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Abstract

Background:

In recent literature, it has been suggested that deep neuromuscular block (NMB) improves surgical conditions during laparoscopy; however, the evidence supporting this statement is limited, and this was not investigated in laparoscopic bariatric surgery. Moreover, residual NMB could impair postoperative respiratory function. We tested the hypotheses that deep NMB could improve the quality of surgical conditions for laparoscopic bariatric surgery compared with moderate NMB and investigated whether deep NMB puts patients at risk for postoperative respiratory impairment compared with moderate NMB.

Methods:

Sixty patients were evenly randomized over a deep NMB group (rocuronium bolus and infusion maintaining a posttetanic count of 1–2) and a moderate NMB group (rocuronium bolus and top-ups maintaining a train-of-four count of 1–2). Anesthesia was induced and maintained with propofol and remifentanil. The primary outcome measures were the quality of surgical conditions assessed by a single surgeon using a 5-point rating scale (1 = extremely poor, 5 = optimal), the number of intra-abdominal pressure increases >18 cmH2O and the duration of surgery. Secondary outcome measure was the postoperative pulmonary function assessed by peak expiratory flow, forced expiratory volume in 1 second, and forced vital capacity, and by the need for postoperative respiratory support. Data are presented as mean ± standard deviation with estimated treatment effect (ETE: mean difference [95% confidence interval]) for group comparisons.

Results:

There was no statistically significant difference in the surgeon's rating regarding the quality of the surgical field between the deep and moderate NMB group (4.2 ± 1.0 vs 3.9 ± 1.1; P = .16, respectively; ETE: 0.4 [-0.1, 0.9]). There was no difference in the proportional rating of surgical conditions over the 5-point rating scale between both groups (P = .91). The number of intra-abdominal pressure increases >18 cmH_2O and the duration of surgery were not statistically different between the deep and moderate NMB group (0.2 ± 0.9 vs 0.3 ± 1.0; P = .69; ETE: -0.1 [-0.5, 0.4] and 61.3 ± 15.1 minutes vs 70.6 ± 20.8 minutes; P = .07, ETE: -9.3 [-18.8, 0.1], respectively). All the pulmonary function tests were considerably impaired in both groups when compared with baseline (P < .001). There was no statistically signifcant difference in the decrease in peak expiratory flow, forced expiratory volume in 1 second, and forced vital capacity (expressed as % change from baseline) between the deep and the moderate NMB group.

Conclusions:

Compared with a moderate NMB, there was insuffcient evidence to conclude that deep NMB improves surgical conditions during laparoscopic bariatric surgery. Postoperative pulmonary function was substantially decreased after laparoscopic bariatric surgery independently of the NMB regime that was used. The study is limited by a small sample size.
(Anesth Analg 2017;124:1469–75)

Introduction

Laparoscopic bariatric surgery poses special demands on the anesthesiologist and surgeon. The surgeon requires a good visualization of the surgical field to perform the operation, whereas the anesthesiologist is concerned with adequate postoperative respiratory function in these morbidly obese patients. In recent literature, it has been suggested that deep neuromuscular block (NMB) improves surgical conditions during laparoscopy. The evidence supporting this statement, however, is limited[1] and pertains mainly to laparoscopic surgery for cholecystectomy,[2,3] gynecologic,[4,5] and urologic[6] disorders. The "pro/con" debate pertaining to the advantages of deep NMB is still ongoing.[7,8] Because laparoscopy significantly reduces the time span for recovery from intraoperative NMB, deep NMB puts the patient at risk for residual postoperative NMB and associated respiratory complications.

Jones et al[9] found that recovery from a rocuronium induced posttetanic count (PTC) of 1 to 2 to a train-of-four ratio (TOFR) of 0.9 with a single dose of neostigmine 70 μg/kg takes 50 minutes, which is considerably longer than the time interval from the end of pneumoperitoneum to the end of skin closure. Even minimal residual NMB with a TOFR of 0.8 is associated with impaired respiratory function, as witnessed by reductions of forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) in healthy volunteers.[10,11] Moreover, a postoperative TOFR <0.7 may be associated with adverse events.[12–14]

Obese patients are at an even greater risk for these postoperative respiratory complications. In a recent study, 100% of patients after bariatric surgery had at least one hypoxic event (oxygen saturation <90% for more than 30 seconds).[15] Restrictive ventilatory defects clearly are associated with body mass index (BMI) and obesity hypoventilation syndrome. Because respiratory failure is responsible for 12% of mortalities after bariatric surgery, optimal respiratory care for these patients is of primary importance.[16] Adequate reversal of NMB plays an important role herein. Sugammadex is a cyclodextrin molecule that encapsulates and inactivates rocuronium and vecuronium, allowing a dose-dependent reversal of deep NMB

within 5 minutes.[9] A first indication that deep NMB and reversal with sugammadex could be beneficial in morbidly obese patients recently was presented by Carron et al[17] in a high-risk cardiac patient undergoing a laparoscopic gastrectomy.

