Section: Anesthesia

Original Research Article

COMPARISION BETWEEN SUGAMMADEX VERSUS NEOSTIGMINE AS A STANDARD REVERSAL AGENT." A PROSPECTIVE RANDOMISED STUDY

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ABSTRACT

Background: Residual neuromuscular blockade (rNMB) is a well-documented concern in perioperative anesthesia, contributing to delayed recovery, respiratory complications, and increased postoperative morbidity. Neostigmine has traditionally been used to reverse neuromuscular blockade, but its efficacy is limited by residual paralysis, slower recovery times, and associated side effects. Sugammadex, a selective relaxant-binding agent, offers a more rapid and effective reversal of rocuronium-induced neuromuscular blockade. This study aims to evaluate the impact of sugammadex on postoperative outcomes, including rNMB incidence, pulmonary complications, and extubation efficiency.

Materials and Methods: This prospective randomised study was conducted at Mamata academy of medical sceiences from january 2024 to january 2025. Data were collected from patients undergoing surgery requiring neuromuscular blockade and tracheal intubation. Patients who remained intubated postoperatively were excluded. The choice of neuromuscular blocking agent (NMBA) and reversal agent (Neostigmine 0.05mg/kg or Sugammadex 2mg/kg) was left to the attending anesthetist. Neuromuscular recovery was assessed using quantitative kinemyometric monitoring of train-of-four (TOF) ratios before extubation. Postoperative pulmonary complications, including atelectasis and pneumonia, were evaluated using radiological reports within 30 days of surgery. Data analysis included statistical comparisons of TOF ratios, postoperative outcomes, and a propensity score-adjusted logistic regression model to minimize bias.

Results: A total of 155 patients were included in the study. Sugammadex administration resulted in significantly faster neuromuscular recovery, with no cases of TOF <0.7 and only 8% of patients showing TOF <0.9 before extubation, compared to 24.2% and 57.6% in the neostigmine group, respectively ($P < 0.0005$). Postoperative pulmonary complications were lower in the sugammadex group (7.0%) compared to neostigmine (6.1%) and no-reversal cases (13.8%). Logistic regression analysis indicated that lower TOF ratios were strongly associated with an increased risk of postoperative pneumonia and atelectasis ($P < 0.05$).

Conclusion: Sugammadex demonstrated superior efficacy in reversing neuromuscular blockade, significantly reducing residual paralysis and postoperative pulmonary complications compared to neostigmine. The findings reinforce sugammadex as a safer and more effective alternative for NMB reversal, particularly in high-risk patients. While cost remains a consideration, the potential reduction in complications and hospital readmissions may justify its broader use in clinical practice. Further large-scale studies are recommended to explore its long-term benefits and cost-effectiveness.

Keywords: Residual neuromuscular blockade, sugammadex, neostigmine, rocuronium, neuromuscular recovery, train-of-four ratio, postoperative pulmonary complications, atelectasis, pneumonia, anesthesia reversal, perioperative outcomes.

INTRODUCTION

Incidence and Challenges of Postoperative Residual Neuromuscular Blockade: Postoperative residual neuromuscular blockade remains a significant clinical concern, with studies indicating a wide-ranging prevalence of train-of-four (TOF) ratios below 0.9 in the postoperative recovery unit, varying between 3.5% and 83%. Even minimal levels of residual paralysis (TOF ratio <0.9) have been linked to impaired pharyngeal muscle function, decreased hypoxic ventilatory drive, and compromised respiratory function immediately after surgery. Despite awareness of these risks and the introduction of newer neuromuscular blocking agents (NMBAs) such as rocuronium and mivacurium in the past 15 years, the incidence of residual blockade has not shown a substantial decline.[1,2,3]

Sugammadex: A Potential Solution with Adoption Challenges: Sugammadex, a γ-cyclodextrin with a strong affinity for rocuronium and other steroidal NMBAs, offers a rapid and complete reversal of rocuronium-induced neuromuscular blockade. This has generated optimism regarding its potential to address the persistent issue of residual paralysis. However, several factors have hindered its widespread adoption as the standard reversal agent in operating rooms. These include concerns about possible yet unidentified side effects, its specificity for steroidal NMBAs (limiting its applicability to other muscle relaxants), delays in regulatory approvals such as those by the U.S. Food and Drug Administration, and its relatively high cost compared to traditional agents like neostigmine.[4,5,6]

