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Comparative Study Between Neostigmine Versus Sugammadex in Obese Patients Undergoing Laparoscopic Surgery

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Abstract: Background: Complete and rapid reversal of the effects of neuromuscular blocker drugs is a primary element of safety in anaesthesia. Neuromuscular conduction that is not completely improved leads to post-operative residual curarisation and the development of complications that are related to respiration. Aim of the Work: to compare between the effect of neostigmine and sugammadex on the duration of the recovery from neuromuscular blocking agents and postoperative residual curarization and respiratory complications in the obese patients undergoing laparscopic surgery. Patients and Methods: We carried out this randomized clinical study on sixty four patients operated upon at General Surgery Department at Armed Forces Hospitals. Patients and Methods: In this study, 64 patients of either sex with average age ranging from 18-65 years, ASA (I, II), submitted for bariatric gastric sleeveoperation were included in this study. Patients were randomly classified into 2 equal groups; Group S (sugammadex, n = 32) and group N (neostigmine, n = 32). Results: no significant differences between both groups regarding age, gender, BMI and ASA. But, we showed statistically a high significant difference between both groups regarding $TOF_{0.9}$ and significant differences between both groups regarding PACU and operative room time. Conclusion: This study verified the efficiency of sugammadex over neostigmine for full and timely reversal of neuromuscular blockade induced by a rocuronium, in morbidly obese patients undergoing laparoscopic bariatric surgery.

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1. Introduction

Obesity is a medical condition in which excess body fat has been accumulated to the extent that it may have an adverse effect on health, leading to reduced life expectancy. Although obesity is excess fat, in a practical setting it is difficult to determine this directly, therefore obesity is commonly assessed using the body mass index (BMI) which is a convenient parameter for documenting the incidence of obesity [(1)]. According to the BMI, obesity is defined as a body mass index of 30 kg/m^2 or higher, whereas individuals whose BMI is between 25 and 29.9 kg/m2 are termed overweight or Preobese [(2)].

Laparoscopy is widely used in the surgical treatment of a number of diseases. Its advantages are generally believed to lie on its minimal invasiveness, better cosmetic outcome and shorter length of hospital stay. Many surgical procedures are significantly longer in duration when performed with laparoscopic techniques. Taken together, these factors impose special care for the management of mechanical ventilation during laparoscopic surgery [(3)].

Bariatric surgery is necessary for individuals who have a body mass index (BMI) ≥ 40, or more than 100 pounds overweight. and their BMI ≥ 35 and at least one or more obesity-related co-morbidities such as type II diabetes (T2DM), hypertension, sleep apnea and other respiratory disorders, non-alcoholic fatty liver disease, osteoarthritis, lipid abnormalities, gastrointestinal disorders, or heart disease [(4)].

Bariatric surgery can be defined as surgery that modifies the gastrointestinal tract with the purpose of decreasing calorie consumption and therefore decreasing weight. There are several different types of bariatric surgery, including malabsorptive, restrictive and mixed [(5)].

Neuromuscular Blocking Drugs (NMBDs) are used in anesthesia to impair neuromuscular transmission and provide skeletal muscle relaxation. These drugs enable the anesthesiologist to perform tracheal intubation, facilitate ventilation and to provide optimal surgical operating conditions. NMBDs are quaternary ammonium compounds structurally similar to Acetylcholine (Ach); they act

mostly at the post-junctional nicotinic receptor of the neuromuscular junction. NMBDs may be agonists (depolarizing NMBDs) like succinylcholin or antagonists (non-depolarizing NMBDs) which are two groups; benzlisoquinolinium compounds and aminosteroid compounds [6].

Neostigmine methylsulfate is a cholinesterase inhibitor commonly used for reversal of non-depolarizing neuromuscular blockade. Neuraxial administration of neostigmine as an analgesic agent is still in an experimental stage. A severe nausea side effect limits its intrathecal application. Recent studies employing epidural neostigmine have reported effective analgesia, opioid, and local anesthetic sparing effects, and reduction in opioid-related side effects [7].

