Post-tetanic count and train-of-four responses during 
neuromuscular block produced by vecuronium and infusion of 
nicardipine

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We have examined onset and recovery of neuromuscular block produced by vecuronium using 
either post-tetanic count (PTC), or the first twitch of the train-of-four (TOF) (T1/T0) and 
TOF ratio (T4/T1) during continuous infusion of nicardipine. Sixty adult patients were allocated 
to one of four groups of 15 patients each: nicardipine–PTC, nicardipine–TOF, control–PTC 
and control–TOF. In the nicardipine–PTC and nicardipine–TOF groups, nicardipine 0.03 mg 
kg\(^{-1}\) was given before vecuronium 0.1 mg kg\(^{-1}\) and a continuous infusion of nicardipine was 
started immediately at a rate of 2 \(\mu\)g kg\(^{-1}\) min\(^{-1}\). Mean time from administration of vecuronium 
to onset of neuromuscular block in the nicardipine–PTC and nicardipine–TOF groups was 
significantly shorter than in the control–PTC and control–TOF groups (166 (SD 39) vs 
220 (28) s; \(P<0.05\)). There was no significant difference in recovery of PTC between the nicardipine– 
PTC and control–PTC groups or in recovery of TOF ratio in the nicardipine–TOF and control– 
TOF groups. However, during recovery, T1/T0 in the nicardipine–TOF group was significantly 
less than that in the control–TOF group, 60–100 min after administration of vecuronium.

Keywords: neuromuscular block, measurement of response; neuromuscular block, vecuronium; 
calcium channel block, nicardipine

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Calcium channel blockers enhance the action of neuromuscular blocking drugs.\(^{1-5}\) In previous reports,\(^{1-5}\) single 
twitch height or the first response of the train-of-four (TOF) (T1/T0) were measured after bolus injection or during 
continuous infusion of a calcium channel blocker. However, no previous studies have investigated post-tetanic count 
(PTC) and TOF ratio (T4/T1) during infusion of such drugs.

PTC and TOF ratio provide an indication of the prejunctional effect of neuromuscular blocking drugs,\(^{6}\) while T1/ 
T0 represents the effect at the postjunctional nicotinic receptor.\(^{6}\) Calcium channel blockers augment neuromuscular 
block by acting at the postjunctional region; they have no apparent effect at the putative prejunctional receptors.\(^{1,2}\) 
Therefore, we postulated that during infusion of a calcium channel blocker, T1/T0 would be decreased but PTC or TOF 
ratio would not change in patients receiving vecuronium.

Methods and results

The study was approved by our Local Ethics Committee 
and written informed consent was obtained from each patient. We studied 60 adult patients, ASA I or II, undergoing 
elective general anaesthesia. Patients were allocated randomly to one of four groups of 15 patients each: nicardipine– 
PTC, nicardipine–TOF, control–PTC and control–TOF. No patient had neuromuscular, hepatic, renal or cardiac 
disorders or was receiving any drug known to affect neuromuscular transmission.

Premedication comprised atropine 0.01 mg kg\(^{-1}\) and 
hydroxyzine 1.0 mg kg\(^{-1}\) i.m., 30 min before induction of 
aesthesia. In the operating theatre, two surface stimulating 
electrodes were positioned over the ulnar nerve at the wrist. 
A force displacement transducer which was connected to 
a neuromuscular transmission analyser (Myograph 2000, 
Biometer International, Odense, Denmark) was attached 
to the thumb of the investigated arm. Thumb preload was 
adjusted to 250 g.

In the nicardipine–PTC and nicardipine–TOF groups, 
before induction of anaesthesia, nicardipine 0.03 mg kg\(^{-1}\) 
was given i.v. Immediately after administration of nicardipine, 
propofol 2 mg kg\(^{-1}\) was given and a continuous infusion of 
nicardipine at a rate of 2 \(\mu\)g kg\(^{-1}\) min\(^{-1}\) was started.

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each group, after loss of the eyelash reflex was confirmed, TOF stimuli were given at 50 mA every 12 s using an electrical nerve stimulator (Myotest DBS, Biometer International, Odense, Denmark). Four single twitch stimuli consisting of 0.2-ms duration square waves were applied at 2 Hz. Adduction of the thumb was measured mechanically using the neuromuscular transmission analyser. The height of T1 (the first response in the TOF) was regarded as control (T0). When a control reading was recorded, vecuronium 0.1 mg kg\(^{-1}\) was administered i.v. to facilitate tracheal intubation. In the control–PTC and control–TOF groups, anaesthesia was induced in the same manner as in the nicardipine groups, except that nicardipine was not given. After administration of vecuronium, disappearance of the T1 response was regarded as the time to onset of neuromuscular block. This time was measured in 30 patients in the nicardipine–PTC and nicardipine–TOF groups, and was compared with the 30 patients in the control–PTC and control–TOF groups.

