Print ISSN: 2321-6379
Online ISSN: 2321-595X

Original Article

Effect of Sugammadex and Neostigmine-Glycopyrrolate on Post-operative Nausea and Vomiting in Middle Ear Surgeries: A Comparative Study

Chavi Sethi[1], Chitrangana Gupta[2], Shubam Achari[3]

[1]Associate Professor, Department of Anesthesia, MLB Medical College, Jhansi, Uttar Pradesh, India, [2]Assistant Professor, Department of Anesthesia, MLB Medical College, Jhansi, Uttar Pradesh, India, [3]Junior Resident, Department of Anesthesia, MLB Medical College, Jhansi, Uttar Pradesh, India

Abstract

Background and Objectives: Post-operative emesis is one of the most common and significant problems in modern anesthetic practice, especially in today's era of a growing trend toward daycare surgeries. Our study is focused on comparing the effects of neostigmine and sugammadex on the antagonism of neuromuscular blockage, specifically in relation to the incidence of post-operative nausea and vomiting (PONV) in patients undergoing elective middle ear surgery.

Materials and Methods: In this prospective, randomized, double-blinded study, a group of 140 patients of the American Society of Anesthesiology I or II, either sex, aged 18–65 years who underwent elective middle ear surgery under general anesthesia were recruited. The objective of the study was to compare the effects of two different medications for reversing neuromuscular blockade. Group I received neostigmine 2.5 mg in combination with glycopyrrolate 0.5 mg, while Group II received sugammadex 2 mg/kg. The assessment of PONV scores and the requirement for anti-emetic rescue was conducted upon arrival in the post-anesthesia recovery unit, as well as at specific time intervals following the reversal.

Results: Patients in Group II experienced a significantly lower incidence of PONV compared to those in Group I during the 0–2 h interval post-operative (P = 0.002). The occurrence of PONV was similar during other time intervals. The significance of the rescue antiemetic was evident as patients in Group I received a higher number of doses.

Conclusion: Our findings suggest that sugammadex shows potential for reducing the occurrence of PONV in elective middle ear surgery and can be used as an alternative to neostigmine.

Key words: Neostigmine, Post-operative nausea and vomiting, Sugammadex

INTRODUCTION

Post-operative emesis is a common occurrence following ear, nose, and throat surgeries unless preventive measures are taken. Experiencing nausea or vomiting after surgery can worsen the condition of the patient, resulting in a longer recovery period and a delay in release from the hospital.[1] Approximately 20–30% of patients may experience post-operative nausea and vomiting (PONV) after receiving general anesthesia.[2] Neostigmine is an anticholinesterase inhibitor that helps counteract muscle paralysis caused by non-depolarizing muscle relaxants. It does this by forming a complex with an enzyme, which leads to an increase in the concentration of acetylcholine at the neuromuscular junction. It is believed to potentially contribute to the occurrence of PONV by inducing gastric spasms, reducing barrier pressure, and intensifying afferent input to the central vomiting center.[3] Muscle paralysis may be treated with the specific gamma-cyclodextrin medication sugammadex. Encapsulating aminosteroid-non-depolarizing muscle relaxants stops their function. It has a more rapid onset of action compared to neostigmine and does not cause the undesirable muscarinic side effects

Access this article online

www.ijss-sn.com

Month of Submission : 02-2024
Month of Peer Review : 03-2024
Month of Acceptance : 04-2024
Month of Publishing : 04-2024

Corresponding Author: Dr. Shubam Achari, Department of Anesthesia, MLB Medical College, Jhansi, Uttar Pradesh, India.

that are often seen with neostigmine administration.[4,5] However, the studies on the effects of sugammadex on PONV among patients undergoing elective middle ear surgery are very limited. The hypothesis of our study was that utilizing sugammadex to counteract the impact of neuromuscular blocker agents would result in a decrease in PONV following elective middle ear surgery in comparison to neostigmine.

Objective of the Study

1. To determine the association that exists between the choice of reversal agent (neostigmine versus sugammadex) used and PONV occurrence, which was measured by utilizing a four-point verbal descriptive scale[6] in patients undergoing elective middle ear surgery.
2. The secondary objective was to determine if the choice of reversal agent (neostigmine or sugammadex) had any impact on the requirement for rescue antiemetics and the incidence of post-operative side effects during the first 24 h post-operatively.

