e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2024; 16(5); 293-297

Original Research Article

Sugammadex versus Neostigmine as a Reversal Agent in Obese Patients and its Postoperative Efficiency

Stuti Kumari[1], Ravi Kumar[2], Nitin Ojha[3], Bijoy Kumar[4]

[1]Senior Resident, Department of Anaesthesia & Intensive Care, Nalanda Medical College and Hospital, Patna, Bihar, India

[2]Senior Resident, Department of Anaesthesia & Intensive Care, Nalanda Medical College and Hospital, Patna, Bihar, India

3Assistant Professor, Department of Anaesthesia & Intensive Care, Nalanda Medical College and Hospital, Patna, Bihar, India

[4]Professor and HOD, Department of Anaesthesia & Intensive Care, Nalanda Medical College and Hospital, Patna, Bihar, India

Received: 20-02-2024 / Revised: 10-03-2024 / Accepted: 15-04-2024
Corresponding Author: Dr. Ravi Kumar
Conflict of interest: Nil

Abstract

Aim: The aim of the present study was to compare the benefits and harms of sugammadex and neostigmine in obese patients and its post-operative efficiency.

Methods: The present study was conducted in the Department of Anaesthesia & Intensive Care, Nalanda Medical College and Hospital, Patna, Bihar, India. 100 obese patients were included in the study.

Results: Demographic and baseline characteristics including gender, age, race, ASA physical status, and preoperative diagnosis were similar between groups. The median age was 49 [44, 65] years old in Group N and 57 [47, 63] years old in Group S (p = 0.72). Moreover, 56% of patients in Group N were males, whereas 60% in Group S were females. The median body mass index (BMI) was slightly higher in Group S when compared to Group N. The median time elapsed from neuromuscular blockade reversal administration to extubation was slightly shorter in the Group S when compared to Group N. Overall, the median time elapsed from neuromuscular blockade reversal administration to OR readiness-for-discharge was similar between Group S and Group N. Cholecystectomy was the most common procedure performed in both groups. There were no statistically significant differences in median length of anesthesia or surgery between groups. The median length of hospital stay (Phase II and/or hospitalization) was similar between groups (166 [102, 245] min for Group N versus 118 [83, 175] min for Group S; p = 0.11). In addition, the total time of hospitalization for Group N was 543 and 466.5 min for Group S. The overall incidence of adverse events was 23% and there were not statistical difference among groups. However, postoperative nausea and vomiting, urinary retention, and shortness of breath were the most common perioperative complications.

Conclusion: Sugammadex offers a significantly faster, predictable, and safer recovery profile from neuromuscular blockade than neostigmine in patients undergoing outpatient surgical abdominal procedures in obese patients.

Keywords: sugammadex, neostigmine, obese patients, post-operative efficiency

Introduction

Morbid obesity (MO), defined as body mass index (BMI) >40 kg.m−2, occurs in 2%–5% in the Western societies. The worldwide increase in the incidence of obesity has led to an increased demand for bariatric surgery, which offers an important treatment for these patients. [1,2] An increased risk for postoperative respiratory complications from general anesthesia and paralysis makes adequate reversal from neuromuscular blockade (NMB) crucial in MO patients. Acetylcholine inhibitors, such as neostigmine, have been conventionally used to reverse NMB. Their action on muscarinic cholinergic receptors causes undesirable side effects such as bradycardia, hypotension, bronchoconstriction, airway secretions, and increased gastrointestinal motility. They are also associated with unpredictable reversal and a risk of postoperative residual curarization (PORC). [3,4]

The discovery of sugammadex was considered a revolution in the domain of neuromuscular reversal.

[5] Sugammadex is a synthetically modified gamma-cyclodextrin that is specifically designed to encapsulate rocuronium and vecuronium and reverse their effects. Two recent systematic review and meta-analysis (SR and MA) have compared the efficacy and safety of sugammadex and neostigmine in reversing NMB in adults and have found sugammadex to allow a faster neuromuscular recovery from rocuronium-induced NMB, with fewer adverse effects. [6,7] This can result in a reduced duration of anesthesia, higher flow of patients through the operating theater, and more efficient use of healthcare resources. [7]