In the present randomized, double-blind, clinical trial, we build on these findings and are the first to test the hypotheses that deep NMB could improve the quality of surgical conditions for laparoscopic bariatric surgery compared with moderate NMB. The primary objective of this study was to analyze the effect of deep NMB on surgical conditions (using a 5-point rating scale, the number of intra-abdominal pressure rises >18 cmH2O, and the duration of surgery) compared with a moderate NMB. Because deep NMB puts patients at risk for residual postoperative NMB, we tested a second hypothesis that deep NMB could decrease postoperative pulmonary function. Therefore, the secondary objective was to analyze the effect of deep NMB on peak expiratory flow (PEF), FEV1, and FVC compared with moderate NMB and to assess the need for postoperative respiratory support. This study was funded by a grant from Merck, Sharp & Dohme (grant nr. 8646-085 MISP40977).

METHODS

Study Design

In this single-center, randomized, double-blind, clinical trial, we investigated the effect of deep versus moderate NMB with rocuronium on surgical conditions and postoperative respiratory function. The trial was conducted at the Ziekenhuis Oost-Limburg after approval by the local ethics committee (Comité Medische Ethiek Ziekenhuis Oost-Limburg) and was registered on clinicaltrials.gov (registration number: NCT01748643) and EudraCT (registration number: 2012-005533-37) before patient enrollment. The study started in April 2013 and ended in January 2015 when the objective of 60 enrolled patients had been reached. Written informed consent was obtained from all patients before inclusion in the trial.

Participants

Patients were recruited from a multidisciplinary weight loss program in our hospital. Eligible patients were older 18 years of age and were obese or morbidly obese as defined by a BMI of >30 kg/m^2 and >40 kg/m^2, respectively, and were scheduled to undergo a laparoscopic gastric bypass surgery. Patients with an American Society of Anesthesiologist physical status class IV or greater were excluded from the study. Inclusion and exclusion criteria are presented in Table 1.

Table 1. Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
1. Obese or morbidly obese as defned by a BMI > 30 and >40 kg/m^2, respectively	1. Neuromuscular disorders
2. American Society of Anesthesiologists physical status class I, II, or III	2. Allergies to, or contraindication for muscle relaxants, neuromuscular reversing agents, anesthetics, narcotics
3. Able to give written informed consent	3. History of malignant hyperthermia
	4. Pregnancy or lactation
	5. Renal insuffciency defned as serum creatinine of 2× the upper normal limit, glomerular fltration rate <60 mL/min, urine output of <0.5 mL/kg/h for at least 6 h
	6. Chronic obstructive pulmonary disease GOLD classifcation 2 or higher
	7. Clinical, radiographic or laboratory fndings suggesting upper or lower airway infection
	8. Congestive heart failure
	9. Pickwick syndrome
	10. Psychiatric illness inhibiting cooperation with study protocol or possibly obscuring results

Interventions

The surgical and anesthesia technique were the same for both study groups except for maintaining and reversing NMB. In the deep NMB-group, a PTC of 1 to 2 twitches was maintained, and NMB was reversed with sugammadex at the end of surgery. In the moderate NMB group, a TOF count of 1 to 2 was maintained and NMB was reversed with a combination of neostigmine and glycopyrolate at the end of surgery. All patients were operated by one abdominal surgeon, who was experienced in laparoscopic gastric bypass surgery. Pneumoperitoneum was obtained by insufflating CO_2 through a Veress needle until a steady pressure of 18 mm Hg was reached, and this pressure was maintained throughout the procedure.

After we applied standard hemodynamic and respiratory monitoring (3-lead ECG, noninvasive blood pressure manometer, pulse oxymeter), an 18-gauge intravenous cannula was placed in a forearm vein and an infusion with Plasmalyte A was started. After 3 minutes of preoxygenation (100% oxygen by mask) in slight anti-Trendelenburg position, anesthesia was induced with propofol 1% (Diprivan 1%; AstraZeneca, Zoetermeer, the Netherlands) and remifentanil (Ultiva; GlaxoWellcome, Barnard Castle, UK) until the patient lost consciousness. NMB was monitored by acceleromyography of the adductor pollicis muscle with the TOFWatch SX[18] (Organon, Dublin, Ireland): after we degreased the skin, 2 electrocardiogram electrodes were placed over the ulnar nerve at the wrist. After calibration and supramaximal stimulation, an intubation dose of rocuronium (Esmeron, Merck, Sharpe and Dohme, Hoddesdon, UK) of 0.6 mg/kg (lean body mass) was administered and the patient was intubated. Assessment of NMB was performed every 5 minutes.

Anesthesia was maintained throughout the duration of surgery with propofol 1% target-controlled infusion (Alaris, CareFusion, U.K. Marsh model) and remifentanil 0.15–0.5 μg/kg/min. Dosing was left at the discretion of the attending anesthesiologist. Patients were ventilated with an oxygen/air mixture of 50:50 to achieve an end-tidal CO_2 of 30–35 mm Hg. Cefazoline 2 g (Cefazoline Mylan, Mylan, Athens, Greece) and paracetamol 1 g (Perfusalgan; BristolMyers Squibb, Agen, France) were administered after intubation. We used the definitions by Kopman and Naguib[1] for the depth of NMB (deep NMB: PTC >1 but no response to a TOF stimulation; moderate NMB: TOF count of 1–3). In the deep NMB group, a continuous rocuronium infusion of 0.6 mg/kg (lean body mass)/h was started and titrated to a PTC of 1 to 2 twitches. At the end of surgery, NMB was reversed with sugammadex 4 mg/kg (Bridion; Merck, Sharpe & Dome, Hoddesdon, UK) in the deep NMB group. In the moderate NMB group, top-ups of rocuronium (10 mg) were given to maintain a TOF count of 1 to 2.

