Effects of rocuronium and vecuronium on intracranial pressure, mean arterial pressure and heart rate in neurosurgical patients

W. M. SCHRAMM, K. STRASSER, A. BARTUNEK, H. GILLY AND C. K. SPISS

Summary

We have evaluated the effects of a single bolus dose of rocuronium 0.6 mg kg$^{-1}$ (group 1, $n = 10$) or vecuronium 0.1 mg kg$^{-1}$ (group 2, $n = 10$) on intracranial pressure (ICP), mean arterial pressure (MAP), cerebral perfusion pressure (CPP) and heart rate (HR) in 20 neurosurgical patients undergoing mechanical ventilation of the lungs during continuous sedation with sufentanil and midazolam. Before and after neuromuscular block using twice the ED$_{90}$ of the blockers, ICP, MAP, CPP and HR were recorded continuously for 15 min. Treatment caused no significant changes in ICP, CPP or MAP and there was no evidence of histamine release. Mean maximum block in the rocuronium group was slightly less than that in the vecuronium group (95.9 (3.1) % vs 100%; ns) The difference between the two groups in onset time (rocuronium 142 (62) s, vecuronium 192 (64) s; $P = 0.04$) was significant. Patients in the rocuronium group showed a slight (7 (4)%) but significant ($P = 0.003$) increase in heart rate. (Br. J. Anaesth. 1996; 77: 607–611)

Key words


For neurosurgery the use of drugs which do not increase or preferentially decrease intracranial pressure (ICP) is preferred. For emergency neurosurgery, rapid sequence intubation is often performed as fasting conditions in patients with subarachnoid haemorrhages, severe head injury or intracerebral bleeding are often unknown. Suxamethonium is often used to facilitate tracheal intubation because of its rapid onset, but it has the disadvantage of increasing intracranial pressure. Other non-depolarizing agents such as vecuronium and atracurium dibesylate have no direct effect on ICP; however, their onset of action is considered too long for rapid sequence intubation. Rocuronium is a non-depolarizing neuromuscular blocking agent with a faster onset than all currently available non-depolarizing agents, approaching that of suxamethonium.

There are no previous studies of the effects of rocuronium on cerebral dynamics. Because of the rapid onset of action of rocuronium, we have compared the effects of rocuronium with those of vecuronium on ICP, mean arterial pressure (MAP), cerebral perfusion pressure (CPP) ($= \text{MAP} - \text{ICP}$) and heart rate (HR) in neurosurgical patients.

Patients and methods

After approval from the local Ethics Committee, we studied 20 ASA I–III patients, aged 18–65 yr. Patients known or suspected of having neuromuscular disorders, metabolic diseases, impaired renal function or impaired hepatic function were excluded. As osteoclastical trepanation interferes with the normal relationship between MAP and ICP, such patients were also excluded from this study. Five patients did not meet the inclusion criteria and these were replaced in order to have a total of 10 evaluable patients in each group. The investigation was performed in the neurosurgical intensive care unit, on postoperative or conservatively treated patients (table 1), after a stabilization period of at least 6 h without neuromuscular block. The lungs of all patients were ventilated in a volume-controlled mode with an air–oxygen mixture ($F_{O_2} = 0.3–0.4$) and received, at least 6 h before the start of the study, continuous sedation with sufentanil 1–3 µg kg$^{-1}$ h$^{-1}$ and midazolam 0.05–0.15 mg kg$^{-1}$ h$^{-1}$ until at least the end of the study. An extradural probe (Gaeltec, Gaeltec Ltd, Scotland) or an intraventricular catheter (Cordis, Cordis Corporation, USA) was in situ for ICP measurements. Temperature (36–37 $^\circ$C) and ventilation (end-tidal carbon dioxide concentration 4–4.5 kPa) were kept constant throughout the study.

In the intensive care unit, an arterial cannula, neuromuscular block monitoring equipment (Myotest MK II, Biometer Odense, Denmark) and an end-tidal carbon dioxide sensor were attached.

WOLFGANG M. SCHRAMM*, MD, KARIN STRASSER, MD, A. BARTUNEK, MD, CHRISTIAN K. SPISS, MD, Department of Anaesthesia and General Intensive Care, University of Vienna, Austria, HERMANN GILLY, PhD, Boltzmann Institute for Experimental Anaesthesiology and Research in Intensive Care Medicine. Accepted for publication: July 4, 1996.

