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ORIGINAL ARTICLE

Deep neuromuscular block improves surgical conditions during laparoscopic hysterectomy

A randomised controlled trial

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BACKGROUND The benefit of inducing deep neuromuscular block to improve laparoscopic surgical conditions is controversial.

OBJECTIVE The goal of this study was to determine the depth of neuromuscular block needed to guarantee excellent operating conditions during laparoscopic hysterectomy.

DESIGN A randomised controlled trial.

SETTING A single-centre study performed between February 2011 and May 2012.

PATIENTS One hundred and two women of ASA physical status 1 or 2 gave consent to participate and were allocated randomly to one of two groups.

INTERVENTION Under desflurane general anaesthesia, patients in Group S (shallow block), neuromuscular blockade was induced by administration of rocuronium 0.45 mg kg^{-1} followed by spontaneous recovery or a rescue bolus dose of 5 mg if surgical conditions were unacceptable. In Group D (deep block), neuromuscular block was induced by administration of rocuronium 0.6 mg kg^{-1} and maintained by bolus doses of 5 mg if the train-of-four count exceeded two, using adductor pollicis electromyography.

MAIN OUTCOME MEASURES With a stable pneumoperitoneum (13 mmHg), the surgeon scored the quality of the surgical field every 10 min as excellent (1), good but not optimal (2), poor but acceptable (3) or unacceptable (4). The groups were compared using the Cochran–Armitage trend test. The level of neuromuscular blockade was recorded each time the surgical field score exceeded 1.

RESULTS For groups S and D, respectively, the maximum surgical field scores were 1 in 21 and 34 patients, 2 in 11 and 11 patients, 3 in 4 and 5 patients and 4 in 14 and 0 patients. A trend towards higher scores was demonstrated in group S ($P < 0.001$). Surgical field scores of 2, 3 and 4 occurred only when the train-of-four count was at least 1, 2 and 3, respectively.

CONCLUSION Inducing deep neuromuscular block (train-of-four count <1) significantly improved surgical field scores and made it possible to completely prevent unacceptable surgical conditions.

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Introduction

Neuromuscular blocking agents (NMBAs) are used routinely to provide the anaesthesiologist, the surgeon and the patient with adequate intubation and surgical conditions.[1] The benefit of maintaining deep neuromuscular block (NMB)[2] to improve intra-abdominal surgical operating conditions has seldom been investigated. During retropubic prostatectomy by laparotomy, King *et al.*[3] demonstrated that adequate surgical conditions were provided in many patients without an NMBA, although unacceptable conditions were more frequent than in patients who had received one. Wallace *et al.*[4] demonstrated that NMB is necessary to prevent high pressure events during laparoscopy and to improve surgical conditions. However, when Chassard *et al.*[5] questioned surgeons about the quality of relaxation when performing laparoscopic gynaecological procedures with

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or without NMB, they did not find any difference. Similarly, Williams *et al.*[6] demonstrated lower initial intra-abdominal pressure and better conditions for umbilical port placement in the paralysed group, with identical surgical conditions and intra-abdominal volume.

For several years, maintaining deep NMB to improve surgical conditions was controversial because of the risk and consequences related to awareness[7] and residual curarisation at the end of surgery.[8] Sugammadex is a new reversal agent that allows more rapid and complete reversal of deep rocuronium-induced NMB than neostigmine.[9] It offers the ability to maintain deep NMB throughout the operation and guarantee rapid reversal after the end of surgery, which may improve surgical access and enhance the visual field without delaying or compromising the safety of extubation.[10]

It is unclear whether deep NMB is required routinely to provide adequate surgical conditions during laparoscopy in patients who are properly anaesthetised using modern techniques. It is also not clear whether NMB must be maintained at a specific depth throughout the surgical procedure.

The goal of this randomised controlled study was to test the hypothesis that deep rocuronium-induced NMB decreases the frequency of unacceptable operating conditions during pelvic laparoscopy, as evaluated by a surgeon and confirmed by objective evidence of high insufflation pressure events. For each patient, the maximum surgical field score (i.e. the worst surgical condition) reached during the entire procedure was the primary outcome measure. We also aimed to determine the depth of NMB (secondary outcome measure) required to guarantee excellent operating conditions during pelvic laparoscopy.

