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Original Research Article

An Observational Study to Evaluate Optimised Reversal with and Without Quantitative Train of four Monitoring with Injection Vecuronium Bromide

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Abstract

Background and aims: Postoperative residual neuromuscular block is a serious complication after general anesthesia which endangers the patient safety. The aim of the study is to assess the reversal after neuromuscular blockade without Train Of Four (TOF) monitoring and reversal using quantitative TOF monitoring. **Method:** This prospective, single centre, observational study includes 60 patients of American society of Anaesthesiologists (ASA) grade 1 and 2 requiring general anaesthesia for elective surgeries of <3 hour duration. The cohort of patients was formed as those who received reversal strategy based on train of four quantitative monitoring (group A) and those who received optimal neostigmine reversal strategy without train of four monitoring (group B). All patients were monitored for total dose and time duration since last dose of vecuronium bromide administered, dose of neostigmine, reversal extubation time, TOF value in recovery room, pulse rate, blood pressure (BP), airway problems, respiration patterns, oxygen saturation, nausea and vomiting during and after 30 minute (min) in the recovery room. Observation, tabulation, statistical analysis done using Chi-Square Test, one way ANOVA test by SPSS version 20 software. **Results:** The time interval between administration of neostigmine and tracheal extubation of group B was longer (16.10±1.88) min than group A (13.40±2.08) min. The TOF ratio in recovery room in group A was (0.96±0.05) and in group B was (0.91±0.1). **Conclusion:** The study concluded that anaesthetists should not rely on clinical criteria alone, even when using an intermediate-acting neuromuscular blocking agent. However in absence of neuromuscular monitoring, optimised use of reversal agent can reduce the chances of adverse events.

Key words: neuromuscular monitoring, vecuronium bromide, neostigmine

1. INTRODUCTION

Postoperative residual neuromuscular block, defined as the train-of-four ratio <0.9[1], is associated with an increased risk of postoperative hypoxaemia, airway obstruction, pneumonia, coma and mortality. Regarding both efficacy and safety, the key for successful reversal of neuromuscular blockade is to use neostigmine "appropriately," optimizing the dosage and timing of administration under close monitoring.

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Vecuronium is an intermediate acting, non depolarizing neuromuscular blocking agent used commonly to induce muscle relaxation during surgery, poses risk of residual paralysis. Several objective, i.e. quantitative methods for assessing and monitoring the degree of neuromuscular block have been developed over time. On the basis of best available evidence, current recommendation support a Train of Four (TOF) (T4 / T1) ratio of 0.9 or more as appropriate indication of adequate recovery from neuromuscular transmission block. However, the device is not widely available with only 9.4 – 22.7% of clinicians who had quantitative train of four monitoring in their practice[2,3] . When it is not available, the chance of successful reversal may be increased by optimal administration of neostigmine. Recent studies have shown that that the depth of blockade -based neostigmine dosing and reversal – extubation time has an important role in decreasing the incidence of residual paralysis[4,5,6]. The aim of this study is to assess the reversal after neuromuscular blockade and evaluate and compare the reversal with and without TOF monitoring. We also study the occurrence of any post operative residual paralysis.

2. METHOD

This prospective, single centre, observational study was conducted in our medical college Hospital after the approval from Institutional Ethics Committee ECR/1055/Inst/MP/2018. Period of study from January 2019 to July 2020. Sixty patients of either sex, aged 16-60 years, belonging to American society of Anaesthesiologists (ASA) I and II who were posted for elective surgery requiring general anaesthesia were included. Patient refusal, patient requiring elective ventilation or post surgery intensive care admission, those with BMI >35kg/m^2, hepatic disease (liver enzyme value >50% normal value), renal insufficiency (Serum Creatinine >1.8mg/dL), neuromuscular disease, consumption of drugs known to affect neuromuscular transmission, contraindications to neostigmine, history of hypersensitivity or allergic to anaesthetic agent given and difficulty accessing the train of four measuring device in the ulnar nerve were excluded. A thorough preanaesthetic assessment was done and an informed written consent was obtained from the patients.