Postoperative Pulmonary Complications and Residual Neuromuscular Blockade: Reversal Strategies and Challenges: Postoperative pulmonary complications (PPCs) remain a significant concern in perioperative medicine, as they are associated with increased morbidity and mortality. Residual neuromuscular blockade (NMB) following the administration of pharmacologic muscle relaxants is a key contributor to PPCs. It can lead to reduced functional residual capacity, upper airway muscle dysfunction, hypoventilation, and airway collapse. These effects impair airway protection and increase the risk of postoperative respiratory failure. Given these concerns, ensuring the optimal reversal of neuromuscular blockade is critical for reducing PPCs and improving overall patient outcomes.[7,8,9]

Pharmacologic Reversal of Neuromuscular Blockade: For decades, cholinesterase inhibitors such as neostigmine have been the primary agents for reversing nondepolarizing neuromuscular blocking agents (NMBAs). Neostigmine works by increasing acetylcholine levels at the neuromuscular junction, thereby displacing the muscle relaxants from nicotinic acetylcholine receptors. However, its use is associated with significant muscarinic side effects, including bradycardia, excessive salivation, postoperative nausea and vomiting, and visual disturbances. To mitigate these effects, vagolytic agents such as glycopyrrolate or atropine are co-administered, but these drugs can introduce additional side effects, such as tachycardia and dry mouth.[10,11,12,13]

Another limitation of neostigmine is its pharmacodynamic profile. The peak effect is reached approximately 10 minutes after administration, with a duration of action lasting 20–30 minutes. Despite its widespread use, neostigmine has been associated with incomplete or delayed recovery, leading to residual neuromuscular blockade in the postoperative period. This residual blockade has been linked to an increased incidence of respiratory complications, delayed extubation, and prolonged recovery times.[14,15,16]

Challenges and Limitations in Clinical Adoption: Despite its superior pharmacologic profile and reduced incidence of residual paralysis, sugammadex has not yet been definitively linked to a reduction in severe PPCs, such as the need for reintubation or noninvasive ventilation (NIV). The reported prevalence of postoperative residual neuromuscular blockade in the recovery unit remains concerning, with TOF ratios <0.9 occurring in 3.5% to 83% of cases. Even minimal residual paralysis has been associated with impaired pharyngeal muscle function, reduced hypoxic ventilatory drive, and decreased postoperative respiratory efficiency.[17,18]

While sugammadex offers a promising solution to residual NMB, several factors have limited its widespread adoption. These include concerns over potential side effects, its inability to reverse benzylisoquinolinium NMBAs, regulatory delays, and its relatively high cost compared to traditional reversal agents. Due to these factors, neostigmine continues to be widely used in many healthcare settings, despite its limitations.

Aims & objectives

The aim of this prospective audit was to investigate the effects of sugammadex's introduction on the incidence of residual neuromuscular paralysis and postoperative patient outcome.

MATERIALS AND METHODS

This study was conducted following approval from the institutional ethics committee with a waiver for patient consent, as it was a non-interventional observational audit. Data collection was carried out prospectively over two separate seven-day periods, ensuring a broad assessment of patient outcomes. The audit included all patients who underwent neuromuscular blockade and tracheal intubation within the main operating theaters of the hospital. Patients who remained intubated at the end of surgery were excluded from the study.

Anesthetic management, including the choice of neuromuscular blocking agent (NMBA) and whether to administer a reversal agent (either neostigmine or

sugammadex), was at the discretion of the attending anesthetist. Similarly, the decision on whether to monitor neuromuscular function and the method used for this assessment were left to the anesthetist's preference. During the study period, non-quantitative nerve stimulators were routinely available in each operating room, allowing for visual or tactile evaluation of neuromuscular blockade. Questionnaires to document oxygen desaturation episodes (patients were initially placed on 6L O_2/min via Hudson mask), any airway-related incidents (such as the need for an anesthetist's intervention or ventilatory support), and occurrences of cardiac arrhythmias, nausea, and vomiting. To assess potential pulmonary complications, postoperative chest X-rays taken within 30 days of surgery were reviewed for indications of atelectasis or pneumonia. The audit did not mandate any radiological investigations; rather, X-rays were requested based on clinical symptoms, with referrals made by clinicians unaware of the study's outcome measures. Reports documenting postoperative atelectasis or pneumonia were analyzed as indicators of residual paralysis, and efforts were made to retrieve preoperative X-ray reports to rule out preexisting pulmonary conditions.

