COMPARISON OF SUGAMMADEX WITH NEOSTIGMINE FOR REVERSAL OF VECURONIUM INDUCED NEUROMUSCULAR BLOCKADE: A RANDOMIZED CONTROLLED TRIAL

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KEYWORDS

Neuromuscular Blockade; Residual Neuromuscular Blockade, Train-Of-Four (TOF) Monitoring, Postoperative Complications, Reversal Agents

ABSTRACT

Introduction: Neuromuscular blocking drugs (NMBDs) are commonly used in anesthesia, but residual neuromuscular blockade (RNMB) post-surgery can lead to serious complications such as hypoxia and airway obstruction. Acetylcholinesterase inhibitors like neostigmine have been traditionally used for reversal, though they come with side effects. Sugammadex, a newer agent, offers faster reversal and fewer complications. This study aims to compare the efficacy and safety of sugammadex with neostigmine in reversing vecuronium-induced neuromuscular blockade and assess associated adverse effects.

Methods: A randomized controlled trial was conducted at Shri Guru Ram Rai Institute of Medical and Health Sciences, Dehradun. Sixty patients were enrolled after ethical approval and informed consent. Group A received sugammadex (2 mg/kg), while Group B received neostigmine (0.05 mg/kg). Patients were monitored for reversal time, efficacy, complications, and post-operative recovery. Data were analyzed using statistical methods, including p-values, mean, standard deviation (SD), interquartile range (IQR), and 95% confidence intervals.

Results: In Group A, 93.3% of patients achieved TOF ratio 0.9 in under 10 minutes, compared to 50.0% in Group B. The efficacy of reversal was 93.3% in Group A and 83.3% in Group B. The incidence of post-operative complications was lower in Group A (13.3%) compared to Group B (20.0%). No significant differences were found in ASA classification, age, or surgical duration between the groups. Statistical analysis showed p-values > 0.05 for baseline characteristics, indicating comparability.

Conclusion: Sugammadex is a faster and more effective agent for reversing neuromuscular blockade compared to neostigmine, with a lower incidence of complications. Both drugs showed similar results in hospital stay and ICU admission. Sugammadex is recommended for quicker recovery and fewer adverse effects, enhancing the recovery process in surgical settings.

1. Introduction:

Neuromuscular blocking drugs (NMBDs) are essential in anaesthesia, ensuring smooth surgeries and facilitating tracheal intubation. However, residual neuromuscular blockade (RNMB) after surgery can lead to serious complications like hypoxia, airway obstruction, and increased mortality (1-3). Thus, effective reversal is vital to patient recovery.

Acetylcholinesterase inhibitors like neostigmine have been the standard for reversing NMBDs, but they carry risks such as bradycardia, hypotension, and nausea (4-5). Anticholinergic drugs like glycopyrrolate are often used to counteract these effects, but they also have side effects, including tachycardia and confusion (6).

Sugammadex, a novel drug, offers a promising alternative by rapidly reversing neuromuscular

blockade induced by rocuronium and, to a lesser extent, vecuronium (7-8). Despite its success with rocuronium, limited data exist on its effectiveness with vecuronium (9-11). This study aims to compare sugammadex and neostigmine in reversing vecuronium-induced neuromuscular blockade and assess the potential adverse effects of these treatments. Through this, we aim to determine the optimal pharmacological approach for safer and faster reversal of profound neuromuscular blockade.

2. Material And Methods

This randomized controlled trial was conducted in our institute after obtaining ethical approval from the Institutional Ethics Committee. Sixty adult patients scheduled for elective surgery under general anaesthesia were recruited based on inclusion and exclusion criteria, and written informed consent was obtained.

Monitoring was performed using standard intraoperative parameters, including non-invasive arterial blood pressure (NIBP), electrocardiogram (ECG), pulse oximetry, and end-tidal CO_2 monitoring. Neuromuscular function was assessed through acceleromyography (TOF-Watch SX) at the adductor pollicis muscle, with repetitive train-of-four (TOF) stimulation administered to the ulnar nerve every 15 seconds until complete neuromuscular recovery (TOF ratio ≥0.9) was achieved. Central body temperature was maintained above 35°C, and postoperative monitoring continued in the recovery room for at least 60 minutes, assessing for signs of muscle weakness, hypoxia, airway obstruction, or recurrent neuromuscular blockade.

Patients were randomly assigned to two groups. Group A received sugammadex 2 mg/kg IV, while Group B received neostigmine 0.05 mg/kg IV with glycopyrrolate 10 µg/kg IV. Anesthesia was induced using propofol (1.5–2.0 mg/kg) and fentanyl (2.0 µg/kg) and maintained with sevoflurane (1.5–1.8 vol%) in an air–oxygen mixture. Neuromuscular blockade was achieved with vecuronium (0.1 mg/kg), and maintenance doses (0.02–0.03 mg/kg) were given as required. Reversal agents were administered upon the reappearance of the second twitch (T2) in the TOF response.

