

Clinical Recovery and Train-of-Four Ratio Measured Mechanically and Electromyographically Following Atracurium

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Indices of clinical recovery were compared with mechanically (adductor pollicis muscle) and electromyographically (first dorsal interosseal muscle) recorded train-of-four (TOF) ratios during antagonism of atracurium blockade in 23 healthy neurolept anesthetized patients. Clinical recovery was evaluated from the ability to lift the head, sustain headlift for 5 or 10 s, protrude the tongue, open the eyes, and the presence of ptosis of the eyelids. In all patients the mechanical TOF ratio was recorded. In 17 patients TOF ratios based on measurements of the potential area and the amplitude of the major negative deflection of the compound EMG response were recorded as well. At each TOF ratio interval of 0.05 from a TOF ratio of 0.5–0.85, the number of patients being able to perform the individual tests was recorded. Further, the mechanical TOF ratio during recovery was compared with the EMG TOF ratios. Headlift could not be sustained for 5 s in any patient at a TOF ratio of 0.5, whether recorded mechanically or by EMG, and TOF ratio had to recover to 0.8 before all patients could sustain headlift for 5 s. All patients could open the eyes and protrude the tongue at a TOF ratio of 0.65, and ptosis remained present during the entire testing period. There was no statistically significant difference between the mechanical and the EMG methods with regard to the TOF ratios at which the tests could be performed. During recovery a linear relationship was found between mechanical TOF ratios and the square root of the EMG TOF ratios. It is concluded that the TOF ratio, whether recorded mechanically or by EMG, must exceed 0.8 to exclude residual curarization from atracurium blockade. (Key words: Measurement techniques: electromyography. Neuromuscular relaxants: atracurium. Neuromuscular transmission.)

A COMMON CRITERION for adequate clinical recovery following nondepolarizing neuromuscular blockade has been a train-of-four (TOF) ratio of 0.7.¹⁻³ This ratio was derived from studies in which clinical recovery from long-acting relaxants was compared with the evoked mechanical twitch of the adductor pollicis muscle. However, it has recently been suggested that a TOF ratio of only 0.5 is compatible with safe recovery following intermediate duration of action relaxants, such as atracurium.^{4,5}

Although mechanical twitch recordings are still used in most studies involving neuromuscular blocking drugs, there has been a growing interest in the electromyographical (EMG) method. In many studies the two meth-

ods have been compared,⁶⁻¹² but the actual relationship between clinical recovery and the electromyographically recorded response to peripheral nerve stimulation has not been established. We therefore compared indices of clinical recovery with mechanically and electromyographically recorded TOF ratios during antagonism of atracurium blockade. We also established the specific TOF ratio that is indicative of safe clinical recovery using atracurium.

Materials and Methods

A microprocessor controlled unit developed in our laboratory, which incorporated a Myotest nerve stimulator (Biometer),¹³ was used to monitor neuromuscular transmission. This unit delivered simultaneous recordings of the compound EMG response and the mechanical twitch. For the EMG recording, small gelled silver-silver chloride surface electrodes were used. The EMG response was gated (18 ms), band pass filtered (0.5 Hz to 1 kHz), amplified ($\times 1,000$), analog to digital converted, and stored in the memory of the computer. To avoid recording of the stimulus artifact, a manually adjustable delay (1–3 ms) was incorporated. The area (I) contained within the negative deflection of the compound EMG signal and the amplitude (P) of that deflection from the isoelectric line were calculated by the computing unit. The mechanical response (M) was measured by a force displacement transducer (Statham UC 3 gold cell), and similar to the EMG response, it was stored in the memory after analog to digital conversion. The TOF ratio (T4) of the EMG (IT4 or PT4) and the mechanical response (MT4) were continuously shown at the display of the computer and printed out. The mechanical response and a reconstituted analogue waveform of the compound EMG response with a time expansion of $\times 80$ were recorded continuously.

