ACCELERATED RECOVERY FROM COMBINED ATRACURIUM-VECURIUM NEUROMUSCULAR BLOCK

J. A. STIRT

It was observed fortuitously that relatively small doses of atracurium in combination with vecuronium seemed to produce complete neuromuscular block, with a distinctly more rapid recovery of muscle twitch, than when a single, larger intubating dose of each relaxant alone was used.

Combinations of non-depolarizing neuromuscular blockers have been used in numerous clinical studies in man [1-5]. Two previous reports have demonstrated more rapid recovery from the same degree of block in patients given potentiating combinations of blockers (pancuronium-dimethyltubocurarine [3] or pancuronium-tubocurarine [4]) than those given a single agent.

A prospective investigation of the combined use of atracurium and vecuronium was performed to study and quantify this phenomenon in more detail.

SUMMARY

Patients given combinations of non-depolarizing neuromuscular blocking drugs have been reported to recover from neuromuscular block more rapidly than patients given a single drug. This study was designed to assess if this phenomenon occurred with the combination of atracurium and vecuronium. During nitrous oxide-fentanyl anaesthesia, 30 adult patients were allocated randomly to receive atracurium 0.5 mg kg\(^{-1}\), vecuronium 0.1 mg kg\(^{-1}\), or a combination of atracurium 0.125 mg kg\(^{-1}\) + vecuronium 0.025 mg kg\(^{-1}\). All patients had 100% neuromuscular block, and times to block onset did not differ significantly between the three groups. Recovery to 10, 25, 50 and 90% of control twitch height was significantly faster in the group receiving the combination of drugs.

METHODS AND RESULTS

The study was approved by the institution's Human Investigation Committee, and written informed consent was obtained from all patients. We studied 30 adult patients, ASA physical status I or II. No premedication was given. After application of an arterial pressure cuff and electrocardiographic electrodes, anaesthesia was induced with thiopentone 4-6 mg kg\(^{-1}\) i.v. and maintained with fentanyl 3-5 µg kg\(^{-1}\) i.v. and 67% nitrous oxide in oxygen.

Neuromuscular block was monitored using a chart recorder and a force transducer (Grass FT-10) which measured adductor pollicus twitch tension in response to supramaximal ulnar nerve stimulation at 0.15 Hz delivered for a duration of 0.15 ms via 25-gauge needles placed subcutaneously.

Patients were allocated randomly to receive atracurium 0.5 mg kg\(^{-1}\) (4 x ED\(_{90}\)), vecuronium 0.1 mg kg\(^{-1}\) (4 x ED\(_{90}\)), or atracurium 0.125 mg kg\(^{-1}\) (ED\(_{90}\)) followed immediately by vecuronium 0.025 mg kg\(^{-1}\) (ED\(_{90}\)). We measured the times to initial twitch depression and to maximum twitch depression, the magnitude of neuromuscular block produced and the times to 10, 25, 50, 75 and 90% recovery of initial twitch height.

Statistical analysis was performed using one-way analysis of variance (ANOVA); groups which differed significantly by ANOVA were tested with two-tailed t tests (Bonferroni correction) to determine differences between groups. \(P < 0.05\) was considered significant.

Mean ages and weights did not differ significantly between the three groups. All patients had 100% neuromuscular block (table I). Times to
TABLE I. Neuromuscular block and recovery (mean (SEM)) following atracurium 0.5 mg kg\(^{-1}\), vecuronium 0.1 mg kg\(^{-1}\), or atracurium 0.125 mg kg\(^{-1}\) + vecuronium 0.025 mg kg\(^{-1}\). Significant differences (P < 0.05) compared with: * atracurium 0.5 mg kg\(^{-1}\) and vecuronium 0.1 mg kg\(^{-1}\) groups; † atracurium 0.5 mg kg\(^{-1}\) group.

