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Effect of Tetanus on Subsequent Neuromuscular Monitoring in Patients Receiving Vecuronium

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The current study evaluated the effects of tetanic stimulation on neuromuscular responses to serial train-of-four (TOF) and double-burst stimulation (DBS). For TOF monitoring (n = 13), a degree of neuromuscular blockade was achieved with an intravenous vecuronium infusion such that the ratio of fourth twitch (T_4) to first twitch (T_1), T_4/T_1, was stable at a value between 0.1 and 0.7. Four seconds after a 5-s, 50-Hz tetanic stimulus was delivered, TOF monitoring was resumed at 10-s intervals. Significant changes were noted for T_1, T_4, and T_4/T_1, with median increases of 38, 250, and 93%, respectively. The median times for T_1, T_4, and T_4/T_1 to return to within 10% of their pretetanic (baseline) values were 34, 43, and 34 s, respectively (P = nonsignificant [NS] among times to recovery). A 100-Hz tetanic stimulus induced 50, 300, and 178% median increases of T_1, T_4, and T_4/T_1, while corresponding values for recovery times were 53, 73, and 54 s. For DBS monitoring (n = 14), tetanic stimulation (50-Hz, 5-s) induced 38, 300, and 153% median increases of the $DBS_{3,3}$ parameters (first response [D_1], second response [D_2], and their ratio [$D_2 \neq D_1$], respectively). The posttetanic effects on D_1, D_2, and D_2/D_1 persisted for 43, 66, and 46 s, respectively. For $DBS_{3,2}$, median posttetanic (50-Hz, 5-s) increases were 41, 275, and 176%, while corresponding times to recovery were 43, 43, and 43 s. Although the data indicate that the posttetanic percent increase was at least 10 times larger at greater degrees of blockade (T_4/T_1 = 0.1) than at lesser degrees (T_4/T_1 = 0.7), all T_4/T_1 and D_2/D_1 ratios returned to within 10% of baseline in 125 s or less after 5-s tetanic stimulation. (Key words: Monitoring, neuromuscular: double-burst stimulation, fade, nerve stimulator, posttetanic facilitation, tetanic stimulation, time to recovery, train-of-four. Relaxants: neuromuscular: vecuronium.)

ANESTHESIOLOGISTS commonly use train-of-four (TOF) monitoring to assess the degree of neuromuscular blockade.[1,2] However, the visual and/or tactile evaluation of fade in response to TOF stimulation may be inaccurate, especially when the TOF ratio (the ratio of the fourth response [T_4] to the first response [T_1]) is between 0.4–0.7.[3] Double-burst stimulation (DBS) has been introduced to overcome this limitation, since fade demonstrated by the second minitetanic burst of DBS is more readily detected by tactile means than is fade to TOF.[4,¶] Nevertheless, many anesthesiologists still rely upon response to a 5-s tetanic stimulus to supplement the assessment provided by less intense stimulation (TOF).[5,6] A tetanic stimulus, however, alters subsequent neuromuscular responses. Testing of neuromuscular function during the period of posttetanic "facilitation" may lead to overestimation of the evoked TOF or DBS response. It had been reported that posttetanic increase of adductor pollicis twitch response to ulnar nerve stimulation may last for more than 11 min[7] and up to 30 min,[8] and it has even been proposed that tetanic stimulation may result in "complete recovery of neuromuscular conduction."[9] Alternatively, in the context of pronounced nondepolarizing blockade, it recently has been shown that tetanic stimulation at 6-min intervals (during assessment of posttetanic count) did not alter the time to spontaneous return of the first detectable twitch response.[10] The current study sought to determine the degree and duration of posttetanic effects at lesser degrees of blockade, *i.e.*, at TOF (or DBS) ratios between 0.1 and 0.7, during a vecuronium infusion.

Materials and Methods

The effects of a 5-s tetanic stimulation on subsequent TOF and DBS monitoring were tested in the following settings: 1) a single 50-Hz tetanus on TOF monitoring; 2) a second, subsequent 50-Hz tetanus on TOF monitoring; 3) a single 100-Hz tetanus on TOF monitoring; 4) a second, subsequent 100-Hz tetanus on TOF monitoring; 5) a single 50-Hz tetanus on $DBS_{3,3}$; 6) a second, subsequent 50-Hz tetanus on $DBS_{3,3}$; 7) a single 50-Hz tetanus on $DBS_{3,2}$; and 8) a second, subsequent 50-Hz tetanus on $DBS_{3,2}$.