Twenty-three women, ASA physical status 1 or 2 scheduled for elective surgery, gave informed consent to the study. The protocol for the study was approved by the local Ethics Committee. None of the patients had neuromuscular disease or received any drugs that might alter neuromuscular function. The patients ranged in age from 25 to 70 yr. One hour before anesthesia, diazepam 0.2 mg/kg was given orally for preanesthetic medication. Anesthesia was induced with droperidol 5–10 mg, fentanyl 0.1–0.2 mg, and thiopental 3–5 mg/kg iv and maintained with 66% nitrous oxide in oxygen and supplementary doses of fentanyl 0.05–0.1 mg iv. Ventilation was controlled at a level sufficient to maintain normocap-

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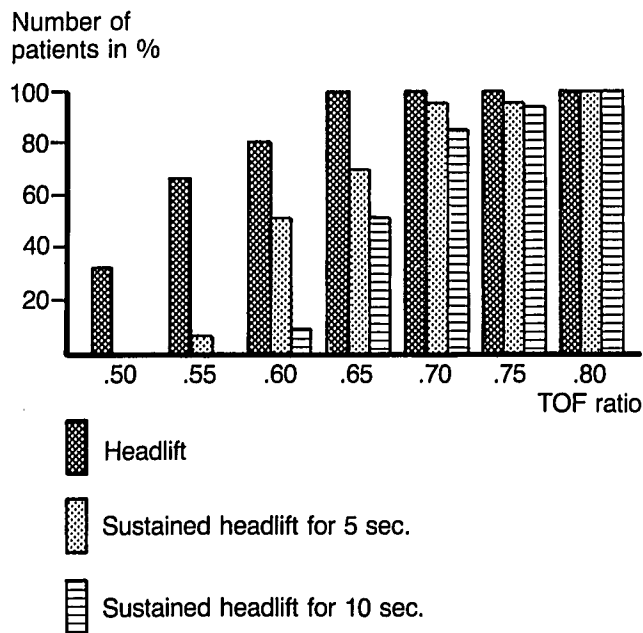


FIG. 1. Percentage of patients being able to lift the head, to sustain headlift for 5 s, or for 10 s, respectively, in relation to mechanically measured TOF ratio during induced recovery from atracurium-induced blockade.

nia as determined by intermittent analysis of arterial blood gases. Peripheral temperature was monitored from a cutaneous probe placed on the dorsum of the hand from which the response to peripheral nerve stimulation was recorded.

Following induction of anesthesia the ulnar nerve was stimulated at the wrist through cutaneous electrodes. In all patients neuromuscular transmission was monitored using supramaximal TOF nerve stimulation by measuring the mechanical response of the adductor pollicis muscle as previously described.¹⁴ Thumb preload was adjusted to between 250 and 300 g. Sixteen of the patients had the EMG response monitored from the first dorsal interosseal muscle from the same hand. When stable control responses of both the EMG and the mechanical twitch were obtained, tracheal intubation was performed following a bolus injection of atracurium 0.4 mg/kg. Using a continuous infusion of atracurium ($0.78 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$), the block was maintained at a deep level corresponding to one or two responses being present after a 50-Hz tetanic stimulation for 5 s (post tetanic count [PTC] of 1 or 2).¹⁵ At the end of surgery neuromuscular recovery was induced by neostigmine 0.06 mg/kg preceded by glycopyrrolate 0.012 mg/kg at a median PTC level of 7 (3–16). TOF ratio was continuously recorded as soon as the TOF response reappeared during recovery. When a mechanical TOF ratio of 0.45–0.50 was reached, N_2O was turned off and 100% O_2 was given. Tracheal extubation was performed at a mechanical TOF ratio of 0.5 if the

patient was awake and the respiration was judged to be sufficient from the movement of the breathing bag. All patients received doxapram 0.3 mg/kg to counteract central respiratory depression.

After tracheal extubation clinical recovery was evaluated from five different tests: the patient's ability to lift the head, to sustain headlift for 5 s or for 10 s, open the eyes, protrude the tongue, and the presence of ptosis of eyelids. The patient was asked to perform each of the tests every 2–3 min, and the number of seconds headlift could be sustained was observed. The TOF ratio at which the individual test could be performed was registered. The observer was not aware of the actual TOF ratio during the period of clinical testing. Five seconds of sustained headlift was taken to reflect adequate recovery of neuromuscular blockade.^{16,17} It was not possible to perform tracheal extubation and start the clinical testing in all patients at a mechanical TOF ratio of 0.5, partly because some patients were still asleep and partly because neuromuscular recovery in some patients was too rapid. Therefore, at each TOF ratio interval of 0.05, from a TOF ratio of 0.5–0.85, the number of patients being able to perform the different tests was calculated in relation to the total number of patients tested at that particular level of block. For further evaluation of the EMG and the mechanical response, TOF ratios obtained simultaneously from both methods during recovery were compared. In each patient one or two paired observations were made in each 0.10 TOF ratio interval from a TOF ratio of 0.15 until the stimulation was no longer accepted to the patient. For statistical evaluation of the results the McNemar test for related samples, Student's *t* test, and random coefficient linear regression were used. Significance was assigned at a level of 0.05 or less.