MATERIALS AND METHODS

This prospective, comparative, randomized study was conducted in the Maharani Laxmi Bai Medical College, Jhansi, from July 2023 to September 2023 in 140 patients who underwent elective middle ear surgery after taking approval of the protocol by the Ethical Committee of the Institution with Ethical Committee's number 9617/IEC/I/2022-23 on September 26, 2023. Each participant provided written informed consent for their involvement in the study and the use of their patient data for research and educational purposes. The study was duly registered with the Clinical Trials Registry of India with registration number CTRI/2023/10/058570 on October 12, 2023, accessed from www.ctri.nic.in. The study was conducted following the principles of the Declaration of Helsinki, 2013, and good clinical practice.

The study included patients with American Society of Anesthesiology (ASA) grades I and II, aged between 18 and 65 years, and with a normal coagulation profile. The exclusion criteria were patients with significant cardiovascular, pulmonary, and neuromuscular conditions, as well as those with renal or hepatic dysfunction. Patients with abnormal coagulation profiles or who were hemodynamically unstable were also excluded. In addition, individuals with a body mass index (BMI) >30 kg/m^2 or with allergies or contraindications to any of the study drugs were also not included.

The individuals were divided into two groups [Figure 1]: Group I (neostigmine) and Group II (sugammadex). A block randomization method was employed, with blocks of different sizes, to ensure an equal distribution of participants between the two groups. This was done using a computerized random number list that was prepared before the start of the trial. Every participant received a sealed envelope with a random number inside, generated using a computerized list. The envelope also had their date of birth written on top. The participants were given clear instructions not to open the envelope, and the hospital staff made sure that they followed these instructions. The modality of neuromuscular blockade reversal was implemented based on the group to which participants were assigned through randomization. After the patient had been transferred to the operation theater, a junior resident was given the responsibility of opening the envelopes. Afterward, the resident carefully prepared the study drugs in two syringes, making sure they were exactly the same and assigned them to their respective study groups. The resident did not participate in any further activities during the study. The administration of the reversal agent was based on the randomized groups that the patients were assigned to. Patients in Group I were administered neostigmine 2.5 mg in combination with glycopyrrolate 0.5 mg, while patients in Group II were given sugammadex 2 mg/kg after the surgery was finished.

Before conducting the surgery, patients' risks of PONV were evaluated with the help of the simplified Apfel scoring system.[6]

Risk estimation (%)	1 20%	2 40%	3 60%	4 80%
1 point female gender				
1 point no smoking				
1 point post-operative use of opioids				
1 point for previous history of PONV or motion sickness				

PONV: Post-operative nausea and vomiting

Before administering general anesthesia, all patients were pre-oxygenated for 3–5 min. This was followed by the administration of intravenous injection of fentanyl at a dose of 2 mcg/kg and injection of propofol at a dose of 2 mg/kg. To facilitate orotracheal intubation, the patients were then paralyzed using injection rocuronium at a dose of 0.9 mg/kg. The anesthesia was maintained using sevoflurane to achieve a minimum alveolar concentration of 1.0–1.2 in a mixture of oxygen and air. In the operating room, during the surgery, patients were given a crystalloid infusion of 3–5 mg/kg of normal saline at 0.9% to replenish the fluids lost from dehydration. After the surgery, the administration of anesthetic drugs was stopped, and the patient was manually ventilated with 100% oxygen. As per the randomization schedule, the patients in Group I received intravenous administration of injection neostigmine 2.5 mg in combination with

injection glycopyrralate 0.5 mg for antagonization of neuromuscular blockade. On the other hand, the patients in Group II were given 2 mg/kg of injection sugammadex. The patient underwent extubation following the removal of oropharyngeal secretions. As part of the multimodal analgesia management, a 5% lignocaine patch was applied before the surgery, and a 1 g IV injection of paracetamol was administered every 8 h. In addition, a dose of 4 mg of injection ondansetron IV is administered 1 h before the conclusion of the surgery.

An anesthesiologist who was unaware of the distribution of individuals into the groups evaluated the incidence of PONV and the requirement for rescue antiemetics over a 24-h period following surgery. The 24-h period was divided into 3-time intervals: 0–2 h, 2–6 h, and 6–24 h. The primary outcome of the study was to determine and compare the occurrence of PONV between the study groups, and the secondary outcome was to determine the requirement for additional antiemetic medication for a 24-h period following the surgical procedure and its association with the type of reversal agent used.