*Address for correspondence: Department of Anaesthesia and General Intensive Care, University of Vienna, Intensive Care Unit 13B3, 18–20 Waehringer Guertel, A-1090 Vienna, Austria.
Neuromuscular block was monitored by supramaximal single twitch stimulation of the ulnar nerve at the wrist (single twitches of 0.2 ms duration at 0.1 Hz). Evoked responses were quantified mechanomyographically and recorded with a constant preload of 200–400 g on the adductor pollicis muscle to determine maximal neuromuscular response and onset time (time from administration of the neuromuscular blocking agent to 95% effect). HR, invasive MAP, end-tidal carbon dioxide, ICP and single twitch responses were allowed to stabilize for at least 10 min. Thereafter baseline variables (time T0: ICP T0, MAP T0, HRT0, CPP T0) and arterial blood samples were obtained for measurement of baseline PaCO2. Patients in study group 1 received a single bolus dose of rocuronium 0.6 mg kg⁻¹ and patients in study group 2 a single bolus dose of vecuronium 0.1 mg kg⁻¹ i.v. As rocuronium is approximately six times less potent than vecuronium,⁶⁻¹¹ both doses represent twice the ED₉₀. HR, MAP, end-tidal carbon dioxide and ICP were recorded every minute for 15 min (time T1–T15) after administration of the neuromuscular blocking agent. Changes in ICP (ΔICP = ICP T1–ICP T0), HR (ΔHRT = HRT1–HRT0), MAP (ΔMAP = MAP T1–MAP T0) and CPP (ΔCPP = CPP T1–CPP T0) were calculated for 15 min by subtracting the respective baseline values in both groups. Possible histamine-related reactions such as skin rashes, bronchospasms or severe (±20%) haemodynamic changes were recorded also.

Non-parametric analysis of variance (Friedman) was performed for HR, MAP, ICP and CPP in both the rocuronium and vecuronium groups followed by the multiple comparison Wilcoxon–Wilcox if the Friedman test showed significance. Comparison of baseline variables (ICP T0, MAP T0, CPP T0, HRT0, PaCO₂) and neuromuscular variables in both groups was performed using the Mann–Whitney–Wilcoxon test. Results were considered statistically significant at P < 0.05.

### Results

Characteristics of the 20 patients in the two groups are shown in table 2. Baseline variables did not differ significantly between the two groups. The time course of ΔICP, ΔCPP, ΔMAP and ΔHRT during the 15-min study period is shown in figures 1 and 2. In the rocuronium group, the change in ICP from baseline varied from −3 to +4 mm Hg and in the vecuronium group from −4 to +2 mm Hg. There were no significant changes in ICP, MAP and CPP in each group even though MAP decreased slightly (4%) in the rocuronium group. Patients in the rocuronium group showed a slight (4%) but significant (P = 0.003) increase in HR which peaked 5 min after drug administration and decreased thereafter to baseline values. HR did not change in patients in the vecuronium group. No patient had histamine-related symptoms or adverse clinical events. Mean maximum block in the rocuronium group was slightly lower than that in the vecuronium group (95.9 (3.1) % vs 100%, ns). The difference between the two groups in onset time (rocuronium 142 (62) s, vecuronium 192 (64) s; P = 0.04) was significant (table 2).

