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# Does Perioperative Tactile Evaluation of the Train-of-four Response Influence the Frequency of Postoperative Residual Neuromuscular Blockade?

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**The authors conducted a randomized controlled clinical trial to evaluate the usefulness of perioperative manual evaluation of the response to train-of-four (TOF) nerve stimulation. A total of 80 patients were divided into four groups of 20 each. For two groups (one given vecuronium and one pancuronium), the anesthetists assessed the degree of neuromuscular blockade during operation and during recovery from neuromuscular blockade by manual evaluation of the response to TOF nerve stimulation. In the other two groups, one of which received vecuronium and the other pancuronium, the anesthetists evaluated the degree of neuromuscular blockade solely by clinical criteria. The use of a nerve stimulator was found to have no effect on the dose of relaxant given during anesthesia, on the need for supplementary doses of anticholinesterase in the recovery room, on the time from end of surgery to end of anesthesia, or on the incidence of postoperative residual neuromuscular blockade evaluated clinically. The median (and range of) TOF ratios recorded in the recovery room were 0.75 (0.33–0.96) and 0.79 (0.10–0.97) in the vecuronium groups monitored with and without a nerve stimulator, respectively. These ratios were significantly higher than those found in the pancuronium groups, which were 0.66 (0.06–0.90) and 0.63 (0.29–0.95), respectively. However, no difference was found between the vecuronium and pancuronium groups in the number of patients showing clinical signs of residual neuromuscular blockade, as evaluated by the 5-s head-lift test. All patients with clinical signs of residual neuromuscular blockade had a TOF ratio < 0.70, but the majority of patients (71%) with a TOF ratio < 0.70 were able to sustain head-lift for 5 s. A correlation was found between the peripheral skin temperature and the TOF ratio. It is concluded that under the conditions of this study, no effect of perioperative tactile evaluation of the response to TOF nerve stimulation could be demonstrated. In the avoidance of residual neuromuscular blockade, the choice of relaxant was more decisive than was manual evaluation of the response to TOF nerve stimulation. (Key words: Measuring techniques: neuromuscular blockade. Monitoring: neuromuscular function. Neuromuscular relaxants: pancuronium, vecuronium. Temperature: cooling, monitoring.)**

A HIGH FREQUENCY of postoperative incomplete recovery from competitive neuromuscular blockade has been documented in several studies.[1–4] Among others, we have claimed that perioperative use of a nerve stimulator would decrease the frequency of residual neuromuscular blockade after the use of neuromuscular relaxants.[1,5,6] It has also been suggested that the use of the intermediate-acting relaxants with a more rapid spontaneous recovery may decrease the frequency of residual neuromuscular blockade.[4] However, the impact of neuromuscular monitoring as well as the use of intermediate-acting relaxants upon postoperative recovery has not been established. This study was designed to evaluate whether the use of manual evaluation of response to train-of-four (TOF) nerve stimulation would influence 1) the dose of relaxant used during operation and 2) the frequency of postoperative residual neuromuscular blockade.

## Methods

After a power analysis, 80 adult patients, ASA physical status 1, 2, or 3, scheduled for elective gastrointestinal operations, were included in the study. All gave informed consent to the investigation, and the study protocol was approved by the local Ethics Committee. All patients were free from neuromuscular disease and renal or hepatic failure and received no drug that might have altered neuromuscular function. Diazepam 0.2 $mg \cdot kg^{-1}$ was given orally 1 h before induction of anesthesia. Anesthesia was induced with fentanyl 0.1–0.2 mg, droperidol 5–10 mg, and thiopental 250–350 mg iv and maintained with 66% nitrous oxide in oxygen. Increments of fentanyl 0.05 mg were given if the patient's systolic blood pressure and heart rate exceeded the preinduction value by more than 30%. Ventilation was controlled to maintain normocapnia. Arterial blood gases were measured when requested by the anesthesiologist.

