Postoperative Residual Curarization: Clinical Observation in the Post-anesthesia Care Unit

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Background: Neuromuscular blocking agents (NMBAs) are widely used during the induction and maintenance of anesthesia. Postoperative residual curarization (PORC) following the use of NMBAs still occurs even though intermediate-acting NMBAs were used. Train-of-four (TOF) stimulation is used to quantify the degree of neuromuscular blockade. The TOF ratio of 0.7 in the adductor pollicis muscle was associated with normal respiratory function. Pharyngeal function returned to normal while the TOF ratio reached 0.9. The aim of this study was to survey the PORC in the post-anesthesia care unit (PACU).

Methods: In this observational study, 308 patients who received general anesthesia with NMBAs were enrolled. Residual curarization was evaluated using the TOF-Watch acceleromyograph upon arrival in the PACU. Three consecutive TOF stimulations were applied and recorded at 15-second intervals. Two thresholds of TOF ratios (0.9 and 0.7) were used to assess the presence of residual curarization.

Results: TOF ratios less than 0.7 and 0.9 were observed in 15 (5%), and 97 (31%) patients, respectively. The differences of the TOF ratios between the male and female patients were significant ($p = 0.014$). In terms of weight, the differences between the patients with ratios > 0.9 and $\leqq 0.9$ were significant ($p = 0.013$). There were 67, 49, 15, and three patients who received reversal medication in the > 0.9 group, $\leqq 0.9$ and > 0.7 group, and $\leqq 0.7$ group, respectively. The differences of the TOF ratios between the patients who received and those who did not receive reversal medication were not significant ($p = 0.91$).

Conclusion: PORC is still a clinical problem in the modern PACU. Objective neuromuscular monitoring needs to be performed to ensure patient safety.
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Key words: postoperative residual curarization, neuromuscular blocking agents, neuromuscular monitoring, train-of-four stimulation

Neuromuscular blocking agents (NMBAs) are widely used to facilitate endotracheal intubation during induction of anesthesia and to provide adequate muscle relaxation during operations. However, residual postoperative paralysis following the use of NMBAs, known as postoperative residual curarization (PORC), may result in morbidity and mortality. Theoretically, the incidence of PORC should be reduced with the use of short-acting or intermediate-acting NMBAs, but PORC still occurred even though intermediate-acting NMBAs were used.[1,2] Prevention of PORC depends on meticulous clinical assessment, neuromuscular block monitoring, use of short-acting or intermediate-acting NMBAs, and administration of appropriate reversal medication, such as anticholinesterases. Since the response of Train-of-four (TOF) stimulation of a peripheral nerve is commonly used to quantify the degree of neuromuscular blockade without prior establishment of a control response, it is widely used to identify residual curarization. In 1970, Ali *et al*.[3] reported that a TOF ratio (T4/T1 twitch ratio) of 0.7 in the mechanical adductor pollicis muscle was associated with normal respiratory function while a TOF ratio less than 0.6 correlated with obvious muscle weakness such as ptosis and tracheal tug. The threshold was increased to 0.9 according to recent observations.[4,5] Eriksson *et al*.[4] showed that pharyngeal function did not return to normal until the adductor pollicis TOF ratio reached 0.9. A four- to five-fold increase in the incidence of misdirected swallowing and aspiration was seen in awake, nonanesthetized volunteers that had TOF ratios less than 0.9.[6] In our study, we examined the TOF ratios of patients upon arrival in the postanesthesia care unit (PACU) to survey the PORC in the PACU.

METHODS

This is a prospective, nonrandomized, and observational study. All patients who had undergone general anesthesia with the use of NMBAs were enrolled. The choice of the anesthetic protocol was left to the anesthesiologist in charge of the patient, who was unaware that the patient was to be evaluated. Only two kinds of competitive NMBAs were used in our department, namely, rocuronium and cisatrcurium, and both are intermediate-acting NMBAs.

Upon arrival in the PACU, if the patients met the inclusion criteria, residual curarization was immediately evaluated using TOF-Watch (TOF-Watch acceleromyograph, Organon Teknika, The Netherlands). The ulnar nerve was stimulated with TOF stimulation (4 pulses 0.2 ms in duration, at a frequency of 2 Hz). A supra-maximal stimulation of 50 mA was applied. Three consecutive TOF stimulations were applied and recorded at 15-second intervals. The evoked responses at the thumb were calculated and two thresholds of the TOF ratio (0.9 and 0.7) were used to assess the presence of a residual neuromuscular blockade.