In the post-anesthesia recovery unit after anesthesia, the presence of nausea and vomiting was evaluated using a 4-point verbal descriptive scale, which has been used in previous studies. The scale ranges from 0, indicating no nausea, to 3, indicating multiple episodes of vomiting during the observation period.[7] Patients who experienced vomiting of three or more episodes (PONV score of 3) were administered IV metoclopramide 10 mg as a rescue antiemetic. Patients were carefully monitored to ensure their hemodynamic stability and effective pain management before being transferred to the general ward.

In a previous study conducted by Yagan *et al.* in 2017,[8] the researchers reported the incidence of PONV to be 27% when neostigmine was administered, while the incidence was 7% when sugammadex was administered. Using the comparing proportions formula for the estimation of sample size for the study, 64 patients in each group would be required to detect the desired change with 80% power and 5% significance ($\alpha = 0.05$, $\beta = 0.80$).[17] The minimum sample size from the above formula came out to be 128 for the study, and by adjusting for 10% lost to follow-up, the sample size came out to be 140 patients (70 in each group).

Statistical Analysis

The statistical analysis was conducted using the SPSS statistics software version 23.0 by IBM Corp. in Armonk, NY, USA. The data were initially processed and coded in MS Excel. We conducted the Kolmogorov–Smirnov and Shapiro–Wilk tests to assess the normality of the data. At unpaired t-test was used to compare age, weight, BMI, and surgery duration, depending on the normality of the data. An analysis was conducted using Fisher's exact test to identify any possible associations between gender, PONV scores, post-operative complications, and the type of reversal agent utilized. A $P < 0.05$ was considered statistically significant at the 95% confidence interval.

RESULTS

During the study, a total of 160 patients were evaluated for potential inclusion. However, 10 patients were excluded as they did not meet the criteria, while another 10 patients decided not to participate. Therefore, for the analysis, we included a total of 140 patients, with 70 patients in each group.

There were no statistically significant distinctions observed among the groups in relation to ASA grading, weight, BMI, gender, PONV risk scores, and surgical duration [Table 1]. Group II had a lower incidence of nausea compared to Group I throughout the entire duration. However, this difference was only statistically significant ($P = 0.021$) during the 0–2 h time interval. Specifically, four patients from group II experienced nausea, while 14 patients from group I reported the same. Only one patient from group II experienced vomiting, while in group I, five patients reported vomiting. During the later 24-h monitoring period, there was no statistically significant difference in the occurrence and intensity of PONV between the groups [Table 2].

In addition, there was a statistically significant difference ($P = 0.002$) in the number of patients who received IV metoclopramide 10 mg as a rescue antiemetic between Group I and Group II (23 patients in Group I, 8 patients in Group II, $P = 0.002$). There was no difference in statistical significance among the groups in regard to side effects [Table 3].

DISCUSSION

Our study determined the effects of administration of injection sugammadex and injection neostigmine on the incidence of PONV when used to counteract the effects of neuromuscular blocker agents. We found that sugammadex resulted in a lower incidence of PONV within the first 2 h after surgery, which was statistically significant. Our observations revealed that patients who received sugammadex experienced a significant decrease in the use of antiemetics during the initial 24 h after surgery, in comparison to those who were given neostigmine. Our study provides evidence that using sugammadex to counteract the effects of neuromuscular blocker agents

