Section: Anaesthesiology

Original Research Article

COMPARISON OF AUGMENTATION OF CISATRACURIUM NEUROMUSCULAR BLOCKING EFFECT WITH SEVOFLURANE VS DESFLURANE UNDER GENERAL ANAESTHESIA – A PROSPECTIVE, CONTROLLED, RANDOMISED DOUBLE-BLINDED STUDY

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ABSTRACT

Background: NDMR administration serves as the primary therapy for facilitating endotracheal intubation and an adjuvant therapy for the perioperative maintenance of anaesthesia. Cisatracurium besylate is an intermediate-acting NMB and is three times the potency of atracurium. The inhalational anaesthetics sevoflurane and desflurane both have low blood-gas solubility, resulting in rapid uptake and rapid elimination, allowing faster recovery and making both suitable for daycare surgery. The study aims to evaluate the enhancement of cisatracurium neuromuscular blockade by potent inhalational anaesthetic agents by plotting a dose-response curve for cisatracurium during anaesthesia. **Materials and Methods:** Seventy-five patients of both genders, aged between 18 and 60 years, posted for surgery under general anaesthesia in general surgery and orthopaedics, were selected for the study. Patients are randomly divided into three groups of 25 each. Group S received Cis-atracurium 0.15-2mg/kg plus 1.5 MAC sevoflurane, Group D received Cis-atracurium 0.15-2mg/kg plus 1.5 MAC desflurane, and Group C received Cis-atracurium 0.15-2mg/kg. The primary outcome was to determine the depression of T1/T0 twitch after three cumulative doses of cisatracurium 15microgram/kg during desflurane and sevoflurane, and the secondary outcomes were to determine the interaction of desflurane and sevoflurane on the dose-response curves and pharmacodynamic profile of cisatracurium, duration 25% (referred to the time after injecting the last dose till 25% of T1 recovery), recovery index (which is the time to T1 twitch recovery from 25% to 75%), and interval T1 (time from 25% recovery to a TOF of 0.7). **Result:** Patients receiving sevoflurane and desflurane achieved 95% T1 twitch depression with fewer incremental doses of cisatracurium than the control group. Both volatile anaesthetics produced significantly greater T1 twitch depression at cumulative doses of 15, 30, and 45 µg/kg compared with the control group ($P < 0.001$). The cumulative dose–response curves demonstrated a leftward shift, with significantly lower ED50 (17.45 and 17.28 vs 27.35 µg/kg) and ED95 (39.71 and 39.71 vs 53.05 µg/kg) values in the sevoflurane and desflurane groups, respectively ($P < 0.05$). Recovery from neuromuscular blockade was significantly prolonged in both volatile anaesthetic groups, with delayed recovery of T1 twitch and TOF ratio compared with the control group ($P < 0.05$). No significant difference was observed between the sevoflurane and desflurane groups. **Conclusion:** The neuromuscular blocking effect of cisatracurium was augmented when administered with inhalational agents such as sevoflurane and desflurane, to a similar extent.

INTRODUCTION

General anaesthesia requires endotracheal intubation, which is essential for an anesthesiologist to provide acceptable intubating conditions, with optimal depth of anaesthesia and muscle paralysis, to avoid airway injuries. The neuromuscular junction (NMJ) is an extensively studied model of neural function.[1]