After Human Investigation Committee approval, 13 consenting patients receiving general anesthesia underwent TOF testing and another 14 patients underwent DBS testing. TOF consisted of a series of four impulses at 500-ms intervals. DBS consisted of two mini-tetanic bursts at an interval of 750 ms. All patients were free of neuromuscular disease. Ages ranged from 19 to 77 yr (mean 46 yr), and weights ranged from 45 to 89 kg (mean 68 kg).

In all cases, anesthesia was induced with thiopental (3–6 mg·kg^{-1}), fentanyl (0.5–2.0 μg·kg^{-1}), and/or midazolam (0.02–0.04 mg·kg^{-1}) and was maintained with

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0.25–1.00% end-tidal isoflurane and 66% N_2O in O_2. Tracheal intubation was facilitated by succinylcholine (1 $mg \cdot kg^{-1}$). Approximately 10 min after return of single-twitch response to within 10% of its presuccinylcholine height, a vecuronium bolus (0.01–0.05 $mg \cdot kg^{-1}$) was administered, and a vecuronium infusion was started at 0.5–1.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ to maintain a stable degree of neuromuscular blockade, as defined by a T_4/T_1 ratio that changed by less than 5% over a 10-min period.

Effects on Train-of-Four Monitoring

For TOF testing, a Digistim III nerve stimulator (Neuro Technology, Houston, TX) was interfaced to an oscilloscope (Tektronix 7623A, Tektronix Inc., Beaverton, OR) to confirm delivery of a 50-mA stimulus of 200 μs duration. The stimulator then was applied to the 13 patients *via* cutaneous electrodes (Plia-Cell Infant ECG Electrode, NDM Corp., Dayton, OH), which were placed over the olecranon groove and on the volar aspect of the forearm. The positive electrode was proximal, and the negative electrode was distal.[11] The ipsilateral thumb was attached to a force transducer (Adductor Pollicis Monitor, Medar Corp., Scarsdale, NY) and abducted to achieve a preload of 250 g. The transducer was interfaced to a monitor and to a calibrated strip-chart recorder (Datascope 2000A/2000RS, Datascope Corp., Paramus, NJ). Data were recorded continuously at a chart speed of 1 $mm \cdot s^{-1}$. The amplitude of thumb adduction in response to each of the four stimuli comprising the TOF was estimated to the nearest 0.5 mm by freezing the tracing on the monitor screen and adjusting the built-in monitor reference line in 1-mm increments. The T_4/T_1 ratio then was calculated.

(A) First 5-s Tetanus at 50 Hz

The T_4/T_1 was monitored at 60-s intervals to achieve a ratio within the range of 0.1–0.7. Once the T_4/T_1 ratio had remained stable for at least 10 min, TOF monitoring was changed to the stimulator's preset 10-s interval. Pretetanic baseline values for T_1 twitch height (T_{1pre}), T_4 twitch height (T_{4pre}), and their ratio (T_4/T_{1pre}) were recorded. A supramaximal (60-mA) tetanic stimulus with a frequency of 50-Hz and a duration of 5 s then was delivered. Monitoring of TOF responses was resumed approximately 4 s after the end of the tetanic stimulation and the first posttetanic values of the TOF parameters (T_{1post}, T_{4post}, and T_4/T_{1post}) were recorded. Monitoring then was continued at 10-s intervals until T_1, T_4, and the ratio T_4/T_1 each returned to within 10% of their respective pretetanic baseline values.

For each subject, the increase of T_1, T_4 and T_4/T_1 after tetanus was compared to the corresponding pretetanic value and was termed %increase; *e.g.*, for T_1, %increase = $(T_{1post}-T_{1pre})/T_{1pre} \times 100$. The overall %increase for the 13 subjects was expressed as median and range. For each parameter, the significance of the difference between pre- and posttetanic values was determined with Wilcoxon's signed rank test for nonparametric data, as were the differences in %increase among T_1, T_4, and T_4/T_1.

The relationship between the degree of baseline neuromuscular blockade and the amount of subsequent increase of T_1, T_4, and T_4/T_1 was assessed by exponential regression analysis with baseline T_4/T_1 as the independent variable and %increase as the dependent variable. Then the subjects were grouped according to whether the baseline T_4/T_1 ratio was less than or greater than 0.40. For each TOF parameter, Wilcoxon's rank sum test was used to compare the effect of tetanus on the two groups.

The time to recovery for T_1, T_4, and T_4/T_1 was determined by noting the time at which each parameter returned to within 10% of its respective baseline. Wilcoxon's signed rank test was used to compare the recovery times for T_1, T_4, and T_4/T_1. Differences in all analyses were considered to be significant at the $P < 0.05$ level.