Joshi et al. [8] compared neostigmine induced reversal of vecuronium in normal weight, overweight and obese female patients, objectively using neuromuscular (NM) monitoring. They concluded that neostigmine induced recovery of NMB is delayed in late phases, which may result in vulnerability for associated complications of incomplete recovery. Ensuring safe recovery thus requires objective NM monitoring.

Sugammadex is a completely new possibility of neuromuscular block reversal and introduced to anesthesia practice [9]. **Duarte et al.** [10] compared neuromuscular blockade reversal time induced by continuous infusion of rocuronium and the occurrence of residual postoperative paralysis in morbidly obese patients undergoing laparoscopic bariatric surgery, using three different doses of sugammadex, calculated for ideal weight, ideal weight plus 20% of excess weightor, ideal weight plus 40% of excess weight. They observed no differences between groups with neuromuscular blockade reversal time and frequency of postoperative residual curarization. They concluded that ideal body weight can be used to calculate sugammadex dose to reverse moderate neuromuscular blockade in morbidly obese patients.

Aim of the work

To compare between the effect of neostigmine and sugammadex on the duration of the recovery from neuromuscular blocking agents and postoperative residual curarization and respiratory complications in the obese patients undergoing laparscopic surgery.

2. Patients and methods

After approval by the Local Ethical Committee of General Surgery Department, Armed Forces Hospitals; this randomized clinical study was conducted on 64 patients. Patients were categorized into two groups equally (32 for each group). A written informed consent was obtained from all patients prior to enrolment in this study.

American Society of Anesthesiology physical status (ASA-PS) I and II patients with age ranging from 18-56 years of either sex and body mass index (BMI) > 30 kg/m2, submitted for bariatric laparoscopic surgery under general anesthesia, were eligible for the study.

While American Society of Anesthesiology physical status (ASA- PS) III and IV, patients of either sex< 18 age or ≥ 65, patients with neuromuscular diseases (such as myasthenia gravis) andrespiratory diseases were excluded from the study.

Study groups:

After induction of anesthesia, 64 patients were randomly assigned into two groups to receive 2 mg/ kg sugammadex (group S) or 0.04 mg/kg neostigmine + 0.5 mg atropine (group N). Group randomization was done using sequentially numbered, opaque, sealed envelopes containing computer-generated random allocations in a ratio of 1:1 in balanced blocks of 4.

All patients in the currnet study were subjected to evaluation of the patients includes: A careful history and physical examination, Airway assessment, cardiopulmonary assessment.

All patients were fasted according to standard rules and were premedicated with diazepam 0.1mg/kg by mouth 1 hour before the scheduled time of surgery.

Monitoring:

Patients were monitored using electrocardiography (ECG), non- invasive blood pressure (NIBP), pulse oximetry, capnography and body temparture. A train of four (TOF) Watch (TOF-Watch-SX Monitor, Organon Teknika; Oss, Netherlands) device was used to monitor nerve muscle transmission. Two surface electrodes were placed on the forearm ulnar nerve trace 2-3 cm apart, active and passive electrodes of the acceleromyograph and transducer was placed on the pulp of the thumb. Patients were preoxygenated for three minutes with 100% oxygen. TOF-Watch device was calibrated by supramaximal stimulation at 0.1 Hz frequency before induction.

Procedure:

An intravenous cannula was inserted into a forearm vein and standard anesthesia monitoring (noninvasive blood pressure, electrocardiogram, and oxygen saturation) established on arrival in the operating room. Anesthesia was induced with propofol (2–3 mg/kg) and fentanyl (1–2 ug/kg) and maintained with isoflurane 1% MAC and according to clinical need and anesthesiologist preference.