Sugammadex is a cyclodextrin with a novel mechanism of action and widely reported efficacy for neuromuscular blockade reversal. [8,9] Sugammadex encapsulates the rocuronium molecule creating a stable complex that is removed by the glomeruli, bypassing the hepatobiliary metabolic pathway. [10] The dose of 2 mg/kg is recommended for the reversal of a moderate rocuronium- or vecuronium-induced neuromuscular blockade. Likewise, a dose of 4–8 mg/kg is effective for the reversal of deep neuromuscular blockade and a single dose of 16 mg/kg is advisable to reverse the neuromuscular blockade within 3 min after the administration of 1.2 mg/kg of rocuronium. [11] The use of sugammadex has been linked to a significant reduction in the time for extubation and operating room (OR) readiness for discharge. However, its cost-effectiveness remains unclear. [12] In a systematic review, Paton et al. mentioned the lack of evidence concerning sugammadex cost and "efficient use of resources." The review discussed the cost-effectiveness of the drug based on the United Kingdom practice where OR staff time was evaluated at £4.44 per minute. [13] Similarly, the cost of sugammadex has been identified as one of the main limiting factor for its use in the United States. [14] Reported evidence on the incidence of postoperative pulmonary complications, residual neuromuscular blockade, postoperative nausea and vomiting (PONV), and PACU LOS after the use of sugammadex is highly variable. [15]

The aim of the present study was to compare the benefits and harms of sugammadex and neostigmine in obese patients and its post-operative efficiency.

Materials and Methods

The present study was conducted in the Department of Anaesthesia & Intensive Care, Nalanda Medical College and Hospital, Patna, Bihar, India for one year. 100 obese patients were included in the study.

Inclusion Criteria

Adult patients were eligible for inclusion in the study provided they are American Society of Anesthesiologists Class 1, 2, or 3, scheduled for an elective surgical procedure under general anesthesia using rocuronium for tracheal intubation and maintenance of NMB, and required reversal of NMB.

Exclusion Criteria

Exclusion criteria were any anatomical malformation that might cause difficult intubation; any patient transferred to the intensive care unit after surgery; neuromuscular disorders that could affect the NMB; (family) history of malignant hyperthermia; allergy to opioids/opiates, cyclodextrins including sugammadex, muscle relaxants and their excipients, or other medications used during general anesthesia; administration of toremifene and/or fusidic acid within 24 hours of study drug administration (or plan to administer these drugs within 24 hours after study drug administration); any condition contraindicating neostigmine and/or glycopyrrolate; pregnant females; participation in a previous sugammadex study; participation in another clinical drug study within 30 days inclusive of signing consent for the current study; or a member of, or related to, the investigational staff or sponsor staff.

Eligible patients were randomized on a 1 : 1 basis to receive either sugammadex 2.0 mg/kg or neostigmine 50 μg/kg plus glycopyrrolate 10 μg/kg for NMB reversal. Anesthesia was induced with intravenous propofol and maintained with inhalational sevoflurane. Opioids were administered according to local practice when clinically required. Neuromuscular monitoring was carried out using continuous acceleromyography at the adductor pollicis muscle with the TOF-Watch SX® (Organon Ireland Ltd., a subsidiary of Merck and Co., Swords, Co. Dublin, Ireland).

Following induction of anesthesia, the TOF-Watch SX® device was attached, stabilized, and calibrated. Rocuronium 0.6 mg/kg was administered as a single bolus dose for intubation, and NMB was maintained with one or more doses of 0.1 to 0.2 mg/kg rocuronium as clinically required. After the last dose of rocuronium, at the reappearance of T2, a single intravenous (IV) dose of sugammadex 2.0 mg/kg or a single IV dose of neostigmine 50 μg/kg plus glycopyrrolate 10 μg/kg was administered to reverse the NMB.

Results

Table 1: Demographics and baseline variables

Variable	Overall (n = 100)	Neostigmine (n = 50)	Sugammadex (n = 50)	P-value
Age, years, median [IQR]	54 [45, 63]	49 [44, 65]	57 [47, 63]	0.72
Gender, male, n (%)	48 (48%)	28 (56%)	20 (40%)	0.22
Gender, female, n (%)	52 (52%)	22 (44%)	30 (60%)	
Height, m, median [IQR]	1.7 [2, 1.8]	1.7 [2, 1.9]	1.7 [2, 1.7]	0.23
Weight, kg, median [IQR]	95.3 [80, 102.5]	86.4 [79, 100.9]	92.4 [86, 103.9]	0.48
BMI, kg/m^2 , median [IQR]	30.4 [28, 34.8]	28.2 [27, 33.8]	32.5 [29, 39.1]	0.07
ASA classification, I/II/III, n	10/50/40	10/25/20	0/25/20	0.32
Preoperative diagnosis n (%)				
Calculus of gallbladder/cholecystitis	52 (52)	28	24	
Inguinal hernia	30 (30)	22	8	0.12
Ventral hernia	16 (16)	4	12	
Appendix condition (mass, appendicitis)	2 (2)	2	0	