The patients were randomly allocated into four groups of 20. In groups 1 and 2, the degree of neuromuscular blockade during operation and during reversal of the neuromuscular blockade was assessed by manual evaluation of the response to TOF nerve stimulation. In these patients the ulnar nerve was stimulated supramaximally at the wrist through cutaneous electrodes from a Myotest nerve stimulator (Biometer, Denmark).[5] The ten anesthesiologists participating in the study were experienced in the use of a nerve stimulator. They were instructed to

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try to maintain the block during operation at a level such that one or two responses in the TOF could be felt, and not to antagonize the block unless at least one and preferably two responses in the TOF were present. In groups 3 and 4, the degree of neuromuscular blockade during operation was evaluated solely on the basis of clinical criteria, such as presence of spontaneous muscle activity. Reversal of residual paralysis was not to be attempted unless spontaneous respiration or other indications of spontaneous muscle activity could be observed. Patients in group 1 and 3 received pancuronium and patients in group 2 and 4 vecuronium. The relaxant was given both for tracheal intubation and maintenance of neuromuscular blockade. No exact dose regime was required, except that when given for intubation, a dose of 0.08–0.1 $mg \cdot kg^{-1}$ was recommended. However, if preferred, succinylcholine 1.5 $mg \cdot kg^{-1}$ preceded by pancuronium 0.01 $mg \cdot kg^{-1}$ could be given as an alternative to facilitate tracheal intubation. Neostigmine 2.5 mg preceded by atropine 1.0 mg was given for antagonism of neuromuscular block. One or two supplementary doses of neostigmine 1.25 mg were allowed. Nitrous oxide was discontinued and the lungs ventilated with 100% oxygen after administration of neostigmine. End of anesthesia was defined as the time when 100% oxygen was discontinued. In groups 1 and 2, recovery was considered sufficient when the patient could sustain head-lift for 5 s[7] and there was no manually detectable fade in the TOF response. In groups 3 and 4, neuromuscular recovery was considered sufficient when the patients could sustain head-lift for 5 s.

With the use of a probe (Thermometer MC8700, Exacon) placed on the dorsum of the hand, the peripheral temperature was recorded at the start of reversal, at the end of anesthesia, and at arrival in the recovery room. The central temperature was recorded from the rectum or the esophagus at the end of anesthesia and at arrival in the recovery room.

Upon arrival in the recovery room, all patients received nasal oxygen 3 $l \cdot min^{-1}$. When the anesthetist had departed a TOF ratio was measured from electromechanical twitch recordings (Myograph 2000, Biometer, Denmark).[5] Also, neuromuscular recovery was assessed clinically from the ability to sustain head-lift for 5 s.[7] Residual anesthesia was assessed with the Glasgow Coma Scale,[8] and arterial blood gases were measured. Recordings of the mechanical twitch was continued until a TOF ratio of 0.7 was reached. A TOF ratio less than 0.5 and a $Pa_{CO_2}$ greater than 45 mmHg or clinical signs of residual neuromuscular blockade (5-s sustained head-lift) were used to administer supplementary doses of neostigmine, up to a total dose of 5 mg.

### Statistical Analysis

The Mann-Whitney test was used for comparison of medians. The chi-squared test was used for comparison of residual neuromuscular blockade and TOF ratios (<0.70), peripheral temperature (<28.0° C), hypoxemia ($Pa_{O_2} < 60$ mmHg), and hypercapnia ($Pa_{CO_2} > 45$ mmHg). To compare temperature and TOF measurements, Spearman's test was used. Significance was assessed at the 0.05 level.

## Results

There were no significant differences among the four groups with respect to age or weight of the patients (table 1), or with respect to intraoperative variables, such as duration of anesthesia or doses of anesthetics. There was no effect of neuromuscular monitoring on the total dose of relaxant given or the time from end of surgery to end of anesthesia (table 2).

The results of the postoperative evaluations and measurements are given in table 3. The use of the nerve stimulator did not reduce the incidence of clinical signs of postoperative residual neuromuscular blockade, nor did it influence the postoperative TOF ratios as measured in the recovery room. However, the TOF ratios of patients in the pancuronium groups (groups 1 and 3) were significantly lower than were those of patients in the vecuronium groups (groups 2 and 4). Also, eight patients in the pancuronium groups, but only two patients in the vecuronium groups, had clinical signs of residual neuromuscular blockade. This difference is, however, not statistically significant ($P < 0.10$). No significant relationship was found between residual neuromuscular blockade evaluated clinically or by TOF, and postoperative hypoxemia or hypercapnia.



