

High Incidence of Residual Curarization After Rocuronium Despite Administration of Neostigmine

Neostigmin Uygulamasına Rağmen Rokuronyum Sonrası Yüksek Rezidüel Kürarizasyon Oranları

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ABSTRACT Objective: The aim of the study was to investigate the incidence of postoperative residual curarization (PORC) after rocuronium administration using normalized acceleromyographic (AMG) train-of-four (TOF) ratios. **Material and Methods:** During propofol-fentanyl- nitrous oxide anesthesia, neuromuscular block was monitored using acceleromyography method in 130 patients. A TOF ratio measured at the end of control stimulation was recorded as a baseline TOF value. Neuromuscular block was induced with rocuronium 0.6 mg.kg⁻¹ and antagonized with neostigmine 40 µg.kg⁻¹ at the end of anesthesia. Immediately after the patients' arrival in the postanesthetic care unit (PACU), TOF ratios were measured and normalized (i.e., dividing the raw TOF ratio by the baseline TOF value). The incidences of PORC were determined according to three different TOF threshold values: Normalized AMG-TOF ratio <1; raw AMG-TOF ratio <1; and raw AMG-TOF ratio < 0.9. **Results:** The baseline AMG TOF ratios varied widely 110.8 (91-149) among patients. Considering normalized AMG-TOF ratios <1 as PORC, 77 (63.1%) patients had PORC on arrival to the PACU. Significantly fewer patients had raw TOF ratios < 0.9 (39 subjects, 31.9%), and <1 (67 subjects, 54.9%) than whose normalized TOF ratios <1 (77 subjects, 63.1 %) (p< 0.05). Although not statistically significant, the when it was determined using normalized AMG-TOF ratios rather than using raw AMG-TOF ratios (18.3% and 10%, respectively). **Conclusion:** Despite reversal of neuromuscular block with neostigmine, the incidence of PORC is very high after rocuronium administration.

Key Words: Monitoring, physiologic; rocuronium; complications; neuromuscular blockade

ÖZET Amaç: Bu çalışmada rokuronyum sonrası postoperatif rezidüel kürarizasyon (PORK) sıklığının normalleştirilmiş akseleromyografik (AMG) train-of-four (TOF) oranları kullanılarak belirlenmesi amaçlanmıştır. **Gereç ve Yöntemler:** Propofol-fentanil-nitroz oksit anestezisi sırasında, 130 hastada nöromusküler blok akseleromyografi yöntemiyle monitorize edildi. Kontrol stimülasyonu sonrasında ölçülen TOF oranı bazal TOF değeri olarak kabul edildi. Nöromusküler blok 0.6 mg.kg⁻¹ rokuronyumla sağlandı ve anestezinin sonunda 40 µg.kg⁻¹ neostigminle antagonize edildi. Hastalar postoperatif derlenme odasına geldikten hemen sonra TOF oranları ölçüldü ve normalleştirildi (ham TOF oranının bazal TOF değerine bölünmesiyle). PORK sıklığı üç farklı TOF eşik değerine göre belirlendi: Normalleştirilmiş AMG-TOF oranı < 1; ham AMG-TOF < 1 ve ham AMG-TOF oranı < 0.9. **Bulgular:** Bazal TOF oranları hastalar arasında geniş ölçüde değişkenlik gösterdi 110.8 (91-149). PORK, AMG- TOF oranı < 1 olarak kabul edildiğinde, postoperatif derlenme odasında 77 (%63.1) hastada PORK mevcuttu. Ham TOF oranları<0.9 (39 hasta, % 31.9) ve <1 olan (67 hasta, %54.9) hastaların sayısı normalleştirilmiş TOF oranları<1 olan hastalardan (77 hasta, %63.1) anlamlı olarak düşüktü (p< 0.05). İstatistiksel önemlilik düzeyine ulaşmasa da, şiddetli PORK (TOF<0.7) sıklığı normalleştirilmiş AMG-TOF oranları kullanılarak belirlendiğinde ham AMG-TOF oranlarıyla saptanan değerlere göre daha yüksekti (sırasıyla %18.3 ve %10). **Sonuç:** Neostigmin ile nöromusküler bloğun antagonize edilmesine rağmen rokuronyum sonrası PORK sıklığı son derece yüksektir.

