

## Stimulation with Submaximal Current for Train-of-Four Monitoring

Sorin J. Brull, M.D.,\* Jan Ehrenwerth, M.D.,† David G. Silverman, M.D.†

The present study evaluated responses to train-of-four (TOF) stimulation at a range of stimulating currents. Traditionally TOF has been applied with a supramaximal stimulus but this may be quite uncomfortable for the awake patient. In the first part of this study, 12 healthy volunteers quantified (by 10-cm visual analog scale) the discomfort associated with TOF stimulation at 20, 30, and 50 mA. The median VAS scores were 2, 3, and 6, respectively ( $P < 0.05$  for differences between each group). In the second part, single twitch and TOF responses were compared at 20, 30, and 50 mA in 64 postoperative and in 19 intraoperative patients who had ratios of the fourth to the first twitch ( $T_4/T_1$ ) ranging from 0.15-1.03. In all patients, neuromuscular responses to nerve stimulation were recorded by a mechanogram, and the  $T_4/T_1$  ratios were calculated. Although single twitch heights increased significantly as amperage was increased, there was no statistical difference in the  $T_4/T_1$  ratios at the three different currents. The mean  $\pm$  SD  $T_4/T_1$  ratios at 20, 30, and 50 mA were  $0.795 \pm 0.247$ ,  $0.798 \pm 0.237$ , and  $0.802 \pm 0.233$ , respectively ( $P = ns$ ). It is concluded that TOF monitoring using a submaximal stimulus is more comfortable for the awake patient who is suspected of residual weakness, and that  $T_4/T_1$  testing can be reliably accomplished intraoperatively as well as postoperatively using submaximal stimuli. (Key words: Complications, postoperative: residual curarization. Monitoring, neuromuscular: Mechanogram; neurostimulation; submaximal stimulus; supramaximal stimulus; train-of-four. Pain: Neurostimulation, visual analog scale.)

FIRST PROPOSED over 30 yr ago,<sup>1</sup> the evaluation of neuromuscular response to peripheral nerve stimulation is now routine during general anesthesia. It also can be useful in awake subjects, with several recent reports attesting to the value of evaluating patients in the Post Anesthesia Care Unit (PACU).<sup>2-7</sup> A supramaximal stimulus (*i.e.*, a current that is 10-20% greater than that needed to elicit a maximal motor response) traditionally has been recommended in order to insure depolarization of all components of the nerve.<sup>8,9</sup> An increase in twitch height is noted as the current administered *via* ulnar nerve skin electrodes is increased toward supramaximal. Paulus<sup>8</sup> and Kopman *et al.*<sup>9</sup> have shown that the current required to initiate a detectable muscle contraction *via* cutaneous electrodes is 5-25 mA, while the current required for supramaximal stimulation is 30-60 mA.

Although train-of-four (TOF) stimulation obviates the need for an absolute twitch height for baseline comparisons, it too has been used with a supramaximal current.<sup>10</sup> This may limit its usefulness in the awake patient, as a greater stimulus intensity (*i.e.*, supramaximal) should be associated with more discomfort. Furthermore, if a supramaximal stimulus were indeed required for TOF monitoring, this would lead to uncertainty about determinations obtained without prior confirmation of adequate (*i.e.*, supramaximal) nerve stimulator output. The present study was undertaken to determine if less than supramaximal stimulation could provide reliable TOF monitoring while also reducing discomfort in awake subjects.

### Materials and Methods

Following approval by the institutional Human Investigation Committee, TOF stimulation at three different currents was delivered to 12 unmedicated volunteers in order to evaluate discomfort. TOF stimulation at the same three currents was then delivered to 64 consecutive PACU patients and to 28 anesthetized intraoperative patients in order to evaluate neuromuscular function. In all cases, TOF stimuli were provided by a Digistim III<sup>®</sup> peripheral nerve stimulator (Neuro Technology Inc., Houston, TX). Stimulator output was regulated with a built-in rheostat and was documented on the instrument's liquid crystal display, the accuracy of which was determined with an interfaced calibrated oscilloscope. For each subject, surface (stick-on) electrodes (Pliacell Infant ECG Electrode, NDM Corp., Dayton, OH) were placed with the positive terminal over the olecranon groove and the negative terminal on the ulnar side of the volar forearm.<sup>9</sup>

