

Original Article

A COMPREHENSIVE AND PROSPECTIVE ANALYSIS TO IMPROVE PATIENT OUTCOMES IN POSTOPERATIVE PERIOD BY OPTIMIZING NEOSTIGMINE DOSE AND TIMING WITH THE HELP OF TOF MONITORING

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ABSTRACT

Objective: The objective is to find out the optimum neuromuscular reversal strategy using Train-of-Four (TOF) monitoring in the postoperative period for complete and risk-free recovery without residual paralysis. In this study, the neuromuscular blockade brought on by cisatracurium will be reversed using a neuromuscular monitor (TOF) and neostigmine administered at the best possible time and dose. In addition, we'll look at the prevalence of neuromuscular paralysis that persists after general anesthesia, as some research have revealed that paralysis may worsen and return once patients leave the recovery area.

Methods: A comprehensive prospective, randomized, double-blind and prospective analysis was conducted involving various study groups. Demographic data, residual neuromuscular weakness, negative head lift tests, and Visual Analog Scale (VAS) scores were assessed. TOF monitoring was used regularly to tailor neuromuscular reversal strategies.

Results: Incidence of regression of TOF ratio < 0.9 and incidence of negative head lift test after extubation among different groups were statistically non-significant by Chi square test at 15 min (p value 0.4), 30 min (0.8) and 60 min (p value 0.9).

It also concludes that neuromuscular stimulation given for TOF monitoring is well tolerated by different group of the population in terms of VAS score (mean 3.9, ranging from 3.3 to 3.8).

Conclusion: This research suggests that tailoring strategies of neostigmine dose and time of its administration according to TOF ratio leads to complete recovery of neuromuscular function with all the doses (20/30/40 micrograms/kg). This study emphasizes the use of neuromuscular monitoring guided reversal methods to attain complete recovery without residual paralysis.

Keywords: Neuromuscular reversal, Train-of-Four monitoring, Postoperative outcomes, Anesthesia management, Residual paralysis

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INTRODUCTION

Neuromuscular blocking agents (NMBAs) are indispensable tools in modern anesthesia practice. However, the incomplete reversal of NMBAs may lead to potentially serious postoperative pulmonary complications, including impaired airway function, respiratory distress, and compromised patient safety. Efficient neuromuscular reversal is therefore pivotal to ensuring timely and complete recovery from anesthesia, minimizing patient discomfort, and enhancing postoperative outcomes [1].

Inadequate monitoring or hasty administration of reversal agents can result in residual neuromuscular blockade, where patients regain consciousness while still experiencing compromised muscle function [2]. This not only prolongs the time to extubation but also increases the risk of postoperative respiratory complications, delays in ambulation, need of reintubation and a heightened need for post-anesthesia care [3].

One of the key tools in neuromuscular monitoring is the Train-of-Four (TOF) method, which involves the application of four consecutive electrical stimuli to a peripheral nerve, measuring the corresponding muscle twitch responses [4]. TOF monitoring provides clinicians with valuable insights into the degree of neuromuscular blockade and assists in determining the optimal timing and dosage of reversal agents. It enables a more individualized approach to neuromuscular reversal, ensuring that patients regain full muscle function and respiratory capabilities at the appropriate time [5].

This study presents a comprehensive and prospective analysis that aims to optimize neuromuscular reversal strategies to improve patient outcomes during the postoperative period. By emphasizing the

integration of TOF monitoring into clinical practice, we seek to bridge the gap between theoretical knowledge and practical implementation, fostering safer and more effective anesthesia management [6].

MATERIALS AND METHODS

This was a prospective, randomised, interventional, double-blind experiment. The study got the approval of synopsis from DRC of RUHS, Jaipur and CTRI registration was done (registration number CTRI/2020/08/027270).

Institutional ethics committee of SMS Medical College, Jaipur approves the study. With the informed written consent of all the participants the study was done at the anaesthesia department of SMS Medical College Jaipur in the year of 2021.

At three doses of neostigmine (20, 30 or 40 micro gm/kg), a sample size of 30 participants in each group was determined to be sufficient at a 95% confidence level and 80% power to verify the minimum predicted difference of 2.2 (2.13) minutes in attaining full reversal of neuromuscular block [6].

From all 180 eligible patients six groups of 30 patients each were created by random allocation. Patients in Groups A, B, and C (n=30) got neostigmine (20, 30, and 40 micro g/kg, respectively) with glycopyrrolate at 0.4 TOF ratio.

Patients in Groups E, F and G (n=30) received neostigmine (20, 30 and 40 µg/kg, respectively) with glycopyrrolate at a TOF ratio of 0.6.

To confer the double blinding the anaesthesiologist who gave anaesthesia to patients would be different from the anaesthesiologist who collected and analysed data.