(B) Second 5-s Tetanus at 50 Hz

Two minutes after neuromuscular evoked responses returned to baseline (after the first 5-s tetanic stimulus), a new set of baseline T_1, T_4 and T_4/T_1 values was obtained, after which a subsequent 5-s, 50-Hz tetanic stimulus was delivered. TOF stimulation was resumed at 10-s intervals until T_1, T_4, and T_4/T_1 had returned to within 10% of their respective baseline values. The %increase and time to recovery were determined for each parameter and analyzed as described above for the first 5-s tetanic stimulus, with the exception that the data were not grouped or plotted according to degree of blockade. In addition, the results in part A (First 5-s Tetanus at 50 Hz) were compared to those in part B (Second 5-s Tetanus at 50 Hz by Wilcoxon's signed rank test, with respect to: T_{1pre}, T_{4pre}, and T_4/T_{1pre}; %increase of T_1, T_4, and T_4/T_1; and time to recovery of T_1, T_4, and T_4/T_1.

(C) First and (D) Second 5-s Tetanus at 100 Hz

Three minutes after completion of the first and second tetanus at 50 Hz, baseline T_1, T_4, and T_4/T_1 were recorded, and a 5-s, 100-Hz tetanic stimulus was delivered to the ulnar nerve. Approximately 4 s later, TOF stimulation was resumed at 10-s intervals until T_1, T_4, and T_4/T_1 returned to within 10% of baseline. Two minutes after the return of all parameters to baseline, a repeat set of baseline values was obtained, and the sequence was repeated after a second, 5-s, 100-Hz tetanic stimulus. For each tetanic stimulation, the %increase and times to recovery were measured and analyzed as above. Baseline heights, %increase, and time to recovery of T_1, T_4, and T_4/T_1 were compared (with Wilcoxon's signed rank test) for the first *versus* the second 100-Hz tetanus (seven subjects) and for the first 100-Hz tetanus (seven subjects) *versus* the first 50-Hz tetanus (in the same seven subjects).

EFFECTS ON DOUBLE-BURST MONITORING

For DBS testing, a Myotest monitor (Biometer, Denmark) was bench-tested to confirm accuracy of a 50-mA stimulus of 200-μs duration. The monitor was applied to the volar forearm of a separate group of 14 patients *via* cutaneous rubber electrodes coated with silver–silver chloride gel. The ipsilateral thumb responses to DBS stimulation were recorded as described above for TOF. The amplitude of thumb adduction in response to both stimuli comprising DBS (D_1 and D_2) was estimated to the nearest 0.5 mm, and the D_2/D_1 ratio was calculated.

After initiation of the vecuronium bolus and infusion, the D_2/D_1 ratio of $DBS_{3,3}$ was monitored at 60-s intervals for a minimum of 30 min in order to achieve a ratio within the range of 0.1–0.7. The patients then were randomly assigned to receive either $DBS_{3,3}$ (two bursts of three tetanic stimuli each) or $DBS_{3,2}$ (one burst of three tetanic stimuli followed by a burst of two such stimuli) for subsequent testing.

(E) First and (F) Second 5-s Tetanus at 50 Hz on $DBS_{3,3}$

Once the D_2/D_1 ratio had remained constant for at least 5 min when tested at the stimulator's preset 20-s interval, pretetanic baseline values for D_1 (D_{1pre}), D_2 (D_{2pre}) and their ratio (D_2/D_{1pre}) were recorded. A supramaximal (60-mA) tetanic stimulation with a frequency of 50 Hz and a duration of 5 s then was delivered. $DBS_{3,3}$ was resumed approximately 4 s after the end of the tetanic stimulation, and was continued at 20-s intervals until D_1, D_2, and their ratio (D_{1post}, D_{2post}, and D_2/D_{1post}) each returned to within 10% of their respective pretetanic baseline values. Two minutes later another 5-s, 50-Hz tetanic stimulation was delivered as described above, and monitoring of subsequent responses was resumed 4 s later. Data obtained were analyzed in a manner similar to TOF data for the 50-Hz tetanus.

First and Second 5-s Tetanus at 50 Hz on $DBS_{3,2}$

Data collection and analysis were performed in a manner analogous to that for $DBS_{3,3}$.

