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Original Research Article

Correlation of Kidney Function with the Efficacy of Sugammadex in Reversing Neuromuscular Blockade

Vikram Nath[1], Amrit Kumar[2], Rahul Kumar[3]

[1]Senior Resident, Department of Anaesthesia, Sri Krishna Medical College, Muzaffarpur, Bihar
[2]Senior Resident, Department of Anaesthesia, Sri Krishna Medical College, Muzaffarpur, Bihar
[3]Associate Professor, Department of Anaesthesia, Sri Krishna Medical College, Muzaffarpur, Bihar

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Corresponding Author: Dr. Amrit Kumar
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Abstract:

Background: Residual neuromuscular blockade after surgery can lead to postoperative complications. Sugammadex, a selective relaxant binding agent, rapidly reverses aminosteroidal neuromuscular blockade, but its efficacy may be influenced by kidney function, given its renal excretion. Understanding this relationship is important for safe perioperative management.

Aim: To evaluate the association between kidney function and the efficacy of sugammadex in reversing neuromuscular blockade, as measured by train-of-four (TOF) ratio recovery.

Methods: A prospective observational study was conducted on 100 adult patients undergoing elective surgery under general anesthesia with rocuronium or vecuronium-induced neuromuscular blockade. Patients were categorized into normal (eGFR ≥90 mL/min/1.73 m², n=70) and impaired kidney function groups (eGFR <60 mL/min/1.73 m², n=30). Sugammadex was administered according to standard dosing, and TOF ratio was monitored to assess recovery. Data were analyzed using SPSS version 23.0, with $p<0.05$ considered statistically significant.

Results: Patients with impaired kidney function had significantly longer recovery times to TOF ≥0.9 (5.6 ± 1.4 minutes) compared to those with normal renal function (2.8 ± 0.9 minutes, $p<0.001$). Only 60% of patients with impaired function achieved complete reversal within 5 minutes versus 97.1% of normal patients. A strong negative correlation was observed between eGFR and recovery time ($r = -0.72$, $p<0.001$). Sugammadex was well-tolerated, with minor adverse events reported in 6% of patients and no significant difference between groups.

Conclusion: Sugammadex effectively reverses neuromuscular blockade in patients with normal kidney function; however, its efficacy is reduced in those with impaired renal function, resulting in delayed recovery. Preoperative kidney assessment is essential to anticipate slower reversal.

Recommendations: Clinicians should monitor neuromuscular recovery closely in patients with renal impairment and consider individualized dosing or extended observation to ensure safe reversal of neuromuscular blockade. Further studies are recommended to optimize sugammadex dosing strategies in severe renal dysfunction.

Keywords: Sugammadex, Kidney Function, Neuromuscular Blockade, Train-of-Four, Renal Impairment.

Introduction

Neuromuscular blocking agents (NMBAs) are integral to modern anesthesia practice, facilitating endotracheal intubation, optimal surgical conditions, and controlled ventilation [1]. Non-depolarizing NMBAs such as rocuronium and vecuronium are commonly used; however, residual neuromuscular blockade after surgery can result in significant complications including hypoventilation, airway obstruction, and postoperative pulmonary complications [2]. Therefore, timely and effective reversal of neuromuscular blockade is crucial to ensure patient safety and reduce postoperative morbidity.

Traditionally, acetylcholinesterase inhibitors, such as neostigmine, were used for reversal. These agents increase acetylcholine levels at the neuromuscular junction, thereby competing with NMBAs to restore muscle function [3]. However, acetylcholinesterase inhibitors have several limitations, including a ceiling effect, variable efficacy in deep blockade, and potential cholinergic side effects such as bradycardia, bronchospasm, and nausea [4]. Sugammadex, a modified γ-cyclodextrin, represents a novel approach by directly encapsulating aminosteroidal NMBAs, primarily rocuronium and vecuronium, allowing rapid and predictable reversal even from deep blockade [5].

Pharmacokinetically, sugammadex is largely eliminated via the kidneys, and its clearance is significantly reduced in patients with impaired renal function [6]. Studies have demonstrated that while sugammadex is generally safe in patients with mild to moderate renal impairment, recovery times may be prolonged, and the drug's efficacy may be affected in severe renal dysfunction [7,8]. Considering the increasing prevalence of chronic kidney disease in surgical populations, understanding the impact of renal function on sugammadex efficacy is clinically relevant [9].

Quantitative neuromuscular monitoring, such as (TOF) ratio assessment, provides an objective method to evaluate residual blockade and monitor recovery [10]. Several recent studies have highlighted that renal impairment may delay recovery as measured by TOF ratio, even when standard doses of sugammadex are administered [6,8]. This underscores the importance of individualized perioperative planning, careful dosing, and close monitoring in patients with compromised kidney function.

Despite the growing body of evidence, data on the relationship between kidney function and sugammadex efficacy remain limited, particularly in diverse surgical populations and in real-world clinical settings. This study aims to evaluate the association between kidney function, measured by estimated glomerular filtration rate (eGFR), and the time to neuromuscular recovery following sugammadex administration, providing insights into safe and effective perioperative management in patients with varying degrees of renal function.

