Comparison of suxamethonium and different combinations of rocuronium and mivacurium for rapid tracheal intubation in children†

M. NAGUIB, A. H. SAMARKANDI, A. AMMAR AND A. TURKISTANI

Summary
The use of suxamethonium in children is associated with undesirable side effects. The synergistic effect of a rocuronium–mivacurium combination can be considered as an acceptable alternative to suxamethonium in clinical practice. The calculated ED50 of the rocuronium–mivacurium mixture was only 62% of the predicted value assuming a purely additive interaction. The use of this combination has not been evaluated in children. In this two-part study, we assessed the intubating conditions and pharmacodynamics of suxamethonium, rocuronium, mivacurium or a rocuronium–mivacurium combinations in children. We studied 120 ASA I children of both sexes, aged 3–10 yr. Children were premedicated with trimethazine 2 mg kg⁻¹ orally, and received fentanyl 2 μg kg⁻¹ and propofol 2 mg kg⁻¹ for induction of anaesthesia. They were allocated randomly to receive one of the following drugs or drug combinations: suxamethonium 1.0 mg kg⁻¹, mivacurium 0.2 mg kg⁻¹, rocuronium 0.6 or 0.9 mg kg⁻¹, mivacurium 0.1 mg kg⁻¹ with rocuronium 0.3 mg kg⁻¹, or mivacurium 0.15 mg kg⁻¹ with rocuronium 0.45 mg kg⁻¹. In part 1, 60 s after administration of the neuromuscular blocking drug or drug combination, tracheal intubation was performed in 60 children by mimicking rapid sequence induction, and intubating conditions were evaluated by a blinded investigator according to a standard score. In part 2, neuromuscular monitoring was established before administration of neuromuscular blocking agent(s) and the time from injection of drug or drug combination until complete ablation of T1 (onset) and recovery of T1 to 25% (duration) were recorded in another 60 children. The frequency of distribution of excellent or good intubating conditions in the higher dose of rocuronium and the combination groups were similar to those in the suxamethonium group, but significantly different (P<0.05) from those in the mivacurium group. Mean onset time was faster in the suxamethonium (55.1 (so 11.4) s), rocuronium 0.9 mg kg⁻¹ (70.5 (37.7) s), mivacurium 0.1 mg kg⁻¹ with rocuronium 0.3 mg kg⁻¹ (67 (35.9) s) and mivacurium 0.15 mg kg⁻¹ with rocuronium 0.45 mg kg⁻¹ (55 (26.7) s) groups compared with the mivacurium 0.2 mg kg⁻¹ (116 (26.8) s) and rocuronium 0.6 mg kg⁻¹ (97.9 (29) s) groups. This study demonstrated that the combination of rocuronium 0.45 mg kg⁻¹ and mivacurium 0.15 mg kg⁻¹ could possibly be considered as an acceptable alternative to suxamethonium when rapid sequence induction of anaesthesia is indicated in children because it provides uniform excellent intubating conditions and complete neuromuscular block in <60 s. (Br. J. Anaesth. 1997; 79: 450–455).

Key words

Because it has a brief onset of action and rapid recovery, suxamethonium is still the standard neuromuscular blocking drug for rapid sequence tracheal intubation. However, its use in children is associated with undesirable side effects1–4 that resulted in the recent mandated changes in the suxamethonium package insert by the Food and Drug Administration.5 6 This concern raises an important question on alternate approaches that are available to the clinician to enhance the onset of the available non-depolarizing neuromuscular blocking drugs.7 8

The onset of action of non-depolarizing neuromuscular blocking drugs can be accelerated by the use of high doses of an individual agent,9 10 combinations of blockers11 or by preceding the intubating dose with a priming dose of blocker.12 13 These techniques, however, have not consistently achieved the rapid onset of action of suxamethonium and did not result in uniform intubating conditions matching those after suxamethonium.