Patients were assessed postoperatively for awareness, muscle strength (5-second head-lift test), cough reflex, and any residual neuromuscular blockade every 15 minutes until full recovery. The primary outcome was the time to achieve a TOF ratio ≥0.9, while secondary outcomes included incomplete reversal, recurrent neuromuscular blockade, postoperative respiratory complications, and adverse effects such as bradycardia, nausea, or muscle weakness.

Statistical analysis was performed using SPSS software, with continuous variables compared using the Student's t-test or Mann-Whitney U test and categorical data analyzed via the chi-square test. A p-value < 0.05 was considered statistically significant.

3. Results

Table 1: Socio-demographic characteristics of study participants in Group A (Sugammadex) and Group B (Neostigmine)

	Socio-demographic Characteristics	Group A (Sugammadex)	Group B (Neostigmine)
Age Group	**18-39**	14 (46.7%)	9 (30.0%)
	40-59	14 (46.6%)	18 (60.0%)
	≥ 60	2 (6.7%)	3 (10.0%)
Gender	**Male**	20 (66.7%)	14 (46.7%)
	Female	10 (33.3%)	16 (53.3%)
BMI Category	**Normal**	2 (6.7%)	1 (3.3%)
	Over-weight	1 (3.3%)	2 (6.7%)
	Obese	27 (90.0%)	27 (90.0%)
ASA Class I	**ASA Class I**	7 (23.3%)	6 (20.0%)
	ASA Class II	18 (60.0%)	21 (70.0%)
	ASA Class III	5 (16.7%)	3 (10.0%)

Duration of Surgery	**< 1 hr**	10 (33.3%)	9 (30.0%)
	1-2 hr	15 (50.0%)	14 (46.7%)
	> 2 hr	5 (16.7%)	7 (23.3%)
Vecuronium Dose	**Low**	8 (26.7%)	10 (33.3%)
	Medium	12 (40.0%)	11 (36.7%)
	High	10 (33.3%)	9 (30.0%)

The socio-demographic characteristics of the study participants showed a balanced distribution between the two groups. Group A (Sugammadex) had a higher proportion of male participants (66.7%), while Group B (Neostigmine) had more females (53.3%). Both groups predominantly comprised individuals in the age group of 40-59 years, with similar distributions in BMI and ASA classifications. The duration of surgery was also comparable between the two groups, with most surgeries lasting 1-2 hours, as shown in Table 1.

Table 2: Comparison of Reversal Time, Efficacy, Complications, and Postoperative Outcomes Between Group A (Sugammadex) and Group B (Neostigmine)

	Study Variables	Group A (Sugammadex)	Group B (Neostigmine)
Time taken to reversal	**< 10 min**	20 (66.7%)	7 (23.3%)
	10-20 min	8 (26.7%)	15 (50.0%)
	> 20 min	2 (6.6%)	8 (26.7%)
Efficacy of Reversal Successful	**Yes**	28 (93.3%)	25 (83.3%)
	No	2 (6.7%)	5 (16.7%)
Complication Associated	**Yes**	4 (13.3%)	6 (20.0%)
	No	26 (86.7%)	24 (80.0%)
Time to complication	**< 1 hr**	2 (50.0%)	3 (50.0%)
	1-2 hr	1 (25.0%)	2 (33.3%)
	> 2 hr	1 (25.0%)	1 (16.7%)
Severity of Complication	**Mild**	2 (50.0%)	3 (50.0%)
	Moderate	1 (25.0%)	2 (33.3%)
	Severe	1 (25.0%)	1 (16.7%)
Duration of Hospital Stay	**< 1 day**	20 (66.7%)	19 (63.3%)
	1-3 days	7 (23.3%)	8 (26.7%)
	> 3 days	3 (10.0%)	3 (10.0%)
Need for ICU Admission	**Yes**	2 (6.7%)	3 (10.0%)
	No	28 (93.3%)	27 (90.0%)

Group A (Sugammadex) achieved faster reversal times, with 66.7% of patients reaching the target TOF ratio in less than 10 minutes, compared to only 23.3% in Group B (Neostigmine), as shown in Table 2. Additionally, Group A had a higher rate of successful reversal (93.3%) compared to Group B (83.3%). While the incidence of complications was lower in Group A (13.3%), both groups had similar hospital stay durations and ICU admission rates, indicating comparable post-operative recovery.

Table 3: Comparison of Postoperative Recovery and Adverse Effects Between Group A (Sugammadex) and Group B (Neostigmine)

	Study Variables	Group A (Sugammadex)	Group B (Neostigmine)
Time taken from Injection to TOF ratio	**< 10 min**	28 (93.3%)	15 (50.0%)
	0-20 min	2 (6.7%)	12 (40.0%)
	> 20 min	0 (0.0%)	3 (10.0%)
Incidence of Incomplete Reversal within 30 mins	**Yes**	2 (6.7%)	5 (16.7%)
	No	28 (93.3%)	25 (83.3%)
Incidence of Post-op Recurrent Neuromuscular	**Yes**	3 (10.0%)	5 (16.7%)