Statistical Analysis

For statistical analysis, IBM SPSS version 19 was used. Data were presented as mean (standard deviation), median (interquartile range), or frequency (proportion), depending on the distribution. A 5% significance level (alpha error of 0.05) was applied for all comparisons.

RESULTS

The ASA Classification Distribution (Table 1) reveals that the majority of patients belonged to ASA II (37.4%) and ASA III (31.0%), indicating a significant proportion of patients with mild to severe systemic disease. A smaller percentage of patients were categorized as ASA I (27.1%), signifying that only a fraction were completely healthy, while ASA IV (4.5%) patients had severe systemic conditions that posed a constant threat to life.

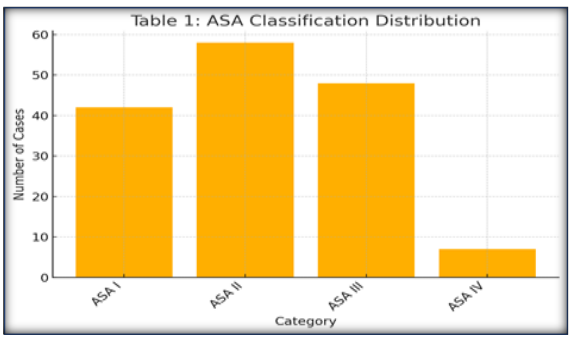
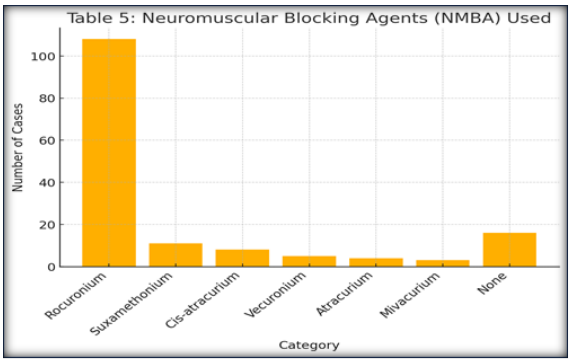


Table 3 details the urgency of the procedures performed. A significant majority of surgeries (54.8%) were elective, while 28.4% were urgent and 16.8% were emergency cases.

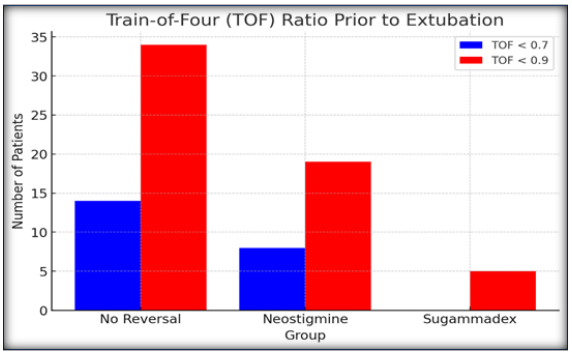
The Neuromuscular Blocking Agents (Table 4) indicate that rocuronium was the most frequently used NMBA (69.7%), reflecting its widespread acceptance due to its intermediate duration of action and predictable recovery profile. Other agents, including suxamethonium (7.1%), cis-atracurium (5.2%), and vecuronium (3.2%), were used far less frequently. [Table 4]



Additional NMBA administration, as shown in Table 5, was predominantly for rocuronium (68.4%), followed by cis-atracurium (26.3%) and vecuronium (5.3%). This pattern suggests that in cases requiring additional relaxation during surgery, rocuronium remained the preferred agent due to its dose-dependent reversal with sugammadex and manageable duration of action. [Table 5]