Neuromuscular blocking agents (NMBAs), also called muscle relaxants, have been in use for almost 75 years. NMBAs can also be classified by their mode of action into depolarising NMBAs (e.g., SCh) and Nondepolarizing NMBAs. NDMR can be classified according to their chemical structure (benzylisoquinolinium or steroidal) or their duration of action (short-, intermediate-, or long-duration). NDMR administration serves as the primary therapy for facilitating endotracheal intubation and as an adjuvant therapy for the perioperative maintenance of anaesthesia and the care of critically ill patients. Among them, cisatracurium besylate is an intermediate-acting NMB. It has a benzyl-iso-quinolinium structure.[2,3] The neuromuscular blocking action of cisatracurium is three times that of atracurium. Different inhalational anaesthetic agents enhance NMB produced by NDMR to a varying degree. The augmentation of neuromuscular blocking effect during sevoflurane or desflurane administration and the reduction of this effect on withdrawal of the short-acting inhalation agent reduce the NMB dose in the perioperative period and eliminate the risk of postoperative residual curarisation. The inhalational anaesthetics sevoflurane and desflurane both have low blood-gas solubility, resulting in rapid uptake and rapid elimination. Their physicochemical properties allow faster recovery and make both suitable for daycare surgery. Qualitative evaluation of neuromuscular monitoring employs a peripheral nerve stimulator to assess the visual or tactile response of the stimulated muscle.[4] Train-of-four (TOF) stimulation was introduced clinically in 1971 and consists of four sequential ST stimuli (T1, T2, T3, and T4) delivered at 2 Hz, with 15 to 20 seconds between stimuli to avoid facilitation of subsequent muscle responses.[5,6] In the presence of NMBs, repeated stimuli cause a diminished release of acetylcholine at the NMJ, leading to decreased muscle contraction amplitude. This study aimed to evaluate the enhancement of cisatracurium neuromuscular blockade by potent inhalational anaesthetic agents by plotting a dose-response curve for cisatracurium during anaesthesia with either 1.5 MAC desflurane or sevoflurane. The primary objective was to determine the depression of T1/T0 twitch after three cumulative doses of cisatracurium (15 microgram/kg) during desflurane and sevoflurane. The secondary objectives were to determine the interaction of desflurane and sevoflurane on the dose-response curves and pharmacodynamic profile of cisatracurium, to measure the duration 25% (which is the time after injection of the last dose till 25% recovery of T1 twitch), recovery index (which is the time to recovery of T1 twitch from 25% to 75%) and interval T1 (from 25% to TOF ratio 0.7).

MATERIALS AND METHODS

After institutional ethics committee approval and written informed consent from patients, 100 patients of both genders, aged between 18 and 60 years, and American Society of Anaesthesiologists class I or II, posted for surgery under general anaesthesia, were selected for the study. The study process is explained to them in their own language, and written informed consent is obtained. Patients were randomly divided into three groups of 25 each. A master list of the drug assigned to each patient was kept in a secure location by a third party not directly connected to the study. This was revealed only to the person administering the drug outside the operating theatre at the time of the study. Only at the end of the study was the list released to the investigator for analysis of the study results. Group C received Cis-atracurium 0.15-2mg/kg, Group S received Cis-atracurium 0.15-2mg/kg plus 1.5 MAC sevoflurane, and Group D received Cis-atracurium 0.15-2mg/kg plus 1.5 MAC desflurane. Patients aged <18 or>60 years, American Society of Anaesthesiology physical status III & IV, renal/hepatic disease, and a history of neuromuscular disease/diabetes were excluded from the study. In this study, patients do not know which group they are assigned to, and the observer who records the data does not know the patients' groups.