Results

EFFECTS ON TRAIN-OF-FOUR MONITORING

(A) First 5-s Tetanus at 50 Hz

Prior to delivery of the first tetanic stimulation, the mean values for T_{1pre}, T_{4pre}, and T_4/T_{1pre} were 11 ± 6 mm, 4 ± 3 mm, and 0.35 ± 0.2, respectively. As noted in table 1, the median increase was 38% for T_1, 250% for T_4, and 93% for the T_4/T_1 ratio; $P < 0.05$ for T_{1pre} *versus* T_{1post}, T_{4pre} *versus* T_{4post}, T_4/T_{1pre} *versus* T_4/T_{1post}, and %increase of T_4 *versus* %increase of T_1. The overall median times to recovery were 34, 43, and 34 s for T_1, T_4, and T_4/T_1, respectively (P = NS for differences among them). All parameters returned to baseline within 74 s.

The relationship between the posttetanic increase of T_4/T_1 and the pretetanic value of T_4/T_1 was demonstrated by $r^2 = 0.86$ (fig. 1). Significantly greater potentiation of T_1, T_4, and T_4/T_1 was noted in the eight subjects with a $T_4/T_{1pre} \leq 0.40$ than in the five subjects with a $T_4/T_{1pre} > 0.40$ (figs. 2*a* and 2*b*)

(B) Second 5-s Tetanus at 50 Hz

Prior to the second tetanus, mean values for T_{1pre}, T_{4pre}, and T_4/T_{1pre} were 11 ± 6 mm, 4 ± 3 mm, and 0.34 ± 0.2, respectively (P = NS between parts A and B). After tetanus, the median %increases were 43, 200, and 117% for T_1, T_4, and T_4/T_1, respectively (table 1); $P < 0.05$ for T_{1pre} *versus* T_{1post}, T_{4pre} *versus* T_{4post}, T_4/T_{1pre} *versus* T_4/T_{1post}, and %increase of T_4 *versus* %increase of T_1. Median recovery times were 35, 35, and 33 s (table 1; P = NS for differences among them).

The consistency of %increase, and more importantly, of recovery times after the two tetanic stimuli is evident in table 1. In all cases T_1, T_4, and T_4/T_1 returned to within 10% of baseline in 74 s or less. There were no significant differences between data after the first and

TABLE 1. Effect of 50-Hz Tetanus on TOF

Tetanus		T_1	T_4	T_4/T_1
1st (n = 13)	Increase (%)	38 (7–129)	250 (38–1,100)	93 (26–555)
	Recovery time (s)	34 (4–66)	43 (23–74)	34 (15–74)
2nd (n = 13)	Increase (%)	43 (0–143)	200 (67–2,100)	117 (36–806)
	Recovery time (s)	35 (3–65)	35 (23–65)	33 (15–65)
Combined (n = 26)	Increase (%)	41 (0–143)	200 (38–2,100)	116 (26–806)
	Recovery time (s)	34 (3–66)	39 (23–74)	34 (15–74)

Values expressed as median (range in parentheses).

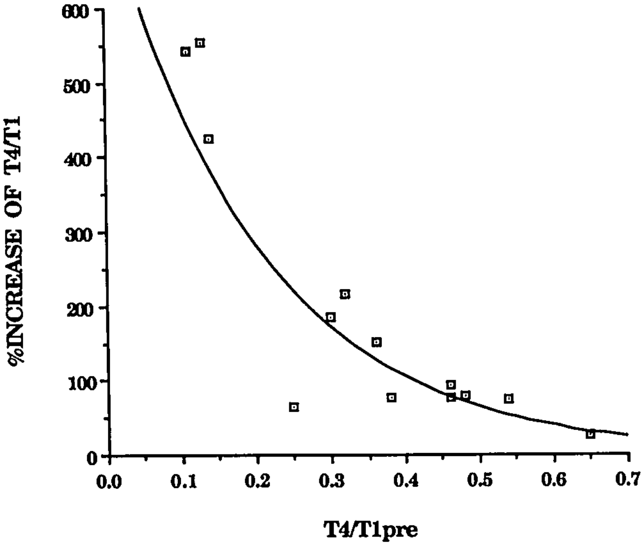

FIG. 1. The relationship between percent increase of T_4/T_1 and degree of blockade (T_4/T_{1pre}). The proportion of the variation in the percent increase of T_4/T_1 that can be explained by an increasing depth of blockade is $r^2 = 0.86$ by exponential regression.

after the second 5-s 50-Hz tetanus with respect to baseline heights, %increase, or recovery times of T_1, T_4, or T_4/T_1.

