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RELATIONSHIP OF POST-TETANIC COUNT AND TRAIN-OF-FOUR RESPONSE DURING INTENSE NEUROMUSCULAR BLOCKADE CAUSED BY ATRACURIUM

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SUMMARY

Atracurium-induced intense neuromuscular blockade was evaluated in 60 randomly selected patients using the post-tetanic count (PTC) and train-of-four (TOF) methods. Thirty patients were anaesthetized with thiopentone, nitrous oxide and halothane, and 30 patients received thiopentone, nitrous oxide and fentanyl. In all patients, the response to post-tetanic single twitch stimulation appeared before the response to TOF stimulation, and a close correlation was found between the number of post-tetanic twitches (PTC) and the time interval between the PTC and the first detectable TOF response. A PTC of zero indicated that the time to first response to TOF stimulation was always more than 8 min. A PTC of 1 meant that the TOF response would appear in, on average, 9 min (95% confidence limits: 4–14 min). Halothane significantly prolonged the time from injection of atracurium to the first response to post-tetanic single twitch stimulation. It is concluded that the relationship between PTC and the time to first response to TOF nerve stimulation makes the PTC method a valuable supplement to TOF nerve stimulation for neuromuscular monitoring during clinical anaesthesia involving atracurium.

The short duration of action and rapid recovery rate of the non-depolarizing neuromuscular blocking agent atracurium (Hughes, 1985) has increased the need for reliable methods to assess objectively the degree of neuromuscular blockade. The ability to predict, in advance, the time for clinical recovery would ensure the precise timing of incremental doses and, hence, smoother clinical neuromuscular blockade.

Mechanical responses to single twitch, tetanic and train-of-four (TOF) nerve stimulation are often used to assess recovery from neuromuscular blockade (Ali and Savarese, 1976). During intense blockade, there is no response to these modes of stimulation, and the degree of blockade cannot be established (Viby-Mogensen, 1982). However, it is possible to quantify part of this so called "period of no response" by applying tetanic stimulation (50 Hz for 5 s) followed by single twitch (1-Hz) stimulation. The number of responses to the post-tetanic single twitch stimulation is called the post-tetanic count or PTC (Viby-Mogensen et al., 1981).

It has been shown that there is a close correlation between PTC and recovery from intense neuromuscular blockade caused by pancuronium (Howardy-Hansen et al., 1984).

The objective of this study was to clarify whether a similar correlation exists between PTC and recovery from blockade caused by atracurium.

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PATIENTS AND METHODS

Sixty surgical patients (32 male, all ASA Class I or II) were included in the study. Informed consent was not sought, since neuromuscular monitoring was considered routine and did not pose any risk to the patients. The study was

approved by the College of Medicine Research Centre of our institution.

The patients were allocated randomly to two groups of 30 patients each. All patients were given lorazepam 2–3 mg by mouth 2 h before induction. Anaesthesia was induced with sodium thiopentone 3–5 mg kg^{-1}. Patients in group 1 were allowed to breathe 1–2% halothane in 50% nitrous oxide and 50% oxygen. Group 2 did not receive halothane, and anaesthesia was maintained with 70% nitrous oxide in oxygen and fentanyl 2–3 μg kg^{-1} i.v.

Neuromuscular monitoring commenced immediately after induction. The ulnar nerve was stimulated using surface electrodes and the mechanical response of the adductor pollicis muscle recorded using the Myograph 2000 neuromuscular transmission analyser. TOF nerve stimulation (repeated at 10-s intervals) was used. After supramaximal stimulation was achieved, a bolus of atracurium 0.6 mg kg^{-1} was injected i.v. The trachea was intubated and the lungs ventilated using a tidal volume of 10 ml kg^{-1} at a rate of 12 b.p.m.

At 6-min intervals, tetanic stimulation (50 Hz) was applied for 5 s followed by a 3-s pause. On each occasion the tetanic stimulation was preceded by a 1-min period of 1-Hz stimulation, which was continued after the 3-s pause. When there was no response to the 1-Hz stimulation or the observed response had faded to zero, TOF mode of stimulation was reinstituted until 1 min preceding the next tetanic stimulation (Viby-Mogensen et al., 1981). The cycle was repeated until 6 min after the first detectable response to the first stimulus in the train-of-four (TOF).

RESULTS

The two groups were similar in respect of age and weight (table I).