MATERIALS AND METHODS

Following approval from the Institutional Ethical Committee (CHU Dinant Godinne om 050, Chairperson Pr P. Evrard, registered in November 2010 at the Belgian Federal Agency for Medicines and Health Products No. B03920109764) and with written informed consent, 102 patients were enrolled in the study between February 2011 and May 2012.

The study population included female patients between 18 and 80 years of age, with an American Society of Anesthesiologists' (ASA) physical status of 1 or 2, scheduled to undergo laparoscopic hysterectomy. We excluded patients suffering from renal or hepatic disease, neurological disorders or allergies to any of the medications used in the study protocol.

Randomisation to one of two treatment groups was performed using the minimisation procedure described by Taves[11] and generalised by Pocock and Simon,[12] which took four criteria into account for allocating treatments: age (18 to 40, 41 to 60, 61 to 80 years); BMI (<20, 20 to 24, 25 to 29, 30 to 34, 35 to 39 $kg\,m^{-2}$); type of surgery (laparoscopic hysterectomy, laparoscopic subtotal hysterectomy or laparoscopic subtotal hysterectomy and cervical sacrofixation); and number of pregnancies (0 to 5). Randomisation was undertaken using customised software.

Patients in Group S (shallow NMB) received a low intubating dose of rocuronium 0.45 $mg\,kg^{-1}$, followed by spontaneous recovery unless the surgical condition was graded 4 (see below). If necessary, neostigmine 50 $\mu g\,kg^{-1}$ was administered at the end of surgery to reverse any residual NMB. Patients in Group D (deep NMB) were given a higher intubating dose of rocuronium 0.6 $mg\,kg^{-1}$ followed by repeated 5-mg bolus doses each time the train-of-four (TOF) count exceeded 2 (this level of blockade commonly corresponds with the end of the clinical duration of NMBAs). Sugammadex 4 $mg\,kg^{-1}$ was administered at the end of surgery to reverse deep NMB.

The surgeon and all the clinical care nurses were blinded to the group assignment throughout the study. The senior anaesthesiologist in charge of the patient strictly observed the following protocol.

Anaesthesia and neuromuscular block management

Premedication comprised lorazepam 0.5 mg given 60 min before arrival in the operating theatre. The monitoring equipment consisted of a three-lead electrocardiogram, noninvasive blood pressure measurement and finger pulse oximetry. An intravenous line containing Ringer lactate solution was inserted into a major left forearm vein.

The anaesthesiologist placed the neuromuscular transmission monitor on the right hand according to good clinical research guidelines,[2] and both arms were placed alongside the body. Stimulating electrodes were applied to the wrist along the ulnar nerve (E152, IMMED; Bio-Protech Inc, Gangwon-do, Korea). We used electromyography (EMG) to record the muscular responses [NeuroMuscular Transmission (NMT) module; GE Healthcare, Buckinghamshire, UK]. A recording electrode was placed on the thenar eminence and over the belly of the adductor pollicis muscle, and the indifferent electrode was placed on the first phalanx of the thumb. The neutral ground electrode was placed over the carpal ligament, on the inner surface of the wrist.

After 3 min of 100% oxygen exposure through a facemask, anaesthesia was induced with intravenous sufentanil 0.15 $\mu g\,kg^{-1}$, ketamine 0.5 $mg\,kg^{-1}$ and propofol 2 to 3 $mg\,kg^{-1}$ and maintained with desflurane 6 to 7% to target a minimum alveolar concentration (MAC) of 1 (Zeus Infinity empowered anaesthesia machine; Drägerwerk AG and Co, Lübeck, Germany). After the patient lost consciousness, ventilation was controlled

manually. The randomised dose of rocuronium was then administered, and tracheal intubation was performed when the evoked muscular responses ceased. Controlled mechanical ventilation was started (a semi-closed circuit, 40 to 45% oxygen in air) and adjusted to produce an end-tidal carbon dioxide concentration within the range of 4.0 to 4.7 kPa. During the study period, the temperatures of the oropharynx and right hand were maintained above 36°C and 32°C, respectively.