All patients were thoroughly evaluated in a pre-anaesthetic checkup, and all relevant investigations were done. On the day of surgery, after securing the IV cannula, the ASA monitors were connected, and all the patients were premedicated with Inj. Midazolam (0.05-0.1mg/kg), Inj. Glycopyrrolate (0.01mg/kg), Inj. Ondansetron (0.1mg/kg), Inj. Fentanyl (1-2mμ/kg). Preoxygenation was done for 3 minutes prior to induction. Induction of general anaesthesia was achieved with Propofol 2-2.5mg/kg IV. After administration of cisatracurium 0.15 - 0.2mg/kg IV in graded increments till ED95 is achieved, assessed by the neuromuscular monitor, patients are intubated with an appropriate-size cuffed endotracheal tube. All the groups received 70% N2O and 30% O2. Inhalational anaesthetics sevoflurane/desflurane were started at 2.5-3.0 MAC, and the concentration was decreased to 1.5 MAC over the next few minutes in the sevoflurane and desflurane groups. The third group did not receive any inhalational anaesthetics and was therefore maintained with propofol at 100 μg/kg/min. End-tidal Pco2 was adjusted to be between 32 and 36 mmHg. Body and skin temperatures above the monitored muscle were maintained at 35-36 °C, respectively, by passive warming. The NIBP cuff was placed on the arm opposite to the site of the neuromuscular monitor. Light anaesthesia or moderate hypertension was treated initially with Inj. Fentanyl 100 microgram IV and, if necessary, 20% increments of end-tidal concentration of inhalational anaesthetic or propofol infusion rate were given. Hypotension was treated initially with fluid infusion and then by decreasing the end-tidal concentration of the inhalational anaesthetic or the propofol infusion rate by 20%. The left arm was primarily used for neuromuscular monitoring and was fixed to the arm board. Neuromuscular monitoring was performed

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using TOF stimulation of the ulnar nerve with surface electrodes placed at the wrist, delivering supramaximal square-wave impulses at 2Hz every 12 seconds for 200 seconds. Cisatracurium was given when steady-state conditions were reached, and there was equilibrium between the inspiratory and desired end-tidal concentrations of inhalation anaesthetics. Cumulative increments of Cisatracurium 15mcg/kg were administered until the depression of the first twitch of 95% was achieved. The subsequent doses were given 4 minutes later, and only if there were three consecutive twitches of identical amplitude.

Along with the depression of the T1 twitch, the following parameters of the NMB will be obtained:

1. Duration 25% (which is the time from injecting the last dose till 25% recovery of T1 twitch)
2. Recovery index (which is the time to T1 recovery from 25% to 75%)
3. Interval T1 (which is the 25% to TOF of 0.7).
4. TOF 0.7 – The time required for the return of TOF to 0.7
5. Cumulative dose-response curve - They were obtained by nonlinear regression in all three groups, showing the ED50, ED95, ED95/ED50 ratio, and the slope of regression in graphs.
6. Hemodynamic parameters - like Heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean arterial pressure (MAP) at baseline, 5mins, 15mins, 30mins, 45mins, 60mins, 90mins, and 120mins.
7. Depression of the T1 twitch - The 95% depression of T1 twitch with the incremental doses of cisatracurium of 15, 30, 45, and 60µg/kg was studied in sevoflurane, desflurane, and the control groups.
8. Duration of the hospital stay

Based on the previous study by Wulf et al. in adults during TIVA, reported recovery indices (25–75% recovery of T1/ T0) of 17 (SD 5), 17 (SEM 1) or 12.6 (SEM 0.6) min after a single dose of cisatracurium 100µg/kg, while recovery to a TOF of 0.7 was 66.7 (SEM 4.9) min. A 20% difference in potency or recovery time is considered clinically relevant, with 80% power and a 5% significance level. With the EPI INFO software, the sample size was determined as 22 per group. In addition to the dropouts or exclusions from the study, a total of 25 patients per group were included.

n = 25 / group

Total = 25 * 3 = 75

Formula: $n = (Z\alpha + Z\beta)2\ 2SD2 / MD2$

SD – Pooled standard deviation

MD – Mean difference

Statistical analysis was performed using Microsoft Excel and IBM SPSS Statistics software (version 28.0; IBM Corp., Armonk, NY, USA). Qualitative variables were expressed as frequencies and percentages, while quantitative variables were expressed as mean ± standard deviation (SD). The Chi-square test was used to assess the statistical significance of differences in categorical variables between the study groups, including gender, American Society of Anesthesiologists (ASA) physical status, diagnosis, comorbidities, and type of surgery. Quantitative variables such as age, weight, duration of surgery, duration of hospital stay, and perioperative haemodynamic parameters, including systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR), were analysed using one-way analysis of variance (ANOVA) to determine statistical significance between groups.