<table>
<thead>
<tr>
<th>Group</th>
<th>Time to initial twitch height depression (min)</th>
<th>Time to maximum neuromuscular block (min)</th>
<th>Time to % recovery from neuromuscular block (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>10(^\circ) 25(^\circ) 50(^\circ) 75(^\circ) 90(^\circ)</td>
</tr>
<tr>
<td>Atracurium 0.5 mg kg(^{-1}) (n = 10)</td>
<td>1.0 (0.2)</td>
<td>3.0 (0.4)</td>
<td>42 (2) 48 (2) 54 (2) 60 (2) 66 (2)</td>
</tr>
<tr>
<td>Vecuronium 0.1 mg kg(^{-1}) (n = 10)</td>
<td>1.0 (0.2)</td>
<td>3.0 (0.3)</td>
<td>38 (2) 43 (2) 50 (3) 58 (4) 66 (4)</td>
</tr>
<tr>
<td>Atracurium 0.125 mg kg(^{-1}) + vecuronium 0.025 mg kg(^{-1}) (n = 10)</td>
<td>1.4 (0.1)</td>
<td>4.2 (0.4)</td>
<td>27 (1)* 32 (1)* 38 (2)* 43 (2)† 48 (2)*</td>
</tr>
</tbody>
</table>

initial and maximal twitch height depression did not differ significantly between the groups (table I).

Profiles of twitch height recovery are also shown in table I. Recovery to 10, 25, 50 and 90 % of control twitch height was significantly faster in the group receiving the atracurium–vecuronium combination than in the other two groups.

COMMENT

Two previous studies [3, 4] using single bolus doses of combinations of non-depolarizing neuromuscular blocking drugs in man demonstrated no significant differences in onset time or maximum block between groups receiving single or combined relaxant drugs. Time to 25 % recovery of twitch height was significantly shorter in groups receiving combinations than in those receiving a single agent [3, 4].

We have studied the combination of atracurium and vecuronium. Although not significantly different, the slightly longer times to initial and maximal twitch height depression in the group receiving the combination of drugs, together with the significantly shorter recovery times in this group, may indicate that the drug combination was less potent than the doses in the single agent groups. This is not surprising, as only 25 % of each of the single relaxant doses was used in the combination group.

The doses of drugs were selected to simulate clinical use. Atracurium 0.5 mg kg\(^{-1}\) and vecuronium 0.1 mg kg\(^{-1}\) are doses used commonly for tracheal intubation in man. Spontaneous recovery from these doses to 25 % of control twitch height has been reported to occur in approximately 40 min, and 90 % recovery in approximately 55 min [6]. The results of our study are consistent with these values.

Twitch tension recovered significantly faster after complete neuromuscular block in the group receiving combined atracurium and vecuronium (table I). Thus neuromuscular block in patients receiving a combined atracurium–vecuronium regimen (2 × ED\(_{90}\) equivalent) was potentially readily reversible (spontaneous recovery to 10 % of control twitch height) 10–15 min before that in patients receiving an intubating dose of either atracurium or vecuronium alone (4 × ED\(_{90}\)). Similarly, spontaneous recovery to 90 % of control twitch height occurred almost 20 min faster (approximately 33 % more rapidly) in the group receiving the drug combination than in either group receiving one agent.

The shorter recovery time produced by a combination of atracurium and vecuronium may be useful in situations where a brief period of intense relaxation is required; use of the doses administered to the combined atracurium–vecuronium group (2 × ED\(_{90}\) equivalent) may produce conditions suitable for intubation in several minutes. This regimen would not be suitable for rapid sequence intubation, although more rapid onset might be obtained by increasing the combined doses.

What other advantages might be offered by the use of a combination of atracurium and vecuronium in the doses used in this study? First, use of the combination of neuromuscular blockers would decrease the expense of producing conditions suitable for intubation, and avoid the use of suxamethonium. In addition, the more rapid recovery might, in some instances, allow for use of smaller than usual doses of relaxant antagonists,
and occasionally obviate the need for their use. Faster recovery may also reduce the frequency of unsuccessful antagonism of neuromuscular block. Finally, the incidence of cardiovascular systemic side effects produced by atracurium may be diminished by the use of the combined regimen described.

REFERENCES