Anahtar Kelimeler: Monitorizasyon, fizyolojik; rokuronyum; komplikasyon; nöromusküler blok

Residual neuromuscular curarization (PORC) in the recovery room is a well recognised phenomenon which can prolong postoperative recovery, impair airway protective reflexes and adversely effect respiratory function.^{1,2} Although the incidence of postoperative residual curarization is lower with intermediate acting neuromuscular blocking drugs such as rocuronium, vecuronium and atracurium when compared to long acting neuromuscular blocking drugs, it may still occur.²⁻⁹ The current generally accepted threshold value for exclusion of PORC is a mechanomyographic train-of-four (TOF) ratio of 0.9.

Due to its fast onset of action and safety profile, rocuronium is one of the most widely used relaxants in many countries.¹⁰ Previous studies determined the incidence of PORC following the administration of rocuronium.³⁻⁹ Despite antagonism of neuromuscular blockade at the end of surgery, up to 17-36% of patients given rocuronium arrived in the postanesthetic care unit (PACU) with objective evidence of PORC.^{3,4,6-9} Acceleromyography (AMG) was used in these previous studies and the acceleromyographic TOF (AMG-TOF) ratio threshold values used to define the presence of residual neuromuscular block were <0.7 ,³⁻⁵ <0.8 ,^{6,7} or <0.9 .^{4,5,8,9} However, the AMG-TOF ratio is often higher than that of the 'gold standard' mechanomyography, and AMG can not detect minor PORC.¹¹⁻¹³ As recently demonstrated by Eikermann et al. even a minor degree of PORC may have clinical consequences.¹⁴ It was demonstrated that recovery of the AMG-TOF ratio to unity and normalization or calibration is required to detect PORC reliably.¹¹ Normalization is the method which is based on correcting a raw TOF ratio displayed on the monitor screen of AMG during recovery by the baseline (control) TOF ratio.^{11,15-17} That is, if, for example, the control AMG-TOF ratio is 1.1, a displayed (raw) TOF value of 0.9 during recovery period corresponds to a normalized TOF ratio of 0.81. However, it is necessary to know the baseline TOF ratio to apply the normalization method. In this case, the simplicity of the automatic calculated TOF ratio is lost.

In the present study, our initial aim was to investigate the real incidence of residual block after rocuronium administration using normalized AMG-TOF ratios. The second aim was to compare the incidences of PORC determined according to the three different TOF threshold values: normalized AMG-TOF ratio <1 ; raw AMG-TOF ratio <1 ; and raw AMG-TOF <0.9 .

MATERIAL AND METHODS

The study protocol was approved by the local ethics committee and written informed consents were obtained from all patients. One hundred and thirty patients between the ages of 18 and 65 years, ASA physical status 1 or 2 requiring muscle relaxants during general anesthesia were enrolled in the study. The estimated duration of surgery was at least 1 h. Major surgeries associated with massive blood loss or fluid replacement were excluded. Patients were excluded from the study if they were suffering from hepatic, renal or neuromuscular disease. Pregnant women and patients receiving medications known to be capable of affecting normal neuromuscular transmission were also excluded. All patients were within 20% of ideal body weight. Premedication consisted of midazolam 0.04 mg.kg⁻¹ intravenously. Indirect blood pressure, heart rate, oxygen saturation by pulse oximetry, and end-tidal CO₂ were monitored in all patients. Anesthesia was induced with propofol 2-2.5 mg.kg⁻¹, and fentanyl 1-2 µg.kg⁻¹, and was maintained by a continuous infusion of propofol 3-4 mg.kg⁻¹.h⁻¹ and 70% nitrous oxide in oxygen. Following induction of anesthesia, a paired of electrodes was applied to the ulnar nerve at the wrist. Contraction of the adductor pollicis was assessed using acceleromyography (TOF Watch SX, Organon Ireland Ltd, Dublin, Ireland). The acceleration transducer was taped to the distal ventral part of the thumb, and the study arm was immobilized with a splint. The other fingertips were tightly fixed with tape. The arm board was adjusted to approximately a 70 degree abduction. 50 mA TOF stimulation (four pulses of 0.2 ms in duration, at a frequency of 2 Hz, 2 s in duration) was performed at the ulnar nerve every 15 s. The TOF ratio measured at the end of

