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SPECIAL ARTICLE

Survey of postoperative residual curarization, acute respiratory events and approach of anesthesiologists

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Abstract
Background and objectives: residual paralysis following the use of neuromuscular blocking drugs (NMBDs) without neuromuscular monitoring remains a clinical problem, even when NMBDs are used. This study surveys postoperative residual curarization and critical respiratory events in the recovery room, as well as the clinical approach to PORC of anesthesiologists in our institution.
Methods: This observational study included 415 patients who received general anesthesia with intermediate-acting NMBDs. Anesthesia was maintained by non-participating anesthesiologists who were blinded to the study. Neuromuscular monitoring was performed upon arrival in the recovery room. A CRE was defined as requiring airway support, peripheral oxygen saturation <90% and 90–93% despite receiving 3 L/min nasal O2, respiratory rate >20 breaths/min, accessory muscle usage, difficulty with swallowing or speaking, and requiring reintubation. The clinical approach of our anesthesiologists toward reversal agents was examined using an 8-question mini-survey shortly after the study.
Results: The incidence of PORC was 43% ($n = 179$) for TOFR <0.9, and 15% ($n = 61$) for TOFR <0.7. The incidence of TOFR <0.9 was significantly higher in women, in those with ASA physical status 3, and with anesthesia of short duration ($p < 0.05$). In addition, 66% ($n = 272$) of the 415 patients arriving at the recovery room had received neostigmine. A TOFR <0.9 was found in 46% ($n = 126$) of the patients receiving neostigmine.
Conclusions: When routine objective neuromuscular monitoring is not available, PORC remains a clinical problem despite the use of NMBDs. The timing and optimal antagonism of the

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neuromuscular blockade, and routine objective neuromuscular monitoring is recommended to enhance patient safety.

PALAVRAS-CHAVE
Complicações;
Pós-operatório;
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Monitoração;
Bloqueio neuromuscular;
Eventos respiratórias agudos

Pesquisa de curarização residual no pós-operatório, eventos respiratórios agudos e abordagem de anestesiologistas

Resumo
Justificativa e objetivos: A paralisia residual após o uso de bloqueadores neuromusculares (BNMs) sem monitoração neuromuscular continua sendo um problema clínico, mesmo quando BNMs são usados. Este estudo pesquisou a curarização residual pós-operatória e os eventos respiratórios críticos em sala de recuperação, bem como a abordagem clínica da CRPO feita pelos anestesiologistas em nossa instituição.
Métodos: Este estudo observacional incluiu 415 pacientes que receberam anestesia geral com BNMs de ação intermediária. A manutenção da anestesia foi feita por anestesiologistas não participantes, ''cegos'' para o estudo. A monitoração neuromuscular foi realizada no momento da chegada à sala de recuperação. Um ERC foi definido como necessidade de suporte ventilatório; saturação periférica de oxigênio <90% e 90-93%, a despeito de receber 3 L/min de O2 via cânula nasal; frequência respiratória >20 bpm; uso de musculatura acessória; dificuldade de engolir ou falar e necessidade de reintubação. A abordagem clínica de nossos anestesiologistas, em relação aos agentes de reversão, foi avaliada usando um miniquestionário de oito perguntas logo após o estudo.
Resultados: A incidência de CRPO foi de 43% (n = 179) para a SQE <0 e 15% (n = 61) para a SQE <0,7. A incidência de SQE <0,9 foi significativamente maior em mulheres, pacientes com estado físico ASA III e com anestesia de curta duração (p < 0,05). Além disso, 66% (n = 272) dos 415 pacientes que chegam à sala de recuperação haviam recebido neostigmina. Uma SQE <0,9 foi encontrada em 46% (n = 126) dos pacientes que receberam neostigmina.
Conclusão: Quando a monitoração neuromuscular objetiva de rotina não está disponível, a CRPO continua sendo um problema clínico, a despeito do uso de BNMs. O momento e o antagonismo ideais do bloqueio neuromuscular e a monitoração neuromuscular objetiva de rotina são recomendados para aumentar a segurança do paciente.