Patient characteristics were expressed as mean ± SD. The Student's t-test was used to compare the patients with and without PORC. Results were considered statistically significant when $p \leqq 0.05$.

RESULTS

Three hundred and eight patients met the inclusion criteria and were evaluated. Demographic data of these patients are shown in Table 1. Among the 308 patients, 211 (69%) had TOF ratios higher than 0.9, 82 (27%) had TOF ratios lower than 0.9 and higher than 0.7, and 15 (5%) had TOF ratios lower than 0.7 upon arrival in the PACU. No significant differences were seen among the ages of these three groups (52.63 ± 17.49 vs 51.06 ± 17.65 $p = 0.49$; 52.63 ± 17.49 vs. 55.73 ± 14.91 $p = 0.45$; 51.06 ± 17.65 vs 55.73 ± 14.91 $p = 0.29$).

In a total of 126 male patients, 28 (22%) showed TOF ratios lower than 0.9 and four (3%) were lower than 0.7. In a total of 182 female patients, 69 (38%) had TOF ratios lower than 0.9 and 11 (6%) were lower than 0.7. The differences of TOF ratios the between male and female patients was significant ($p = 0.014$).

Table 1. Patient Characteristics

TOF ratio	Total	> 0.9	$\leqq$ 0.9 and > 0.7	$\leqq$ 0.7
Number (n)	308	211	82	15
Age (years)	52.36±17.39	52.63±17.49	51.06±17.65	55.73±14.91
Sex (M/F)	126/182	98/113	24/58	4/11
Weight (kg)	62.80±11.62	61.73±11.85	65.20±10.83	65.60±18.03
Received reverse before extubation (n)	67	49	15	3

Data are mean ± SD or number of patients.

In terms of weight, the differences between those with TOF ratios > 0.9 and those with TOF ratios $\leqq$ 0.9 was significant (61.73 $\pm$ 11.85 vs 65.14 $\pm$ 10.81 p = 0.013). However, the average weight did not differ significantly between those with TOF ratios $\leqq$ 0.7 and those with TOF ratios > 0.9 (61.73 $\pm$ 11.85 vs 65.60 $\pm$ 18.03 p = 0.31). The average weight difference between those with TOF ratios $\leqq$ 0.7 and those with TOF ratios $\leqq$ 0.9 and > 0.7 was also not significant (65.20 $\pm$ 10.83 vs 65.60 $\pm$ 18.03 p = 0.89).

All patients included in this study were extubated prior to transfer to the PACU. Before extubation, there were 67, 49, 15, and three patients who received reversal medication, in those with TOF ratios > 0.9, $\leqq$ 0.9, > 0.7, and $\leqq$ 0.7, respectively. Of the 241 patients who did not receive reversal medication, 80 (33%) showed TOF ratios lower than 0.9, and 12 (5%) showed TOF ratios lower than 0.7. Of the 67 patients who received reversal medication, 17 (25%) showed TOF ratios lower than 0.9, and three (4%) showed TOF ratios lower than 0.7. The difference of the TOF ratios between the patients who received and did not receive reversal medications was not significant (p = 0.91).

DISCUSSION

Muscle relaxants are given to facilitate tracheal intubation and to maintain an adequate level of paralysis according to surgical need. Since 1979, residual neuromuscular blockade has been pointed out in patients in the PACU.[7] The incidence of PORC correlated with the duration of the NMBAs. The longer the duration, the more frequent the occurrence of PORC.[8] Despite the widespread use of intermediate-acting NMBAs (vecuronium, rocuronium, atracurium, and cisatracurium), PORC is still frequent in the PACU.[9-11]

Residual paralysis can be assessed using clinical tests. Test results such as eye opening, tongue protrusion, and coughing ability are unreliable. The ability to sustain head lift, leg lift, or strong hand grip for more than 5 seconds proved to be reliable indicators of recovery.[12] However, to assess neuromuscular function with these clinical tests requires that patients are awake, cooperative, and without the residual effects of other anesthetic medication upon arrival in the PACU.[13] These conditions are not always possible to achieve. The accelerometry of the TOF ratios in the adductor pollicis muscle is a more useful objective monitoring technique to evaluate PORC than the subjective visual/tactile assessment methods.[14,15] At the TOF ratio of 0.7, the respiratory mechanics (vital capacity, peak expiratory flow rate) return to near control values[16] but the hypoxic ventilatory response is reduced by 30% in awake volunteers.[17] However, the time course of the pharyngeal dysfunction and dyscoordination is markedly longer than that of the peripheral skeletal muscle groups, such as the diaphragm, larynx, hand, and face.[18,19] Partial paralysis can reduce pharyngeal muscle tone and disturb swallowing patterns.[6] This may result in upper airway obstruction and tracheal aspiration. The airway protection and control are not recovered until an adductor pollicis TOF ratio of 0.9 is reached.[4,6]

