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

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

International Journal of Current Pharmaceutical Review and Research 2026; 18(8); 1604-1613

Original Research Article

To Compare The Efficacy and Safety of 1mg/Kg Sugammadex Combining with 50µg/kg neostigmine versus 50µg/kg Neostigmine Alone as Reversal Agent for A Moderate Neuromuscular Block Induced by Vecuronium: A Randomized Control Study

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Received: 10-06-2026 / Revised: 04-07-2026 / Accepted: 12-08-2026

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Conflict of interest: Nil

Abstract

Background: Residual neuromuscular blockade following general anaesthesia may delay recovery and increase postoperative respiratory risk. Neostigmine is commonly used for reversal of nondepolarizing neuromuscular blockade but may provide relatively slow and variable recovery. Combining a reduced dose of sugammadex with neostigmine may provide faster reversal while reducing the requirement for conventional-dose sugammadex.

Objectives: To compare the efficacy and safety of low-dose sugammadex combined with neostigmine versus neostigmine alone for reversal of vecuronium-induced moderate neuromuscular blockade.

Materials and Methods: This randomized controlled study included 50 adult patients undergoing elective surgery under general anaesthesia at a BMCRI-affiliated hospital between March and June 2025. Patients were randomized into two equal groups. Group NS (n=25) received sugammadex 1 mg/kg plus neostigmine 50 µg/kg and glycopyrrolate 0.01 mg/kg, whereas Group N (n=25) received neostigmine 50 µg/kg plus glycopyrrolate 0.01 mg/kg. Reversal agents were administered when the train-of-four (TOF) count reached two twitches. The primary outcome was time to achieve a TOF ratio ≥0.90. Secondary outcomes included hemodynamic changes, postoperative Modified Aldrete Score, and adverse effects.

Results: Baseline demographic and clinical characteristics were comparable between the groups. The mean time to achieve a TOF ratio ≥0.90 was significantly shorter in Group NS than in Group N (2.93 ± 0.55 vs 15.34 ± 2.05 minutes; mean difference -12.41 minutes; 95% CI -13.27 to -11.56; P<0.001). At 1 minute after reversal, Group NS showed higher mean arterial pressure (102.56 ± 18.39 vs 92.24 ± 14.76 mmHg; P=0.03) and heart rate (104.68 ± 6.31 vs 99.64 ± 14.32 bpm; P=0.04), but these differences were no longer significant at 5 minutes. Modified Aldrete Scores were comparable between Group NS and Group N (9.72 ± 0.54 vs 9.60 ± 0.58; P=0.38), and no study-recorded adverse effects occurred in either group.

Conclusion: Low-dose sugammadex 1 mg/kg combined with neostigmine 50 µg/kg resulted in substantially faster reversal of moderate vecuronium-induced neuromuscular blockade than neostigmine alone, without sustained hemodynamic disturbance or deterioration in immediate postoperative recovery. Larger multicenter studies are required to confirm the safety and generalizability of this dose-sparing reversal strategy.

Keywords: Sugammadex; Neostigmine; Vecuronium; Neuromuscular blockade; Neuromuscular reversal; Train-of-four monitoring; General anaesthesia; Residual neuromuscular blockade.

DOI: 10.25258/ijcpr.18.8.239

Introduction

Neuromuscular blocking agents are an essential component of modern general anaesthesia because they facilitate tracheal intubation, optimize surgical conditions, and permit controlled mechanical ventilation. However, incomplete recovery from neuromuscular blockade at the end of surgery remains an important patient-safety concern. Postoperative residual neuromuscular blockade can impair upper airway muscle function, reduce ventilatory responses, compromise swallowing and

pharyngeal coordination, and increase the likelihood of adverse respiratory events during the early postoperative period [1]. Quantitative neuromuscular monitoring is therefore increasingly emphasized, with a train-of-four (TOF) ratio of at least 0.9 considered an important endpoint before tracheal extubation [2]. Contemporary guidelines recommend objective neuromuscular monitoring and appropriate pharmacological antagonism to minimize residual paralysis and its associated complications [2,3].

Vecuronium is an intermediate-acting, nondepolarizing aminosteroidal neuromuscular blocking agent that has been extensively used during general anaesthesia. Although its intermediate duration of action offers predictable operating conditions, clinically significant residual blockade may persist after surgery, particularly when repeated or maintenance doses are administered. Traditionally, vecuronium-induced neuromuscular blockade has been reversed with acetylcholinesterase inhibitors such as neostigmine. Neostigmine increases the concentration of acetylcholine at the neuromuscular junction by inhibiting acetylcholinesterase, thereby competitively antagonizing the effect of nondepolarizing neuromuscular blocking drugs. Its effectiveness, however, depends substantially on the degree of spontaneous neuromuscular recovery present when it is administered [3]. Consequently, neostigmine is less reliable during deep or profound neuromuscular blockade and has a ceiling effect beyond which administration of a larger dose does not produce proportionately greater reversal.