Patients received a facemask and spontaneously ventilated to keep arterial oxygen saturation at 96% or higher and to maintain normocapnia. Body temperature was maintained at 35.0°C or higher. Neuromuscular monitoring was carried out according to international consensus guidelines, using evoked

electromyography of the adductor pollicis muscle using the neuromuscular transmission module in a S/5 GE Datex Light monitor (GE Datex Medical Instrumentation, Inc., Tewksbury, MA). Using electromyography avoids a common problem seen with acceleromyography (*i.e.*, TOF ratios above 1.0).

The forearm was immobilized and surface skin electrodes were placed over the ulnar nerve proximal to the wrist. Before calibration, tetanic stimulation of the ulnar nerve was performed. Then, stimulation was switched to TOF mode (70-mA current; 0.2-ms pulse duration, 2 Hz frequency) every 12 s. After at least 3 min of stable twitch responses, calibration of the system was performed automatically to find individual supramaximal stimulation. After this calibration, the ulnar nerve was stimulated with supramaximal TOF stimulation at 15-s intervals and the evoked electromyogram of the adductor pollicis muscle was recorded. However, recalibration was performed if stimulation was not stable for at least 3 min postcalibration.

Neuromuscular transmission and its suppression were described by parameters related to the TOF stimulation patterns (i.e., the response to the four stimulations [T1–T4] related to baseline values and the ratio of the fourth to first twitch response of a TOF complex [TOF ratio]).

Skin temperature was measured at the site of the neuromuscular measurements and maintained at 32.0°C or higher using heating blankets. After 3 min of stabilization of the electromyography recording, 0.6 mg/kg rocuronium was injected. The trachea was intubated when T1 was 0. During surgery, maintenance doses of 0.1– 0.2 mg/kg rocuronium were injected according to clinical need. When the surgical procedure did not require further neuromuscular block, spontaneous recovery from the neuromuscular block was allowed to a TOF ratio of 0.5.

At this point, the study medication which are 64 patients were randomly assigned into two groups to receive 2 mg/ kg sugammadex (group S) or 0.04 mg/kg neostigmine + 0.5 mg atropine (group N). Neuromuscular monitoring was continued until the end of the surgical procedure, and at least 10 min after the TOF ratio reached 0.9 at least. At the end of surgery and emergence of anesthesia, the awake patient was extubated. Heart rate and mean arterial blood pressure were recorded before the injection of the study medication and then 2, 5, 10, and 20 min afterward.

Patients were kept in the recovery room for a minimum of 60 min. Oxygen saturation; respiration rate, heart rate, and blood pressure were routinely monitored. Arterial blood gases (ABG) was done 30 min after admission of patient to recovery room. Any signs of reoccurrence of muscle weakness were recorded. Therefore at several time points (every 15 min and before discharge from the recovery room), the consciousness level (*i.e.*, awake and oriented, arousable with minimal stimulation, or responsive only to tactile stimulation) were assessed.

Cooperative patients were asked to open their eyes for 5 s, perform a 5-s head lift test, a 5-s arm lift test and were asked to swallow 20-ml bolus of plain water. Then a test for general muscle weakness was performed using the Medical Research Council Scale; 0 _ no movement, 1 _ flicker is perceptible in the muscle, 2 _ movement only if gravity eliminated, 3 _ can move limb against gravity, 4 _ can move against gravity and some resistance exerted by examiner, 5 _ normal power. The blinded safety assessor performed these postoperative clinical assessments. Chest x ray was done before patient discharge from recovery room. The study was finished for a patient after discharge from the recovery room to the regular ward.

The anesthesiologist of the patient and the safety assessor also monitored all patients for adverse effects (AE). However, if there was doubt about AE classification or severity, the safety assessor decided AE coding. AEs were defined as drug related if the investigator considered them to be definitely, probably, or possibly related to the study drug.