Individual dose–response curves were generated by plotting the logarithm of the administered dose against the logit transformation of T1 twitch depression relative to baseline. The curves were constructed using a nonlinear regression model to describe the relationship between dose and response based on the pharmacological dose–response equation. The regression curve was expressed as: $y = mx + b$

x = explanatory variable (log dose)

y = dependent variable (logit transformation of T1 twitch depression)

m = slope of the regression curve

b = intercept of the regression curve

The median effective dose (ED50) and slope of the regression curve were estimated as regression parameters. The ED95, defined as the dose producing the desired effect in 95% of patients, was calculated from the regression curve. The 95% confidence intervals (CI) were calculated for ED50, ED95, the ED95/ED50 ratio, and the slope of the regression curve. A p-value <0.05 was considered statistically significant.

RESULTS

Of the 75 screened patients, all those who met the inclusion criteria were randomly allocated to the three groups. The Consolidated Standards of Reporting Trials (CONSORT) flowchart is shown in Figure 1. Both groups were similar in terms of demographics and ASA classification ($P > 0.05$) [Table 1]. All 75 recruited patients completed the study.

Administration of cisatracurium resulted in varying degrees of T1 twitch depression among all three groups. The sevoflurane and desflurane groups achieved 95% T1 depression with fewer incremental doses compared with the control group [Table 2]. A significantly greater neuromuscular blocking effect was observed in the volatile anaesthetic groups compared with the control group at cumulative cisatracurium doses of 15, 30, and 45 µg/kg ($P < 0.001$) [Figure 2].

The cumulative dose–response curves demonstrated enhanced sensitivity to cisatracurium with sevoflurane and desflurane anaesthesia [Table 3]. The narrow 95% confidence intervals indicated limited inter-individual variability. ED50, ED95, ED95/ED50 ratio, and regression slope were derived from the dose–response curves. ED50 and ED95

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were significantly lower in the sevoflurane and desflurane groups than in the control group ($P < 0.05$) [Table 4]. The ED95/ED50 ratio and regression slope also showed significant differences among groups ($P < 0.001$).

Recovery parameters showed significant differences among the groups, with altered recovery profiles following exposure to volatile anaesthetic. The time to achieve T1 and TOF recovery differed significantly between groups ($P < 0.05$) [Table 5].

Haemodynamic parameters, including heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure, were recorded at baseline and at 5, 15, 30, 45, 60, 90, and 120 minutes during the procedure. Comparison between the groups was performed using one-way analysis of variance (ANOVA). No statistically significant differences were observed in haemodynamic parameters between the two groups, indicating comparable haemodynamic stability.

Table 1: Demographic profile between the groups

Variables		Group S	Group D	Group C	P value
Age (years)		39.24±5.333	41.72± 5.466	39.24±5.371	0.532
Gender	Female	22 (88%)	18 (72%)	16 (64%)	0.065
	Male	3 (12%)	7 (28%)	9 (36%)	
Weight (kgs)		63.20±5.124	64.10±4.967	63.80±5.967	0.742
Height (cms)		151.68±3.78	151.16±5.41	151.68±3.78	0.890
BMI (kg/m2)		27.47±2.10	28.05±2.35	27.72±2.20	0.88
ASA n (%)	1	23 (92%)	23 (92%)	23 (92%)	0.902
	2	2 (8%)	2 (8%)	2 (8%)	

Values are expressed as (mean±SD) or number (percentage). BMI: body mass index; ASA American Society of Anaesthesiologists – Kilograms; cms – centimetres.