On the day of the surgery, peripheral venous access was secured using 18G or 20G intravenous (IV) cannula. All standard monitors were attached to the patients. Perioperative baseline heart rate (HR), Blood pressure (BP), spO_2 and electrocardiography was noted. Premedication was done with midazolam 1 mg IV and IV glycopyrrolate 0.2 mg. Anaesthesia was induced with propofol 2 mg/kg IV, fentanyl 2 µg/kg IV and vecuronium 0.1 mg/kg IV for tracheal intubation. Anaesthesia was maintained with sevoflurane 0.5-2% with N_2O/ O_2 in the ratio 50:50%. Ventilation was adjusted to maintain the $Etco_2$ in the range of 35 – 45 mm of Hg.

All the patients had two electrodes on the forearm. The distal electrode was placed at the wrist crest, whereas the proximal electrode was placed 3-6 cm proximal from the distal one at the course of ulnar nerve. All TOF device cables was then connected to the electrodes and the transducer will be taped to the distal phalanx of the thumb. An incremental dose of vecuronium 1mg was given as and when required. Reversal of neuromuscular blockade was done using neostigmine and glycopyrrolate.

The groups were allocated based on the surgery list of that day; every alternate patient were included in group A while other alternates on same day were included in group B. In group A, neostigmine was given at a dose according to the measured TOF values and body weight. The TOF stimulation of 50 mA was given without calibration. The neostigmine administration was delayed if TOF count value was 0–1. Subjects who have TOF count of 2–

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE11, 2023

4 received 50 µg/kg of IV neostigmine. If the TOF ratio was ≤ 0.40 and in the range of 0.40–0.70, then neostigmine dosing of 40 and 30 µg/kg IV, respectively, was given. Patient was then extubated after a TOF ratio of 0.9

In group B, we recorded the time since last vecuronium administration and assessed the patient's spontaneous breathing effort. The reversal strategy was based on the fact that the duration of action of vecuronium will be equal to the TOF count of 4; the tidal volume will return to the normal when the TOF ratio is >0.40 and the diaphragm muscles will fully recover if the TOF ratio is >0.70. In addition, any attempts of reversal should be delayed by at least 40 minutes after vecuronium administration if there are no signs of recovery. When the time since last vecuronium was >40 minutes without evidence of spontaneous breathing, 50 µg/kg of IV neostigmine was given. When minimal spontaneous breathing was detected, 40 µg/kg and 30 µg/kg of IV neostigmine was given, if time since last vecuronium was ≤40 minutes and ≥40 minutes before reversal, respectively. Patient was extubated when he/she was able to do arm lift, head lift, swallowing and eye opening[7]. Local anaesthestia was administered along the incision at the end of surgery and post operative analgesia was maintained with NSAIDS and tramadol.

The primary outcome of the study was the proportion of patients who had residual paralysis in the recovery room based on the threshold TOF value <0.90 in both groups. Oxygen supplementation was done via facemask or nasal probe at 3-4 L/minute. Non-invasive BP and spO_2 monitors, ECG leads and TOF devices was attached to all patients on arrival at the recovery room, and the TOF value was measured by the second researcher who did not know the type of intervention given. The variables recorded were total dose and time duration since last dose of vecuronium bromide was administered, dose of neostigmine administered, reversal extubation time, TOF value in the recovery room, pulse rate, blood pressure, airway problems, respiration patterns, oxygen saturation, nausea and vomiting during and after 30 min in the recovery room.

Statistical analysis was done using IBM SPSS Statistics V22.0®. Data comparison was done by applying specific statistical tests to find out the statistical significance of the comparisons. The qualitative data were expressed in the proportions and percentages and the quantitative data was expressed as mean and standard deviations (SD). The difference in proportion was analysed by one-way ANOVA test and the difference in means were analyzed by using Student's 'T' test. The significance level for tests was determined as 95% (P< 0.05).