The method of randomisation was computerised by using a sequentially numbered sealed envelope approach.

Any patient of either sex, with age 20-40 y, weight 40-70 kgs and belonging to ASA I or II class posted for surgery under general anesthesia (duration lasting from 60-150 min) was included in study.

Patients with history of any known neuromuscular disease/cardiac/respiratory/hepatic or renal disease were excluded. Patients using drugs that affect NM blockage, such as gentamycin, CCB, phenytoin, steroids, frusemide, magnesium, lithium, procainamide, etc. were also excluded.

Anesthesia technique: On the day before surgery, every patient informed about the anaesthetic technique and postoperative course. Every patient underwent a thorough pre-anesthetic examination including investigations.

Following explanations of the research protocol, all patients had the option to withdraw from the research at any time.

After confirming patient's identity and pre-anesthesia fasting, all patients were anesthetised and intubated by similar standard protocol. All patients underwent standard electrocardiogram (ECG), capnography, non-invasive blood pressure (NIBP), pulse rate, pulse oximetry (SpO₂), temperature, and bispectral index (BIS) procedures.

After completion of surgery, every patient was given neostigmine along with glycopyrrolate in dose according to group allocated.

TOF monitoring was done regularly during all the period.

Before surgery patient received pre-medication I. V. fentanyl (1.5mcg/kg) and glycopyrrolate (5mcg/kg). Induction was done with Propofol 2 mg/kg. Then gave cis-atracurium (0.15 mg/kg) for full relaxation. Maintenance was done with sevoflurane and oxygen-nitrous oxide combination. EtCO₂ were kept within range of 30-35 mmHg. Additional doses of cisatracurium were administered

throughout the surgery to keep the TOF count below 2. Throughout the process, the patients' peripheral core temperature was maintained between 35 and 37 °C.

Acceleromyography (AMG) was used to track neuromuscular function. According to the Stockholm revision of acceptable clinical research practises, 200732 the study used a neuromuscular monitor. After the surgery when a TOF ratio of 0.4 or 0.6 was observed, neostigmine was administered in accordance with group allocation at an established dose. Also noticed were TOF ratios at 15, 30, and 60 min following extubation. Our outcome variable was to compare the duration of achieving full reversal (TOF =1.0) of cis atracurium-induced neuromuscular block after administration of different doses of neostigmine (20, 30 and 40 mcg/kg) at the different intensity of neuromuscular block (TOF ratio 0.4 or 0.6), incidences of residual neuromuscular paralysis by ToF monitor or clinical method and acceptability of neuromuscular stimulation for ToF monitoring.

Statistical analysis

Quantitative data were summarised using the mean and standard deviation. Two independent samples were used in a "student t-test" to compare the means between the two groups. Proportions were used to show qualitative data. To evaluate the disparities in proportions between the groups, the CHI-SQUARE TEST was employed. All statistical analyses were performed using a 95% confidence interval. All of the quantitative variables were examined using the appropriate one-way ANOVA or KUSKAL-WALLIS test. Post hoc analysis was performed to look for intergroup comparison. A p-value<0.05 was taken as statistically significant.

RESULTS

Both the groups were comparable in relation to their demographics and baseline characteristics like age, gender, Height, Weight and ASA grading. The total cumulative dose of cisatracurium given and total duration of surgery were also consistent among groups (non-significant).

Table 1: Time to achieve TOF ratio 1.0 among various study groups

Neostigmine dose	Time taken in TOF from 0.4 to TOF 1.0 (min)	Time taken in TOF from 0.6 to TOF 1.0 (min)
20 mcg/kg	8.20(±0.56) Group A	7.72(±0.43) Group D
30 mcg/kg	6.52(±0.52) Group B	6.34(±0.51) Group E
40 mcg/kg	6.28(±0.25) Group C	6.17(±0.53) Group F

Table 1 shows that all neostigmine dosages (20/30/40 mcg/kg) are 100% effective in achieving TOF ratios to TOF 1.0 or complete recovery. Post-hoc analysis of variants using ANOVA test was conducted. The time it took to attain the TOF 1.0 target in our study

for 30 mcg/kg at TOF 0.6 (Group E), 40 mcg/kg at TOF 0.4 (Group C), and 40 mcg/kg at TOF 0.6 (Group F) was statistically non-significant (p 0.05). All other groups have a significantly high time for complete reversal.