Table 2: Depression of T1/T0 after three Cumulative Doses of Cisatracurium

GROUP	T1/T0 %				P-value
	15µg/kg	30µg/kg	45µg/kg	60µg/kg	
GROUP S	37.44±1.758	90.44±1.685	98.16±0.943	-	<0.001*
GROUP D	38.00±2.082	90.20±1.443	98.28±0.891	-	
GROUP C	14.64±1.075	70.28±1.400	90.68±1.701	95.44±0.768	

Values are expressed as (mean±SD). * P value – significant

Table 3: Dose–response relationship between cumulative cisatracurium dose and T1 twitch depression among study groups

Cumulative cisatracurium dose (µg/kg)	Group S T1 depression (%) (95% CI)	Group D T1 depression (%) (95% CI)	Group C T1 depression (%) (95% CI)	P value
15	37.44 ± 1.758% (36.71–38.71)	38.00 ± 2.082% (37.14–38.86)	14.64 14.64 ± 1.075% (14.196–15.084)	<0.001*
30	90.44 ± 1.685 (89.74–91.14)	90.20 ± 1.443 (89.60–90.80)	70.28 ± 1.400 (69.702–70.858)	<0.001*
45	98.16 ± 0.943 (97.77–98.55)	98.28 ± 0.891 (97.91–98.65)	90.68 ± 1.701 (89.978–91.382)	<0.001*
60	-	-	95.44 ± 0.768 (95.123–95.757)	-

Values are expressed as (mean±SD). * P value – significant

Table 4: ED50, ED95, ED95/ED50 Ratio and the Slope of Regression among the three Groups

Variables	GROUP S	GROUP D	GROUP C	P value
ED50(µg/kg)	17.45±0.728 (17.15 to 17.75)	17.28±0.838 (16.93 to 17.62)	27.35±0.360 (27.21 to 27.50)	0.045*
ED95(µg/kg)	39.71±0.426 (39.54 to 39.89)	39.71±0.405 (39.54 to 39.88)	53.05±0.453 (52.86 to 53.24)	0.036
ED95/ED50	2.279±0.099 (2.23 to 2.32)	2.303±0.114 (2.25 to 2.35)	1.93±0.025 (1.92 to 1.95)	<0.001*
SLOPE OF REGRESSION	2.024±0.072 (1.99-2.054)	2.009±0.006 (1.97 to 2.043)	1.752±0.033 (1.73 to 1.76)	<0.001*

Values are expressed as (mean±SD). * P value – significant

Table 5: Recovery from NMB During Desflurane, Sevoflurane, and Control Group After Equi-Effective Doses of Cisatracurium

Variable	Group S	Group D	Group C	P value
T25 duration (min)	18.12 ± 1.42	16.44 ± 1.47	15.48 ± 1.25	0.045*
T75 duration (min)	37.64 ± 1.57	38.88 ± 0.97	35.64 ± 1.15	
T25–75 duration (min)	19.52 ± 2.43	22.44 ± 1.87	20.24 ± 1.85	
TOF 0.7 duration (min)	46.92 ± 2.69	47.80 ± 2.34	34.60 ± 1.15	

Values are expressed as (mean±SD). * P value – significant.

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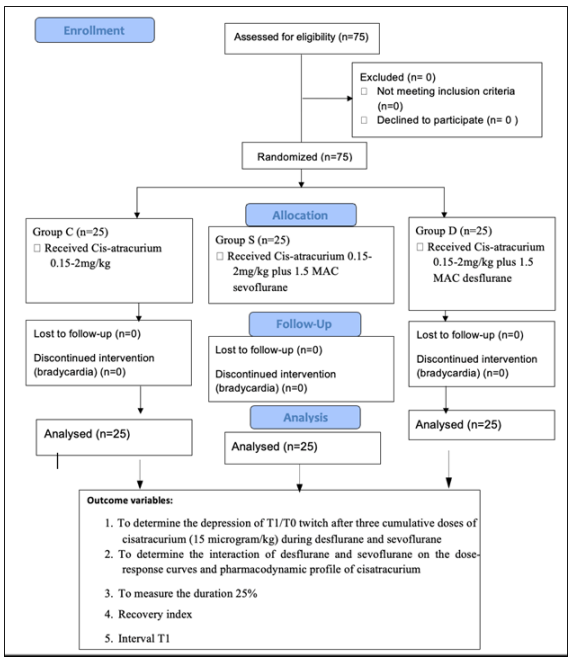