After administration of vecuronium in the nicardipine–PTC and control–PTC groups, PTC was measured every 5 min. A 50-Hz tetanic stimulation was delivered at 50 mA for 5 s, and after a pause of 3 s, 20 single twitch stimuli of 0.2-ms duration square waves were given at 50 mA. The number of detectable muscular contractions in response to the single twitch stimuli was regarded as the PTC. In the nicardipine–PTC and control–PTC groups, times from administration of vecuronium to return of PTC1 (the first response to the 20 single twitch stimuli delivered after tetanic stimulation) and the time courses of recovery of PTC were compared. In the nicardipine–TOF and control–TOF groups, times from administration of vecuronium to return of T1, T2, T3 and T4 (the first, second, third and fourth response of the TOF) were compared between the two groups. Also, T1/T0 and T4/T1 were recorded every 10 min and were compared between the nicardipine–TOF and control–TOF groups.

In each group, anaesthesia was maintained with 66% nitrous oxide in oxygen and 1.0% end-tidal isoflurane. Patients’ lungs were ventilated to maintain normocapnia (\(PE_{\text{CO}_2}\) 4.1–5.0 kPa). End-tidal concentrations of anaesthetic agents and \(PE_{\text{CO}_2}\) were measured using a multiple-gas monitor (Capnomac Ultima, Datex Inc., Helsinki, Finland).

Results are expressed as number or mean (SD). Patient data in the four groups were compared using analysis of variance (ANOVA) and Scheffe’s multiple comparison. Times to onset of neuromuscular block in the nicardipine–PTC and nicardipine–TOF groups and in the control–PTC and control–TOF groups, times to return of PTC1 in the nicardipine–PTC and control–PTC groups, and times to return of T1, T2, T3 and T4 in the nicardipine–TOF and control–TOF groups were compared using the unpaired t test. Recovery of PTC was compared in the nicardipine–PTC and control–PTC groups using the Kruskal–Wallis test followed by the Mann–Whitney U test with Bonferroni’s adjustment. Comparison of recoveries of T1/T0 and T4/T1 were made using ANOVA followed by the unpaired t test with Bonferroni’s adjustment. \(P<0.05\) was considered statistically significant. Statistical analyses were performed using a statistical package (Stat 123, Sinkoukoueki Inc., Tokyo, Japan) running on a personal computer (NEC PC-9821 Na 15, NEC Inc., Tokyo, Japan).

Patient data were comparable in the four groups. Mean time to onset of neuromuscular block in the 30 patients in the nicardipine–PTC and nicardipine–TOF groups was significantly shorter than that in the 30 patients in the control–PTC and control–TOF groups (166 (SD 39) vs 220 (28) s; \(P<0.05\)).

Times from administration of vecuronium to return of PTC1 did not differ significantly between the nicardipine–PTC and control–PTC groups (22.3 (10.0) vs 19.7 (4.4) min).

Fig 1 Mean (SD) recovery of post-tetanic count (PTC) (A), T1/T0 (B) and T4/T1 (TOF ratio) (C) after administration of vecuronium 0.1 mg kg\(^{-1}\) in the nicardipine and control groups. There was no significant difference in recovery of PTC or T4/T1 between groups. For recovery of T1/T0, \(*P<0.05\) between groups.
min; ns). In contrast, mean times to return of T1, T2, T3 and T4 in the nicardipine–TOF group were significantly longer than those in the control–TOF group (38.1 (13.9) vs 28.3 (11.2) min for T1; 48.5 (17.8) vs 36.7 (8.9) min for T2; 54.9 (19.3) vs 42.9 (9.6) min for T3; and 57.9 (20.3) vs 45.1 (9.9) min for T4; P<0.05).

Recovery of PTC did not differ significantly between the nicardipine–PTC and control–PTC groups (Fig. 1A). T1/T0 in the nicardipine–toF group was significantly lower than that in the control–TOF group, 60–100 min after administration of vecuronium (Fig. 1B) (P<0.05). TOF ratios did not differ significantly between the nicardipine–TOF and control–TOF groups (Fig. 1C).

**Comment**

In this study, we found that the onset of vecuronium-induced neuromuscular block was faster after bolus administration of nicardipine, as has been reported previously with nicardipine and diltiazem.3,4 During infusion of nicardipine, return of PTC1 and recovery of PTC or TOF ratio were not delayed, but return of T1, T2, T3 and T4, and recovery of T1/T0 were slower.

PTC and the TOF ratio are thought to represent the degree of neuromuscular block at the prejunctional region of the neuromuscular junction.6 But it has been reported that calcium channel blockers enhance neuromuscular block by acting mainly at the postjunctional region.1 Therefore, it was not surprising that recovery of PTC or TOF ratio was not delayed, even during nicardipine infusion. As shown in Figure 1A, although recovery of PTC in the nicardipine–PTC group was relatively slower than in the control–PTC group, the difference between the two groups was not significant. As shown in Figure 1C, the time courses of recovery of TOF ratio in the nicardipine–TOF and control–TOF groups were comparable. In contrast, T1/T0 recovery was decreased in patients receiving nicardipine (Fig. 1B).

T1/T0 is thought to represent the postjunctional effect of neuromuscular block, which is also potentiated by administration of nicardipine. Similarly, time from administration of a neuromuscular blocking drug to return of PTC1 and T1, T2, T3 and T4 are related to the prejunctional and postjunctional effects of neuromuscular block, respectively.6

Our findings that times from administration of vecuronium to return of PTC1 were comparable between the nicardipine–PTC and control–PTC groups, but times to return of T1, T2, T3 and T4 in the nicardipine–TOF group were significantly longer than those in the control–TOF group were considered predictable.

**References**