https://doi.org/10.62587/AFRJMS.3.2.2026.145-155 ISSN: 3006-7421

African Research Journal of Medical Sciences

Journal homepage: https://www.afrjms.com

Research Paper **Open Access**

Sugammadex versus neostigmine for reversal of rocuronium-induced neuromuscular blockade under general anaesthesia: A randomised controlled study

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Article Info
Volume 3, Issue 2, July 2026
Received : 25 December 2025
Accepted : 18 August 2026
Published : 09 November 2026
doi: 10.62587/AFRJMS.3.2.2026.145-155

Abstract

Background: Reversal of rocuronium-induced neuromuscular blockade is important for achieving adequate recovery before extubation. Sugammadex and neostigmine differ in their mechanisms of action and speed of reversal. **Aim:** To compare sugammadex and neostigmine for reversal of rocuronium-induced neuromuscular blockade under general anaesthesia. **Methods:** This randomised controlled study included 60 participants, with 30 assigned to receive sugammadex and 30 to receive neostigmine. The groups were compared for baseline characteristics, time to achieve a train-of-four (TOF) ratio of at least 0.9, extubation time, time to reach an Aldrete score of at least 9, haemodynamic measurements after reversal, and adverse effects. **Results:** Baseline characteristics were comparable between groups. Mean time to reach a TOF ratio of at least 0.9 was shorter with sugammadex than with neostigmine (2.9 ± 2.2 vs 9.1 ± 3.5 minutes; mean difference −6.20 minutes, 95% CI −7.72 to −4.68; $p < 0.001$). Recovery to TOF ≥0.9 within 3 minutes occurred in 70.0% and 6.7% of participants, respectively ($p < 0.001$). Mean extubation time was 6.8 ± 1.6 minutes with sugammadex and 10.2 ± 2.1 minutes with neostigmine; mean time to Aldrete score ≥9 was 13.8 ± 2.9 and 18.9 ± 3.6 minutes, respectively (both $p < 0.001$). Haemodynamic differences were not consistent across measurement times. Bradycardia and postoperative nausea and vomiting were numerically less frequent with sugammadex, but neither individual comparison was statistically significant. The composite adverse-event rate was lower with sugammadex (13.3% vs 40.0%; $p = 0.020$). **Conclusion:** Sugammadex was associated with faster neuromuscular recovery, extubation, and early recovery than neostigmine in this study. The haemodynamic and adverse-event findings should be interpreted cautiously given the small sample and multiple unadjusted haemodynamic comparisons.

Keywords: *Sugammadex, Neostigmine, Neuromuscular blockade*

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1. Introduction

Neuromuscular blocking agents are used during general anaesthesia to facilitate tracheal intubation and provide suitable operating conditions. Their effects may persist after surgery, however, causing residual neuromuscular blockade (RNMB) (Brueckmann *et al.*, 2015). Incomplete recovery can impair upper airway function and ventilation and has been associated with critical respiratory events in the post-anaesthesia care unit (PACU). Murphy *et al.* (2008) described the clinical importance of RNMB in patients experiencing critical respiratory events. Quantitative neuromuscular monitoring helps identify incomplete recovery; a train-of-four (TOF) ratio of at least 0.9 is generally used as the threshold before extubation (Thilen *et al.*, 2023).

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Rocuronium is a non-depolarising neuromuscular blocking agent commonly used during general anaesthesia. Neostigmine reverses neuromuscular blockade by inhibiting acetylcholinesterase and increasing acetylcholine at the neuromuscular junction. Its effectiveness depends on the degree of spontaneous recovery, and its muscarinic effects may cause bradycardia, increased secretions, or gastrointestinal symptoms; an anticholinergic drug is therefore co-administered. Sugammadex reverses rocuronium through selective binding, reducing the free concentration of the drug and allowing neuromuscular transmission to recover.

