Assessment of residual curarization using low-current stimulation

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The present study employed train-of-four (TOF) stimulation at a current of 20 mA to assess the incidence and degree of residual neuromuscular blockade in 64 randomly selected Post Anesthesia Care Unit (PACU) patients. Group C (Control, n = 10) had received anaesthesia without nondepolarizing muscle relaxant; Group V (n = 25) had received vecuronium; and Group P (n = 29) had received pancuronium. At the end of surgery, each patient had been considered by his anaesthetist to have adequate neuromuscular function on the basis of clinical signs and tactile or visual evaluation of responses to TOF stimulation. However, upon testing in the PACU 15 min later, 45% (13 of 29) of Group P patients and 8% (2 of 25) of Group V patients had a TOF ratio <0.70. This study indicates that residual curarization may be commonly encountered following long-acting relaxants despite qualitative intraoperative TOF monitoring. The present incidence, detected at a current of 20 mA, is consistent with previous reports which employed supramaximal TOF stimulation. We conclude that despite intraoperative monitoring, residual curarization following long-acting nondepolarizing agents is common and that it may be detected with TOF at a low stimulating current (20 mA).

La présente étude a utilisé l'ondée-de-quatre (TOF) avec des courants de 20 mA afin d'évaluer l'incidence et le degré de blocage neuromusculaire résiduel chez 64 patients choisis au

hasard dans l'unité des soins postanesthésiques (PACU). Le groupe C (Contrôle, n = 10) a reçu de l'anesthésie sans relaxant musculaire nondépolarisant; le Groupe V (n = 25) a reçu du vécuronium; et le Groupe P (n = 29) a reçu du pancuronium. A la fin de la chirurgie, chaque patient fut considéré par son anesthésiste comme ayant une fonction neuromusculaire adéquate sur la base des signes cliniques tactiles et les évaluations visuelles des réponses de la stimulation avec une ondée-de-quatre. Cependant, lors de la stimulation au PACU 15 minutes plus tard, 45% (13 de 29) du Groupe de patients P et 8% (2 de 25) avaient un ratio de TOF <0,70. Cette étude indique que la curarisation résiduelle peut survenir fréquemment après les relaxants à longue action malgré une surveillance qualitative intraopératoire du TOF. L'incidence trouvée, détectée avec un courant de 20 mA, est en accord avec des études antérieures qui emploient la stimulation supramaximale de TOF. On conclut que malgré une surveillance intraopératoire, la curarisation résiduelle après des agents non-dépolarisants à longue action est fréquente et qu'elle pourrait être détectée par une stimulation avec un TOF avec un courant de 20 mA.

Key words

MEASUREMENT TECHNIQUES: neuromuscular blockade, train-of-four;

NEUROMUSCULAR RELAXANTS: pancuronium, vecuronium;

RECOVERY: residual curarization.

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In the past decade, several investigators have noted that, despite apparently adequate clinical reversal of neuromuscular blocking (NMB) agents, a considerable number of patients showed evidence of inadequate neuromuscular function when tested in the post-anaesthesia care unit (PACU).¹⁻⁵ Recent evidence has suggested that this problem is less common following reversal of newer relaxants of intermediate duration.⁴⁻⁶

Despite the high incidence of residual blockade, neurostimulation in the PACU is used infrequently as it can be uncomfortable for awake patients.⁷ We recently reported that train-of-four (TOF) stimulation with 20 and 30 milliamperes (mA) currents consistently provided TOF ratios comparable with those obtained using a supramaximal current of 50 mA.⁸ This may be important in testing awake patients, since higher stimulating currents are associated with more discomfort.^{7,8} The present report assesses whether an incidence of residual blockade comparable to that reported at other institutions could be identified by neuromuscular testing at a submaximal current of 20 mA in the 64 PACU patients evaluated in our

previous study.⁸ In contrast to several recent reports,¹⁻⁵ all patients in the present study had been assessed intraoperatively with a blockade monitor to guide maintenance of NMB therapy. Moreover, in distinction to a previous report where a blockade monitor was employed in 74% of patients intraoperatively to monitor the level of blockade but not necessarily to assess the adequacy of reversal,⁴ all patients in the present study were also tested for adequacy of reversal by visual or tactile responses to neurostimulation.

Methods

For the present investigation, consistent delivery of a 20 mA current by a Digistim III nerve stimulator (Neuro Technology Inc., Houston, TX) was first confirmed by comparing its LCD display to the voltage generated on an interfaced Tektronix 7623A (Tektronix Inc. Beaverton, OR) oscilloscope. A decade box provided variable resistances ranging from 470 to 2,200 ohms.