control stimulation was recorded as a control value. Thereafter, each patient received a single intravenous bolus of rocuronium, $0.6 \text{ mg} \cdot \text{kg}^{-1}$ for tracheal intubation. Following tracheal intubation, the display of TOF Watch SX was covered by an adhesive tape. Maintenance doses of 10 mg rocuronium were administered if required. An upper extremity forced air warming device was placed on all patients to maintain nasopharyngeal temperature $>35^\circ\text{C}$ and arm temperature $>32^\circ\text{C}$. Ventilation was controlled to maintain normocapnia. When the surgical procedure was completed, anesthetic agents were discontinued and neuromuscular blockade was reversed with neostigmine $40 \mu\text{g} \cdot \text{kg}^{-1}$ and atropine $15 \mu\text{g} \cdot \text{kg}^{-1}$. The anesthetists were instructed to assess patients for adequacy of neuromuscular reversal using standard clinical criteria used in our department. Head lift five doconts or hand grip, eye opening on command and tidal volume $> 5 \cdot \text{kg}^{-1}$ were the minimal requirements, all other tests of residual paresis were at the discretion of the anesthetist conducting the case. When the anesthetist determined that full recovery of neuromuscular function was present, the trachea was extubated. The total doses of fentanyl, rocuronium and neostigmine, estimated blood loss, time intervals from the last dose of rocuronium to neostigmine administration, and from neostigmine administration to TOF measurements were recorded.

In the recovery room, an investigator blinded to the study protocol carried out assessment of residual block. The arm was put into the same position as control TOF ratio had been obtained. Four consecutive TOF measurements were obtained, and the average of the closest two values was recorded. Normalized TOFs were calculated by dividing the TOF noted on the acceleromyographic monitor display screen by the control value, as previously suggested.¹⁵

Patients were instructed in the use of 100 mm visual analog scale (VAS) score (from 0 mm= no pain to 100 mm= intractable pain) in the preoperative holding area. Before the patient left the recovery room, discomfort associated with neuromuscular stimulation was evaluated using VAS.

PORC was defined as a normalized TOF ratio less than 1. However, the incidences of PORC were determined according to the three different TOF threshold values: normalized AMG-TOF ratio <1 ; raw AMG-TOF ratio <1 ; and raw AMG-TOF <0.9 . The incidences of severe PORC were also determined according to the two different TOF threshold values: normalized AMG-TOF ratio <0.7 and raw AMG-TOF ratio <0.7 .

Data are expressed as the number of patients, mean \pm SD or median, and range. Results were considered statistically significant when $p \leq 0.05$. A student's t-test was used to analyse patient characteristics (patient demographics or perioperative variables), and to compare the patients with and without PORC. Chi-square test was used for categorical variables. Fisher's exact test was used when expected values were below five. The proportions of subjects having TOF ratios less than the predefined threshold values in the PACU were analyzed using McNemar's chi-squared test. The sensitivity, specificity and predictive values of raw AMG-TOFs <0.9 and 1 to detect PORC (defined as a normalized TOF ratio <1) were calculated according to standard formulae, and values were expressed as percentage and 95% CI.¹⁸

RESULTS

Of the 130 patients, six were excluded because their core temperature was low ($<35^\circ\text{C}$) when they arrived to PACU, and another two patients were also excluded for missing data on important variables. There was no significant difference between the patients with and without PORC with respect to patient demographics or perioperative variables with student's t test (unshown data). Patient demographics and perioperative variables are presented for the whole patient group in Tables 1 and 2, respectively.