The first responses to post-tetanic twitch stimulation (PTTS) were seen at mean times of 34.4 and 30.3 min after the injection of atracurium in groups 1 and 2, respectively ($P < 0.05$, table I). In comparison, the first detectable response to TOF stimulation appeared after mean times of 41.9 min (group 1) and 38.1 min (group 2) (ns). When no response to PTTS was seen, time to first detectable response to TOF nerve stimulation was always more than 8 min. The mean numbers of post-tetanic twitches at the time of the first detectable response to TOF stimulation were 7.6 in group 1 and 8.0 in group 2 (ns).

During a trial of pancuronium-induced neuromuscular blockade, a close linear relation was found between the time to first detectable response to TOF nerve stimulation and the square root of PTC (Viby-Mogensen et al., 1981). This relationship can be expressed as:

$$t = a + b\sqrt{\text{PTC}}$$

where PTC is post-tetanic count, t is time from a given PTC to the first detectable TOF response, a is a constant (intercept) and b is the regression coefficient (slope).

Because of the rapid recovery rate of atracurium only two, or sometimes three, non-zero readings were obtained per patient in the present study. Therefore, each patient's regression coefficient could not be evaluated. Instead, for each group, all patient data were pooled and the optimal regression coefficient evaluated by the standard least squares method. As the objective of the PTC

TABLE I. *Age and weight distribution, and neuromuscular effect of atracurium 0.6 mg kg^{-1} in the two groups of patients. Group 1 = halothane* (n = 30)*; group 2 = fentanyl* (n = 30)*. PTTS = Post-tetanic twitch stimulation; TOF = train-of-four nerve stimulation; PTC = post-tetanic count = number of responses to PTTS. * Statistically significant difference between groups* (P < 0.05)

	Group 1			Group 2		
	Mean	SD	Range	Mean	SD	Range
Age (yr)	33.4	12.9	18–76	35.4	11.7	18–60
Weight (kg)	63.5	12.7	42–88	69.0	13.4	44–99
Time (min) from injection to first response to:						
PTTS *	34.4	7.5	19–48	30.3	7.3	18–48
TOF *	41.9	8.0	25–58	38.1	7.6	28–60
PTC at first response to TOF	7.6	1.6	6–10	8.0	2.0	4–11
	(n = 11)			(n = 11)		

method is to predict how soon after a given PTC the first detectable reaction to TOF will appear, and counts of 12 or more always occurred after the first response to TOF, these counts were excluded from the analysis.

The indices of regression are presented in table II. In both groups, there was a highly significant correlation between the square root of the PTC and the time-interval between a given PTC and the first detectable TOF response. Using standard methods, the estimated slopes of the two curves (*b*) were tested, but no significant difference was found. Using the pooled estimate of the slope (−4.9), the intercepts of the two curves (*a*) were then evaluated and tested. These intercepts, 14.1 for group 1 (halothane) and 13.2 for group 2 (fentanyl), were found to differ significantly. This implies that, throughout the PTC range of 1–12, the time before TOF for any given PTC was, on average, 1 min longer for the halothane group. However, this difference was not clinically significant. Therefore, both sets of data were combined and the overall curve (with 95% confidence intervals) is shown (fig. 1). The individual results have also been plotted to show the goodness-of-fit. It appears from figure 1 that a PTC of 1 indicates that the first detectable response to TOF would appear in, on average, 9 min, with 95% of the responses appearing between 4 and 14 min. The average time to first reaction to TOF corresponding to other PTC values can be read from the graph.

TABLE II. *Regression indices. SD = Standard deviation of the difference between observed and predicted values*

	Group 1	Group 2	Combined
a	14.8	12.5	13.7
b	−5.2	−4.5	−4.9
SD	2.42	2.05	2.29
Correlation coeff.	−0.848	−0.873	−0.85
Significance of correlation	$P<0.001$	$P<0.001$	$P<0.001$