Introduction

Neuromuscular blocking drugs (NMBDs) are used to facilitate endotracheal intubation during induction of anesthesia. Residual postoperative paralysis following the use of muscle relaxants agents, known as postoperative residual curarization (PORC), may increase postoperative pulmonary complications, morbidity and mortality.[1,2] For many years a train-of-four ratio (TOFR) of 0.7 was considered sufficient to exclude PORC; nowadays, however, to exclude clinically significant PORC it is considered that the TOFR should be $\geq$0.9.[3,4] PORC is associated with weakness of upper airway muscles, airway obstruction, impaired pharyngeal function leading to increased risk for aspiration, inadequate recovery of pulmonary function, and impaired hypoxic ventilatory response.[2,5] The incidence of PORC in the recovery room/post-anesthesia care unit (PACU) varies widely, with reported frequencies ranging from 9 to 47%.[2,6–9] Critical respiratory events (CREs) during early recovery from general anesthesia are not uncommon and their etiology is multifactorial. Anesthetic variables associated with postoperative CREs include the use of opioids and NMBDs during general anesthesia.[2,10]

This prospective observational study aimed to determine the incidence of PORC in the early recovery period, anticholinesterase application ratios and doses, adverse respiratory events of PORC, and the current approach of anesthesiologists to PORC without routine monitorization in our institution.

Materials and methods

Patients and study protocol

This prospective, observer-blinded observational study was approved by the local Ethical Committee (Clinical Trial-number 024/2010). A total of 415 patients (ASA Physical Status 1–3, aged 18–65 years) who were operated under general anesthesia using intermediate-acting muscle relaxants between April 2010 and June 2010 were enrolled in the recovery room. Exclusion criteria were patients with

neuromuscular diseases, severe kidney or liver diseases, those undergoing total intravenous anesthesia, and patients with a body temperature $\leq$35 °C. Premedication and choice of anesthetic protocol, giving anticholinesterase were left to the discretion of the anesthesiologist in charge of the patient, who was unaware that the patient was to be included in this study.

Data collection

Patients were subject to routine monitoring immediately after arrival at the recovery room. Patients' electrocardiogram, peripheral oxygen saturation (SpO_2), non-invasive blood pressure, and body temperature (Genius™ 2 IR Tympanic Thermometer Ltd., Gosport, UK) were measured, and supplemental oxygen (3 L/min) was provided to all patients.

PORC was assessed in the recovery room by an anesthesiologist unaware of the study. The neuromuscular function of the Adductor pollicis muscle was monitored using the TOF-Watch SX® acceleromyograph. The skin was washed with alcohol, and an acceleromyograph probe was placed on the distal ventral part of the thumb. The remaining fingertips were tightly fixed with tape. The ulnar nerve was stimulated. The TOF tracing was stabilized by administering 1 min of repetitive TOF stimulation followed by a 5-s, 50-Hz tetanic stimulation, and then another 3–4 min period of repetitive TOF stimulation. The CAL 2 mode was used to determine the supramaximal threshold and to calibrate the transducer of the acceleromyograph. After calibration of the device, the ratio of three values was recorded having assessed the three TOFR at 15-s intervals in each patient and we use mean of these three values. Patients with a TOFR of <0.7, 0.7–0.9, and >0.9 were regarded as having severe PORC, mild to moderate PORC, and sufficient neuromuscular recovery, respectively. The following parameters were assessed and recorded in the intraoperative anesthesia records: age, bodyweight (BW), type of surgery, duration of anesthesia (i.e. period between induction of anesthesia and arrival at the recovery room), the type of intermediate-acting NMBDs used, duration of the last NMBD (period between the last NMBD and the TOFR recording in the recovery room), neostigmine dose and time administered, and reversal time (period between neostigmine administration and TOF recording in the recovery room). Moreover, the following parameters were examined/recorded to assess respiratory status: need for airway support, upper airway obstruction, respiratory rate, accessory muscle use, difficulty with swallowing or speaking, and reintubation.

Patients with a peripheral oxygen saturation (SpO_2) <90% despite 3 L/min O_2 nasal cannula were regarded as having severe hypoxia, those with 90–93% as having mild to moderate hypoxia, and those with SpO_2 > 93% as having normoxia.[2,11] Approach to treatment of PORC left choice of anesthesia unaware of the study. For the survey part of this study, the clinical approach of our anesthesiologists (n = 21) toward neostigmine was explored using a mini-survey (8 questions) shortly after the clinical study.[12] These (anonymous) questionnaires were collected in enclosed envelopes.