Measuring:

The primary outcome measure of the study is the time (min) to obtain a TOF 0.9 after the administration of the reversal agent. The secondary outcome measures are the operation room time (min), PACU time (min), frequency of respiratory complication as cough, breath holding, increased secretion, desaturation (SpO2≤90), hypoxemia (PaO2<60) (which detected by doing Arterial blood gases (ABG) after 30 min from admission of patient to recovery room), apnea and pulmonary disorders (atelectasis, pneumonia and others) (which detected by doing of chest x ray before patient discharge from recovery room) and ICU admission (reversal, anaesthesia care, complication treatment).

Statistical analysis

Data were checked entered and analyzed by using SPSS version 22. Data were represented as mean ± SD for quantitative variables and frequency and percentage for categorical variables. Chi squared and t test were used when appropriate. P less than 0.05 is considered statistically significant.

3. Results

Table (1): Characteristics of the studied groups

	Sugammadex (n = 32)	Neostigmine (n = 32)	Test of significance	p
Age (years)				
Mean ± SD	37.6 ± 12.3	38 ± 11	t =	0.89
Range	18-65	18-65	0.13	(NS)
Gender				
Male	19 (59.5%)	18 (56.3%)	X^2 =	0.8
Female	13 (40.6%)	14 (43.8%)	0.06	(NS)
BMI				
Mean ± SD	34.6 ± 3.5	33.9 ± 3	t =	0.4
Range	30-41	31-42	0.8	(NS)

Table (1) shows the demographic and preoperative data of both groups. No significant differences were found between both groups regarding age, gender and BMI.

Table (2): ASA among studied groups

ASA	Sugammadex (n = 32)		Neostigmine (n = 32)	
	No	%	No	%
I	25	78.1	23	71.9
II	7	21.9	9	28.1

Table (2) shows thatno significant difference was found between both groups regarding ASA.

Table (3): Heart rate and mean arterial blood pressure

	Neostigmine group	Sugammadex group	p
Heart rate (HR)			
Baseline	73 ± 12	75 ± 11.5	NS
2 minutes	95 ± 11	84.8 ± 10.9	HS
5 minutes	90 ± 10	89 ± 12	NS
10 minutes	78 ± 10	80 ± 11	NS
20 minutes	74 ± 10	76 ± 12	NS
Mean arterial blood pressure (MAP)			
Baseline	86 ± 13.8	87.5 ± 14	NS
2 minutes	101 ± 15	85.6 ± 12	HS
5 minutes	97 ± 12	89.9 ± 11	NS
10 minutes	86 ± 11	90 ± 10.9	NS
20 minutes	85 ± 12	86 ± 10	NS

Table (3) shows no significant differences between both groups regarding heart rate and mean arterial blood pressure, except for HR and MAP at 2 minutes which exhibited statistically high significant differences.

Table (4): $TOF_{0.9}$ among studied groups (minute).

$TOF_{0.9}$ (min)	Sugammadex (n = 32)	Neostigmine (n = 32)	Test of significance	p
Mean ± SD	1.4 ± 0.4	5.6 ± 2.1	10.7	< 0.001
Range	0.8-2	3-9.9		(HS)

Table (4) shows statistically a high significant difference between both groups regarding $TOF_{0.9}$.

Table (5): Operation room time and PACU time (minutes)

	Sugammadex (n = 32)	Neostigmine (n = 32)	T	p
Operative room time				
Mean ± SD	78.3 ± 23.4	91.4 ± 26	2.1	0.03 (S)
Range	50-130	60-150		
PACU				
Mean ± SD	16.8 ± 5.1	21.8 ± 7.7	2.86	0.05 (S)
Range	10-30	15-45		

Table (5) shows statistically significant differences between both groups regarding PACU and operative room time.

Table (6): Respiration-related complications (desaturation) ($SpO_{2 \leq 90\%}$)

SpO_2	Sugammadex (n = 32)		Neostigmine (n = 32)		X^2	P
	No	%	No	%		
≤ 90%	2	6.3	7	21.9	2.07	0.15(NS)
> 90%	30	93.7	25	78.1		

Table (6) shows a non-significant difference between both groups regarding SpO_2.