The automatic calibration sequence of the NMT module was initiated under general anaesthesia before administration of the NMBA: a search for the supramaximal stimulation level, calibration of the twitch height, followed automatically by 2-Hz TOF stimulations every 20 s. The EMG responses (TOF count, T1 and TOF ratio) were recorded online and displayed on the monitoring screen. In the event of suboptimal surgical conditions in the absence of a TOF response, a posttetanic count (PTC) was undertaken, and TOF stimulation automatically resumed after 3 min.

After the trachea had been intubated and the patient placed on the operating table horizontally with the legs in the lithotomy position, we determined the haemodynamic baseline before the surgical procedure began. During the operation, if the heart rate and/or the arterial pressure decreased by more than 20% from the baseline, we administered a fluid challenge (250 ml of Ringer lactate solution) and, if necessary, ephedrine 5 mg. If heart rate and/or blood pressure increased by more than 20%, we administered sufentanil 5 μg and, if that was insufficient, the concentration of desflurane was increased to 1.2 MAC for the remainder of the procedure.

Postoperative pain and nausea were minimised by administering paracetamol 1 g, tramadol 1 mg kg^{-1}, alizapride 50 mg and dehydrobenzperidol 0.625 mg 30 min before the end of surgery. We added butylhyoscine 10 mg to prevent spasms caused by the urinary catheter.

Surgery and evaluation of surgical conditions

The surgical operation began with intraperitoneal insufflation of CO_2 with a Veress needle at the umbilicus. The insufflation pressure was set and monitored at 13 mmHg throughout the procedure. Three additional ports were placed in the suprapubic area. The patient was placed in the maximal Trendelenburg position at 45° for the duration of the surgery (Maquet, Ardon, France). A cannula was placed in the cervix for appropriate uterine mobilisation. The round ligaments were coagulated and cut with scissors. When adnexectomy was required, the infundibulopelvic ligament was also coagulated and cut. The uterine vessels were dissected with bipolar coagulation and cut. When subtotal hysterectomy was performed, unipolar scissors were used to cut the cervix and separate it from the corpus, which was removed through a 15-mm trocar after morcellation. When sacrofixation was performed, a monofilament polypropylene mesh was placed in the cervix and the opposite side of the mesh fixed to the anterior sacral ligament using a 5-mm tacking device. When total hysterectomy was performed, a vaginal incision was made around a uterine mobiliser equipped with a vaginal cupula. The completely freed uterus was then pulled into the vagina and morcellated if necessary. The vagina was sutured laparoscopically using one running suture. The pelvis was then rinsed with isotonic saline solution and a pelvic drain left in the pouch of Douglas for 24 h.

Once the camera was installed through the umbilical port and every 10 min thereafter, or at any time at which the surgical conditions were deemed to be inadequate, the senior surgeon in charge of the study, who had ample experience in the surgery being performed,[13,14] assessed the exposure of the surgical field on a four-grade numerical scale that has been previously used in the literature:[3,5,6] excellent (1); good but not optimal (2); poor but acceptable (3); or unacceptable and impossible to continue the operation (4).

The surgeon was blinded to the NMT monitor and was accustomed to conducting such evaluations on a routine basis before the study began. We recorded the NMB level corresponding to all evaluations with a score greater than 1. If condition 4 was reported, a relief bolus dose of rocuronium 5 mg was administered immediately, irrespective of the group.

The entire laparoscopic procedure and the intra-abdominal pressure levels were recorded to enable any subsequent analysis that might prove necessary.

At the end of the surgery, the abdominal cavity was emptied of gas and the abdominal ports were removed. The patient was placed flat, and the laparoscopic incisions were sutured.