(C) First 5-s Tetanus at 100 Hz

Prior to the first tetanus at 100 Hz, values for T_{1pre}, T_{4pre}, and T_4/T_{1pre} were 11 ± 6 mm, 4 ± 3 mm, and 0.31 ± 0.1, respectively (P = NS for Groups A *vs.* C). Median %increases were 50, 300, and 178%, respectively (table 2); $P < 0.05$ for T_{1pre} *versus* T_{1post}, T_{4pre} *versus* T_{4post}, T_4/T_{1pre} *versus* T_4/T_{1post}, and %increase of T_4 *versus* %increase of T_1. Median times to recovery were 53, 73, and 54 s, respectively (table 2; P = NS).

The median %increases after tetanus at 50 Hz (part A) for the seven subjects who were also studied after tetanus at 100 Hz (part C) were 40, 260, and 152% for T_1, T_4, and T_4/T_1, respectively. The corresponding recovery times were 34, 34, and 33 s. There were no significant differences between these two sets of data with respect to baseline heights and %increase in the seven subjects. However, the recovery times for T_1, T_4, and T_4/T_1 after the first 100-Hz tetanus were significantly greater than the corresponding values after the first 50-Hz tetanus.

(D) Second 5-s Tetanus at 100 Hz

Prior to the second tetanus at 100 Hz, values for T_{1pre}, T_{4pre}, and T_4/T_{1pre} were 11 ± 6 mm, 4 ± 3 mm, and 0.30 ± 0.1, respectively (P = NS for parts C *vs.* D). Median %increase values were 50, 300, and 200%, respectively (table 2); $P < 0.05$ for T_{1pre} *versus* T_{1post}, T_{4pre} *versus* T_{4post}, T_4/T_{1pre} *versus* T_4/T_{1post}, and %increase of T_4 *versus* %increase of T_1. Median recovery times were 63, 73, and 64 s, respectively (table 2); $P < 0.05$ for T_1 *versus* T_4; P = NS for T_1 *versus* T_4/T_1 and T_4 *versus* T_4/T_1. Comparison to data obtained after the first 100-Hz tetanus revealed no significant differences with respect to baseline heights, %increase, and recovery times of T_1, T_4, and T_4/T_1. In all cases, T_4, T_1, and T_4/T_1 returned to within 10% of baseline in 125 s or less.

EFFECTS ON DOUBLE-BURST MONITORING

(E) First 5-s Tetanus at 50 Hz on $DBS_{3,3}$

Prior to the first tetanus, D_{1pre}, D_{2pre}, and D_2/D_{1pre} were 13 ± 6 mm, 5 ± 2 mm, and 0.40 ± 0.1, respectively. Median %increases were 38, 300, and 153% for D_1, D_2 and D_2/D_1, respectively (table 3); $P < 0.05$ for D_{1pre} *versus* D_{1post}, D_{2pre} *versus* D_{2post}, D_2/D_{1pre} *versus* D_2/D_{1post}, and %increase of D_2 *versus* %increase of D_1. The respective median recovery times for D_1, D_2, and D_2/D_1 of $DBS_{3,3}$ were 43, 66, and 46 s (table 3; P = NS).

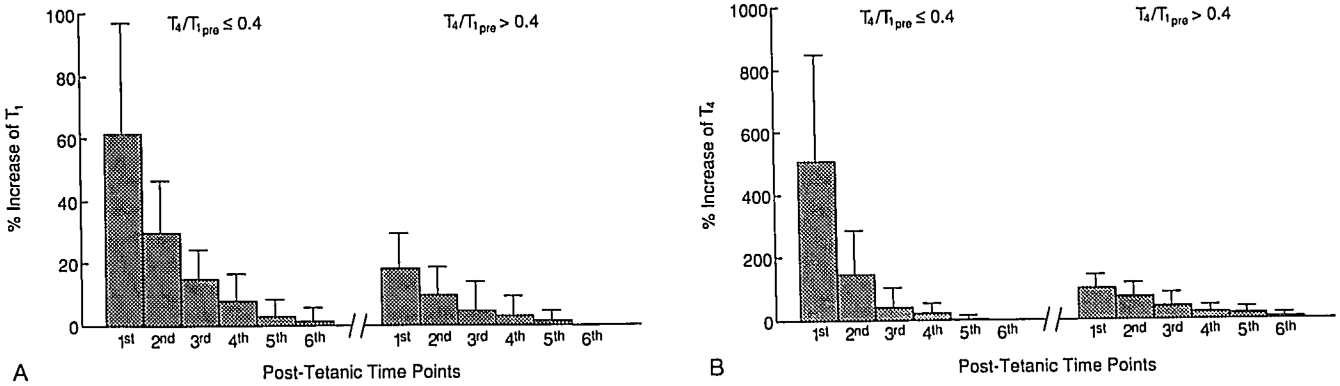

FIG. 2. Percent increase of (*A*) T_1 and (*B*) T_4 at each 10-s interval after 5-s tetanic stimulation at 50 Hz in the $T_4/T_{1pre} \leq 0.40$ and $T_4/T_{1pre} > 0.40$ subgroups. Values are plotted as mean ± SD.