At the end of surgery, NMB was reversed with a combination of neostigmine 50 μg/kg (lean body mass) and glycopyrolate (Robinul-Neostigmine; Eumedica, Brussels, Belgium). In both groups, patients were extubated when the TOF ratio was >0.9. Remifentanil infusion was stopped 15 minutes before the conclusion of surgery. At the same time, fentanyl 100 μg (GlaxoSmithKline, Torrile, Italy) was administered to provide initial postoperative analgesia.

Outcome Measures

The primary outcome measure was the overall quality of surgical conditions during the entire laparoscopy procedure assessed by a single surgeon using a 5-point rating scale (1 = extremely poor, 2 = poor, 3 = acceptable, 4 = good, 5 = optimal)[6] at the end of the surgery. Although used in previous studies, the 5-point surgical rating scale remains a subjective tool and different surgeons could rate the quality of the surgical conditions differently. Therefore, we added 2 more objective outcome parameters to investigate the surgical conditions.

One such parameter was the number of intra-abdominal pressure increases >18 cmH_2O not related to manipulation of the abdominal wall (eg, insertion of trocars) as measured by the peritoneal CO_2 insufflator, and the other one was the duration of surgery measured from the first skin incision to completion of skin closure.

Secondary outcome measures were the postoperative pulmonary function and the need for postoperative respiratory support. Pulmonary function was assessed by measuring PEF, FEV1, and FVC with the Vitalograph micro model 6300 (Buckingham, UK) electronic portable peak flowmeter. Portable peak flowmeters give highly reproducible data, and the technology on which the Vitalograph is based has the least over-reading in the mid- and low-flow range.[19] A mean of 3 measurements in the upright posture in bed (upper body raised 45°) before and after surgery was used for statistical analysis. Baseline pulmonary function tests were performed during the preoperative anesthesiology consultation. Postoperative tests were performed in the recovery room. A modified observer's assessment of alertness scale[20] was determined at the time of postoperative pulmonary function measurements to exclude sedation as a cause of reduced pulmonary function. Respiratory function was furthermore assessed by the need for reintubation or noninvasive respiratory support such as continuous positive airway pressure or bilevel positive airway pressure. Other registered parameters were as follows: total dose of propofol, remifentanil and rocuronium, and time interval from TOFR >0.9 to pulmonary function tests.

Blinding and Randomization

Patients were randomized within 3 strata (BMI 30–34 kg/ m^2, BMI 35–39 kg/m^2, BMI >40 kg/m^2) so that the treatment assignments were balanced within each stratum. Randomization was performed by the anesthesiologist responsible for the anesthesia and consisted of pulling a closed envelope from 1 of the 3 boxes labeled "BMI 30–34 kg/m^2," "BMI 35–39 kg/m^2," or "BMI > 40 kg/m^2." Each box contained an equal amount of cards reading deep and moderate NMB in closed envelopes. The cards were made unreadable by wrapping them in aluminum foil. The anesthesiologist performing the anesthesia was not involved in outcome assessment.

The patient and the surgeon were both blinded to the treatment. To blind the surgeon, each patient had a syringe marked "rocuronium" in a syringe pump attached to the intravenous line. In the moderate NMB group, the syringe contained normal saline 0.9%, whereas in the deep NMB group, the syringe contained actual rocuronium. During surgery, the "rocuronium" syringe pumps in both groups were operated by the anesthesiologist as if they contained the active drug. The hand of the patient used to monitor NMB was hidden from the view of the surgeon under the sterile drapes.

Statistical Methods

All analyses were preceded by tests for normality (D'Agostino and Pearson).[21] Differences in the primary outcome measure (quality of surgical conditions) assessed by a 5-point surgical rating scale, the number of intra-abdominal pressure rises >18 cmH_2O, and the duration of surgery were analyzed by a Mann-Whitney U test. Differences in proportion in the different surgical ratings between the 2 study groups also were examined with the Mann-Whitney U test. No adjustment was made to the significance criterion for having 3 primary outcome variables. The secondary outcome measure was assessed by comparing the mean percent change from baseline in PEF, FEV1, and FVC in both groups with the Student t test. Data are presented as mean ± standard deviation with estimated treatment effect (ETE: mean difference [95% confidence interval]) for group comparisons. $P < .05$ was considered statistically

significant. Statistical analyses were performed using Prism 5.0d (GraphPad Software, San Diego, CA). The clinically meaningful difference in quality of surgical conditions on a 5-point surgical rating scale has not been determined. We proposed that a difference of 2 points on a 5-point rating scale could be considered clinically meaningful. To detect this difference with a standard deviation of 3 and a power of 90% with a significance level set at α = 0.05, we calculated that a sample size of 24 patients per group would be needed.[22] To compensate for an estimated dropout rate of 20%, we included 30 patients per group.

