GKDA Derg 22(1):24-28, 2016
doi:10.5222/GKDAD.2016.028

Klinik Çalışma

Postoperative Residual Curarization in Postanesthesia Care Unit: Relationship with Clinical Tests

Gonca OĞUZ*, Süheyla ÜNVER*, Gülşah AÇIKGÖZ*, Oruç Emre SOLMAZ*, Yeliz İrem TUNÇEL*

ABSTRACT

Introduction: The residual effects of neuromuscular blocking agents may persist into early postoperative period. Although train-of-four stimulation is used to evaluate the degree of neuromuscular blockade, many anesthetists still prefer clinical tests. A train-of-four ratio of 0.9 is accepted as a threshold for adequate respiratory function. In this study, the incidence of postoperative residual curarization in postanesthesia care unit and the relation of train-of-four ratios with clinical tests were investigated.

***Material and Method:** A total of 128 patients who underwent surgical procedures under general anesthesia were included in the study. Residual curarization was assessed using train-of-four monitorization upon arrival in the postanesthesia care unit. At the same time, the skills of lifting one's head for 5 min, eye opening, hand grip and tongue protrusion were evaluated. Need for additional neostigmine, verbal or mechanical stimulation for respiration and reintubation were also recorded.*

***Results:** Train-of-four ratios of ≤0.7, 0.7-0.9, and ≥9 were detected in 18%, 32.8%, and 49.2% of the patients, respectively. Train-of-four values showed weak-moderate positive correlation with head lift, and hand grip. The correlation coefficient was most significant with head lift (0.318, p=0.000). A negative correlation existed with American Society of Anesthesiologists classification (-0.289, p=0.001). Eleven of 23 patients with train-of-four ratios of ≤0.7 were able to sustain 5s head lift, while the number increased to 56 of 63 when train-of-four ratio was ≥0.9.*

***Discussion and Conclusion:** Incomplete recovery from neuromuscular blocking agents is an important problem in postoperative care units. The clinical tests are not well correlated with postoperative residual paresis. Objective neuromuscular monitoring and optimal reversal must be performed to improve patient outcomes.*

Keywords: *postoperative, residual curarization, neuromuscular monitorization*

ÖZ

Postanestezi Bakım Ünitesinde Görülen Postoperatif Rezidüel Kürarizasyon: Klinik Testlerle İlişkisi

***Amaç:** Nöromusküler blokörlerin rezidüel etkileri erken postoperatif döneme uzayabilir. Nöromusküler bloğun derecesini değerlendirmede train-of-four stimülasyonu kullanılmakla beraber, birçok anestezist hâlâ klinik testleri tercih etmektedir. Yeterli solunum fonksiyonu için train-of-four oranının eşik değeri 0.9 olarak kabul edilmektedir. Bu çalışmada, postanestezi bakım ünitesinde görülen postoperatif rezidüel kürarizasyon sıklığı ve train-of-four oranlarının klinik testlerle ilişkisi araştırıldı.*

***Gereç ve Yöntem:** Çalışmaya genel anestezi altında cerrahi girişim uygulanan 128 hasta dâhil edildi. Rezidüel kürarizasyon postanestezi bakım ünitesinde train-of-four stimülasyon ile ölçüldü. Aynı zamanda, 5 saniye başını kaldırabilme, göz açma, el sıkma ve dil çıkarma becerileri de değerlendirildi. Ek neostigmin gereksinimi, solunum için sözel veya mekanik stimülasyon ve reentübasyon kaydedildi.*

***Bulgular:** Hastaların %18'inin train-of-four oranı ≤0.7, % 32.8'i 0.7-0.9 ve %49.2'si ≥0.9'du. Train-of-four oranları baş kaldırma ve el sıkmayla zayıf-orta derecede pozitif korelasyon gösterdi. Korelasyon katsayısı en fazla baş kaldırmayla anlamlıydı (0.318, p=0.000). Amerikan Anestezistler Derneği sınıflandırması ile korelasyon negatif olarak bulundu (-0.289, p=0.001). Train-of-four oranı ≤0.7 olan 23 hastanın 11'i 5 saniye baş kaldırabilirken, train-of-four ≥0.9 olduğunda bu sayı 63 hastada 56'ya yükseldi.*

***Tartışma ve Sonuç:** Postoperatif bakım ünitelerinde nöromusküler blokörlerden yetersiz derlenme önemli bir sorundur. Klinik testler postoperatif rezidüel parezi ile iyi korelasyon göstermemektedir. Hasta sonuçlarını iyileştirmek için objektif nöromusküler monitörizasyon ve optimal antagonizma uygulanmalıdır.*

