

Neostigmine versus sugammadex on post-operative recovery following bariatric surgery

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ABSTRACT

OBJECTIVE: The purpose of our study was to compare the recovery characteristics and side effects of sugammadex (SM) and neostigmine (NT) in morbidly obese patients undergoing bariatric surgery. Residual neuromuscular block is a serious condition that increases pulmonary complications after anesthesia. Although acetylcholinesterase inhibitors help reverse this block, they may be insufficient, especially when administered with inhalational anesthetics. SM, a selective antagonist, may be more effective in reversing the block.

METHODS: Patients were randomly divided into NT group (Group NT, n=34) and SM group (Group SM, n=34). For the induction, fentanyl (1–1.5 µg/kg), propofol (2–3 mg/kg), and rocuronium (0.6 mg/kg) were used. For the maintenance, 50% O₂ + air, 1% sevoflurane, and remifentanyl (0.5–0.3 µg/kg/min) were used. Additional rocuronium was given to maintain the train of four (TOF) ratio ≤2. On completion of surgery and when the TOF ratio was 2, group NT received 50 µg/kg of NT with 20 µg/kg of atropine, whereas group SM received 2 mg/kg of SM. Hemodynamic parameters and peripheral oxygen saturation (SpO₂) were recorded every 10 min first, and every 5 min after the reversal agents were given. When the TOF ratio was 0.9 or higher, time to reach a TOF ratio of 0.9, and time to extubation were recorded. Patients were observed in the recovery room for 30 min for adverse effects.

RESULTS: Demographic characteristics of the patients and total rocuronium use in two groups were similar (p>0.05). Time to extubation, time to TOF ratio of 0.9, time until patients responded to stimuli, time until cooperation, and time until orientation were significantly shorter in the SM group than in the NT group. Time to reach the Aldrete score of 9 was also significantly shorter in the SM group (p<0.05). In the post-operative period, hemodynamic variables and side effects such as respiratory difficulty, nausea, vomiting, hypo/hypertension, and presence of pain showed no statistically significant differences between the groups (p>0.05).

CONCLUSION: Considering the high risk of post-operative respiratory insufficiency in morbidly obese patients, SM could be a safer choice in this patient group.

Keywords: Bariatric surgery; NT, SM.

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Post-operative residual curarization (PORC) is one of anesthesia's most important post-operative complications. PORC occurs when the effects of muscle re-

laxants partially persist in the spontaneously breathing extubated patient [1]. PORC delays anesthesia recovery, possibly resulting in aspiration of stomach contents, re-

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spiratory failure, hypoxia, and even cardiopulmonary arrest. Airway control becomes more difficult and functional residual capacity is lower with increasing weight in morbidly obese patients. PORC increases with age and its rate is further increased with obesity [2].

In morbidly obese patients receiving neostigmine (NT) to reverse the effects of muscle relaxants, it is known that muscle relaxants sequestered in fat tissue are reintroduced into the bloodstream after the antidote is cleared, thereby causing respiratory insufficiency. NT has important adverse effects including bradycardia and increased secretions [3].

Sugammadex (SM), which was developed selectively against aminosteroid neuromuscular blockers, rocuronium, and vecuronium, was a cyclodextrin composed of eight glucose monomers arranged cylindrically. In blood plasma, one SM molecule mechanically binds one rocuronium or vecuronium molecule and thus decreases their plasma concentrations. This forms a gradient-causing transit of rocuronium and vecuronium from all extravascular spaces toward the blood, allowing for speedy elimination and decurarization. Recurarization or muscarinic adverse effects are not expected in decurarization of such a mechanism. It is suggested that the selective binder of rocuronium and vecuronium, SM, does not leave a residue [4].

The purpose of our study was to compare the effects of two antidotes in terms of the time to reach a train-of-four (TOF) ratio of 0.9, post-operative recovery properties, post-operative respiratory complications, and adverse effects in morbidly obese patients undergoing bariatric surgery.