RESULTS

Study Population

Seventy-four patients were assessed for eligibility. Fourteen patients were excluded: 11 patients declined to participate, 1 patient had renal insuffciency, and 2 patients had previous gastric banding surgery. Sixty patients were randomized, 30 to each treatment group. Each treatment group contained an equal amount of patients per stratum: 1 patient in the BMI 30–34 kg/m$_2$ stratum, 20 patients in the BMI 35–39 kg/ m^2 stratum, and 9 patients in the BMI >40 kg/m$_2$ stratum. All patients received the allocated treatment and none were lost to follow-up. In total, 60 patients completed the study (Figure 1). The baseline characteristics of the 2 study groups were similar (Table 2).

Table 2. Baseline Characteristics of the Study

Characteristic	Deep NMB Group (n = 30)	Moderate NMB Group (n = 30)
Age (y)	41 ± 13	42 ± 11
Sex no. (%)		
Male	8 (27%)	4 (13%)
Female	22 (73%)	26 (87%)
BMI (kg/m2)	40 ± 3	41 ± 7
Preoperative pulmonary function tests		
PEF (L/min)	314 ± 109	276 ± 81
FEV1 (L)	2.4 ± 0.9	2.2 ± 0.6
FVC (L)	3.0 ± 0.9	2.7 ± 0.8
FEV1/FVC	84 ± 8	82 ± 9

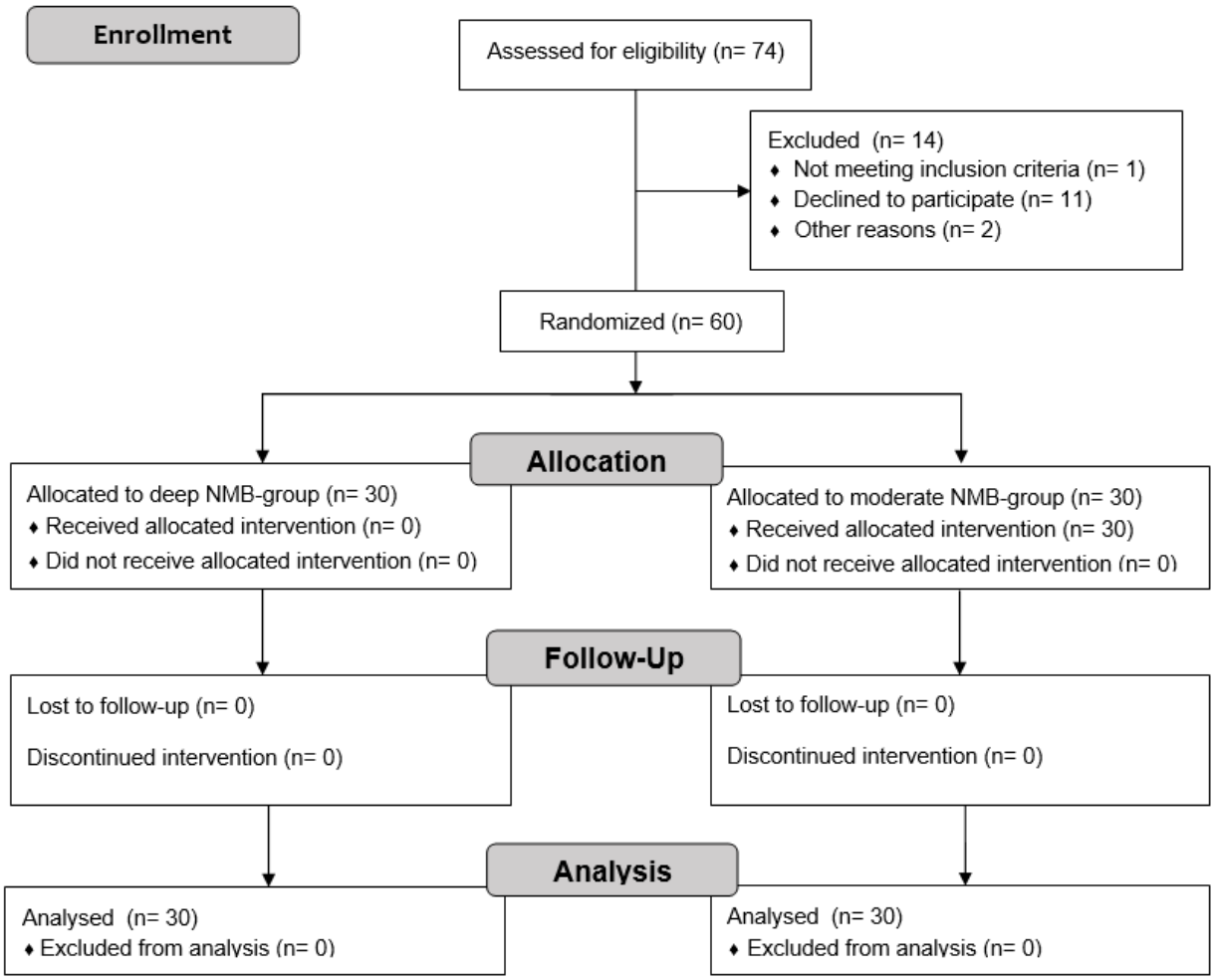
Table 2*. Data are presented as mean ± standard deviation. Abbreviations: BMI, body mass index; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; NMB, neuromuscular block; PEF; peak expiratory flow.*