The baseline TOF ratio was 110.8 (91-149). The baseline TOF ratios of 1.01 and above were present in 71 (58.1%) patients. However, the baseline TOF ratios of 99 and below (91-98) were seen in 29 (23.7%) patients.

Considering normalized AMG-TOF ratios <1 as PORC, 77 (63.1%) patients had PORC on arrival

Sample size	122
Age (yr)	44.8 ± 12.5
Sex (M/F)	35/87
ASA physical status(I/II)	76/46
Weight (kg)	69.6 ± 11.6
Height (cm)	162.4 ± 9.9
Operative procedures	
General	42
Gynecologic	28
Plastic	16
Neurologic	24
Orthopedic	6
Urological	6

Fentanyl dose (µg)	133.3 ± 96.8
Rocuronium dose (mg)	51.7 ± 12.5
Number of redoses of rocuronium	0 (0-4)
Patients receiving rocuronium within 45 min of neostigmine	5 (4.1%)
Time from last dose of rocuronium to injection of neostigmine (min)	79.3 ± 25.1
Neostigmine dose to TOF measurement (min)	16.3 ± 7.7
Dose tramadol (mg)	104.1 ± 37.7
Duration of anesthesia (min)	138.4 ± 51.2
Blood loss (mL)	381 ± 328
Temperature at the end of procedure (°C)	35.6 ± 0.45

Data are mean ± SD, median (range), or number of patients (%).
TOF: Train-of-four.

to the PACU. Significantly fewer patients had raw TOF ratios <0.9 (39 subjects, 31.9%), and <1 (67 subjects, 54.9%) when compared to the ones with normalized TOF ratios <1 (77 subjects, 63.1) (Tablo 3, p< 0.05).

The incidence of severe PORC (TOF <0.7) was higher when normalized AMG-TOF ratios were

taken into consideration rather than the raw values (18.3% and 10%, respectively), even though the difference did not reach statistical significance (Table 3).

When PORC was defined as a normalized TOF ratio less than 1, PORC was present in 100% of patients whose raw TOF ratios were <0.9 (positive predictive value, Table 4). However, complete recovery (normalized TOF ratio ≥1) was seen in 45 (54.2%) of the 83 patients who had raw AMG-TOF ratios ≥ 0.9 (Negative predictive value, Table 4). Among 67 patients who had raw TOF ratios <1, 62 (92.5%) patients also had normalized TOF ratios <1 (positive predictive value, Table 4). Among 55 patients who had raw TOF ratios ≥1, 39 (70.9%) also had normalized AMG TOF ratios ≥1 (negative predictive value, Table 4).

Only five (4.1%) patients remembered TOF measurements that were performed in the PACU. The mean VAS score in these five patients was 24 ± 23 mm.

DISCUSSION

The time interval from tracheal extubation to complete recovery of neuromuscular function is a relatively unsafe period during which the patients may be at risk for adverse respiratory events. PORC has been found as an important contributing factor in the development of critical respiratory events including upper airway obstruction and hypoxemia during this immediate postoperative period resulting in pulmonary complications.^{8,19} Recovery of neuromuscular function should be achieved prior to tracheal extubation to ensure acceptable recovery of pharyngeal and respiratory muscle strength and to reduce the risk of respiratory complications. Recovery of neuromuscular function including nor-

	Normalized TOF ratio <1	Raw TOF ratio <0.9	Raw TOF ratio <1
The incidence of PORC	77 (63.1%)*	39 (31.9%)	67 (54.9%)
	Normalized TOF ratio <0.7	Raw TOF ratio <0.7	
The incidence of severe PORC	22 (18.3)	12 (10%)	

*Significantly different from those of raw TOF ratios of 0.9 and 1 (p< 0.05).
PORC: Postoperative residual curarization.
TOF: Train-of-four.