MATERIALS AND METHODS

The study was conducted with 68 morbidly obese patients who were aged 18–65 years, had American society of anesthesiologist physical status scores of I to III, and underwent elective laparoscopic bariatric surgery between September 25, 2014, and March 25th, 2015, at the General Surgery Clinics of Haydarpasa Numune Training and Research Hospital, University of Health Sciences, Istanbul.

The study was approved by our hospital's ethical board (decision no. AEK 2014/KK77) and conducted according to the Helsinki ethical principles for medical research involving human subjects. Each patient gave written consent for inclusion in the study. Simple ran-

Highlight key points

- Times to extubation, TOF ratio of 0.9, respond the verbal stimuli, cooperation, and orientation were significantly shorter in the SM group than in the NT group
- Time to reach the Aldrete score of 9 was significantly shorter in the SM group
- In the post-operative period, hemodynamic variables and side effects such as respiratory difficulty, nausea, vomiting, hypo/hypertension, and presence of pain showed no statistically significant differences between the groups
- Considering the high risk of post-operative respiratory insufficiency with morbid obese patients, SM could be a safer choice in this patient group.

domization placed 34 patients in the NT group and 34 patients in the SM group.

Patients with a body mass index (BMI) >35 kg/m², aged 18–65 years, and undergoing bariatric surgery under general anesthesia with an expected surgical time under 120 min were included in the study. Exclusion criteria were BMI under 35 kg/m², having known drug allergy, muscle disorders, organ insufficiency, and age under 18 or above 65 years.

Patients were premedicated with 0.5 mg of atropine intramuscular (IM) and 10 mg of diazepam IM 30 min before the operation. In the operation room, all patients were under electrocardiography, non-invasive blood pressure, and peripheral oxygen saturation monitoring. An acceleromyograph device (TOF Watch SX) was set up to stimulate the ulnar nerve to evaluate neuromuscular blockage. An intravenous (IV) line was placed in the hand with an 18–20 G cannula. Fentanyl (1–1.5 µ/kg) and 2–3 mg/kg of propofol were administered. For muscle relaxation, 0.6 mg/kg of rocuronium was given following TOF calibration. The patient was intubated when the TOF reading was zero. For anesthesia maintenance, 50% O₂ + air, 1% sevoflurane, and 0.5–0.3 µg/kg/min of remifentanyl were given. Additional rocuronium was given if necessary to maintain the TOF ratio ≤2. On completion of surgery and when the TOF ratio was 2, group NT received 50 µg/kg of NT with 20 µg/kg of atropine, whereas group SM received 2 mg/kg of SM (Bridion®, Merck Sharp and Dohme-MSD, The Netherlands). Inhaled anesthetics and remifentanyl were stopped only after TOF measurements were complete to prevent possible pain. Thirty milligrams of tenoxicam and 1 g of paracetamol were given IV 30 min before the end of the operation for post-operative analgesia. No

narcotic analgesics were given. Peak heart rate (PHR), mean blood pressure, and peripheral capillary oxygen saturation (SpO_2) were measured at 5, 10, 20, 30, 45, 60, 75, and 90 min beginning from anesthesia induction. For TOF measurements, the device was calibrated after induction with propofol and before administration of rocuronium. Time was kept after rocuronium injection (0 min). TOF was measured with four supramaximal stimuli of 2 Hz every 0.5 s with the device's automatic measurement mode until intubation. Time to intubation, start of surgery, and end of surgery were recorded. Time to intubation was measured as the time from calibration to a TOF of zero. After surgery and when the TOF was 2, the timer was reset. The TOF device was again set to 15-s automatic measurement mode. Heart rate, mean arterial pressure (MAP), and SpO_2 were recorded at 0, 5, 10, 15, and 20 min. TOF recordings were stopped when the TOF ratio was 0.9 or higher. Anesthesia maintenance was stopped when the TOF ratio was 0.9. After completion of surgery, beginning from the reset time, time to reach a TOF ratio of 0.9, and time to extubation were recorded. Patients were observed in the recovery room for 30 min for adverse effects (nausea, vomiting, blurred vision, and others). Those with Aldrete scores ≥ 9 were transferred to the ward.