Statistical analysis

All statistical analyses were performed using SPSS (the statistical package for social sciences) Version 15.0 (SPSS, Inc., Chicago, IL, USA). For continuous variables, mean and standard deviation were presented; for categorical variables, frequency and percentage values were presented. Chi-square test and Fischer's exact test were used to compare categorical variables. To compare the two groups, Student's t test was used for parametric conditions, and Mann–Whitney U test was used for non-parametric conditions. In order to compare three or more groups, one-way analysis of variance was used for parametric conditions, and Kruskal–Wallis H test was used for non-parametric conditions. Predictor factors of PORC were determined through univariate logistic regression. All parameters with $p < 0.05$ in univariate analyses were included in a multivariate logistic regression model. A p-value of $\leq$0.05 was considered statistically significant.

Results

A total of 415 patients met the inclusion criteria and were evaluated. Of these, 255 underwent non-abdominal procedures and 160 underwent abdominal procedures. Table 1 presents the demographic data and clinical characteristics of the 415 patients.

Postoperative residual curarization

The incidence of PORC was 43% (n = 179) for a TOFR <0.9, and 15% (n = 61) for a TOFR <0.7. The TOFR was $\geq$0.9 in 56% (n = 236) of the all patients.

Table 1 Demographic and anesthesiology data of the study group (n = 415).

Gender (M/F) n/(%)	Age (years)	Weight (kg)	ASA 1/2/3 n (%)	Duration of anesthesia (min)	Type of surgery Abdominal/ non-abdominal (n)	Sevo/Des/Iso n
202(48.7)/213 (51.3)	43.87 ± 14.14	73.24 ± 13.06	159(38.3)/201 (48.4)/55(13.3)	106.10 ± 45.98	160/255	300/84/31

Data are mean ± SD, or number of patients (n) and percent (%).
ASA, American Society of Anesthesiologists; Sevo, sevoflurane; Des, desflurane; Iso, isoflurane.

Table 2 Train-of-four ratio in relation to demographic/clinical data.

Characteristic	TOF ratio				*P* value
	<0.7 (*n* = 61)	0.7–0.8 (*n* = 43)	0.8–0.9 (*n* = 75)	>0.9 (*n* = 236)	
Age (year)	49.9 ± 11.7[a]	46.5 ± 13.2[a]	46.6 ± 12.2[a]	41.0 ± 14.8	<0.001
Gender n (%)					
Male	24 (11.9)	21 (10.4)	30 (14.8)	127 (62.9)	0.038
Female	37 (17.4)	22 (10.3)	45 (21.1)	109 (51.2)	
Weight (kg)	75.5 ± 14.8	72.8 ± 14.5	73.0 ± 13.0	72.8 ± 12.3	NS
ASA n (%)					
1	17 (10.7)	11 (6.9)	24 (15.1)	107 (67.3)	0.003
2	34 (16.9)	25 (12.4)	39 (19.4)	103 (51.2)	
3	10 (18.2)	7 (12.7)	12 (21.8)	26 (47.3)	
Duration of anesthesia (min)	83.9 ± 37.1[a]	95.6 ± 41.0[a]	95.9 ± 41.9[a]	116.9 ± 47.1	<0.001
TFL TOF (min)	67.4 ± 27.3[a]	73.6 ± 28.4[a]	88.0 ± 37.7[a,b]	109.4 ± 43.0	<0.001
Reversal time (min)	10.5 ± 4.4[a,c]	10.7 ± 4.2[a,c]	12.3 ± 4.8	12.4 ± 4.3[b]	0.040
Neosigmine (mg)	1.3 ± 0.5	1.1 ± 0.3	1.3 ± 0.4	1.2 ± 0.4	>0.05
Body temp. (OC)	35.7(0.4)	35.7 (0.3)	35.8 (0.3)	35.7 (0.4)	>0.05

ASA, American Society of Anesthesiologists; TOF, train-of-four; TFL TOF, time from last NMBD to TOF recording in recovery room (min); reversal time, time between reversal and assessment of TOF ratio in recovery room (min).
[a] $p < 0.001$ versus TOF >0.9.
[b] $p < 0.001$ versus TOF <0.7.
[c] $p < 0.05$ versus TOF 0.8–0.9.

Most of the patients showing insufficient recovery (TOFR <0.7 and <0.9) were female, ASA physical status 3, had anesthesia of short duration, and had a higher than average age ($p < 0.05$) (Tables 2 and 3).