3. RESULT

A total of sixty patients were enrolled for the study which included 30 patients in each group and all the participants who were enrolled completed the study. The demographic profile of the patients were comparable among both the groups in terms of age, sex and duration of the surgery. All the parameters were noted in the form of mean ± standard deviation (SD). A 'P' value < 0.05 was taken as significant and 'P' value of <0.001 was taken as highly significant (Table 1).

The total dose of vecuronium bromide including intubating dose given in group A and group B was 7.1 ± 1.63 mg and 6.9 ± 1.61 mg, respectively (p=0.63, non- significant). In this study, time between the last dose of vecuronium bromide and administration of neostigmine in group A and group B was 40.7 ± 5.7 and 39.77 ± 6.86 minutes respectively (p=0.9, non-significant). The total neostigmine dose in group A was 2.60 ± 0.39mg and in group B was 2.62 ± 0.42mg (p= 0.945, non- significant).

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE11, 2023

The time interval between administration of neostigmine and tracheal extubation of group B (16.10 ± 1.88 minutes) was significantly longer than group A (13.40 ± 2.08 minutes) (p < 0.001, highly significant). The TOF ratio in recovery room in group A (0.96±0.05) was higher than the group B (0.91±0.1) (p < 0.05, significant). The differences in mean pulse rate, mean systolic blood pressure, mean diastolic pressure, mean respiratory rate and mean spO2 were not statistically significant in both the groups. Two cases in group B presented with respiratory distress during immediate post operative period requiring nasopharyngeal airway (p=0.4, non significant). No patient in our study required reintubation. One patient in both group had incidence of post op nausea and vomiting (table 2).