Table (7): Respiration-related complications (hypoxemia) ($PaO_2 \leq 60$ mmHg)

paO_2	Sugammadex (n = 32)		Neostigmine (n = 32)		X^2	P
	No	%	No	%		
≤ 60mmHg	3	9.4	7	21.9	1.9	0.16(NS)
> 60mmHg	29	90.6	25	78.1		

Table (7) shows a non-significant difference between both groups regarding PaO_2.

Table (8): Other complications

	Sugammadex (n = 32)		Neostigmine (n = 32)		X^2	p
	No	%	No	%		
Cough	3	9.4	10	31.3	4.73	0.029(S)
Breath holding	1	3.1	5	15.6	1.66	0.19(NS)
Secretion	3	9.4	5	15.6	0.14	0.7(NS)
Atelectasis	0	0	2	6.3	0.52	0.43(NS)
Pneumonia	2	6.3	3	9.4	0.22	0.6(NS)
ICU admission	2	6.3	8	25	4.27	0.03(S)

Table (8) shows non-significant differences between both groups regarding complications, except for cough and ICU admission which exhibited statistically significant differences.

4. Discussion

Obese patients pose a significant challenge to anesthetic management. The physiological and anthropometric changes associated with obesity alter the pharmacokinetic properties of most drugs. Obese individuals are often excluded from clinical trials despite the growing recognition of the impact of obesity on pharmacokinetic and pharmacodynamic properties of the drugs. Dosing information in the package inserts is usually based on the kilogram of RBW, which can result in incorrect doses when applied to the obese patients [(11)].

Over decades, the incidence of obesity has tripled, and number of obese patients undergoing surgery has also increased. Diseases associated with obesity such as diabetes, hypertension, cardiopulmonary diseases and obstructive sleep apnoea reduce the margin of safety of anaesthetic drugs. Body composition, regional blood flow and tissue affinity alter distribution of drugs in these patients posing a significant challenge to anaesthesiologist [(12)].

Life style interventions are seldom associated with long-lasting results. Accordingly, requests for bariatric surgery have dramatically increased in recent years, with the majority of the procedures performed

through laparoscopic approach, which is a valid option to open surgery and demonstrated to reduce major complications [13].

Bariatric surgery has become very popular as long-term treatment of morbid obesity caused by the fact that long term weight loss is better sustained in surgically treated patients compared to conventional treatment. Laparoscopic bariatric procedures are the preferred technique [14].

Morbidly obese patients undergoing anaesthesia for general surgery are at high risk for respiratory complications following reversal of NMB. There is considerable interest in assessing the efficacy of anaesthetic reversal agents on respiratory function. The ideal reversal agent should have a fast onset, an efficient compelte reversal, a longer half life than NMBDs and has few adverse effects [15].

Postoperative residual curarization (PORC) is defined as residual paresis after emergence from general anaesthesia with neuromuscular blocking drug. The presence of PORC attenuates the normal ventilatory response to hypoxia by impairing adequate function of the carotid body. PORC may impair coughing, as well as increasing the likelihood of atelectasis. It has been shown that even a small degree of PORC increases the incidence of critical respiratory events [16]. Reliance on clinical signs and symptoms to determine degree of reversal of neuromuscular function is not effective and only careful monitoring of neuromuscular function (in our study through assessment of TOF) can accurately detect PORC.

Neostigmine increases the risk of bronchospasm because of its muscarinic and pro-secretory effects. These side effects can be blunted by co-administration of an anti-muscarinic drug such as glycopyrrolate, but the duration of action of neostigmine can outlast that of the vagolytic agent [16].

Sugammadex, a synthetic γ cyclodextrin encapsulate the aminosteroid NMBDs such as rocuronium and vecuronium forming an inclusion complex with reduction of their free plasma concentration which leads to passive diffusion of NMBDs from the neuromuscular junctions into the central compartment through a concentration gradient resulting in rapid reversal of neuromuscular blockade [17].

