COMPARISON OF LOW DOSE SUGAMMADEX WITH NEOSTIGMINE PLUS GLYCOPYRROLATE VERSUS NEOSTIGMINE PLUS GLYCOPYRROLATE FOR EXTUBATION

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ABSTRACT

Background: Residual neuromuscular blockade remains a significant cause of delayed recovery and postoperative respiratory complications following general anaesthesia. Neostigmine with glycopyrrolate is the conventional reversal regimen but may be associated with incomplete recovery. Sugammadex provides rapid and predictable reversal of aminosteroidal neuromuscular blocking agents. The use of low-dose sugammadex in combination with conventional reversal may improve recovery while minimizing cost. **Objectives:** To compare recovery characteristics following conventional reversal with neostigmine and glycopyrrolate versus neostigmine and glycopyrrolate followed by sugammadex 0.5 mg/kg. **Methods:** This prospective comparative study included 60 adult patients (ASA I–II) undergoing surgery under general anaesthesia with vecuronium-induced neuromuscular blockade. Patients were randomized into two groups of 30 each. Group N received neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg. Group S received neostigmine 0.05 mg/kg, glycopyrrolate 0.01 mg/kg, and sugammadex 0.5 mg/kg. The primary outcome was extubation time. Secondary outcomes included time of eye opening, response to verbal commands, residual neuromuscular blockade, postoperative complications. **Results:** Baseline demographic and surgical characteristics were comparable between groups. Group S demonstrated significantly faster recovery than Group N. Extubation time was significantly reduced in Group S (8.20 ± 1.70 min) versus Group N (14.10 ± 2.90 min) ($p<0.001$). Eye opening, spontaneous respiration, and response to verbal commands occurred significantly earlier in Group S ($p<0.001$ for all comparisons). PACU stay was significantly shorter in Group S (55.20 ± 10.80 min) compared with Group N (74.50 ± 13.40 min) ($p<0.001$). Residual neuromuscular blockade occurred in 16.7% of patients in Group N and none in Group S ($p=0.020$). **Conclusion:** The addition of low-dose sugammadex (0.5 mg/kg) to conventional neostigmine-glycopyrrolate reversal significantly improved neuromuscular recovery, reduced extubation time, shortened PACU stay, and decreased residual neuromuscular blockade. This combination may represent a safe and effective strategy for improving postoperative recovery following general anaesthesia.

Keywords: Neuromuscular blockade; Neostigmine; Glycopyrrolate; Sugammadex; Extubation time; Residual neuromuscular blockade.

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INTRODUCTION

Neuromuscular blocking agents (NMBAs) are an essential component of modern general anaesthesia. They facilitate tracheal intubation, provide optimal muscle relaxation, and improve surgical conditions across a wide range of procedures. However, successful anaesthetic management depends not only on achieving adequate intraoperative neuromuscular blockade but also on ensuring complete recovery before extubation, as residual neuromuscular blockade (RNMB) continues to be an important cause of postoperative morbidity.[1]

Residual neuromuscular blockade may impair upper airway muscle function, reduce ventilatory reserve, and increase the risk of airway obstruction, hypoxaemia, aspiration, and delayed recovery in the post-anaesthesia care unit (PACU). Importantly, studies have demonstrated that clinically significant residual paralysis can persist even in patients who appear to have recovered adequately, making RNMB a continuing concern for patient safety and postoperative respiratory outcomes.[9–11]

For many years, the combination of neostigmine and glycopyrrolate has been the standard method for reversing non-depolarizing neuromuscular blockade. Neostigmine acts by inhibiting acetylcholinesterase, thereby increasing acetylcholine availability at the neuromuscular junction, while glycopyrrolate is administered to counteract the muscarinic side effects of neostigmine. Owing to its effectiveness, low cost, and widespread availability, this combination remains the most commonly used reversal regimen in routine clinical practice.[12,13]

