Post-tetanic count at adductor pollicis is a better indicator of early diaphragmatic recovery than train-of-four count at corrugator supercilii

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Background. Because the intensity of neuromuscular block at the diaphragm (DIA) is indirectly assessed, the electromyographic measurements of the DIA (DIA EMG) from surface electrodes were related to information provided by visual estimation of neuromuscular transmission at the adductor pollicis (AP) and the corrugator supercilii (CSC) during recovery from vecuronium block.

Methods. Twelve adult patients were studied during balanced anaesthesia. After induction of anaesthesia and tracheal intubation without neuromuscular blocking agent, supramaximal stimulations were applied to phrenic, ulnar and facial nerves. During recovery from vecuronium 0.1 mg kg⁻¹ an independent observer blinded to DIA EMG counted visually detectable train-of-four (TOF) at CSC (TOF CSC) and post-tetanic AP (PTC AP) responses. Times to recovery of PTC AP = 1, ≤ 5, < 10 and ≥ 10, and TOF CSC = 1–4 responses were related to DIA EMG. Values are means (SD).

Results. Reappearance of the first response to PTC AP occurred significantly (P < 0.05) earlier and for a lower recovery of DIA EMG than that of TOF CSC [24 (8) min vs 33 (9) min, and 10 (10)% vs 25 (8)%], respectively. With PTC AP ≤ 5 response, DIA EMG recovery was 21 (1)% and 47 (9), respectively.

Conclusions. PTC AP may better reflect early recovery of vecuronium-induced DIA paralysis than TOF CSC. The findings suggested that PTC AP ≤ 5 warranted deep neuromuscular block of the DIA.

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Neuromuscular blocking agents (NMBAs) are frequently administered to achieve neuromuscular block at the targeted muscles of the thorax and the abdomen including the diaphragm (DIA). Of interest, the DIA is considered to be the most resistant muscle to NMBAs, which means that compared with other more sensitive muscles it requires a larger dose and is prone to earlier recovery. Although strict control of neuromuscular transmission at the DIA seems critical for some central types of surgery, direct clinical monitoring of neuromuscular transmission at this muscle is lacking. Therefore, indirect assessment of neuromuscular transmission at the DIA might be of interest. Post-tetanic twitches count (PTC) has been developed to predict return of the adductor pollicis (AP) muscle reactivity during recovery from deep neuromuscular block, but is not related to DIA recovery. Recently, a recovery profile resembling that of muscles resistant-to-NMBA was demonstrated for the corrugator supercilii (CSC) muscle.
suggesting that monitoring of neuromuscular transmission at this muscle might be informative on DIA relaxation. Because very few objective data exist explaining the relationships between neuromuscular transmission monitoring at peripheral muscles and DIA relaxation, we compared information provided by visual estimation of neuromuscular transmission at the AP and CSC muscles with electromyographic measurements of the DIA (DIAEMG).

**Methods**

After institutional ethical approval and with their informed consent, we studied 12 adult patients (eight men), ASA grade I or II, about to undergo elective long duration peripheral orthopaedic surgery of the lower limb under general anaesthesia. Exclusion consisted of a history of previous abnormal response to neuromuscular agents. All patients were free from renal or hepatic disease, and were not taking drugs known to interfere with neuromuscular function.

**Anaesthetic management**

No premedication was given. Anaesthesia was induced with propofol 2.5–3 mg kg\(^{-1}\) and fentanyl 2 µg kg\(^{-1}\). Orotracheal intubation was performed 2 min later without using NMBA. Anaesthesia was maintained with an inhaled mixture of \(\text{N}_2\text{O}/\text{O}_2/\text{isoflurane}\) (60%/40%/0.6–0.8%) and supplemented by bolus doses of fentanyl 1 µg kg\(^{-1}\) every 30 min. Ventilation was controlled to maintain the end-tidal carbon dioxide concentration between 4 and 4.5 kPa. During surgery patients laid supine and were covered with a warm air-heating blanket. Tympanic temperature was monitored.