Anahtar kelimeler: *postoperatif, rezidüel kürarizasyon, nöromusküler monitörizasyon*

Alındığı tarih: 16.02.2016
Kabul tarihi: 17.03.2016
* Dr. A.Y. Ankara Onkoloji Eğitim ve Araştırma Hastanesi, Anesteziyoloji ve Reanimasyon Kliniği
Yazışma adresi: Doç. Dr. Gonca Oğuz, Hukukçu Dostlar Sitesi 495. Sok. No: 13 Çayyolu / Ankara
e-mail: goncatuncel@hotmail.com

INTRODUCTION

Neuromuscular blocking agents (NMBAs) are commonly used by the anesthetists to facilitate endotracheal intubation during induction of anesthesia and to provide adequate muscle relaxation during surgery. The residual effects of NMBAs may persist into the early postoperative period despite the use of monitorization and reversal agents [1]. Although the clinical importance of the residual neuromuscular blockade (NMB) in the postanesthesia care unit (PACU) has been pointed out since 1979, there are still 33-64% incidence rates of inadequate neuromuscular recovery of patients on arrival to the PACU [3-7].

Train-of-four (TOF) stimulation of a peripheral nerve is commonly used to evaluate the degree of neuromuscular blockade without the necessity of first establishing control or baseline values. A few decades ago, a TOF ratio of 0.7-0.8 was proposed as the acceptable level for adequate respiratory function. The threshold was increased to 0.9 as it was demonstrated in volunteer studies that TOF fade ratios of <0.7-0.9 are associated with upper airway obstruction, [6] inadequate recovery of pulmonary function, [6] reduced pharyngeal muscle coordination, an increased risk for aspiration [8] and an impaired hypoxic ventilatory response [9]. On routine basis, most of the clinicians use clinical tests to assess the level of recovery from neuromuscular blockade at the end of anesthesia [10]. Unaware of the insufficiency of such tests to show up significant degrees of NMB, ability to sustain head lift or hand grip for 5s, eye opening, tongue protrusion or leg lift are widely used without quantitative monitoring of NM function.

The primary aim of the present study was to detect the incidence of postoperative residual curarization in PACU. The relation of TOF ratios with clinical tests were also evaluated as second outcome measures.

MATERIALS and METHODS

This prospective, non-randomized study was approved by institutional ethics committee and written informed consent was obtained from all subjects. One hundred and thirty patients scheduled for surgical procedures requiring the use of NMBAs were enrolled in the study. Exclusion criteria included presence of morbid obesity, neuromuscular disease, use of drugs known to interfere with neuromuscular transmission, severe renal or hepatic dysfunction.

The choice of the premedication, anesthetic protocol, reversal use to antagonize NMBAs and extubation criteria were at the discretion of the anesthesiologist in charge of the patient, who was unaware that the patient was to be evaluated.

Immediately after arrival in the PACU, the patients were monitored with TOF watch SX (Organon, Ireland) to evaluate residual curarization. A pair of electrodes was applied over the ulnar nerve at the wrist. The probe was positioned on the distal volar aspect of the thumb and the other finger tips were tightly fixed with tape. The ulnar nerve was stimulated with TOF stimulation (4 pulses 0.2 ms in duration, at a frequency of 2 Hz). The current intensity was 50 mA in all patients and five consecutive TOF stimulations at 10s intervals were applied. After excluding the highest and lowest values, the arithmetical mean of the three remainder values were accepted as the measured TOF ratio of the patient. At the same time, the ability of 5s head lift, eye opening, hand grip and tongue protrusion were evaluated. Additional neostigmine need, verbal or mechanical stimulation (airway maneuver) for respiration and reintubation were also noted.

Statistical analysis was performed using SPSS 15 for Windows. Patients' characteristics were expressed as mean±SD, TOF ratios as number and percentages. Spearman correlation test was used to analyze the correlation between TOF values and non-normally distributed variables, Pearson correlation test for normally distributed ones. The study was found to have a power of 0.96 for the correlation between TOF ratio and head lift, and 0.76 for the correlation between TOF ratio and hand grip. A p value of <0.05 was considered as statistically significant.

RESULTS

A total of 128 patients were evaluated in this study. Two patients were excluded from the analysis because of missing data. Demographic data were presented in Table 1. Fifty-two (40.6%) patients were female and 76 (59.4%) were male. Most of the patients (65.6%) were in American Society of Anesthesiologists II

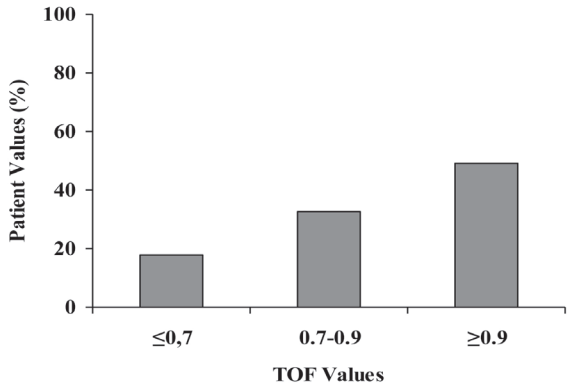

Figure 1. Number of patients according to TOF values (%).