Despite its widespread use, neostigmine has several limitations. Its effectiveness depends on the degree of spontaneous recovery, is less reliable in deeper neuromuscular blockade, and is limited by a ceiling effect, which may result in incomplete reversal and postoperative residual paralysis despite appropriate administration.[10,13]

Sugammadex has transformed the reversal of aminosteroidal neuromuscular blockers such as rocuronium and vecuronium. As a modified γ-cyclodextrin, it selectively encapsulates these agents, rapidly reversing neuromuscular blockade without inhibiting acetylcholinesterase. This results in faster, more predictable recovery, a lower incidence of residual neuromuscular blockade, and eliminates the need for concomitant anticholinergic drugs.[3,5,14,15]

Although sugammadex provides rapid and reliable reversal of neuromuscular blockade, its high cost limits routine use, particularly in resource-limited settings. This has led to interest in more cost-effective strategies, such as adding low-dose sugammadex to conventional neostigmine–glycopyrrolate reversal. The complementary mechanisms of these agents may enhance neuromuscular recovery while reducing the need for standard doses of sugammadex.(16,17)

However, evidence supporting this approach, particularly in vecuronium-induced neuromuscular blockade, remains limited.[17,18] Therefore, the present prospective randomized comparative study was undertaken to evaluate the effect of adding low-dose sugammadex (0.5 mg/kg) to conventional neostigmine–glycopyrrolate reversal. Recovery characteristics, extubation profile, residual neuromuscular blockade, postoperative complications, and overall recovery outcomes were compared between the two reversal strategies.

METHODOLOGY

Study Design

This prospective comparative study was conducted in the Department of Anaesthesiology at a tertiary care teaching hospital.

Study Duration

The study was conducted over a period of six months from the date of Institutional Ethics Committee approval.

Study Setting

The study was carried out in the operation theatres and post-anaesthesia care unit (PACU) of a tertiary care teaching hospital.

Sample Size Calculation

The sample size was calculated based on previous studies evaluating neuromuscular recovery following reversal with sugammadex and neostigmine. A minimum of 27 patients per group was required. To compensate for potential dropouts and protocol deviations, 30 patients were included in each group, resulting in a total sample size of 60 patients.

Group Allocation

Group N = 30 patients

Group S = 30 patients

Study Population

Adult patients undergoing elective surgical procedures under general anaesthesia requiring neuromuscular blockade with vecuronium were considered for inclusion.

Inclusion Criteria

- Patients aged 18–60 years.
- Either sex.
- ASA Physical Status I and II.
- Elective surgical procedures under general anaesthesia.
- Requirement of vecuronium-induced neuromuscular blockade.
- Patients willing to provide written informed consent.

Exclusion Criteria

- Refusal to participate.
- ASA Physical Status III or above.
- Known hypersensitivity to neostigmine, glycopyrrolate, vecuronium, or sugammadex.

- Significant renal impairment (serum creatinine >2 mg/dL).
- Significant hepatic dysfunction.
- Neuromuscular disorders such as myasthenia gravis or muscular dystrophy.
- Pregnancy and lactation.
- Anticipated difficult airway.
- Emergency surgeries.
- Patients receiving medications known to interfere with neuromuscular transmission.

PROCEDURE

Allocation

Patients meeting the eligibility criteria were allocated into two groups.

