TETANIC FADE DURING RECOVERY FROM VECURONIUM BLOCK: COMPARISON OF SYSTEMIC AND ISOLATED FOREARM ADMINISTRATION

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SUMMARY

We have compared the degree of tetanic fade relative to twitch depression occurring after isolated forearm block with vecuronium and that after systemic i.v. injection. Fifteen patients received either vecuronium 0.3 mg into an isolated forearm or vecuronium 0.05 mg kg\(^{-1}\) systemically. Adductor pollicis mechanomyography was used to monitor recovery of twitch height at 0.2 Hz. At 25, 50, 75 and 100% recovery of twitch height, a 5-s, 50-Hz tetanus was administered and tetanic fade ratio measured. There was significantly less tetanic fade in the isolated forearm group (P < 0.01; unpaired t-test) at 25, 50 and 75% twitch height. This suggests that twitch depression and tetanic fade are independently mediated effects of vecuronium. (Br. J. Anaesth. 1993; 70: 581-582)

KEY WORDS

There is considerable evidence that twitch depression and fade produced by non-depolarizing neuromuscular blocking drugs are separate effects, mediated at different sites within the neuromuscular junction [1], although this model has been questioned recently [2, 3]. Bowman and Webb [4] noted that different techniques of drug administration in cats may produce different degrees of fade relative to twitch height, suggesting that the two effects are mediated independently. In this study, we investigated the degree of tetanic fade that is produced in the human adductor pollicis muscle using two different techniques of drug administration—systemic i.v. injection and isolated forearm block.

METHODS AND RESULTS

After obtaining approval by the Hospital Research Ethics Committee, we studied 15 consenting patients (ASA grade I or II), allocated randomly to one of two groups: group 1 = systemic vecuronium 0.05 mg kg\(^{-1}\); group 2 = isolated forearm vecuronium 0.3 mg. The dose of vecuronium used in each group was selected to produce 100% twitch block and have a comparable duration of action to allow assessment of fade during recovery.

Patients with medical conditions or receiving drugs known to affect neuromuscular function were excluded. All patients received i.m. pethidine 1 mg kg\(^{-1}\) with promethazine 25 mg 1 h before operation. Anaesthesia was induced with i.v. propofol 2-3 mg kg\(^{-1}\) and maintained with propofol infused at 6-10 mg kg\(^{-1}\) h\(^{-1}\) and 60% nitrous oxide in oxygen. After administration of systemic vecuronium to patients in group 1, the trachea was intubated and the lungs ventilated to maintain end-tidal carbon dioxide tension in the range 4.5-5.5 kPa. Patients in group 2 breathed spontaneously via a nasopharyngeal airway.

The ulnar nerve at the right wrist (group 1) or both wrists (group 2) was stimulated supramaximally (0.2 Hz, 0.2 ms duration) via adhesive electrodes. The mechanical evoked response of the adductor pollicis muscle was measured using a modified 20-kg load cell taped to the hand with a preload of 200-300 g, and recorded on a paper chart recorder. After 10 min, a control tetanus (50 Hz for 5 s) was administered. Ten minutes later, in group 1, vecuronium 0.05 mg kg\(^{-1}\) was administered i.v. into the contralateral arm; in group 2, a pneumatic tourniquet was inflated to greater than arterial pressure on the patient's right forearm and vecuronium 0.3 mg diluted in 20 ml of saline was injected into a vein on the dorsum of this hand. In both groups, 100% twitch depression was produced in all cases. In group 2 the arterial tourniquet was deflated after 3 min. Neuromuscular block in both groups was allowed to recover spontaneously. At 25, 50, 75 and 100% of control twitch height, a tetanic stimulus (50 Hz for 5 s) was administered to each monitored hand in both groups. During tetanic stimulation, the gain and speed of the chart recorder were adjusted to enable recordings of the response to be made.

The ratio between the tension at the end of the 5-s tetanus to the maximum tension developed initially (tetanic fade ratio (TFR)) was calculated for each tetanus. The time to 25% recovery of twitch height (T\(_{25\text{-}50}\)) and the 25-75% recovery index (RI) also were


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measured for each patient. The TFR at each level of twitch recovery ($T_{25}$ and RI) in the two groups were compared by unpaired Student's t test.

The groups were comparable in age and weight (table I). There was no significant difference between groups in $T_{25}$, indicating that the doses chosen were approximately equi-effective in terms of twitch depression. RI was significantly smaller in the isolated arm group ($P < 0.05$, unpaired Student's t test). There was no significant difference between the control TFR in each group. There was no measurable effect in the contralateral arm, distributed to the general circulation. This produces rapid onset of twitch depression by its persistence in the biophase after tourniquet release. This produces rapid onset of twitch depression, but may be inadequate time for binding to fade sites to occur.

After tourniquet release in the isolated forearm, the small dose of neuromuscular blocker is distributed to the general circulation. This produces no measurable effect in the contralateral arm, implying that the plasma concentration of drug is small during recovery. However, despite the small plasma concentration, depression of twitch height persists in the isolated forearm for a significant duration. In the present study, mean time for recovery to 75% twitch height was 25.2 min in the isolated forearm group, compared with 29.9 min in the systemic group. This slow recovery of twitch height in the isolated forearm is presumed to be caused by drug persisting in the biophase after tourniquet release, despite the small plasma concentration. In the absence of significant circulating drug, however, it appears that fade sites are not readily blocked by drug sustaining continued twitch depression by its persistence in the biophase. This again suggests that the sites for these two effects are distinct and may be subject to local factors affecting the ease of access and binding to each.

COMMENT

In this study the same drug, administered in two different ways, produced differing degrees of tetanic fade relative to twitch depression, suggesting that the two effects are mediated independently. This finding supports that of Bowman and Webb [4], who observed that fade of the tetanic response to stimulation at 50 Hz in the cat soleus muscle was much less marked after block was produced by a small dose of tubocurarine administered i.a. than after similar twitch depression produced by a larger i.v. dose. Bowman [1] interpreted their findings as evidence that twitch depression and fade are consequences of separate actions of a competitive neuromuscular blocker; he postulated that less fade might be produced after arterial injection because there was less time for binding to "fade sites" to occur, as the drug was washed rapidly through the muscle and diluted in the general circulation. He also proposed [1] that a slower rate of binding to the fade sites would explain the different time course of twitch depression and fade observed clinically [5]. This explanation has been questioned, however [2, 3], by workers who have challenged the dual receptor hypothesis and consider that the different time course of fade and twitch depression may be a pharmacokinetic artefact. A slow rate of binding to fade sites would, however, explain the relatively little fade seen in the isolated forearm. In this technique, drug is concentrated in the muscle for 3 min before tourniquet release. This produces rapid onset of twitch depression, but may be inadequate time for binding to fade sites to occur.

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REFERENCES