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Accelographic Train-of-four at Near-threshold Currents

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The authors evaluated train-of-four (TOF) fade, as quantified by accelography, in response to neurostimulation at currents ranging from 10 to 60 mA. This was done to determine the range of currents over which measurements of fade remain consistent. In 31 patients (ASA Physical Status 1, 2, and 3), anesthesia was induced with fentanyl, midazolam, and thiopental and was maintained with isoflurane and 66% nitrous oxide in oxygen. Surface stimulating electrodes were placed over the ulnar nerve, and an acceleration transducer was placed on the thumb. Succinylcholine was administered to facilitate tracheal intubation; after neuromuscular recovery, a bolus of vecuronium (0.01–0.05 $mg \cdot kg^{-1}$) and an infusion (0.25–1.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$) were administered. After documentation of a stable TOF ratio, accelographic TOF responses were quantified in response to 200-μs stimulation at 10, 15, 20, 30, 40, 50, and 60 mA, in random order. A total of 95 data sets were collected at different depths of blockade. The TOF ratios maintained intercurrent consistency (P = not significant by nonparametric repeated measures analysis of variance), except at currents near the fourth-twitch (T_4) threshold current. This inconsistency was eliminated by testing at ≥ 10 mA above threshold. TOF ratios obtained at 10 mA above T_4 threshold correlated highly with those at 60 mA (Spearman r value = 0.94). The authors conclude that the TOF ratio is consistent over a wide range of stimulating currents and that testing with submaximal currents can be performed reliably at ≥ 10 mA above the T_4 threshold. (Key words: Monitoring, neuromuscular: accelography; adductor pollicis monitor; nerve stimulation; train-of-four. Relaxants, neuromuscular: vecuronium.)

ALTHOUGH the relationship between fade in response to peripheral neurostimulation and clinical adequacy of neuromuscular function is not defined clearly, anesthesiologists nevertheless monitor the degree of fade to assess the depth of nondepolarizing blockade. This typically is achieved by monitoring adductor pollicis response to supramaximal train-of-four (TOF) stimulation of the ulnar nerve. When precise monitoring is sought, the ratio of the fourth twitch height to the first (T_4/T_1) may be determined with an adductor pollicis force transducer.

Recently, it was reported that fade in response to TOF stimulation remained consistent at stimulating currents of 20, 30, and 50 mA.[1] Because low-current stimulation causes significantly less discomfort than supramaximal stimulation,[2] it may be indicated for testing of awake patients. The current study used accelography to determine the consistency of TOF responses at seven stimulating currents, beginning as low as 10 mA. In the context of nondepolarizing blockade, accelography provides TOF ratios equal to those obtained by force transduction while eliminating the need to establish and maintain preload.[3–6] The accelograph's microprocessor permits rapid adjustment of stimulating current and easy recording of responses, thereby making the instrument particularly useful for multiple intercurrent comparisons. Using this technique, we sought to address concerns that assessment of TOF fade may be distorted at near-threshold currents, especially near currents that cause selective loss of the fourth twitch (*i.e.*, $T_4/T_1 = 0$ at a low current despite a measurable ratio at higher currents).[7–9] Specifically, we sought to determine the range of currents over which TOF fade remained consistent and then to establish guidelines for low-current neurostimulation.

Materials and Methods

After approval was obtained from the institutional Human Investigation Committee, we studied 31 consenting patients (ASA Physical Status 1, 2, and 3) undergoing general anesthesia for elective surgical procedures. Patients were between 35 and 70 yr of age, within 50% of ideal body weight, free of known neuromuscular disease, and not receiving any medication known to affect neuromuscular transmission. Preinduction medication consisted of intravenous fentanyl (1–3 $\mu g \cdot kg^{-1}$) and midazolam (0.01–0.04 $mg \cdot kg^{-1}$). The cutaneous electrodes of the accelograph (Biometer, Copenhagen, Denmark) were applied to the arm opposite the blood pressure cuff, with the positive electrode over the proximal and the negative electrode over the distal forearm.[10] The miniature acceleration transducer was taped to the ipsilateral thumb, and the accelograph was adjusted to deliver sets of 200-μs, square-wave impulses to the ulnar nerve at a frequency of 2.0 Hz for TOF stimulation every 15 s.