- Patients fulfilling the inclusion and exclusion criteria were selected for the study.
- A detailed pre-anaesthetic evaluation was performed one day before surgery.
- During the pre-anaesthetic assessment, the patient's age, sex, weight, height, body mass index (BMI), ASA physical status, medical comorbidities, and relevant laboratory and radiological investigations were recorded.
- The anaesthetic procedure, study protocol, and possible risks were explained to all patients, and written informed consent was obtained.
- All patients were kept nil per oral (NPO) according to standard fasting guidelines before surgery.
- After arrival in the operating room, intravenous access was secured.
- Standard ASA monitors were attached, including electrocardiography (ECG), non-invasive blood pressure (NIBP), pulse oximetry (SpO_2), end-tidal carbon dioxide ($EtCO_2$).
- Baseline haemodynamic parameters, including heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and oxygen saturation (SpO_2), were recorded before induction of anaesthesia.
- Three minutes before induction of anaesthesia, all patients were premedicated with intravenous midazolam 0.02 mg/kg and fentanyl 2 µg/kg.
- General anaesthesia was induced with propofol 2 mg/kg IV. After the loss of consciousness, vecuronium 0.08 mg/kg IV was administered to achieve adequate neuromuscular blockade. Once satisfactory muscle relaxation was achieved, the trachea was intubated using an appropriately sized cuffed endotracheal tube. Correct tube placement was confirmed by bilateral chest auscultation and continuous capnography.
- Anaesthesia was maintained with an oxygen–air mixture and sevoflurane (1–2 MAC). Patients were mechanically ventilated, with ventilatory settings adjusted to maintain an end-tidal carbon dioxide ($EtCO_2$) concentration between 35 and 40 mmHg. Additional doses of vecuronium were administered as required during surgery.
- At the completion of surgery, patients received the assigned reversal regimen according to their study group. Patients in Group N received inj.neostigmine 0.05 mg/kg IV together with inj.glycopyrrolate 0.01 mg/kg IV. Patients in Group S received the same doses of neostigmine and glycopyrrolate, followed immediately by inj.sugammadex 0.5 mg/kg IV.
- Recovery from neuromuscular blockade was evaluated by TOF monitoring, recording the time to eye opening, time to extubation, time to obey verbal commands, and time to adequate spontaneous respiration. After extubation, all patients were transferred to the post-anaesthesia care unit (PACU) for further observation.
- During the PACU stay, the duration of PACU stay, incidence of postoperative residual curarization (PORC), clinical muscle weakness, requirement for airway support, and need for re-intubation were assessed and documented. Patients were also monitored for adverse events, including bradycardia, tachycardia, hypotension, hypertension, oxygen desaturation, nausea, vomiting, bronchospasm, and allergic reactions.
- Haemodynamic parameters, including heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP), were recorded at baseline, before reversal, 1, 3, 5, and 10 minutes after reversal, at extubation, and 15 minutes after extubation.

Postoperative Monitoring

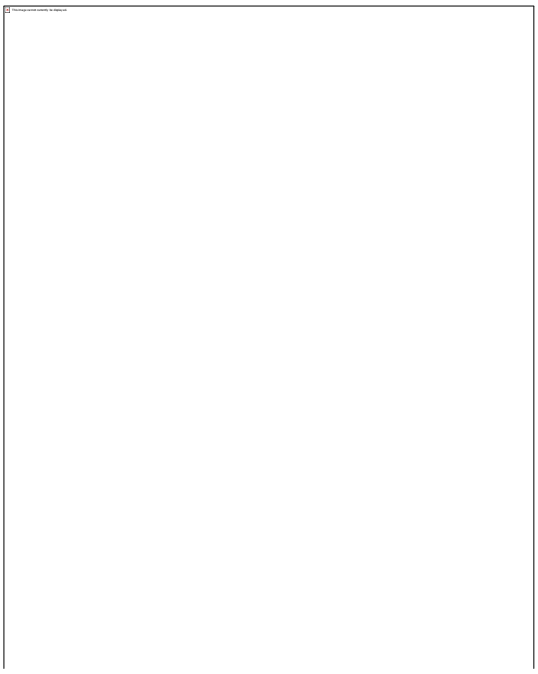
Patients were observed in PACU for: Heart rate, Blood pressure, Respiratory rate, Oxygen saturation, Airway patency, Neuromuscular recovery and recovery data were recorded by the investigator.