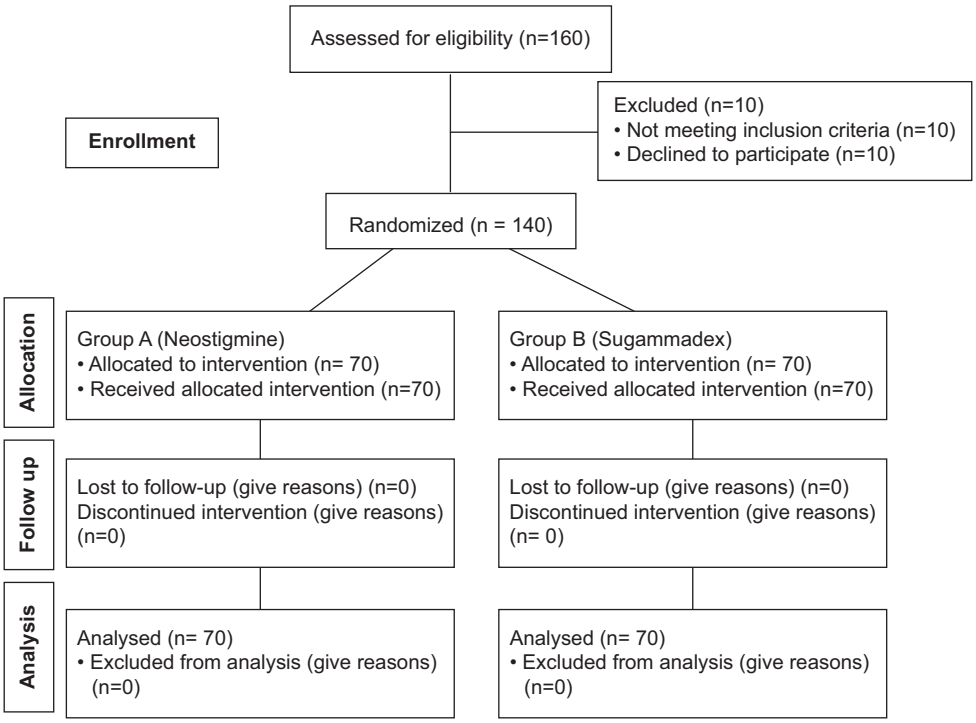

Figure 1: Consolidated standards of reporting trials (CONSORT) flow diagram

Table 1: Demographic variables of the participants

Demographic data	Group I (*n*=70)	Group II (*n*=70)	P-value
ASA 1 and 2	50/20	47/23	0.826
Age (in years)	42.9±13.6	39.8±14.3	0.705
Weight (in kg)	62±9.2	61±10.5	0.331
BMI (kg/m^2)	23.9±3.5	22.8±3.6	0.508
Gender (F/M)	40/30	38/32	0.205
Apfel score 0/1/2/3	14/20/28/8	15/17/23/15	0.825
Surgery time (in minutes)	119±24.9	122±23.9	0.201

BMI: Body mass index, F/M: Female/male, ASA: American Society of Anesthesiologists. Data are presented as mean±SD or frequencies. APFEL SCORE-1 point-female gender. 1 point – non-smoker, 1 point-history of PONV/history of Motion sickness, 1 point-post-operative opioid analgesia. *P*<0.05 considered significant.

Table 2: Incidence and severity of PONV and antiemetic treatment in groups

PONV	Group I (*n*=70%)	Group II (*n*=70%)	*P*-value
PONV at PACU from 0 to 2 h			
0	50 (71.42)	65 (92.85)	0.021
1	14 (19.71)	4 (5.71)	
2	5 (7)	1 (1.42)	
3	1 (1.4)	0	
PONV at PACU from 2 to 6 h			
0	64 (91.46)	66 (94.28)	0.896
1	5 (7.14)	4 (5.71)	
2	1 (1.4)	0 (0)	
3	0 (0)	0 (0)	
PONV at PACU from 6 to 24 h			
0	67 (95.71)	70 (100)	0.708
1	3 (4.28)	0 (0)	
2	0 (0)	0 (0)	
3	0 (0)	0 (0)	
Need for Rescue Antiemetics	23 (33.85)	8 (11.42)	0.002

Data are presented as frequencies and percentages. PONV, Post-operative nausea and vomiting; PACU, Post-anesthetic care unit. PONV was evaluated as follows: 0=not nauseated, 1=nauseated, not vomiting, 2=nauseated, one to two episodes of vomiting, 3=nauseated, more than two episodes of vomiting. *P*<0.05 considered significant

can reduce PONV after elective middle ear surgery, when compared to neostigmine. The strength of our study is its randomized and double-blinded design, which enhances its credibility.

PONV, described as nausea and/or vomiting that occurs within 24 h after having surgery, affects a significant number of patients, with higher rates observed in high-risk individuals.[9,10] Our study found that sugammadex had a much lower occurrence of PONV compared to neostigmine within the first 2 h after reversal.