Rocuronium and mivacurium are non-depolarizing neuromuscular blocking agents that have recently been introduced into clinical practice. Rocuronium has a brief onset and an intermediate

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duration of action. Mivacurium has a considerably shorter duration of action than any other currently used non-depolarizing agent. The speed of onset of rocuronium at the recommended intubating dose (0.6 mg kg\(^{-1}\)) is slower than that of suxamethonium.\(^{10,13}\) Naguib\(^{14}\) demonstrated that mixtures of rocuronium and mivacurium are synergistic in humans. The calculated ED\(_{90}\) of a rocuronium and mivacurium mixture (38.8 μg kg\(^{-1}\) for rocuronium and 11.4 μg kg\(^{-1}\) for mivacurium) was only 62% of the predicted value (125 μg kg\(^{-1}\) for rocuronium and 37 μg kg\(^{-1}\) for mivacurium) assuming a purely additive interaction.\(^{14}\)

Because of the dangers of hyperkalaemic cardiac arrest after suxamethonium in children with unrecognized muscular dystrophy,\(^{1-4}\) there have now been moves to limit the use of suxamethonium in children.\(^{7-8}\) Hopkins\(^{8}\) has indicated that there would be good reason not to use suxamethonium if another drug had the same advantages with fewer side effects. Therefore, the use of a rocuronium–mivacurium combination may be a reasonable alternative to suxamethonium for rapid sequence induction in children.

This two-part study was designed to assess the intubating conditions of single bolus doses of suxamethonium, rocuronium, mivacurium or different combinations of rocuronium and mivacurium in a simulated rapid sequence induction in children, and to measure onset time and duration of action of the drugs or drug combinations. This study differs from previous investigations because it included the suxamethonium group as a control, and because it compared multiple doses of rocuronium and different combinations of rocuronium and mivacurium under clinically relevant conditions.

### Patients and methods

After obtaining institutional approval and informed consent from the children’s parents, we studied 120 ASA I children of both sexes, aged 3–10 yr (mean 5.3 yr) and weighing 12–40 (mean 20.2 (sd 7) kg. All patients were undergoing elective procedures, had no neuromuscular, renal or hepatic diseases, and were not receiving any drug known to interfere with neuromuscular function.

All patients received trimeprazine, 2 mg kg\(^{-1}\) orally, and a local anaesthetic cream (EMLA, Astra Pharmaceuticals) was applied to the previewed puncture site 90 min before induction of anaesthesia. ECG, haemoglobin oxygen saturation by pulse oximetry (\(S_{\text{Po}}\)) and arterial pressure were monitored. Temperature was monitored by a nasopharyngeal thermistor and maintained at 36.5±0.5°C.

#### PART 1: RAPID SEQUENCE INDUCTION STUDY

In the first part of the study we compared the quality of neuromuscular block induced by different drugs in the context of rapid sequence induction. Sixty children were allocated randomly to one of six groups (\(n=10\) in each) to receive suxamethonium 1.0 mg kg\(^{-1}\) (2 × ED\(_{90}\))\(^{15}\) (control group), mivacurium 0.2 mg kg\(^{-1}\) (2 × ED\(_{90}\)), rocuronium 0.6 mg kg\(^{-1}\) (2 × ED\(_{90}\)), rocuronium 0.9 mg kg\(^{-1}\) (3 × ED\(_{95}\)), mivacurium 0.1 mg kg\(^{-1}\) (1 × ED\(_{95}\)) with rocuronium 0.3 mg kg\(^{-1}\) (1 × ED\(_{95}\)), or mivacurium 0.15 mg kg\(^{-1}\) (1.5 × ED\(_{95}\)) with rocuronium 0.45 mg kg\(^{-1}\) (1.5 × ED\(_{95}\)). After preoxygenation with 100% oxygen for 3 min, anaesthesia was induced with fentanyl 2 μg kg\(^{-1}\) and propofol 2 mg kg\(^{-1}\) followed by the neuromuscular blocking drug or drug combination. Neuromuscular blocking drugs or drug combinations were injected over 5 s. When a combination of drugs was used, each was administered simultaneously by the same i.v. route. To maintain blinding, patients who received a single neuromuscular blocking drug had a simultaneous injection of a placebo (0.9% sodium chloride). Sixty seconds after the end of injection, the trachea was intubated in all patients by the same experienced anaesthetist who was unaware of the patient’s grouping. He assessed intubating conditions using the following criteria\(^{16}\): excellent = jaw relaxed, vocal cords abducted and immobile, and no diaphragmatic movement; good = jaw relaxed, vocal cords abducted and immobile, and some diaphragmatic movement; poor = jaw relaxed, vocal cords moving, and coughing or bucking; and inadequate = jaw not relaxed and vocal cords closed. Cricoid pressure was applied during insertion of the tube. The ulnar nerve was stimulated supramaximally at the wrist with square pulses of 0.2 ms duration, delivered in a train-of-four (TOF) sequence at 2 Hz every 12 s, using a Myotest peripheral nerve stimulator (Biometer International, Odense, Denmark). The resultant contraction of the adductor pollicis muscle was evaluated by tactile assessment of thumb adduction by another investigator. The number of contractions (TOF count) felt at the time of intubation was recorded.