Statistical Analysis

Data were entered into Microsoft Excel and analysed using IBM SPSS Statistics version 28. Results were presented as tables and graphs. Continuous variables were expressed using appropriate descriptive statistics, while categorical

variables were presented as frequencies and percentages.

Data normality was assessed using the Shapiro–Wilk test. Continuous variables were compared using the independent t-test for normally distributed data and the Mann–Whitney U test for non-normally distributed data. Categorical variables were analysed using the Chi-square test or Fisher's exact test, as appropriate. Changes in repeated measurements over time were analysed using repeated-measures ANOVA followed by post hoc analysis. A p-value <0.05 was considered statistically significant.



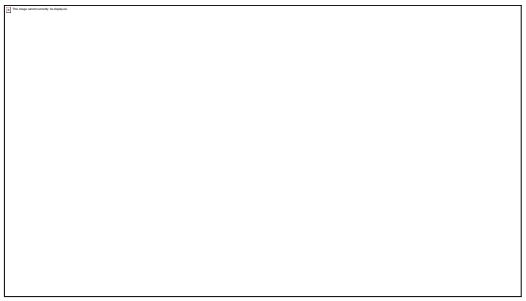
RESULTS

A total of 60 patients undergoing surgery under general anaesthesia with vecuronium-induced neuromuscular blockade were enrolled and completed the study. Patients were allocated into two equal groups: Group N (Neostigmine + Glycopyrrolate, n = 30) and Group S (Neostigmine + Glycopyrrolate followed by Sugammadex 0.5 mg/kg, n = 30). All patients were included in the final analysis.

Table 1: Demographic Characteristics

Variable	Group N (n=30)	Group S (n=30)	p-value
Age (years)	40.63 ± 10.96	41.63 ± 9.96	0.713
Weight (kg)	65.02 ± 7.54	63.44 ± 8.69	0.453
BMI (kg/m²)	23.63 ± 3.49	23.15 ± 3.25	0.584
Male	18 (60.0%)	17 (56.7%)	0.796
Female	12 (40.0%)	13 (43.3%)	
ASA I	17 (56.7%)	18 (60.0%)	0.796
ASA II	13 (43.3%)	12 (40.0%)	
Duration of surgery (min)	95.17 ± 21.19	96.27 ± 16.19	0.822

There was no statistically significant difference between Group N and Group S in age, weight, or BMI (all p > 0.05), indicating comparable baseline demographic characteristics.



GRAPH 1: COMPARISON OF DEMOGRAPHIC CHARACTERISTICS

GRAPH 2: COMPARISON OF DEMOGRAPHIC CHARACTERISTICS

The distribution of gender and ASA physical status was comparable between the two groups. No statistically significant differences were observed between the groups (p = 0.796), indicating that both groups were well matched with respect to baseline clinical characteristics.

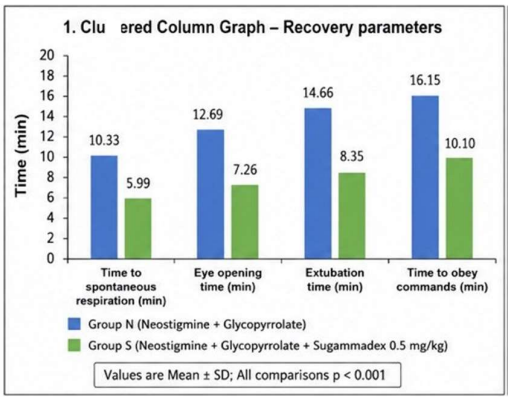
The mean duration of surgery was 95.17 ± 21.19 minutes in Group N and 96.27 ± 16.19 minutes in Group S. The difference was not statistically significant (p = 0.822). These findings indicate that both groups were comparable with respect to intraoperative surgical duration.