TABLE 2. Effect of 100-Hz Tetanus on TOF

Tetanus		T_1	T_4	T_4/T_1
1st (n = 7)	Increase (%)	50 (13–138)	300 (183–1,300)	178 (140–900)
	Recovery time (s)	53 (13–104)	73 (43–104)	54 (23–104)
2nd (n = 7)	Increase (%)	50 (14–171)	300 (150–1,400)	200 (107–900)
	Recovery time (s)	63 (14–85)	73 (43–125)	64 (33–83)
Combined (n = 14)	Increase (%)	50 (13–171)	300 (150–1,400)	189 (107–900)
	Recovery time (s)	58 (13–104)	73 (43–125)	64 (23–104)

Values expressed as median (range).

(F) Second 5-s Tetanus at 50 Hz on $DBS_{3,3}$

Prior to the second tetanus, D_{1pre}, D_{2pre}, and D_2/D_{1pre} were 12 ± 5 mm, 5 ± 2 mm, and 0.39 ± 0.1, respectively. Mean %increases were 30, 317, and 152% for D_1, D_2, and D_2/D_1, respectively (table 3); $P < 0.05$ for D_{1pre} *versus* D_{1post}, D_{2pre} *versus* D_{2post}, D_2/D_{1pre} *versus* D_2/D_{1post}, and %increase of D_2 *versus* %increase of D_1. Median recovery times were 43, 43, and 43 s, respectively (table 3; P = NS). There were no significant differences between data of the first and second tetanus on $DBS_{3,3}$ with respect to baseline heights, %increase, or recovery times of D_1, D_2, or D_2/D_1. In all cases, D_1, D_2, and D_2/D_1 returned to within 10% of baseline in 103 s or less.

(G) First 5-s Tetanus at 50 Hz on $DBS_{3,2}$

Prior to the first tetanus, D_{1pre}, D_{2pre}, and D_2/D_{1pre} were 14 ± 7 mm, 4 ± 4 mm, and 0.30 ± 0.1, respectively. Median %increases were 41, 275, and 176% for D_1, D_2 and D_2/D_1, respectively (table 4); $P < 0.05$ for D_{1pre} *versus* D_{1post}, D_{2pre} *versus* D_{2post}, D_2/D_{1pre} *versus* D_2/D_{1post}, and %increase of D_2 *versus* %increase of D_1. Median recovery times for D_1, D_2, and D_2/D_1 of $DBS_{3,2}$ were 43, 43, and 43 s (table 4; P = NS).

(H) Second 5-s Tetanus at 50 Hz on $DBS_{3,2}$

Prior to the second tetanus, D_{1pre}, D_{2pre}, and D_2/D_{1pre} were 15 ± 8 mm, 4 ± 3 mm, and 0.27 ± 0.2, respectively. Median %increases were 38, 300, and 107% for D_1, D_2, and D_2/D_1, respectively (table 4); $P < 0.05$ for D_{1pre} *versus* D_{1post}, D_{2pre} *versus* D_{2post}, D_2/D_{1pre} *versus* D_2/D_{1post}, and %increase of D_2 *versus* %increase of D_1. Median recovery times were 43, 63, and 43 s, respectively (table 4; P = NS). There were no significant differences between the first and second tetanus on $DBS_{3,2}$ with respect to baseline heights, %increase, or recovery times of D_1, D_2, or D_2/D_1. In all cases of $DBS_{3,2}$ testing, D_1, D_2, and D_2/D_1 returned to within 10% of baseline in 103 s or less.

Discussion

After tetanic stimulation, increased release of acetylcholine[12] may be manifested clinically by posttetanic count,[10,13] augmented single-twitch height,[14] and a decrease in fade in response to TOF and DBS. Although the minitetanic bursts of DBS are different from the individual twitches of TOF, we noted comparable findings for TOF, $DBS_{3,3}$, and $DBS_{3,2}$ with regard to the degree and duration of posttetanic "facilitation."