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Diagnosis</th>
<th>Sex</th>
<th>ICP measurement</th>
<th>Age (yr)</th>
<th>Weight (kg)</th>
<th>Neuromuscular blocker</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>Intracerebral bleeding</td>
<td>M</td>
<td>Extradural</td>
<td>32</td>
<td>100</td>
<td>Vecuronium</td>
</tr>
<tr>
<td>6</td>
<td>Astrocytoma III</td>
<td>M</td>
<td>Intravenous</td>
<td>42</td>
<td>100</td>
<td>Vecuronium</td>
</tr>
<tr>
<td>7</td>
<td>Comm. post. aneur., SAH</td>
<td>M</td>
<td>Intravenous</td>
<td>32</td>
<td>95</td>
<td>Rocuronium</td>
</tr>
<tr>
<td>8</td>
<td>Comm. ant. aneur., SAH</td>
<td>M</td>
<td>Extradural</td>
<td>59</td>
<td>80</td>
<td>Vecuronium</td>
</tr>
<tr>
<td>9</td>
<td>Astrocytoma III</td>
<td>M</td>
<td>Extradural</td>
<td>42</td>
<td>79</td>
<td>Rocuronium</td>
</tr>
<tr>
<td>10</td>
<td>Aneur. middle cerebral art., SAH</td>
<td>F</td>
<td>Intravenous</td>
<td>56</td>
<td>80</td>
<td>Rocuronium</td>
</tr>
<tr>
<td>11</td>
<td>Aneur. middle cerebral art., SAH</td>
<td>F</td>
<td>Intravenous</td>
<td>27</td>
<td>55</td>
<td>Vecuronium</td>
</tr>
<tr>
<td>12</td>
<td>Meningioma temp. dext.</td>
<td>F</td>
<td>Extradural</td>
<td>34</td>
<td>75</td>
<td>Rocuronium</td>
</tr>
<tr>
<td>13</td>
<td>Aneur. middle cerebral art., SAH</td>
<td>F</td>
<td>Intravenous</td>
<td>37</td>
<td>80</td>
<td>Vecuronium</td>
</tr>
<tr>
<td>14</td>
<td>Meningioma oefact.</td>
<td>F</td>
<td>Extradural</td>
<td>58</td>
<td>92</td>
<td>Vecuronium</td>
</tr>
<tr>
<td>15</td>
<td>Angioma parieto-occ. dext.</td>
<td>M</td>
<td>Extradural</td>
<td>43</td>
<td>85</td>
<td>Vecuronium</td>
</tr>
<tr>
<td>16</td>
<td>Aneur. comm. ant., SAH</td>
<td>M</td>
<td>Intravenous</td>
<td>43</td>
<td>110</td>
<td>Rocuronium</td>
</tr>
<tr>
<td>17</td>
<td>Intracerebral haematomy</td>
<td>M</td>
<td>Extradural</td>
<td>25</td>
<td>65</td>
<td>Vecuronium</td>
</tr>
<tr>
<td>18</td>
<td>Intracerebral haematomy</td>
<td>F</td>
<td>Extradural</td>
<td>43</td>
<td>75</td>
<td>Vecuronium</td>
</tr>
<tr>
<td>19</td>
<td>Meningioma sphenoidale</td>
<td>F</td>
<td>Extradural</td>
<td>63</td>
<td>75</td>
<td>Rocuronium</td>
</tr>
<tr>
<td>20</td>
<td>Comm. ant. aneur., SAH</td>
<td>F</td>
<td>Extradural</td>
<td>51</td>
<td>75</td>
<td>Rocuronium</td>
</tr>
<tr>
<td>21</td>
<td>Comm. ant. aneur., SAH</td>
<td>M</td>
<td>Extradural</td>
<td>51</td>
<td>85</td>
<td>Rocuronium</td>
</tr>
<tr>
<td>22</td>
<td>Aneur. middle cerebral art., SAH</td>
<td>M</td>
<td>Intravenous</td>
<td>51</td>
<td>85</td>
<td>Vecuronium</td>
</tr>
<tr>
<td>23</td>
<td>Comm. ant. aneur., SAH</td>
<td>M</td>
<td>Intravenous</td>
<td>60</td>
<td>70</td>
<td>Rocuronium</td>
</tr>
<tr>
<td>24</td>
<td>Intracerebral haematomy</td>
<td>M</td>
<td>Extradural</td>
<td>41</td>
<td>75</td>
<td>Rocuronium</td>
</tr>
</tbody>
</table>

### Table 2

Patient-related data and baseline variables (mean (SD or range) or number). n = 10 for each group. ICP = Intracranial pressure, MAP = mean arterial pressure, HR = heart rate, CPP = cerebral perfusion pressure (CPP = MAP – ICP)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Sex</th>
<th>ICP measurement</th>
<th>Age (yr)</th>
<th>Weight (kg)</th>
<th>Rocuronium</th>
<th>Vecuronium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (cm)</td>
<td>173 (5.8)</td>
<td>47.3 (32–63)</td>
<td>41.7 (25–59)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>81.9 (12.1)</td>
<td>142 (62) s</td>
<td>192 (64) s</td>
<td>4.4 (0.3)</td>
<td>4.4 (0.2)</td>
<td></td>
</tr>
</tbody>
</table>

Table 1 Patient data. Twenty neurosurgical patients received 2 × ED₉₀ of either rocuronium or vecuronium. SAH = Subarachnoid haemorrhage.
Neuromuscular block and cerebral dynamics

Discussion

In this study ICP was measured after administration of rocuronium 0.6 mg kg\(^{-1}\) or vecuronium 0.1 mg kg\(^{-1}\) in adult neurosurgical patients undergoing mechanical ventilation and continuous sedation with sufentanil and midazolam. To avoid any impact of concomitant neuromuscular block during the study, only intermediate-acting neuromuscular blocking agents were used for tracheal intubation during the pre-study period. In this study we attempted to control and minimize confounding factors that could influence ICP. External stimuli such as noise, touch and tracheal suction which might alter ICP were either avoided or held constant during the study. Reliable monitoring of ICP with either an intraventricular or extradural probe was achieved as measurements were performed only after a stabilization interval of at least 6 h. Recording of ICP during surgery could have been confounded by surgical manipulation. ICP was measured extradurally in 12 and intraventricularly in eight patients. Although it has been shown that extradural pressure correlates closely with intraventricular pressure over a wide range in animals and in clinical practice,\(^{13}\) we decided to include approximately the same number of patients with ICP measured extradurally and intraventricularly. As our study was undertaken in both six patients with extradural ICP measurement and four patients with intraventricular ICP measurement, a possible impact of measurement technique was excluded. However, both are accepted methods of ICP measurement and this study aimed to detect changes from baseline rather than absolute values. The non-parametric statistical analysis of choice to detect only changes in ICP from the baseline in a time span (figs 1, 2) was therefore the Friedman test.

