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## Evaluation of Intense Neuromuscular Blockade Caused by Vecuronium Using Posttetanic Count (PTC)

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Injection of a non-depolarizing relaxant in a dose sufficient for smooth tracheal intubation causes intense neuromuscular blockade of the peripheral muscles indicated by disappearance of the response to train-of-four (TOF) and single twitch stimulation.<sup>1</sup> It is possible to quantify part of this period of no response by applying tetanic stimulation (50 Hz for 5 s) followed by 1 Hz stimulation and observing the posttetanic single twitch response (posttetanic count or PTC). A close correlation was found to exist between PTC and recovery from intense blockade caused by pancuronium.<sup>2,3</sup>

The objective of the present study was to evaluate the relationship between PTC and recovery from intense neuromuscular blockade caused by vecuronium.

### METHODS AND MATERIALS

The study plan was approved by the College of Medicine Research Center of our institution. Informed consent was not sought, because neuromuscular monitoring is considered routine, is non-invasive, and does not pose any risk to the patient. No patient had any neuromuscular

disease or received any drug that might influence neuromuscular function.

Sixty adult patients (ASA physical status I-II) undergoing intraabdominal or orthopedic procedures were studied. The patients ranged in age from 16-65 yr (mean: 32 yr), and there were 20 females and 40 males. All patients were given lorazepam 1-3 mg orally 2-4 h before induction. The patients were divided randomly into two groups of 30 each. In all patients, anesthesia was induced with sodium thiopental 3-5 mg · kg<sup>-1</sup> body weight. Patients in group 1 were then allowed to breathe halothane in 50% O<sub>2</sub> with N<sub>2</sub>O sufficient to achieve surgical plane of anesthesia (0.6-2.0% inspired halothane concentration as indicated by a Fluotec Mark III vaporizer). Patients in group 2 breathed 30% O<sub>2</sub> with N<sub>2</sub>O, supplemented with fentanyl 2-4 mg · kg<sup>-1</sup>. Following induction of anesthesia, the ulnar nerve was stimulated at the wrist through cutaneous electrodes, and the response of the adductor pollicis muscle was recorded using the Myograph 2000 neuromuscular transmission analyzer.<sup>2</sup> TOF nerve stimulation was used every 12 s. After supramaximal stimulation was achieved, 0.1 mg · kg<sup>-1</sup> body weight vecuronium was given intravenously. The trachea was intubated when the response to TOF stimulation had disappeared, and the patients were ventilated with a tidal volume of 10 ml · kg<sup>-1</sup> and a respiratory rate of 12 min<sup>-1</sup>, the aim being to maintain normocapnia (arterial blood gas measurements were made periodically). As cooling of the patients was not a problem in Saudi Arabia, body temperature was not monitored routinely. Every 6 min, the mode of nerve stimulation was changed: 1 Hz twitch stimulation was given for 1 min, followed by tetanic stimulation (50 Hz) for 5 s. After a pause of 3 s, the single twitch stimulation was resumed. If there was no response to this stimulation (PTC = 0), or when the observed response had faded to zero, the TOF mode of stimulation was reinstated until

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the next cycle.<sup>2</sup> The last tetanic stimulation was given 6 min after the first response to TOF stimulation had reappeared.

Patients assigned to either halothane or fentanyl were compared by the Chi-square test (for sex) and Student's *t* test (for age and weight). Other pairs of means were also tested by Student's *t* test and variances by the *F* test. The regression curves were fitted using the standard least square method. For all tests, a significance level of 0.05 was used.

RESULTS

The two groups were similar in age, sex, and weight distribution. After the injection of vecuronium, the first response to posttetanic twitch stimulation (PTTS) was seen at a mean time of 19.8 min for the halothane group and 18.4 min for the fentanyl group (N.S.) (table 1). The first detectable response to the TOF stimulation appeared at 26.8 min for the halothane group, and at 25.5 min for the fentanyl group (N.S.). When no response to PTTS was seen, time to the appearance of the response to TOF nerve stimulation was always more than 7 min. The post-tetanic count (PTC) at the appearance of the first TOF response was 9.7 (mean) for the halothane group and 10.0 (mean) for the fentanyl group (N.S.).

In the previous trials using pancuronium, a close correlation was found to exist between the square root of PTC and the time to the onset of TOF response from that PTC.<sup>2,3</sup> This can be expressed as:

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

where *t* = the interval between a given PTC and the first detectable response to TOF stimulation; *a* = a constant (intercept), and *b* = the regression coefficient (slope) of this linear relationship.