Clinical data have already demonstrated the efficacy and tolerability of sugammadex for the reversal of moderate and deep neuromuscular blockade [18].

The clinical safety and efficacy of sugammadex for reversal of rocuronium-induced NMB has been confirmed. There is also evidence that it produces more rapid NMB recovery than neostigmine, however there is relatively limited data pertaining to its physiological effects in morbidly obese patients, who are particularly high risk for adverse respiratory events in the immediate post-operative period [16].

Suzuki et al. [19] demonstrated that neostigmine significantly impairs upper airway dilator muscle activity when given after recovery from neuromuscular blockade, whereas a reversal dose of sugammadex given under the same conditions does not affect genioglossus muscle activity and normal breathing.

To date, there has not been a study comparing the respiratory recovery of morbidly obese patients following NMB reversal with sugammadex or neostigmine. The objective of this study was to compare between the effect of neostigmine and sugammadex on the duration of the recovery from neuromuscular blocking agents and postoperative residual curarization and respiratory complications in the obese patients undergoing laparscopic surgery. We carried out this randomized clinical study on sixty four patients operated upon at General Surgery Department– Armed Forces Hospitals.

In this study, 64 patients of either sex with average age ranging from 18-65 years, ASA (I, II), submitted for bariatric gastric sleeveoperation were included in this study. Patients were randomly classified into 2 equal groups; Group S (sugammadex, n = 32) and group N (neostigmine, n = 32).

Our study found no significant differences between both groups regarding age, gender, BMI and ASA. **Joshi et al.** [8] compared neostigmine induced reversal of vecuronium in normal weight, overweight and obese female patients, objectively using neuromuscular (NM) monitoring. Twenty female patients each belonging to normal weight, overweight and obese, based on body mass index, requiring general anaesthesia were recruited for this prospective cross sectional study. They found that time taken for recovery of TOF to 0.5 following reversal was comparable in all three groups. Recovery of TOF ratio to 0.7 was delayed in obese as compared to normal weight group. Furthermore, recovery of TOF to 0.9 was delayed in both overweight and obese patients, which was statistically significant. Duration of surgery was comparable among all three groups.

Johnson et al. [20] determined whether sugammadex, a selective reversal agent is associated with better respiratory recovery than neostigmine following the reversal of anaesthesia-associated neuromuscular blockade by rocuronium in the morbidly obese. Peak Expiratory Flow Rate a surrogate marker for respiratory function, was the primary outcome measured and secondary outcome measures included post-operative nausea and vomiting, pain and head lifting. Of the 40 patients who underwent elective laparoscopic bariatric surgery or laparoscopic cholecystectomy, 20 were reversed

with sugammadex and 20 with neostigmine and glycopyrrolate. There was no significant difference between patient characteristics.

Our study showed statistically a high significant difference between both groups regarding $TOF_{0.9}$ and significant differences between both groups regarding PACU and operative room time. Our finding correlated with that of **Carron et al.** [21], who demonstrated that use of sugammadex as a reversal agent in the morbidly obese is associated with much shorter reversal and total anaesthetic times than neostigmine. They found better PONV in their sugammadex group.

Suzuki et al. [19] found that time required to recover to TOF ratio of 0.5 and 0.7 were comparable between the groups and the late phase of recovery to 0.9 was delayed in overweight (3.3–28.5 min) and obese groups (13.5–41.0 min). This was attributed to over dose of vecuronium in obese patients.

Johnson et al. [20] found that secondary outcome measures of time to TOF 0.9 and time to head lift were significantly shorter in patients receiving sugammadex as compared to those patients receiving neostigmine and glycopyrrolate.

