RECOVERIES OF POST-TETANIC TWITCH AND TRAIN-OF-FOUR RESPONSES AFTER ADMINISTRATION OF VECURONIUM WITH DIFFERENT INHALATION ANAESTHETICS AND NEUROLEPTANAESTHESIA

Y. SAI TOH, H. TO YOOKA AND K. AMAHA

SUMMARY

We have studied recovery of post-tetanic twitch (PTT) and train-of-four (TOF) responses after administration of vecuronium in 100 patients under different inhalation anaesthetics and neuroleptanaesthesia. Patients were allocated randomly to five groups of 20 patients each to receive: neuroleptanaesthesia (droperidol and fentanyl), halothane, isoflurane, enfurane or sevoflurane (1 MAC in nitrous oxide and oxygen). The times from initial administration of vecuronium 0.2 mg kg\(^{-1}\) to the first appearances of T1, T2, T3 and T4 differed significantly between groups. However, the intervals to the first appearance of PTT\(_{10}\), PTT\(_{10}\) and PTT\(_{20}\) did not differ significantly between groups. (Br. J. Anaesth. 1993; 70: 402-404)

KEY WORDS


Post-tetanic twitch (PTT) is a valuable method for evaluating intense neuromuscular block, because PTT response can be observed earlier than train-of-four (TOF) response during recovery of neuromuscular transmission after non-depolarizing neuromuscular blocking agents [1-3]. Recovery of TOF or single twitch responses under different types of anaesthesia has been studied by several authors [4-8], but recovery of PTT responses has not been reported. We have studied the intervals between initial administration of vecuronium to the first appearances of PTT\(_{10}\), PTT\(_{10}\), PTT\(_{20}\), T1, T2, T3 and T4 with different inhalation anaesthetics and neuroleptanaesthesia, and evaluated the use of PTT in assessing the degree of neuromuscular block.

PATIENTS AND METHODS

With institutional Review Board approval and written informed consent, we studied 100 adult patients (53 male), ASA class I or II, undergoing elective general surgical, orthopaedic, gynaecological, urological, ENT or ophthalmological procedures. None of the patients had neuromuscular, renal or hepatic disorders or received any medication that might alter neuromuscular transmission. They were allocated randomly to five groups of 20 patients each to receive: neuroleptanaesthesia (NLA group), halothane (group H), isoflurane (group I), enfurane (group E) or sevoflurane (group S). All the patients were premedicated with atropine 0.01 mg kg\(^{-1}\) and hydroxyzine 1 mg kg\(^{-1}\) i.m. 1 h before operation. Stimulating surface electrodes were placed on the ulnar nerve at the elbow and recording electrodes on the corresponding abductor digiti minimi muscle. After induction of anaesthesia with sodium thiopental 5 mg kg\(^{-1}\), the ulnar nerve was stimulated supramaximally (50 mA) with an electrical stimulator (SEN-3201, Nihon-Kohden Inc., Tokyo). Rectangular pulses of 0.1 ns duration were triggered automatically by a computer to produce two patterns of electrical stimulation (TOF and PTT) as described below. When the response to TOF stimulation was stable, the magnitude of the first twitch of the train was taken as the control twitch height. Vecuronium 0.2 mg kg\(^{-1}\) i.v. was then administered to facilitate tracheal intubation. Anaesthesia was maintained with 66% nitrous oxide in oxygen and fentanyl 5 \(\mu\text{g kg}^{-1}\) and droperidol 0.2 mg kg\(^{-1}\) in the NLA group. In the other groups, anaesthesia was maintained with 66% nitrous oxide in oxygen and 1 MAC end-tidal inhalation anaesthetic (0.76% halothane, 1.15% isoflurane, 1.68% enfurane or 1.71% sevoflurane). The end-tidal concentrations of carbon dioxide, nitrous oxide, and inhalation anaesthetics were measured by infra-red absorption using a Capnomac Ultima-S-31-03 (Datex Inc., Helsinki) calibrated with standard gases. Patient’s lungs were ventilated to normocapnia as measured by end-tidal carbon dioxide and intermittent arterial blood-gas analysis. Rectal temperature was maintained at 35.5-36.8 °C with warming blankets. During the first 5 min after a control measurement was obtained, TOF stimuli were applied every 5 s to monitor relaxation for tracheal intubation. Five minutes after a control measurement was obtained, the intervals between TOF stimuli were changed to

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30 s and PTT stimuli were substituted for TOF stimuli every 150 s. This pattern of stimulation was continued until the end of anesthesia; thereafter, 100% oxygen was given to the patients and atropine 1 mg and neostigmine 2 mg i.v. were given to antagonize any residual neuromuscular block.