Because of the short duration of action of vecuronium, only two or three PTC determinations per patient could be made before the onset of TOF response. It was, therefore, not possible to evaluate each patient's correlation coefficient. The data from each group were pooled, and the optimal regression coefficient was evaluated. The correlation coefficients (with their levels of significance), the regression coefficients, and the residual standard deviations are shown in table 2. The lines fitted both sets of data with correlation coefficients of -0.85 for both the halothane and fentanyl groups. The regression coefficients for the halothane and fentanyl groups were then tested for similarity. Neither the slopes (*b* coefficients) nor the intercepts (*a* coefficients) showed any significant difference. Both sets of data were then pooled, and the combined line of best fit evaluated (fig. 1). The individual points are also plotted to show the goodness of fit. From this graph, the expected time of onset of TOF response

TABLE 1. Neuromuscular Effect of Vecuronium 0.1 mg · kg<sup>-1</sup> in the Two Groups of Patients

	Halothane (n = 30)			Fentanyl (n = 30)		
	Mean	SD	Range	Mean	SD	Range
Min from injection to first response to:						
PTTS	19.8	3.6*	12-30	18.4	5.2*	6-24
TOF	26.8	4.8	18-40	25.5	5.7	18-37
PTC at first response to TOF	9.7 (n = 12)	3.8	6-17	10.0 (n = 11)	2.8	6-15

PTTS = posttetanic twitch stimulation; TOF = train-of-four nerve stimulation; PTC = posttetanic count = number of responses to PTTS.  
\* Indicates a statistically significant difference between the variance of the two groups.

can be predicted from the PTC. For example, a PTC of 1 indicates that the response to TOF would appear, on average in 8 min, with the response for 95% of patients occurring between 4 and 13 min.

DISCUSSION

The response to PTTS appeared an average of 8.5 min (range 6-15 min) before the first detectable response to TOF stimulation. Further, a close correlation was found between PTC and time to a response to TOF stimulation (fig. 1). The PTC method is thus the only method of nerve stimulation that allows the clinician to evaluate, in a more quantitative fashion, intense neuromuscular blockade following vecuronium. The advantage of this technique is most obvious following intubation in situations where it is crucial to avoid sudden movements of the respiratory muscles. Following intubation with vecuronium, it is possible, using the PTC method, to get an indication of when the response to TOF nerve stimulation will reappear. If there is no response at all to PTTS (PTC = 0), the neuromuscular blockade is still intense, and it will take at least 7 min before a response to TOF stimulation will appear. On the other hand, a PTC of, for instance, 8-9 indicates that a response to TOF is imminent (fig. 1).

TABLE 2. Regression Parameters

	Halothane	Fentanyl	Combined
<i>a</i> (intercept)	12.4	12.3	12.4
<i>b</i> (slope)	-4.0	-3.7	-3.9
Sy*	2.35	2.09	2.22
Correlation coefficient	-0.85	-0.85	-0.85
Significance of the correlation	0.01	0.01	0.01

\* The standard deviation of the difference between observed and predicted values.