After anesthesia was induced with thiopental (4–6 $mg \cdot kg^{-1}$), the baseline responses to the four impulses of TOF stimulation were recorded on the accelograph's interfaced printer: thumb acceleration was translated into individual "twitch heights" (T_1, T_2, T_3, and T_4) and the baseline T_4/T_1 ratio was calculated. Then, tracheal intubation was facilitated with intravenous succinylcholine

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(1 mg · kg^{-1}), and anesthesia was maintained with isoflurane (0.25–1.0% end-tidal) and 66% nitrous oxide in oxygen. After neuromuscular recovery from the effects of succinylcholine, a bolus of vecuronium (0.01–0.05 mg · kg^{-1}) was administered, and a continuous vecuronium infusion was started at 0.25–1.5 μg · kg^{-1} · min^{-1} to achieve a spectrum of T_4/T_1 ratios.

When the T_4/T_1 ratio obtained at a stimulating current of 60 mA (monitored at the instrument's default interval of 15 s) exhibited less than a 5% change during a 10-min period, the accelograph was adjusted to deliver sets of TOF stimuli at 10, 15, 20, 30, 40, 50, and 60 mA in random order. Responses were tested twice at each current to permit intracurrent, as well as intercurrent, comparisons. When responses to each of four impulses to TOF stimulation at a given current were detected by the accelograph, the T_4/T_1 ratio was calculated for that current. In most cases, the calculation was accomplished by the accelograph's microprocessor. However, when the T_4 response was very small (*e.g.*, as a result of pronounced blockade or because of low-current stimulation), the accelograph printed a line that represented the individual responses but did not provide the numeric "heights" of T_1 and T_4 or calculate the T_4/T_1 ratio. In such cases, the lines representing T_1 and T_4 were measured manually, and T_4/T_1 was calculated by an investigator who was unaware of the stimulating current intensity or the degree of blockade.

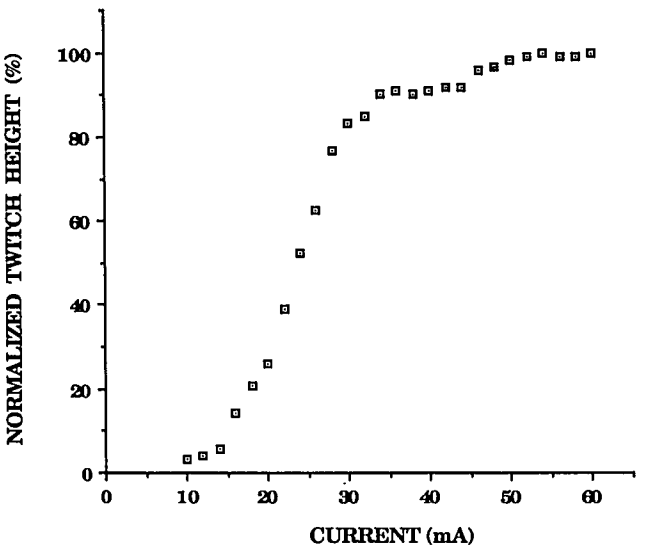

FIG. 1. Accelographic T_1 height (normalized to the height obtained at the highest current, 60 mA) as a function of stimulating current in a single subject. The data, obtained at 2-mA increments in the absence of nondepolarizing blockade, are consistent with a logarithmic relationship (r = 0.99). After an interval of rapidly increasing height, there was a slow increase to a plateau. A similar relationship was present in each of the seven data sets evaluated in this manner, with the exception that a consistent "maximal" response was not always elicited within the range of stimulating currents.