NMBD management

In the present study, the moderate muscle relaxant agents used were vecuronium, rocuronium and atracurium, which

Table 3 Logistic regression analysis of risk factors for PORC.

	OR	% 95 CI	*p*
Univariate logistic regression			
Age (year)	1.036	1.021–1.051	<0.001
Gender (male[a]/female)	1.616	1.092–2.391	0.016
Weight (kg)	1.006	0.991–1.021	0.430
ASA			
I[*]	1		
II	1.958	1.272–3.014	0.002
III	2.295	1.229–4.286	0.009
Duration of Anesthesia (min)	0.987	0.982–0.991	<0.001
Neuromuscular blocking drug			
Atracurium[a]	1	–	
Vecuronium	1.744	0.601–5.063	0.306
Rocuronium	2.640	0.832–8.375	0.099
TFL TOF (min)	0.978	0.972–0.984	<0.001
Neostigmine administration (no[a]/yes)	1.465	0.968–2.219	0.071
Reversal time (min)	1.008	0.979–1.037	0.602
Neostigmine dose (mg)	1.271	0.951–1.697	0.105
Multivariate logistic regression			
Age (year)	1.039	1.022–1.056	<0.001
Gender (male/female)	1.568	1.010–2.433	0.045
TFL TOF (min)	0.980	0.973–0.987	<0.001

R-Sup-NMBDs, Receiving supplementary NMBDs; TFL TOF, Time from last NMBD to TOF recording in recovery room (min); OR, Odd's ratio; 95% CI, 95% Confidence interval.
[a] Reference category.

Table 4 Administration of neostigmin related demographic data.

Characteristic	Neostigmine administration?		*p* value
	Yes (*n*:272)	No (*n*:143)	
Age (year)	45.06 ± 14.14	41.60 ± 13.90	0.017
ASA n (%)			
I (*n* = 159)	92 (57.9)	67 (42.1)	0.020
II (*n* = 201)	138 (68.7)	63 (31.3)	
III (*n* = 55)	42 (76.4)	13 (23.6)	
Duration of anesthesia (min)	95.61 ± 41.80	126.05 ± 47.09	<0.001
TFL TOF (min)	83.42 ± 34.08	118.92 ± 46.34	<0.001

ASA, American Society of Anesthesiologists; TFL TOF, time from last NMBD to TOF recording in recovery room (min).

were applied in 335, 63 and 17 patients, respectively. TOFR < 0.9 was 42.1% for vecuronium, 52.4% for rocuronium and 29.4% for atracurium.

Reversal of NMB agents

On arrival in the recovery room, 65.5% (*n* = 272) of the 415 patients had received neostigmine, whereas the remainder 34.5% (*n* = 143) had not. A TOFR <0.9 was estimated in 46.3% (*n* = 126) of the patients receiving neostigmine, and in 14.7% (*n* = 40) of this group the TOFR was <0.7. Table 4 presents data on neostigmine administration in relation to demographic characteristics. Patients receiving neostigmine were of higher average age, had anesthesia of shorter duration, and the period between administration of the last muscle relaxant and TOFR assessment was shorter. Another finding was that the neostigmine dose did not change according to the TOFR; an average dose of 20 ± 10 μg/kg neostigmine was applied. In patients not receiving neostigmine, the average time after the last NMBD dose was 118.92 ± 46.34 min, compared with 83.42 ± 34.08 min in those who received neostigmine ($p < 0.001$). The period between the administration of neostigmine and TOFR assessment was 10.5 ± 4.4 min in patients with a TOFR <0.7 and 12.4 ± 4.3 min in those with a TOFR >0.9 min (Table 2).

Respiratory status

Table 5 presents data on the relation between PORC and CREs. Accordingly, in patients with a TOFR ≥0.7 the SpO_2 was proportionally high, while in those with a TOFR <0.7 it was proportionally low. Use of airway support and respiratory complications were higher in patients with TOFR <0.7. In our 415 patients, 14 of 17 patients (82.4%) with an SpO_2 ≤90% had a TOFR ≤0.9. Only 3 patients (17.6%) had an SpO_2 ≤90% despite a TOFR >0.9. SpO_2 was ≥93% in 307 patients. Airway support was applied in 42.6% of the patients with a TOFR <0.7, and in 31.9% of those with a TOFR >0.9 (Table 6).