Figure 1: CONSORT

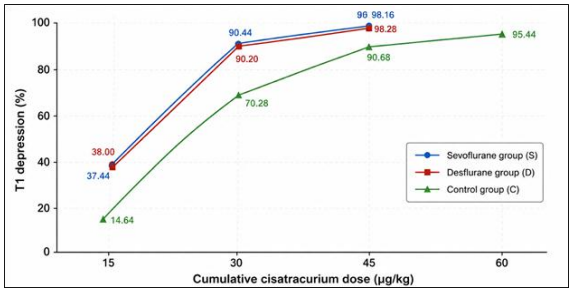

Figure 2: Cumulative Dose-Response Curves for Cisatracurium in Patients Anesthetised with Sevoflurane, Desflurane and Control Groups

DISCUSSION

General anaesthesia involves a medically induced state of unconsciousness with loss of protective reflexes. Neuromuscular blockers (NMBs) are essential components of anaesthetic practice, facilitating endotracheal intubation and mechanical ventilation, supporting surgical conditions, and reducing anaesthetic requirements and oxygen consumption.[8] Since their introduction by Griffith and Johnson in 1942, NMBAs have significantly transformed anaesthetic practice.[9] They act at the neuromuscular junction by binding to postsynaptic nicotinic acetylcholine receptors, thereby inhibiting acetylcholine-mediated neuromuscular transmission. Cisatracurium is an intermediate-acting benzylisoquinolinium non-depolarising neuromuscular blocker with predictable pharmacodynamics, cardiovascular stability, and minimal histamine release. As an isomer of atracurium, it provides effective neuromuscular blockade with fewer adverse effects.[7-9] Volatile anaesthetics such as sevoflurane and desflurane possess low blood–gas solubility, allowing rapid onset and recovery. However, they enhance the effects of non-depolarising neuromuscular blockers through potentiation, mediated by pre-junctional effects, altered muscle blood flow, and central muscle relaxation mechanisms. This interaction is dose- and duration-dependent and results in reduced ED50 and ED95 requirements compared with intravenous anaesthesia.[10-13]

The potentiation of neuromuscular blockade by volatile agents may prolong recovery and increase the risk of delayed emergence. This is attributed to equilibration of anaesthetic concentrations among the end-tidal gas, blood, and muscle compartments, resulting in prolonged neuromuscular effects.[9,14] Therefore, this study was undertaken to evaluate the influence of sevoflurane and desflurane on the dose–response relationship and pharmacodynamic profile of cisatracurium. In the present study, both volatile anaesthetics enhanced the neuromuscular blocking effect of cisatracurium to a similar extent.

The present study demonstrated that maintaining anaesthesia with sevoflurane or desflurane significantly potentiated the neuromuscular-blocking effect of cisatracurium compared with the control group. Both volatile anaesthetics produced greater T1 twitch depression at lower cumulative doses of cisatracurium, resulting in a leftward shift of the cumulative dose–response curve and lower ED50 and ED95 values. However, no appreciable difference was observed between sevoflurane and desflurane, indicating a comparable potentiating effect of both agents.

Our findings are consistent with those of Wulf et al,[9] who demonstrated that desflurane, sevoflurane, and isoflurane enhanced the neuromuscular blocking effect of cisatracurium compared with total intravenous anaesthesia (TIVA), with significant reductions in ED50 and ED95. A similar leftward displacement of the dose–response curves during volatile anaesthesia was observed, with no significant change in the slopes of the regression curves. Likewise, Ashraf et al,[7] reported reduced dose requirements of cisatracurium and rocuronium during sevoflurane anaesthesia compared with propofol, confirming the potentiating effect of volatile agents on non-depolarising neuromuscular blockers.