Neostigmine or sugammadex was administered depending on the group and the level of the NMB, and their effects were monitored until a TOF ratio higher than 0.9 was obtained before the administration of desflurane was interrupted and the patient was awakened and the trachea extubated. Patients were then transferred to the postanaesthesia care unit.

Statistics

The individual maximum surgical field scores obtained in the two groups were compared with each other using the Cochran–Armitage trend test. Treatment failure was defined as a grade 4 surgical field score at any time during surgery. The total sample size enabling the detection of a proportion of treatment failure between group D (0%) and group S (25%) with an α error rate of 0.05 and a power of 0.90 was calculated as 86 patients using G*Power 3 software.[15] We randomised 51 patients per group.

Statistical tests were performed using SPSS 15.0 statistical software (SPSS Inc., Chicago, Illinois, USA). *P* values less than 0.05 were considered statistically significant.

Results

Of the 100 patients initially enrolled, two were excluded after randomisation because of an intraoperative violation of the protocol (inappropriate magnesium administration at induction, and failure to apply the protocol) and were prospectively replaced by two other patients, also randomised. The final analysis included 100 patients (50 in group S and 50 in group D) (Fig. 1). The details of the patients' characteristics, which were similar in each group, are summarised in Table 1.

Respectively for groups S and D, the mean ± SD duration of surgery was 74 ± 23 and 69 ± 22 min, allowing for 348 and 306 surgical field scores, the average values of which were 1.3 ± 0.8 and 1.1 ± 0.4. The maximum field scores in Groups S and D, respectively, were 1 in 21 (42%) and 34 (68%) patients; 2 in 11 (22%) and 11 (22%) patients; 3 in four (8%) and five (10%) patients; and 4 (treatment failure) in 14 (28%) and 0 patients. Most level 3 surgical field scores and all of the level 4 scores were associated with a high pressure alarm from the insufflator. The results are shown in Fig. 2. The Cochran–Armitage trend test confirmed the trend towards higher (i.e. worse) scores in group S ($P < 0.001$).

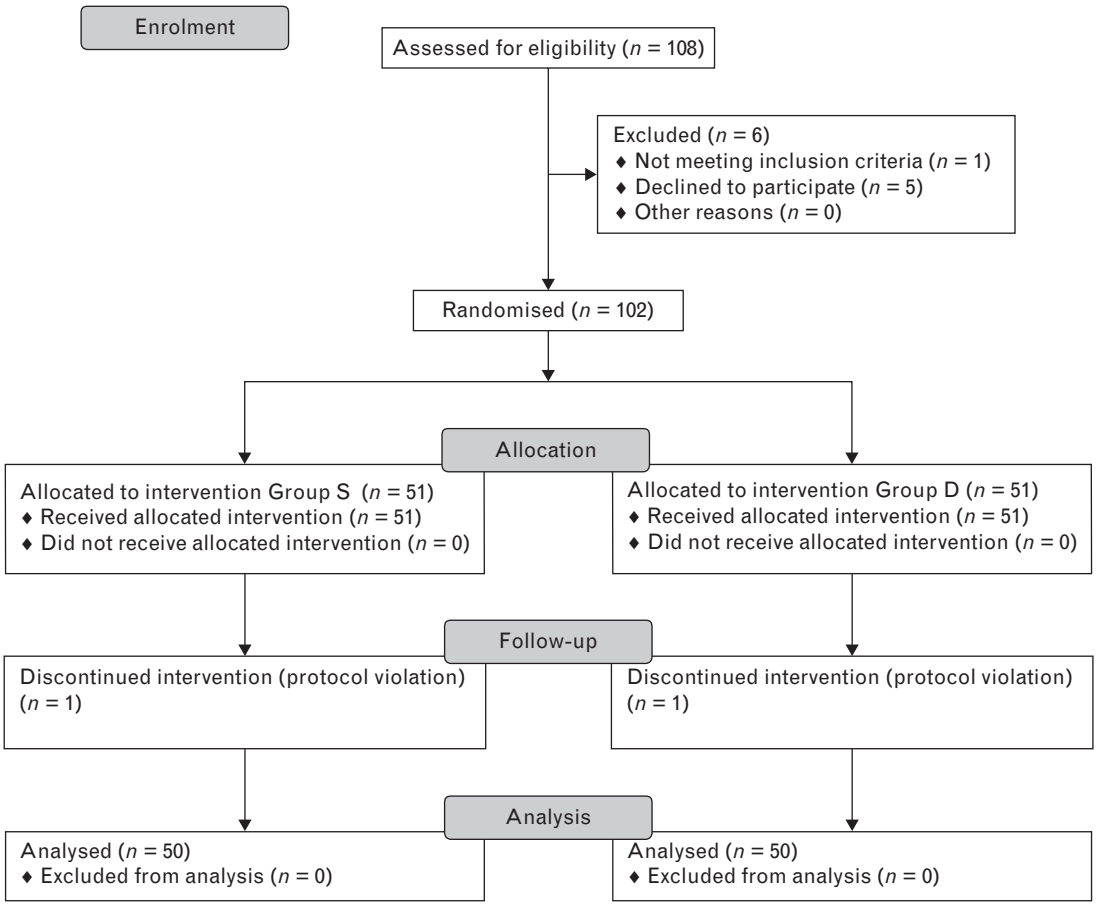
Table 1 Characteristics of the patient groups