Block			
	No	27 (90.0%)	25 (83.3%)
Muscle Weakness	**Yes**	3 (10.0%)	5 (16.7%)
	No	27 (90.0%)	25 (83.3%)
Force of Coughing	**Yes**	2 (6.7%)	4 (13.3%)
	No	28 (93.3%)	26 (86.7%)
Ease of Swallowing	**Yes**	4 (13.3%)	6 (20.0%)
	No	26 (86.7%)	24 (80.0%)
Critical Respiratory Events	**Yes**	2 (6.7%)	4 (13.3%)
	No	28 (93.3%)	26 (86.7%)
Critical Circulatory Events	**Yes**	2 (6.7%)	3 (10.0%)
	No	28 (93.3%)	27 (90.0%)

As shown in Table 3, Group A (Sugammadex) demonstrated significantly faster reversal times, with 93.3% of patients achieving the desired TOF ratio in less than 10 minutes, compared to 50.0% in Group B (Neostigmine). Additionally, Group A had a lower incidence of incomplete reversal (6.7%) and post-operative recurrent neuromuscular block (10.0%). Adverse effects such as muscle weakness, coughing, and difficulty swallowing were less frequent in Group A, indicating that sugammadex may offer a safer and more efficient reversal option compared to neostigmine.

4. Discussion

The study aimed to compare the efficacy and safety of sugammadex and neostigmine in reversing neuromuscular blockade, specifically in terms of time to reversal, incidence of complications, and post-operative outcomes. Group A, which received sugammadex, exhibited significantly faster reversal times compared to Group B, which received neostigmine. Notably, 93.3% of patients in Group A achieved the target TOF ratio in under 10 minutes, while only 50.0% in Group B reached this goal. Additionally, 93.3% of Group A had successful reversal, compared to 83.3% in Group B. The incidence of post-operative complications was also lower in Group A (13.3%) compared to Group B (20.0%).

The ASA classification showed a similar distribution of patients in both groups, with the majority in ASA Class II, and there were no significant differences in age, weight, BMI, or surgical duration. Vecuronium doses varied between the groups, but both groups had a comparable distribution of patients. These findings suggest that the two groups were demographically balanced, ensuring comparability for further analysis.

Previous studies have reported similar demographic patterns. No HJ et al. (12) found that patients before and after applying inverse probability of treatment weighting (IPTW) had comparable distributions in terms of age, sex, BMI, and comorbidities such as diabetes and hypertension. However, after applying IPTW, some variables like ASA class showed residual imbalances, highlighting the importance of weight adjustments in observational studies.

He J et al.(13) also explored the baseline characteristics of patients treated with sugammadex and neostigmine, finding no significant differences between the groups in terms of sex, age, BMI, ASA classification, or vecuronium dose. Their findings align with this study, where no statistically significant differences were noted in the baseline characteristics of the two groups.

In terms of post-operative recovery, Group A exhibited fewer cases of incomplete reversal (6.7%) compared to Group B (16.7%), and the incidence of post-op recurrent neuromuscular block was also lower in Group A (10.0%) than in Group B (16.7%). This is consistent with findings from He J et al.(12) where sugammadex was found to have a faster and more effective reversal compared to neostigmine.

Regarding adverse effects, Group A experienced a lower incidence of complications such as muscle

weakness, coughing, and difficulty swallowing, compared to Group B. These findings support the safety advantage of sugammadex over neostigmine in terms of post-operative recovery and complication rates. Interestingly, Hristovska AM et al.(14) observed that sugammadex had a lower risk of desaturation and postoperative nausea and vomiting (PONV) compared to neostigmine. The study also found that sugammadex was associated with fewer instances of bradycardia, suggesting a more favorable safety profile.

5. Strengths

One of the key strengths of this study is its well-balanced design, with equal sample sizes in both groups, ensuring reliable comparisons. The use of comprehensive data points such as time to reversal, incidence of complications, and ASA classification enhances the depth of the analysis. Additionally, the study design's attention to baseline comparability between the two groups allows for a more robust examination of the drugs' effects. The inclusion of a detailed assessment of post-operative outcomes, including complications and recovery, contributes significantly to its clinical relevance.

6. Limitations

One limitation of the study is its relatively small sample size, which may limit the generalizability of the results to larger populations. Additionally, the study did not include long-term follow-up to assess any delayed complications or effects of the drugs over time. Another limitation is the lack of a placebo group, which could have provided a clearer comparison of the two treatments in the absence of any intervention. Further research with a larger sample and placebo-controlled trials is needed to confirm these findings and enhance their applicability.

7. Conclusion

This study demonstrated that sugammadex is a faster and more effective agent for reversing neuromuscular blockade compared to neostigmine. The findings highlighted sugammadex's superiority in terms of time to reversal and a lower incidence of post-operative complications, such as muscle weakness and coughing. However, both drugs showed comparable results regarding hospital stay and ICU admission, suggesting similar clinical outcomes. This study supports sugammadex as a preferred alternative for neuromuscular blockade reversal, offering advantages in speed and safety, enhancing recovery in surgical settings.

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