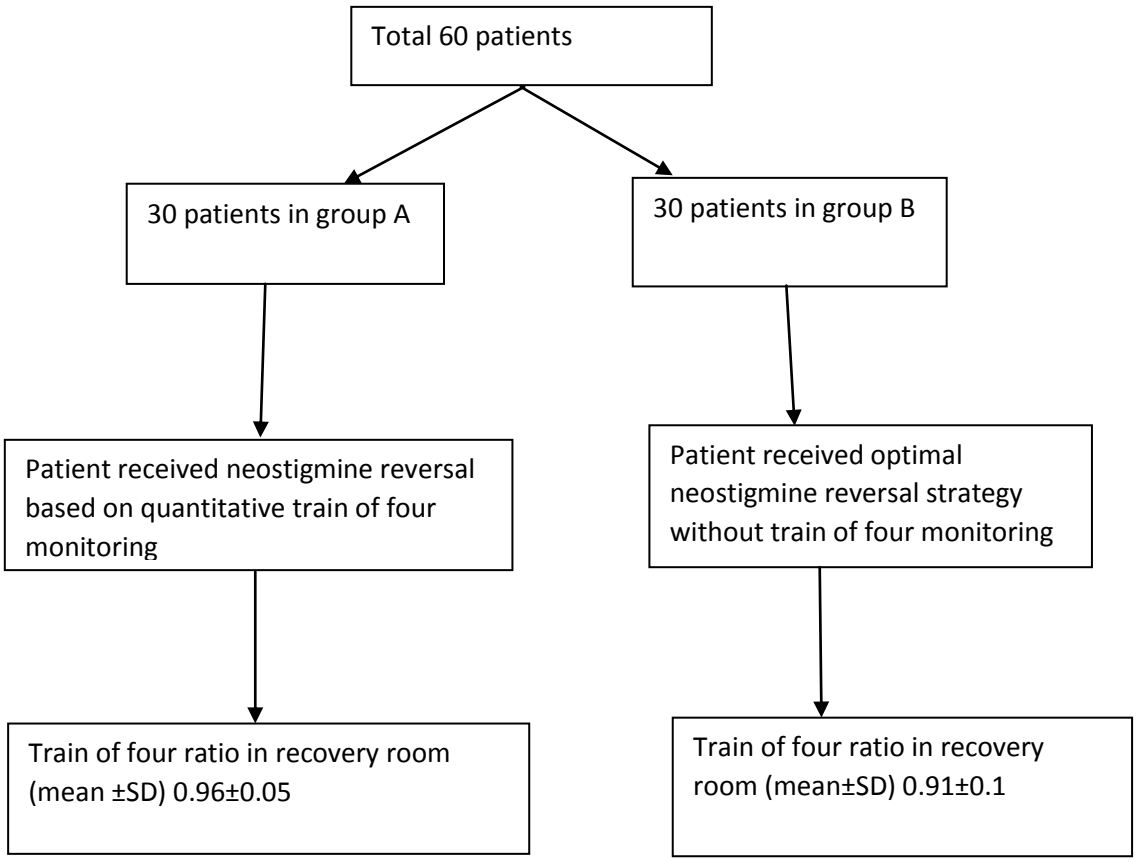


Figure 1: representation of patients recruited for study as per consort diagram

Table 1: shows studied parameters in both groups

Parameters	Group A			Group B			P value
	n	Mean	SD	n	Mean	SD	
Age	30	38.70	11.925	30	35.70	12.069	0.337
Duration of surgery	30	119.17	34.64	30	112.00	36.80	0.441
Total dose of vecuronium bromide (mg)	30	7.10	1.63	30	6.90	1.61	0.633

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE11, 2023

Time since last dose (min)	30	40.07	5.70	30	39.77	6.86	0.970
Total neostigmine dose (mg)	30	2.60	0.39	30	2.62	0.42	0.945
Reversal extubation time	30	13.40	2.08	30	16.10	1.88	<0.001
TOF ratio in recovery room	30	0.96	0.05	30	0.91	0.10	0.042

Figure 2 shows the comparision of reversal extubation time between group A and B.

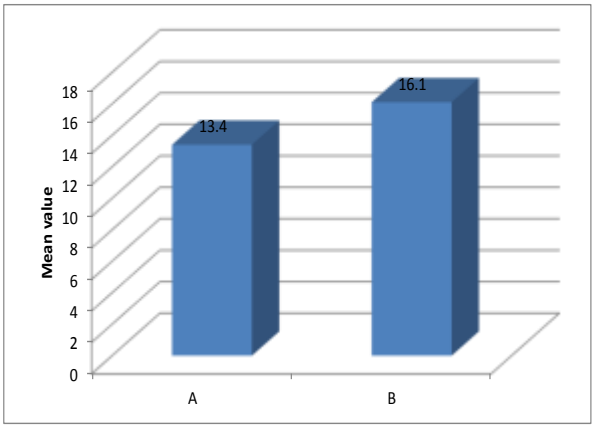
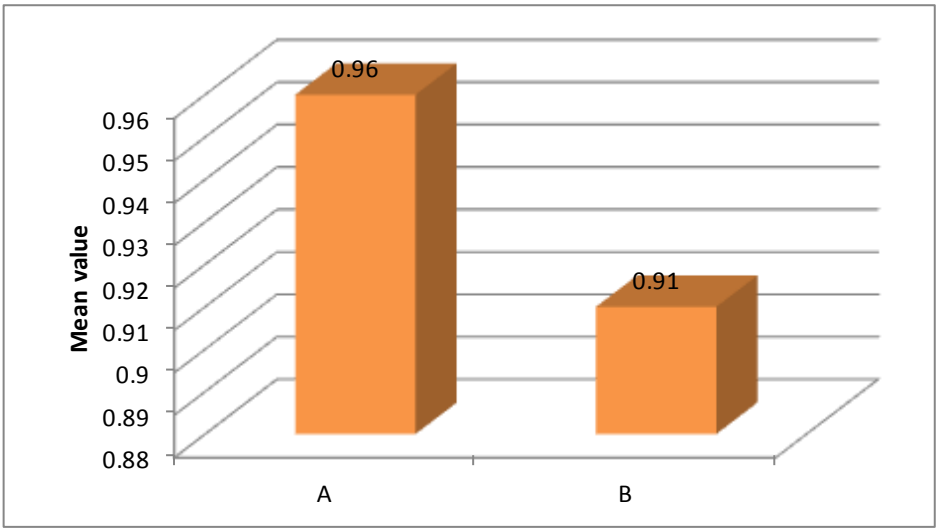


Figure 3 shows comparision of TOF ratio between both groups in recovery room.