TABLE 1. Differences Between Successive Normalized T_4/T_1 Ratios at the Same Current

Stimulating Current Intensity (mA)	Intracurrent Differences: Median (5th–95th percentile)
60 *vs.* 60	0 (−1 to 4)
50 *vs.* 50	0 (−3 to 5)
40 *vs.* 40	0 (−3 to 6)
30 *vs.* 30	0 (−3 to 6)
20 *vs.* 20	0 (−10 to 7)
15 *vs.* 15	0 (−26 to 11)
10 *vs.* 10	−9.5 (−24 to 9)

After evoked responses were recorded at each of the seven currents, the vecuronium infusion was adjusted so that a different T_4/T_1 ratio could be obtained, and a new data set was acquired once a stable level of blockade was confirmed. As many as five such data sets were collected for each patient. In seven patients, an additional data set was obtained in the absence of nondepolarizing relaxant. A total of 95 data sets were collected and analyzed, with a range of T_4/T_1 ratios between 0.1 and 1.0. Unless otherwise specified, pooled data are expressed as mean ± SD (median, 5th–95th percentiles).

T_1 Value

Intracurrent consistency of T_1 was assessed by comparing the two values obtained at the same current with the use of the Wilcoxon signed rank test; $P < 0.05$ was considered statistically significant for this and all subsequent analyses. The first T_1 value then was used for all analyses. The difference in T_1 amplitudes obtained at successive currents was analyzed by Friedman's nonparametric repeated measures analysis of variance. Additionally, the effect of stimulating current on T_1 amplitude was delineated in seven patients by graphic display of the twitch height as a function of current intensity in 2-mA increments.

T_4 and T_4/T_1 Values

Intracurrent differences were assessed as for T_1. To facilitate intercurrent comparisons among the 95 data sets, the individual T_4/T_1 ratios of a given data set were normalized to the T_4/T_1 ratio obtained at 60 mA in that data set (*i.e.*, they were expressed as a percentage of the ratio obtained at 60 mA). Data sets then were grouped according to the lowest of the seven test currents able to evoke a detectable T_4; this was called the "T_4 threshold" current. Intercurrent differences for normalized T_4/T_1 ratios were analyzed by Friedman's nonparametric repeated measures analysis of variance with Tukey's adjustment for multiple comparisons. In view of the incon-

sistent T_4 heights obtained at threshold current, the intercurrent consistency of responses was assessed at ≥ 10 mA above the T_4 threshold. The individual data sets were displayed in a scattergram that compared the T_4/T_1 at 10 mA above the T_4 threshold with the T_4/T_1 at 60 mA for that set. The relationship was analyzed with the use of Spearman's assessment of correlation.

Results

T_1 Value

Intracurrent differences averaged 1.2%, 1%, 0.2%, 0.8%, −0.4%, 1%, and 0.9% at 10, 15, 20, 30, 40, 50, and 60 mA, respectively. The relationship between T_1 acceleration ("T_1 twitch height") and stimulating current was demonstrated by a sigmoidal curve (fig. 1). Overall, the mean height of T_1 increased between 10 and 15 mA, between 15 and 20 mA, and with each 10-mA increment between 20 and 60 mA ($P < 0.05$). As the level of blockade increased, the threshold current likewise increased, and "supramaximal" stimulation often was not achieved at 60 mA.

T_4 and T_4/T_1 Values

Differences between successive T_4/T_1 determinations at the same current (*i.e.*, intracurrent consistency) are summarized in table 1. Differences as great as 24–26% primarily were observed when the evoked responses were too low to be quantified by the accelograph, and thus required manual measurement by the blinded investigator.

The classification of data sets according to the T_4 threshold is illustrated in the top row of table 2. An inverse linear trend was observed between the T_4/T_1 ratio and threshold current: group 1 (n = 7), with a T_4 threshold of 10 mA, had a median T_4/T_1 of 1.0; group 7 (n = 4), with a T_4 threshold of 60 mA, had a median ratio of 0.22. The remainder of table 2 provides the median and 5th–95th percentiles of normalized T_4/T_1 values for each group. The 19% difference between the normalized values at 40 and 60 mA in group 5 constituted the largest intercurrent difference.