Viby-Mogenson *et al*.[7] reported that 42% of the patients have TOF ratio < 0.7 following the use of long-acting NMBAs. Murphy *et al*.[20] reported that among 34 patients who received the intermediate-acting NMBA, rocuronium, 5.9% arrived in the PACU with TOF ratios lower than 0.7 and 29% with TOF ratios lower than 0.9. Our observations were similar to those of Murphy *et al*.[20] showing 5% with TOF ratios lower than 0.7 and 31% with TOF ratios lower than 0.9 upon arrival in the PACU. Our results further showed that female patients tended to have higher rates of PORC than male patients.

Reversal medication is administered at the end of anesthesia to avoid partial paralysis. Anticholinesterases have limited effect against profound blockade because they do not reverse muscle blockade but instead act as competitive agents which increase the agonist concentration to overcome neuromuscular blockade.[21] Our results confirmed that the differences of the TOF ratios between patients who received and did not receive reversal medication were not significant. Hayes *et al*.[12] also reported that there were no significant differences in the incidences of PORC between patients who did or did not reverse their blockades. The administration of reversal medication did not guarantee the lack of partial paralysis in all patients.

The methods for reducing the incidence of PORC were mentioned by Viby-Mogensen *et al*.[5] First, long-acting NMBAs should not be used. Second, the blockade should be antagonized at the end of the procedure, but reversal should not be initi-

ated before two and preferably three or four responses to TOF stimulation are given. If a nerve stimulator is not available, antagonism should not be attempted unless spontaneous muscle activity is present. Third, if a nerve stimulator is available, tactile evaluation of responses to double-burst stimulation (DBS) is preferred over tactile evaluation of the response to TOF stimulation during recovery because it is easier to feel fade in the DBS than in the TOF response. Finally, the clinical signs and symptoms of residual block should be considered in relation to the response to nerve stimulation.

As our results, PORC is still a clinical problem despite the use of intermediate-acting NMBAs. Objective neuromuscular monitoring is an evidence-based practice. It is non-invasive and has little risk. At best, this measurement needs to be performed in the operating room before extubation rather than in the PACU to ensure patient safety.

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術後箭毒殘餘：麻醉後恢復室之臨床觀察

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背 景： 肌肉鬆弛劑在誘導及維持麻醉被廣泛的使用，即使使用中效型肌肉鬆弛劑，手術後箭毒殘餘依然可能發生。4 次成串刺激 (train-of-four stimulation) 可應用於監測肌肉鬆弛劑的殘餘作用，對內收拇肌 4 次成串刺激比值 0.7 與正常呼吸功能恢復相關，4 次成串刺激比值恢復至 0.9，喉部肌肉功能可恢復正常，本篇文章目的爲檢視麻醉後恢復室病患術後箭毒殘餘情形。

方 法： 在這篇臨床觀察研究中，308 名接受全身麻醉並使用肌肉鬆弛劑病患接受評估，箭毒殘餘以 4 次成串刺激在病患送入麻醉後恢復室時予以評估，每位病患皆施以連續 3 次間隔 15 秒的 4 次成串刺激，兩個標準值 (0.9 和 0.7) 用於評估箭毒殘餘情形。

結 果： 分別有 15 名 (5%) 及 97 名 (31%) 病患被觀察到 4 次成串刺激比值小於 0.7 及小於 0.9。4 次成串刺激比值在男性病患與女性病患間有顯著差異 ($p = 0.014$)，在 4 次成串刺激比值 > 0.9 和 ≦ 0.9 病患體重間有明顯差別 ($p = 0.013$)；在全部病患中，4 次成串刺激比值在全部病人、> 0.9、≦ 0.9 且 > 0.7、及 ≦ 0.7 的病患分別有 67，49，15，及 3 名病患接受肌肉鬆弛劑反轉藥物，4 次成串刺激比值在接受與無接受肌肉鬆弛劑反轉藥物病患間並無顯著差異 ($p = 0.91$)。

結 論： 手術後箭毒殘餘在現代麻醉後恢復室依然是一個臨床問題，爲了保證病患安全，客觀的神經肌肉功能監測是必需的。
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關鍵詞： 手術後箭毒殘餘，神經肌肉阻斷劑，神經肌肉監測，4 次成串刺激