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Short Communication

Post-operative residual neuromuscular blockade after the administration of a single intubating dose of intermediate-acting non-depolarising neuromuscular blocking agent in adult elective surgical procedures

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ABSTRACT

Objectives: Post-operative residual neuromuscular blockade may result in life-threatening conditions if not properly managed making it a common and significant concern among anaesthesiologists. Among adult elective surgeries requiring single intubating dose of intermediate-acting non-depolarising neuromuscular blocking agent, the study determined the incidence and risk factors associated with post-operative residual neuromuscular blockade during early post-operative period.

Materials and Methods: A prospective, open-labelled, non-randomised observational study conducted in an operating room and post-anaesthesia care unit. A total of 175 ASA-PS Class I and II patients admitted in the surgical wards scheduled for elective surgical operation and were administered of a single intubating dose of intravenous intermediate-acting non-depolarising neuromuscular blocking drug. The train-of-four (TOF) method of peripheral nerve stimulation detects the presence of post-operative residual neuromuscular blockade.

Results: A significant post-operative residual paralysis was identified in specific age groups (26–35, 46–55 and 56–65), in surgical procedures in the orthopaedic service, and among patients who were given a reversal agent. Residual neuromuscular blockade is still present even if the interval between the last dose of muscle relaxant and the measurement of TOF ratio at the post-anaesthesia care unit was long, however, less than that observed in short interval surgeries.

Conclusion: Clinical importance of residual neuromuscular blockade is still evident up to the present time and the present study recommends routine monitoring of neuromuscular blockade and pharmacologic antagonism in the reversal of non-depolarising neuromuscular blocking drugs.

Keywords: Residual neuromuscular blockade, Atracurium, Rocuronium, Train-of-four stimulation, Neostigmine, Sugammadex

INTRODUCTION

General anaesthesia requires a reversible state that includes hypnosis, amnesia, analgesia, hemodynamic stability and immobility.[1] Neuromuscular blocking drugs (NMBDs) are widely used to ease tracheal intubation[1] and reduce laryngeal trauma,[2] to maintain adequate muscle relaxation during surgery,[1,2] and to assist in mechanical ventilation. If muscular

paralysis is unnecessary throughout the procedure, a single dose of NMBD is given only to facilitate tracheal intubation.[3] To ensure adequate ventilation, cough and patent airway, post-operative restoration of complete muscle strength is important[4] to avoid residual paralysis.[1,2] However, residual neuromuscular blockade (RNMB) is still evident in post-anaesthesia care unit (PACU)[5] interfering pulmonary mechanics and impairing ventilator response to hypoxia,[6] contributing to increased morbidity and mortality.

Routine monitoring is recommended to address RNMB[7] and its management is guided by train-of-four (TOF) stimulation.[8] Two strategies developed to ensure optimal restoration of muscle strength include neuromuscular transmission monitoring and use of reversal agents to antagonise RNMB.[1] This study determined the incidence and risk factors associated with post-operative RNMB during early post-operative period after single intubating dose of intermediate-acting non-depolarising NMBDs (atracurium and rocuronium) using the TOF method of peripheral nerve stimulation.

MATERIALS AND METHODS

Study population, sample size and sampling design

After obtaining approval from Ethics Review Board (ANES 2016-073), 175 American Society of Anaesthesiologists-Physical Status (ASA-PS) Class I and II, aged 18–65 years, admitted in Philippine General Hospital scheduled for elective surgery under general anaesthesia requiring single intubating dose of intermediate-acting NMBD (atracurium or rocuronium) were enrolled in this prospective, open-labelled, non-randomised observational study during the 3-month period between July and September 2016. Those who refused to participate; those who are ventilated using laryngeal mask airways; ASA-PS Class III and above patients; those who used medications interfering neuromuscular transmission; those who have body mass index (BMI) more than 30%; pregnant; those for cardiac, thoracic and major vascular surgeries; surgical procedures requiring massive fluid shift, emergency procedures; patients for elective post-operative ventilation; and those with neuromuscular, renal, hepatic, or metabolic diseases were excluded from the study. The minimum sample size was computed using Cochran's formula based on proportion of post-operative neuromuscular blockade of 13.1%, 5% level of significance and 5% margin of error.

