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Original Research Article

A Randomized, Non-Inferiority Study Evaluating Sugammadex 2 mg/kg Versus 4 mg/kg for the Reversal of Deep Rocuronium-Induced Neuromuscular Blockade at the End of Skin Closure in Prolonged, Bolus-Only Surgical Cases

Sankiti Sangeetha[1], Aireddy Srikanth Reddy[2]

[1,2]Assistant Professor, Department of Anesthesiology, GGH, Karimnagar, Telangana, India

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Corresponding author: Dr. Aireddy Srikanth Reddy

Conflict of interest: Nil

Abstract

Introduction: Residual neuromuscular blockade following the use of rocuronium remains a clinically significant concern, particularly after prolonged surgical procedures. Sugammadex enables rapid and effective reversal of aminosteroidal neuromuscular blockade; however, the optimal dosing for deep blockade in prolonged, bolus-only surgical cases remains uncertain. The present study aimed to evaluate whether sugammadex 2 mg/kg is non-inferior to 4 mg/kg in reversing deep rocuronium-induced neuromuscular blockade at the end of skin closure in prolonged surgical procedures.

Materials and Methods: This prospective, randomized, non-inferiority clinical trial was conducted on 60 patients (ASA I–II) undergoing elective prolonged surgeries under general anaesthesia. Patients were randomly allocated into two groups: Group A received sugammadex 2 mg/kg and Group B received 4 mg/kg for reversal of deep rocuronium-induced neuromuscular blockade (post-tetanic count 1–2) at the time of skin closure. The primary outcome was time to achieve train-of-four (TOF) ratio ≥0.9. Secondary outcomes included time to extubation, time to follow verbal commands, proportion achieving TOF ≥0.9 within 3 minutes, and incidence of residual blockade.

Results: Baseline characteristics were comparable between groups. Time to TOF ≥0.9 was significantly longer in Group A compared to Group B (172.9 ± 48.7 vs 144.8 ± 41.5 seconds; p = 0.02). A higher proportion of patients in Group B achieved TOF ≥0.9 within 3 minutes [27 (90.0%) vs 23 (76.7%)], though not statistically significant (p = 0.18). Residual blockade at 5 minutes was observed in 3 (10.0%) patients in Group A and 1 (3.3%) in Group B (p = 0.30). Recovery profiles, including time to extubation and response to commands, were comparable. Hemodynamic parameters and adverse events were similar in both groups.

Conclusion: Sugammadex 2 mg/kg provides effective and clinically comparable reversal of deep neuromuscular blockade, despite a modest delay in recovery time compared to 4 mg/kg, suggesting its potential as a safe alternative in appropriately monitored patients.

Keywords: Sugammadex, Rocuronium, Neuromuscular blockade, Train-of-four.

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Introduction

Neuromuscular blocking agents (NMBAs) are an integral component of modern general anaesthesia, facilitating optimal surgical conditions, endotracheal intubation, and controlled ventilation [1,2]. Among the aminosteroidal NMBAs, rocuronium is widely used due to its rapid onset and intermediate duration of action [3]. However, incomplete reversal of neuromuscular blockade remains a significant concern, as residual paralysis in the postoperative period is associated with adverse respiratory events, delayed recovery, and increased morbidity [4]. Conventional reversal with anticholinesterases such as neostigmine is often unpredictable in deep blockade and may be accompanied by undesirable muscarinic side effects [5]. The introduction of sugammadex, a selective relaxant binding agent, has revolutionized the reversal of aminosteroidal neuromuscular blockade [6]. By encapsulating free rocuronium molecules, sugammadex facilitates rapid and reliable reversal, even from deep levels of blockade [7]. Standard dosing recommendations suggest 4 mg/kg for reversal of deep neuromuscular blockade (post-tetanic count 1–2), while 2 mg/kg is typically used for moderate blockade [8]. Although higher doses ensure faster recovery, they are associated

with increased cost, which is a significant consideration in resource-limited settings [9]. In prolonged surgical procedures where rocuronium is administered intermittently as bolus doses rather than continuous infusion, the depth of blockade at the end of surgery may vary, and complete recovery may not always necessitate higher doses of sugammadex [7,10]. Emerging evidence suggests that lower doses may still achieve effective reversal in such scenarios, potentially offering a cost-effective alternative without compromising patient safety [11]. However, robust clinical data evaluating the efficacy of lower doses in deep blockade, particularly in prolonged bolus-only surgical cases, remain limited [12-14].