The discomfort associated with TOF stimulation at 20, 30, and 50 mA was assessed in the 12 healthy volunteers. Prior to testing, each subject was oriented to a 10-cm visual analog scoring (VAS) scale for pain, anchored with "no pain" at 0 and "worst pain imaginable" at 10. Each volunteer then underwent stimulation at 20, 30, or 50 mA in random, computer-generated order at 1-min intervals. The first stimulus was repeated later in the sequence to minimize the influence of surprise and anxiety on VAS scores. Ten seconds after each stimulus, the subject was asked to rate his/her pain based on the VAS scale. The overall VAS pain score at each mA was expressed as median with ranges (and 25th to 75th percentiles), and analyzed with Friedman multiple variables test

\* Assistant Professor of Anesthesiology.

† Associate Professor of Anesthesiology.

Received from the Department of Anesthesiology, Yale University School of Medicine, New Haven, Connecticut. Accepted for publication November 21, 1989. Presented in part at the Annual Meeting of the American Society of Anesthesiologists, San Francisco, California, October 1988.

Address reprint requests to Dr. Brull: Department of Anesthesiology, Yale University School of Medicine, 333 Cedar Street, New Haven, Connecticut 06510.

and Wilcoxon signed-rank test for paired nonparametric data. A  $P < 0.05$  was considered statistically significant for this and all subsequent analyses. When multiple comparisons were done, a Bonferroni adjustment was made to the significance level.

The response to TOF testing at the different stimulator current outputs was determined in the 64 postoperative and the 28 intraoperative patients. The sequence of testing was as follows: two TOF determinations (10 s apart) were obtained at a 20-mA output; 2 min later, two determinations were obtained at 30 mA; and after an additional 2 min, determinations were obtained at 50 mA. The force of thumb adduction in response to ulnar nerve stimulation was quantified with a calibrated adductor pollicis monitor (Medar Corp., Scarsdale, NY) interfaced to a strip chart recorder.

The 64 PACU patients had undergone a variety of general anesthetic regimens, 54 of which included nondepolarizing relaxants. The anesthesia teams providing the intraoperative care were not aware that their patients would be subsequently tested in the PACU. In each case, they had considered the return of neuromuscular function to be adequate prior to transfer of the patient to the PACU. This assessment had been made intraoperatively by methods such as absence of fade in response to TOF, sustained head-lift for 5 s, and inspiratory force of greater than  $-30$  cm H<sub>2</sub>O. The 64 patients were then tested in the PACU by an investigator who was not involved in their perioperative management.

For the 28 intraoperative patients, general anesthesia was maintained with oxygen in 66% nitrous oxide plus 0.25–1.0% inspired isoflurane. In each patient, a TOF ratio (range of 0.15–1.03) was maintained constant for at least 5 min by a continuous iv infusion of vecuronium. Once the ratio remained stable, the TOF responses were recorded. If a T<sub>4</sub> response was not obtainable at a given current (as was the case for nine of 28 intraoperative assessments at 20 mA), then the subject was excluded from the main study population because the T<sub>4</sub>/T<sub>1</sub> ratio could not be calculated. In these subjects, only the responses to 30 and 50 mA were compared.

For each patient, the twitch heights of T<sub>1</sub> and T<sub>4</sub> at each mA were recorded and the T<sub>4</sub>/T<sub>1</sub> was calculated. Differences between the neuromuscular responses to the three different currents (*i.e.*, the intercurrent differences for 20 *vs.* 30 mA, 20 *vs.* 50 mA, and 30 *vs.* 50 mA) were analyzed by paired *t* test. These intercurrent differences were compared with the intracurrent differences (20 *vs.* 20 mA, 30 *vs.* 30 mA, and 50 *vs.* 50 mA) using paired *t* test. In addition, the consistency of 20 *versus* 30 mA, 20 *versus* 50 mA, and 30 *versus* 50 mA responses for each patient was determined by linear regression analysis. In order to better appreciate the intercurrent differences at high and low T<sub>4</sub>/T<sub>1</sub> ratios, the ratios were categorized

as  $\leq 0.70$ , 0.71–0.94, or  $\geq 0.95$ , according to their ratios at 50 mA; the ratios obtained at 20 and 30 mA were each compared with the 50 mA values using paired *t* test.