The enhanced neuromuscular blockade produced by volatile anaesthetics has been attributed to several mechanisms, including depression of neuromuscular transmission at the pre- and postsynaptic levels, increased skeletal muscle perfusion facilitating drug delivery, and central muscle relaxation. In addition, volatile anaesthetics increase the sensitivity of the neuromuscular junction to non-depolarising neuromuscular blocking agents in a concentration- and time-dependent manner. These mechanisms explain the reduced dose of cisatracurium required to achieve comparable levels of neuromuscular blockade in the sevoflurane and desflurane groups.

The cumulative dose–response curves in the present study further demonstrated greater sensitivity to cisatracurium during volatile anaesthesia than in the

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control group. Similar observations were reported by Xue et al,[15] who demonstrated a leftward shift of the rocuronium dose–response curve during sevoflurane anaesthesia, and by Lowry et al,[16] who also observed enhanced neuromuscular blockade with volatile anaesthesia compared with intravenous anaesthesia. These findings collectively support the concept that volatile anaesthetics potentiate the pharmacodynamic effects of non-depolarising neuromuscular blocking agents.

The significantly lower ED50 and ED95 values observed in the sevoflurane and desflurane groups suggest that smaller doses of cisatracurium are required to achieve equivalent neuromuscular blockade during volatile anaesthesia. Similar reductions in effective dose requirements have been reported by Wulf et al,[9] and Ashraf et al,[7] reinforcing the need to adjust neuromuscular blocker dosing when volatile anaesthetics are used. The comparable ED95/ED50 ratios across groups indicate that, although cisatracurium potency increased, the overall shape of the dose–response relationship remained largely unchanged.

Recovery from neuromuscular blockade was significantly prolonged in patients receiving sevoflurane and desflurane compared with the control group. Prolongation of recovery indices and delayed recovery of the TOF ratio are well-recognised effects of volatile anaesthetics and have been consistently reported in previous studies. Wulf et al,[9] demonstrated prolonged recovery index and TOF recovery during desflurane and sevoflurane anaesthesia compared with TIVA, while Ashraf et al,[7] and Lowry et al,[16] similarly reported delayed recovery following volatile anaesthesia. This prolongation is thought to result from continued potentiation of neuromuscular blockade by residual concentrations of volatile anaesthetic agents despite their relatively rapid elimination.

An important observation in the present study was the absence of a clinically significant difference between sevoflurane and desflurane in their effects on the pharmacodynamics of cisatracurium. Although desflurane has a lower blood–gas partition coefficient than sevoflurane, both agents produced comparable dose–response characteristics and recovery profiles, suggesting that either volatile anaesthetic exerts a similar potentiating influence on cisatracurium under the conditions of this study. The clinical implication of these findings is that anaesthesiologists should anticipate enhanced neuromuscular blockade and prolonged recovery when administering cisatracurium during sevoflurane or desflurane anaesthesia. Dose adjustment guided by quantitative neuromuscular monitoring may reduce the risk of excessive blockade and postoperative residual neuromuscular weakness.

Limitations: The study evaluated only sevoflurane and desflurane; inclusion of other volatile anaesthetics, such as isoflurane, could provide a broader comparison. End-tidal anaesthetic concentrations were not monitored, which may have influenced the precision of the pharmacodynamic assessment. Potentiation was assessed using an equieffective dosing approach (ED50 and ED95). The use of a fixed-dose neuromuscular blocking regimen may better demonstrate differences in block duration. The study included short-duration surgeries and an exposure time of approximately 10 minutes to volatile anaesthetics; therefore, the findings may not be generalizable to prolonged procedures. Sex-specific differences in neuromuscular blockade were not analysed. The relatively small sample size may limit the generalisability of the findings. Larger, adequately powered studies are required to validate these results and to compare the effects of other neuromuscular blocking agents.

CONCLUSION

Sevoflurane and desflurane similarly potentiated the neuromuscular blocking effect of cisatracurium, producing a leftward shift in the dose–response curve and significantly reducing the ED50 and ED95 compared with the control group.

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