ISSN: 0975-3583, 0976-2833 VOL14, ISSUE11, 2023

Table 2: comparision of adverse events in both the groups

Adverse events	Group		p-value
	A	B	
Respiratory distress	0 (0.0%)	2 (6.7%)	0.492 (Fisher's Exact test)
Reintubation	0	0	1(Fisher's Exact test)
Post operative nausea and vomiting	1(3.3%)	1(3.3%)	1.000

Figure 4: COMPARISION OF RESPIRATORY DISTRESS BETWEEN BOTH GROUPS

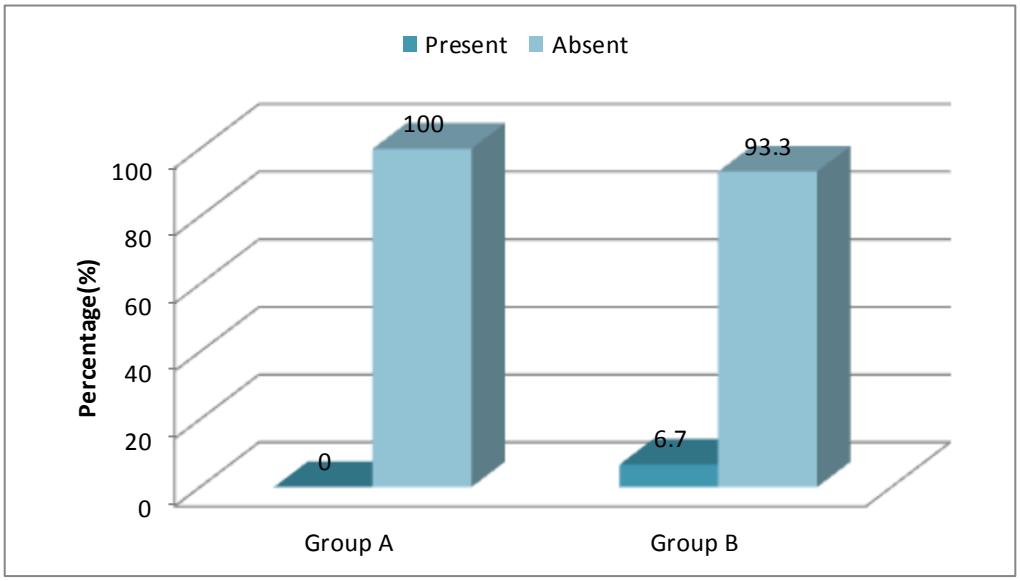


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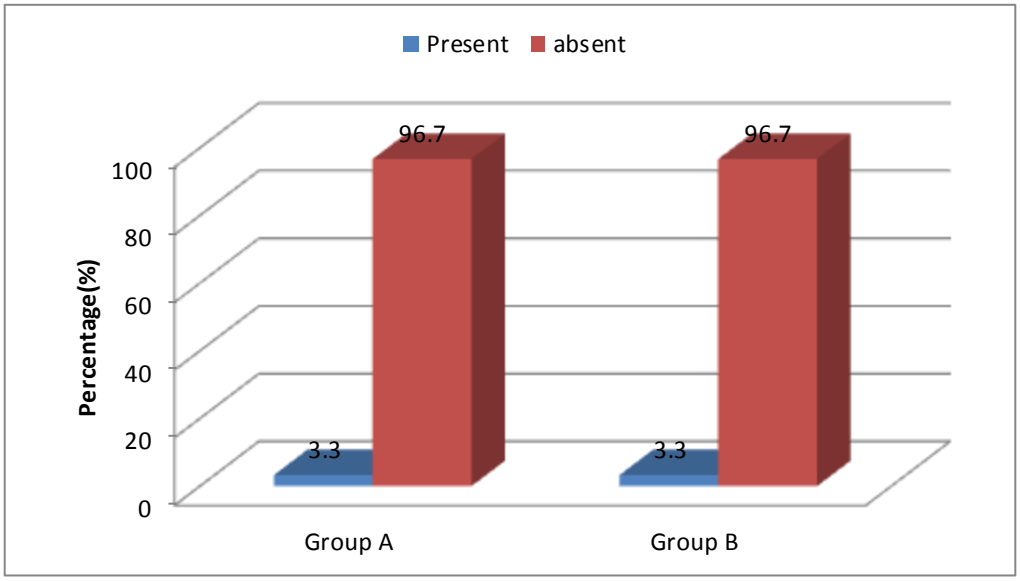
Figure 6: COMPARISION OF POST OPERATIVE NAUSEA AND VOMITING BETWEEN BOTH GROUPS