## Results

Each of the 12 volunteers noted the least discomfort at 20 mA and the most discomfort at 50 mA T<sub>4</sub>/T<sub>1</sub> stimulation. For 20, 30, and 50 mA, the median VAS scores (and their 25th to 75th percentiles) were: 2 (1–3), 3 (3–4.5), and 6 (5–7), respectively ( $P < 0.05$  for 20 *vs.* 30 mA, 20 *vs.* 50 mA, and 30 *vs.* 50 mA).

All 64 PACU and 19 of the 28 intraoperative patients had detectable T<sub>1</sub> and T<sub>4</sub> responses at 20, 30, and 50 mA. For these 83 patients, neuromuscular responses after the first and second TOF stimulations had a mean intracurrent difference of 1.2% or lower at each of the three current amplitudes (*i.e.*,  $0.801 \pm 0.248$  and  $0.789 \pm 0.249$  for the first and second TOF stimulation at 20 mA;  $0.799 \pm 0.237$  and  $0.797 \pm 0.239$  at 30 mA; and  $0.799 \pm 0.236$  and  $0.804 \pm 0.232$  at 50 mA). Thus, the two responses at each current were averaged for all subsequent analyses.

As expected, first twitch heights were significantly different after the 20, 30, and 50 mA stimuli ( $P < 0.05$ ). In the 64 PACU patients, they averaged  $7.07 \pm 5.42$ ,  $11.07 \pm 7.15$ , and  $13.88 \pm 8.37$  mm, respectively. For the 19 intraoperative subjects with responses at all three currents, the respective first twitch heights were  $2.76 \pm 1.26$ ,  $6.07 \pm 2.87$ , and  $8.65 \pm 3.48$ . For the nine patients excluded from the main study population because of lack of measurable T<sub>4</sub>/T<sub>1</sub> response at 20 mA, the twitch heights at 30 and 50 mA were  $3.39 \pm 1.19$  and  $6.89 \pm 2.25$ , respectively.

In contrast, there was no statistical difference in the T<sub>4</sub>/T<sub>1</sub> ratios at the three different amperages. The mean T<sub>4</sub>/T<sub>1</sub> ratios obtained in the PACU patients at 20, 30, and 50 mA were  $0.849 \pm 0.184$ ,  $0.853 \pm 0.175$ , and  $0.855 \pm 0.173$ , respectively; their respective ranges were 0.320–1.030, 0.365–1.000, and 0.365–1.030. For the 19 intraoperative patients with discernible T<sub>1</sub> and T<sub>4</sub> responses at each current, the mean T<sub>4</sub>/T<sub>1</sub> ratios at 20, 30, and 50 mA were  $0.613 \pm 0.336$ ,  $0.615 \pm 0.321$ , and  $0.623 \pm 0.316$ , respectively; their respective ranges were 0.149–1.055, 0.168–1.019, and 0.198–1.060. For the 83 patients, the overall ratios were  $0.795 \pm 0.247$ ,  $0.798 \pm 0.237$ , and  $0.802 \pm 0.233$  at 20, 30, and 50 mA, respectively.

The mean differences between the pairs of T<sub>4</sub>/T<sub>1</sub> ratios at the three currents were  $0.28 \pm 7.3\%$  for 20 *versus* 30 mA,  $0.64 \pm 7.9\%$  for 20 *versus* 50 mA, and  $0.36 \pm 5.2\%$  for 30 *versus* 50 mA. These small intercurrent differences were similar to the intracurrent differences of  $1.22 \pm 5.2\%$  for 20 *versus* 20 mA,  $0.29 \pm 4.9\%$  for 30