Approaches to PORC by anesthesiologists

Table 7 presents the results of our mini-survey among our 21 anesthesiologists shortly after the clinical study. Of these anesthesiologists, 71% (*n* = 15) thought that the incidence of PORC was 0–10%, and only 1 anesthesiologist (5%) mentioned it could be 30–50%. Eight anesthesiologists (38%) always use

Table 5 Critical respiratory events ratio in relation to the TOF ratio.

Variables	TOF ratio				*p*-Value
	<0.7	0.7–0.8	0.8–0.9	>0.9	
SpO_2	92.1 ± 3.7	94.3 ± 2.9[a,b]	94.6 ± 2.7[a,b]	95.6 ± 2.5[a]	<0.001
Requiring Airway support, n (%)					
Yes (*n* = 47)	20 (42.6)	4 (8.5)	8 (17.0)	15 (31.9)	<0.001
No (*n* = 368)	41 (11.1)	39 (10.6)	67 (18.2)	221 (60.1)	
Critical respiratory events, n (%)					
No (*n* = 370)	33 (8.9)	39 (10.5)	69 (18.6)	229 (61.9)	<0.001
Yes (*n* = 45)	28 (62.2)	4 (8.9)	6 (13.3)	7 (15.6)	
Upper airway obstruction	5	2	2	2	
Respiratory rate >20	18	2	1	1	
Accessory muscle usage	4	–	3	3	
Reintubation	1	–	–	–	

Data are mean ± SD, or number of patients and percent (%).
[a] $p < 0.001$ vs. TOF <0.7.
[b] $p < 0.001$ vs. TOF 0.9.

Table 6 Peripheral oxygen saturation (SpO_2) in relation to adequate recovery of TOF (> 0.9) and inadequate recovery of TOF (<0.7).

Peripheral saturation	TOF <0.9 (n = 179)	TOF >0.9 (n = 236)	p-Value
SpO_2 n (%)			
<90% (n = 17)	14 (82.4)	3 (17.6)	
90–93% (n = 96)	60 (62.5)	36 (37.5)	<0.001
>93% (n = 302)	105 (34.8)	197 (65.2)	

Data are number of patients and percent (%).

Table 7 Attitudes regarding management of PORC in our institution (n = 21anesthesiologists).

Question	Options	n	%
What do you estimate the incidence of PORC to be in your clinic?	0–10.0%	15	71
	10.1–20.0%	3	14
	20.1–30.0%	2	10
	30.1–50.0%	1	5
	50.1–70.0%	–	–
When an NMBD has been given, do you always administer neostigmine at the end of surgery?	Yes	8	38
	No	13	62
If answer to the above question was 'No' in what percentage of cases do you omit neostigmine?	1–25%	2	15
	26–50%	5	39
	51–75%	4	31
	76–100%	2	15
How long after administration of neostigmine do you extubate your patiens?	After extubation I administer neostigmine	1	5
	5–10 min	18	86
	11–15 min	2	10
What dose of neostigmine do you usually administer?	2.5 mg	1	5
	<0.05 mg/kg	10	48
	0.05 mg/kg	5	24
	>0.05 mg/kg	–	–
	<2.5 mg	5	24
Do you have any concerns regarding the adverse effects associated with administration of neostigmine/antimuscarinic drugs?	Yes	17	81
	No	4	19
If 'Yes' to the preceding question, what are they?	- Hemodynamic effects	14	67
	- Respiratory effects	8	38
	- Increased nausea and vomiting	10	48
	- Inadequate recovery of neuromuscular function	4	19
	- Other	1	5
Prior to tracheal extubation the TOF monitors should be:	<50–60%	–	–
	61–70%	2	10
	71–80%	4	19
	80–90%	4	19
	91–100%	11	53

neostigmine at the end of surgery. Five of 13 anesthesiologists who do not always use neostigmine reported that they use it at a rate of 26% and 50%. Eighteen anesthesiologists (86%) administer neostigmine 5–10 min before extubation, 2 administer it 10–15 min before extubation, and 1 mentioned that he administered it after extubation. Of these 21 anesthesiologists, 17 (81%) had concerns about the side-effects by the use of reversal agents, 14 (67%) about hemodynamic side-effects, 10 (59%) about nausea/vomiting, and 8 (38%) had concerns about respiratory side-effects. Eleven anesthesiologists (53%) believed that the TOFR should be 0.9 or higher before extubation (Table 7).