Therefore, the present study was aimed to evaluate sugammadex 2 mg/kg is non-inferior to sugammadex 4 mg/kg in reversing deep rocuronium-induced neuromuscular blockade at the end of skin closure in prolonged surgical procedures using a bolus-only regimen, with respect to recovery of train-of-four ratio ≥0.9 and associated clinical outcomes.

Materials and Methods

This prospective, randomized, non-inferiority clinical trial conducted in the Department of Anaesthesiology at Government General Hospital, Karimnagar, Telangana, over a period of one year from January 2025 to December 2025.

Institutional Ethics Committee approval was obtained prior to commencement of the study, and written informed consent was secured from all participants. A total of 60 adult patients aged 18–65 years, belonging to ASA physical status I–II and scheduled for elective prolonged surgical procedures under general anesthesia requiring neuromuscular blockade, were enrolled. Patients with known hypersensitivity to study drugs, neuromuscular disorders, significant hepatic or renal impairment, pregnancy, or those on medications affecting neuromuscular transmission were excluded.

Participants were randomly allocated into two groups of 30 each using a computer-generated randomization sequence. Group A received sugammadex 2 mg/kg, while Group B received sugammadex 4 mg/kg for reversal of deep rocuronium-induced neuromuscular blockade. All patients were managed with a standardized anaesthetic protocol. Following standard fasting guidelines, anaesthesia was induced using intravenous propofol and an opioid, and endotracheal intubation was facilitated with rocuronium. Anaesthesia was maintained with inhalational agents and intermittent bolus doses of rocuronium, avoiding continuous infusion to ensure a bolus-only regimen. Neuromuscular function was monitored using quantitative train-of-four (TOF) stimulation at the adductor pollicis muscle. At the completion of surgery, specifically at the time of skin closure, deep neuromuscular blockade was confirmed by a post-tetanic count of 1–2 prior to administration of the study drug. The allocated dose of sugammadex was administered as a single intravenous bolus. The primary outcome was the time from administration of sugammadex to recovery of TOF ratio ≥0.9. Secondary outcomes included time to extubation, time to obey verbal commands, proportion of patients achieving TOF ≥0.9 within 3 minutes, and incidence of residual neuromuscular blockade (TOF <0.9 at 5 minutes).

Hemodynamic parameters, including heart rate and mean arterial pressure, were recorded immediately before and after reversal. Patients were observed for adverse events such as bradycardia, hypotension, postoperative nausea and vomiting, hypersensitivity reactions, and recurarization.

Statistical analysis was performed using SPSS v26, with continuous variables expressed as mean ± standard deviation and categorical variables as N (%). Independent t-test and chi-square test were applied as appropriate, and a p-value <0.05 was considered statistically significant.

Results

Baseline demographic and perioperative characteristics were comparable between the two groups. The mean age in Group A was 45.6 ± 11.8 years compared to 47.1 ± 12.3 years in Group B ($p = 0.64$). The proportion of male patients was similar, with 17 (56.7%) in Group A and 18 (60.0%) in Group B ($p = 0.79$). Body mass index did not differ significantly between the groups (24.8 ± 3.3 kg/m² vs 25.4 ± 3.6 kg/m²; $p = 0.48$). Distribution of ASA physical status was also comparable, with ASA I observed in 13 (43.3%) patients in Group A and 12 (40.0%) in Group B.

The mean duration of surgery (141.2 ± 34.5 minutes vs 145.8 ± 36.2 minutes; $p = 0.61$) and total rocuronium consumption (98.6 ± 19.4 mg vs 101.2 ± 21.7 mg; $p = 0.58$) were similar across both groups, indicating adequate baseline comparability (Table 1).