**Measurements at the DIA**

The right phrenic nerve was stimulated (single twitches: 0.2 ms at 0.1 Hz) during end expiratory pauses using percutaneous insulated needle electrodes inserted at the inferolateral edge of the sternomastoid muscle. Satisfactory stimulation of the phrenic nerve caused visible hiccupping of the hemidiaphragm. The resulting evoked DIAEMG was measured using Ag–AgCl chloride surface electrodes placed on the right anterior axillary line of the thoracoabdominal wall at the seventh or eighth intercostal space. The signal was amplified and recorded with a gated EMG amplifier using a latency of 2 ms and a window of 20 ms (Viking 2, Nicolet Instruments, Trappes, France). Peak-to-peak amplitude of compound action potential activity of DIAEMG was calculated.

**Peripheral neuromuscular transmission monitoring**

Single twitches (0.2 ms at 0.1 Hz) were applied at the ulnar and facial left nerves through skin Ag–AgCl superficial electrodes. A force transducer (Myotest; Biometer, Odense, Denmark) was used to measure the mechanical response of AP muscle. Acceleromyography (Entrans®, Les Clayes-sous-Bois, France) was used to measure CSC muscle evoked response.

**Clinical protocol**

After supramaximal stimulation intensities had been defined (6 min stability in responses amplitude) for the three muscles, the patients received a bolus dose of vecuronium 0.1 mg kg\(^{-1}\). With 100% block of the mechanical response at the AP muscle, recordings and measurement devices at both the hand and eyebrow were removed and the stimulation pattern of both the ulnar and facial nerves was switched to 5 s (50 Hz) tetanus delivered every 5 min at the ulnar nerve and train-of-four (TOF) applied every minute at the facial nerve, respectively. Visual estimation of neuromuscular transmission performed by an independent observer blinded to DIAEMG consisted of simple count of visually detectable: TOF at the CSC muscle (TOFCSC) and post-tetanic at the AP muscle (PTCAP) responses which were categorized in 1–4 TOFCSC and 1, ≤5, ≤10 and >10 PTCAP responses.

**Data analysis**

Values are means (SD). Calculation of EMG was relative to control values. Times to recovery of PTCAP and TOFCSC responses and the related DIAEMG were compared using a non-parametric Mann–Whitney test.

**Results**

Mean age (range) of patients was 46 (29–69) years and weight 71 (9) kg. No adverse events or clinically important clinical changes occurred during the study. Mean supramaximal stimulation current intensities were of 31, 51 and 29 mA at the phrenic, ulnar and facial nerves, respectively. The time course of vecuronium on DIAEMG is presented in Table 1. Reappearance of PTCAP=1 occurred significantly \((P<0.05)\) earlier and for a lower recovery of DIAEMG than TOFCSC=1 [Tables 1 and 2: 24 (8) min vs 33 (9) min, and 10 (10)% vs 25 (8)%, respectively]. With PTCAP≤5, DIAEMG recovery was 21 (11)% (Table 3). Recovery of TOFCSC=1 and 2 coincided with DIAEMG recovery of 25 (8)% and 47 (9)%, respectively (Table 3).

**Discussion**

PTCAP and TOFCSC gave different information regarding neuromuscular transmission at the DIA. We showed that during recovery from vecuronium blockade, reappearance of the first PTCAP twitches coincided with early DIA recovery, while return of the first and second TOFCSC responses occurred with a significant DIA recovery.
Under the conditions of our study, both PTC\textsubscript{AP} and TOF\textsubscript{CSC} represent possible indirect monitoring strategies to evaluate DIA relaxation during recovery from vecuronium blockade. Monitoring the thumb has the advantage of being accurate at detecting early DIA recovery, but was performed intermittently every 5 min. Of interest, we measured a mean 10% increase of DIA\textsubscript{EMG} between two tetanus stimulations of the ulnar nerve. In contrast, although the first response to TOF\textsubscript{CSC} reappeared later during the recovery stage of the DIA, monitoring the eyebrow was interesting because TOF could be applied every minute at the facial nerve without interfering with neuromuscular transmission at the stimulation site.