Randomised studies have compared these reversal agents using TOF recovery as an outcome (Paech *et al.*, 2018; Kim *et al.*, 2019; Murphy *et al.*, 2021; Huang *et al.*, 2023; Chhabra *et al.*, 2024). Jones *et al.* (2008) reported faster reversal of rocuronium-induced blockade with sugammadex than with neostigmine in patients with profound blockade. Geldner *et al.* (2012) also reported shorter recovery times with sugammadex in a randomised controlled study. These findings support assessment of recovery using quantitative monitoring while also examining haemodynamic changes and adverse effects.

The present study compared sugammadex with neostigmine for reversal of rocuronium-induced neuromuscular blockade in patients undergoing elective ENT surgery under general anaesthesia. Time to achieve a TOF ratio of at least 0.9 was the primary outcome. Haemodynamic parameters and adverse effects were also assessed.

2. Aim and objectives

2.1. Aim

To compare sugammadex and neostigmine for reversal of rocuronium-induced neuromuscular blockade under general anaesthesia.

2.2. Objectives

1. To compare the time taken to achieve a TOF ratio of at least 0.9 following reversal with sugammadex or neostigmine.
2. To compare haemodynamic changes following administration of the reversal drugs.
3. To compare the adverse effects associated with sugammadex and neostigmine.

3. Materials and methods

3.1. Source of data

Data were collected from adult patients admitted to Chamarajanagar Institute of Medical Sciences, Chamarajanagar, who were scheduled for elective ENT surgery under general anaesthesia.

3.2. Study design

The study was conducted as a prospective, randomised, double-blinded comparative study.

3.3. Study location

The study was conducted in the Department of Anaesthesiology, Chamarajanagar Institute of Medical Sciences Hospital, Chamarajanagar, Karnataka.

3.4. Study duration

The study was conducted over 18 months, from June 2024 to December 2025.

3.5. Sample size

The calculated minimum was approximately 27 patients per group. After allowing for a 10% dropout rate, the target was rounded to 30 patients per group. Thus, 60 patients were enrolled, with 30 in each group.

3.6. Inclusion criteria

Patients were included if they:

- Were 18–70 years old.
- Were of either sex and belonged to ASA physical status I or II.

- Were scheduled for elective ENT surgery under general anaesthesia.
- Provided written informed consent to participate.

3.7. Exclusion criteria

Patients were excluded if they had:

- A known allergy to any of the study drugs.
- Pregnancy or were lactating.
- A history of high-dose steroid intake.
- Known cardiac, respiratory, or endocrine disorders.
- Known renal or hepatic dysfunction.
- Suspected neuromuscular disease.
- A planned requirement for postoperative mechanical ventilation.

3.8. Procedure and methodology

After institutional ethics committee approval, eligible patients were assessed during the pre-anaesthetic evaluation. The study procedures, potential risks, and expected benefits were explained, and written informed consent was obtained before enrolment.

Participants were assigned by computer-generated random numbers to one of two groups:

- **Group SR:** Sugammadex 2 mg/kg intravenously.
- **Group NR:** Neostigmine 50 μg/kg with glycopyrrolate 10 μg/kg intravenously.

An anaesthesiologist who was not involved in the study prepared the reversal drug. Both preparations were diluted to 10 mL to maintain blinding of the participant and the investigator conducting the assessment.

On arrival in the preoperative area, standard monitoring with electrocardiography, pulse oximetry, and non-invasive blood pressure was applied. An 18-gauge intravenous cannula was inserted, and Ringer's lactate was administered. Anaesthesia was induced and maintained according to the institutional protocol. Premedication included glycopyrrolate, ondansetron, dexamethasone, and midazolam; lidocaine was administered before induction, followed by propofol and fentanyl. Rocuronium 0.6 mg/kg was administered for tracheal intubation, with supplemental doses of 0.1 mg/kg given when indicated by neuromuscular monitoring.

Neuromuscular function was monitored with an acceleromyographic GE Datex-Ohmeda E-NMT module. Surface electrodes were placed over the ulnar nerve near the wrist, and the forearm was immobilised. Train-of-four stimulation was applied at 15-second intervals, and the evoked response of the adductor pollicis muscle was monitored during surgery.

At the end of surgery, when no further neuromuscular blockade was required, patients were allowed to recover until the second twitch (T2) reappeared. The allocated reversal drug was then administered intravenously. TOF monitoring continued until the TOF ratio reached at least 0.9; the interval from reversal-drug administration to this threshold was recorded.