#### PART 2: PHARMACODYNAMIC STUDY

In the second part of the study we investigated the time course of neuromuscular block induced by the drugs or drug combinations. Premedication and intraoperative monitoring were similar to that described in part 1. Anaesthesia was induced in all patients with fentanyl 2 μg kg\(^{-1}\) and propofol 2 mg kg\(^{-1}\), and the lungs were ventilated via a face mask with 70% nitrous oxide in oxygen. After induction of anaesthesia, patients received a caudal injection of plain 0.25% bupivacaine 1 ml kg\(^{-1}\). If more than 20 ml was used, the concentration of bupivacaine was reduced to 0.1875%. End-tidal concentration of carbon dioxide was maintained at 4.8–5.3 kPa. Incremental doses of propofol were administered as necessary to maintain unconsciousness. Concentrations of nitrous oxide, oxygen and carbon dioxide were measured continuously by a multiple-gas analyser (Capnomac, Datex Instrumentarium Corporation, Helsinki, Finland).

After loss of consciousness, an acceleration transducer (Biometer International, Odense, Denmark) was fastened to the volar side of the interphalangeal joint of the thumb. The ulnar nerve was stimulated supramaximally at the wrist with square...
pulses of 0.2 ms duration, delivered in a train-of-four (TOF) sequence at 2 Hz every 12 s, using a Myotest peripheral nerve stimulator (Biometer International, Odense, Denmark). The resultant contraction of the adductor pollicis muscle was recorded using a neuromuscular function analyser (Myograph 2000, Biometer International, Odense, Denmark). The first twitch (T1) of the TOF was considered the twitch height. The test hand was immobilized in a supine position using an arm board. Free movement during evoked thumb adduction was allowed by fixation of the extended four ulnar fingers by adhesive tape.

After a stable neuromuscular response was obtained, 60 children were allocated randomly to one of six groups (n=10 in each) to receive suxamethonium (control group), mivacurium, rocuronium, or a mivacurium–rocuronium combination in doses similar to those described in part 1. All drugs were administered as a single bolus dose over 5 s. When a combination of drugs was used, each was administered simultaneously by the same i.v. route. Tracheal intubation was performed at maximum block. Intubating conditions were not assessed in this part of the study. The times from injection of neuromuscular blocking drug or drug combination to complete ablation of T1 (onset time), from injection to recovery of T1 to 25% of baseline (clinical duration of action) and from recovery of T25–T75% (recovery index) were recorded.

In patients who received suxamethonium or mivacurium, a blood sample was obtained from an antecubital vein in the arm contralateral to that used for i.v. fluid administration for measurement of plasma cholinesterase (PCHE) activity, dibucaine and fluoride numbers. Plasma cholinesterase activity was measured by the change in absorbance at 600 nm after reduction of butyrylthiocholine to thiocholine, using

\[ \text{Activity} = \frac{\text{Absorbance change at 600 nm}}{\text{Concentration of butyrylthiocholine}} \]

Results

There were no significant differences in distribution of age, weight or sex ratio between the groups (tables 1, 2). Similarly, dibucaine and fluoride numbers and baseline activity of PCHE were similar in all groups.

**PART 1: RAPID SEQUENCE INDUCTION STUDY**

The frequency of distribution of excellent or good intubating conditions in the higher dose of rocuronium and the combination groups were similar to those in the suxamethonium group, but significantly different (P<0.05) from those observed in the mivacurium group (table 1).