Table 2: Incidence of post-extubation TOF ratio<0.9 and Negative Head lift test at different time points

Time interval	Group A		Group B		Group C		Group D		Group E		Group F		Total	
	TOF ratio<0.9	Negative head lift test	TOF ratio<0.9	Negative head lift test	TOF ratio<0.9	Negative head lift test	TOF ratio<0.9	Negative head lift test	TOF ratio<0.9	Negative head lift test	TOF ratio<0.9	Negative head lift test	TOF ratio<0.9	Negative head lift test
15 min	3	5	1	3	0	1	2	4	0	1	0	0	6	14
30 min	8	3	6	1	4	1	3	2	1	0	1	0	23	7
60 min	4	1	3	1	2	0	2	1	1	0	0	0	12	3

Table 3: VAS score

	No. of patients	Total VAS score	Mean	SD	p value
VAS Score 1	18	18	3.3	20	0.9
VAS Score 2	41	82			(NS)
VAS Score 3	37	111			
VAS Score 4	49	196			
VAS Score 5	23	115			
VAS Score 6	12	72			
VAS Score 7-10	0	0			
Total	180	594			

Z Score= 0.115, Here we found the overall mean Visual Analog Score among the patients to be 3.3±20. The p value was 0.9 by Z score which was statistically non-significant.

Table 2 shows that difference among various groups were statistically non-significant by Chi square test for Tof ratio at 15 min (p value 0.4), 30 min (p value 0.8) and 60 min (p value 0.9). The results are also non-significant for negative head lift test with p value of 0.11, 0.33 and 0.82 at three-time points,

During the monitoring, there was also no statistically significant difference in the likelihood of an unfavorable incident between the three groups (p-value 0.68). However, 5.5% of people reported trouble swallowing, and 5% reported nausea and vomiting overall.

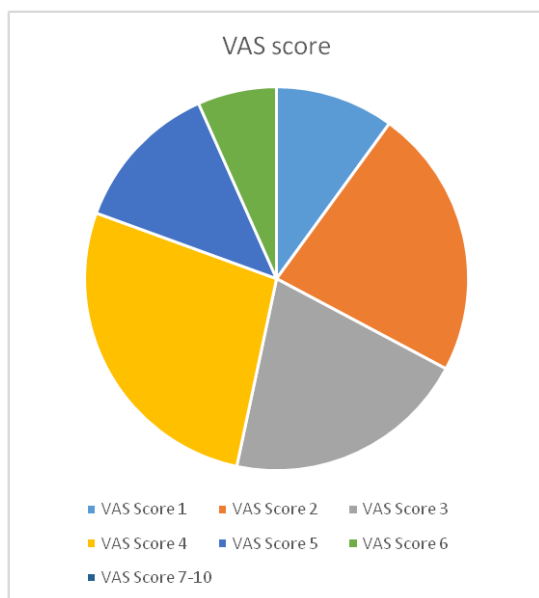


Fig. 1: VAS score

DISCUSSION

This publication investigates the use of Train-of-Four (TOF) monitoring as a means of maximizing the effectiveness of neuromuscular reversal methods during the postoperative phase. The results of the research provide light on the relevance of individualized neuromuscular reversal to improve patient outcomes following anesthesia [8].

The distribution of demographic data among the different groups provides a representative sample, which helped to ensure that demography-related differences did not substantially impact the findings of the research. Similarly, having surgeries of similar lengths and administering equivalent dosages of cisatracurium helped to reduce the number of possible confounding factors, which in turn strengthened the trustworthiness of the results [9].

Incidence of post-extubation TOF ratio < 0.9 and Negative Head lift test at different time points were utilized as a proxy for neuromuscular recovery, and the fact that their incidence remained similar throughout intervals indicated that optimal reversal tactics permitted uniform trends in the recovery of muscle strength. This consistency provides further evidence that TOF-guided neuromuscular reversal is an effective treatment for guaranteeing a prompt and risk-free recovery [10].

The Visual Analog Scale (VAS) ratings that were used to quantify pain indicated that all of the research groups had similar levels of discomfort. It would seem from this that the management of anesthesia and the neuromuscular reversal procedures both contributed to the constant postoperative pain levels.

It is necessary to recognize the limitations of the research, such as the fact that it focused on a certain demography and a specific neuromuscular blocking agent, cisatracurium. Both of these factors might have an effect on the data potential to be generalized [11].

CONCLUSION

This study suggests that tailoring strategies of the neostigmine dose and time of its administration with help of TOF monitoring leads to complete recovery of neuromuscular function after cisatracurium-induced block. This study emphasizes the effectiveness of TOF-guided neuromuscular reversal methods in promoting optimal and risk-free recovery without any residual paralysis. It also concludes that neuromuscular stimulation given for TOF monitoring is well tolerated by different group of the population in terms of VAS score.

Although, the study's focus on cisatracurium-induced blockade might limit the generalizability to other neuromuscular blockers

Future research could expand the applicability of these findings to broader patient populations and different anesthesia scenarios, further enhancing their clinical relevance.

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AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICTS OF INTERESTS

Declared none

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