Demographic and baseline characteristics including gender, age, race, ASA physical status, and preoperative diagnosis were similar between groups. The median age was 49 [44, 65] years old in Group N and 57 [47, 63] years old in Group S (p = 0.72). Moreover, 56% of patients in Group N were males, whereas 60% in Group S were females. The median body mass index (BMI) was slightly higher in Group S when compared to Group N.

Table 2: Perioperative variables

Variable	Overall (n = 100)	Neostigmine (n = 50)	Sugammadex (n = 50)	P-value
Procedure performed n (%)				
Inguinal hernia repair	30 (30)	22	8	
Cholecystectomy	52 (52)	28	24	0.12
Appendectomy	1 (2.7)	1 (5.3)	0 (0.00)	
Ventral hernia repair	16 (16)	4	12	
Length of anesthesia, min, median [IQR]	98 [80, 127]	99 [80, 132]	95 [74, 117]	0.52
Length of surgery, min, median [IQR]	61 [51, 90]	61 [51, 93]	61.5 [51, 78]	0.80
Incision closure to extubation time, min, median [IQR]	6 [3,8]	7 [5,8]	4.5 [2,6]	0.24
IP Administration to extubation time, min, median [IQR]	12 [8, 15]	13 [11, 16]	10.5 [7, 15]	0.16
IP Administration to anesthesia readiness, min, median [IQR]	15 [12, 17]	15 [14, 18]	14 [9, 16]	0.16
Phase I duration, min, median [IQR]	60 [44, 90]	56 [45, 84]	63.5 [44, 118]	0.32
Phase II duration, min, median [IQR]	133 [85, 213]	166 [102, 245]	118 [83, 175]	0.12
Total time hospitalization, min, median [IQR]	510 [415, 604]	543 [430, 625]	466.5 [404, 548]	0.36

The median time elapsed from neuromuscular blockade reversal administration to extubation was slightly shorter in the Group S when compared to Group N. Overall, the median time elapsed from neuromuscular blockade reversal administration to OR readiness-for-discharge was similar between Group S and Group N. Cholecystectomy was the most common procedure performed in both groups. There were no statistically significant differences in median length of anesthesia or surgery between groups. The median length of hospital stay (Phase II and/or hospitalization) was similar between groups (166 [102, 245] min for Group N versus 118 [83, 175] min for Group S; p = 0.11). In addition, the total time of hospitalization for Group N was 543 and 466.5 min for Group S.

Table 3: Postoperative complications

Variables	Overall (n = 100)	Neostigmine (n = 50)	Sugammadex (n = 50)	P-value
Postoperative nausea and vomiting n (%)	14 (14)	3 (6)	1 (22)	0.22
Urinary retention n (%)	6 (6)	3 (5)	0 (0.0)	0.42
Shortness of breath n (%)	3 (3)	3 (1.5)	0 (0.0)	>0.99

The overall incidence of adverse events was 23% and there were not statistical difference among groups. However, postoperative nausea and vomiting, urinary retention, and shortness of breath were the most common perioperative complications.

Discussion

Sugammadex, a modified γ-cyclodextrin, has been used clinically to reverse neuromuscular blockade (NMB) of steroidal neuromuscular blocking drugs (NMBDs). [16] The drug provides fast recovery of neuromuscular function and prevents postoperative residual NMB in patients with severe obesity. [17] Accordingly, sugammadex is recommended for patients with body mass index (BMI) ≥ 35 kg/m2 as an NMB reversal agent in our center after obtaining their informed consent. Although there are several studies exploring the effects of sugammadex on PONV, most of the available evidence suggests that sugammadex only tends to reduce the occurrence of PONV; however, these results failed to reach statistical significance. [18,19]

