COMPARISON OF THE TRAIN-OF-FOUR FADE PROFILES PRODUCED BY VECURONIUM AND ATRACURIUM

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SUMMARY
In this double-blind study, we have allocated randomly 40 ASA I-III patients to one of four groups. After a standard anaesthetic induction, patients received vecuronium 0.08 mg kg\(^{-1}\) or 0.10 mg kg\(^{-1}\), or atracurium 0.4 mg kg\(^{-1}\) or 0.5 mg kg\(^{-1}\). Using an electromyogram (Datex Relaxograph) the train-of-four (TOF) response was measured during onset of and recovery from neuromuscular block. A greater degree of fade of TOF was observed with atracurium during onset of neuromuscular block than with equivalent doses of vecuronium. During recovery of neuromuscular transmission, vecuronium was associated with more fade than atracurium. The differences in the TOF profiles of these two drugs may be important when judging the adequacy of antagonism of neuromuscular block using the TOF response.

KEY WORDS

Different fade characteristics have been described with various non-depolarizing neuromuscular blocking drugs. At onset of neuromuscular block, gallamine is associated with more fade in the train-of-four (TOF) than pancuronium [1] or vecuronium [2]. Similarly, tubocurarine is associated with more fade than pancuronium [3]. For individual blocking drugs, fade differs between onset and offset of block. The neuromuscular block produced by either vecuronium or gallamine has been shown to have more fade during recovery of block than during onset [2].

In this double-blind study, we have sought to make a pharmacodynamic comparison of the neuromuscular effects of vecuronium and atracurium at the manufacturers’ recommended doses on the U.S. data sheets.

METHODS AND RESULTS
After approval from the Human Investigation Committee, 40 consenting patients (ASA I-III) aged 18–65 yr were allocated randomly to one of four groups: group 1 = vecuronium 0.08 mg kg\(^{-1}\); group 2 = vecuronium 0.1 mg kg\(^{-1}\); group 3 = atracurium 0.4 mg kg\(^{-1}\); group 4 = atracurium 0.5 mg kg\(^{-1}\).

Patients taking medication or with medical conditions known to interact with neuromuscular trans-
near the junctional membrane in preparation for result in decreasing amounts of Ach being released junctional block, rapidly repeated stimuli would and is likely to influence the neuromuscular response uptake of isoflurane occurs slowly but continuously (Ach) from storage sites to the readily available sites these receptors results in transfer of acetylcholine neuromuscular junction. Normally, stimulation of nicotine (T4) ratio at onset and offset of neuromuscular block (mean (SD)). Onset: T1 = 50% baseline. Offset: T1 = 25% baseline. * P < 0.05 compared with atracurium within dose group

<table>
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<tr>
<th></th>
<th>Smaller doses</th>
<th>Larger doses</th>
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<tbody>
<tr>
<td></td>
<td>Vecuronium</td>
<td>Atracurium</td>
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<td></td>
<td>0.08 mg kg⁻¹</td>
<td>0.4 mg kg⁻¹</td>
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<tr>
<td>Onset</td>
<td>73 (10) *</td>
<td>60 (12)</td>
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<tr>
<td>Offset</td>
<td>16 (22) *</td>
<td>60 (41)</td>
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vecuronium (table I). During recovery of T1 to 25%, the reappearance of T4 was delayed markedly in the patients receiving vecuronium compared with patients receiving atracurium (table I).

**COMMENT**

The doses of atracurium and vecuronium used in this study had a similar duration of action. However, the faster speed of onset with vecuronium may be clinically useful and may also allow a smaller dose of vecuronium to be given, resulting in a shorter duration of action compared with atracurium. This finding is similar to that of a previous study [4], but differs from another which demonstrated a faster onset time for atracurium [5]. Such differences in speed of onset may be accounted for by the doses of blocking drug used, the end-points measured (e.g. time from injection to maximum effect, time for T1 to decrease from 75% to 25% or 95% to 5% of baseline) the method of measurement (e.g. electromyogram or force transducer) and the muscle group studied. The apparent duration of action may be affected by factors such as the concentration of isoflurane used and the temperature of the muscles being stimulated. All our patients had their arms covered, but active warming was not used. Muscle uptake of isoflurane occurs slowly but continuously and is likely to influence the neuromuscular response increasingly over time. Methodological differences between studies make direct comparison difficult.

It has been suggested that fade in the train-of-four results from block of prejunctional receptors at the neuromuscular junction. Normally, stimulation of these receptors results in transfer of acetylcholine (Ach) from storage sites to the readily available sites near the junctional membrane in preparation for rapid release. Therefore, in the presence of prejunctional block, rapidly repeated stimuli would result in decreasing amounts of Ach being released [6].

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Comparative studies have shown fade to differ between neuromuscular blocking agents [1]. Our study showed atracurium to have the most fade at onset when compared with vecuronium, a finding reported also in another study [5].

Greater fade during offset compared with onset of action of vecuronium has been reported previously, and the importance of measuring fade at both these times stressed [2]. Following a bolus dose of neuromuscular blocker, there are rapidly changing concentrations of drug in the blood and at the sites of action. The time taken for the drug to penetrate through to, and bind to different receptors may result in differing pharmacodynamic effects during this early equilibration phase of block. Our finding may be explained by vecuronium having a greater affinity for the prejunctional receptor than atracurium, but being able to enter and leave the region of the prejunctional receptor only slowly, resulting in a slower onset and offset of prejunctional effects compared with atracurium. In contrast, atracurium would appear to attain its maximal, albeit relatively small, prejunctional effect rapidly. The fact that atracurium undergoes spontaneous degradation may further influence its action by bypassing the need for the drug to diffuse out of the region of the prejunctional receptors.

**ACKNOWLEDGEMENT**

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**REFERENCES**