Table 2: Recovery Profile

Variable	Group N (n=30)	Group S (n=30)	p-value
Extubation time (min)	14.66 ± 2.80	8.35 ± 1.66	<0.001

Time to spontaneous respiration (min)	10.33 ± 1.73	5.99 ± 0.85	<0.001
Eye opening time (min)	12.69 ± 2.30	7.26 ± 1.65	<0.001
Time to obey commands (min)	16.15 ± 2.38	10.10 ± 1.57	<0.001

Recovery parameters were significantly faster in Group S compared to Group N. The mean time to spontaneous respiration, eye opening, extubation, and obeying commands was significantly lower in Group S ($p < 0.001$ for all comparisons). These findings indicate a more rapid postoperative recovery profile in Group S than in Group N.



GRAPH 3: COMPARISON OF RECOVERY PARAMETERS

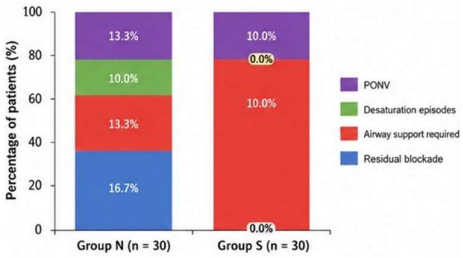
Table 3: Postoperative Complications

Complication	Group N (n=30)	Group S (n=30)	p-value
Residual blockade	5 (16.7%)	0 (0.0%)	0.019
Airway support required	4 (13.3%)	0 (0.0%)	0.038
Desaturation episodes	3 (10.0%)	0 (0.0%)	0.076
Postoperative nausea and vomiting (PONV)	4 (13.3%)	3 (10.0%)	0.688

The incidence of residual neuromuscular blockade was significantly higher in Group N (16.7%) compared to Group S (0%), with a statistically significant difference ($p = 0.019$). Similarly, the requirement for airway support was significantly greater in Group N (13.3%) than in Group S (0%) ($p = 0.038$).

Although desaturation episodes occurred more frequently in Group N (10.0%) than in Group S (0%), the difference did not reach statistical significance ($p = 0.076$). The incidence of postoperative nausea and vomiting (PONV) was comparable between the groups (13.3% vs. 10.0%; $p = 0.688$).

Overall, Group S demonstrated a lower incidence of postoperative respiratory complications and residual neuromuscular blockade compared with Group N.



GRAPH 4: COMPARISON OF POSTOPERATIVE COMPLICATIONS

DISCUSSION

Residual neuromuscular blockade (RNMB) remains an important cause of postoperative morbidity despite advances in anaesthetic monitoring and perioperative care. Inadequate recovery from neuromuscular blockade can result in upper airway obstruction, hypoventilation, aspiration, hypoxemia, delayed extubation, prolonged post-anaesthesia care unit (PACU) stay, and increased healthcare costs. The present prospective randomized comparative study evaluated the efficacy of conventional reversal with neostigmine-glycopyrrolate versus neostigmine-glycopyrrolate supplemented with low-dose sugammadex (0.5 mg/kg) in patients undergoing surgery under general anaesthesia with vecuronium-induced neuromuscular blockade. The study demonstrated that the addition of low-dose sugammadex significantly accelerated recovery and reduced postoperative residual neuromuscular blockade.

Baseline demographic characteristics, including age, body weight, BMI, gender, ASA physical status, duration of surgery, and total vecuronium consumption, were comparable between the two groups. This ensured that the observed differences in postoperative recovery were primarily attributable to the reversal strategy rather than patient- or surgery-related factors. Similar baseline comparability has been reported in previous studies evaluating neuromuscular blockade reversal agents.[1,2]

The principal finding of this study was the significantly faster recovery achieved with low-dose sugammadex. Patients in Group S regained spontaneous respiration, opened their eyes, responded to verbal commands, and were extubated significantly earlier than those in Group N (all $p<0.001$). Notably, mean extubation time decreased from 14.66 ± 2.80 minutes with conventional reversal to 8.35 ± 1.66 minutes with low-dose sugammadex, highlighting its ability to accelerate recovery even at a dose of 0.5 mg/kg.