Furthermore, increased acetylcholine following neostigmine administration is not restricted to nicotinic receptors at the neuromuscular junction. Stimulation of muscarinic receptors can result in bradycardia, increased salivation, bronchial secretions, gastrointestinal activity, and other cholinergic adverse effects. For this reason, neostigmine is routinely administered with an antimuscarinic agent such as glycopyrrolate or atropine. Despite appropriate administration, recovery may remain variable, and residual neuromuscular blockade may occur if neostigmine is administered at an inappropriate depth of blockade [2,3].

Sugammadex introduced a fundamentally different approach to reversal of aminosteroidal neuromuscular blockade. It is a modified γ-cyclodextrin that forms stable complexes with steroidal neuromuscular blocking agents, particularly rocuronium and vecuronium, thereby reducing their free plasma concentrations and promoting their movement away from the neuromuscular junction [4]. Unlike neostigmine, its mechanism does not depend on increasing acetylcholine concentrations, and it therefore does not require routine coadministration of an antimuscarinic drug. Clinical studies have demonstrated that sugammadex can rapidly and effectively reverse vecuronium-induced neuromuscular blockade. In a multicenter randomized controlled trial, Khuenl-Brady et al. reported substantially faster reversal of vecuronium-induced blockade with sugammadex than with neostigmine [4]. Dose-response studies have similarly demonstrated effective reversal of both moderate and deep vecuronium-induced blockade with appropriately selected doses of sugammadex [5].

Although standard doses of sugammadex provide rapid and predictable recovery, the possibility of using lower doses has attracted increasing interest. Asztalos et al. investigated low-dose sugammadex for reversal of vecuronium-induced blockade at a TOF count of four and demonstrated that the efficacy of reversal was clearly dose dependent; a dose of 1.0 mg/kg was more effective than 0.5 mg/kg, although the possibility of recurrent neuromuscular blockade after inadequate dosing remained a concern [6]. More recently, He et al. demonstrated that both sugammadex and neostigmine could antagonize shallow residual vecuronium-induced neuromuscular blockade, but the required dose and reliability of reversal differed between the two agents [7]. These observations indicate that reducing the dose of sugammadex may be feasible in selected stages of recovery but requires careful dosing and quantitative neuromuscular monitoring.

An alternative strategy is to combine a reduced dose of sugammadex with neostigmine. The theoretical advantage of this approach is based on their complementary mechanisms: sugammadex directly decreases the concentration of free vecuronium molecules, whereas neostigmine increases acetylcholine availability at the neuromuscular junction. Clinical studies involving rocuronium have provided preliminary evidence supporting this concept. Cheong et al. demonstrated that combining sugammadex with neostigmine could reduce the amount of sugammadex required for reversal of moderate rocuronium-induced neuromuscular blockade, although muscarinic adverse effects related to neostigmine remained an important consideration [8]. Similarly, Aouad et al. reported that half-dose sugammadex combined with neostigmine was non-inferior to full-dose sugammadex for reversal of deep rocuronium-induced blockade, suggesting that combination therapy may provide an effective dose-sparing strategy [9].

Systematic evidence comparing sugammadex and neostigmine further indicates that sugammadex generally produces faster and more reliable recovery and may be associated with fewer reversal-related

adverse events [10]. However, most investigations of combined low-dose sugammadex and neostigmine have focused on rocuronium, while evidence specifically addressing vecuronium-induced neuromuscular blockade remains limited. Considering the established responsiveness of vecuronium to sugammadex and the different pharmacological mechanisms of the two reversal agents, evaluating a low-dose sugammadex–neostigmine combination may identify an effective strategy capable of achieving reliable recovery while reducing exposure to full-dose sugammadex.

Therefore, the present randomized controlled trial was designed to compare the efficacy and safety of a low-dose sugammadex–neostigmine combination with neostigmine alone for reversal of vecuronium-induced neuromuscular blockade. The study primarily aims to determine whether combination therapy provides faster and more reliable neuromuscular recovery while maintaining acceptable hemodynamic stability and a favorable adverse-effect profile. Such evidence may help define a practical alternative reversal strategy for patients receiving vecuronium during general anaesthesia.

Materials and Methods

Study design and setting: This randomized controlled, double blinded parallel-group clinical study was conducted at a Bangalore Medical College and Research Institute (BMCRI)-affiliated hospital over a 3-month period between March and June 2025. Ethical clearance was obtained from the Institutional Ethics Committee before commencement of the study. The study included 50 adult patients undergoing elective surgery under general anaesthesia. Written informed consent was obtained from all participants before enrolment. The study was designed to compare the efficacy and safety of low-dose sugammadex combined with neostigmine versus neostigmine alone for reversal of vecuronium-induced moderate neuromuscular blockade.