Statistical Analysis

To provide an alpha of 0.05 and power of 80%, we decided to include 68 patients.

The number cruncher statistical system 2007 (Kaysville, Utah, USA) was used for statistical analysis. Besides descriptive statistics (mean, standard deviation, median, frequency, ratio, minimum, and maximum), incomparision of quantitative data, Student's t-test was used for parameters with normal distribution and Mann-Whitney U test was used for parameters without normal distribution. For the comparison of qualitative data, Pearson's Chi-square test, Fisher's exact test, and Yates's continuity correction test were used. Significance was set at $p < 0.01$ or $p < 0.05$.

RESULTS

The ages of the patients ranged between 20 and 60 years with a mean of 39.56 ± 10.97 years. Age, height, BMI, duration of anesthesia, and operative times showed no statistically significant differences between the groups ($p > 0.05$) (Table 1).

TABLE 1. Demographic characteristics of groups

	Group NT (n=34)	Group SM (n=34)	p
Age (years)			
Min-Max (median)	22-59 (38)	20-60 (38)	^a 0.476
Weight (kg)			
Min-Max (median)	105-191 (127)	91-175 (123)	^b 0.068
Height (cm)			
Min-Max (median)	150-195 (160)	151-180 (165)	^b 0.389
BMI (kg/m ²)			
Min-Max (median)	40-57 (48)	36-58 (45.2)	^b 0.156
Anesthesia duration (min)			
Min-Max (median)	60-160 (110)	57-240 (120)	^b 0.116
Operation time (min)			
Min-Max (median)	50-140 (95)	45-230 (100)	^b 0.311

NT: Neostigmine; SM: Sugammadex; a: Student t-test; b: Mann-Whitney U test; *: $P < 0.05$.

There was no significant difference in terms of measurements of total rocuronium use between the groups. Time to extubation, time to TOF ratio of 0.9, time until patients responded to stimuli, time until cooperation, and time until orientation were significantly shorter in the SM group than in the NT group. The time to an Aldrete score of 9 in the SM group was significantly shorter than in the NT group (Table 2).

The MAP and PHR of the patients after induction, intubation, ending of anesthesia, and extubation showed no statistically significant difference between the groups ($p > 0.05$).

Post-operative respiratory insufficiency, nausea, vomiting, hypotension, hypertension, and presence of pain showed no statistically significant difference between the groups ($p > 0.05$) (Table 3).

DISCUSSION

Bariatric operations are short and widespread interventions with short lengths of stay. The morbidly obese patient group brings risk of anesthetic redistribution and longer time of post-operative anesthetic recovery [5, 6]. A higher incidence of PORC in morbidly obese patients has been shown in literature [1, 2], thus it is important to prevent PORC in this population, which already has high risk of post-operative respira-

TABLE 2. Recovery properties of groups

		Group NT (n=34)	Group SM (n=34)	^b p
Total rocuronium (mg)	Min–Max(median)	100–140 (120)	90–150 (130)	0.340
Time to extubation (min)	Min–Max (Median)	1–25 (5)	1–14 (3)	0.001**
Time to TOF ratio of 0.9 (min) (n=68)	Min–Max (Median)	3–15 (6)	1–14 (3)	0.001**
Time until response to verbal stimuli (min)	Min–Max (Median)	2–17 (6)	1–16 (4)	0.001**
Time until cooperation (min) (n=68)	Min–Max (Median)	3–19 (7)	1–9 (4)	0.001**
Time until orientation (min)	Min–Max (Median)	4–20 (10)	1–18 (5)	0.001**
Time to Aldrete score = 9 (min) (n=68)	Min–Max (Median)	1–15 (6)	1–15 (4)	0.001**