Data were collected from all study participants arriving in PACU between 8:00 am and 6:00 pm, Monday through Friday, over a 3-month period (July to September 2016). The data included basic demographic information, pre-operative diagnosis, pre-existing medical conditions, pre-operative medications, data related to surgery and anaesthesia (i.e., surgical service/type of surgery, duration of surgery and anaesthesia, induction and maintenance agents, non-depolarising NMBD and reversal agents used and duration from extubation to transfer to PACU), volatile anaesthetic and opioids used and TOF ratio. The following warranted withdrawal from the study: (a) patients who received additional doses of NMBD throughout the procedure; (b) withdrawal of participation at any point in the study; and (c) death of participant before or after the acquisition of TOF ratio.

Pre-operative course

An approved written informed consent form was obtained during pre-operative evaluation and included in the chart. The patient information form was also included in the chart where risk factors were identified.

Intraoperative course

Upon arrival in the operating room, the patient was placed on the operating table and kept warm. Monitoring included blood pressure apparatus, electrocardiography, pulse oximetry and/or capnography. Choice of drugs for pre-medication, induction and maintenance and post-operative pain control was at the discretion of the primary anaesthesiologist. After preoxygenation with 100% oxygen, induction agents were given. All patients received a single intubating dose of intravenous intermediate-acting non-depolarising NMBD (atracurium or rocuronium) to facilitate tracheal intubation and did not receive subsequent doses. Manual lung ventilation proceeded before performing endotracheal intubation. The adequacy of recovery, decision to extubate the trachea, decision to give reversal agents (sugammadex or neostigmine) and transfer to PACU were at the discretion of the primary anaesthesiologist.

Post-operative course

The patients transferred to PACU were quickly checked if they meet the study criteria. Post-operative residual neuromuscular block (PRNMB) defined as TOF ratio of <0.9 is the outcome measure. Monitoring of TOF ratio was obtained using TOF-Watch® Organon. The patients were evaluated on arrival (baseline) and 15, 30 and 60 min thereafter.

Data and statistical analyses

Descriptive statistics were reported as means with standard deviations for continuous quantitative variables while frequency counts and percentages for categorical qualitative variables. Comparison of proportions involving two groups

was done using *z*-test while comparison involving three or more groups made use of a Chi-square test. Multiple logistic regression analysis was employed in identifying significant risk factors associated with PRNMB. All analyses were carried out at 5% level of significance using Statistical Analysis Systems (SAS®) software.

RESULTS

Patient characteristics and risk factors associated with PRNMB were identified [Table 1]. Intermediate acting non-depolarising NMBDs were administered in the following distribution: 137 (78.29%) and 38 (21.71%) for atracurium and rocuronium, respectively. Only 117 (66.85%) patients were given reversal of neuromuscular blockade, wherein 114 (97.44%) and 3 (2.56%) were given neostigmine and sugammadex, respectively. The duration of 71 (40.57%) surgeries was 3 h or less, while 104 (59.43%) surgeries lasted for more than 3 h. The mean duration of anaesthesia was 209.67 min. For those surgeries lasted for 3 h or less, 49 (69.01%) had 60 min or less duration from time of extubation to arrival at PACU, while 22 (30.99%) had duration more than 60 min. For surgeries lasted for more than 3 h, 86 (82.69%) had 60 min or less duration from time of extubation to arrival at PACU, while 18 (17.31%) had duration of more than 60 min.

A significant PRNMB was identified in age groups 26–35, 46–55 and 56–65, and among the services, only orthopaedic

Table 1: Patient characteristics and associated post-operative residual neuromuscular blockade rates determined by multiple logistic regression analysis.