Consciousness and clinical recovery were assessed. In conscious, cooperative patients, a five-second head-lift test, handgrip, arm lift, and eye opening were assessed. Patients who had recovered and were haemodynamically stable were extubated. Heart rate and blood pressure were recorded before reversal and at 5, 10, 15, 30, 60, and 120 minutes after administration. After extubation, oxygen saturation, respiratory rate, and heart rate were monitored in the recovery room for at least 60 minutes. Patients were observed for signs of recurrent blockade, including respiratory-rate changes or oxygen saturation below 90%. A further clinical assessment of neuromuscular recovery and respiratory adequacy was performed at least 10 hours after study-drug administration.

The time to achieve an Aldrete score of at least 9, extubation time, haemodynamic measurements, and adverse events including bradycardia and postoperative nausea and vomiting were also recorded.

3.9. Sample processing

No biological samples were collected or processed. Patient and perioperative data were recorded in a structured proforma and entered into a master chart. Data were checked for completeness and coded before statistical analysis. Continuous outcomes included time to TOF ratio ≥0.9, extubation time, time to Aldrete score ≥9, and haemodynamic measurements. Categorical outcomes included ASA class, clinical recovery findings, and adverse events.

3.10. Statistical methods

Data were entered in Microsoft Excel 2019 and analysed using Epi Info version 7.2.6. Continuous variables were summarised using mean and standard deviation when normally distributed; medians were used for skewed data. Categorical variables were presented as frequencies and percentages.

The independent-samples t test was used to compare normally distributed continuous outcomes between groups. The Mann–Whitney U test was used for skewed continuous outcomes. Categorical variables were compared using the chi-square test or Fisher's exact test when expected cell counts were small. A two-sided p value below 0.05 was considered statistically significant.

Clinical Trials Registry of India registration number: CTRI/2025/03/082137.

4. Results

The two groups were comparable at baseline (Table 1). Mean age was 36.97 ± 9.80 years in the sugammadex group and 38.63 ± 10.07 years in the neostigmine group, with a mean difference of −1.66 years (95% CI: −6.80 to 3.48; $p = 0.520$). There were no statistically significant between-group differences in sex, height, weight, or BMI (all $p > 0.05$). ASA physical status was also similar: 40.0% of patients in the sugammadex group and 30.0% in the neostigmine group were ASA I, while the remaining patients were ASA II ($p = 0.417$).

Table 1: Baseline characteristics and group comparability

Characteristic	Sugammadex (n=30)	Neostigmine (n=30)	Difference (95% CI)	Test statistic	*p* value
Age, years, mean (SD)	36.97 (9.80)	38.63 (10.07)	−1.66 (−6.80 to 3.48) years	Welch $t = -0.65$	0.520
Male sex, n (%)	14 (46.7)	15 (50.0)	−3.3 percentage points (−26.9 to 20.7)	$\chi^2 = 0.07$	0.796
Height, cm, mean (SD)	163.69 (6.31)	165.16 (6.51)	−1.47 (−4.78 to 1.84) cm	Welch $t = -0.89$	0.378
Weight, kg, mean (SD)	60.70 (6.74)	64.14 (8.81)	−3.44 (−7.50 to 0.62) kg	Welch $t = -1.70$	0.095
BMI, kg/m², mean (SD)	22.63 (1.98)	23.45 (2.27)	−0.82 (−1.92 to 0.28) kg/m²	Welch $t = -1.49$	0.142
ASA physical status I, n (%)	12 (40.0)	9 (30.0)	10.0 percentage points (−13.6 to 32.1)	$\chi^2 = 0.66$	0.417
ASA physical status II, n (%)	18 (60.0)	21 (70.0)			

The mean time to achieve a TOF ratio of at least 0.9 was shorter in the sugammadex group than in the neostigmine group (2.9 ± 2.2 vs 9.1 ± 3.5 minutes; mean difference: −6.20 minutes, 95% CI: −7.72 to −4.68; < 0.001) (Table 2). Recovery within 3 minutes occurred in 70.0% of the sugammadex group compared with

6.7% of the neostigmine group. Conversely, recovery taking more than 10 minutes was recorded in 3.3% and 56.7%, respectively. Extubation and attainment of an Aldrete score of at least 9 were also faster in the sugammadex group (both $p < 0.001$).