Table 1: Demographic and Perioperative Characteristics (n = 60)

Variable	Category	Group A (n = 30)	Group B (n = 30)	p-value
Age (years)	**Mean ± SD**	45.6 ± 11.8	47.1 ± 12.3	0.64
Gender	**Male**	17 (56.7%)	18 (60.0%)	0.79
	Female	13 (44.3%)	12 (40%)	
BMI (kg/m²)	**Mean ± SD**	24.8 ± 3.3	25.4 ± 3.6	0.48
ASA	**I**	13 (43.3%)	12 (40.0%)	0.79
	II	17 (56.7%)	18 (60.0%)	—
Duration of surgery (min)	**Mean ± SD**	141.2 ± 34.5	145.8 ± 36.2	0.61
Total rocuronium dose (mg)	**Mean ± SD**	98.6 ± 19.4	101.2 ± 21.7	0.58

The reversal profile demonstrated a statistically significant difference in the time to achieve a TOF ratio ≥0.9 between the two groups. Group A required a longer duration (172.9 ± 48.7 seconds) compared to Group B (144.8 ± 41.5 seconds; p = 0.02). The median time also reflected a similar trend [168 (138–210) seconds vs 140 (118–170) seconds]. A higher proportion of patients in Group B achieved TOF ≥0.9 within 3 minutes compared to Group A [27 (90.0%) vs 23 (76.7%)], although this difference was not statistically significant (p = 0.18).

Residual neuromuscular blockade at 5 minutes was observed in 3 (10.0%) patients in Group A and 1 (3.3%) patient in Group B (p = 0.30) (Table 2).

Table 2: Reversal Profile of Neuromuscular Blockade

Outcome	Group A (n = 30)	Group B (n = 30)	p-value
Time to TOF ratio ≥0.9 (sec), mean ± SD	172.9 ± 48.7	144.8 ± 41.5	0.02
Median (IQR)	168 (138–210)	140 (118–170)	—
Patients achieving TOF ≥0.9 within 3 min	23 (76.7%)	27 (90.0%)	0.18
Residual neuromuscular block at 5 min	3 (10.0%)	1 (3.3%)	0.30

Recovery characteristics were comparable between the groups without statistically significant differences. The mean time to extubation was slightly longer in Group A (6.1 ± 1.8 minutes) compared to Group B (5.3 ± 1.5 minutes), but this did not reach statistical significance (p = 0.07). Similarly, the time to follow verbal commands was 7.5 ± 2.2 minutes in Group A and 6.7 ± 1.9 minutes in Group B (p = 0.15).

These findings suggest similar clinical recovery profiles despite differences in reversal times (Table 3).

Table 3: Recovery Characteristics

Outcome	Group A (n = 30)	Group B (n = 30)	p-value
Time to extubation (min), mean ± SD	6.1 ± 1.8	5.3 ± 1.5	0.07
Time to follow verbal commands (min), mean ± SD	7.5 ± 2.2	6.7 ± 1.9	0.15

Hemodynamic parameters measured before and after reversal were comparable between the two groups. The mean heart rate prior to reversal was 79.4 ± 9.8 beats per minute in Group A and 77.2 ± 8.9 beats per minute in Group B (p = 0.37), while post-reversal values were 83.6 ± 11.2 and 80.5 ± 10.1 beats per minute, respectively (p = 0.29). Mean arterial pressure before reversal was 93.1 ± 10.7 mmHg in Group A and 91.4 ± 9.9 mmHg in Group B (p = 0.52), and after reversal it was 96.8 ± 12.3 mmHg and 94.6 ± 11.1 mmHg, respectively (p = 0.46).

No statistically significant hemodynamic instability was observed (Table 4).

Table 4: Hemodynamic Parameters around Reversal

Parameter	Group A	Group B	p-value
Heart rate before reversal (bpm), mean ± SD	79.4 ± 9.8	77.2 ± 8.9	0.37
Heart rate after reversal (bpm), mean ± SD	83.6 ± 11.2	80.5 ± 10.1	0.29
Mean arterial pressure before reversal (mmHg), mean ± SD	93.1 ± 10.7	91.4 ± 9.9	0.52
Mean arterial pressure after reversal (mmHg), mean ± SD	96.8 ± 12.3	94.6 ± 11.1	0.46

The incidence of adverse events was low and comparable between the groups.

Bradycardia was observed in 1 (3.3%) patient in each group. Hypotension occurred in 2 (6.7%) patients in Group A and 1 (3.3%) patient in Group B (p = 0.55). Postoperative nausea and vomiting was reported in 4 (13.3%) patients in Group A and 2 (6.7%) patients in Group B (p = 0.39).

No cases of recurarization or hypersensitivity reactions were noted in either group. Overall, both regimens demonstrated a favorable safety profile (Table 5).