Study population: Patients aged 18-60 years, belonging to American Society of Anaesthesiologists physical status I or II, who were scheduled for elective surgery under general anaesthesia and were willing to provide written informed consent were considered eligible for participation.

Patients unwilling to participate, those undergoing emergency surgery, patients with a history of alcohol or drug abuse, known allergy to any of the study medications, or deranged renal function were excluded.

Sample size calculation: The sample size was calculated based on the study by Aouad et al**.**, using the reported difference in the duration required to achieve recovery of the train-of-four (TOF) ratio to 0.90. For the calculation, a 95% confidence level ($Z1-\alpha=1.96$), 80% statistical power ($Z1-\beta=0.84$), standard deviations of 1.9 and 0.8 in the two comparison groups, respectively, and an allocation ratio of 1:1 were considered. The calculated minimum sample size was 25 patients in each group, yielding a total study population of 50 patients.

Randomization and allocation: Following pre-anaesthetic evaluation and confirmation of eligibility, the 50 enrolled participants were randomized in a 1:1 ratio into two groups of 25 patients each. Random allocation was performed using computer-generated random numbers, and group allocation was concealed using the sealed-envelope technique. The groups were designated as follows:

- Group NS (n = 25)**:** Sugammadex 1 mg/kg plus neostigmine 50 µg/kg and glycopyrrolate 0.01 mg/kg.
- Group N (n = 25): Neostigmine 50 µg/kg plus glycopyrrolate 0.01 mg/kg.

Double blinded study

Both the patients and the assessor are blinded.

Pre-anesthetic assessment and monitoring: All participants underwent routine pre-anesthetic evaluation before surgery. After arrival in the operating room, standard monitoring was instituted. Baseline parameters, including heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and neuromuscular function, were recorded. Neuromuscular blockade was assessed using quantitative train-of-four monitoring.

General anaesthesia was administered according to the institutional anaesthesia protocol. After securing the airway with an endotracheal tube, patients were mechanically ventilated. Anaesthesia was maintained with sevoflurane at approximately 1 minimum alveolar concentration (MAC). Vecuronium was used as the nondepolarizing neuromuscular blocking agent according to the study protocol.

Neuromuscular monitoring and reversal protocol: At the end of the surgical procedure, TOF stimulation was performed at 20-second intervals to assess the depth of residual neuromuscular blockade. Reversal medication was administered when the TOF count had recovered to two twitches, representing moderate residual neuromuscular blockade.

Patients allocated to Group NS received intravenous sugammadex 1mg/kg in combination with neostigmine 50 µg/kg and glycopyrrolate 0.01

mg/kg. Patients in Group N received intravenous neostigmine 50 µg/kg together with glycopyrrolate 0.01 mg/kg.

Following administration of the reversal agents, quantitative neuromuscular monitoring was continued. The interval between administration of the reversal drug and achievement of a TOF ratio ≥0.90 was recorded in seconds and constituted the principal measure of neuromuscular recovery.

Extubation and postoperative recovery: Tracheal extubation was performed after the TOF ratio reached ≥0.90 and the patient fulfilled standard clinical criteria for safe extubation. Patients were subsequently assessed for postoperative recovery using the Modified Aldrete Score. Patients achieving a score of ≥9 were considered to have achieved satisfactory early postoperative recovery and were transferred to the post-anaesthesia care unit (PACU).

Outcome measures: The primary outcome was the time required for adequate reversal of vecuronium-induced moderate neuromuscular blockade, defined as the time from administration of the assigned reversal regimen at a TOF count of two until achievement of a TOF ratio ≥0.90. The study specifies comparison of this outcome between sugammadex 1 mg/kg combined with neostigmine 50 µg/kg and neostigmine 50 µg/kg alone.

The secondary outcome included peri-reversal hemodynamic changes, evidence of residual neuromuscular blockade, postoperative recovery assessed using the Modified Aldrete Score, and postoperative adverse effects, including postoperative nausea and vomiting.

Hemodynamic variables were evaluated before reversal and during the early post-reversal period. Based on the study analysis, heart rate and mean arterial pressure were assessed at baseline before reversal, 1 minute after reversal, and 5 minutes after reversal. The study used repeated-measures analysis for evaluation of serial hemodynamic changes.

Safety assessment: Patients were observed throughout neuromuscular recovery and during the immediate postoperative period for clinically apparent adverse events associated with the reversal medications. Particular attention was given to hemodynamic instability and postoperative adverse effects, including nausea and vomiting. The occurrence or absence of adverse effects was documented for both groups. The study subsequently compared the proportion of patients experiencing adverse events between treatment groups.