TABLE 4: Sensitivity, specificity and predictive values of AMG-TOF of 0.9 and 1 to detect PORC (defined as a normalized AMG-TOF ratio less than 1).

AMG TOF ratio	Sensitivity	Specificity	Negative predictive value	Positive predictive value
0.9	50% (41.1-58.9)	100% (100-100)	54.2% (46-64)	100% (100-100)
1	79.5% (72.3-86.7)	88.6% (83-94.2)	70.9% (62.8-79)	92.5% (87.8-97.2)

Values are presented as percent and 95% confidence interval.

AMG-TOF: Acceleromyographic train-of-four.

mal pharyngeal function requires a mechanomyographic adductor pollicis TOF ratio of 0.9 or greater.¹³ Moreover, when a mechanomyographic TOF ratio is <0.9, there is a significant decrease in carotid body chemosensitivity to hypoxia. However, AMG is the most widely used method for monitoring neuromuscular function. The baseline AMG-TOF ratio often exceeds 1 and it is difficult to exclude a mechanomyographic TOF value <0.9. Even though TOF recovery to 1 has been recommended to exclude PORC reliably when using AMG, the average baseline TOF ratio is higher than 1 and the recovery of raw AMG-TOF ratio to 1 can not assure adequate neuromuscular function in every patient.¹⁴ Impaired FIV1, high MEF50/MIF50 ratio, and difficult swallowing may occur at a raw AMG-TOF ratio of 1.¹⁴ A previous study aimed to determine the AMG TOF ratio that detects PORC (defined as a mechanomyographic TOF <0.9) with a 95% probability.¹¹ The negative predictive value of normalized AMG TOF of 0.9 in detecting PORC (defined as a mechanomyographic TOF ratio less than 0.9) was found as 89% (95% CI, 70-98), which did not allow reliable detection of PORC.¹¹ Thus, TOF recovery to 1 and normalization or calibration have been recommended to exclude PORC reliably when using AMG.¹¹ In the current study, PORC was defined as a normalized AMG-TOF ratio smaller than 1, and the incidence of PORC was found very high (64%). In other words, only about 36% of the patients had recovered completely in the PACU approximately 16 min after neostigmine administration. The incidence of severe PORC (TOF <0.7) was also higher when normalized AMG-TOF ratios were taken into consideration rather than the raw values (18.3% and 10%, respectively), even though the difference did not reach statistical significance. These results constitute additional evidence for alarmingly high incidences of PORC.

In previous studies, the incidence of PORC was investigated using AMG in patients following rocuronium administration.³⁻⁹ After a single dose of rocuronium and no reversal, the incidence of PORC (defined as a raw AMG-TOF <0.9) was found as 45% on arrival in the PACU.⁵ Kim et al. investigated PORC (defined as a raw TOF ratio <0.7) after administration of either rocuronium or vecuronium with reversal by pyridostigmine in 602 consecutive patients.³ Twenty percent of patients had a TOF <0.7 in the recovery room.³ Despite a protocol designed to limit PORC (careful intraoperative management of rocuronium administration, monitoring, and administration of reversal agent at a TOF count of 2), Murphy et al. showed that 32% of patients had PORC (defined as a raw AMG-TOF ratios <0.9) in the PACU.⁴ In the current study, despite reversal with neostigmine, the incidence of PORC (defined as a normalized AMG-TOF <1) was found as 64%. However, if PORC had been defined as a raw AMG-TOF <0.9, the incidence of PORC would have been found as low as 31.9 in the PACU, similar to the study conducted by Murphy et al.⁴ In this case, slight levels of residual paralysis (mechanomyographic TOF ratio 0.7-0.9) can not be reliably detected.