Primary Outcome

The distribution of patients over the 5-point surgical rating scale in the deep and moderate NMB group is presented in Figure 2. There was no statistically significant difference in the surgeon's rating regarding the quality of the surgical field between the deep and moderate NMB group (4.2 ± 1.0 vs 3.9 ± 1.1; P = .16, respectively; ETE: 0.4 [-0.1, 0.9]). There was no difference in the proportional rating of surgical conditions over the 5-point rating scale between both groups (P = .91). The number of intra-abdominal pressure rises >18 cmH_2O were not

statistically different between the deep and moderate NMB-group (0.2 ± 0.9 vs 0.3 ± 1.0; P = .69, respectively; ETE: -0.1 [-0.5, 0.4]). The duration of surgery was not different between the deep NMB group and the moderate NMB group (61.3 ± 15.1 minutes vs 70.6 ± 20.8 minutes; P = .07, respectively; ETE: -9.3 minutes [-18.8, 0.1]).

Figure 1. CONSORT 2010 Flow Diagram



Secondary Outcomes

After surgery, all the pulmonary function tests were considerably impaired in both groups when compared with baseline (Table 3). There was no statistically significant difference in the decrease in PEF, FEV1, and FVC (expressed as % change from baseline) between the deep and the moderate NMB group (PEV: 51.3% ± 31.6% vs 51.5% ± 19.0%; P = .97, respectively; ETE: -0.2% [-13.8, 15.6], FEV1: 45.2% ± 36.4% vs 48.8% ± 19.6%; P = .64, respectively; ETE: -3.6% [-15.0, 11.0] and FVC: 51.9% ± 16.4% vs 49.0% ± 22.6%; P = .58, respectively; ETE: 2.9% [-7.2, 17.6]).

The modified observer's assessment of alertness scale at the time of pulmonary function testing was not different between the 2 groups (4.9 ± 0.5 vs 4.9 ± 0.3; P = .76). In the deep NMB group, 2 patients required postoperative noninvasive continuous positive airway pressure

versus 1 patient in the moderate NMB-group (P = .6). No patient needed reintubation after surgery. The total dose of propofol, remifentanil and rocuronium, and time from a TOFR >0.9 to pulmonary function testing in both groups are presented in Table 4.

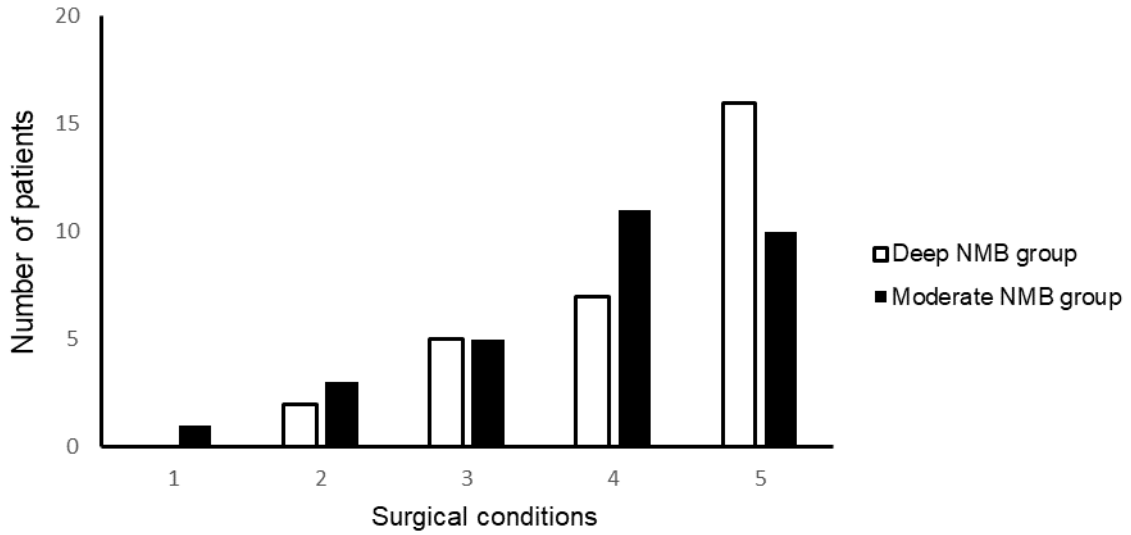


Figure 2*. Distribution of patients over the surgical rating scale. Surgical conditions were assessed by one surgeon using a 5-point rating scale (1 = extremely poor, 2 = poor, 3 = acceptable, 4 = good, 5 = optimal). Deep NMB, posttetanic count of 1–2; moderate NMB, train-of-four count of 1–2. NMB indicates neuromuscular block.*