Statistical analysis: Continuous variables were summarized as mean ± standard deviation (SD) and categorical variables as frequency and percentage. Baseline continuous characteristics and recovery time between the two independent groups were compared using the independent Student's t-test. Categorical variables were compared using the Chi-square test, wherever applicable. Serial hemodynamic variables measured before reversal and at 1 and 5 minutes after reversal were analyzed using repeated-measures analysis of variance (ANOVA). The Modified Aldrete Score was compared between groups using the Mann-Whitney U test, consistent with the statistical analyses reported in the thesis. A two-sided P value <0.05 was considered statistically significant.

Results

A total of 50 patients were included in the final analysis, with 25 patients allocated to the sugammadex-neostigmine combination group (Group NS) and 25 to the neostigmine-alone group (Group N). Baseline demographic characteristics, including age, sex, body weight, and comorbidity profile, were comparable between the groups, indicating satisfactory baseline balance.

Table 1: Baseline demographic and clinical characteristics of the study groups

Characteristic	Group NS (n=25)	Group N (n=25)	P value
Age, years, mean ± SD	46.20 ± 11.20	44.08 ± 9.59	0.48
Age range, years	21-60	25-64	—
Male, n (%)	12 (48.0)	11 (44.0)	0.78
Female, n (%)	13 (52.0)	14 (56.0)	
Weight, kg, mean ± SD	65.64 ± 9.96	64.36 ± 15.03	0.72
T2DM, n (%)	2 (8.0)	3 (12.0)	0.78*
Hypertension, n (%)	1 (4.0)	1 (4.0)	
T2DM + hypertension, n (%)	1 (4.0)	2 (8.0)	
Asthma, n (%)	0 (0.0)	1 (4.0)	
No comorbidity, n (%)	21 (84.0)	18 (72.0)	

*P value represents comparison of overall distribution of comorbidities.

There were no statistically significant differences between the groups with respect to age, sex, body weight, or comorbidity profile. Mean age was 46.20 ± 11.20 years in Group NS and 44.08 ± 9.59 years in Group N (P=0.48). The proportion of males was 48.0% and 44.0%, respectively (P=0.78). Mean body weight was also comparable

between Group NS and Group N (65.64 ± 9.96 vs 64.36 ± 15.03 kg; P=0.72). Most participants had no documented comorbidity, accounting for 84.0% in Group NS and 72.0% in Group N.

Table 2: Comparison of neuromuscular recovery time between the study groups

Parameter	Group NS (n=25)	Group N (n=25)	Mean difference	95% CI	P value
Time to TOF ratio ≥0.90, min	2.93 ± 0.55	15.34 ± 2.05	-12.41	-13.27 to -11.56	<0.001

The primary efficacy outcome demonstrated a marked difference between the two reversal strategies. Patients receiving low-dose sugammadex in combination with neostigmine achieved a TOF ratio ≥0.90 in 2.93 ± 0.55 minutes, compared with 15.34 ± 2.05 minutes among patients receiving neostigmine alone. The mean between-group difference was -12.41 minutes (95% CI -13.27 to -11.56), representing substantially faster neuromuscular recovery with combination therapy (P<0.001).

Table 3: Comparison of hemodynamic parameters during neuromuscular reversal

Parameter	Time point	Group NS (n=25), mean ± SD	Group N (n=25), mean ± SD	Mean difference	P value
MAP, mmHg	Before reversal	95.72 ± 14.49	94.36 ± 15.55	1.36	0.75
	1 min after reversal	102.56 ± 18.39	92.24 ± 14.76	10.32	0.03
	5 min after reversal	101.40 ± 18.13	94.08 ± 16.86	7.32	0.15
Heart rate, bpm	Before reversal	97.68 ± 11.87	102.04 ± 16.59	-4.36	0.29
	1 min after reversal	104.68 ± 6.31	99.64 ± 14.32	5.04	0.04
	5 min after reversal	101.44 ± 8.55	100.44 ± 15.32	1.00	0.78

Baseline MAP was comparable between groups. At 1 minute following administration of the reversal agents, Group NS demonstrated a higher MAP than Group N (102.56 ± 18.39 vs 92.24 ± 14.76 mmHg; P=0.03). By 5 minutes, the difference was no longer statistically significant. Similarly, baseline heart rate did not differ significantly; however, at 1 minute after reversal, Group NS demonstrated a modestly higher mean heart rate (104.68 ± 6.31 vs 99.64 ± 14.32 bpm; P=0.04). The difference disappeared by 5 minutes.

Repeated-measures analysis showed that the overall temporal change in MAP was not statistically significant within either Group NS (P=0.08) or Group N (P=0.54). Similarly, changes in heart rate over the three measurement points were not significant within Group NS (P=0.10) or Group N (P=0.75).