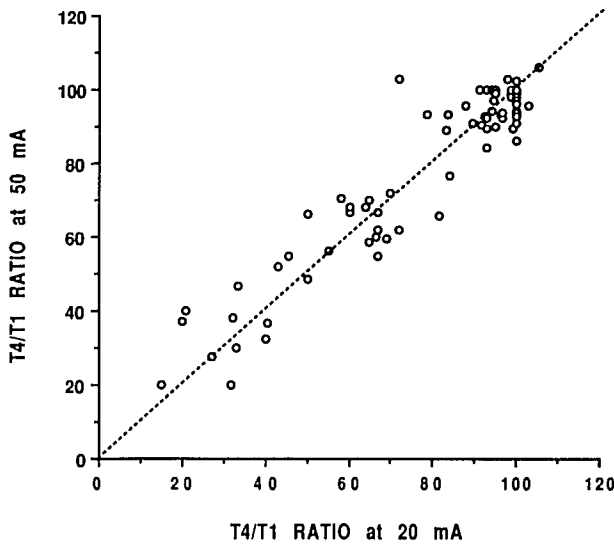


FIG. 1. Scattergram of  $T_4/T_1$  at 20 mA versus  $T_4/T_1$  at 50 mA for each of the patients tested ( $n = 83$ ). Dotted line represents line of identity;  $r^2 = 0.897$ .

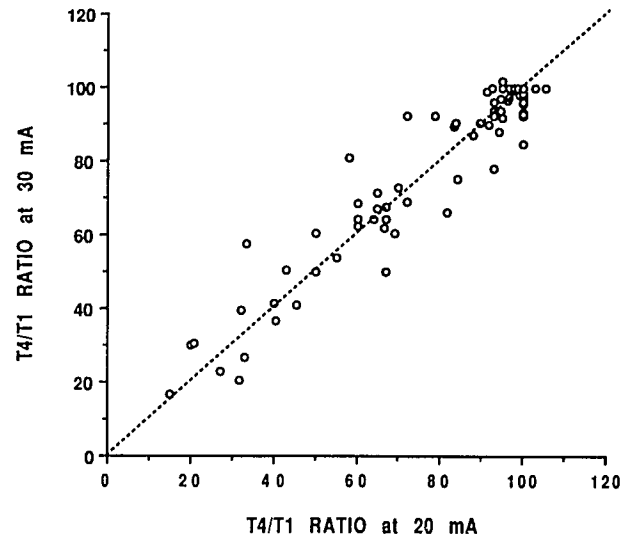


FIG. 3. Scattergram of  $T_4/T_1$  at 20 mA versus  $T_4/T_1$  at 30 mA for each of the patients tested ( $n = 83$ ). Dotted line represents line of identity;  $r^2 = 0.912$ .

versus 30 mA, and  $0.48 \pm 3.9\%$  for 50 versus 50 mA ( $P = ns$ ).

The consistency of the  $T_4/T_1$  ratio at different milliamperages in each of the 83 subjects is illustrated in figures 1, 2, and 3. For 20 versus 50 mA, 30 versus 50 mA, and 20 versus 30 mA, the high degree of linear association is represented by  $r$  values of 0.95, 0.98, and 0.96, respectively, each having a significant slope ( $PR > F = 0.0001$ ).

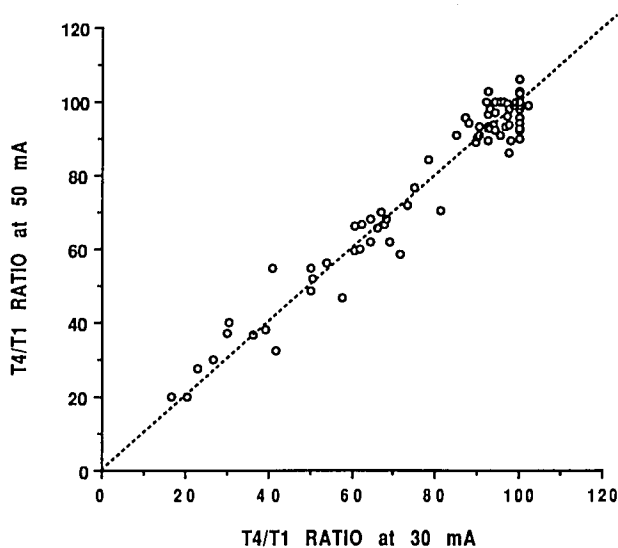


FIG. 2. Scattergram of  $T_4/T_1$  at 30 mA versus  $T_4/T_1$  at 50 mA for each of the patients tested ( $n = 83$ ). Dotted line represents line of identity;  $r^2 = 0.952$ .