Table 1. Demographic characteristics, average TOF value, NMBAs, neuromuscular monitorization and neostigmine use.

Gender (n,%)	
Female	52 (40.6%)
Male	76 (59.4%)
Age (year)	52.3±14.9
Weight (kg)	71.0±13.9
ASA (n,%)	
I	18 (14.1%)
II	84 (65.6%)
III	26 (20.3%)
Duration of anesthesia (min)	164.4±95.9
Average TOF value (n, mean ± SD)	128 (0.87±0.182)
Rocuronium/vecuronium/atracurium use (%)	68.8% / 28.1% / 3.1%
Intraoperative neuromuscular monitorization (n,%)	6 (4.7%)
Neostigmine use (mg)	1.5±0.5

Data are presented as mean ± SD, number or percentages

(ASA) group. Only 6 patients (4.7%) were monitored intraoperatively for the assessment of neuromuscular block. Rocuronium was the most frequently used NMBA (68.8%).

The TOF ratios of the patients are shown at Figure 1. The mean TOF ratio of all patients was 0.87±0.182. Train-of-four ratios of ≤0.7, 0.7-0.9, and ≥ 9 were detected in 18%, 32.8%, and 49.2% of the patients, respectively. The TOF ratios showed weak-moderate positive correlation with head lift and hand grip. The correlation coefficient was most significant with head lift (0.318, p=0.000) (Table 2). The correlation was negative with ASA classification (-0.289, p=0.001).

The distribution of the number of patients according to the TOF ratio and clinical tests are presented in Table III. Eleven of 23 patients with TOF≤0.7 were able to sustain 5 s head lift, while the number increased to 56 of 63 when TOF≥0.9. Nineteen patients grasped hand at TOF≤0.7, and 62 at TOF≥0.9.

Table 2. Correlation of TOF values with other variables.

	Correlation coefficient	p
Age	-0,147	0.980
Weight	0.127	0.119
ASA	-0.289**	0.001
Duration of anesthesia (min)	-0.175*	0.048
Time passed from last NMB dose	0.087	0.331
Head lift	0.318**	0.000
Eye opening	0.141	0.112
Tongue protrusion	0.145	0.103
Hand grip	0.232**	0.008

0-0.25 none or very weak correlation, 0.25-0.5 weak to moderate correlation, 0.5-0.75 good correlation, 0.75-1 very good correlation.

In the PACU, 6 patients (4.6%) had a need for verbal stimulation, 2 (1.5%) airway placement, 2 (1.5%) chin lift and 1 (0.7%) additional neostigmine as respiratory support. Re-intubation was not required for any patient. None of the patients complained or showed any sign of discomfort due to TOF stimulation.

DISCUSSION

The clinical importance of the residual effects of the NMBAs lasting after surgery has been of interest since 1970 [11]. Residual NM block has been defined by correlating signs and symptoms of muscle weakness with TOF fade ratios in volunteer studies [8,9]. While in 1970's, a TOF ratio of 0.7 was acceptable for normal respiratory mechanics, Ericksson et al reported that even partial NMB (TOF of 0.7) impairs the ventilatory response leading to hypoxia suggesting an effect of nondepolarizing relaxants on carotid body hypoxic chemosensitivity [12]. Volunteer studies with vecuronium established upper airway obstruction at TOF 0.8 and pharyngeal dysfunction with aspiration at TOF <0.9. Therefore, based on the available evidence, a TOF ratio of at least 0.9 is required for adequate neuromuscular recovery [13]. There is also strong evidence indicating that even light levels of postoperative residual curarization are able to produce an increased incidence of adverse effects like hypoxia and atelectasis as well as an increased length of stay in PACU [14,15].

In the present study, we have found the prevelance of residual NMB to be high in our PACU. Fifty-one percent of the patients had a TOF ratio of ≤0.9 showing the existence of a clinically significant residual curarization. The incidence of residual neuromuscu-

lar block varies widely among studies, with reported frequencies ranging from 2% to 64% [16,17]. Our results also represent a high level among the reported incidences.