The number of TOF count felt at the time of intubation was significantly greater in the mivacurium, rocuronium 0.6 mg kg\(^{-1}\) and mivacurium 0.1 mg kg\(^{-1}\)-rocuronium 0.3 mg kg\(^{-1}\) groups compared with the suxamethonium group (P<0.01; Dunnett’s test), rocuronium 0.9 mg kg\(^{-1}\) group or the mivacurium 0.15 mg kg\(^{-1}\)-rocuronium 0.45 mg kg\(^{-1}\) combination group (P<0.05; Student–Newman–Keuls multiple range test) (table 1).

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (yr)</th>
<th>Weight (kg)</th>
<th>Sex (M/F)</th>
<th>Excellent</th>
<th>Good</th>
<th>Poor</th>
<th>Inadequate</th>
<th>TOF count (u.ml(^{-1}))</th>
<th>PCHE activity (u.ml(^{-1}))</th>
<th>Dibucaine number</th>
<th>Fluoride number</th>
</tr>
</thead>
<tbody>
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<td>5.1</td>
<td>20.1 (7.1)</td>
<td>7/3</td>
<td>9</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>[0.4 (0.7)]</td>
<td>9.4 (1.5)</td>
<td>88.9 (2.2)</td>
<td>47.4 (1.9)</td>
</tr>
<tr>
<td>1.0 mg kg(^{-1})</td>
<td>[3–8]</td>
<td>[13.5–34]</td>
<td></td>
<td>[0–2]</td>
<td>[7.8–13]</td>
<td>[86–94]</td>
<td>[44–50]</td>
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<tr>
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<td>24 (10.1)</td>
<td>8/2</td>
<td>5</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>[0.4]</td>
<td>8.9 (1.2)</td>
<td>88.9 (1.6)</td>
<td>49.1 (3.5)</td>
</tr>
<tr>
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<td>[13–40]</td>
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<td>[4]</td>
<td>[6.7–10.9]</td>
<td>[86–91]</td>
<td>[45–55]</td>
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<td></td>
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<tr>
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<td>16.7 (2.8)</td>
<td>7/3</td>
<td>7</td>
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<td>[3.5 (0.8)]</td>
<td>—</td>
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</tr>
<tr>
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<td></td>
<td>[2–4]</td>
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<td>—</td>
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<td>—</td>
<td></td>
</tr>
<tr>
<td>Mivacurium</td>
<td>5.5</td>
<td>22.8 (6.5)</td>
<td>7/3</td>
<td>10*</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>[0–3]</td>
<td>8.8 (1.1)</td>
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<tr>
<td>0.9 mg kg(^{-1})</td>
<td>[3–5]</td>
<td>[14–35]</td>
<td></td>
<td>[0–4]</td>
<td>[7.4–12.4]</td>
<td>[86–90]</td>
<td>[47–55]</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Mivacurium + rocuronium</td>
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<td>18.4 (4.9)</td>
<td>8/2</td>
<td>9</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>[2.4 (1.8)]</td>
<td>9.3 (1.8)</td>
<td>88.2 (1.5)</td>
<td>47.9 (2.7)</td>
</tr>
<tr>
<td>0.3 mg kg(^{-1})</td>
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<td>[13–30]</td>
<td></td>
<td>[0–4]</td>
<td>[7.4–12.9]</td>
<td>[86–90]</td>
<td>[47–55]</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Mivacurium + rocuronium</td>
<td>5.6</td>
<td>19.4 (7.3)</td>
<td>6/4</td>
<td>10*</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>[1.2 (1.7)]</td>
<td>9.9 (1.5)</td>
<td>88.3 (1.2)</td>
<td>46.7 (1.7)</td>
</tr>
<tr>
<td>0.15 mg kg(^{-1})</td>
<td>[3–10]</td>
<td>[12–34]</td>
<td></td>
<td>[0–4]</td>
<td>[7.4–12.9]</td>
<td>[86–90]</td>
<td>[44–49]</td>
<td></td>
<td></td>
<td></td>
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</table>

*P<0.05 vs suxamethonium group (Dunnett’s mean comparison between the control group and other groups); †P<0.01 vs suxamethonium group (Dunnett’s mean comparison between the control group and other groups); ‡P<0.05 vs other groups (Student–Newman–Keuls multiple range test) (table 1).
Table 2 Pharmacodynamic study. Patient, onset and recovery data (mean (SD) [range] (n=10 in each group). Onset time = time interval between completion of injection of the neuromuscular blocking drug or drug combination and time to maximal depression of T1; Duration = time interval between completion of injection of the neuromuscular blocking drug or drug combination and time to T1 recovery to 25% of control; recovery index = time from T25% to T75% of recovery. *P<0.05, **P<0.01 vs suxamethonium group (Dunnett’s mean comparison between the control group and other groups); †P<0.05 vs other groups (Student–Newman–Keuls multiple range test for groups that received rocuronium, mivacurium or their combinations)