Discussion

In the present study which included 415 patients, the incidence of PORC was 15% in those with a TOFR <0.7 and 43% in those with a TOFR <0.9. Furthermore, the rate of sufficient recovery (TOFR >0.9) was 57%, and 65.5% of

these patients had received neostigmine at an average dose of 20 ± 10 μg/kg, generally administered 10–12 min before extubation.

A TOFR <0.9 was estimated in 46% of the patients who received neostigmine ($n = 126$), and 14% ($n = 40$) of this group had a TOFR <0.7. However, among our 21 anesthesiologists, 71% ($n = 15$) believed that the incidence of PORC in our institute was 0–10%. The study also shows that patients with insufficient recovery (TOFR <0.7 to <0.9) were older than average, more often female, had an ASA score 3, and a shorter duration of anesthesia.

Of our 415 patients, in the recovery room 45 had CREs symptoms and 62% of these 45 patients had a TOFR <0.7. Of the total group, 84% had a TOFR $\leq$0.9.

The incidence of PORC did not decrease over time. In other randomized prospective studies, the incidence of PORC was reported to have changed in relation to differences between the study designs.[2,6–9] For example, Debaene et al.[8] determined the percentage of patients in the PACU with a TOFR <0.7 and <0.9 after receiving a single intubating dose of an intermediate-acting NMBD (vecuronium, rocuronium, or atracurium). Muscular paralysis was not antagonized intraoperatively. A TOFR <0.7 in 16% of patients (15.9% received rocuronium, 16.9% received atracurium, 17% received vecuronium) and <0.9 in 45% of patients (45% received rocuronium, 41.6% received atracurium, 46.8% received vecuronium) were observed postoperatively and TOFR >0.9 was observed in only 55% of patients in the recovery room.[8] In our study we found that TOFR <0.9 was 42% with vecuronium, 52% with rocuronium and 30% with atracurium.

Cammu et al.[7] assessed the occurrence of PORC in patients undergoing outpatient and inpatient surgical procedures. Neuromuscular monitoring and reversal agent was used in only 12% and 25% of patients, respectively. A TOFR <0.9 was found in 47% of the inpatients and in 38% of the outpatients.

In their observational study, Butterly et al.[1] reported that reversal agents are frequently used; 78% of their study population received neostigmine at a mean dose of 2.5 ($\pm$1.2) mg. Basic nerve stimulators were applied routinely in operating rooms and anesthetizing locations, and the incidence of PORC was 22%. The higher incidence of PORC in our institution might be attributable to a lower anticholinesterase application rate (66%), a lower mean neostigmine dose (20 μg/kg), lack of routine neuromuscular monitoring, and may depend on low awareness for PORC.

Antagonism of neuromuscular blockade with cholinesterase inhibitors at the end of the surgery reduces the incidence of PORC, the length of stay in the recovery room, and pulmonary complications.[1,2,5,6,9,13] However, the moment of antagonism plays an important role in these patients. If antagonism is performed shortly before extubation, the neuromuscular block is often insufficiently antagonized, thus increasing the risk of PORC.[14] If intraoperative objective neuromuscular monitoring can not be applied, it is recommended that the patient be constantly antagonized long before extubation to avoid PORC associated with the depth of neuromuscular blockade.[5,8] Muphy et al.[9] investigated the incidence of PORC in the recovery room and in the pre-extubation period among 120 patients (ASA 1–2) using rocuronium under intraoperative neuromuscular monitoring; all subjects were reversed with neostigmine at a TOF count of 2–4. The average period from the injection of neostigmine to the recording of TOFR at the time of extubation regarding the clinical criteria was 8 ± 6 min. During extubation, the percentage of patients with a TOFR <0.7 was 58% and that of patients with a TOFR <0.9 was 88%. They also reported that the period from injecting neostigmine to the TOFR assessment in the recovery room was 19 ± 7 min; the incidence of PORC was 8% and 32% for patients with a TOFR $\leq$0.7 and 0.9, respectively.[9]