Following approval by the institutional Human Investigation Committee, 64 patients who were sufficiently awake and cooperative were studied within 15 min of PACU arrival. Patients were excluded from analysis if they were <18 or >90 yr of age, <50% or >150% of ideal body weight, ASA physical status 4 or 5, if they had a known or suspected history of neuromuscular disease or were receiving medications known to affect neuromuscular function. Patients were assessed by: (1) ability to sustain head-lift for five seconds; and (2) TOF stimulation at 20 mA. For TOF testing, surface electrodes were placed over the olecranon groove and volar forearm, and the ipsilateral thumb was inserted in a calibrated adductor pollicis monitor (Medar Corp., Scarsdale, NY) interfaced to a monitor and a stripchart recorder (Datascope 2000A/RS, Datascope Corp., Paramus, NJ). The ratio of the fourth to the first twitch (T_4/T_1 ratio) was then determined after each of two sets of TOF stimulation at 20 mA with a 20-sec interval between sets, and the difference between these readings was calculated.

Patients were categorized retrospectively according to their intraoperative anaesthetic regimen: control group (C) received regional or general inhalational anaesthesia (enflurane or isoflurane) without nondepolarizing agents ($n = 10$); vecuronium group (V) received general inhalational anaesthesia (halothane, enflurane or isoflurane) with vecuronium as the sole nondepolarizing agent ($n = 25$); and pancuronium group (P) received general inhalational anaesthesia (enflurane or isoflurane) with pancuronium as the sole nondepolarizing agent ($n = 29$). The investigator had been blinded to intraoperative technique, and the anaesthesia care provider had not been informed that the patient would be evaluated postoperatively.

Analysis was performed as follows: the three patient

FIGURE Train-of-four ratios during testing in the PACU. Bars represent distribution of T_4/T_1 ratios in the three patient groups.

groups were compared with regard to T_4/T_1 ratio using Wilcoxon rank sum test. The incidence with which the T_4/T_1 ratio was less than 0.70, ASA status classification, inhalational and intravenous anaesthetics received, antibiotics received, ability to maintain head-lift, and the sex distribution among the three groups were compared with chi-square analysis. The differences in age, weight, temperature, duration of anaesthesia, initial and maintenance doses of NMB agents, time from last dose of relaxant to time of testing of TOF, and dose of reversal agents were compared using ANOVA with Duncan's multiple range test for multiple comparisons.

Results

Testing of the neuromuscular monitor confirmed consistency of current output at the resistances tested. For an LCD reading of 20 mA, the Tektronix oscilloscope readings were 23.5, 22.1, 20.9 and 19.5 mA at resistances of 470, 1000, 1500 and 2200 ohms, respectively. During clinical testing, the mean difference between the two successive T_4/T_1 determinations at 20 mA was <2%, and the first T_4/T_1 determination was therefore used for subsequent analyses.

Despite being considered adequately reversed while still in the operating room at the end of surgery, 15 of the 64 patients evaluated had a $T_4/T_1 < 0.70$ when tested in the PACU. As noted in the Figure, 13 of the 29 patients (45%) in Group P had a T_4/T_1 ratio <0.70. In contrast, only two of 24 patients (8%) of Group V and no Group C patients evidenced a T_4/T_1 ratio <0.70. The two Group V patients who showed a $T_4/T_1 < 0.70$ in the PACU (i.e.,

TABLE I T_4/T_1 ratio at 20 mA

	Mean $\pm$ SD	Range
Group C ($n = 10$)	0.98 ± 0.04	0.92–1.03
Group V ($n = 25$)	0.94 ± 0.09	0.65–1.00
Group P ($n = 29$)	$0.72 \pm 0.20^*$	0.32–1.00

* $P < 0.05$ for Groups P vs C and P vs V.

ratios of 0.63 and 0.65) were the two who had received a relatively large dose of vecuronium ($0.25 \text{ mg} \cdot \text{kg}^{-1}$) to facilitate rapid intubation. Overall, patients who received pancuronium (Group P) had a mean T_4/T_1 ratio of 0.72 ± 0.20 , which was lower than the mean values of 0.98 and 0.94 for Groups C and V, respectively ($P < 0.05$ for Group P vs V and Group P vs C) (Table I).

Sixty-one of the 64 patients were sufficiently awake and cooperative to undergo clinical testing (i.e., head-lift) in the PACU. One patient was unable to sustain head-lift for five seconds; this Group P patient had a $T_4/T_1 = 0.37$. The three patients who were unable to cooperate with clinical testing were likewise all in Group P; their TOF ratios were 0.43, 0.94, and 0.97. All patients in Group P and 23 of the 25 patients in Group V received neostigmine and glycopyrrolate at the conclusion of surgery (NS for difference between groups with respect to dosage).