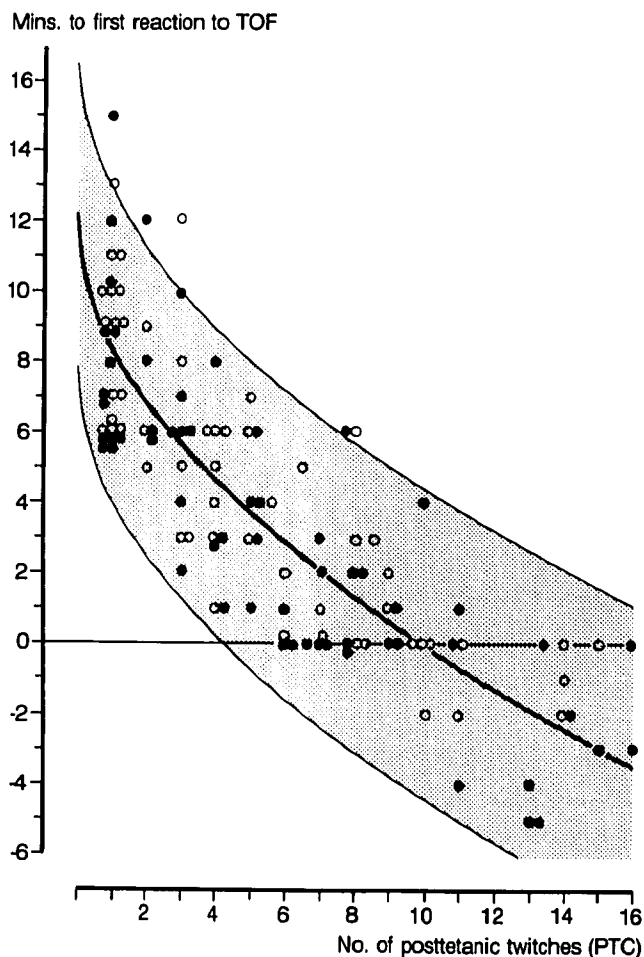


FIG. 1. Relationship between the posttetic count (PTC) and time to onset of the response to TOF stimulation during neuromuscular blockade caused by vecuronium. The individual data points and the predicted mean curve with 95% confidence limits are shown.  $\circ$  = halothane group;  $\bullet$  = fentanyl group.

The diaphragm is less sensitive to neuromuscular blocking drugs than the peripheral muscles.<sup>4</sup> Hiccup, bucking, and coughing may therefore occur during surgical procedures, in spite of total abolition of the response to TOF stimulation. When it is important to avoid sudden movements during anesthesia, for example, in major ophthalmic surgery,\* the PTC method can be used to quantify the more intense blockade that is necessary to prevent such movements. Thus far, the correlation between the PTC of the peripheral muscles and the degree of paralysis of the diaphragm has not been investigated. However, studies in progress indicate that, to exclude any bucking or coughing, *i.e.*, to ensure total diaphragmatic

paralysis, the neuromuscular blockade of the peripheral muscles should be so intense that no response to PTTS (PTC = 0) can be elicited.

In addition, the PTC method may be useful whenever there is no response to TOF nerve stimulation. Although there are few clinical indications for producing a neuromuscular blockade that eliminates all response of the TOF, in reality, this frequently happens. If, for instance, there is no response to TOF stimulation at the end of a case, the PTC will indicate how long it is going to take before reversal of the neuromuscular block can be initiated (*i.e.*, at least one response to TOF stimulation is present).

The physiologic basis for the PTC method is that the enhancement of posttetanic twitch tension (posttetanic facilitation) in patients partially paralyzed with a new depolarizing muscle relaxant remains constant, regardless of the magnitude of neuromuscular blockade.<sup>5</sup> Therefore, the response to PTTS appears earlier than the twitch and the TOF response during recovery from intense neuromuscular blockade.<sup>2</sup> However, the degree of posttetanic facilitation and, thus, the PTC is dependent upon the frequency and the duration of the tetanic stimulus, the time lapse between the conclusion of the tetanic stimulus and the first posttetanic single stimulus, the frequency of the single twitch stimuli, and, probably, also on the duration of the single twitch stimulation before the tetanic stimulus. All of our studies with the PTC method have been performed using 1 min 1 Hz twitch stimulation before a 50 Hz tetanic stimulation given for 5 s, with a time lapse after the tetanic stimulation of 3 s.<sup>2,3</sup> Further, to exclude that the tetanic stimulation, in itself, influences recovery of neuromuscular blockade, the tetanic stimulations have never been given more often than every 6 min.<sup>3</sup> A prerequisite for the use of the PTC nomograms published by us is, therefore, that these variables are not changed (studies are in progress to see if it is possible to shorten the period of pretetanic twitch stimulation, without changing the relationship between the PTC and the TOF response).

The present study was performed in normal individuals following injection of a bolus of vecuronium. As vecuronium may accumulate, a different relationship probably exists between PTC and TOF following a long-lasting infusion of the drug, and in patients with severe liver or kidney disease. This problem remains to be investigated.

In conclusion, following vecuronium  $0.1 \text{ mg} \cdot \text{kg}^{-1} \text{ iv}$ , a close correlation was found between the number of posttetanic twitches (the posttetic count or PTC) and the time of onset of the TOF response. The response to posttetanic twitch stimulation appeared, on the average, 8.5 min before the first detectable response to TOF stimulation. A PTC of 8–9 indicated that a response to TOF

\* Hunter JM, Kelly JM, Jones RS: Atracurium infusion in major ophthalmic surgery. *Eur J Anaesth* 4:9–15, 1987.

was imminent. Thus, the PTC method allows the anesthesiologist to evaluate, in a more quantitative fashion, vecuronium-induced intense neuromuscular blockade.

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