Recovery to TOF ratio of 0.7 and 0.9 was delayed in overweight and obese, which may represent a balance between spontaneous recovery (elimination of drug from plasma) from overdosed vecuronium induced block and the waning reversal effect of neostigmine. Residual paralysis causes increased airway collapsibility in obese individuals. Clinical parameters used for NM recovery such as patient's ability to maintain a 5 s head lift and hand grip maybe present at TOF ratio of 0.7 and does not ensure complete recovery [22]. **Fuchs-Buder et al.** [23] indicated that low levels of residual paralysis corresponding to TOF ratio 0.7– 0.9 may be harmful.

Our study showed non-significant differences between both groups regarding complications, except for cough and ICU admission which exhibited statistically significant differences. **Suzuki et al.** [19] used a dose of 40 ug/kg CBW of neostigmine in the morbidly obese. We used a dose of 50 ug/kg CBW of neostigmine, which did not appear to cause an increased incidence of side effects.

Baurain et al. [24] studied the conditions to optimize the reversal action of neostigmine upon vecuronium induced NMB and concluded that in order to obtain the highest NM transmission recovery (TOF of 0.9), 40 mcg/kg dose of neostigmine has to be given at 25–50% recovery of twitch height. Increasing the dose of neostigmine to 80 mcg/kg did not accelerate the recovery.

According to **Donati et al.** [25], higher doses of neostigmine (50 µg/kg) can antagonize the block more rapidly than smaller doses (5, 10, 20 µg/kg). To reverse the profound block, maximum dose of neostigmine (70–80 µg/kg) may be used for a better recovery profile.

Kopman and Eikermann [26] used low dose of neostigmine (15–20 µg/kg for TOF count of four and 40–50 µg/kg for TOF count of two or three) to minimise potential cardiovascular and respiratory side effects when NMB was not intense. The recommended dose of neostigmine is 40–80 µg/kg, not exceeding a total of 5 mg. In obese subjects, recovery of NM function after reversal with neostigmine is found to be incomplete as compared to normal weight subjects.

Sugammadex is a specifically designed gamma cyclodextrin and selective relaxant binding drug that rapidly reverses the effects of rocuronium and vecuronium induced block. Decisions with regard to dosage and timing of neostigmine in overweight and obese patients require clinical and NM monitoring for a safe recovery [27].

Van Lancker et al. [28] found that the use of sugammadex based on ideal or ideal plus 20% weight delayed the reversal of neuromuscular blockade. They found there was no difference between ideal weight plus40% and total weight and concluded that sugammadex is effective for reversal of rocuronium blockade after recovery from the second TOF response, with 2 mg.kg−1, based on ideal weight plus 40%. However, even in the ideal weight and 20% corrected weight groups, which had significantly longer recovery times, these authors did not find a significantly longer duration for tracheal extubation or opening of the eyes, nor any postoperative complications related to residual curarization.

Laurado et al. [29] compared sugammadex usingadjusted ideal weight by level of neuromuscular blockade in laparoscopic bariatric surgeries. They used 2 mg.kg−1sugammadex to reverse moderate blockade (classified as two or more TOF responses) and 4 mg.kg−1for deep blockade (classified as TOF 0 and 12 or fewer PTC responses). In both groups, sugammadex was administered for ideal weight. They found a delay in motor recovery and high rates of patients responding to sugammadex slowly or not at all. They concluded that the use of sugammadex based on ideal weight is insufficient or unsafe for moderate or deep blockade. Two aspects of the study, however, should be considered: first, the groups studied (moderate and deep blockade) were not randomized, a recognized by the authors themselves; second, unusually for management of recovery from motor blockade, the authors accepted a maximum time of only 2 min for reversal of moderate blockade and 3 min for deep blockade. After this, if the TOF did not reach a level of 0.9, a second 2 mg. kg−1dose of sugammadex was administered in either group. In a

self-analysis of this course of action, the authors agree that if more time had been allowed for recovery from blockade before administering the second dose, more patients who used sugammadex on the basis of ideal weight could have achieved a TOF of over 90%, which would have modified the conclusions. In our opinion, the indication of the second dose of sugammadex so soon after the initial dose added bases on the findings on insufficient recovery of neuromuscular blockade when it was used sugammadex based on ideal weight and, equally, on the possible complications arising from the use of such calculation that were not actually found.