Mean duration from the start of anaesthesia to the time when patients arrived in the PACU (i.e., total anaesthesia time) was 200 min for Group P, longer than for both Group C (145 min) and Group V (146 min) ($P < 0.05$). There were no significant differences with respect to age, sex, ASA physical status, antibiotic therapy, dose of reversal agents, duration from reversal to time of TOF testing, or incidence of intraoperative hypo- or hyperthermia (Table II).

Discussion

The current study corroborates previous reports^{1–6} that “residual” neuromuscular blockade, defined by a T_4/T_1 ratio < 0.70 , is common. The 45% incidence of residual blockade following the use of pancuronium and the 8% incidence following the use of vecuronium observed in the present study confirm the lesser likelihood of residual blockade when shorter-acting agents are used. This difference may be attributed to the longer half-life of pancuronium and to the existence of active metabolites. The former difference appeared to have been nullified when a high dose of vecuronium ($0.25 \text{ mg} \cdot \text{kg}^{-1}$) was used. Differing affinities for presynaptic receptors and/or tendencies for channel block may further contribute to the difference in residual effects of relaxants.

Ideally, intraoperative monitoring should document both readiness for reversal as well as adequacy of

TABLE II Mean demographic values

	Group C	Group V	Group P	P values
Age (yr)	47	40	50	NS
Weight (kg)	74	72	64	NS
Temperature in PACU (°C)	35.6	36.0	35.7	NS
Neostigmine dose (mg)	—	2.4	3.2	NS
Duration of surgery (min)	146	149	202	$P < 0.05$ for Group P vs V Group P vs C

subsequent recovery. In the present study, partial PACU curarization was not avoided by intraoperative visual and tactile assessment of the responses to TOF and/or tetanic stimulation. If partial curarization is due to only partial reversal (i.e., is “residual”), then more effective intraoperative monitoring is required. Although mechanographic assessment of response to supramaximal neuromuscular stimulation is the standard for assessment of residual blockade, its intraoperative use is limited by relatively elaborate set-ups. Alternatively, it has been shown that the absence of fade to TOF stimulation by tactile and visual means does not exclude partial curarization.⁹ Perhaps qualitative assessment by double-burst stimulation^{10,11} or less cumbersome electromyographic and accelerographic techniques^{12,13} will be helpful.

Postoperatively, neuromuscular testing is further limited by patient discomfort. The use of less painful, submaximal stimulating currents may facilitate such monitoring.⁷ The consistency of the T_4/T_1 ratio in response to currents of 20, 30 and 50 mA has recently been reported.^{8,14} An inter-current difference of less than 2% was noted for T_4/T_1 ratios (ranging from 0.1 to 1.0) obtained mechanographically, as long as all four twitches were detectable at the lower currents.^{8,9} All PACU patients in the current investigation were able to demonstrate four twitches to TOF stimulation, and testing at 20 mA proved to be consistent and well-tolerated.

Our findings are similar to other reports which have documented the inability to detect residual blockade in PACU patients using clinical criteria (Table III). The lack of sensitivity of head-lift testing to detect blockade in the present study was demonstrated by the fact that only one patient who was awake enough to cooperate with clinical testing was unable to sustain head-lift for more than five seconds. This patient had a TOF ratio of 0.37 and was in Group P.

It should be noted that there is controversy with respect to both the TOF value and to the clinical tests which indicate adequate reversal. Dupuis *et al.*¹⁷ have documented the differences between electromyographic and

TABLE III

Author and year of study	No. and percent of patients able to cooperate with clinical testing		No. of patients with TOF ratio < 0.70	No. of patients clinically weak with TOF ratio < 0.70	No. of patients weak TOF > 0.70
	n	%			
Lennmarken-1984 ³	46	(96)	12	3	0
Beemer-1986 ²	62	(62)	15	8	2
Bevan-1988 ⁴	113	(76)	12	5	3
Andersen-1988 ⁵	58	(97)	6	3	9
Viby-Mogensen-1979 ¹	68	(94)	30	15	1
Brull-1990	61	(95)	15	1	0

mechanographic TOF determinations as indicators of adequate clinical function. Dodgson *et al.*¹⁵ and Pavlin *et al.*¹⁶ reported that, although ventilatory function may be normal, upper airway musculature may be significantly compromised.

In conclusion, the present study emphasizes the potential for residual neuromuscular blockade in PACU patients. A better appreciation of the factors involved in residual blockade would be gained if intraoperative neuromuscular monitoring were performed quantitatively rather than qualitatively. Our data revealed that at our institution, the current intraoperative practice of clinical assessment plus neuromuscular monitoring did not necessarily prevent postoperative residual curarization, particularly in patients who received long-acting relaxants. Patients administered the shorter-acting agent vecuronium appeared to have better postoperative neuromuscular function. Train-of-four stimulation at 20 mA may be a sensitive method of detecting residual curarization when using a force transducer.

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