The incidence of postoperative residual paralysis following the use of long and intermediate-acting NMBAs has been studied in different clinical trials [3,18,19]. These studies have demonstrated that the risk of observing a TOF ratio of <0.7 in the PACU is reduced when shorter acting agents are administered. In 1979, Vigby-Mogensen et al have reported that 42% of patients who were administered long-acting NMBAs and 2.5 mg doses of neostigmine had a TOF ratio of <0.7 on arrival to the PACU [2]. Although the presence of postoperative residual NMB seems to be related to the duration of action of the NMBA, several recent studies have also documented a high incidence of this complication when shorter-acting NMBAs are used in the operating room [1]. Debaene et al.have showed that residual paralysis is common after a single dose of an intermediate -acting muscle relaxant even more than 2h after the administration of the drug [19].

In daily practice, residual neuromuscular paralysis is frequently assessed using some clinical bedside tests like head and leg lift, hand grip or tongue protrusion. However, these tests require awake and cooperative patients. The residual effects of other anesthetic, sedative or analgesic medications must also be excluded. In addition, many clinical tests are not specific for the respiratory function and cannot be used clinically to evaluate respiratory muscle function [20]. Although a 5s head lift is the widely accepted traditional test performed in the operating room, it is regarded as an insensitive test of neuromuscular recovery. Ali et al observed that no patients with a TOF ratio of <0.4 were able to sustain a 3 s head lift, while all patients with a TOF ratio of>0.6 could perform this task [21]. Kopman et al [22] found that the test was passed at an average TOF value of 0.62±0.09 (range, 0.48-0.75). There are also other studies showing that some subjects can perform a 5s head lift even with TOF ratios as low as 0.25-04 [23]. Therefore, these results show us that it's not possible to exclude residual neuromuscular block even in the presence of capability of 5s head lift.

In our study, we have evaluated the ability of 5s head lift, eye opening, hand grip and tongue protrusion upon arrival in the PACU. Many of the patients were capable of performing those clinical tests despite the presence of clinically significant residual blockade as shown in Table 3. Although the correlation was most significant with 5s head lift, it was only of weak-moderate degree and approximately half of the patients with TOF of <0.7 were able to lift their heads for 5s.

Table 3. Distribution of clinical tests according to TOF values (n, %).

	Head lift	Eye opening	Tongue protrusion	Hand grip
TOF≤0.7 n=23	11	22	21	19
TOF=0.7-0.9 n=42	34	40	39	38
TOF≥0.9 n=63	56	63	62	62
Total n=128	101 (78.9%)	125 (97.7%)	122 (95.3%)	119 (93%)

The recovery of neuromuscular block should be assessed prior to tracheal extubation in order to ensure enough recovery of respiratory and pharyngeal function and reduce the risk of respiratory complications. Murphy et al have shown that critical respiratory events in the postanesthesia care unit are closely associated with a high incidence of severe residual blockade [24]. Similarly, a Scandinavian group has also demonstrated that pulmonary complications like pneumonia or atelectasis were observed 3 times more frequently in patients with TOF ratios of <0.7 (16.9%) compared to one with TOF ratios of ≥0.7 (4.8%) [15]. Our study was not designed to evaluate the incidence of adverse respiratory effects but we have noted the additional efforts to support the respiration of the patients. In the PACU, 6 patients required verbal stimulation, 2 airway placement (n=2), chin lift (n=2) and additional neostigmine (n=1) as respiratory support. None of the patients were re-intubated.

Some anesthetists do not prefer to administer reversal agents at the end of anesthesia unless the patient has significant residual weakness. This approach is frequently based on the fear of potential side effects of neostigmine such as nausea and vomiting, bradycardia, etc. In our study, only two patients did not receive any reversal agent. All of the other patients had received

neostigmine with atropine at the end of the surgery, but the mean dose used was 1.5±0.5 mg which was a very low dose to fully antagonize the residual NMB. This may be due to avoid the side effects of neostigmine as many anesthetists do. Sugammadex, the first selective relaxant binding agent indicated to reverse the neuromuscular blockade, may be a better choice offering advantages with rapid reversal properties and minimal side effects [25]. In a very recent study, it has been shown to eliminate residual neuromuscular blockade and associated clinically significant symptoms of partial paralysis [26]. Although it is also available in our country, it is unfortunately used only for limited indications because of its high cost.

In the present study, we have showed that incomplete recovery from non-depolarizing NMBAs still continues to be an important problem in modern PACUs. The frequently used clinical tests are not well correlated with postoperative residual paresis and several preventive techniques must be used to reduce the risk. We think that avoidance of long-acting muscle relaxants, routine use of neuromuscular monitoring in the operating room and reversal of neuromuscular blockade properly may improve patient outcomes by reducing the incidence of postoperative residual curarization and its associated complications.

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