Our study has methodological limitations. We used electromyography to evaluate the neuromuscular block of the DIA. We are aware that mechanical measurements of the force generated by the DIA would have been more pertinent for clinical extrapolation of our results. Moreover, we applied supramaximal single twitch to the phrenic nerve which is certainly a less intense stimulus than tetanus-like stimulation resulting from clinical stimulation. However, the method used in the present study is certainly the least invasive validated method to evaluate NMBA effects on the DIA.\textsuperscript{1–3} Additionally, we used a visual estimation to quantify neuromuscular transmission at the AP and CSC muscles. Tactile assessment of AP muscle responses would have been more reliable, but we preferred using the same method of neuromuscular transmission monitoring for the two studied muscles. Visual neuromuscular transmission monitoring at the thumb and the eyebrow was performed by trained physicians. Before beginning the study, we analysed and controlled the accuracy of our visual monitoring. We observed a high precision in visual TOF count at CSC muscle, and a modest overestimation of the number of counted twitches when PTC\textsubscript{AP} is >5. Of interest, by using four different categories of PTC\textsubscript{AP} the precision of twitch detection was restored. Therefore, we believe that our technique of visual neuromuscular transmission monitoring is reliable. Also, we applied two different methods for determining supramaximal current intensity at AP and CSC muscles, which might have affected our results, possibly explaining the relatively low

<table>
<thead>
<tr>
<th>PTC\textsubscript{AP} Number of twitches</th>
<th>Time to recovery (min)</th>
<th>TOF\textsubscript{CSC} Number of responses</th>
<th>Time to recovery (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>24 (8)*</td>
<td>1</td>
<td>33 (9)</td>
</tr>
<tr>
<td>≤5</td>
<td>29 (9)</td>
<td>2</td>
<td>38 (11)</td>
</tr>
<tr>
<td>≤10</td>
<td>34 (7)</td>
<td>3</td>
<td>44 (9)</td>
</tr>
<tr>
<td>&gt;10</td>
<td>39 (9)</td>
<td>4</td>
<td>52 (10)</td>
</tr>
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Our findings may be useful for daily clinical practice in anaesthesia when neuromuscular block of the DIA is mandatory. Although there is no indisputable study that has demonstrated the clinical relevance of DIA paralysis for optimal surgical conditions, we assume that muscular recovery of the DIA may alter the safety of certain types of central surgery. Indeed, spontaneous DIA movements during laparoscopic procedures of the thorax or the upper abdomen may have dramatic consequences for the patient and seriously compromise surgical success.

Our results confirm that the DIA began recovering while PTC\textsubscript{AP} still equals zero.\textsuperscript{7} However, PTC\textsubscript{AP} was a reliable method of assessment of early DIA recovery. Allowing recovery of PTC\textsubscript{AP} ≤5 led to low DIA recovery. If our results were confirmed, this threshold of five PTC\textsubscript{AP} responses could be used to titrate NMBA administration in order to reach and maintain an intense block at the DIA. Because abdominal muscles have been shown to be more sensitive to NMBA than the DIA,\textsuperscript{3,8} maintaining PTC\textsubscript{AP} ≤5 may prevent hiccups, bucking and coughing that have been shown to occur during surgical procedures despite total abolition of the AP muscle TOF response.\textsuperscript{9}

We also showed that the clinical duration of action of vecuronium on the DIA (time to recovery of 25% control activity) almost coincided with reappearance of the first TOF\textsubscript{CSC} response. This interesting finding suggests that if deep neuromuscular block is mandatory at the DIA, re-injection of NMBA should be performed without delay just after the first TOF\textsubscript{CSC} response has returned. Moreover, our data suggest that the CSC muscle may not be reliable in detecting early diaphragmatic recovery, although its own recovery profile is similar to that of muscles resistant to NMBA.
supramaximal current intensities we characterized for facial and ulnar nerve stimulation. However, we have previously demonstrated that acceleromyography and mechanomyography were interchangeable methods to evaluate evoked muscle response characteristics for AP and CSC muscles. Finally, by using isoflurane to maintain anaesthesia, we have certainly increased the duration and variability of the effects of vecuronium, but we aimed to perform this trial in conditions strictly mimicking clinical practice trial of anaesthesia.

**Conclusion**

In conclusion, we demonstrated that PTC\textsubscript{AP} and TOF\textsubscript{CSC} were two indirect methods allowing different estimation of DIA recovery. Our data suggest that PTC\textsubscript{AP} may better reflect early recovery of vecuronium-induced DIA paralysis than TOF\textsubscript{CSC}. PTC at the AP muscle allows detection of early diaphragm recovery from vecuronium neuromuscular block.

**Acknowledgement**

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