Normalization of acceleromyographic train-of-four ratio by baseline value for detecting residual neuromuscular block

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Background. This study was designed to recognize the importance of normalizing postoperative acceleromyographic train-of-four (TOF) ratio by the baseline TOF value obtained before neuromuscular block for ensuring adequate recovery of neuromuscular function.

Methods. In 120 patients, TOF responses of the adductor pollicis to the ulnar nerve stimulation were monitored by acceleromyography (AMG) during anaesthesia using propofol, fentanyl and nitrous oxide. Control TOF stimuli were administered for 30 min. A TOF ratio measured at the end of control stimulation was regarded as a baseline value. Neuromuscular block was induced with vecuronium 0.1 mg kg\(^{-1}\) and was allowed to recover spontaneously. Duration to a TOF ratio of 0.9 as calculated by AMG (DUR-raw 0.9) was compared with that of 0.9 as corrected by the baseline TOF ratio (i.e. 0.9×baseline TOF ratio; DUR-real 0.9).

Results. Baseline TOF ratios ranged from 0.95 to 1.47. The average TOF ratios observed every 5 min were constant throughout control stimulation from at time zero mean (SD) [range]; 1.11 (0.09) [0.94–1.42] to at 30 min 1.13 (0.11) [0.95–1.47]. The DUR-real 0.9 was 91.0 (18.0) [51.3–131.0] min and was significantly longer than the DUR-raw 0.9 (81.2 (16.3) [41.3–123.0] min).

Conclusions. Baseline TOF ratios measured by AMG are usually more than 1.0 and vary widely among patients. Therefore a TOF ratio of 0.9 displayed postoperatively on AMG does not always represent adequate recovery of neuromuscular function and should be normalized by baseline value to reliably detect residual paralysis.

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Mechanomyography (MMG) is gold the standard for monitoring neuromuscular function, while acceleromyography (AMG) is increasingly being used in a clinical setting because it is relatively inexpensive, easy to set up, and able to detect neuromuscular block with accuracy. However, anaesthetists should pay attention to a unique characteristic of AMG. When compared with MMG, the baseline train-of-four (TOF) ratio measured using AMG is significantly higher (i.e. the TOF ratio >1.0).\(^{2–4}\) Baseline TOF ratio measured using MMG is usually 1.0 or very close to 1.0,\(^{2}\) therefore a TOF ratio observed by MMG during recovery from neuromuscular block should be regarded as a real value of TOF ratio. Nevertheless, average baseline TOF ratio measured with AMG is 1.10–1.20,\(^{2–4}\) therefore it may be essential to correct a raw TOF ratio displayed on the monitor screen of AMG during recovery by the baseline TOF ratio for ensuring adequate TOF recovery and avoiding residual paralysis. This study was designed to emphasize the importance of recording baseline TOF ratio for improving detection of postoperative residual neuromuscular block using AMG.

Methods

After approval of the protocol by the hospital Ethics Committee on Human Rights in Research, a hundred and twenty female patients consented to participate in the study. Patients were ASA I or II, 27–59 yr of age [mean (SD) 44.2 (8.6) yr] undergoing elective gynaecological surgery. In all the patients neuromuscular, hepatic, renal, endocrine or metabolic disorders were excluded. Also obesity (BMI>25) and...
intake of drugs that might interfere with neuromuscular transmission were excluded.

The patients were premedicated with midazolam 0.05 mg kg\(^{-1}\) i.m. 45 min before the induction of anaesthesia. On arrival in the operating room, monitors as appropriate for routine anaesthetic care (ECG, non-invasive arterial pressure and pulse oximetry) were applied. An i.v. infusion of acetated Ringer’s solution was started in the right forearm and was administered at an infusion rate of 8–10 ml kg\(^{-1}\) h\(^{-1}\). An epidural catheter was inserted via intervertebral space between Th12 and L1 and introduced 5 cm cephalad. A test dose of 2 ml of mepivacaine 2% was injected into epidural space, followed by a bolus of 0.15 ml kg\(^{-1}\) of mepivacaine 2%. Mepivacaine 2% (0.1 ml kg\(^{-1}\)) was repetitively given every 45–60 min throughout the surgery. General anaesthesia was induced with fentanyl 2–4 \(\mu\)g kg\(^{-1}\) and propofol 2–2.5 mg kg\(^{-1}\) i.v. while patients received 100% oxygen through an anaesthesia facemask. Laryngeal mask insertion was accomplished without aid of neuromuscular blocking agents. Anaesthesia was maintained by a continuous infusion of propofol 3–4 mg kg\(^{-1}\) h\(^{-1}\), intermittent administrations of fentanyl as required, and inhalation of nitrous oxide 67% in oxygen. Ventilation was adjusted to keep the end-tidal carbon dioxide within the range of 4.3–5.1 kPa using a Multigas Unit AG-920R\(^\text{TM}\) (Nihon Kohden, Tokyo, Japan).