Another study by McCaul et al.[14] included 40 patients of ASA I using atracurium. During neuromuscular block antagonism, the TOFR <0.7 patients were found to be 70%, while the same ratio was found in 65% of the patients during extubation. Compared with patients with a PORC TOFR >0.7, patients with a TOFR <0.7 during extubation had shorter procedures, and deeper neuromuscular block at the time of neostigmine administration. In that study, it was established that the period from the moment the muscle relaxant was applied to the recording TOFR was 6 ± 1 min for patients with TOFR <0.7, and 15 ± 4 min for those with a TOFR >0.7.[14] In the present study, the period from anticholinesterase application to TOFR measurement was 10.5 ± 4.4 min for those with a TOFR <0.7 and 12.4 ± 4.3 min for those with q TOFR >0.9, which supports the results of McCaul et al. Furthermore, Baillard et al.[6] investigating 435 patients in 1995, 130 in 2000, and 101 in 2002, studied the factors affecting PORC with early changes in clinical anesthesia applications. Within this period, concomitant with an increase in the average age of the patients, their weight, duration of surgery, use of intraoperative neuromuscular monitoring and reversal of residual paralysis, the incidence of PORC showed a marked decrease from 60% to 5%.

Postoperative respiratory events are the most common adverse outcomes associated with residual paralysis reported in both observational and randomized clinical studies. In 1994, Rose et al.[10] prospectively examined patient (age >60 yr, male gender, diabetic, and obese), surgical (emergencies and cases >4 h) and anesthetic factors (premedication, induction with thiopental, fentanyl >2.0 $\mu g\,kg^{-1}$, fentanyl and morphine combination, and atracurium >0.25 $mg\,kg^{-1}\,h^{-1}$) associated with CREs in the PACU. Murphy et al.[2] assessed and quantified the severity of neuromuscular blockade in patients with signs or symptoms of CREs in the PACU. A total of 7459 patients received a general anesthetic during the 1-year study period, of whom 61 (1%) developed a CRE. Forty-two of these patients were matched with controls and constituted the study group for statistical analysis. A high incidence of several residual blockades was observed in patients with CREs, which was absent in control patients without CREs.[2]

In another randomized, prospective and placebo-controlled trial, Sauer et al.[15] studied the effect of CREs on the incidence of PORC by dividing 114 patients into a neostigmine and placebo group after general anesthesia in the PACU. Among patients receiving rocuronium, 39% were discovered to have CREs and the incidence of hypoxemia (SpO_2) was significantly higher in the placebo group than in the neostigmine group.

In a survey comparing PORC in the USA and Europe, the use of routine reversal agents was 18% in Europe and 34%

in the USA.[12] The incidence of neuromuscular monitoring in the operating room was 22.7% in the USA compared with 70.2% in Europe. In Europe, 54% of the participants applied neostigmine 3–5 min before extubation and only 5% of them waited ≥10 min; in the USA these figures were 39% waited 3–5 min, 46% waited 6–10 min, and 13% waited 10 min before extubation. With respect to the neostigmine dose, 60% of the participants from Europe administered a dose of 2.5 mg, whereas 49% of the participants in the USA administered this drug on a milligram per kilogram basis rather than a fixed dose. Most participants from both Europe (83.7%) and the USA (86%) reported concerns about the adverse effects of anticholinesterases and antimuscarinic drugs.[12] In our institution, routine use of a reversal agent is similar to that used in the USA (i.e. 38%). Among our anesthesiologists, a lower awareness of PORC and a higher incidence of neuromuscular blockade is probably associated with the lack of routine neuromuscular monitoring in our institute.

The present study has some limitations. First, because it is difficult to establish a cause-effect relation in observational studies, we may not have revealed other factors affecting PORC. Second, we were unable to establish the incidence of PORC or the depth of neuromuscular block during extubation since objective neuromuscular monitoring is not applied in any of our operating rooms. Third, the CREs might have been influenced by unknown clinical variables; in addition, their long-term effects remain unknown as CREs could only be monitored before departure from the recovery room. Fourth, because the patients stayed in the recovery room for varying lengths of time, we were unable to check the effects of the TOFR in relation to the duration of stay in the recovery room.

In summary, when routine objective neuromuscular monitoring is not available, PORC remains a clinical problem despite the use of intermediate-acting NMBDs. Older patients, female patients, ASA physical status 3, shorter anesthesia procedures, patients with a short time to the last NMBD dose, and early extubation after antagonism of a neuromuscular blockade may be at risk of PORC and CREs. The timing and optimal antagonism of the neuromuscular blockade, and routine objective neuromuscular monitoring is recommended to enhance patient safety.

Conflicts of interest

The authors declare no conflicts of interest.

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