Demographic and baseline characteristics including gender, age, race, ASA physical status, and preoperative diagnosis were similar between groups. The median age was 49 [44, 65] years old in Group N and 57 [47, 63] years old in Group S (p = 0.72). Moreover, 56% of patients in Group N were males, whereas 60% in Group S were females. The median body mass index (BMI) was slightly higher in Group S when compared to Group N. The median time elapsed from neuromuscular blockade reversal administration to extubation was slightly shorter in the Group S when compared to Group N. Overall, the median time elapsed from neuromuscular blockade reversal administration to OR readiness-for-discharge was similar between Group S and Group N. In an open parallel study, Sacan et al [20] reported a significant reduction on the times to achieve TOF ratios of 0.7, 0.8, and 0.9 in patients receiving sugammadex when compared to edrophonium and neostigmine groups (p < 0.05). In addition, sugammadex administration has been associated with a faster deep neuromuscular blockade (1–2 PTC responses) reversal and a greater predictability to a TOF ratio of 0.9 within 5 min in comparison with neostigmine (98% versus 11%, respectively). [21,22]

Morbid obesity, procedure performed, anesthesia type, past medical history of hypertension and scheduled surgery duration have been identified as the main factors associated with a prolonged PACU LOS in outpatient care centers. [23] In addition, intraoperative surgical training activities caused significant delays in the last stage of the surgery in our academic institution, which could have resulted in subsequent prolongation of the OR-to-PACU readiness-for-discharge times and PACU LOS, regardless of the type of procedure and randomization group. Cholecystectomy was the most common procedure performed in both groups. There were no statistically significant differences in median length of anesthesia or surgery between groups. The median length of hospital stay (Phase II and/or hospitalization) was similar between groups (166 [102, 245] min for Group N versus 118 [83, 175] min for Group S; p = 0.11). In addition, the total time of hospitalization for Group N was 543 and 466.5 min for Group S. The overall incidence of adverse events was 23% and there were not statistical difference among groups. However, postoperative nausea and vomiting, urinary retention, and shortness of breath were the most common perioperative complications.

In contrast, sugammadex does not interfere with the acetylcholinesterase receptor system. In addition, the use of sugammadex has been linked to a faster and predictable reversal of any degree of neuromuscular blockade, reduced incidence of residual neuromuscular block and more efficient utilization of healthcare resources. [24] However, hypersensitivity reactions, cough, oral discomfort, increased partial thromboplastin time (PTT), severe bradycardia, and asystole have been also described after its administration. [25,26] Postoperative nausea and vomiting was the only adverse effect reported in Group S in our study. Nevertheless, prolongation of the hospitalization was not necessary in any of these patients.

Conclusion

Sugammadex offers a significantly faster, predictable, and safer recovery profile from neuromuscular blockade than neostigmine in patients undergoing outpatient surgical abdominal procedures in obese patients.

References

1. Casati A, Putzu M. Anesthesia in the obese patient: pharmacokinetic considerations. J Clin Anesth. 2005 Mar;17(2):134-45.