Qualitative characteristics	**Total *n* (%)**	**With post-operative RNMB *n* (% of subgroup total)**	**OR (95% CI)**
Age			
18–25	26 (14.86)	13 (50.00)	-
26–35	40 (22.86)	26 (65.00)	6.79 (1.63–28.25)
36–45	46 (26.29)	23 (50.00)	1.88 (0.55–6.58)
46–55	36 (20.57)	26 (72.22)	8.50 (1.82–39.70)
56–65	27 (15.43)	18 (66.67)	5.96 (1.11–32.04)
Sex			
Male	65 (37.14)	40 (61.54)	0.60 (0.22–1.62)
Female	110 (62.86)	66 (60.00)	-
ASA-PS classification			
I	123 (70.29)	75 (60.98)	-
II	52 (29.71)	31 (59.62)	0.58 (0.20–1.68)
Procedure/service			
General surgery	73 (41.71)	45 (61.64)	-
Gynaecology	15 (8.57)	5 (33.33)	0.39 (0.08–1.92)
Neurosurgery	6 (3.43)	1 (16.67)	0.06 (0.01–0.70)
Otorhinolaryngology	42 (24.00)	30 (71.43)	2.32 (0.71–7.59)
Orthopaedics	15 (8.57)	9 (60.00)	15.39 (2.52–94.13)
Plastics	5 (2.86)	4 (80.00)	7.60 (0.35–166.44)
Urology	19 (10.86)	12 (63.16)	2.97 (0.67–13.15)
Non-depolarising NMBD used during induction			
Atracurium	137 (78.29)	81 (59.12)	-
Rocuronium	38 (21.71)	25 (65.79)	0.76 (0.26–0.16)
Use of reversal agent			
Without	58 (33.14)	15 (25.86)	-
With	117 (66.86)	91 (77.78)	32.28 (10.91–95.53)
Reversal agent			
Neostigmine	114 (65.14)	90 (78.95)	-
Sugammadex	3 (1.71)	1 (33.33)	0.41 (0.22–7.75)
Continuous variables	**[Mean±SD]**		**OR (95% CI)**
Age (years)	40.67±12.83		1.01 (0.99–1.04)
Anaesthesia duration (minutes)	209.67±83.35		0.99 (0.985–0.994)
Extubation-time to recovery room (minutes)	50.06±17.08		1.00 (0.98–1.02)

RNMB: Residual neuromuscular blockade, ASA-PS: American Society of Anaesthesiologists-Physical Status, NMBD: Neuromuscular blocking drug, SD: Standard deviation, CI: Confidence interval

service showed significant PRNMB. Moreover, patients who were given a reversal agent showed significant finding of PRNMB. The frequencies of RNMB at baseline, 15, 30 and 60 min were 106 (60.57%), 66 (37.71%), 33 (18.86%) and 13 (7.43%), respectively. Among the 71 patients with procedures lasting for 3 h or less, there were 57 (80.28%), 37 (52.11%), 23 (32.39%) and 12 (16.90%) cases with TOF < 0.9 immediately on arrival at PACU (baseline) and 15, 30 and 60 min, respectively, and were given reversal drugs at the end of operation. Among the 104 patients whose operation lasted more than 3 h, 49 (47.12%), 29 (27.88%), 10 (9.62%) and 1 (0.96%) had TOF < 0.9 at baseline and 15, 30 and 60 min, respectively. Among the 46 patients whose operation lasted for more than 3 h and was given reversal, 38 (82.61%), 23 (50%), 9 (19.57%) and 2 (4.35%) had TOF < 0.9 at baseline, 15, 30 and 60 min, respectively. Residual neuromuscular blockade may still be present even if the interval between last dose of muscle relaxant and measurement of TOF ratio at the PACU was long, however, less than that observed in short-interval surgeries.

DISCUSSION

Post-operative residual neuromuscular blockade (PRNMB) is based on correlation between signs and symptoms of muscle weakness after intraoperative use of non-depolarising NMBDs and TOF ratios. Train-of-four ratio of ≥ 0.9 is the new acceptable gold standard[5] since with TOF ratio of 0.7–0.9, impaired airway protective reflexes, higher risk of aspiration, upper airway obstruction, decrease hypoxic ventilator response and symptoms of muscle weakness still occurred.

Neuromuscular blocking agents are used to improve conditions for tracheal intubation, provide immobility during surgery and facilitate mechanical ventilation. It is important to ensure that the effects of these agents have worn off or are reversed before the patient regains consciousness.

The incidence of RNMB after single dose of intermediate acting non-depolarising neuromuscular blocking agents (NMBAs) was 45% and may persist after 2 h of stay in the PACU.[1] The risk was even higher in surgical procedures lasting for less than 2 h causing partial paralysis.[1] Recently, two common strategies are used to prevent RNMB, namely neuromuscular transmission monitoring and reversal of neuromuscular blockade using pharmacologic agents.[1]

Creation and implementation of guidelines for monitoring neuromuscular block is vital to all patients receiving NMBAs and its reversal to prevent post-operative residual paralysis[9] and its complications.

Recent studies mentioned sugammadex as an attractive reversal agent in preventing RNMB as it has been shown to be safer and more reliable than the traditional agents such as neostigmine.[10]

CONCLUSION

Administration of a single intubating dose of neuromuscular blocking drugs in a surgical procedure does not guarantee complete recovery of neuromuscular transmission. Residual neuromuscular blockade may still be present even after a long procedure. Patients who were given reversal agent do not guarantee complete recovery or less residual paralysis compared to those who did not receive the drug which necessitates further evaluation.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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