Table 3. Postoperative Pulmonary Function Tests				
Postoperative Pulmonary Function Tests	**Deep NMB Group**	**Moderate NMB Group**		
PEF (L/min)	141 ± 79[a]	126 ± 44[a]		
FEV1 (L)	1.1 ± 0.5[a]	1.1 ± 0.4[a]		
FVC (L)	1.4 ± 0.5[a]	1.2 ± 0.6[a]		
Percent Change From Baseline				
	Deep NMB Group	**Moderate NMB Group**	***P***	**Estimated Treatment Effect**
PEF (L/min)	51.3 ± 31.6%	51.5 ± 19.0%	.97	-0.2% [-13.8, 15.6]
FEV1 (L)	45.2 ± 36.4%	48.8 ± 19.6%	.64	-3.6% [-15.0, 11.0]
FVC (L)	51.9 ± 16.4%	49.0 ± 22.6%	.58	2.9% [-7.2, 17.6]

Table 3. *Student t test was used to compare data between both groups. Data are presented as mean ± standard deviation. Estimated treatment effect is presented as mean difference [95% confdence interval].*
Abbreviations: FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; NMB, neuromuscular block; PEF, peak expiratory flow.
[a] *P = .0001 compared with preoperative pulmonary function tests*

Table 4. Anesthetic Dosages, Duration of Surgery, and Time Interval From a TOFR > 0.9 to Pulmonary Function Tests			
Parameter	**Deep NMB Group**	**Moderate NMB Group**	***P***
Total dose propofol (mg/kg)	13.7 ± 2.4	13.8 ± 2.3	.86
Total dose remifentanil (µg/kg)	22.0 ± 7.4	23.4 ± 8.9	.51
Total dose rocuronium (mg/kg)	1.0 ± 0.3	0.7 ± 0.2	.0001
Duration of surgery (min)	61.3 ± 15.1	70.6 ± 20.8	.07
Time from a TOFR > 0.9 to pulmonary function tests (h)	2.1 ± 0.8	2.2 ± 1.0	.83

Table 4*. Student t test was used to compare anesthetic dosages between both groups. A Mann-Whitney U test was used to compare the duration of surgery. Data are presented as mean ± standard deviation.*
Abbreviations: NMB, neuromuscular block; TOFR, train-of-four ratio

DISCUSSION

Deep NMB failed to improve the surgeon's rating of operating conditions when compared with moderate NMB in patients undergoing laparoscopic gastric bypass surgery. There was no difference in the number of intra-abdominal pressure increases or the duration of surgery between both groups.

Investigators whom reported an improved effect of deep NMB during laparoscopy often compared it with a very shallow or no NMB.[2,4,5] This, however, does not reflect clinical practice, where a certain degree of muscle relaxation is maintained during laparoscopic procedures. So, the question we should be asking ourselves is as follows: "is there an added value of deep NMB compared over moderate NMB" rather than "is deep NMB superior to a shallow or no NMB"?

To complicate matters even further, investigators frequently use various definitions of deep, moderate, and shallow NMB adding to the difficulty of comparing these studies. Often the term "moderate NMB" is used for conditions following a single intubation dose of rocuronium after which neuromuscular function is spontaneously allowed to return to normal over the course of the surgery. With TOF stimulation, however, T1 reappears 21 minutes after an intubation dose of 0.6 mg/kg rocuronium and after 28 minutes T1 is at 25% of its initial value[23] corresponding to a shallow NMB for the remainder of the operation. Therefore, studies comparing deep NMB to a "true" moderate NMB are scarce.

In one such study, Staehr-Rye et al[3] investigated whether deep NMB was associated with a greater proportion of optimal surgical conditions during low-pressure pneumoperitoneum (8 mm Hg) for laparoscopic cholecystectomy compared with moderate NMB. Optimal surgical space conditions were found in 28% of patients in the deep NMB group versus 4% in the moderate NMB group (P = .05). The conversion rate to a high-pressure pneumoperitoneum (12 mm Hg) and median duration of anesthesia were similar between the 2 groups. The authors concluded that deep NMB marginally improved surgical conditions.

Our findings and those by Staehr-Rye et al[3] are in line with an earlier observation that deep NMB only minimally enlarged the surgical space (distance from the sacral promontory to the edge of the trocar) by 0.3 cm compared with no NMB.[4] The effect of such a small improvement on the quality of the surgical field is indeed questionable.

In contrast, Martini et al[6] found improved surgical conditions with deep NMB (PTC 1–2, compared with a moderate NMB: TOFcount 1–2) in patients undergoing laparoscopic prostatectomy or nephrectomy. Nonetheless, the improved surgical conditions did not result in a shorter duration of surgery

Several explanations are possible for the discrepancy with our results. First, the retroperitoneal localization of the surgical field for prostatectomy and nephrectomy is more confined and surrounded by muscles than an intraperitoneal surgical field and consequently could benefit more from deep NMB. Second, different surgeons could rate operating conditions differently, as was demonstrated in the same study. Finally, the range of end-tidal CO_2 pressures was less controlled in the study by Martini et al[6] (33–56 mm Hg). Because high end-tidal CO_2 pressures stimulate the respiratory center in the brainstem, which in turn activates the phrenic nerve and the diaphragm,[24] this could induce a bias. The percentage of optimal surgical ratings in our study (55%) is lower than previously reported with deep NMB (68%–88%).[5,25] This can be explained by the obesity of our patients. The increased abdominal wall mass and intraperitoneal fat can lead to decreased intraperitoneal volume expansion and therefore visibility for equal pneumoperitoneum pressures.