The avoidance of long acting neuromuscular blocking drugs, the use of routine neuromuscular monitoring in the operating room, the avoidance of total twitch suppression, and the reversal of neuromuscular blockade at a TOF count of 2-3 decrease the incidence of PORC.³ Incidence of residual block increases with reduced core temperature, use of pyridostigmine (which is less potent than neostigmine), large doses of neuromuscular blocking drug relative to the duration of surgery, short intervals between administration of last dose of neuromuscular blocking drug to antagonize neuromuscular block, and antagonism to extubation.^{3,19} In the

present study, neuromuscular block was not monitored from rocuronium administration in the operating room until TOF measurement in the PACU, and this could have contributed to the high incidence of PORC. The protocol of this study was designed to reflect standard clinical practice in our clinic. Neuromuscular monitoring is used mostly in the PACU in our clinic, and PORC is defined as raw TOF ratio <0.9 . We wanted to know the positive and negative predictive values of raw AMG-TOFs <0.9 and 1 , when a normalized AMF-TOF ratio of 1 was accepted as the threshold value to exclude PORC. Second, the average time interval between neostigmine administration and TOF measurement was relatively short (16 min) in the current study. It is well known that the incidence of PORC may be reduced if antagonism of neuromuscular blockade is initiated 20-30 min before tracheal extubation.¹⁹

The baseline AMG-TOF ratios varied widely [110.8 (91-149)] in the current study, similar to previous studies.^{11,16,17,20} Even though the baseline TOF ratios were >1 in 71 (58.1%) patients, they were <1 in 29 (23.7%) patients. Thus, if PORC had been considered as a raw TOF ratio less than 1 in this study, five patients would have been erroneously accepted as having PORC (positive predictive value; 92%). The negative predictive value of raw AMG TOF of 1 was better than that of 0.9 (70.9% and 54%, respectively). The positive predictive value of raw AMG-TOF of 0.9 was 1 , but its sensitivity was low (50%) and its negative predictive value (54%) was not reliable enough to detect PORC.

Even though raw TOF ratios are helpful in detecting PORC, it seems, due to wide variation of baseline TOF ratios (91-149), that it is not possible

to detect PORC reliably without measurement of baseline TOF ratio. We believe that this result constitutes additional evidence necessary to monitor neuromuscular function before administration of neuromuscular blocking drugs until complete recovery of neuromuscular function. However, in clinical practice, AMG monitoring is often applied subsequent to the administration of neuromuscular blocking drugs, without having had an initial calibration. In this situation, because its negative predictive value is higher than 0.9 , the TOF threshold ratio for residual block should be 1 instead of 0.9 .

The stimulating current was manually set at 50 mA in the current study. A stimulation current of at least 45 mA is required for accuracy and precision of TOF monitoring.²¹

Fifty mA may result in painful muscle contractions in awake, unpremedicated patients. In a previous study,⁴ TOF stimulating currents of 50 mA were used in patients in the PACU. Only nine (8%) patients recalled TOF measurements and mean VAS scores in these patients were 25 ± 13 mm.⁴ Similarly, five (4.1%) patients recalled TOF measurements and mean VAS scores were 24 ± 23 mm on a 100 mm scale in the current study. Probably, due to analgesic and amnesic effects of anesthetic agents persist in the immediate recovery period, TOF measurements did not disturb most of the patients.

In conclusion; despite reversal with neostigmine, the incidence of PORC is very high during the early PACU admission. Due to wide variation of baseline TOF ratios by AMG, it is not possible to detect PORC reliably without measurement of baseline TOF ratio.

REFERENCES

1. Arbous MS, Meursing AE, van Kleef JW, de Lange JJ, Spoormans HH, Touw P, et al. Impact of anesthesia management characteristics on severe morbidity and mortality. *Anesthesiology* 2005;102(2):257-68.
2. Karmarkar SG, Divatia JV, Kulkarni AP, Patil VP, Mehta P. Residual neuromuscular blockade in the recovery room: Does the choice of the muscle relaxants matter?. *J Anaesth Clin Pharmacol* 2006;22(1):21-6.
3. Kim KS, Lew SH, Cho HY, Cheong MA. Residual paralysis induced by either vecuronium or rocuronium after reversal with pyridostigmine. *Anesth Analg* 2002;95(6):1656-60.