Table 4: Comparison of total vecuronium dose between the study groups

Parameter	Group NS (n=25)	Group N (n=25)	Mean difference	P value
Vecuronium dose, mg	10.00 ± 1.45	9.74 ± 1.45	0.26	0.545

The mean total vecuronium dose documented in Group NS was 10.00 ± 1.45 mg compared with 9.74 ± 1.45 mg in Group N. The mean difference was 0.26 mg and was statistically insignificant (P=0.545).

Table 5: Comparison of postoperative Modified Aldrete scores

Parameter	Group NS (n=25)	Group N (n=25)	Mean difference	95% CI	P value
Modified Aldrete score	9.72 ± 0.54	9.60 ± 0.58	0.12	-0.20 to 0.44	0.38

Both groups demonstrated satisfactory postoperative recovery. The mean Modified Aldrete Score was 9.72 ± 0.54 in Group NS and 9.60 ± 0.58 in Group N. The between-group difference of 0.12 was not statistically significant (95% CI -0.20 to 0.44; P=0.38), demonstrating comparable immediate postoperative recovery scores.

Table 6: Comparison of postoperative side effects between the study groups

Side effects	Group NS (n=25), n (%)	Group N (n=25), n (%)
Present	0 (0.0)	0 (0.0)
Absent	25 (100.0)	25 (100.0)

No recorded postoperative side effects occurred in either treatment group. All 25 patients in Group NS and all 25 patients in Group N were documented as having no adverse effects during the study observation period. Consequently, a meaningful between-group statistical comparison could not be calculated because there were no events in either group.

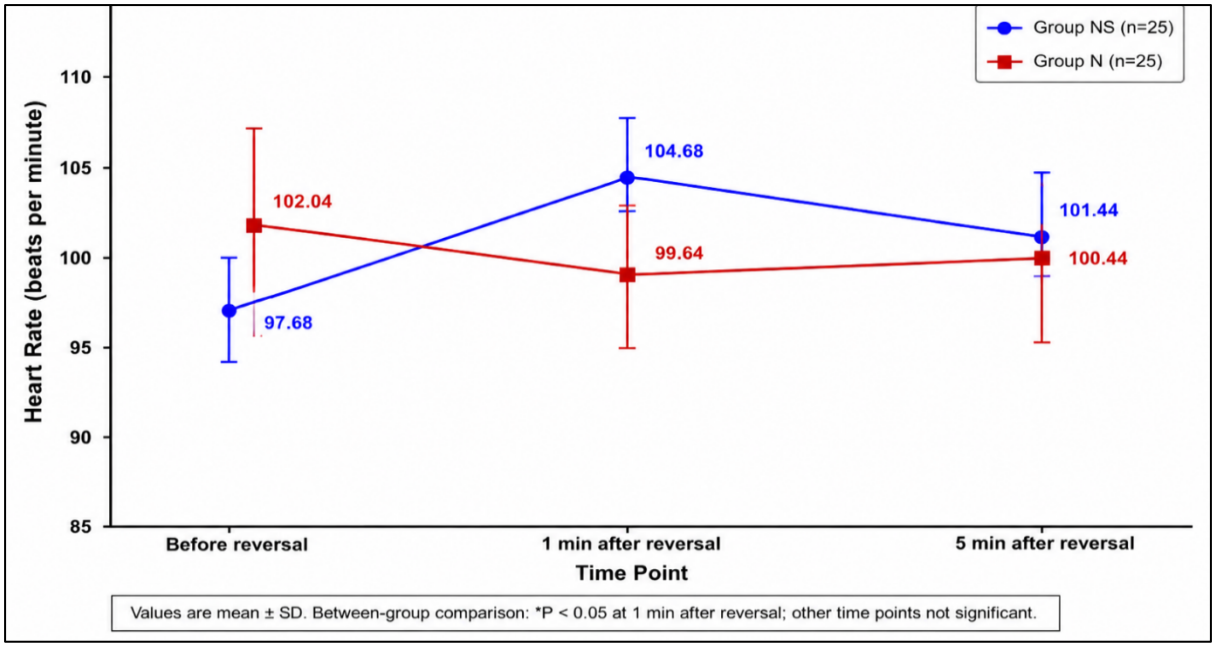

Figure 1: Changes in heart rate during neuromuscular reversal

Figure 1 showing the mean heart rate (beats per minute) in the sugammadex-neostigmine group (Group NS) and the neostigmine-alone group (Group N) at three time points: before reversal, 1 minute after reversal, and 5 minutes after reversal. Group NS showed an increase in mean heart rate from 97.68 bpm before reversal to 104.68 bpm at 1 minute, followed by a slight decline to 101.44 bpm at 5 minutes. In contrast, Group N demonstrated a relatively stable trend, with mean heart rates of 102.04 bpm before reversal, 99.64 bpm at 1 minute, and 100.44 bpm at 5 minutes. A statistically significant difference between the groups was observed at 1 minute after reversal (P = 0.04), while differences before reversal and at 5 minutes were not statistically significant. Overall, the figure illustrates a transient early rise in heart rate in the combination group, with convergence of values between groups by 5 minutes.