Pulmonary function was impaired significantly after laparoscopic bariatric surgery in the deep as well as the moderate NMB group. There was no difference between both groups with respect to the extent of impairment (45%–52% decrease from baseline) in PEF, FEV1, and FVC. Given that respiratory function tests are highly dependent on patient cooperation, we determined the alertness of patients before testing the pulmonary function. In both groups, we found mean sedation scores of 5, i.e., the patients responded readily to their name spoken in a normal tone. Blobner et al[2] found similar decreases in PEF, FEV1, and FVC after laparoscopic cholecystectomy in nonobese patients irrespective of the use of deep NMB. The pulmonary function tests showed no sign of recovery within the first 24 hours after surgery. The investigators found no difference in postoperative pain scores related to the use of deep NMB. In the latter study, patients were also extubated when TOFR was >0.9.

These findings suggest that the use of NMB agents is not responsible for postoperative respiratory impairment as long as NMB is adequately monitored and reversed at the end of surgery. Pulmonary atelectasis is probably the main cause of decreased postoperative pulmonary function. Baltieri et al[26] found that atelectasis was present in 25% of patients after laparotomy for bariatric surgery. This number may be even higher after laparoscopic bariatric surgery because of the cranial displacement of the diaphragm caused by the pneumoperitoneum. Only postoperative bilevel positive airway pressure decreased the incidence of atelectasis. A major limitation is the fact that the study was underpowered. Ideally, the sample size should have been a total of 98 patients. As such, negative results should not be interpreted as lack of an effect but more studies are needed to definitively answer the research question.

In conclusion, there was insufficient evidence to conclude that deep NMB improves surgical conditions during laparoscopic bariatric surgery compared with a moderate NMB. Postoperative pulmonary function is substantially decreased after laparoscopic bariatric surgery independently of the NMB regime that is used.

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Title: The Effect of Deep Versus Moderate Neuromuscular Block on Surgical Conditions and Postoperative Respiratory Function in Bariatric Laparoscopic Surgery: A andomized, Double Blind Clinical Trial

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Abstract: BACKGROUND: In recent literature, it has been suggested that deep neuromuscular block (NMB) improves surgical conditions during laparoscopy; however, the evidence supporting this statement is limited, and this was not investigated in laparoscopic bariatric surgery. Moreover, residual NMB could impair postoperative respiratory function. We tested the hypotheses that deep NMB could improve the quality of surgical conditions for laparoscopic bariatric surgery compared with moderate NMB and. investigated whether deep NMB puts patients at risk for postoperative respiratory impairment compared with moderate NMB.

METHODS: Sixty patients were evenly randomized over a deep NMB group (rocuronium bolus and infusion maintaining a posttetanic count of 1-2) and a moderate NMB group (rocuronium bolus and top-ups maintaining a train-of-four count of 1-2). Anesthesia was induced and maintained with propofol and remifentanil. The primary outcome measures were the quality of surgical conditions assessed by a single surgeon using a 5-point rating scale (1 = extremely poor, 5 = optimal), the number of intra-abdominal pressure increases >= 18 cmH(2)O and the duration of surgery. Secondary outcome measure was the postoperative pulmonary function assessed by peak expiratory flow, forced expiratory volume in 1 second, and forced vital capacity, and by the need for postoperative respiratory support. Data are presented as mean +/- standard deviation with estimated treatment effect (ETE: mean difference [95% confidence interval]) for group comparisons.

RESULTS: There was no statistically significant difference in the surgeon's rating regarding the quality of the surgical field between the deep and moderate NMB group (4.2 +/- 1.0 vs 3.9 +/- 1.1; P = .16, respectively; ETE: 0.4 [-0.1, 0.9]). There was no difference in the proportional rating of surgical conditions over the 5-point rating scale between both groups (P =.91). The number of intra-abdominal pressure increases >18 cmH(2)O and the duration of surgery were not statistically different between the deep and moderate NMB group (0.2 +/- 0.9 vs 0.3 +/- 1.0; P = .69; ETE: -0.1 [-0.5, 0.4] and 61.3 +/- 15.1 minutes vs 70.6 +/- 20.8 minutes; P = .07, ETE: -9.3 [-18.8, 0.1], respectively). All the pulmonary function tests were considerably impaired in both groups when compared with baseline (P < .001). There was no statistically significant difference in the decrease in peak expiratory flow, forced expiratory volume in 1 second, and forced vital capacity (expressed as % change from baseline) between the deep and the moderate NMB group.