	Group S	Group D
Age (years)	51.7 ± 10.9	49.9 ± 9.8
BMI (kg m^{-2})	25.9 ± 4.9	26.7 ± 5.3
Type of surgery		
LH	43	43
LASH	2	3
LASH and sacrofixation	5	4
Number of pregnancies		
0/1/2/3/4/5 or more	7/5/24/6/7/1	2/16/19/11/6/2

Data are presented as mean ± SD or numbers of patients. LASH, laparoscopic subtotal hysterectomy; LH, laparoscopic hysterectomy.

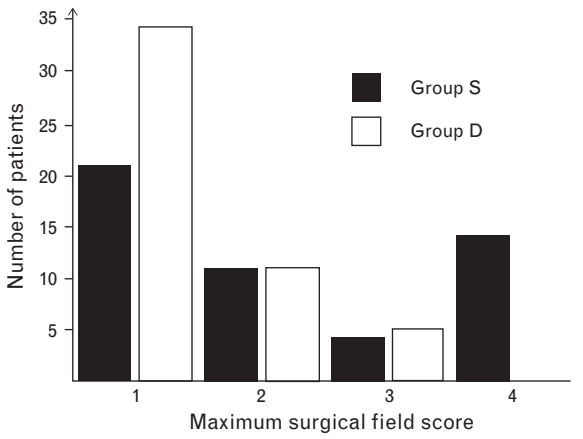
The levels of NMB monitoring recorded at the times at which suboptimal surgical conditions occurred are shown in Fig. 3. Surgical field scores 2, 3 and 4 occurred only when the TOF count was at least 1, 2 and 3, respectively.

Fig. 1



CONSORT flow diagram.

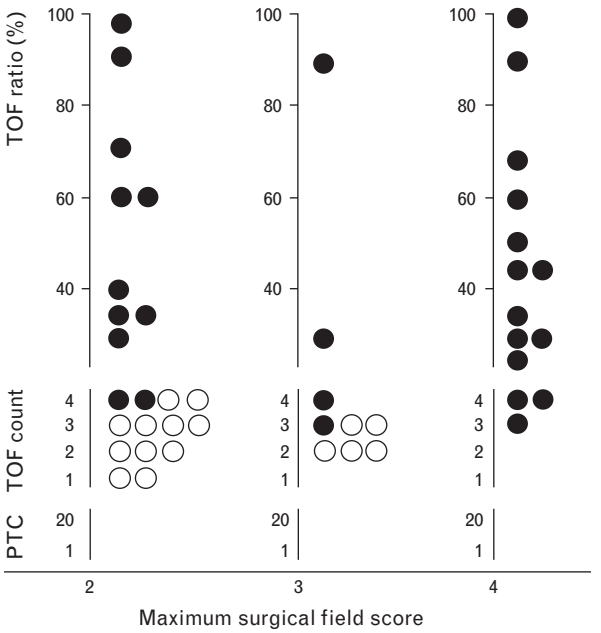
Fig. 2



Maximum surgical field scores in Group S (shallow block) and Group D (deep block). See text for details. The Cochran–Armitage trend test confirmed the trend towards higher scores in group S ($P < 0.001$).