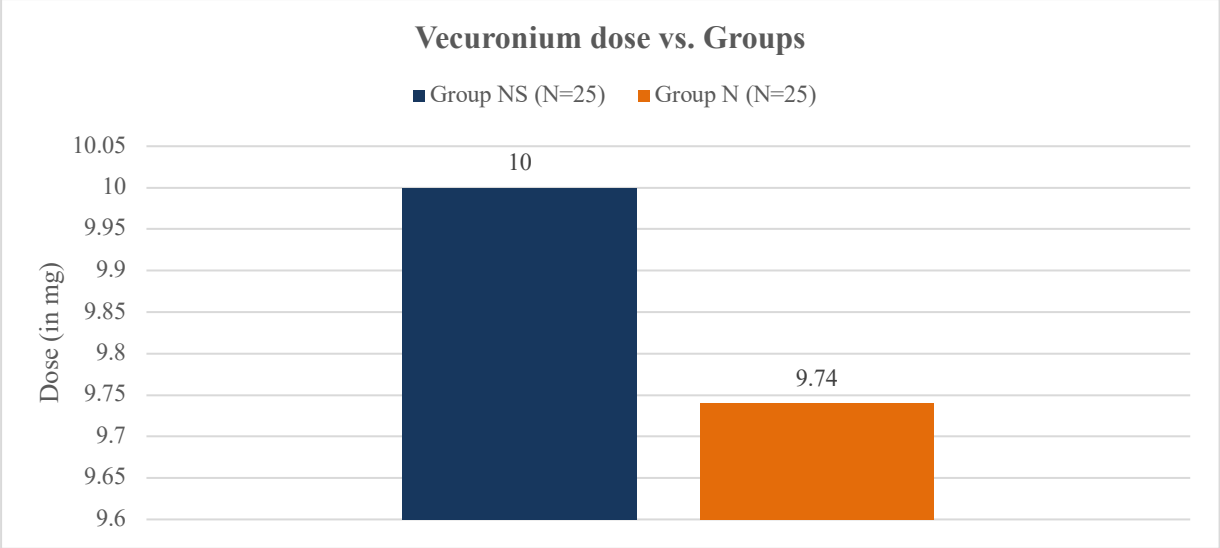

Figure 2: Comparison of mean total Vecuronium dose between the study groups

Figure 2 showing the mean total vecuronium dose administered in the two study groups. Both groups received a relatively similar mean dose of vecuronium, with Group NS averaging 10.00 ±1.45 mg and Group N receiving 9.74 ±1.45 mg. There was no statistically significant difference in vecuronium dose used between the two groups.(p=0.545).

Discussion

The present randomized controlled study evaluated the efficacy and safety of low-dose sugammadex 1 mg/kg combined with neostigmine 50 µg/kg compared with neostigmine 50 µg/kg alone for reversal of vecuronium-induced moderate neuromuscular blockade. The principal finding was

that combination therapy produced a markedly faster recovery of neuromuscular function. The mean time required to achieve a train-of-four (TOF) ratio ≥0.90 was 2.93 ± 0.55 minutes in Group NS compared with 15.34 ± 2.05 minutes in Group N, corresponding to a mean difference of -12.41 minutes (95% CI -13.27 to -11.56; P<0.001). This represents a substantial pharmacodynamic advantage for the low-dose sugammadex-neostigmine strategy and suggests that combining agents with complementary mechanisms may provide effective reversal while limiting the amount of sugammadex required.

The rapid recovery observed in the combination group is pharmacologically plausible. Sugammadex directly encapsulates free aminosteroidal neuromuscular blocking molecules, whereas neostigmine increases acetylcholine concentration at the neuromuscular junction by inhibiting acetylcholinesterase. Consequently, the two agents act through fundamentally different mechanisms. Suy et al. demonstrated a clear dose-response relationship for sugammadex in both rocuronium- and vecuronium-induced moderate blockade. In patients receiving vecuronium, sugammadex 1 mg/kg administered at the reappearance of the second twitch produced a mean recovery time to a TOF ratio of 0.90 of approximately 2.5 minutes, whereas recovery following placebo was considerably slower [11]. The recovery time of 2.93 minutes observed in the present combination group is therefore biologically consistent with previous vecuronium-specific pharmacodynamic evidence, although the present study differs by combining low-dose sugammadex with neostigmine.