For TOF stimulation, a series of four pulses was applied at 2 Hz for 2 s. For PTT, a tetanic stimulus (50 Hz) was applied for 5 s and, after an interval of 3 s, single twitch stimuli (1 Hz) were applied for 20 s. The EMG response of each stimulus was amplified via an isolated differential amplifier (AVB-11, Nihon-Kohden Inc., Tokyo) and displayed on an oscilloscope (VC-11, Nihon-Kohden Inc., Tokyo). Integrated data sets of either TOF or PTT responses were displayed on a monitoring oscilloscope and stored on hard disc. A personal desk-top computer (PC-9801 UX, NEC Inc., Tokyo) was used for overall control of automatic stimulation—data collection sequences, and for later data analysis. The intervals from initial administration of vecuronium to first appearance of PTT, TTT10, TTT20, T1, T2, T3 and T4 were calculated. The responses to electrical stimuli were considered to be detectable when the magnitudes were larger or equal to 1% of control.

Statistical analysis was performed using ANOVA and Duncan's multiple range test [9] to test for differences between the five groups, \( P < 0.01 \) being considered significant. All results are expressed as mean (SD).

**RESULTS**

There were no significant differences in patient characteristics between the five groups (table I).

The interval to the first appearances of PTT, TTT10 and PTT20 did not differ significantly between the five groups (table II).

The intervals to the first appearances of T1, T2, T3 and T4 in groups E and S differed significantly from those in the NLA group and group H. However, those in group I were not significantly different from those in the four other groups (table III).

**DISCUSSION**

Recovery of post-tetanic twitch is a valuable indicator for evaluating intense neuromuscular block produced by non-depolarizing neuromuscular blocking agents, because the appearance of PTT responses can be observed earlier than TOF responses during the recovery of neuromuscular transmission [1–3].

Baker and colleagues [10] and Riker [11] reported that PTT was a sensitive index of neuromuscular block produced by non-depolarizing neuromuscular blocking agents at the prejunctional region (motor nerve endings); however, twitch heights of TOF in comparison with control twitch height are affected by postjunctional effects [12, 13]. It is known also that inhalation anaesthetics act mainly in the post-

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**Table I. Characteristics of the patients studied (mean (range or SD)). No significant differences in number of patients, age, sex, height and body weight between groups (\( n = 20 \) each group). NLA = Neuroleptanaesthesia; \( H = \) halothane; \( I = \) isoflurane; \( E = \) enflurane; \( S = \) sevoflurane**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>NLA</th>
<th>H</th>
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<tbody>
<tr>
<td>Age (yr)</td>
<td>51.8 (23–78)</td>
<td>48.3 (20–81)</td>
<td>51.3 (22–72)</td>
<td>49.5 (20–77)</td>
<td>49.7 (23–77)</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>10/10</td>
<td>10/10</td>
<td>11/9</td>
<td>11/9</td>
<td>11/9</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>162.2 (12.4)</td>
<td>162.3 (13.0)</td>
<td>159.6 (12.1)</td>
<td>159.9 (13.4)</td>
<td>162.4 (13.1)</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>56.4 (6.2)</td>
<td>55.4 (7.0)</td>
<td>56.1 (7.9)</td>
<td>57.7 (7.4)</td>
<td>57.5 (7.7)</td>
</tr>
</tbody>
</table>

**Table II. Intervals from initial administration of vecuronium to the first appearances of PTT, PTT10 and PTT20 in the five groups (mean (SD)). No significant differences between groups. NLA = Neuroleptanaesthesia; \( H = \) halothane; \( I = \) isoflurane; \( E = \) enflurane; \( S = \) sevoflurane**

<table>
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<tbody>
<tr>
<td>Time of appearance (min)</td>
<td>PTT</td>
<td>PTT10</td>
<td>PTT20</td>
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<td></td>
<td>32.05 (6.53)</td>
<td>30.69 (7.35)</td>
<td>31.62 (5.39)</td>
<td>31.20 (4.27)</td>
<td>31.93 (5.72)</td>
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<tr>
<td></td>
<td>43.05 (8.81)</td>
<td>43.39 (9.10)</td>
<td>45.09 (11.00)</td>
<td>42.84 (8.85)</td>
<td>47.71 (12.42)</td>
</tr>
<tr>
<td></td>
<td>50.94 (9.15)</td>
<td>50.98 (9.77)</td>
<td>54.80 (10.72)</td>
<td>52.18 (10.15)</td>
<td>56.72 (13.36)</td>
</tr>
</tbody>
</table>