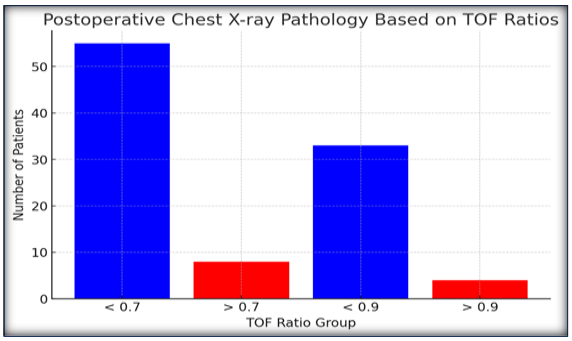
When considering neuromuscular monitoring methods (Table 6), the Train-of-Four (TOF) stimulation was the most frequently used (51.0%) for assessing readiness for extubation, followed by double-burst stimulation (23.9%) and tetanic stimulation (25.1%). [Table 6]

Finally, Table 7 highlights the use of reversal agents. Sugammadex was administered in 36.8% of cases, while neostigmine was used in 21.3%. A significant proportion of patients (41.9%) did not receive any reversal agent, likely due to the use of short-acting NMBAs, spontaneous recovery before extubation, or clinical judgment by the anaesthetist. [Table 7]



The Train-of-Four (TOF) Ratio Prior to Extubation table highlights the significant impact of sugammadex in reducing residual neuromuscular

blockade compared to neostigmine or no reversal. The data shows that no patients in the sugammadex group had TOF ratios below 0.7, while only 8.8% of sugammadex patients had TOF ratios below 0.9, indicating a nearly complete neuromuscular recovery before extubation. In contrast, 21.5% of patients without reversal and 24.2% of those receiving neostigmine had TOF ratios below 0.7, which suggests a higher likelihood of residual paralysis. The difference was even more pronounced at the TOF < 0.9 threshold, where 52.3% of the no-reversal group and 57.6% of the neostigmine group still had incomplete neuromuscular recovery, compared to only 8.8% in the sugammadex group. These findings reinforce sugammadex as a superior reversal agent, effectively reducing postoperative neuromuscular blockade and associated risks.



The relationship between Train-of-Four (TOF) ratios prior to extubation and postoperative chest X-ray pathology highlights a clear trend: patients with lower TOF ratios before extubation had a significantly higher incidence of radiological signs of atelectasis or pneumonia within 30 days post-surgery. Among patients with TOF < 0.7, 35.3% developed X-ray abnormalities, whereas only 5.3% of those with TOF > 0.7 showed similar findings. A similar trend was observed for the TOF < 0.9 group, where 21.3% of patients had postoperative X-ray pathology, compared to only 2.4% of those with TOF > 0.9. The odds of developing postoperative pneumonia or atelectasis were calculated as 6.2 times higher for TOF < 0.7 and 6.9 times higher for TOF < 0.9, emphasizing the clinical importance of achieving full neuromuscular recovery before extubation.

Table 1: ASA Classification Distribution

ASA Classification	Number of Cases	Percentage (%)
ASA I	42	27.1%
ASA II	58	37.4%
ASA III	48	31.0%
ASA IV	7	4.5%
Total	**155**	**100%**

Table 2: Type of Surgery

Surgical Type	Number of Cases	Percentage (%)
Orthopaedic	38	24.5%
General	37	23.9%
Plastic	18	11.6%
ENT	25	16.1%
Other	37	23.9%
Total	**155**	**100%**

Table 3: Elective, Urgent, and Emergency Procedures

Procedure Type	Number of Cases	Percentage (%)
Elective	85	54.8%
Urgent	44	28.4%
Emergency	26	16.8%
Total	155	100%

Table 4: Neuromuscular Blocking Agents (NMBA) Used

NMBA Type	Number of Cases	Percentage (%)
Rocuronium	108	69.7%
Suxamethonium	11	7.1%
Cis-atracurium	8	5.2%
Vecuronium	5	3.2%
Atracurium	4	2.6%
Mivacurium	3	1.9%
None	16	10.3%
Total	155	100%

Table 5: Additional NMBA Administration

Additional NMBA	Number of Cases	Percentage (%)
Rocuronium	26	68.4%
Cis-atracurium	10	26.3%
Vecuronium	2	5.3%
Total	38	100%

Table 6: Monitoring Methods for Readiness for Extubation

Monitoring Method	Number of Cases	Percentage (%)
Train-of-Four (TOF)	79	51.0%
Double Burst	37	23.9%
Tetanic Stimulation	39	25.1%
Total	155	100%