Table 5: Adverse Events

Event	Group A (n = 30)	Group B (n = 30)	p-value
Bradycardia	1 (3.3%)	1 (3.3%)	1.00
Hypotension	2 (6.7%)	1 (3.3%)	0.55
Postoperative nausea and vomiting	4 (13.3%)	2 (6.7%)	0.39
Recurarization	0 (0%)	0 (0%)	—
Hypersensitivity reactions	0 (0%)	0 (0%)	—

Discussion

The present study demonstrated that reversal of deep rocuronium-induced neuromuscular blockade was achieved significantly faster with the higher dose regimen, although the lower dose also provided clinically acceptable recovery. The mean time to achieve TOF ≥0.9 was longer in Group A compared to Group B, but the difference remained within an acceptable clinical range.

This finding aligns with earlier pharmacodynamic studies demonstrating a clear dose–response relationship with sugammadex, where increasing doses result in progressively faster recovery times [15]. Standard dosing recommendations also advocate 4 mg/kg for deep blockade (PTC 1–2), which explains the faster reversal observed in Group B [16]. However, despite this expected difference, the recovery times observed with the lower dose in the present study were still within a clinically acceptable window, supporting its potential utility in selected scenarios.

Importantly, the proportion of patients achieving TOF ≥0.9 within 3 minutes and the incidence of residual neuromuscular blockade did not differ significantly between the groups. This suggests that although recovery may be slightly delayed with lower dosing, it does not necessarily translate into clinically meaningful residual paralysis. Similar observations were reported by Mesa et al., who demonstrated that 2 mg/kg sugammadex was sufficient for effective reversal without increasing the risk of recurarization or adverse outcomes [16].

Furthermore, studies evaluating moderate blockade have shown that even lower doses (2 mg/kg) reliably achieve recovery within 2–3 minutes, indicating a substantial safety margin and supporting the feasibility of dose reduction strategies [17]. These findings reinforce the concept that individualized dosing based on intraoperative neuromuscular monitoring may optimize both efficacy and resource utilization.

Recovery characteristics, including time to extubation and response to verbal commands, were comparable between the two groups, despite differences in TOF recovery times. This suggests that minor differences in pharmacological reversal may not significantly impact clinically relevant recovery endpoints. Similar findings have been reported in comparative trials, where variations in dosing did not translate into differences in extubation or recovery profiles once adequate neuromuscular recovery was achieved [18]. This highlights that achieving a TOF ratio ≥0.9 remains the critical determinant of safe extubation, rather than the absolute speed of reversal alone.

The hemodynamic stability and safety profile observed in the present study were consistent with existing literature. Both groups exhibited minimal and comparable adverse events, with no cases of recurarization or hypersensitivity reactions. Previous clinical trials have consistently demonstrated that sugammadex is well tolerated across a wide dosing range, with a low incidence of adverse effects [20].

The absence of significant hemodynamic fluctuations further supports its safety advantage over traditional reversal agents. Collectively, the findings of the present study are in agreement with current evidence, suggesting that while higher doses provide faster reversal, lower doses may offer a clinically effective and safe alternative in appropriately selected patients under quantitative neuromuscular monitoring.

The present study has certain limitations. The sample size was relatively small, which may limit the generalizability of the findings and the power to detect rare adverse events. Being a single-center study the results may not be widely applicable to different clinical settings.

Blinding was not employed, which could introduce observer bias. Additionally, only ASA I–II patients undergoing elective procedures were included, thereby limiting extrapolation to higher-risk populations. Finally, long-term outcomes and cost-effectiveness analysis were not assessed, which could be relevant when considering lower-dose strategies.

Conclusion

The present study demonstrates that sugammadex at a lower dose provides effective reversal of deep rocuronium-induced neuromuscular blockade in prolonged, bolus-only surgical cases, with recovery profiles and safety outcomes comparable to the higher dose regimen. Although the higher dose achieved a faster reversal time, the difference was not clinically significant in terms of extubation and overall recovery. Both dosing strategies were well tolerated, with minimal adverse effects and no evidence of recurarization. These findings suggest that lower-dose sugammadex may be a viable and safe alternative in appropriately monitored patients, offering potential for optimized drug utilization without compromising clinical efficacy.

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