As shown in the bottom row of table 2, significant intercurrent differences were observed in 5 of the 55 intercurrent comparisons. Each significant intercurrent difference involved comparison of a T_4/T_1 ratio obtained at the T_4 threshold current with that at a higher current. No significant intercurrent differences were evident when comparisons involved ratios obtained at ≥ 10 mA greater than the T_4 threshold. The near-equivalence of T_4/T_1 ratios obtained at 10 mA above the T_4 threshold to those obtained at 60 mA is illustrated in figure 2. Testing at

TABLE 2. T_4/T_1 Values Grouped According to T_4 Threshold

	1 Sets with T_4/T_1 at 10–60 mA (n = 7)	2 Sets with T_4/T_1 at 15–60 mA (n = 10)	3 Sets with T_4/T_1 at 20–60 mA (n = 45)	4 Sets with T_4/T_1 at 30–60 mA (n = 16)	5 Sets with T_4/T_1 at 40–60 mA (n = 10)	6 Sets with T_4/T_1 at 50–60 mA (n = 3)	7 Sets with T_4/T_1 at 60 mA (n = 4)
T_4/T_1 at 60 mA*	1.0 (0.91–1.12)	1.02 (0.24–1.13)	0.43 (0.20–1.13)	0.23 (0.08–0.70)	0.27 (0.13–0.73)	0.28 (0.24–0.87)	0.22 (0.11–0.28)
Normalized T_4/T_1†							
10 mA	90 (67–110)	—	—	—	—	—	—
15 mA	96 (69–128)	94 (73–129)	—	—	—	—	—
20 mA	103 (79–116)	107 (80–125)	94 (71–138)	—	—	—	—
30 mA	97 (85–110)	106 (67–120)	92 (70–132)	104 (67–195)	—	—	—
40 mA	98 (77–116)	106 (85–110)	95 (75–129)	100 (64–119)	81 (31–117)	—	—
50 mA	99 (90–100)	101 (86–107)	100 (81–120)	96 (57–111)	90 (69–122)	100 (75–125)	—
60 mA	100	100	100	100	100	100	100
Significant intercurrent differences‡	10 *vs.* 20 mA	15 *vs.* 20 mA 15 *vs.* 30 mA 15 *vs.* 40 mA	None	None	40 *vs.* 60 mA	None	None

Values are median and 5th–95th percentiles.
Dash indicates that T_4 response was not detected at this current for data sets in this group.
* The T_4/T_1 ratio at 60 mA indicates the depth of blockade for each subset.
† To facilitate comparisons, the T_4/T_1 obtained at each of the currents in a given data set was normalized to the value obtained at 60 mA.
‡ Significant intercurrent differences were limited to comparisons that involved a value obtained at a threshold current.

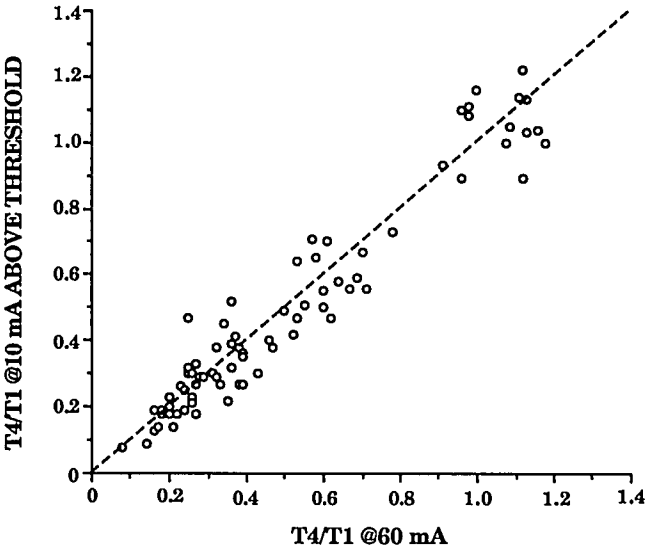

FIG. 2. Linear association of accelographic T_4/T_1 ratios at 10 mA above the T_4 threshold of a given data set to the T_4/T_1 obtained at 60 mA for the same set ($r = 0.94$). The line of identity is provided for illustration. For this comparison, sets with a T_4 threshold of 15 mA (group 2) were excluded, since responses at 10 mA above this threshold (*i.e.*, at 25 mA) were not obtained. Sets with T_4 thresholds greater than or equal to 50 mA also were excluded because 10 mA above this would be greater than the maximal current used (*i.e.*, ≥60 mA). When the data in group 2 were included, the overall mean difference between T_4/T_1 values obtained at 60 mA and those obtained at 10–15 mA above threshold was 0.01 ± 0.08.