ISSN: 0975-3583, 0976-2833 VOL14, ISSUE11, 2023

4. DISCUSSION

Incomplete neuromuscular recovery is sometimes associated with critical respiratory events in post anaesthesia care unit[8]. The risk of these adverse respiratory events during early recovery from anaesthesia can be reduced by intraoperative use of neuromuscular monitoring. But the availability of neuromuscular monitors is scarce especially in developing countries. There are studies which have reported incidences of post operative residual curarization despite use of neuromuscular monitoring[9],[10]. Our study aims to assess the reversal with and without neuromuscular monitoring and study whether optimised dose of neostigmine is adequate to prevent post operative residual paralysis.

According to a study post operative residual paralysis (TOF ratio <0.9) is associated with several factors i.e. the absence of perioperative neuromuscular monitoring, the use of pyridostigmine, which is less potent than neostigmine, a larger dose of vecuronium, shorter time from the last neuromuscular blocker to TOF monitoring, or peripheral cooling[11]. In our study, we have used neostigmine, temperature was maintained between 36-37 degree celsius and there was no statistical significant difference seen in total dose of vecuronium bromide between group A (7.1±1.63) mg and group B (6.9±1.61mg), (p=0.63). Another group of authors[12] also suggested that either the administration of neostigmine should be delayed until an advanced degree of prereversal recovery has occurred (i.e. a T1 >25% of baseline), or after injection of neostigmine recovery times longer than 15 min will be required. In our study time between last dose of vecuronium bromide and administration of neostigmine in both the groups were also comparable. The total neostigmine dose was also comparable in between group A (2.60±0.39) and group B(2.62±0.42).

In a study[13] conducted on 72 patients with rocuronium as muscle relaxant the reversal extubation time in patients with quantitative neuromuscular monitoring was shorter (12.3±8.4 minutes) then in patients with optimised reversal without quantitative neuromuscular monitoring (17.4±4.8 minutes). We also found the same as in our study also the reversal extubation time of group B was longer (16.10±1.88 minutes) than group A (13.40±2.08 minutes) which was statistical significant (p=0.0001). Figure 2 shows the comparision of reversal extubation time between group A and B. But in their study 1 case in TOF group and 6 cases in other group had residual paralysis in the recovery room which is in contrast to our study where no case in TOF group had residual paralysis. Studies have observed that by applying the objective neuromuscular monitoring patients could be safely extubated at the end of surgery (after achieving the TOF >0.9) even without using neostigmine and concluded that the use of quantitative neuromuscular monitoring is associated with decreased incidence of residual neuromuscular blockade in recovery room[14],[15].] In the recovery room 2 patients of group B had respiratory distress (p=0.4, statistical insignificant). TOF ratio in recovery room was more in group A (0.96±0.05) as compared to group B (0.91±0.1) and the difference was statistical significant (p=0.042) (Figure 3). In our study no patient required reintubation in recovery room and one case in each group had incidence of post operative nausea and vomiting. A similar study by another group also not found any significant difference of adverse events in both the groups[13].