Subgrouping of the 83 patients according to the  $T_4/T_1$  at 50 mA resulted in 28 patients with a ratio of  $\leq 0.70$ , 25 with a ratio between 0.70 and 0.95, and 30 with a ratio  $\geq 0.95$ . The mean  $T_4/T_1$  ratios at 50 mA in these subgroups were  $0.513 \pm 0.157$ ,  $0.894 \pm 0.067$ , and  $0.995 \pm 0.022$ , respectively. The mean  $T_4/T_1$  values after 20 mA and 30 mA for patients grouped according to their 50 mA values revealed no statistically significant differences (table 1). The 12 intraoperative patients with ratios  $\leq 0.70$  had a mean  $T_4/T_1$  at 50 mA of  $0.410 \pm 0.164$ . Intercurrent consistency was maintained at these lower ratios; the respective values at 20 and 30 mA were  $0.387 \pm 0.182$  and  $0.403 \pm 0.183$  ( $P = ns$ ).

### Discussion

The consistency of the  $T_4/T_1$  ratios at 20, 30, and 50 mA over a wide spectrum of depths of clinical neuro-

TABLE 1.  $T_4/T_1$  Ratios at 20, 30, and 50 mA

Classification* at 50 mA	20 mA	30 mA	50 mA
$\leq 0.70$ ( $n = 28$ )	$0.500 \pm 0.182$	$0.506 \pm 0.169$	$0.513 \pm 0.157$
$> 0.70, < 0.95$ ( $n = 25$ )	$0.915 \pm 0.104$	$0.916 \pm 0.079$	$0.894 \pm 0.067$
$\geq 0.95$ ( $n = 30$ )	$0.972 \pm 0.060$	$0.972 \pm 0.035$	$0.995 \pm 0.022$

Mean  $\pm$  SD.

\* Data categorized according to  $T_4/T_1$  ratio at 50 mA. For example, if a given subject evidenced  $T_4/T_1$  at 50 mA of  $\leq 0.70$  and a  $T_4/T_1$  ratio at 20 mA of  $> 0.70$ , the subject was grouped only according to the 50 mA value (i.e., placed in  $\leq 0.70$  group).

muscular blockade refutes the classical teaching that, like the single twitch, the  $T_4/T_1$  ratio should be performed with a supramaximal stimulus.<sup>8-12</sup> Although first twitch height doubled in size as current was increased from 20 to 50 mA, it appears that each myoneural unit's individual and hence the overall  $T_4/T_1$  ratio, did not change. The measured individual heights of  $T_4$  and  $T_1$  increased proportionally as additional neuromuscular units were stimulated. Once a sufficient current was achieved, the combined  $T_4/T_1$  ratio of all fibers apparently behaved similarly, regardless of the number of individual neuromuscular units that were stimulated. As noted in table 1, mean  $T_4/T_1$  ratios at 20 and 30 mA were within 3% of the ratios defined at 50 mA throughout the spectrum of blockade.

The consistency of  $T_4/T_1$  ratios at varying output currents is reassuring from a clinical standpoint. Prior to the present investigation, we randomly evaluated eight neurostimulating units at our institution to determine the range of current outputs.<sup>13</sup> Maximum output ranged from 16–64 mA. This finding was of some concern because the requirements for supramaximal stimulation of the ulnar nerve *via* cutaneous electrodes range from 30–60 mA.<sup>8,9</sup> However, the present study documented a consistency of  $T_4/T_1$  within a wide range of stimulus currents.