After tetanus, there was augmentation of T_1 and D_1, and to a greater extent, of T_4 and D_2. These changes did not cause a prolonged period of altered monitoring in the T_4/T_1 (or D_2/D_1 of $DBS_{3,3}$) range of 0.1–0.7. T_4/T_1 and D_2/D_1 returned to their pretetanic baselines within 2 min. Although T_1 and T_4 responses were increased by as much as 143 and 2,100%, respectively, after a 50-Hz tetanic stimulus, they always returned to within 10% of baseline within 74 s. Similarly, D_1 and D_2 responses for $DBS_{3,3}$ were increased by as much as 175 and 1100%, respectively, and returned to within 10% of baseline in less than 103 s. Corresponding values for $DBS_{3,2}$ were 213 and 1,600% increase, with a maximum time to recovery of 103 s.

TABLE 3. Effect of 50-Hz Tetanus on $DBS_{3,3}$

Tetanus		D_1	D_2	D_2/D_1
1st (n = 7)	Increase (%)	38 (17–119)	300 (69–656)	153 (45–244)
	Recovery time (s)	43 (23–66)	66 (43–103)	46 (43–83)
2nd (n = 7)	Increase (%)	30 (0–175)	317 (56–1,100)	152 (65–336)
	Recovery time (s)	43 (3–63)	43 (23–83)	43 (23–63)
Combined (n = 14)	Increase (%)	34 (0–175)	308 (56–1,100)	153 (45–336)
	Recovery time (s)	43 (3–66)	63 (23–103)	43 (23–83)

Values expressed as median (range).

TABLE 4. Effect of 50-Hz Tetanus on $DBS_{3,2}$

Tetanus		D_1	D_2	D_2/D_1
1st (n = 7)	Increase (%)	41 (20–213)	275 (91–1,600)	176 (49–935)
	Recovery time (s)	43 (43–63)	43 (43–103)	43 (23–103)
2nd (n = 7)	Increase (%)	38 (13–150)	300 (45–1,500)	107 (5–1,052)
	Recovery time (s)	43 (23–63)	63 (43–103)	43 (3–103)
Combined (n = 14)	Increase (%)	39 (13–213)	288 (45–1,600)	142 (5–1,052)
	Recovery time (s)	43 (23–63)	43 (43–103)	43 (3–103)

Values expressed as median (range).

Consistent with reports by other investigators with respect to single twitch,[5,15] the %increase in the current study was greater at increased depth of blockade. This accounts for the wide range of %increase, as reported in tables 1–4. An inconsistency of our monitoring technique, while theoretically possible, is not likely in view of the return of posttetanic values to baseline, and in light of a previous report which noted a less than 2% difference between successive readings.[16] The median %increase of T_1 was 46% when the pretetanic T_4/T_1 ratio was less than 0.40, and 12% when T_4/T_{1pre} was greater than 0.40. Corresponding values for T_4 were 300 and 100%. At greater degrees of blockade, the augmentation of T_1 approached that seen with equivalent depressions of T_4. While, in the current study, the depth of blockade did not affect the time to recovery to the same degree that it affected %increase, this does not preclude marked prolongation at greater degrees of blockade. The magnitude and duration of posttetanic effects depend not only on the extent of neuromuscular blockade, but also on the nature of neurostimulation.[5,17–20] As tetanic frequency was increased from 50 to 100 Hz, we noted no significant change in %increase and only a slight (albeit statistically significant) increase in recovery times.

The current study was performed during a steady state of blockade, and during isoflurane inhalation anesthesia, in order to permit comparison among testing regimens within the context of routine clinical care. It is possible that the degree and duration of posttetanic "facilitation" may differ slightly during onset compared to recovery, since the relationship of T_4 to T_1 may differ at these times.[21] In light of reports that succinylcholine alters the depth and duration of subsequent nondepolarizing block,[22] slight differences may be noted if succinylcholine is not used. The nature and concentration of the inhalation agents, and perhaps more importantly, the nature of relaxant, may be relevant. With respect to the latter, an agent with a more pronounced presynaptic effect (*e.g.*, curare) may be associated with more pronounced posttetanic effects. In addition, the relatively short duration of posttetanic facilitation noted may be attributable, in part, to the stable plasma levels of vecuronium provided by the continuous infusion.