TABLE 1. Patient Characteristics

| | Nerve Stimulator | | No Nerve Stimulator | |
|---|---|---|---|---|
| | Group 1: Pancuronium | Group 2: Vecuronium | Group 3: Pancuronium | Group 4: Vecuronium |
| Age (yr) | 66 (50–70) | 67 (50–72) | 64 (58–73) | 73 (66–78) |
| Weight (kg) | 61 (54–66) | 71 (57–76) | 67 (55–83) | 67 (59–77) |
| Female:male | 15:5 | 10:10 | 14:6 | 9:11 |

Values are median and interquartile ranges (in parentheses); n = 20 in each group.

TABLE 2. Intraoperative Variables

| | Nerve Stimulator | | No Nerve Stimulator | |
|---|---|---|---|---|
| | Group 1: Pancuronium | Group 2: Vecuronium | Group 3: Pancuronium | Group 4: Vecuronium |
| Duration of anesthesia (min) | 200 (163–251) | 218 (175–265) | 181 (152–256) | 229 (174–274) |
| Relaxant (mg) | 8.0 (6.5–9.5) | 13.5 (12.0–16.5) | 7.5 (6.5–12.0) | 12.5 (10.5–17.5) |
| Central temperature at reversal (° C) | 36.0 (35.5–36.2) | 35.8 (35.0–36.6) | 36.0 (35.6–36.6) | 36.3 (35.7–36.8) |
| Peripheral temperature at reversal (° C) | 27.5 (24.3–32.7) | 28.3 (26.1–30.0) | 30.8 (26.5–34.2) | 27.8 (25.3–29.0) |
| Time from end of surgery to end of anesthesia (min) | 20.0 (15.0–33.3) | 20.0 (15.0–32.5) | 20.5 (10.0–30.0) | 20.0 (15.0–30.0) |

Values are medians and interquartile ranges (in parentheses).

The individual TOF ratios recorded in the recovery room are shown in figure 1. Although all patients with clinical signs of residual neuromuscular blockade had a TOF ratio < 0.70, the majority of patients with a TOF ratio < 0.70 (71.4%) were found to have recovered adequately when evaluated clinically. The use of a nerve stimulator had no statistically significant effect on the number of patients requiring a supplementary dose of neostigmine in the recovery ward. (Nine patients monitored with and eight patients without a nerve stimulator required neostigmine.)

No statistically significant differences in central temperature were found among the four groups (tables 2 and 3). However, a statistically significant positive correlation was found between the peripheral temperature measured in the recovery room and the TOF ratio ($P < 0.007$) (fig. 2). However, residual neuromuscular blockade as evaluated clinically could not be correlated to peripheral temperature. There was no correlation between the TOF ratio and either the central temperature or the peripheral temperature at the start of reversal.

## Discussion

We have previously suggested that neuromuscular blocking agents are more accurately administered if neuromuscular function is monitored during operation.[5] In the current study, we investigated the effect of routine tactile evaluation of the TOF response. Contrary to our expectations, we found that the use of a nerve stimulator neither saved time nor influenced the consumption of relaxants or the frequency of postoperative residual neuromuscular blockade.

The degree of neuromuscular blockade during surgical anesthesia is easily evaluated with a nerve stimulator, by counting the number of responses felt in the TOF response.[5] We therefore expected that access to a nerve stimulator would result in a more precise evaluation of a

TABLE 3. Postoperative Variables

| | Nerve Stimulator | | No Nerve Stimulator | |
|---|---|---|---|---|
| | Group 1: Pancuronium | Group 2: Vecuronium | Group 3: Pancuronium | Group 4: Vecuronium |
| Number of patients with clinical signs of residual neuromuscular blockade | 3 | 2 | 5 | 0 |
| TOF ratio | 0.66 (0.06–0.90) | 0.75* (0.33–0.96) | 0.63 (0.29–0.95) | 0.79* (0.10–0.97) |
| Central temperature in the recovery room (° C) | 36.3 (36.0–36.8) | 36.3 (35.4–36.7) | 36.4 (36.0–37.0) | 36.3 (35.8–37.1) |
| Peripheral temperature in the recovery room (° C) | 25.7 (22.7–30.2) | 25.7 (22.4–30.3) | 25.5 (23.1–32.0) | 25.9 (23.1–33.9) |
| Glasgow Coma Scale | 15 (13–15) | 15 (14–15) | 14 (8–15) | 15 (14–15) |
| $Pa_{O_2}$ (mmHg) | 94.5 (64.5–177.0) | 99.0 (58.5–156.0) | 117.8 (66.0–186.0) | 89.3 (55.5–186.0) |
| $Pa_{CO_2}$ (mmHg) | 42.8 (30.8–53.3) | 42.8 (33.8–54.8) | 42.8 (30.8–51.0) | 42.0 (35.3–50.3) |

Values are medians and ranges (in parentheses) where applicable.
* A statistically significant difference ($P < 0.01$) between patients receiving pancuronium (groups 1 and 3) and vecuronium (groups 2 and 4).