The reliability of  $T_4/T_1$  testing at 20 mA suggests that one could deliberately use such a low amperage for evaluating the degree of neuromuscular block in awake patients or patients emerging from anesthesia. The VAS scores of the 12 volunteers clearly indicate that discomfort increases as milliamperage is increased. Discomfort was not recorded in the 64 PACU patients because an attempt was made to evaluate these patients soon after arrival in the PACU when they were awake but still sedated. Although we cannot extrapolate the pain scores reported by awake volunteers to patients recovering from anesthesia, most PACU patients would be awake enough to experience discomfort.

We conclude that, with the aid of a mechanogram,  $T_4/T_1$  testing can be accomplished reliably in patients without using a supramaximal stimulus. In the 83 patients with detectable  $T_1$  and  $T_4$  responses at 20, 30, and 50 mA, the  $T_4/T_1$  ratio remained consistent at each current. The use of submaximal currents should be of particular value in testing awake patients in whom presence of residual neuromuscular blockade is suspected. All 64 awake patients in the present study had neuromuscular responses of sufficient amplitude to permit recording at the lowest

(*i.e.*, 20 mA), and thus least uncomfortable, current. In the intraoperative setting, however, stimulation at low currents did not always elicit detectable contractions in patients with a marked degree of blockade. Although it would not improve the accuracy of the recorded  $T_4/T_1$  ratio so long as all four twitches are present, the use of a supramaximal stimulating current in this setting would provide larger individual twitch heights and facilitate the visual and/or tactile assessment of the  $T_4/T_1$  ratio. Lower currents might prove to be most practical in the awake patient, where recordings of TOF responses at submaximal currents are as reliable as, and more comfortable than, monitoring at supramaximal current.

The authors wish to thank Jacki Fitzpatrick for her secretarial assistance, Terry O'Connor, M.P.H., for biostatistical analysis, and Luke Kitahata, M.D., Ph.D., for reviewing this manuscript.

### References

1. Christie TH, Churchill-Davidson HC: St. Thomas' Hospital nerve stimulator in diagnosis of prolonged apnea. *Lancet* 1:776–778, 1958
2. Viby-Mogensen J, Jorgensen BC, Ording H: Residual curarization in the recovery room. *ANESTHESIOLOGY* 50:539–541, 1979
3. Bevan DR, Smith CE, Donati F: Postoperative neuromuscular blockade: A comparison between atracurium, vecuronium, and pancuronium. *ANESTHESIOLOGY* 69:272–276, 1988
4. Beemer GH, Rozental P: Postoperative neuromuscular function. *Anaesth Intensive Care* 14:41–45, 1986
5. Lennmarken C, Lofstrom JB: Partial curarization in the postoperative period. *Acta Anaesthesiol Scand* 28:260–262, 1984
6. Andersen BN, Madsen JV, Schurizek BA, Juhl B: Residual curarization: A comparative study of atracurium and pancuronium. *Acta Anaesthesiol Scand* 32:79–81, 1988
7. Brull SJ, Silverman DG, Ehrenwerth J: Problems of recovery and residual neuromuscular blockade: Pancuronium *vs.* vecuronium (abstract). *ANESTHESIOLOGY* 69:A473, 1988
8. Paulus DA: Electrical signals, *Problems in Anesthesia Monitoring*. Edited by Gravenstein N, Kirby RR, Brown DL. Philadelphia, J.B. Lippincott, 1987, pp 21–26
9. Kopman AF, Lawson D: Milliamperage requirements for supramaximal stimulation of the ulnar nerve with surface electrodes. *ANESTHESIOLOGY* 61:83–85, 1984
10. Ali HH, Utting JE, Gray TC: Stimulus frequency in the detection of neuromuscular block in humans. *Br J Anaesth* 42:967–977, 1970
11. Ali HH, Utting JE, Gray TC: Quantitative assessment of residual antidepolarizing block (Parts I and II). *Br J Anaesth* 43:473–485, 1971
12. Ali HH, Savarese JJ: Monitoring of neuromuscular function. *ANESTHESIOLOGY* 45:216–249, 1976
13. Brull SJ, Elwood J, Ehrenwerth J, Silverman DG: Train of four assessment at various monitor currents (abstract). *ANESTHESIOLOGY* 69:A468, 1988