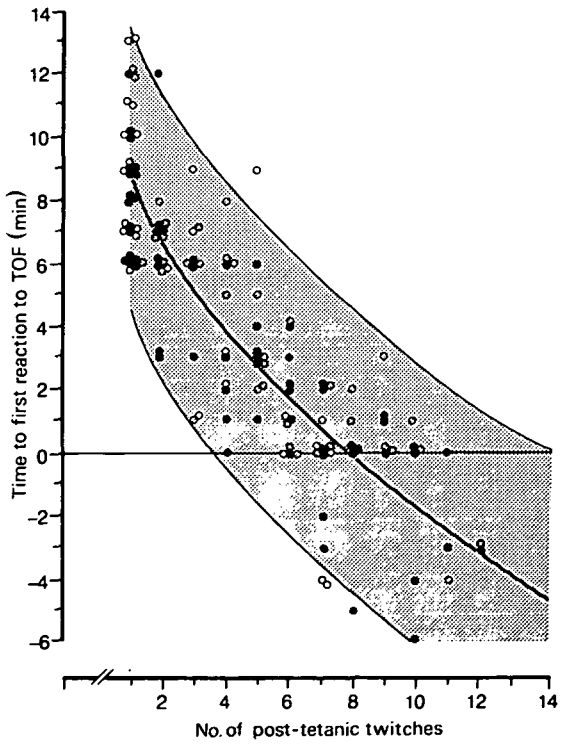

FIG. 1. Pooled data of 60 patients showing the relationship of post-tetanic count (PTC) and time of onset of TOF response. The predicted mean curve with 95% confidence limits are shown. ○ = Halothane group; ● = fentanyl group.

DISCUSSION

Our results indicate that, during intense neuromuscular blockade caused by atracurium, the PTC method gives early warning of the onset of neuromuscular recovery, offering the opportunity to maintain stable and smooth muscle relaxation.

The response to PTTS appeared, on average, 9 min (range 6–15 min) before the first detectable response to TOF stimulation. Further, a close correlation was found between PTC and the time-interval between the PTC and the first detectable response to TOF nerve stimulation (fig. 1). This implies that, even though a patient seems totally relaxed clinically, and no response to TOF or to single twitch stimulation can be elicited, it is still possible—using the PTC method—to evaluate the degree of blockade and, for instance, to decide when it will be necessary to give supplementary doses of atracurium. If there is no response at all to PTTS (PTC = 0), the blockade is still intense and it will take at least 8 min before the first response to TOF will appear. On the other hand, a PTC of, for instance, 6 or 7 would indicate that the first response to TOF is imminent (fig. 1).

The relationship between PTC and TOF found in this study differs from that present during neuromuscular blockade caused by pancuronium (Viby-Mogensen et al., 1981). Figure 2 shows the predicted mean curves (and 95% confidence limits) of the correlation between PTC and the time to first reaction to TOF for both pancu-

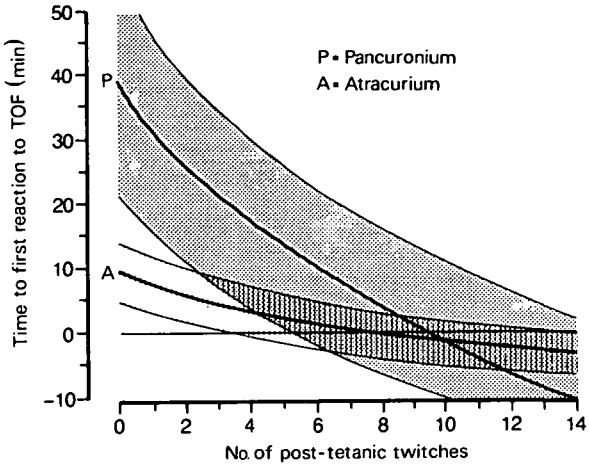

FIG. 2. Comparison of the relationship of post-tetanic count (PTC) and onset of TOF response for pancuronium (Viby-Mogensen et al., 1981) and atracurium. The predicted mean curves with 95% confidence limits are shown.

ronium (Viby-Mogensen et al., 1981) and atracurium. As would be expected, the slopes as well as the positions of the two curves differ. For example, during pancuronium-induced blockade a PTC of 2 indicates that the first TOF response will appear in 25 min. Contrary to this, during intense blockade caused by atracurium, a PTC of 2 would indicate that the first response to TOF would appear in, on average, 7 min. Therefore, whenever the PTC method is used to quantify intense non-depolarizing neuromuscular blockade, it is imperative to take into consideration the neuromuscular blocking drug used.

In summary, during intense atracurium-induced neuromuscular blockade, the time to the return of response to TOF stimulation may be derived from the PTC. It has previously been shown that the response to PTTS can be felt and counted (the PTC) with reasonable accuracy (Howardy-Hansen et al., 1984). In view of this, and the rapid recovery rate of atracurium, the PTC method appears to be a valuable supplement to TOF nerve stimulation during clinical anaesthesia involving atracurium.

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