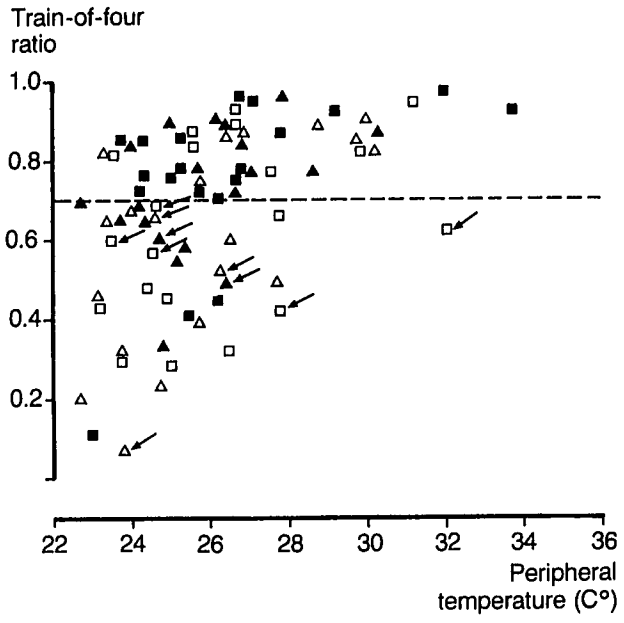


FIG. 1. Train-of-four ratios in the four groups of 20 patients each on arrival in the recovery room. Arrows indicate patients with clinical signs of residual neuromuscular blockade.

patient's need for relaxant as well as for neostigmine. However, our results may have been influenced by the fact that we performed our study in a department with a long-standing interest in neuromuscular blocking agents and in neuromuscular monitoring. Thus, it is conceivable that the anesthetists involved were very conscious about the risks of residual neuromuscular blockade; used small doses of muscle relaxants; and never tried to reverse the block before any spontaneous movements were present. This may have introduced a bias in favor of the groups in which nerve stimulators were not used.

In studying the effect of using the nerve stimulator during reversal of neuromuscular block, we found that access to tactile evaluation of the TOF ratio did not decrease the number of patients with low TOF ratios. We cannot exclude the possibility that the low peripheral temperatures masked an effect of the nerve stimulator. However, this is not likely, since residual neuromuscular blockade evaluated clinically was not reduced among patients monitored with a nerve stimulator, and no difference was found in peripheral temperature among the four groups of patients. The TOF ratios recorded mechanically varied considerably among four groups (fig. 1). Our results in this respect are in accordance with previous studies documenting that an apparently normal response (no detectable fade) to TOF stimulation judged by feel does not exclude residual neuromuscular blockade.[6] It remains to be shown whether during recovery the use of a stimulation pattern, in which the response is more easily evaluated by feel (*i.e.*, double-burst stimulation[9,10]), may decrease the number of patients with residual neuromuscular block.

A TOF ratio of 0.7–0.8 is normally taken to reflect sufficient recovery of neuromuscular function,[11,12] and 5-s sustained head-lift is normally not seen at TOF ratios below 0.55–0.60.[11] It was surprising, therefore, to find so many patients with low TOF ratios who were able to sustain head-lift for 5 s. Of 19 patients, 16 were found to have recovered clinically even though the TOF ratios recorded were lower than 0.50. It is, however, noteworthy that the peripheral temperatures in the current study generally were low, and that there was a correlation between the peripheral temperature and the TOF ratio. This finding is in accordance with recent findings that peripheral cooling even at stable and normal core temperature may cause a decrease in measured TOF ratio.[13] It is therefore likely that the poor correlation between

