Comparison of duration of neuromuscular blocking effect of atracurium and vecuronium in young and elderly patients

V. Slavov, M. Khalil, J. C. Merle, M. M. Agostini, R. Ruggier and P. Duvaldestin

Summary
In a controlled, randomized study, we evaluated duration of neuromuscular block in 80 patients undergoing routine abdominal surgery. Forty patients were aged 18-50 yr (control group) and 40 patients were more than 65 yr (elderly group). All patients had normal plasma creatinine concentrations. After induction of anaesthesia, patients were allocated randomly to receive either atracurium 0.5 mg kg\(^{-1}\) or vecuronium 0.1 mg kg\(^{-1}\) to facilitate tracheal intubation. Monitoring of the evoked response of the adductor pollicis muscle to supramaximal single twitch ulnar nerve stimulation every 10 s was performed and measured with a strain gauge. Repeat doses of atracurium 0.1 mg kg\(^{-1}\) or vecuronium 0.02 mg kg\(^{-1}\) were administered when the adductor pollicis response recovered to 25% of the control twitch height. We found that the duration of action of the initial dose of atracurium was similar in the control and elderly groups, and it did not vary after repeated doses. However, the initial dose of vecuronium caused a significantly longer period of clinical block in the elderly group compared with the controls, and the duration of action of repeated doses was longer in the elderly group. We conclude that as there is a risk of prolonged effect of vecuronium in the elderly, monitoring of neuromuscular function is recommended in this group. Alternatively, atracurium should be preferred for prolonged surgery in elderly patients.

Key words

Atracurium and vecuronium are non-depolarizing neuromuscular blocking agents of intermediate duration of action. The relatively short duration of action of these blockers is explained by their pharmacokinetic profile. The plasma clearance of atracurium and vecuronium is approximately 5 ml min\(^{-1}\) kg\(^{-1}\) instead of 2 ml min\(^{-1}\) kg\(^{-1}\) for most longer-acting agents [1, 2]. Because of these characteristics, these agents are claimed to be non-cumulative, at least in healthy patients [3]. In patients with severe renal failure, vecuronium has been shown to exhibit some cumulation [4]. This is not surprising as alterations in the pharmacokinetics of vecuronium in patients with renal insufficiency have been demonstrated [5]. In contrast, in patients with renal failure, atracurium has no cumulative effects [6]. Elderly patients represent a significant proportion of the patient population undergoing abdominal surgery. In these patients, we suggest that vecuronium may exert a prolonged and cumulative effect.

The aim of the present study was to investigate the clinical duration of action of atracurium and vecuronium when administered repeatedly to elderly patients and compare these data with findings in younger subjects.

Methods and results
The study was approved by the Hospital Ethics Committee. After obtaining informed written consent, we studied 40 patients aged 18-50 yr (control group) and 40 patients more than 65 yr (elderly group) undergoing abdominal surgery. All patients had preoperative plasma creatinine concentrations within the normal range (65-115 umol litre\(^{-1}\)). All patients were ASA I-II, with no known or suspected neuromuscular diseases and were not undergoing treatment with drugs known to interfere with neuromuscular transmission.

Patients were premedicated with oral flunitrazepam 1 mg, 2 h before induction of anaesthesia. Cephazolin 1 g was infused i.v. over 5 min as prophylactic antibiotherapy. Anaesthesia was induced with thiopentone 4-7 mg kg\(^{-1}\) and fentanyl 2 \(\mu\)g kg\(^{-1}\), and maintained with 50-70% nitrous oxide in oxygen, using controlled ventilation and repeated doses of fentanyl 1 \(\mu\)g kg\(^{-1}\) as necessary. To prevent hypothermia, a hot-air blanket (Bair Hugger) was placed over the upper body and arms throughout the procedure. Tympanic and skin surface (thenar eminence) temperatures were recorded throughout surgery.

The evoked response of the adductor pollicis
muscle to supramaximal single twitch ulnar nerve stimulation was measured every 10 s. The evoked strength of the adductor pollicis contraction was measured in all patients with a strain gauge (ELH11, Entran, Clayes-sous-Bois, France). Patients were allocated randomly to receive either atracurium or vecuronium for neuromuscular block. An initial i.v. dose of atracurium 0.5 mg kg\(^{-1}\) or vecuronium 0.1 mg kg\(^{-1}\) was administered when the adductor pollicis response recovered to 25% of control twitch height. Towards the end of surgery, residual neuromuscular block was antagonized with neostigmine 40 μg kg\(^{-1}\) and atropine 20 μg kg\(^{-1}\).