TOF: Trainoffour; NT: Neostigmine; SM: Sugammadex; b: Mann-Whitney U test; **: P<0.01.

tory complications. One of the most important factors in PORC prevention is effective decurarization. NT is a cholinesterase inhibitor used for antagonizing neuromuscular blockers and has the undesired adverse effects of bradycardia, increased secretions in airways, and bronchospasm [7, 8]. In addition, studies have shown that time to a TOF ratio of 0.9 is longer with NT in morbidly obese patients compared with patients of normal weight [9].

Geldner et al. [10] compared SM and NT in different depths of neuromuscular blockage in their study conducted with 140 patients undergoing laparoscopic surgery. In all depths, including deep neuromuscular blockage, SM was found to have a faster effect.

Gaszynski et al. [11] compared SM and NT in morbidly obese patients and found SM to be preventive against post-operative residue, and safe in morbidly obese patients, whereas NT had several adverse effects such as needing longer times for neuromuscular blockage reversal. In their study on bariatric surgery in obese patients, Carron et al. [12] stressed faster recovery times with SM than with NT and that SM could be preferred in this patient group.

With faster recovery times shown with SM in bariatric surgery, other studies on other surgeries and short interventions documented parallel results [13, 14]. Kara et al. [15] compared SM and NT in 80 pediatric outpatients aged between 2 and 12 years. SM was given at a dose of 2 mg/kg and NT 30 µg/kg. Similar to our study, the authors found significantly shorter time to a TOF ratio of 0.9 and time to extubation with SM. Ammar et al. [16] also found similar results with 60 patients of the same age group.

TABLE 3. Post-operative adverse effects of groups

	Group NT (%)	Group SM (%)	p
Respiratory insufficiency	23.5	11.7	^c 0.691
Nausea	20.5	14.7	^c 0.999
Vomiting	2.9	0	^d 0.999
Hypotension	0	2.9	^d 0.426
Hypertension	44	26	^c 0.706
Pain	14.7	20.5	^c 0.374

NT: Neostigmine; SM: Sugammadex; c: Yates's continuity correction test; d: Fisher's exact test.

Schepens et al. [17] used EMG to investigate the effects of NT and SM on the diaphragm and observed SM to be considerably more effective in restoring diaphragm activity. Same authors designed a second study with the hypothesis that NT could potentiate the effects of SM. In that study, one group received NT only, one group received SM only, but the third group received SM 3 min after NT. Both diaphragm and intercostal muscular restorations were investigated using EMG. The striking result of the study was that diaphragm EMG recovery was better in the group that received SM alone than in the other two groups [18].

In a study, SM was found have lower incidence of post-operative residual blockage, radiologic atelectasis, and pneumonia within 30 days compared to NT [19]. Llauradó et al. [20] reported less post-operative chest X-ray changes with SM, but no difference in post-operative mechanical ventilation requirement in their study that compared SM and NT in 160 patients undergoing bariatric surgery.

Unal et al. [21] compared SM and NT as antidotes in 74 patients with an average BMI of 28 kg/m² undergoing surgery for obstructive sleep apnea syndrome (OSAS). Anesthesia was maintained with desflurane. SM was given at a dose of 2 mg/kg and NT 40 µg/kg, together with 0.5 mg of atropine. Time to TOF ratio of 0.9 was 2 min in the SM group and 8 min in the NT group, with a significant difference, similar to our study. Again, similar to our results, the rate of post-operative bradycardia was higher in the NT group. Unal et al. [21] found higher incidences of post-operative respiratory complications in all groups and especially in the NT group, which was different from the results of our study.

The results of Unal et al. [21] differed from ours in that they observed more post-operative respiratory system complications in general, with higher rates in the NT group. We believe that the disparity between their results and ours can be accounted for by the fact that the surgery in their study concerned the upper respiratory tract and the patients had OSAS. Nevertheless, their results were valuable because they studied a specific group of patients with OSAS and showed less post-operative complications with SM.