Table 2: Neuromuscular recovery and related recovery outcomes

Outcome	Sugammadex (n=30)	Neostigmine (n=30)	Difference (95% CI)	Test statistic	*p* value
Time to TOF ratio ≥0.9, min, mean (SD)	2.9 (2.2)	9.1 (3.5)	−6.20 (−7.72 to −4.68) min	Welch $t = -8.22$	<0.001
Achieved TOF ratio ≥0.9 within 3 min, n (%)	21 (70.0)	2 (6.7)	63.3 percentage points (40.2 to 77.5)	Fisher exact test	<0.001
Achieved TOF ratio ≥0.9 after 10 min, n (%)	1 (3.3)	17 (56.7)	−53.3 percentage points (−69.5 to −31.4)	Fisher exact test	<0.001
Extubation time, min, mean (SD)	6.8 (1.6)	10.2 (2.1)	−3.40 (−4.37 to −2.43) min	Welch $t = -7.05$	<0.001
Time to Aldrete score ≥9, min, mean (SD)	13.8 (2.9)	18.9 (3.6)	−5.10 (−6.79 to −3.41) min	Welch $t = -6.04$	<0.001

Mean systolic blood pressure did not differ significantly between groups at any measured time point (all $p > 0.05$) (Table 3). Heart rate differed significantly at 0 minutes and 10 minutes after reversal ($p = 0.008$ and $p = 0.048$, respectively); the remaining heart-rate comparisons were not statistically significant. Diastolic blood pressure was higher in the sugammadex group at 0, 15, and 60 minutes ($p = 0.027$, $p = 0.021$, and $p = 0.036$, respectively), with no significant differences at the other time points.

Table 3: Haemodynamic measurements after reversal					
Parameter and time	**Sugammadex, mean (SD)**	**Neostigmine, mean (SD)**	**Mean difference (95% CI)**	**Welch *t***	***p* value**
Heart rate, beats/min					
0 min	80.20 (11.50)	73.60 (6.30)	6.60 (1.78 to 11.42)	2.76	0.008
5 min	76.10 (13.94)	82.23 (12.47)	−6.13 (−12.97 to 0.71)	−1.80	0.078
10 min	75.60 (13.47)	82.30 (12.21)	−6.70 (−13.35 to −0.05)	−2.02	0.048
15 min	75.27 (12.89)	81.37 (11.42)	−6.10 (−12.40 to 0.20)	−1.94	0.057
30 min	77.53 (10.44)	80.97 (11.54)	−3.44 (−9.13 to 2.25)	−1.21	0.231
60 min	76.03 (11.48)	80.20 (11.18)	−4.17 (−10.03 to 1.69)	−1.43	0.159
120 min	77.57 (11.13)	79.03 (12.44)	−1.46 (−7.56 to 4.64)	−0.48	0.634
Systolic blood pressure, mmHg					
0 min	130.13 (12.71)	128.67 (10.36)	1.46 (−4.54 to 7.46)	0.49	0.628
5 min	129.87 (13.23)	126.00 (10.72)	3.87 (−2.36 to 10.10)	1.25	0.218
10 min	127.20 (11.95)	125.60 (8.63)	1.60 (−3.80 to 7.00)	0.60	0.555
15 min	128.67 (12.89)	124.80 (8.65)	3.87 (−1.82 to 9.56)	1.37	0.178
30 min	126.13 (10.49)	124.27 (8.55)	1.86 (−3.09 to 6.81)	0.75	0.455
60 min	124.00 (9.68)	122.93 (7.36)	1.07 (−3.38 to 5.52)	0.48	0.632
120 min	124.00 (10.09)	122.93 (8.51)	1.07 (−3.76 to 5.90)	0.44	0.659
Diastolic blood pressure, mmHg					
0 min	76.93 (7.74)	72.13 (8.57)	4.80 (0.58 to 9.02)	2.28	0.027
5 min	71.60 (7.41)	70.40 (7.49)	1.20 (−2.65 to 5.05)	0.62	0.535
10 min	71.20 (6.75)	70.80 (6.80)	0.40 (−3.10 to 3.90)	0.23	0.820
15 min	72.00 (8.59)	67.33 (6.40)	4.67 (0.75 to 8.59)	2.39	0.021
30 min	73.07 (8.41)	70.13 (7.95)	2.94 (−1.29 to 7.17)	1.39	0.169
60 min	73.73 (9.22)	68.93 (8.07)	4.80 (0.32 to 9.28)	2.15	0.036
120 min	69.33 (7.84)	70.00 (8.21)	−0.67 (−4.82 to 3.48)	−0.32	0.748