Loupec et al. [30] exploredwhether titrating sugammadex to IBW using a range of doses would identify a dose at which there is suitably rapid and complete reversal from NMB. Neuromuscular blockade was monitored in 50 patients using acceleromyography at the adductor pollicis. At the end of surgery with deep rocuronium-induced neuromuscular blockade, patients randomly received sugammadex 4 $mg.kg^{-1}$ (high dose group), 2 $mg.kg^{-1}$ (middle dose group), or 1 $mg.kg^{-1}$ (low dose group) of ideal body weight. After administration of the first dose of sugammadex, the mean (SD) recovery time (censored at 600 s) from deep neuromuscular blockade was significantly shorter in the high-dose group vs the middle-dose group, or low-dose group. Success rate from neuromuscular blockade reversal defined by a train-of-four ≥ 0.9 within 10 min after sugammadex administration, were 93%, 77% and 22% for these high, middle and low-dose groups respectively. They recommended that, in morbidly obese patients, a reversal dose of 4 $mg.kg^{-1}$ of sugammadex based on IBW, as this allows reversal of deep rocuronium-induced NMB within a practically acceptable time period.

De Robertis et al. [31] analyzed and compared the costs and the recovery times after sugammadex or neostigmine administration, and estimated the time of operating theater occupancy (time from "starting anesthesia" to when the patient was transferred to the postanesthesia care unit [PACU]), in morbidly obese patients undergoing bariatric surgery. They concluded that the clinical application of a TOF-driven protocol to reverse neuromuscular paralysis in morbidly obese patients should be encouraged. Sugammadex use is associated with a faster recovery and a higher health care costs. However, the main benefit is the time saved in the operating room, which could be used in more productivity, such as increasing the number of surgical procedures to perform.

Da Silva et al. [32] determined the minimum effective dose of sugammadex in 90% of obese patients (ED 90) required to complete the reversal of rocuronium-induced moderate neuromuscular blockage using the up-and-down design of biased coin (BCD) in patients with grade III obesity submitted to bariatric surgery. They conclued that the ED90 dose for sugammadex to reverse rocuronium-induced neuromuscular blockade was 2.39mg/kg within a mean infusion time of 213 seconds.

Evron et al. [33] compared the effects of neostigmine vs. sugammadex on critical respiratory events and late respiratory complications in morbidly obese patients undergoing laparoscopic sleeve gastrectomy surgery. They concluded that the use of sugammadex as compared to neostigmine following laparoscopic sleeve gastrectomy surgery was associated with higher postoperative oxyhemoglobin saturation despite deeper muscle relaxation (lower TOF count) before the administration of reversal agent.

Durate et al. [10] observed no differences between groups with neuromuscular blockade reversal time and frequency of postoperative residual curarization. Ideal body weight can be used to calculate sugammadex dose to reverse moderate neuromuscular blockade in morbidly obese patients. **Johnson et al.** [20] found that patients reversed with sugammadex had a significantly higher post-operative PEFR as compared to those reversed with neostigmine and glycopyrrolate group.

In conclusion, although sugammadex shows effective rapid reversal of NMBDs, its cost still high and may still be considered as major limiting factors for its widespread use in our country. Therefore, use of neostigmine as a reversal agent continues to be relevant.

Conclusion

The number of patients studied was small, but nonetheless sufficient to demonstrate that compared to neostigmine, sugammadex leads to better recovery of respiratory function following reversal of NMB of general anaesthesia in morbidly obese patients. This study verified the efficiency of sugammadex over neostigmine for full and timely reversal of neuromuscular blockade induced by a rocuronium, in morbidly obese patients undergoing laparoscopic bariatric surgery.

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