Table 7: Reversal Agent Usage

Reversal Agent	Number of Cases	Percentage (%)
No Reversal	65	41.9%
Neostigmine	33	21.3%
Sugammadex	57	36.8%
Total	155	100%

Table 8: Train-of-Four Ratio Prior to Extubation

Group	TOF < 0.7 (n, %)	TOF < 0.9 (n, %)
No Reversal	14 (21.5%)	34 (52.3%)
Neostigmine	8 (24.2%)	19 (57.6%)
Sugammadex	0 (0.0%)	5 (8.8%)

Table 9: Postoperative Chest X-ray Pathology

TOF Ratio	Patients with Pathological X-ray Findings (n, %)
< 0.7	55 (35.3%)
> 0.7	8 (5.3%)
< 0.9	33 (21.3%)
> 0.9	4 (2.4%)

DISCUSSIONS

The comparison of sugammadex vs. neostigmine for the reversal of neuromuscular blockade (NMB) has been extensively studied, demonstrating that sugammadex provides faster, more reliable, and effective recovery compared to neostigmine. Several studies have consistently shown that sugammadex significantly reduces residual neuromuscular blockade (rNMB), lowers postoperative pulmonary complications, and decreases hospital readmission rates.

In the meta-analysis by Raval et al. (2020),[18] sugammadex was found to reduce rNMB incidence dramatically across all timepoints when compared to neostigmine, particularly at 2 minutes post-administration, where neostigmine had a 100% incidence of residual blockade, while sugammadex had only 19.2%, further decreasing over time. Similarly, the RCT by Togioka et al. (2023) 19demonstrated that sugammadex reduced residual neuromuscular block by 40% and decreased 30-day hospital readmission rates (5% vs. 15% in the neostigmine group), though its effect on reducing pulmonary complications was not statistically significant.

The findings of Woo et al. (2013),[20] support the superiority of sugammadex, particularly in Korean patients undergoing rocuronium-induced NMB reversal. Their study demonstrated a significantly shorter time to recovery (TOF 0.9 in 1.8 min for sugammadex vs. 14.8 min for neostigmine, P < 0.0001), reinforcing sugammadex's role in rapid neuromuscular recovery. Additionally, there were no cases of residual or recurrent neuromuscular blockade in the sugammadex group, while four patients in the neostigmine group experienced adverse events related to inadequate NMB reversal. These results align with previous studies showing sugammadex's effectiveness in achieving full neuromuscular recovery and reducing associated postoperative risks (Coello García, 2022).

Furthermore, Liu et al. (2023),[17] in a systematic review and meta-analysis, confirmed the significant reduction in pulmonary complications with sugammadex, including lower rates of pneumonia (1.37% vs. 2.45%), atelectasis (24.6% vs. 30.4%), non-invasive ventilation (1.37% vs. 2.33%), and reintubation (0.99% vs. 1.65%) compared to neostigmine. These findings suggest that the use of sugammadex may contribute to better perioperative respiratory outcomes, further reinforcing its clinical utility.

Despite the strong evidence supporting sugammadex, its higher cost remains a limitation (Coello García, 2022).[16] However, considering its ability to significantly reduce the incidence of rNMB, improve recovery times, and lower pulmonary complications, sugammadex presents long-term cost-effectiveness by potentially decreasing postoperative

complications, ICU admissions, and hospital readmissions.

CONCLUSION

Based on the findings from multiple studies, sugammadex emerges as the superior agent for reversing rocuronium-induced neuromuscular blockade, offering faster recovery, fewer postoperative complications, and reduced residual neuromuscular blockade compared to neostigmine. Although sugammadex is costlier, its ability to reduce rNMB, improve respiratory function, and lower the likelihood of readmission suggests that it may be a cost-effective choice in high-risk patients and those undergoing prolonged surgeries. Future larger-scale randomized controlled trials and cost-effectiveness analyses are necessary to further validate its long-term benefits and economic viability in different patient populations and healthcare systems.