In conclusion, for the level of blockade evidenced by a T_4/T_1 or D_2/D_1 ratio between 0.1 and 0.7 during continuous vecuronium infusion, assessment can be supplemented by the use of a 5-s, 50–100 Hz tetanic stimulus without distorting subsequent TOF or DBS monitoring for an unacceptably long period of time. As expected, a greater stimulus intensity (*i.e.*, tetanus at 100 Hz) produced a slightly longer posttetanic effect. Nevertheless, in all cases T_4/T_1 and D_2/D_1 returned to baseline within 2 min.

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References

1. Ali HH, Kitz RJ: Evaluation of recovery from nondepolarizing neuromuscular block, using a digital neuromuscular transmission analyzer: Preliminary report. Anesth Analg 52:740–745, 1973
2. Ali HH, Savarese JJ: Monitoring of neuromuscular function. ANESTHESIOLOGY 45:216–249, 1976
3. Viby-Mogensen J, Jensen NH, Engbaek J, Ording H, Skovgaard LT, Chraemmer-Jorgensen B: Tactile and visual evaluation of the response to train-of-four nerve stimulation. ANESTHESIOLOGY 63:440–443, 1985
4. Engbaek J, Ostergaard D, Viby-Mogensen J: Double burst stimulation (DBS): A new pattern of nerve stimulation to identify residual neuromuscular block. Br J Anaesth 62:274–278, 1989
5. Gissen AJ, Katz RL: Twitch, tetanus and posttetanic potentiation as indices of nerve-muscle block in man. ANESTHESIOLOGY 30: 481–487, 1969
6. Waud BE, Waud DR: The relation between the response to "train-of-four" stimulation and receptor occlusion during competitive neuromuscular block. ANESTHESIOLOGY 37:413–416, 1972
7. Hughes JR, Morrell RM: Posttetanic changes in the human neuromuscular system. J Appl Physiol 11:51–57, 1957
8. Lee C, Katz RL: Neuromuscular pharmacology: A clinical update and commentary. Br J Anaesth 52:173–188, 1980
9. Feldman SA, Tyrrell MF: A new theory of the termination of action of the muscle relaxants. Proc R Soc Med 63:692–695, 1970.
10. Howardy-Hansen P, Viby-Mogensen J, Gottschau A, Skovgaard LT, Chraemmer-Jorgensen B, Engbaek J: Tactile evaluation of the posttetanic count (PTC). ANESTHESIOLOGY 60:372–374, 1984
11. Rosenberg H, Greenhow DE: Peripheral nerve stimulator performance: The influence of output polarity and electrode placement. Can Anaesth Soc J 25:424–426, 1978

12. Brooks VB, Theis RE: Reduction of quantum content during neuromuscular transmission. J Physiol (Lond) 162:298–310, 1962
13. Muchhal KK, Viby-Mogensen J, Fernando PUE, Tamilarasan A, Bonsu AK, Lambourne A: Evaluation of intense neuromuscular blockade caused by vecuronium using posttetanic count (PTC). ANESTHESIOLOGY 66:846–849, 1987
14. Wali FA, Bradshaw EG, Suer AH: Clinical assessment of neuromuscular blockade produced by vecuronium using twitch, train of four, tetanus and post-tetanic twitch responses to the adductor pollicis muscle. Acta Anaesthesiol Belg 39:35–42, 1988
15. Katz RL: Electromyographic and mechanical effects of suxamethonium and tubocurarine on twitch, tetanic and post-tetanic responses. Br J Anaesth 45:849–859, 1973
16. Brull SJ, Ehrenwerth J, Silverman DG: Stimulation with submaximal current for train-of-four monitoring. ANESTHESIOLOGY 72:629–632, 1990.
17. Stanec A, Heyduk J, Stanec G, Orkin LR: Tetanic fade and post-tetanic tension in the absence of neuromuscular blocking agents in anesthetized man. Anesth Analg 57:102–107, 1978
18. Ali HH, Utting JE, Gray C: Stimulus frequency in the detection of neuromuscular block in humans. Br J Anaesth 42:967–978, 1970
19. Liley AW, North KAK: An electrical investigation of the effects of repetitive stimulation on mammalian neuromuscular junction. J Neurophysiol 16:509–527, 1953
20. Blackman JG: Stimulus frequency and neuromuscular block. Br J Pharmacol 20:5–16, 1963
21. Turner GA, Williams JD, Baker DJ: Train-of-four fade during onset and recovery of neuromuscular block: A study in non-anesthetized subjects. Br J Anaesth 62:279–286, 1989
22. Ono K, Manabe N, Ohta Y, Morita K, Kosaka F: Influence of suxamethonium on the action of subsequently administered vecuronium or pancuronium. Br J Anaesth 62:324–326, 1989