Our results showed no difference in terms of rates of nausea and vomiting between the two groups, similar to the study of Geldner et al. [10]; however, some studies have shown this rate to be lower in patients on SM [22, 23].

High doses of NT are insufficient for reversal of block after high dose rocuronium use. Even if the first application is effective, the duration of action will be shorter after reaching the effect, and recurrence may be seen in the resulting neuromuscular blocker encounter. Therefore, the total dose of rocuronium used will affect reversal of the neuromuscular block. In our study, no significant difference was found between the two groups in terms of total rocuronium dose (Table 2, $p=0.340>0.01$). Total rocuronium dose used in the study by Carron et al. [12] did not show a significant difference between the two groups, similar to our study.

Conclusion

Recovery is faster with SM than with NT in morbidly obese patients following bariatric surgery, and the two agents are not significantly different in terms of adverse effects. Considering the high risk of post-operative respiratory insufficiency in morbidly obese patients, SM could be a safer choice in this patient group.

Ethics Committee Approval: The Haydarpasa Numune Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 27.10.2014, number: AEK 2014/KK77).

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REFERENCES

1. Arbous MS, Meursing AE, van Kleef JW, de Lange JJ, Spoormans HH, Touw P, et al. Impact of anesthesia management characteristics on severe morbidity and mortality. *Anesthesiology* 2005;102:257–68.
2. Murphy GS, Szokol JW, Marymont JH, Greenberg SB, Avram MJ, Vender JS. Residual neuromuscular blockade and critical respiratory events in the postanesthesia care unit. *Anesth Analg* 2008;107:130–7.
3. Baillard C, Clec'h C, Catineau J, Salhi F, Gehan G, Cupa M, et al. Post-operative residual neuromuscular block: a survey of management. *Br J Anaesth* 2005;95:622–6. [CrossRef]
4. Meistelman C, Fuchs-Buder T, Raft J. Sugammadex development and use in clinical practice. *Curr Anesthesiol Rep* 2013;2:122–9. [CrossRef]
5. Raeder J. Bariatric procedures as day/short stay surgery: is it possible and reasonable? *Curr Opin Anaesthesiol* 2007;20:508–12. [CrossRef]
6. Murphy GS, Szokol JW, Marymont JH, Greenberg SB, Avram MJ, Vender JS. Residual neuromuscular blockade and critical respiratory events in the postanesthesia care unit. *Anesth Analg* 2008;107:130–7.
7. Eikermann M, Fassbender P, Malhotra A, Takahashi M, Kubo S, Jordan AS, et al. Unwarranted administration of acetylcholinesterase inhibitors can impair genioglossus and diaphragm muscle function. *Anesthesiology* 2007;107:621–9. [CrossRef]
8. Plaud B, Debaene B, Donati F, Marty J. Residual paralysis after emergence from anesthesia. *Anesthesiology* 2010;112:1013–22. [CrossRef]
9. Carron M, Freo U, Ori C. Sugammadex for treatment of postoperative residual curarization in a morbidly obese patient. *Can J Anaesth* 2012;59:813–4. [CrossRef]
10. Geldner G, Niskanen M, Laurila P, Mizikov V, Hübler M, Beck G, et al. A randomised controlled trial comparing sugammadex and neostigmine at different depths of neuromuscular blockade in patients undergoing laparoscopic surgery. *Anaesthesia* 2012;67:991–8. [CrossRef]
11. Gaszynski T, Szewczyk T, Gaszynski W. Randomized comparison of sugammadex and neostigmine for reversal of rocuronium-induced muscle relaxation in morbidly obese undergoing general anaesthesia. *Br J Anaesth* 2012;108:236–9. [CrossRef]
12. Carron M, Veronese S, Foletto M, Ori C. Sugammadex allows fast-track bariatric surgery. *Obes Surg* 2013;23:1558–63. [CrossRef]
13. Choi ES, Oh AY, Koo BW, Hwang JW, Han JW, Seo KS, et al. Comparison of reversal with neostigmine of low-dose rocuronium vs. reversal with sugammadex of high-dose rocuronium for a short procedure. *Anaesthesia* 2017;72:1185–90. [CrossRef]
14. Abad-Gurumeta A, Ripollés-Melchor J, Casans-Francés R, Espinosa A, Martínez-Hurtado E, Fernández-Pérez C, et al; Evidence Anaesthesia Review Group. A systematic review of sugammadex vs neostigmine for reversal of neuromuscular blockade. *Anaesthesia* 2015;70:1441–52.