In a study, Yagan *et al.*,[8] found that sugammadex 2 mg/kg had a notably lower occurrence of PONV compared to neostigmine 50 μg/kg with atropine during the 1st h after surgery. In addition, there was less need for antiemetic medication within 24 h of monitoring in a diverse group of surgical patients. In another study, Tas Tuna *et al.*,[11] found that there was no notable variation in the occurrence of PONV at different time intervals between patients who were administered neostigmine 40 μg/kg (with atropine) and patients who received sugammadex 2 mg/kg during laparoscopic cholecystectomy. Interestingly, none of the patients in their study were given antiemetic prophylaxis.

Table 3: Post-operative side effects

Side effect	Group A (*n*=70%)	Group B (*n*=70)	*P*-value
Headache	5 (7.14)	3 (4.28)	0.901
Hypertension	2 (2.85)	4 (6.1)	0.110
Bradycardia	4 (5.71)	0	0.567
Coughing	2 (2.85)	2 (2.85)	0.890
Shivering	0	1 (1.42)	0.105
Sore throat	2 (2.85)	3 (4.28)	0.608

Data are presented as frequencies and percentages. *P*<0.05 considered significant

In a similar study, Paech *et al.*,[12] discovered that there was no notable variation in PONV between the administration of sugammadex 2 mg/kg and neostigmine 40 μg/kg in patients who were undergoing laparoscopic gynecological procedures.

In their study, the patients were only administered a single prophylactic antiemetic (dexamethasone 4 mg), and ondansetron was not administered as a standard practice.

Comparative studies on the reversal of rocuronium-induced neuromuscular blockade using sugammadex and neostigmine revealed that the incidence of PONV was slightly lower in the sugammadex group compared to the neostigmine group. However, this difference did not reach statistical significance.

In a study conducted by Løvstad *et al.*,[7] the effects of neostigmine 50 μg/kg compared to a placebo on PONV were examined in patients undergoing laparoscopic gynecology procedures. The results revealed a significant increase in PONV during the first 6 h after surgery. In our investigation, neostigmine was administered at a standard dosage of 2.5 mg (equivalent to an average of 36 μg/kg). Despite the fact that the amount of neostigmine given to patients in our study was lower than in previous studies, none of our patients experienced any lingering paralysis after surgery.

However, there have been doubts raised about the clinical significance of neostigmine's impact on PONV. After analyzing 15 different studies, it was determined in a meta-analysis that there is not enough evidence to support the claim that neostigmine increases the risk of PONV.[13] A study investigating the effects of PONV after abdominal hysterectomy operations compared two groups. One group allowed for natural recovery from neuromuscular blockage induced by mivacurium, while the other group received 2 mg of neostigmine as an antagonist. No significant difference was found between the groups in terms of both nausea and vomiting. Ultimately, they concluded that the utilization of neostigmine to counteract neuromuscular blockage did not lead to a higher occurrence or intensity of PONV.[14]

Our study findings align with the research conducted by Koyuncu *et al.*,[15] which also observed a lower incidence of PONV in patients treated with sugammadex. However, the occurrence of PONV during the 24-h monitoring period showed different and elevated outcomes compared to our study.

In our study, during the post-operative 24-h monitoring period, there was significant variation in the administration of anti-emetic treatment with metoclopramide between the sugammadex group and the neostigmine group. Specifically, only 11% of patients in the sugammadex group received antiemetic treatment, compared to 34% in the neostigmine group. In a retrospective study, Ledowski *et al.*,[16] found that the group treated with sugammadex required less anti-emetic medication in the PACU.

CONCLUSION

The findings of the current study suggest that sugammadex may be a promising option for reducing the occurrence of PONV in elective middle ear surgery. When it comes to PONV, sugammadex could be a more suitable option for patients at high risk or in situations where this PONV is undesirable.

Limitation of the Study

A potential drawback of our study is that it is based solely on data collected from a single hospital. However, it is widely recognized that conducting a study involving multiple hospitals would offer a more thorough analysis of the characteristics we are investigating.