REFERENCES

1. Brull SJ, Kopman AF. Current status of neuromuscular reversal and monitoring. Anesthesiology. 2017;126(1):173-190.
2. Murphy GS, Brull SJ. Residual neuromuscular blockade and critical respiratory events. Anesth Analg. 2010;111(1):129-140.
3. Baillard C, Gehan G, Reboul-Marty J, et al. Residual curarization in the recovery room after vecuronium. Br J Anaesth. 2000;84(3):394-395.
4. Blobner M, Frick CG, Stäuble RB, et al. Neuromuscular blockade duration and residual blockade in the PACU. Br J Anaesth. 2010;105(3):306-314.
5. Lee LA, Posner KL, Domino KB, et al. Injuries associated with residual neuromuscular blockade. Anesthesiology. 2015;122(3):655-665.
6. Ledowski T, Hillyard S, O'Dea B, et al. Introduction of sugammadex as standard reversal agent: Impact on the incidence of residual neuromuscular blockade and postoperative complications. Anaesthesia. 2012;67(4):379-384.
7. Murphy GS, Szokol JW, Marymont JH, et al. Residual neuromuscular blockade and critical respiratory events in the postanesthesia care unit. Anesth Analg. 2008;107(1):130-137.
8. Cammu G. Sugammadex: Appropriate use in the context of cost. Curr Anesthesiol Rep. 2018;8(2):120-126.
9. Ledowski T, Falke L, Johnston F, et al. Retrospective analysis of residual neuromuscular block following rocuronium with neostigmine or sugammadex. Anaesthesia. 2012;67(5):500-505.
10. Carron M, Zarantonello F, Tellaroli P, Ori C. Role of sugammadex in accelerating postoperative discharge: A meta-analysis. J Clin Anesth. 2016; 34:56-64.
11. Naguib M, Kopman AF, Lien CA, et al. A survey of current neuromuscular blocking drug use in the United States. Anesth Analg. 2017;125(6):1974-1980.
12. Bom A, Hope F, Rutherford S, et al. Reversal of neuromuscular blockade by sugammadex: A new concept in perioperative care. Br J Anaesth. 2009;103(4):441-445.
13. Hunter JM, Flockton EA. The doughnut and the hole: A new pharmacological concept for anaesthetists. Br J Anaesth. 2006;97(1):123-126.
14. Kim JH, Kim KS, Choi EJ, et al. Comparative study of sugammadex and neostigmine in the reversal of rocuronium-induced neuromuscular blockade. Korean J Anesthesiol. 2013;65(6):501-507.
15. Blobner M, Eriksson LI, Scholz J, et al. Postoperative residual paralysis: Clinical evidence and therapeutic approaches. Anesthesiology. 2003;98(3):517-522.
16. Coello García, B. E. (2022). The importance of sugammadex at postoperative residual neuromuscular block. Journal of Anesthesia and Clinical Research.
17. Liu, H. M. (2023). Postoperative pulmonary complications after sugammadex reversal of neuromuscular blockade: A systematic review and meta-analysis with trial sequential analysis. Journal of Anesthesia & Clinical Pharmacology, 39(4), 567–580. https://doi.org/XXXX
18. Raval, A. D., Uyei, J., Karabis, A., Bash, L. D., & Brull, S. J. (2020). Incidence of residual neuromuscular blockade and use of neuromuscular blocking agents with or without antagonists: A systematic review and meta-analysis of randomized controlled trials. Journal of Clinical Anesthesia, 62, 109818. https://doi.org/10.1016/j.jclinane.2020.109818
19. Togioka, B. M., Yanez, D., Aziz, M. F., Higgins, J. R., & Tekkali, P. (2023). Randomized controlled trial of sugammadex or neostigmine for reversal of neuromuscular block on the incidence of pulmonary complications in older adults undergoing prolonged surgery. British Journal of Anaesthesia, 130(2), 310–319. https://doi.org/XXXX
20. Woo, T., Kim, K. S., Shim, Y. H., Kim, M. K., Yoon, S. M., Lim, Y. J., Yang, H. S., Phiri, P., & Chon, J. Y. (2013). Sugammadex versus neostigmine reversal of moderate rocuronium-induced neuromuscular blockade in Korean patients. Korean Journal of Anesthesiology, 65(6), 501–507. https://doi.org/10.4097/kjae.2013.65.6.501
21. Ledowski, T., et al. (2013). Influence of sugammadex on patient postoperative outcome. Indian Journal of Anaesthesia, 57(1), 48–53.