The duration of the initial dose (clinical block period) was defined as the time which elapsed between initial administration until recovery of twitch height to 25% of control twitch height. The duration of the repeated doses was the time from administration until recovery of twitch height to 25% of its control twitch height.

The results are given as the mean (SD). Intergroup and intra-group comparisons were performed by analysis of variance with the Bonferroni test and the paired Student’s \(t\) test, respectively. \(P < 0.05\) was considered significant.

There were no statistical differences in patient characteristics, duration of surgery or central body temperature towards the end of surgery between the groups. The initial intubating dose of atracurium and vecuronium caused complete abolition of twitch height.

Table 1 shows that the duration of action of the initial dose of atracurium 0.5 mg kg\(^{-1}\) was similar in the control and elderly group (47 (14) and 46 (12) min, respectively). However, the initial dose of vecuronium 0.1 mg kg\(^{-1}\) caused a significantly \((P < 0.01)\) longer period of clinical relaxation in the elderly group (50 (18) min) compared with the control group (36 (8) min).

There were up to nine repeat doses of neuromuscular blockers administered. The duration of action of repeated doses of atracurium did not increase with the number of doses in the control or elderly groups. However, the duration of action of repeated doses of vecuronium was longer in the elderly than in control group.

### Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Initial dose</th>
<th>Maintenance dose (No.)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Atracurium</td>
<td>46 (12)</td>
<td>24 (11)</td>
<td>25 (11)</td>
<td>24 (13)</td>
<td>22 (6)</td>
<td>22 (6)</td>
<td>20 (6)</td>
<td>21 (5)</td>
<td>28 (17, 18)</td>
<td>17 (19)</td>
</tr>
<tr>
<td></td>
<td>Vecuronium</td>
<td>36 (8)</td>
<td>22 (7)</td>
<td>22 (6)</td>
<td>22 (7)</td>
<td>23 (10)</td>
<td>22 (6)</td>
<td>20 (3)</td>
<td>21 (3)</td>
<td>24 (28)</td>
<td>—</td>
</tr>
<tr>
<td>Elderly</td>
<td>Atracurium</td>
<td>47 (14)</td>
<td>22 (8)</td>
<td>24 (6)</td>
<td>23 (7)</td>
<td>23 (5)</td>
<td>23 (3)</td>
<td>23 (3)</td>
<td>19, 26, 25</td>
<td>17</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>Vecuronium</td>
<td>50 (18)*</td>
<td>28 (14)*</td>
<td>36 (19)*</td>
<td>31 (10)*</td>
<td>33 (8)*</td>
<td>38 (10)*</td>
<td>44, 42, 27</td>
<td>45</td>
<td>44</td>
<td>53</td>
</tr>
</tbody>
</table>

"Comment"

The principal finding of this study was that vecuronium exerted a longer duration of action in elderly patients whereas atracurium produced the same duration of action in the elderly as in younger adults.

Vecuronium owes its relatively short duration of action to rapid distribution kinetics such that recovery occurs largely during the distribution phase. In contrast, atracurium is rapidly degraded by a pathway which is independent of hepatic and renal function, so that pharmacological recovery occurs largely during the elimination phase. Our data for atracurium demonstrated no alteration in recovery in elderly patients. Despite normal plasma creatinine concentrations in the elderly subjects of the present study, it is known that decreased glomerular filtration rate progresses with ageing, which may explain why the plasma clearance of vecuronium decreased whereas that of atracurium remained unchanged.

The prolonged effect of vecuronium observed here may be explained in part by a decreased rate of elimination of vecuronium in elderly subjects. For a small single dose, the duration of action is dependent on distribution processes whereas for a large single or cumulative dose, the duration of action of neuromuscular blocker is influenced mainly by elimination.

We conclude that there is a risk of prolonged duration of action of vecuronium in the elderly. Therefore, monitoring of neuromuscular function is recommended in elderly patients receiving vecuronium. However, even after prolonged, repeated administration, atracurium exerted the same effect in the elderly as in younger adults and should therefore be preferred for prolonged surgery.

### References

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