REFERENCES

1. Mishra AR, Srivastava U, Kumar D, Saraswat N, Kumar A, Payal YS, *et al*. Nausea and vomiting after ENT surgeries: A comparison between ondansetron, metoclopramide and small dose of propofol. Indian J Otolaryngol Head Neck Surg 2010;62:29-31.
2. Kooij FO, Vos N, Siebenga P, Klok T, Hollmann MW, Kal JE. Automated reminders decrease postoperative nausea and vomiting incidence in a general surgical population. Br J Anaesth 2012;108:961-5.
3. Peck T, Harris B. Pharmacology for Anaesthesia and Intensive Care. Cambridge, New York: Cambridge University Press; 2021.
4. Bom A, Bradley M, Cameron K, Clark JK, Van Egmond J, Feilden H, *et al*. Novel concept of reversing neuromuscular block: Chemical encapsulation of rocuronium bromide by a cyclodextrina cyclodextri cyclodext. Angew Chem Int Ed Engl 2002;41:265-70.
5. Abrishami A, Ho J, Wong J, Yin L, Chung F. Sugammadex, a selective reversal medication for preventing postoperative residual neuromuscular blockade. Cochrane Database Syst Rev 2009;4:CD007362.
6. Apfel CC, Läärä E, Koivuranta M, Greim CA, Roewer N. A simplified risk score for predicting postoperative nausea and vomiting: Conclusions from cross-validations between two centers. Anesthesiology 1999;91:693-700.
7. Løvstad RZ, Thagaard KS, Berner NS, Raeder JC. Neostigmine 50 microg kg(-1) with glycopyrrolate increases postoperative nausea in women after laparoscopic gynaecological surgery. Acta Anaesthesiol Scand 2001;45:495-500.

8. Yagan Ö, Tas N, Mutlu T, Hanci V. Comparison of the effects of sugammadex and neostigmine on postoperative nausea and vomiting. Rev Bras Anestesiol 2017;67:147-52.
9. Kim SI, Kim SC, Baek YH, Ok SY, Kim SH. Comparison of ramosetron with ondansetron for prevention of postoperative nausea and vomiting in patients undergoing gynaecological surgery. Br J Anaesth 2009;103:549-53.
10. McCracken G, Houston P, Lefebvre G, Society of Obstetricians and Gynecologists of Canada. Guideline for the management of postoperative nausea and vomiting. J Obstet Gynaecol Can 2008;30:600-7, 608-16.
11. Tas Tuna A, Palabiyik O, Orhan M, Sonbahar T, Sayhan H, Tomak Y. Does sugammadex administration affect postoperative nausea and vomiting after laparoscopic cholecystectomy: A prospective, double-blind, randomized study. Surg Laparosc Endosc Percutan Tech 2017;27:237-40.
12. Paech MJ, Kaye R, Baber C, Nathan EA. Recovery characteristics of patients receiving either sugammadex or neostigmine and glycopyrrolate for reversal of neuromuscular block: A randomised controlled trial. Anaesthesia 2018;73:340-7.
13. Cheng CR, Sessler DI, Apfel CC. Does neostigmine administratio n produce a clinically important increase in postoperative nausea and vomiting? Anesth Analg 2005;101:1349-55.
14. Hovorka J, Korttila K, Nelskylä K, Soikkeli A, Sarvela J, Paatero H, *et al*. Reversal of neuromus-cular blockade with neostigmine has no effect on the incidence or severity of postoperative nausea and vomiting. Anesth Analg 1997;85:1359-61.
15. Koyuncu O, Turhanoglu S, Ozbakis Akkurt C, Karcıoglu M, Ozkan M, Ozer C, *et al*. Comparison of sugammadex and conventional reversal on postoperative nausea and vomiting: A randomized, blinded trial. J Clin Anesth 2015;27:51-6.
16. Ledowski T, Falke L, Johnston F, Gillies E, Greenaway M, De Mel A, *et al*. Retrospective investigation of postoperative outcome after reversal of residual neuromuscular blockade: Sugammadex, neostigmine or noreversal. Eur J Anaesthesiol 2014;31:423-9.
17. Jain A, Mittal A, Sharma S, Deep A. Comparative evaluation of intrathecal dexmedetomidine and fentanyl as an adjuvant for combined spinal-epidural analgesia for labor. Anesth Essays Res 2022;16:197-202.

How to cite this article: Sethi C, Gupta C, Achari S. Effect of Sugammadex and Neostigmine-Glycopyrrolate on Post-operative Nausea and Vomiting in Middle Ear Surgeries: A Comparative Study. Int J Sci Stud 2024;12(1):21-26.

Source of Support: Nil, **Conflicts of Interest:** None declared.