After having obtained stable depth of anaesthesia, the study arm was immobilized and the left ulnar nerve was stimulated at the wrist with square-wave, automatically detected supramaximal stimuli of 0.2 ms duration, delivered in a TOF mode at 2 Hz every 15 s. The acceleration transducer was taped to the volar aspect of the thumb at the interpharyngeal joint and contraction of the ipsilateral adductor pollicis muscle was measured using AMG (TOFguard\(^\text{TM}\), Organon Teknika NV, Turnhout, Belgium). The thumb was allowed to move freely without a preload. Control TOF stimuli were administered for 30 min to observe and stabilize potentiation of the first twitch of TOF (%T1 potentiation) and TOF ratios. A TOF ratio measured at the end of control stimulation was regarded as a baseline value. Immediately after control stimulation all patients received vecuronium 0.1 mg kg\(^{-1}\) i.v.

The following variables were measured or calculated: onset time (min) from the time of bolus injection of vecuronium to maximum depression of T1; duration (min) from the injection of vecuronium to spontaneous recovery of T1 to 25% of control (DUR25); time (min) to recovery of T1 from 25 to 75% (recovery index, RI); interval (min) from the injection of vecuronium to spontaneous recovery to TOF ratio of 0.9 (actual read of the TOF ratio is expressed as ‘90%’ on the screen of TOFguard\(^\text{TM}\) displayed on the AMG screen (DUR-raw 0.9), and that to corrected TOF ratio of 0.9, i.e. 0.9×baseline TOF ratio (DUR-real 0.9). All data were collected on a memory card of AMG and analysed on a desktop computer. Skin temperature over the thenar muscles was recorded every 15 s throughout the experiment using a surface probe attached in AMG unit and it was kept >32°C. Rectal temperature was measured using Mon-a-Therm\(^\text{TM}\) (Mallinckrodt, Anesthesia Products Inc., St Louis, USA) and maintained >36°C using a warming mattress and blanket (ThermaCare\(^\text{TM}\) and Medi-Therm II\(^\text{TM}\), Gaymer Industries, Inc., NY).

Data are presented as mean (SD) [range]. Statistical analysis was performed using StatView\(^\text{TM}\) software for Windows (SAS Institute, Cary, NC). Analysis of variance was used for multiple comparisons. A P-value of <0.05 was considered statistically significant. If a significant P-value was obtained in multiple comparisons, further group comparisons were made using Bonferroni post hoc test. Difference between two indices was compared using the unpaired Student’s t-test.

**Results**

Data for eight patients were excluded from analysis of results because twitch and TOF ratio did not recover to the baseline values as a result of the baseline shift, therefore, data for 112 patients were analysed in this study.

A progressive increase in %T1 was observed during control TOF stimulation (Table 1). Individual %T1 was maximally potentiated to 140.3 (23.0) [92–192]% after 15.4 (6.4) [3–29] min of the stimulation. In contrast, average TOF ratios were constant with time throughout 30 min of control stimulation and there were no significant differences in the TOF ratios at time zero (1.11 (0.09) [0.94–1.42]) and at 30 min (1.13 (0.11) [0.95–1.47]). Figure 1 shows marked spread of baseline TOF ratios obtained after 30 min of control stimulation. The baseline TOF ratios of 1.01 and above [range: 1.03–1.47] were seen in 100 (out of 112) patients.

After vecuronium, complete block was obtained in every patient. The onset time, DUR25 and RI were 1.9 (0.4) [1.0–3.3] min, 45.8 (9.9) [29.5–78.0] min and 19.9 (6.5) [11.0–33.0] min, respectively. In the patients who showed baseline TOF ratios of 1.01 and above (n=100), a statistically significant difference was seen between DUR-raw 0.9 and DUR-real 0.9 (81.2 (16.3) [41.3–123.0] min vs 91.0 (18.0) [51.3–131.0] min). The time difference between the time

**Table 1** Progress of %T1 and TOF ratios during control stimulation. Data are presented as mean (SD) [range]. # P<0.05 compared with the measurements at 5 min