Results

Among the 23 patients having the mechanical twitch recorded, only 10 and 15 patients were tested at a TOF ratio of 0.5 and 0.55, respectively. All patients were tested at a TOF ratio of 0.6. Among the 16 patients whose neuromuscular response was recorded both mechanically and by EMG, 8 and 12 patients, respectively, were tested at a mechanically measured TOF ratio of 0.5 and 0.55. At a TOF ratio of 0.6 or greater, all 16 patients were tested. Mean peripheral surface temperatures (ranges) at induction of anesthesia, at the time of injection of neostigmine, and when TOF ratio had reached 0.7 were 30.7°C (28.6 – 34.3°C), 33.0°C (28.4 – 35.0°C), and 32.3°C (28.1 – 34.2°C), respectively.

Figure 1 shows the results of the headlift tests from all patients having the mechanical twitch recorded. The percentages of patients at each TOF ratio interval being able

to lift the head, to sustain headlift for 5 s, and for 10 s are presented. Headlift could not be sustained for 5 s by any patients at a TOF ratio of 0.5, and by only 52% of the patients at a TOF ratio of 0.6. At a TOF ratio of 0.70 and 0.75, one patient was still not able to sustain headlift for 5 s.

Mean values (ranges) of the MT4 at which the head could be lifted, sustained for 5 s and for 10 s were 57.8 (50–65), 64.1 (55–80), and 67.9 (60–80), respectively. Median time (range) from a MT4 of 0.5 to sufficient recovery as reflected in 5 s sustained headlift was 6.3 min (1.8–11.2).

Figure 2 shows the results of the headlift tests from the patients having both the mechanical twitch and the EMG recorded. Only results obtained with the IT4 are presented because there was no statistically significant difference between IT4 and PT4 with respect to the number of patients being able to perform the headlift tests. Below a TOF ratio of 0.60–0.65, more patients were able to perform the tests for headlift if quantitation was made from the EMG compared with the mechanical twitch. However, a statistically significant difference between the two methods used was only found at a TOF ratio of 0.55 in the test for 5 s sustained headlift. The electromyographically measured TOF ratio also had to recover to 0.8 before all patients were able to sustain headlift for 5 s.

All patients were able to open the eyes at the time of extubation. Eighty percent of the patients were able to protrude the tongue at a MT4 of 0.5, and all patients were able to do so at a MT4 of 0.65. Ptosis was present in all patients during the period of clinical testing. There was no statistically significant difference between the mechanical and the EMG method regarding the ability to open the eyes, protrude the tongue, or presence of ptosis of the eyelids.

The relationship between TOF ratios recorded mechanically and electromyographically was investigated. For each patient a linear relationship was adequate to describe the relation between both MT4 and $\sqrt{IT4}$ as well as between MT4 and $\sqrt{PT4}$. The individual regression lines varied among patients for both the relationship between MT4 and $\sqrt{IT4}$ as well as for that between MT4 and $\sqrt{PT4}$. Under the assumption of bivariate normality of the individual regression parameters (true unknown level for an electromyographic response of 0.5 and slope of the lines), prediction areas for the mechanical response MT4, given the EMG response IT4 or PT4, were constructed. The estimated mean (\pm SE) of the regression coefficients β and α for both relationships noted above are given in table 1. The estimated regression lines with 95% prediction limits for these relationships are shown in figures 3 and 4, respectively. Individual observations have been plotted to show the goodness-of-fit.