We used sufentanil and midazolam for sedation.

Figure 1 Changes from baseline of intracranial pressure (ICP), cerebral perfusion pressure (CPP), mean arterial pressure (MAP) and heart rate (HR) after administration of vecuronium 0.1 mg kg\(^{-1}\) (mean, SD).

Figure 2 Changes from baseline of intracranial pressure (ICP), cerebral perfusion pressure (CPP), mean arterial pressure (MAP) and heart rate (HR) after administration of rocuronium 0.6 mg kg\(^{-1}\) (mean, SD). *\(P < 0.05\).
There is controversy on the effects of sufentanil on ICP but recent studies have shown that sufentanil exerts minimal influence on ICP.14 In patients sedated adequately with sufentanil, concomitant haemodynamic changes15 are critical for adequate CPP, therefore, the infusion rate of sedating drugs remained unchanged before and during the study.

There was no significant change from baseline in MAP in the two groups during the 15-min study. The rocuronium group showed a transient increase in HR (fig. 1) which peaked 5 min after administration of the neuromuscular blocking agent. The fact that patients were stable before the beginning of the study might have contributed to the marked cardiovascular stability noted in this study. Increases in HR from baseline, probably because of a vagal blocking effect, did not exceed 7% and MAP did not decrease by more than 4% in the rocuronium group. These changes were not clinically important. Our results concur with a report on dose-related HR increases associated with rocuronium in humans.16,17 As the drug possesses no ganglionic blocking effect or histamine-releasing properties,18,19 a substantial decrease in MAP was unlikely. CPP is calculated from MAP and ICP, which were not influenced by either blocker and therefore CPP was not impaired.

A reduction in cerebral perfusion and venous blood return caused by coughing or poor synchronization with the ventilator results in increased cerebral oedema. In neurosurgical patients, neuromuscular block is important to avoid brisk bucking, straining and coughing during laryngoscopy and tracheal intubation. In neurological patients with severe head injuries or subarachnoid haemorrhages who are restless and demonstrate difficulty in artificial ventilation in spite of sedatives and analgesics, neuromuscular block may be the treatment of choice to prevent an increase in ICP.20,21

It is known that tubocurarine may increase ICP22 by ganglionic block which may also produce arterial hypotension. If an increase in ICP occurs concomitantly with a decrease in MAP, a substantial decrease in CPP occurs. In patients with disturbed autoregulation, increased MAP after administration of pancuronium could be a disadvantage. Atracurium has the potential to release histamine, but in humans as in animals,23 atracurium has been shown to have minimal effect on ICP. Vecuronium does not induce histamine release nor does it change MAP or HR. In patients with brain tumours, vecuronium had minimal effects on ICP.2,19 which was consistent with our results. From the point of view of direct cerebral effects, non-depolarizing neuromuscular agents, such as pancuronium,25 vecuronium,2,19 and atracurium, that do not increase ICP, are appropriate for use during neurosurgical procedures and for intubation. Good-to-excellent intubating conditions should exist to limit the increase in ICP which may be caused by intubation. The use of suxamethonium to facilitate tracheal intubation in neurosurgical patients has been associated with an increase in ICP for 4–6 min.26 The mechanism of this effect has been ascribed to transient EEG desynchronization secondary to muscle fasciculation and concomitant increase in cerebral blood flow and cerebral blood volume27–31 and to a transient increase in intra-abdominal pressure caused by muscle fasciculations leading to increased central venous pressure and intracerebral venous pressure.32 Thus the increase in ICP is thought to be specific for depolarizing neuromuscular blocking agents. The use of suxamethonium therefore has been declining in clinical neuroanaesthetic practice, with the exception of emergency situations, such as the patient with a full stomach in whom rapid sequence induction is recommended.

Rocuronium is the first non-depolarizing neuromuscular blocking agent with a rapid onset (approaching that of suxamethonium) and good-to-excellent intubating conditions.6,7 The results of our study suggest that rocuronium may be used for neurosurgical patients without the risks associated with suxamethonium.

Acknowledgement
We thank Organon Teknika, Belgium, for generous support and assistance in the study of emergency situations, such as the patient with a full stomach in whom rapid sequence induction is recommended. Rocuronium is the first non-depolarizing neuromuscular blocking agent with a rapid onset (approaching that of suxamethonium) and good-to-excellent intubating conditions.6,7 The results of our study suggest that rocuronium may be used for neurosurgical patients without the risks associated with suxamethonium.

References