CONCLUSIONS: Compared with a moderate NMB, there was insufficient evidence to conclude that deep NMB improves surgical conditions during laparoscopic bariatric surgery. Postoperative pulmonary function was substantially decreased after laparoscopic bariatric surgery independently of the NMB regime that was used. The study is limited by a small sample size.

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Nederlandstalige samenvatting

Het Effect van Diepe versus gemiddelde neuromusculaire blokkade op chirurgische condities en postoperatieve respiratoire functie in bariatrische laparoscopische chirurgie: een gerandomiseerde, dubbel geblindeerde klinische studie

Inleiding

Laparoscopische bariatrische chirurgie stelt zowel de chirurg als de anesthesist voor specifieke problemen. De chirurg heeft een goede visualisatie nodig van het chirurgische veld om de heelkunde te kunnen uitvoeren; de anesthesist is dan weer bezorgd om de postoperatieve longfunctie bij deze obese patiënten. In recente literatuur wordt gesuggereerd dat een diep neuromusculair blok (NMB) de chirurgische condities tijdens laparoscopie zou kunnen verbeteren. Het wetenschappelijk bewijs dat deze stelling ondersteunt, is echter beperkt. Bovendien werden deze stellingen nog niet onderzocht in bariatrische laparoscopische chirurgie.
In deze klinische studie testen we de hypothese dat een diep NMB de chirurgische condities kan bevorderen vergeleken met een gemiddeld NMB. Omdat een diep NMB de patiënt potentieel blootstelt aan een verhoogd risico op restcurarisatie, testen we de secundaire hypothese dat diep NMB de postoperatieve longfunctietesten nadelig zou beïnvloeden.

Methode

60 Patiënten werden geïncludeerd uit het multidisciplinaire gewichtsverlies programma van het ziekenhuis Oost-Limburg. Deze werden gelijkmatig gerandomiseerd over twee groepen. Een groep werd peroperatief behandeld met een diep NMB (een rocuronium bolus gevolgd door een continue infusie met als doel een *posttetanic count* van 1-2). De andere groep werd behandeld met een matig NMB (rocuronium bolus met nadien boli rocuronium met als doel een *train-of-four count* van 1-2). Anesthesie werd geïnduceerd en onderhouden door middel van propofol en remifentanil.
De primaire uitkomstvariabele was de algemene toestand van het chirurgische veld, dus de zichtbaarheid en werkruimte voor de chirurg welke éénmalig werden gescoord door de chirurg. Hiervoor werden de chirurgische condities op een schaal van 5 punten gescoord op het einde van de ingreep (1= zeer slecht, 2=slecht, 3= acceptabel, 4=goed, 5=optimaal). Hoewel deze schaal reeds in andere studies werd gebruikt, blijft het een subjectieve inschatting. Daarom werden er ook twee meer objectieve uitkomsten geanalyseerd. Ten eerste werden het aantal intra-abdominale drukstijgingen boven de 18cmH_2O, niet gerelateerd aan chirurgische manipulatie van de buikwand, geteld. Ten tweede werd de tijd bijgehouden tussen incisie en het beëindigen van de hechtingen. Secundaire uitkomstvariabelen waren postoperatieve longfunctie, welke werd gemeten door het afnemen van de PEF, FEV1 en FVC en de nood aan postoperatieve ademhalingsondersteuning.

De data worden weergegeven als gemiddelde ± standaard deviatie met het geschatte behandelingseffect (*estimated treatment effect* ETE: gemiddeld verschil [95% betrouwbaarheids interval])

Resultaten

Er was geen statistisch significant verschil in de chirurgische beoordeling van de expositie van het operatieveld tussen de diepe en matige NMB groep (respectievelijk 4.2 ± 1.0 vs. 3.9 ± 1.1; P = .16; ETE: 0.4 [−0.1, 0.9]). Er was geen verschil in de proportionele beoordeling van de chirurgische condities over de 5-punts beoordelingsschaal tussen beide groepen. (p=.91). Het aantal intra-abdominale drukstijgingen >18 cmH_2O was niet statistisch significant verschillend tussen de diepe en matige NMB groep (respectievelijk 0.2 ± 0.9 vs 0.3 ± 1.0; P = .69,; ETE: −0.1 [−0.5, 0.4]). Er werd geen statistisch significant verschil gevonden tussen de diepe en de matige NMB groep (respectievelijk 61.3 ± 15.1 min vs 70.6 ± 20.8 min; P = .07; ETE: −9.3 minuten [−18.8, 0.1]).
Na heelkunde waren alle longfunctietesten duidelijk gestoord in beide groepen in vergelijking met de startwaarden. Er was geen statistisch significant verschil in de afname van PEF, FEV1 en FVC (uitgedrukt als % verschil tegenover de preoperatieve waarde) tussen de diepe en matige NMB groep.

Conclusie

In vergelijking met een matig NMB was er onvoldoende bewijs om te kunnen concluderen dat een diep NMB de chirurgische condities kan verbeteren tijdens laparoscopische bariatrische chirurgie. De postoperatieve longfunctie was substantieel gedaald na laparoscopische bariatrische chirurgie onafhankelijk van het gebruikte NMB diepte. De studie is gelimiteerd door de kleine sample size.