10 mA above the T_4 threshold also eliminated the possibility that stimulation might be performed at a current intensity between the thresholds for T_1 and T_4; this would result in "selective loss" of T_4.

Discussion

New monitoring techniques such as accelography[3–6] and the use of low stimulating current to minimize discomfort in awake patients[1,2] are recent attempts aimed at improving neuromuscular testing and detection of residual blockade. The current study has documented the consistency of and some of the potential errors associated with these approaches.

Although the current data suggest that fade in response to TOF is consistent over a wide range of stimulating currents, this is not to indicate that any submaximal current could be used. We recommend that assessments be performed at ≥ 10 mA above the T_4 threshold. Otherwise, an assessment performed at a near-threshold current might elicit a spuriously low T_4/T_1 ratio: when the stimulating current is between the thresholds for T_1 and T_4, the T_4/T_1 ratio will be registered as zero because of selective loss of T_4; at currents slightly above the T_4 threshold, T_4 may be falsely low. The latter is attributable to the fact that a number of fibers must contract before a contractile response is detected (*i.e.*, overcoming elastic forces). The influence of such an "offset" decreases as the stimulating current is increased progressively above the threshold current. At 10 mA above the T_4 threshold, the overall effect is minimal. Although the difference between the reading at 10 mA above threshold and that at 60 mA was as high as 20% (fig. 2), there was not a consistent bias. Moreover, comparable differences were observed during intracurrent comparisons.

The resolution of monitoring equipment also may affect the intercurrent consistency of TOF determinations. In the setting of intense blockade or during stimulation with very low current, twitch heights may be very low and their precise measurement may be difficult to accomplish. The accelograph's microprocessor may obviate this problem by providing precise delineation of the T_4/T_1 ratio. However, this device likewise may introduce limitations in these settings, primarily because it currently is not programmed to report digital values for twitch height or calculate a TOF ratio when T_1 is less than 20% of its baseline height. Normally, this would be of little clinical consequence during nondepolarizing blockade, because the presence of a detectable T_4 response is unlikely when T_1 is depressed to this degree. However, factors such as arm repositioning or changes in skin resistance may alter twitch height (as compared with baseline) without altering neuromuscular function. This limitation may have contributed to the greater variability encountered at low twitch heights (*i.e.*, during greater degrees of blockade and especially at lower currents), because one of the investigators measured these responses manually. In addition, the accelograph will not even display a twitch response if it is less than 3% of its baseline height. This may account for the lack of recorded T_4 responses at lower currents in some data sets.

Another limitation of the accelograph was evident in the current data but does not affect clinical assessments significantly: in the absence of blockade, the accelographic T_4/T_1 may be greater than 1.0 (fig. 2). This feature has been reported by other investigators.[4,5] It may be attributable to the lack of positional consistency before each contraction (*i.e.*, after the initial [T_1] response, the subsequent contractions [T_2, T_3, and T_4] do not necessarily start from the same resting position because thumb position is not maintained by constant preload).

Although we were concerned primarily with the potential limitations of testing at low current, it should be remembered that accuracy of TOF monitoring is not necessarily assured by neurostimulation at high current intensity.[9] As shown in the current study, which used accelography, and prior investigations, which used force transduction,[11] stimulation with a relatively high current does not necessarily ensure a supramaximal response. In addition, high currents may directly stimulate long flexors in the forearm or induce repetitive depolarization,[12] thereby modifying neuromuscular assessment.

In conclusion, the current data confirm that the accelographic TOF ratio remains consistent over a wide range of stimulating currents. The potential clinical shortcomings of testing at low current (*i.e.*, selective loss or depression of T_4, resulting in a spuriously low T_4/T_1) are alleviated by neurostimulation at ≥ 10 mA above the T_4 threshold current.

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