Because of the interruption of the procedure and the removal of the intra-abdominal instruments in cases in which unacceptable surgical conditions occurred (score 4), no complication occurred during surgery or during the postoperative period.

Fig. 3



Levels of neuromuscular block recovery when suboptimal surgical field scores occurred. The posttetanic count (PTC), train-of-four (TOF) count and TOF ratio are depicted at the time when the maximum surgical field score was recorded in each patient if surgical conditions were suboptimal (score 2, 3 or 4), which never occurred at a TOF count <1. See text for details. ● Group S (shallow block); ○ Group D (deep block).

Discussion

The results of this study confirmed the hypothesis that deep rocuronium-induced NMB significantly decreased the incidence of unacceptable surgical conditions. Although excellent operating conditions were frequently obtained without intermittent bolus doses of rocuronium, maintaining deep NMB significantly improved the surgical conditions and made it possible to prevent completely abdominal wall muscular contractions that induce poor or unacceptable surgical conditions. Under general anaesthesia with desflurane, pelvic laparoscopy conditions were always excellent if no TOF response was observed in the EMG of the adductor pollicis.

Comparing deep NMB with placebo during retropubic open prostatectomy, King *et al.*[3] concluded that the use of muscle relaxants in adequately anaesthetised patients might not be indicated because isoflurane-fentanyl anaesthesia alone produced a good to excellent surgical field in approximately two-thirds of patients. Conversely, we demonstrated that only deep NMB significantly improved the laparoscopic surgical field and prevented difficult or unacceptable surgical conditions that could interrupt the procedure or pose a threat to patient safety.

Deep NMB is defined as the depth of blockade measured at the adductor pollicis between PTC 1 up to but not including a TOF count of 1.[2] The major indications for deep NMB are tracheal intubation and surgery.[1] During surgery, hypnotics, analgesia and deep NMB guarantee the absence of unexpected movement by the patient at a time when precision is critical. NMBAs induce a deep dose-dependent relaxation that allow the muscles to stretch to their maximum length more effectively than with other anaesthetic techniques.[16] The muscle relaxation contributes to providing the surgeon with the best possible working space, particularly during laparoscopic procedures. The effects of NMBAs on patients vary considerably among individuals, and postoperative residual curarisation exposes patients to an additional risk.[8] Consequently, quantitative neuromuscular transmission monitoring has been recommended to adjust the depth of the block precisely during surgery and to exclude any residual blockade before extubation of the trachea.[17,18] Specifically, a deep level of NMB at the adductor pollicis (PTC 1 to 5) has been recommended during surgery,[19,20] and a TOF ratio higher than 0.9 was determined as the minimum level to safely perform tracheal extubation.[8]

Our study demonstrated that deep NMB prevents any untimely contractions of the abdominal wall during laparoscopy. Suboptimal operating conditions only occurred after the reappearance of the TOF responses, just above the block level defined as deep.[2] Conversely, below this level of the reappearance of a TOF response, the operating conditions were always excellent. Consequently, in the specific conditions of our study

(pelvic laparoscopy under anaesthesia with desflurane in the lithotomy and Trendelenburg positions, and pneumoperitoneum of 13 mmHg), it does not appear necessary to deepen the NMB to PTC 1 to 5 to ensure adequate abdominal relaxation.

In group D, our protocol allowed NMB to recover to a TOF count of 2 before a further bolus of rocuronium was administered to reinduce deep NMB. Higher levels of recovery (TOF count of 3 or 4) were recorded on a few occasions in which the monitor immediately reached that level or during the time required for the new bolus administration to become effective (see Fig. 3). Once the upper limit of deep NMB had been exceeded, suboptimal operating conditions occurred (scores 2 and even 3), even in group D. This finding confirmed that the maximum admissible level of recovery to maintain excellent operating conditions in all of the patients was a TOF count at the adductor pollicis of less than 1.