Bradycardia occurred in 3.3% of patients in the sugammadex group and 16.7% in the neostigmine group, while postoperative nausea and vomiting occurred in 10.0% and 23.3%, respectively (Table 4). Neither individual comparison was statistically significant ($p = 0.195$ and $p = 0.299$). The composite adverse-event rate was lower in the sugammadex group than in the neostigmine group (13.3% vs 40.0%; risk difference: −26.7 percentage points, 95% CI: −46.1 to −4.2; $p = 0.020$).

Table 4: Adverse effects					
Adverse effect	**Sugammadex (n=30), n (%)**	**Neostigmine (n=30), n (%)**	**Risk difference (95% CI), percentage points**	**Test statistic**	***p* value**
Bradycardia	1 (3.3)	5 (16.7)	−13.3 (−30.5 to 2.9)	Fisher exact test	0.195
Postoperative nausea and vomiting	3 (10.0)	7 (23.3)	−13.3 (−32.1 to 6.1)	Fisher exact test	0.299
Any composite adverse event	4 (13.3)	12 (40.0)	−26.7 (−46.1 to −4.2)	$\chi^2 = 5.45$	0.020

5. Discussion

5.1. Baseline characteristics

The sugammadex and neostigmine groups were similar in age, sex, height, weight, BMI, and ASA physical status; none of the between-group comparisons was statistically significant (all $p > 0.05$). This balance supports the comparability of the groups, although nonsignificant tests do not establish that the groups were identical. The results apply most directly to this relatively young, low-risk study population. Trials involving older or higher-risk patients, such as those by Togioka *et al.* (2020) and Ledowski *et al.* (2021), studied a different population and assessed additional outcomes such as postoperative pulmonary complications.

5.2. Neuromuscular recovery and related outcomes

Recovery to a TOF ratio of at least 0.9 was faster with sugammadex than with neostigmine in this study: 2.9 versus 9.1 minutes, a mean difference of −6.2 minutes. This is consistent with the direction of effect reported in comparative reviews. Hristovska *et al.* (2017) and Hristovska *et al.* (2018) found substantially faster recovery with sugammadex in adults; in their pooled analysis of moderate block, recovery took approximately 2.0 minutes with sugammadex and 12.9 minutes with neostigmine. These pooled estimates are not directly interchangeable with the present results because reversal time depends on block depth, dose, monitoring method, and study protocol.

The early recovery pattern in the present study was also pronounced: 70.0% of patients in the sugammadex group reached TOF ≥0.9 within 3 minutes, compared with 6.7% in the neostigmine group. Kaufhold *et al.* (2016) similarly found that neostigmine did not reliably reverse residual block to a TOF ratio of 0.9 within 10 minutes in their dose-finding study. In randomised studies, Moon *et al.* (2020) and Farag *et al.* (2021) also reported faster neuromuscular recovery with sugammadex. Farag *et al.* (2021), however, did not find that the faster reversal necessarily produced a significant difference in extubation time in their neurointerventional setting.

The shorter extubation time and time to Aldrete score ≥9 in the present study are consistent with earlier recovery milestones, but they should not be interpreted as proof of shorter PACU stay or better longer-term recovery. In the DATA trial, Piccioni *et al.* (2024) found faster recovery to TOF ≥0.9 and earlier extubation with sugammadex, but no significant difference in PACU stay or hospital length of stay. A randomised trial in patients with obstructive sleep apnoea undergoing bariatric surgery likewise found no difference in operating-room discharge time or postoperative complications (Ajetunmobi *et al.*, 2025).