This rapid recovery is explained by sugammadex's unique mechanism of action. Unlike neostigmine, which indirectly reverses neuromuscular blockade by inhibiting acetylcholinesterase, sugammadex directly encapsulates aminosteroidal neuromuscular blocking agents, producing rapid and predictable reversal. These findings are consistent with those of Jones et al.[3] and Blobner et al.[4], who also reported faster and more reliable recovery with sugammadex than with neostigmine.

A notable finding was the complete absence of residual neuromuscular blockade (RNMB) in the sugammadex group, whereas 16.7% of patients receiving conventional reversal had residual blockade. This is clinically significant because RNMB is associated with impaired airway function and postoperative respiratory complications. Similar observations have been reported by Murphy et al., who demonstrated that residual paralysis after neostigmine reversal contributes to adverse respiratory outcomes.[5]

Postoperative airway support was also required less frequently with sugammadex. Four patients in the conventional reversal group required airway support, whereas none in the sugammadex group did. Although the incidence of desaturation was not statistically significant, it occurred only in Group N. These findings are in agreement with Brueckmann et al., who reported fewer postoperative respiratory complications with sugammadex.[6] More complete recovery of pharyngeal and respiratory muscle function likely explains the improved airway stability after extubation.

The faster recovery observed with sugammadex is clinically important. Earlier eye opening and response to verbal commands indicate quicker restoration of neurological function, allowing earlier postoperative assessment, improved patient satisfaction, smoother operating room turnover, and reduced PACU workload. Similar findings have been reported by Ledowski et al., who demonstrated better early postoperative recovery and higher clinician satisfaction with sugammadex.[7]

These findings are particularly relevant in resource-limited settings, where the cost of sugammadex limits its routine use. Although the recommended dose is 2–4 mg/kg, our results suggest that a low dose of 0.5 mg/kg, administered after conventional reversal, can provide meaningful clinical benefits while reducing treatment costs.

Although sugammadex is more expensive than neostigmine, its use may shorten PACU stay, decrease postoperative respiratory complications and airway interventions, and improve operating room efficiency, potentially offsetting its higher acquisition cost. Similar observations have been reported by Carron et al.[8] However, further pharmacoeconomic studies are needed to confirm the cost-effectiveness of this low-dose approach.

This study has several strengths. It was a prospective, randomized study with standardized anaesthetic and neuromuscular monitoring protocols. Baseline characteristics were comparable between groups, reducing selection bias, and the outcomes assessed were clinically relevant. Additionally, the study evaluated a low-dose sugammadex regimen, an area with limited published evidence.

Some limitations should be acknowledged. The study was conducted at a single centre with a relatively small sample size, which may limit generalizability. Only ASA I–II patients undergoing elective surgery were included, so the findings may not be applicable to high-risk patients or those with significant comorbidities. In addition, only vecuronium-induced neuromuscular blockade was evaluated, and quantitative TOF recovery beyond clinical recovery parameters was not assessed as a primary outcome.

In conclusion, adding low-dose sugammadex (0.5 mg/kg) to conventional neostigmine-glycopyrrolate reversal significantly improved recovery from vecuronium-induced neuromuscular blockade. Patients demonstrated earlier spontaneous breathing, faster extubation, quicker neurological recovery, and fewer residual neuromuscular blockade-related respiratory complications. These findings suggest that low-dose sugammadex is an effective, safe, and potentially cost-effective strategy for enhancing postoperative recovery after general anaesthesia.

CONCLUSION

The addition of sugammadex 0.5 mg/kg to conventional neostigmine-glycopyrrolate reversal significantly improves recovery following vecuronium-induced neuromuscular blockade and it is an effective, safe, and potentially cost-conscious strategy for improving postoperative recovery and patient safety following general anaesthesia.

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