4. Murphy GS, Szokol JW, Marymont JH, Franklin M, Avram MJ, Vender JS. Residual paralysis at the time of tracheal extubation. *Anesth Analg* 2005;100(6):1840-5.
5. Debaene B, Plaud B, Dilly MP, Donati F. Residual paralysis in the PACU after a single intubating dose of nondepolarizing muscle relaxants with an intermediate duration of action. *Anesthesiology* 2003;98(5):1042-8.
6. Gätke MR, Viby-Mogensen J, Rosenstock C, Jensen FS, Skovgaard LT. Postoperative muscle paralysis after rocuronium: less residual block when acceleromyography is used. *Acta Anaesthesiol Scand* 2002;46(2):207-13.
7. Hayes AH, Mirakhor RK, Breslin DS, Reid JE, McCourt KC. Postoperative residual block after intermediate acting neuromuscular blocking drugs. *Anaesthesia* 2001;56(4):312-8.
8. Murphy GS, Szokol JW, Marymont JH, Greenberg SB, Avram MJ, Vender JS, et al. Intraoperative acceleromyographic monitoring reduces the risk of residual neuromuscular blockade and adverse respiratory events in the postanesthesia care unit. *Anesthesiology* 2008;109(3):389-98.
9. Maybauer DM, Geldner G, Blobner M, Pühringer F, Hofmockel R, Rex C, et al. Incidence and duration of residual paralysis at the end of surgery after multiple administrations of cisatracurium and rocuronium. *Anaesthesia* 2007;62(1):12-7.
10. Özcengiz D. [Neuromuscular blockers]. *Türkiye Klinikleri J Anest Reanim* 2005;3(3):116-30.
11. Capron F, Alla F, Hottier C, Meistelman C, Fuchs-Buder T. Can acceleromyography detect low levels of residual paralysis? A probability approach to detect a mechanomyographic train-of-four ratio of 0.9. *Anesthesiology* 2004;100(5):1119-24.
12. Claudius C, Viby-Mogensen J. Acceleromyography for use in scientific and clinical practice: a systematic review of the evidence. *Anesthesiology* 2008;108(6):1117-40.
13. Murphy GS. Residual neuromuscular blockade: incidence, assessment, and relevance in the postoperative period. *Minerva Anestesiol* 2006;72(3):97-109.
14. Eikermann M, Groeben H, Hüsing J, Peters J. Accelerometry of adductor pollicis muscle predicts recovery of respiratory function from neuromuscular blockade. *Anesthesiology* 2003;98(6):1333-7.
15. Kopman AF. Measurement and monitoring of neuromuscular blockade. *Curr Opin Anaesthesiol* 2002;15(4):415-20.
16. Suzuki T, Fukano N, Kitajima O, Saeki S, Ogawa S. Normalization of acceleromyographic train-of-four ratio by baseline value for detecting residual neuromuscular block. *Br J Anaesth* 2006;96(1):44-7.
17. Kopman AF. Normalization of the acceleromyographic train-of-four ratio. *Acta Anaesthesiol Scand* 2005;49(10):1575-6.
18. Dawson-Saunders B. Estimating and comparing proportions. In: Dawson-Saunders B, Trap RG, editors. *Basic and Clinical Biostatistics*. 2nd ed. London: Prentice-Hall International Inc; 1994. p.43.
19. McCaul C, Tobin E, Boylan JF, McShane AJ. Atracurium is associated with postoperative residual curarisation. *Br J Anaesth* 2002;89(5):766-9.
20. Kopman AF, Chin W, Cyriac J. Acceleromyography versus electromyography: an ipsilateral comparison of the indirectly evoked neuromuscular response to train-of-four stimulation. *Acta Anaesthesiol Scand* 2005;49(3):316-22.
21. Helbo-Hansen HS, Bang U, Nielsen HK, Skovgaard LT. The accuracy of train-of-four monitoring at varying stimulating currents. *Anesthesiology* 1992;76(2):199-203.