15. Kara T, Ozbagriacik O, Turk HS, Isil CT, Gokuc O, Unsal O, et al. Sugammadex versus neostigmine in pediatric patients: a prospective randomized study. [Article in Portuguese]. *Rev Bras Anesthesiol* 2014;64:400–5. [\[CrossRef\]](#)
16. Ammar AS, Mahmoud KM, Kasemy ZA. A comparison of sugammadex and neostigmine for reversal of rocuronium-induced neuromuscular blockade in children. *Acta Anaesthesiol Scand* 2017;61:374–80.
17. Schepens T, Cammu G, Saldien V, De Neve N, Jorens PG, Foubert L, et al. Electromyographic activity of the diaphragm during neostigmine or sugammadex-enhanced recovery after neuromuscular blockade with rocuronium: a randomised controlled study in healthy volunteers. *Eur J Anaesthesiol* 2015;32:49–57. [\[CrossRef\]](#)
18. Cammu G, Schepens T, De Neve N, Wildemeersch D, Foubert L, Jorens PG. Diaphragmatic and intercostal electromyographic activity during neostigmine, sugammadex and neostigmine-sugammadex-enhanced recovery after neuromuscular blockade: A randomised controlled volunteer study. *Eur J Anaesthesiol* 2017;34:8–15. [\[CrossRef\]](#)
19. Ledowski T, Hillyard S, O'Dea B, Archer R, Vilas-Boas F, Kyle B. Introduction of sugammadex as standard reversal agent: Impact on the incidence of residual neuromuscular blockade and postoperative patient outcome. *Indian J Anaesth* 2013;57:46–51. [\[CrossRef\]](#)
20. Llauradó S, Sabaté A, Ferreres E, Camprubí I, Cabrera A. Postoperative respiratory outcomes in laparoscopic bariatric surgery: comparison of a prospective group of patients whose neuromuscular blockade was reverted with sugammadex and a historical one reverted with neostigmine. *Rev Esp Anesthesiol Reanim* 2014;61:565–70. [\[CrossRef\]](#)
21. Ünal DY, Baran İ, Mutlu M, Ural G, Akkaya T, Özlü O. Comparison of sugammadex versus neostigmine costs and respiratory complications in patients with obstructive sleep apnoea. *Turk J Anaesthesiol Reanim* 2015;43:387–95. [\[CrossRef\]](#)
22. Martinez-Ubieto J, Ortega-Lucea S, Pascual-Bellosta A, Arazo-Iglesias I, Gil-Bona J, et al. Prospective study of residual neuromuscular block and postoperative respiratory complications in patients reversed with neostigmine versus sugammadex. *Minerva Anesthesiol* 2016;82:735–42.
23. Batistaki C, Tentés P, Deligiannidi P, Karakosta A, Florou P, Kostopaniagiotou G. Residual neuromuscular blockade in a real life clinical setting: correlation with sugammadex or neostigmine administration. *Minerva Anesthesiol* 2016;82:550–8.
24. Carron M, Veronese S, Foletto M, Ori C. Sugammadex allows fast-track bariatric surgery. *Obes Surg* 2013;23:1558–63. [\[CrossRef\]](#)