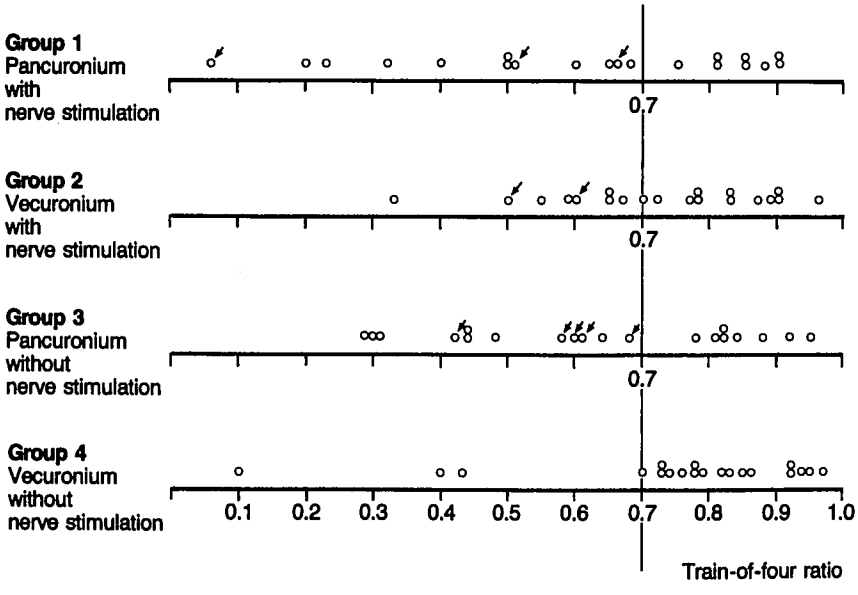


FIG. 2. Relationship between train-of-four ratio and peripheral temperature on arrival in the recovery room. Open triangles = group 1 (pancuronium with nerve stimulator); filled triangles = group 2 (vecuronium with nerve stimulator); open squares = group 3 (pancuronium without nerve stimulator); and filled squares = group 4 (vecuronium without nerve stimulator). Arrows indicate patients with clinical signs of residual neuromuscular blockade.

TOF ratio evaluated peripherally and the sustained head-lift test was due to the low peripheral temperatures.

Recently, it has been argued that the clinical test used in the current study is not a sensitive test of residual neuromuscular blockade, since both inspiratory and expiratory force can be reduced in patients performing a 5-s sustained head-lift.[14] However, this argument is in contrast to the findings of Pavlin *et al.*,[15] who suggest that the ability to sustain head-lift for 5 s is associated with sufficient strength to protect against both airway aspiration and obstruction. Also, the test is still widely accepted and used as a test of sufficient neuromuscular recovery.

In the current study, the overall incidence of residual neuromuscular blockade as evaluated clinically was only 12.5% (10/80; fig. 1) as compared to 24% in our previous study.[1] This difference is caused primarily by the low incidence of residual neuromuscular blockade among patients given vecuronium (2 of 40 = 5%) in the current study. A similar low frequency of residual neuromuscular blockade after intermediate-acting relaxants has been documented previously.[4,16]

We were not able to demonstrate any relationship between residual neuromuscular blockade, whether evaluated by TOF or clinically, and $Pa_{CO_2}$ or $Pa_{O_2}$ in the recovery room. This finding is in accordance with the findings of Pavlin *et al.*,[15] who showed that ventilation postoperatively as evaluated from $Pa_{CO_2}$ is adequate even when maximal inspiratory force is reduced and when muscles responsible for airway protection are nonfunctional. Thus, $Pa_{CO_2}$ is a poor indicator of residual neuromuscular blockade. Furthermore, as already pointed out, the low TOF ratios often recorded may have been caused by low peripheral temperatures. The low TOF ratio may therefore not have reflected the status of the respiratory muscles. Also, the number of patients with clinical signs of residual neuromuscular blockade was low. $Pa_{O_2}$ and $Pa_{CO_2}$ were evaluated from isolated blood samples and episodes of reduced $Pa_{O_2}$ or increased $Pa_{CO_2}$ may have occurred without being noticed.

In conclusion, perioperative manual evaluation of the response to TOF nerve stimulation influenced neither the dose of relaxant used during operation nor the frequency of postoperative residual neuromuscular blockade evaluated clinically or by TOF ratio recordings. The higher TOF ratios found among patients given vecuronium suggest that the choice of relaxant may be more important than tactile evaluation of the response to TOF nerve stimulation if residual neuromuscular blockade is to be avoided. We could not demonstrate that manual evaluation of the response to TOF nerve stimulation had any clinical effect. It remains to be shown, however, whether mechanical or electromyographic measurement of the TOF response or the use of a stimulation pattern in which the response is more easily evaluated manually may show a clinical effect.

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