The occasional difficulties encountered by the surgeon that caused suboptimal evaluations (scores 2, 3 and 4) were always linked to the muscle tone of the abdominal wall. Cyclical contractions (scores 2 or 3) or sudden contractions (scores 3 or 4, with high pressure events) of the abdominal wall caused untimely movements of the surgical instruments passing through it. These movements cause the surgeon's work to be more difficult or even dangerous, risking injury to the patient's intraperitoneal organs with needles, scissors or electrocoagulation devices. Preventing such movements is a matter of patient safety.

Laparoscopic surgeons recommend a low insufflation pressure (8 rather than 12 to 15 mmHg) to reduce postoperative complications including pain and pulmonary complications, and length of hospital stay.[21,22] It has not been clearly established whether this low insufflation pressure impairs surgical conditions or increases the duration of surgery or the risk of complications. It is probable that inducing and maintaining deep NMB makes it easier to obtain a satisfactory intraperitoneal working space despite a lower insufflation pressure.[23] This finding has yet to be confirmed by further studies.

Different surgical approaches (laparotomy or laparoscopy, upper abdomen or pelvic areas) do not have the same requirements. Numerous elements are involved in establishing optimal operating conditions, including the depth of anaesthesia, the adequacy of analgesia, deep NMB, the position of the patient on the operating table, the intraperitoneal insufflation pressure, a previous history of pregnancy or laparoscopic surgery and various aspects of the patient's anatomy (including obesity, tumour or intra-abdominal disease).[16,23–25] In this study, we aimed to isolate the influence of deep NMB. In clinical practice, the combination of various actions dependent on the circumstances contributes towards improving the operating conditions on a case-by-case basis.

Our study has some limitations. The four-grade rating scale used to evaluate the surgical field subjectively has not been validated for this purpose; however, it has been used in the past by other, similar studies.[3,5,6] Recently, Martini *et al.*[26] investigated surgical conditions during laparoscopic prostatectomy or nephrectomy. Although demonstrating results with a similar trend, they used a different inverted 5-grade rating scale, making proper comparison with our study difficult. Future studies should determine the best way to rate laparoscopic access, field exposure and surgical conditions.

Clinically relevant concentrations of halogenated vapours potentiate the depth of NMB.[27] Different anaesthetic techniques might alter the results.[2] The results of our study should be comparable with those of King *et al.*[3] and Williams *et al.*,[6] who used isoflurane-based anaesthesia, and our technique was similar to clinical practice in many hospitals.

We monitored neuromuscular transmission using EMG of the adductor pollicis muscle, a validated method that can be used with the hand alongside the body without compromising the quality of the measurement.[2] Acceleromyography, a more widely used technique, is less precise than EMG and overestimates NMB recovery.[28] Maintaining a TOF count less than 1 to guarantee excellent operating conditions (during pelvic laparoscopy) is probably a valid recommendation for this method as well, although this point should be confirmed by further studies.

Conclusion

Permanent optimal surgical conditions were obtained when deep NMB was maintained throughout laparoscopic hysterectomy. The deep block prevented the occurrence of any unacceptable surgical conditions, which were occasional but could be deleterious for the patient. Using EMG under general anaesthesia with desflurane, the level of NMB to maintain optimal surgical conditions was demonstrated by a TOF count less than 1.

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Conflicts of interest: Philippe E. Dubois and Olivier Donnez have received honoraria in the last 2 years for lectures and travel expenses to meetings organised by the Merck company, but there were no conflicts of interest in the preparation of the present manuscript. The other authors had no conflict of interest.

Presentation: preliminary data from this study were presented as poster presentations at the annual congress of the French Society of Anaesthesia in Paris on 22 September 2012, and at the Belgian Society of Anaesthesiology (resident meeting) on 29 September 2012.

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