The magnitude of the difference between the two groups also agrees with randomized evidence showing the greater speed and predictability of sugammadex-containing reversal strategies compared with conventional anticholinesterase reversal. Geldner et al., in a randomized controlled study of patients undergoing laparoscopic surgery, demonstrated that sugammadex achieved substantially faster recovery than neostigmine across different depths of neuromuscular blockade [12]. Similarly, Blobner et al. reported a geometric mean time to recovery of the TOF ratio to 0.90 of 1.5 minutes with sugammadex versus 18.6 minutes with neostigmine, with 98% of sugammadex-treated patients recovering within 5 minutes compared with only 11% receiving neostigmine [13]. Although these studies primarily involved rocuronium, the fundamental principle is relevant because both rocuronium and vecuronium are aminosteroidal neuromuscular blocking agents susceptible to encapsulation by sugammadex.

Jones et al. further demonstrated the limitations of neostigmine when substantial neuromuscular blockade remains. In their randomized trial of profound rocuronium-induced blockade, the geometric mean recovery time to a TOF ratio of 0.90 was 2.9 minutes with sugammadex compared with 50.4 minutes following neostigmine plus glycopyrrolate [14]. While the present study investigated moderate rather than profound blockade, its findings follow the same overall pharmacodynamic pattern. Neostigmine depends on sufficient spontaneous recovery and has a ceiling effect, whereas sugammadex decreases the concentration of free steroidal neuromuscular blocker directly. The addition of even a low dose of sugammadex may therefore shift the equilibrium sufficiently to facilitate rapid recovery, while simultaneously allowing neostigmine-mediated enhancement of cholinergic transmission.

An important clinical implication of the faster TOF recovery is the potential reduction in residual neuromuscular blockade. Recovery to a quantitative TOF ratio ≥0.90 is an accepted physiological endpoint for adequate reversal because incomplete recovery below this threshold is associated with impaired upper airway function and respiratory vulnerability. Brueckmann et al. found residual blockade at PACU admission in 0 of 74 patients receiving sugammadex compared with 33 of 76 patients receiving usual-care reversal, predominantly neostigmine/glycopyrrolate. Sugammadex also reduced the interval between reversal administration and readiness for operating-room discharge [15]. The present findings therefore support the concept that a sugammadex-containing strategy can improve the speed and predictability of neuromuscular recovery even when the dose of sugammadex is lower than the conventional 2 mg/kg dose used for moderate blockade.

The clinical significance of reliable neuromuscular recovery extends beyond operating-room efficiency. Residual neuromuscular blockade has been associated with adverse postoperative respiratory outcomes. In the large multicenter STRONGER cohort analysis, Kheterpal et al. compared more than 45,000 matched surgical patients receiving sugammadex or neostigmine and reported a lower incidence of major postoperative pulmonary complications among patients reversed with sugammadex [16]. However, the relationship between reversal agent and postoperative pulmonary outcomes is not completely uniform across all observational datasets, and patient characteristics, monitoring practices, depth of block, and surgical procedures can influence these outcomes. Therefore, although the faster quantitative recovery observed in the present study is clinically encouraging, the current sample size was not designed to demonstrate differences in uncommon pulmonary complications.

Hemodynamic assessment revealed an interesting but transient pattern. Before reversal, mean arterial pressure was comparable between Group NS and Group N (95.72 ± 14.49 vs 94.36 ± 15.55 mmHg;

P=0.75). At 1 minute following reversal, MAP was significantly higher in Group NS (102.56 ± 18.39 vs 92.24 ± 14.76 mmHg; P=0.03), whereas at 5 minutes the difference was no longer statistically significant (P=0.15). A similar pattern was observed for heart rate: values were comparable before reversal, but Group NS demonstrated a higher heart rate at 1 minute (104.68 ± 6.31 vs 99.64 ± 14.32 bpm; P=0.04), followed by convergence at 5 minutes (P=0.78).

Importantly, repeated-measures analyses did not demonstrate a statistically significant overall temporal change in MAP within Group NS (P=0.08) or Group N (P=0.54), and corresponding heart-rate changes were also nonsignificant (P=0.10 and P=0.75, respectively). These findings suggest that the significant 1-minute intergroup differences were brief physiological changes rather than sustained hemodynamic instability. Nevertheless, their mechanism cannot be determined from the available data. The combination group received sugammadex, neostigmine, and glycopyrrolate, and therefore the transient cardiovascular response should not be attributed specifically to sugammadex. Larger safety studies have generally shown acceptable cardiovascular tolerability of sugammadex. Herring et al., in a randomized double-blind study that included higher-risk ASA III-IV surgical patients receiving rocuronium or vecuronium, found sugammadex to have an acceptable overall and cardiac safety profile when compared with neostigmine/glycopyrrolate [17].