There are some limitations in our study. In some patients intraoperatively sometimes error occured during TOF monitoring. It might be due to loose attachment of monitors or loosening of electrodes during surgery so it can effect the administered dose of vecuronium bromide. Also the time of administration of neostigmine is not constant between both groups so it might effect the result of study. The sample size of study is also small so the results of study might not represent the whole population.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE11, 2023

5. CONCLUSION

This study shows that there are chances of residual neuromuscular block with vecuronium bromide after reversal with neostigmine. Therefore, anaesthetists should not rely on clinical criteria alone, even while using an intermediate-acting neuromuscular blocking agent and opt for neuromuscular monitoring whenever feasible. However, in absence of neuromuscular monitoring, optimised use of reversal agent can reduce the chances of adverse events.

6. REFERENCES

1. Miller. *miller's anesthesia Reversal (antagonism) of neuromuscular blockade*. (2020).
2. Naguib, M. *et al.* A survey of current management of neuromuscular block in the United States and Europe. *Anesth. Analg.* **111**, 110–119 (2010).
3. Grayling, M. & Sweeney, B. P. Recovery from neuromuscular blockade: a survey of practice. *Anaesthesia* **62**, 806–809 (2007).
4. Kopman, A. F. Residual neuromuscular blockade and adverse postoperative outcomes: An update. *Curr. Anesthesiol. Rep.* **6**, 178–184 (2016).
5. Meyer, M. J., Bateman, B. T., Kurth, T. & Eikermann, M. Neostigmine reversal doesn't improve postoperative respiratory safety. *BMJ (Clinical research ed.)* vol. 346 f1460 (2013).
6. Donati, F. Neuromuscular blocking drugs for the new millennium: current practice, future trends--comparative pharmacology of neuromuscular blocking drugs. *Anesth. Analg.* **90**, S2–S6 (2000).
7. Unterbuchner, C. *et al.* Development of an algorithm using clinical tests to avoid post-operative residual neuromuscular block. *BMC Anesthesiol.* **17**, 101 (2017).
8. Murphy, G. S. *et al.* Intraoperative acceleromyographic monitoring reduces the risk of residual neuromuscular blockade and adverse respiratory events in the postanesthesia care unit. *Anesthesiology* **109**, 389–398 (2008).
9. Fortier, L.-P. *et al.* The RECITE Study: A Canadian Prospective, Multicenter Study of the Incidence and Severity of Residual Neuromuscular Blockade. *Anesth. Analg.* **121**, 366–372 (2015).
10. Naguib, M., Kopman, A. F. & Ensor, J. E. Neuromuscular monitoring and postoperative residual curarisation: a meta-analysis. *Br. J. Anaesth.* **98**, 302–316 (2007).
11. Kim, K. S., Lew, S. H., Cho, H. Y. & Cheong, M. A. Residual paralysis induced by either vecuronium or rocuronium after reversal with pyridostigmine. *Anesth. Analg.* **95**, 1656–60, table of contents (2002).
12. Tajaate, N., Schreiber, J.-U., Fuchs-Buder, T., Jelting, Y. & Kranke, P. Neostigmine-based reversal of intermediate acting neuromuscular blocking agents to prevent postoperative residual paralysis: A systematic review. *Eur. J. Anaesthesiol.* **35**, 184–192 (2018).
13. Wardhana, A., Kurniawaty, J. & Uyun, Y. Optimised reversal without train-of-four monitoring versus reversal using quantitative train-of-four monitoring: An equivalence study. *Indian J. Anaesth.* **63**, 361–367 (2019).
14. Domenech, G. *et al.* Usefulness of intra-operative neuromuscular blockade monitoring and reversal agents for postoperative residual neuromuscular blockade: a retrospective observational study. *BMC Anesthesiol.* **19**, 143 (2019).
15. Goyal, S. *et al.* Reversal agents: do we need to administer with neuromuscular monitoring - an observational study. *Indian J. Anaesth.* **62**, 219–224 (2018).