5.3. Haemodynamic measurements

The present results do not show a consistent haemodynamic difference across all measurement times. There were isolated nominal differences in heart rate and diastolic blood pressure, while systolic blood pressure did not differ significantly at any time point. Because these were separate, unadjusted comparisons across multiple time points, the isolated p values should be interpreted cautiously: some may reflect chance findings. Tsai *et al.* (2023) reported more stable haemodynamic changes with sugammadex in

neurointerventional anaesthesia, but their procedure, patient context, and use of accompanying medication differ from this study. The present table therefore supports a cautious conclusion of no clear, sustained haemodynamic advantage.

5.4. Adverse effects

Bradycardia and postoperative nausea and vomiting were numerically less frequent with sugammadex, but neither individual comparison was statistically significant. With only 30 participants per group, the study had limited ability to detect differences in relatively uncommon events. Hsieh *et al.* (2023), in a meta-analysis of 40 randomised trials, reported a modestly lower risk of postoperative nausea and vomiting with sugammadex; however, evidence on individual adverse effects has varied across reviews and trials. The 2023 American Society of Anesthesiologists guideline (Thilen *et al.*, 2023) emphasises quantitative monitoring and adequate recovery before extubation, while the comparative evidence for specific adverse effects remains less definitive than the evidence for faster reversal.

The composite adverse-event rate was lower with sugammadex (13.3% versus 40.0%, $p = 0.020$). This finding is worth reporting, but it should be interpreted in light of the small number of events and the composite outcome. Broader clinical-outcome studies have not been fully consistent: some observational analyses reported fewer pulmonary complications with sugammadex (Kheterpal *et al.*, 2020; Colquhoun *et al.*, 2023), while randomised or other cohort studies have reported no clear difference (Togioka *et al.*, 2020; Olesnicky *et al.*, 2022; Ren *et al.*, 2024). Olesnicky *et al.* (2024) reviewed patient morbidity and recovery outcomes and highlighted uncertainty in translating faster neuromuscular reversal into consistent improvements in broader postoperative outcomes. This study itself was too small and narrow in scope to determine whether either drug changes the risk of rare or serious postoperative complications.

6. Conclusion

Sugammadex produced faster reversal of rocuronium-induced neuromuscular blockade than neostigmine in this study. Patients receiving sugammadex reached a TOF ratio of at least 0.9 sooner and had shorter extubation and recovery times. Haemodynamic measurements showed no consistent pattern of between-group differences, and the individual rates of bradycardia and postoperative nausea and vomiting were not significantly different. The lower composite adverse-event rate with sugammadex should be interpreted cautiously because the study included few participants and events. Overall, the findings support more rapid neuromuscular recovery with sugammadex in the study population.

7. Limitations of the study

- The sample was small, with 30 participants in each group; the study may have lacked power to detect differences in uncommon adverse events.
- The findings may not generalise to older adults, patients with significant comorbidities, or patients undergoing emergency or high-risk procedures.
- Haemodynamic comparisons were made separately at multiple time points without adjustment for multiple testing; isolated significant results may have occurred by chance.
- Recovery-time estimates and associated test statistics were recalculated from the reported means, standard deviations, and sample sizes. The source did not provide the Mann–Whitney U statistics for these outcomes.
- The available results do not provide enough detail to assess the effects of reversal-drug dose, depth of neuromuscular blockade at reversal, or monitoring method on recovery.
- The study assessed short-term recovery outcomes and was not designed to establish differences in rare serious complications or longer-term postoperative outcomes.

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Cite this article as: Kapadam Pavan Sai Kumar Reddy, Darshan M.S. and Soumya M.V. (2026). Sugammadex versus neostigmine for reversal of rocuronium-induced neuromuscular blockade under general anaesthesia: A randomised controlled study. *African Research Journal of Medical Sciences*, 3(2): 145-155. doi: 10.62587/AFRJMS.3.2.2026.145-155.