Methodology

Study Design: This study was designed as a prospective observational study.

Study Setting: The study was carried out in the operating rooms and post-anesthesia care units (PACU), where neuromuscular blockade and its reversal could be monitored under standardized conditions.

Participants: A total of 100 adult patients scheduled for elective surgeries under general anesthesia requiring neuromuscular blockade were enrolled in the study. Patients were selected consecutively based on eligibility criteria to ensure adequate representation of different levels of kidney function.

Inclusion Criteria

Participants were included if they met the following criteria:

- Adults aged 18–75 years.
- Scheduled for elective surgery under general anesthesia with planned use of non-depolarizing neuromuscular blocking agents.
- Provided written informed consent.
- Preoperative assessment including serum creatinine and estimated glomerular filtration rate (eGFR) was available.

Exclusion Criteria

Participants were excluded if they met any of the following criteria:

- History of neuromuscular disorders (e.g., myasthenia gravis).
- Known hypersensitivity to sugammadex or rocuronium/vecuronium.
- Severe hepatic impairment.
- Pregnancy or lactation.
- Emergency surgeries or conditions affecting neuromuscular monitoring accuracy.

Bias: Potential sources of bias were addressed through standardization of anesthesia protocols, neuromuscular monitoring, and timing of sugammadex administration. Observer bias was minimized by using objective (TOF) measurements. Selection bias was limited by enrolling consecutive eligible patients, and data analysis was performed by a statistician blinded to the patients' renal function categories.

Data Collection: Data collected included demographic variables (age, sex, weight), preoperative kidney function (serum creatinine, eGFR), type and dose of neuromuscular blocking agent, dose of sugammadex, and TOF ratio at recovery. All measurements were recorded on standardized case report forms by trained staff.

Procedure: After induction of anesthesia, patients received a non-depolarizing neuromuscular blocking agent (rocuronium or vecuronium). Neuromuscular function was monitored using a TOF monitor at the adductor pollicis. At the end of surgery, sugammadex was administered at recommended doses according to the degree of neuromuscular blockade. Recovery was defined as a TOF ratio ≥ 0.9, and the time to recovery was recorded. Kidney function was assessed preoperatively, and patients were categorized into normal or impaired renal function groups for analysis.

Statistical Analysis: Data were analyzed using SPSS version 23.0. Continuous variables were expressed as mean ± standard deviation (SD) or median (interquartile range) depending on normality. Categorical variables were presented as frequencies and percentages. Comparisons between groups were performed using independent t-tests or Mann-Whitney U tests for continuous variables and Chi-square or Fisher's exact tests for categorical

variables. Correlation between kidney function and time to recovery was assessed using Pearson or Spearman correlation coefficients. A p-value <0.05 was considered statistically significant.

Results

A total of 100 patients were enrolled in the study. The mean age was 52.3 ± 12.1 years, with 58 males (58%) and 42 females (42%). Based on preoperative kidney function, 70 patients had normal renal function (eGFR ≥90 mL/min/1.73 m²), while 30 patients had impaired renal function (eGFR <60 mL/min/1.73 m²). Baseline characteristics, including age, sex, weight, and comorbidities, were comparable between the groups.

Table 1: Baseline Demographics of Participants

Variable	Normal Kidney Function (n=70)	Impaired Kidney Function (n=30)	p-value
Age (years, mean ± SD)	50.8 ± 11.9	55.6 ± 12.3	0.08
Male, n (%)	40 (57.1%)	18 (60%)	0.78
Female, n (%)	30 (42.9%)	12 (40%)	0.78
Weight (kg, mean ± SD)	70.4 ± 10.2	72.1 ± 11.5	0.42
Hypertension, n (%)	22 (31.4%)	12 (40%)	0.37
Diabetes Mellitus, n (%)	18 (25.7%)	10 (33.3%)	0.42

The two groups were statistically similar in terms of age, sex distribution, weight, and common comorbidities (p>0.05), suggesting a balanced comparison.

Sugammadex Dose and Neuromuscular Recovery: All patients received sugammadex at a dose of 2 mg/kg for moderate blockade and 4 mg/kg for deep blockade. The mean time to TOF ratio ≥0.9 differed between the groups:

- **Normal renal function:** 2.8 ± 0.9 minutes
- **Impaired renal function:** 5.6 ± 1.4 minutes

Table 2: Sugammadex Efficacy Based on Renal Function

Parameter	Normal Kidney Function (n=70)	Impaired Kidney Function (n=30)	p-value
Dose of Sugammadex (mg/kg)	2.9 ± 0.6	3.0 ± 0.7	0.48
Time to TOF ≥0.9 (minutes)	2.8 ± 0.9	5.6 ± 1.4	<0.001
Complete Reversal at 5 min, n (%)	68 (97.1%)	18 (60%)	<0.001

Patients with impaired renal function took significantly longer to achieve full neuromuscular recovery compared to patients with normal kidney function. While the dose of sugammadex was similar between groups, the efficacy was reduced in the impaired group (p<0.001).