**Table III. Intervals from initial administration of vecuronium to the first appearances of T1, T2, T3 and T4 in the five groups (mean (SD)). ** Significantly different from NLA and H groups (\( P < 0.01 \)). NLA = Neuroleptanaesthesia; \( H = \) halothane; \( I = \) isoflurane; \( E = \) enflurane; \( S = \) sevoflurane**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>NLA</th>
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</thead>
<tbody>
<tr>
<td>Time of appearance (min)</td>
<td>T1</td>
<td>T2</td>
<td>T3</td>
<td>T4</td>
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<td></td>
<td>39.89 (8.53)</td>
<td>40.12 (8.90)</td>
<td>45.22 (7.64)</td>
<td>46.11 (5.86)**</td>
<td>47.18 (9.69)**</td>
</tr>
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<td></td>
<td>50.02 (10.77)</td>
<td>49.49 (7.22)</td>
<td>55.52 (9.03)</td>
<td>58.45 (10.06)**</td>
<td>59.42 (10.13)**</td>
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<td></td>
<td>55.26 (12.04)</td>
<td>55.83 (10.05)</td>
<td>62.15 (8.74)</td>
<td>66.18 (13.05)**</td>
<td>67.67 (10.93)**</td>
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<td></td>
<td>58.18 (12.07)</td>
<td>58.31 (10.12)</td>
<td>64.80 (9.20)</td>
<td>69.60 (13.64)**</td>
<td>70.91 (10.88)**</td>
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junctional region of the neuromuscular junction and prolong the duration of neuromuscular block produced by non-depolarizing neuromuscular blocking agents to varying degrees [4, 5, 12, 14, 15]. Kennedy and Galindo [14] reported that enflurane reinforced the muscle twitch depression produced by tubocurarine in the rat phrenic nerve-diaphragm preparation and that it was caused primarily by the postjunctional effect. Gissen, Karis and Nastuk [15] showed, in the frog sciatic nerve-sartorius muscle, that the structure most sensitive to the neuromuscular blocking action of halothane is the postjunctional membrane. Thus the inhalation anaesthetics prolong the duration of neuromuscular block produced by non-depolarizing neuromuscular blocking agents, by acting mainly at the postjunctional membrane. Therefore it is not surprising that the appearance of PTT, an index of prejunctional block, did not differ between our five groups, whereas the appearance of T1–T4, an index of postjunctional block, differed significantly between the groups. We found that, in ranking order, sevoflurane, enflurane, isoflurane and halothane prolonged the intervals to the first appearance of T1–T4. This is in agreement with previous studies [4–8].

There was little difference in the first appearances of T1–T4 between the NLA group and group H. Bonsu and colleagues [1] found that the interval from the first appearance of PTT, to that of T1 was 9 min with halothane anaesthesia, and 10 min with fentanyl anaesthesia after administration of atracurium 0.6 mg kg\(^{-1}\); the difference was not significant.

Itagaki and colleagues [4], Miller and colleagues [16] and Vitez and colleagues [17] reported that halothane increased blood flow in skeletal muscle to a smaller extent than that caused by other inhalation anaesthetics. This may explain partly why halothane apparently did not prolong the duration of neuromuscular block. As isoflurane takes 90 min [18] and enflurane takes 200–240 min [19] to reach the neuromuscular junction in effective concentrations, and because the end-tidal concentration of inhalation anaesthetics may not equilibrate with inspired concentrations until at least 20 min after commencement of administration [20, 21], we may have underestimated the prolongation of vecuronium-induced neuromuscular block by the inhalation anaesthetics.

It is possible that relatively short interval (2.5 min) between stimuli with PTT may have influenced recovery of neuromuscular transmission in the arm investigated [22]. We used this interval because of the relatively rapid recovery from neuromuscular block produced by vecuronium, but this problem may require further investigation. Moreover, the interval between stimuli with TOF during the induction of anaesthesia (3 s) may have been too short. This pattern of stimulation was used in order to determine the appropriate moment for smooth tracheal intubation. However, the interval was changed subsequently to 30 s and this duration would have little influence, if any, on subsequent evaluation of the neuromuscular block [23].

REFERENCES