<table>
<thead>
<tr>
<th></th>
<th>Time zero</th>
<th>5 min</th>
<th>10 min</th>
<th>15 min</th>
<th>20 min</th>
<th>25 min</th>
<th>30 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>%T1</td>
<td>100</td>
<td>[121.3 (14.4)</td>
<td>[131.3 (19.4)]#</td>
<td>[134.5 (21.7)]#</td>
<td>[136.4 (22.8)]#</td>
<td>[136.9 (21.5)]#</td>
<td>[136.4 (21.7)]#</td>
</tr>
<tr>
<td>TOF ratio</td>
<td>1.11 (0.09)</td>
<td>1.11 (0.10)</td>
<td>1.12 (0.09)</td>
<td>1.13 (0.10)</td>
<td>1.12 (0.11)</td>
<td>1.12 (0.10)</td>
<td>1.13 (0.11)</td>
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<td></td>
<td>[0.94–1.47]</td>
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needed to recover to DUR-raw 0.9 and that to DUR-real 0.9 was 10.0 (5.2) [3.0–26.8] min. Least-squares linear regression analysis proved a significant correlation between baseline TOF ratios and the time differences between DUR-real 0.9 and DUR-raw 0.9 ($Y=44.9X-41.6$; $Y$-time difference, $X$-baseline TOF ratio; $R^2=0.645; n=100$; Fig. 2).

Discussion

The present study showed a similar result to the former studies\(^2\text{–}^4\) with regard to average baseline TOF ratio of more than 1.0 measured using AMG at the adductor pollicis before neuromuscular block. However, it also showed a marked spread in the baseline TOF ratios, ranging from 0.95 to 1.47. The wide spread of the ratios most probably contributes to an error in assessing recovery from neuromuscular block, particularly in cases with a baseline TOF ratio >1.0. For maximum baseline TOF ratio of 1.47 observed in the study, a TOF ratio of 0.9 displayed on the screen of AMG (actual read on the display is ‘90%’) corresponds to just 0.61 of the baseline value. In this case, to reach real TOF ratio of 0.9 normalized by the baseline value (i.e. 1.47×0.9=1.32) >20 min were further required (Fig. 2). Average time interval between DUR-raw 0.9 and DUR-real 0.9 was 10 min in the present study. Even in the short period, there is the probability that patients would feel unpleasant symptoms resulting from residual paralysis.\(^5\) Anaesthetists cannot be too careful in avoiding postoperative residual neuromuscular block and the possible risk of causing regurgitation and aspiration of gastric content.\(^6,7\) impaired ventilatory regulation to hypoxia\(^8\) and pulmonary complications.\(^9\) It is therefore important to commence neuromuscular monitoring before the onset of neuromuscular block to get a baseline TOF ratio that can be used to normalize TOF ratios during recovery from block.

An acceleromyographic TOF ratio cannot detect minor residual paralysis when used as an isolated assessment at the end of anaesthesia if a baseline TOF value was not recorded.

However, the former studies\(^10\text{–}^11\) proposed that even a TOF ratio without normalization predicted the time to complete recovery. At uncalibrated acceleromyographic TOF ratio of 0.9, complete recovery occurred within 4 min (95% confidence interval, 2.7–5.8 min).\(^10\) In addition, to elucidate residual paralysis reliably, TOF recovery to 1.0 is recommended when using AMG.\(^11\) The proposals must be surely helpful for eliminating the risk of postoperative residual paralysis when a baseline TOF ratio is not observed before neuromuscular block. Based on our results of this study that average baseline TOF ratio is 1.11 at time 0, the normalized TOF ratio of 0.9 observed during recovery from neuromuscular block should be 0.99 on AMG monitor screen. This finding is consistent with the results of the former study.\(^11\) Taking into consideration the fact that the considerable spread of all baseline TOF ratios ranged from 0.95 to 1.47 was seen in this study, however, it is reasonable that the recovery of an acceleromyographic TOF ratio to 1.0 cannot fully assure adequate neuromuscular function in every patient.

The mechanism of a baseline TOF ratio of >1.0 when measured using AMG has not been elucidated,\(^2\) but, a possible explanation for the problem is that the non-restrained thumb without a preload might not return to exactly the same baseline position after each TOF stimulus.\(^12\) Gradual twitch potentiation, i.e. the staircase phenomenon\(^13\text{–}^14\) was observed during control stimulation, but in contrast, the baseline TOF ratios were consistently stable. Not only T1, but also T2, T3 and T4 were increased in the same proportion by repetitive TOF stimuli, therefore TOF ratios measured during control stimulation were constant. This result suggests that a sufficient time of stimulation is essential for stabilizing twitch height, but is not necessary for evaluating TOF ratio. In usual clinical settings, it is not easy to set up and calibrate the neuromuscular monitor immediately after induction of anaesthesia. However, it is
possible to get the baseline TOF ratio before the administration of a neuromuscular blocking agent in a relatively short period of time. Therefore, we propose that TOF monitoring should be used primarily rather than T1 height monitoring in routine anaesthesia.

In conclusion, a TOF ratio showing adequate recovery for maintaining normal neuromuscular transmission varies individually and mostly exceeds 1.0 when evaluated by AMG. Although routine use of AMG in clinical practice is recommended to avoid postoperative residual neuromuscular block and improve patient safety using its easy set-up and operation to advantage, we have to recognize the characteristics of acceleromyographic TOF responses.

References