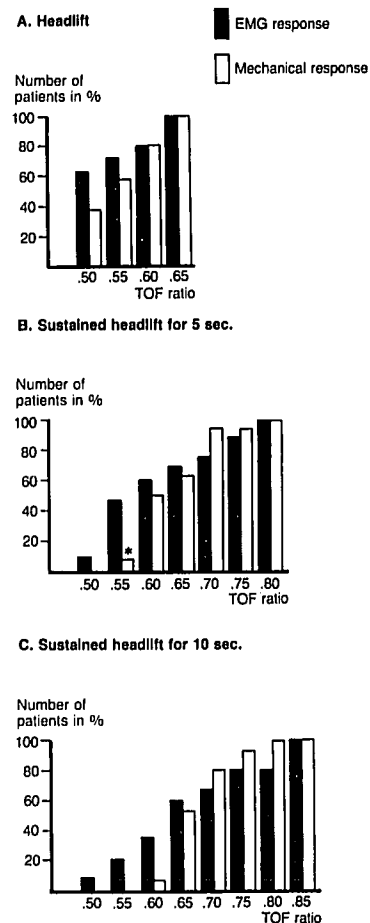


FIG. 2. Percentage of patients being able to lift the head (A), sustain headlift for 5 s (B), or for 10 s (C) in relation to TOF ratio as quantitated both from the mechanical twitch response and the integrated compound electromyogram during induced recovery from atracurium blockade. *Statistically significant difference ($P < 0.05$) between the two methods.

Discussion

The results of the present study suggest that the well-known relationship between clinical recovery and mechanically recorded TOF ratio as established several years ago for the longer-acting relaxants¹⁻³ also exists for the intermediate-acting relaxant atracurium. They further suggest that this relationship is applicable whether TOF ratio is recorded mechanically or by EMG.

Clinical tests, such as the sustained headlift, protrusion of the tongue, and sustained eye opening, are simple to perform and have been widely used in the clinical assessment of neuromuscular recovery.^{1,2,16,18} Among these tests a 5 s sustained headlift has normally been taken to reflect adequate recovery.^{16,17} In the present study 96%

TABLE 1. The Estimated Mean (\pm SE) for the Regression Coefficients β and α from the Linear Relationship Between MT4 and $\sqrt{IT4}$ and Between MT4 and $\sqrt{PT4}$

	IT4	PT4
α	0.546 \pm 0.012	0.538 \pm 0.012
β	1.225 \pm 0.040	1.264 \pm 0.042

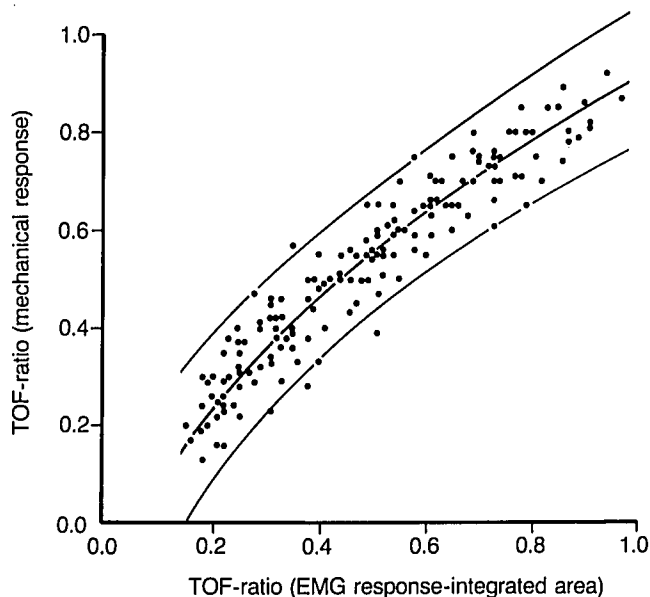


FIG. 3. Scattergram and estimated regression line of simultaneous TOF ratios recorded from the mechanical twitch and the integrated area of the negative deflection of the electromyogram; 95% prediction limits are given. Number of observations = 171.

of the patients were able to sustain headlift for 5 s at a TOF ratio of 0.70. At this level all patients were able to protrude the tongue and open the eyes widely. These findings are almost identical with the results of several previous reports in which longer-acting relaxants were used.^{1,2,18} However, even though a TOF ratio of 0.7 for