Postoperative recovery assessed using the Modified Aldrete Score was similar between groups. Group NS had a mean score of 9.72 ± 0.54, while Group N had a mean score of 9.60 ± 0.58; the mean difference of 0.12 was not statistically significant (P=0.38). This indicates that although combination therapy markedly accelerated quantitative neuromuscular recovery, both groups ultimately achieved satisfactory immediate post-anesthesia recovery. Such a finding is clinically reasonable because the Aldrete Score reflects several domains, including activity, respiration, circulation, consciousness, and oxygen saturation, rather than neuromuscular recovery alone. Thus, a substantial difference in TOF recovery does not necessarily translate into an equally large difference in a global recovery score once patients have fulfilled extubation and PACU-transfer criteria.

No recorded postoperative adverse effects occurred in either group, with all 25 patients in each group classified as free of study-recorded side effects. This finding supports short-term tolerability but should be interpreted cautiously. With only 25 patients per treatment arm and no events, the present trial is underpowered to exclude uncommon adverse reactions. In particular, a zero-event finding should not be interpreted as evidence that the regimens are risk-free. Previous randomized evidence has suggested that differences between reversal agents may be most apparent for specific events such as nausea, vomiting, or bradycardia. Yağan et al. reported significantly less nausea and/or vomiting during the first postoperative hour with sugammadex compared with neostigmine and lower rescue antiemetic use during 24-hour follow-up [18]. More recent pooled evidence has similarly shown faster recovery and reductions in residual blockade and selected postoperative complications with sugammadex compared with neostigmine [19]. However, the present trial assessed a combination strategy rather than conventional-dose sugammadex monotherapy, so these safety findings cannot be directly extrapolated.

Additionally Group NS received 10.00± 1.45 mg of vecuronium and group N received 9.74± 1.45 mg of vecuronium with a mean difference of 0.26 and p value of 0.545. There was no statistical difference in the dose of vecuronium used between the groups.

Another strength of the present study was the use of quantitative TOF monitoring and a predefined recovery threshold of ≥0.90. This provides a more objective endpoint than clinical signs such as sustained head lift, hand grip, or tidal volume, which may fail to identify residual blockade. Brueckmann et al. demonstrated that clinically important residual paralysis could persist despite routine reversal practices, reinforcing the value of objective quantitative monitoring [15]. The clear separation in recovery times in the present study therefore represents a physiologically meaningful outcome rather than reliance on subjective assessment alone.

The findings should nevertheless be interpreted in the context of several limitations. First, the sample size was relatively small and adequate principally for detecting a difference in TOF recovery time rather than uncommon adverse events. Second, the study was conducted at a single institutional setting over a short period, which may limit generalizability. Third, although immediate hemodynamics, Aldrete score, and adverse effects were assessed, longer postoperative respiratory outcomes and patient-centered recovery measures were not evaluated. Finally, the trial compared the combination regimen with neostigmine alone and did not include a conventional-dose sugammadex group. Consequently, it demonstrates the superiority of the low-dose combination over neostigmine but cannot establish whether the combination is noninferior to standard-dose sugammadex.

Overall, the present study demonstrates that sugammadex 1 mg/kg combined with neostigmine 50 µg/kg provides substantially faster reversal of vecuronium-induced moderate neuromuscular blockade than neostigmine 50 µg/kg alone, with recovery to TOF ≥0.90 occurring approximately 12

minutes earlier on average. Immediate postoperative recovery scores were comparable, hemodynamic differences were transient, and no adverse events were recorded in either group. These results are consistent with the wider evidence demonstrating the speed and predictability of sugammadex-mediated aminosteroidal neuromuscular reversal [11-15,19]. The combination strategy therefore represents a potentially useful dose-sparing approach, particularly where the acquisition cost of conventional-dose sugammadex limits routine use. Nevertheless, adequately powered multicenter randomized trials comparing low-dose combination therapy directly with standard-dose sugammadex, incorporating blinded quantitative neuromuscular assessment, standardized cumulative vecuronium exposure, economic evaluation, and clinically meaningful postoperative respiratory endpoints are warranted before routine implementation.

Conclusion

In this randomized controlled study, the combination of low-dose sugammadex 1 mg/kg with neostigmine 50 µg/kg produced substantially faster reversal of vecuronium-induced moderate neuromuscular blockade than neostigmine 50 µg/kg alone. The mean time to achieve a TOF ratio ≥0.90 was 2.93 ± 0.55 minutes in the combination group compared with 15.34 ± 2.05 minutes in the neostigmine group, demonstrating a highly significant reduction in recovery time (P<0.001). Although transient differences in heart rate and mean arterial pressure were observed at 1 minute after reversal, these differences were not sustained at 5 minutes, and overall within-group hemodynamic changes were not statistically significant. Immediate postoperative recovery was comparable between the groups, as reflected by similar Modified Aldrete scores, and no study-recorded adverse effects were observed in either group.

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