2. Buchwald H, Oien DM. Metabolic/bariatric surgery Worldwide 2008. Obes Surg. 2009 Dec; 19(12):1605-11.
3. Caldwell JE. Clinical limitations of acetylcholinesterase antagonists. J Crit Care. 2009 Mar;24(1):21-8.
4. Keating GM. Sugammadex: A Review of Neuromuscular Blockade Reversal. Drugs. 2016 Jul;76(10):1041-52.
5. Sacan O, White PF, Tufanogullari B, Klein K. Sugammadex reversal of rocuronium-induced neuromuscular blockade: a comparison with neostigmine-glycopyrrolate and edrophonium-atropine. Anesth Analg. 2007 Mar;104(3):569-74.
6. Hristovska AM, Duch P, Allingstrup M, Afshari A. The comparative efficacy and safety of sugammadex and neostigmine in reversing neuromuscular blockade in adults. A Cochrane systematic review with meta-analysis and trial sequential analysis. Anaesthesia. 2018 May;73(5):631-641.
7. Carron M, Zarantonello F, Lazzarotto N, Tellaroli P, Ori C. Role of sugammadex in accelerating postoperative discharge: A meta-analysis. J Clin Anesth. 2017 Jun;39:38-44.
8. Nag K, Singh DR, Shetti AN, Kumar H, Sivashanmugam T, Parthasarathy S. Sugammadex: A revolutionary drug in neuromuscular pharmacology. Anesthesia Essays and Researches. 2013 Sep 1;7(3):302-6.
9. Keating GM. Sugammadex: a review of neuromuscular blockade reversal. Drugs. 2016 Jul;76:1041-52.
10. Kovac AL. Sugammadex: the first selective binding reversal agent for neuromuscular block. Journal of clinical Anesthesia. 2009 Sep 1;21(6):444-53.
11. US Food and Drug Administration. BRIDION®(sugammadex) Injection, for intravenous use.
12. Carron M, Zarantonello F, Tellaroli P, Ori C. Efficacy and safety of sugammadex compared to neostigmine for reversal of neuromuscular blockade: a meta-analysis of randomized controlled trials. Journal of clinical anesthesia. 2016 Dec 1;35:1-2.
13. Paton F, Paulden M, Chambers D, Heirs M, Duffy S, Hunter JM, Sculpher M, Woolacott N. Sugammadex compared with neostigmine/glycopyrrolate for routine reversal of neuromuscular block: a systematic review and economic evaluation. British journal of anaesthesia. 2010 Nov 1;105(5):558-67.
14. Deyhim N, Beck A, Balk J, Liebl MG. Impact of Sugammadex Versus Neostigmine/ Glycopyrrolate on Perioperative Efficiency. Clinicoecon Outcomes Res. 2020 Jan 31;12: 69-79.
15. Brett K, Farrah K. Sugammadex for the reversal of rocuronium-induced neuromuscular blockade in surgical patients: a review of clinical effectiveness.
16. Swerdlow B, Osborne-Smith L. Sugammadex: pharmacometrics, clinical utility, and adverse effects. AANA J. 2022;90(2):133–40.
17. Subramani Y, Querney J, He S, Nagappa M, Yang H, Fayad A. Efficacy and safety of sugammadex versus neostigmine in reversing neuromuscular blockade in morbidly obese adult patients: a systematic review and meta-analysis. Anesth Essays Res. 2021;15(1):111–8.
18. Ba YF, Liu YN, He SH, Li HM, Wang HR, Zhu JP, et al. Analysis of sugammadex for antagonistic neuromuscular block in patients with radical resection of lung cancer under thoracoscope. Zhonghua Yi Xue Za Zhi. 2020; 100(3):213–9.
19. Hristovska AM, Duch P, Allingstrup M, Afshari A. Efficacy and safety of sugammadex versus neostigmine in reversing neuromuscular blockade in adults. Cochrane Database Syst Rev. 2017;8(8):Cd012763.
20. Sacan O, White PF, Tufanogullari B, Klein K. Sugammadex reversal of rocuronium-induced neuromuscular blockade: a comparison with neostigmine–glycopyrrolate and edrophonium–atropine. Anesthesia & Analgesia. 2007 Mar 1;104(3):569-74.
21. Blobner M, Eriksson LI, Scholz J, Motsch J, Della Rocca G, Prins ME. Reversal of rocuronium-induced neuromuscular blockade with sugammadex compared with neostigmine during sevoflurane anaesthesia: results of a randomised, controlled trial. European Journal of Anaesthesiology| EJA. 2010 Oct 1;27(10): 874-81.
22. Jones RK, Caldwell JE, Brull SJ, Soto RG. Reversal of profound rocuronium-induced blockade with sugammadex: a randomized comparison with neostigmine. The Journal of the American Society of Anesthesiologists. 2008 Nov 1;109(5):816-24.
23. Gabriel RA, Waterman RS, Kim J, Ohno-Machado L. A predictive model for extended postanesthesia care unit length of stay in outpatient surgeries. Anesthesia & Analgesia. 2017 May 1;124(5):1529-36.
24. Cada DJ, Levien TL, Baker DE. Sugammadex. Hospital Pharmacy. 2016 Jul;51(7):585-96.
25. Pühringer FK, Rex C, Sielenkämper AW, Claudius C, Larsen PB, Prins ME, Eikermann M, Khuenl-Brady KS. Reversal of profound, high-dose rocuronium-induced neuromuscular blockade by sugammadex at two different time points: an international, multicenter, randomized, dose-finding, safety assessor-blinded, phase II trial. The Journal of the American Society of Anesthesiologists. 2008 Aug 1;109(2):188-97.
26. Bhavani SS. Severe bradycardia and asystole after sugammadex. British Journal of Anaesthesia. 2018 Jul 1;121(1):95-6.