Correlation Between eGFR and Recovery Time: A negative correlation was observed between eGFR and time to TOF ≥0.9 (r = -0.72, p<0.001), indicating that lower kidney function was associated with slower neuromuscular recovery.

Table 3: Correlation of Kidney Function with Recovery Time

Parameter	Correlation Coefficient (r)	p-value
eGFR vs TOF ≥0.9 (min)	-0.72	<0.001

The strong negative correlation confirms that renal impairment significantly delays sugammadex-mediated reversal of neuromuscular blockade.

Adverse Events: Minor adverse events were observed in 6 patients (6%), including transient hypotension (n=3) and mild nausea (n=3). There was no significant difference in adverse events between normal and impaired kidney function groups (p=0.83).

Table 4: Adverse Events

Adverse Event	Normal Kidney Function (n=70)	Impaired Kidney Function (n=30)	p-value
Hypotension	2	1	0.88
Nausea	2	1	0.88
Total, n (%)	4 (5.7%)	2 (6.7%)	0.83

Sugammadex was well-tolerated across all participants, with low incidence of minor adverse effects and no serious complications.

Summary

- Patients with impaired renal function required longer recovery times despite similar sugammadex doses.
- There was a significant negative correlation between eGFR and time to neuromuscular recovery.
- Sugammadex was generally safe with low and comparable rates of minor adverse events across groups.

Discussion

In this study of 100 patients undergoing elective surgery with neuromuscular blockade, participants were divided into normal (n=70) and impaired (n=30) kidney function groups. Baseline characteristics, including age, sex, weight, and comorbidities, were similar between the groups, ensuring a balanced comparison.

The efficacy of sugammadex differed significantly based on renal function. Patients with normal kidney function achieved a TOF ratio ≥0.9 in an average of 2.8 ± 0.9 minutes, whereas those with impaired renal function required 5.6 ± 1.4 minutes. Despite receiving similar doses of sugammadex, only 60% of patients with impaired kidney function reached complete reversal within 5 minutes, compared to 97.1% of patients with normal function. This demonstrates that reduced kidney function can delay neuromuscular recovery, likely due to slower drug clearance and altered pharmacokinetics.

A strong negative correlation ($r = -0.72$, $p<0.001$) was observed between eGFR and time to TOF ≥0.9, indicating that lower kidney function is closely associated with delayed reversal of neuromuscular blockade. Sugammadex was well-tolerated overall, with only minor adverse events such as transient hypotension and mild nausea reported in 6% of patients, with no significant difference between groups, confirming the safety of the drug even in patients with renal impairment.

These findings highlight the importance of considering renal function in anesthesia management, as impaired kidney function can significantly prolong the time to neuromuscular recovery despite standard sugammadex dosing. Preoperative assessment of kidney function can help clinicians anticipate delayed reversal and optimize patient monitoring in the perioperative period.

Recent evidence has explored the correlation between kidney function and the efficacy and safety of sugammadex in reversing neuromuscular blockade. Several clinical studies demonstrate that sugammadex maintains efficacy in patients with mild to moderate (CKD), but its clearance is significantly reduced, raising safety concerns in severe impairment. De Souza et al. confirmed that sugammadex effectively reversed neuromuscular block in CKD patients, but impaired renal clearance necessitated caution in patients with advanced disease [9].

Case reports and series focusing on dialysis patients also indicate successful reversal, but because sugammadex is almost exclusively renally excreted, drug accumulation and delayed clearance were observed, suggesting that its use in this group should remain contraindicated [10]. Population pharmacokinetic analyses by Miller et al. further supported these findings, showing that plasma concentrations and half-life of sugammadex are significantly prolonged in severe renal impairment [11].

Comparative reviews concluded that sugammadex is generally safe for use in patients with normal and mild renal impairment but should be avoided in severe CKD and end-stage renal disease due to risk of recurrence of neuromuscular block [12]. A prospective observational study highlighted that while reversal was still effective in moderate renal dysfunction, monitoring and extended postoperative vigilance were essential to avoid complications [13].

Additionally, a systematic review on perioperative outcomes reaffirmed the efficacy of sugammadex in patients with reduced renal function but emphasized insufficient safety data in dialysis populations [14]. Finally, experimental pharmacology work demonstrated that sugammadex concentration remains elevated in renal failure for more than 24 hours, directly correlating with reduced creatinine clearance [15]. In summary, sugammadex reliably reverses neuromuscular blockade across kidney function groups, but delayed clearance in severe CKD and dialysis patients raises safety concerns, making its use contraindicated in advanced renal failure.

Conclusion

Sugammadex effectively reverses neuromuscular blockade in patients with normal kidney function, but its efficacy is reduced in those with impaired renal function, resulting in delayed recovery. Preoperative assessment of kidney function is important to anticipate slower reversal, while the drug remains safe with minimal adverse effects.

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