactin and thyroid hormone levels.

Only one previous study in 1987 assessed gonadal function in diabetic men with ED (mainly type 2 patients) and showed decreased FT as well as increased urinary LH [12]. However, the drawbacks of the latter report were an absence of adrenal hormones determination as well as a lack of a diabetic control group with normal sexual function. On the other hand, a few and sometimes contradictory reports have dealt with sexual hormones in type 1 diabetic subjects, without considering, as in our own study, their distribution according to ED. Thus, Small *et al.* found normal values of basal adrenal hormones [13] while Loviselli *et al.* observed low levels of DHEA-S [14] as did Cough *et al.* in a group of poorly controlled patients (HbA_1 > 10%) [15]. Regarding gonadal hormones, Ali *et al.* also observed low serum and urinary testosterone levels as well as high FSH and LH in 100 type 1 diabetic males with neuropathy when compared with patients without neuropathy [16]. The latter results are in accordance with those of Handelsman *et al.* who also observed in 28 type 1 diabetic men high levels of gonadotropins, when compared to controls [17]. Low FT and DHT levels were also reported in 20 type 1 diabetic patients before glycaemic optimization [18] while Areola *et al.* reported decreased total testosterone and DHT levels but normal FSH and LH values in a group of type 1 diabetic adolescents [19].

In our study, as well as in previous reports, decreased adrenal and gonadal androgens levels could result from advancing age, as reported in non-diabetic individuals [20, 21]. We performed therefore a multiple logistic regression analysis which confirmed that diabetic patients with ED present a decrease of minor androgens (DHEA-S, Δ_4), independently of age and duration of diabetes.

Several drugs are well known for contributing to ED [22]. However, to our knowledge, ACE-inhibitors and antidepressant medications (which were more frequently used in our [ED +] patients) have no proven influence on adrenal steroidogenesis *per se*. Moreover, our data showed no difference in hormonal pattern after excluding subjects receiving an antidepressive therapy.

It remains to be investigated whether this decrease of hormones is the result of an altered androgen metabolism or of a diminished adrenal secretory rate, potentially due to a defect in the activity of the cytochrome P450C17 in the reticularis zona, as previously reported in elderly subjects with decreased DHEA-S [23]. Higher daily insulin dose, as shown in our patients with ED (when using multiple regression analysis), could also have an inhibitory effect on the adrenal enzymatic activitiy [14]. Finally, it cannot be excluded that low sexual activity by itself could also contribute to low levels of androgens. As far as FT levels are concerned, there was no significant association with ED in multivariate analysis. It is however of interest to note that diabetes-specific morphological testicular

alterations have been described in impotent diabetic men [12, 24]. Increased SHBG values were observed in our patients with ED as consequence of lower androgen concentrations. Older age could also contribute to the increased SHBG levels, as recently indicated [25], but the association with ED remained statistically significant even when controlled for age.

Others have observed slightly decreased levels of adrenal and gonadal hormones in non-diabetic patients with ED. Thus, very recently, Reiter *et al.* reported reduced levels of DHEA in males (< 60 years old) with ED when compared with age-matched healthy volunteers [26]. Moreover, Longcope *et al.* also observed that even a slight decrease in bioavailable testosterone could result in a decline in sexual fonction and a reduced ability to achieve spontaneous erections [25]. In this view, it is worth mentioning recent data suggesting that oral DHEA treatment may be of benefit in the therapy of ED [27]. Arlt *et al.* [28] and Baulieu *et al.* [29] also reported a significant increase in most libido parameters after oral DHEA supplementation in women with adrenal insufficiency and in normal aging women, respectively. Similarly, in diabetic men with reduced FT and increased LH, Murray *et al.* showed a clinical response to androgens [12]. Nevertheless, caution is needed and the place and benefits of androgen replacement (DHEA and/or testosterone) have to be further investigated in face of their potential side effects in type 1 diabetic patients in whom ED is clearly multifactorial.

Neuropathy and macroangiopathy are also important causes of ED. Our results also demonstrate, in accordance with previous studies [1, 5-8], that peripheral and autonomic neuropathy, as well as macrovascular disease were significantly more frequent among men with ED. Moreover, ED was associated with a higher prevalence of retinopathy and nephropathy. Finally as previously reported [1], we confirm an association between ED and high blood pressure levels. Depression problems were also more frequent in patients with ED. The direction causality association is unknown, either reflecting a cause of ED and/or its consequence, as patients with ED are more prone to suffer from depression [29].

In conclusion, a high frequency of ED was observed in a Belgian cohort of type 1 diabetic patients. ED was of multifactorial origin. However, our data show a possible association with low androgenicity, alongside other well-established etiological factors such as age, depressive mood, angiopathy and/or neuropathy. A confounding effect of these latter factors on low adrenal androgens cannot be formally ruled out from our data set, although we provide little convincing evidence that such is the case. Further studies are needed in order to determine the place of an eventual androgen replacement therapy in patients with ED.

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