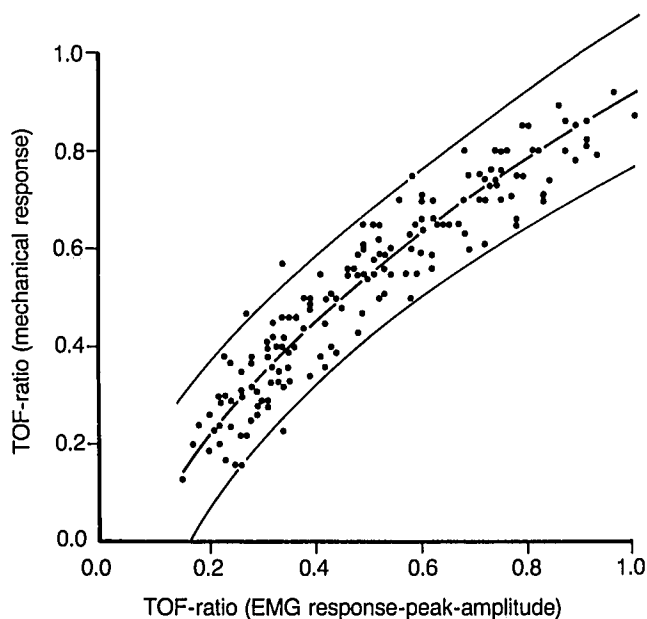


FIG. 4. Scattergram and estimated regression line of simultaneous TOF ratios recorded from the mechanical twitch and the amplitude of the negative deflection of the electromyogram; 95% prediction limits are given. Number of observations = 171.

many years has been taken to reflect adequate recovery, some patients, both in previous reports and in the present study, were not able to sustain headlift for 5 s unless the TOF ratio had recovered to 0.75–0.80. Clinicians using the TOF method should therefore realize that some individuals may still suffer from residual clinically important paralysis following both longer-acting relaxants and atracurium even at a TOF ratio of 0.70.

Only recently has it been suggested that a TOF ratio above 0.50 is compatible with safe reversal of atracurium-induced neuromuscular blockade.^{4,5} This is in contrast to our findings showing that no patients were able to sustain headlift for 5 s at a TOF ratio of 0.50. We have no obvious explanation for this discrepancy except that in our study recovery was induced from an intense level of blockade as quantitated by the PTC. Thus, recovery may have proceeded more slowly, enabling us to relate clinical recovery and TOF ratio in a more precise way.

The TOF ratio of the evoked mechanical and EMG responses have been compared in several previous studies using either electrical amplitude^{6,8,11} or the area of the compound EMG response.^{9,10,12} Generally, a close relationship is found between mechanical twitch recordings and the EMG during recovery from nondepolarizing blockade, but an actual comparison of different parameters of the EMG response has only been made during onset.¹⁹ Our results suggest that the TOF ratio of the electrical amplitude and of the area of the negative deflection of the compound EMG response can be used interchangeably to assess recovery from atracurium blockade. Our study further indicates that the mechanical and the EMG responses are similar in their relation to clinical recovery from atracurium blockade. Irrespective of the method used, residual neuromuscular blockade could not be excluded unless the TOF ratio had recovered to 0.80. Some differences could, however, be observed. Thus, in some patients the EMG response initially recovered more slowly than the mechanical response. This explains why at a TOF ratio below 0.6–0.65 patients were able to perform headlift tests when evaluated from the EMG response compared with that from the mechanical twitch. These differences between recovery of the EMG and the mechanical twitch response are also reflected in the estimated lines of regression as shown in figures 3 and 4. Our findings of a linear relationship between MT4 and the square root of the EMG recorded TOF ratio suggest a slower initial recovery of the EMG response. This finding is in contrast to the results of several previous studies comparing mechanical twitch and EMG during recovery from atracurium blockade.^{9–12} In those studies mechanical TOF ratio recovered more slowly than that of the EMG. The differences are unlikely to be explained by different measuring principles^{9–12} because we found an almost identical recovery of the IT4 and the PT4. Other meth-

odologic differences may explain the lack of agreement between our results and those of others. Thus, in the studies of Kopman⁹ and Carter *et al.*,¹² simultaneous data observations of the EMG and the mechanical TOF ratio were apparently pooled without estimation of regression lines of individual patients. The actual relationship may thus have been obscured. Furthermore, in previous studies the mechanical twitch of the adductor pollicis muscle has been compared with the EMG response of either the hypothenar^{9,10} or the thenar muscle.^{11,12} In contrast, Shanks *et al.*⁸ recorded the EMG from the same position as used in the present study, and they found that the mechanical twitch response to an ED₅₀ dose of alcuronium was significantly less depressed than was the compound EMG. Thus, the difference between our results and those of others may also be due to differences in sensitivity of different muscles of the hand to nondepolarizing relaxants.

In conclusion, residual paralysis from atracurium-induced neuromuscular blockade cannot be excluded unless TOF ratio as measured mechanically or electromyographically has recovered to 0.8.

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