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (yrs)</th>
<th>Weight (kg)</th>
<th>Sex (M/F)</th>
<th>Sex (M/F)</th>
<th>Dibucaine number (Reference range 3.5–13 u.ml⁻¹)</th>
<th>Fluoride number (Reference range 27–42 u.ml⁻¹)</th>
<th>Onset time (s)</th>
<th>Duration (min)</th>
<th>Recovery index (min)</th>
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<td>8/2</td>
<td></td>
<td>88.8 (1.7)</td>
<td>48.3 (2.1)</td>
<td>55.1 (11.4)</td>
<td>4.2 (1.4)</td>
<td>1.3 (0.4)</td>
</tr>
<tr>
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<td>[13.5–28.5]</td>
<td></td>
<td></td>
<td>[87–92]</td>
<td>[45–52]</td>
<td>[35–75]</td>
<td>[2.2–6.3]</td>
<td>[0.7–1.7]</td>
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<tr>
<td>Mivacurium</td>
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<td>19 (6.8)</td>
<td>7/3</td>
<td></td>
<td>88.1 (1.5)</td>
<td>46.7 (1.3)</td>
<td>116 (26.8)</td>
<td>10.4 (1.5)*</td>
<td>4.2 (0.7)*†</td>
</tr>
<tr>
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<td>[12–33]</td>
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<td>[85–90]</td>
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<td>[85–160]</td>
<td>[8.1–12.4]</td>
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<td>Rocuronium</td>
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<td>21.1 (7.7)</td>
<td>9/1</td>
<td></td>
<td>—</td>
<td>—</td>
<td>97.9 (29)**†</td>
<td>23.7 (5.1)**†</td>
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<td>70.5 (37.7)</td>
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<td>10.1 (3.1)****</td>
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<td>[24.8–45.1]</td>
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<td>8/2</td>
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<td>67 (35.9)</td>
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<td>[10–22]</td>
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<tr>
<td>0.3 mg kg⁻¹</td>
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<td>19 (4.8)</td>
<td>8/2</td>
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<td>47.2 (1.4)</td>
<td>55 (26.7)</td>
<td>25.3 (4.6)*****</td>
<td>9.9 (2.4)**</td>
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<td></td>
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<td>[85–91]</td>
<td>[45–49]</td>
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<td>[18.3–35.1]</td>
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<td></td>
<td>[7.8–11.5]</td>
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</tr>
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</table>

PART 2: PHARMACODYNAMIC STUDY

Onset time was faster in the suxamethonium 1.0 mg kg⁻¹, rocuronium 0.9 mg kg⁻¹ and combination groups compared with the mivacurium 0.2 mg kg⁻¹ and rocuronium 0.6 mg kg⁻¹ groups (table 2). Clinical duration and recovery index were shortest in the suxamethonium group compared with all other groups (P<0.05 or less). In patients who received non-depolarizing neuromuscular blocking drugs or drug combinations, clinical duration was longest in the rocuronium 0.9 mg kg⁻¹ group (P<0.05) and shortest in the mivacurium 0.2 mg kg⁻¹ group and mivacurium 0.1 mg kg⁻¹–rocuronium 0.3 mg kg⁻¹ combination group (P<0.05). Recovery index was shortest (P<0.05) in the mivacurium group compared with the other groups who received rocuronium or drug combinations.

Discussion

We have assessed for the first time the potential of different doses of rocuronium and different combinations of rocuronium and mivacurium for rapid sequence induction in children compared with suxamethonium. This study demonstrated that children who received the combination of mivacurium 0.15 mg kg⁻¹ and rocuronium 0.45 mg kg⁻¹ were similar to those who received suxamethonium in having uniform excellent tracheal intubating conditions and an onset of complete paralysis of <60 s. However, clinical duration of neuromuscular block was six times as long in the former group (P<0.01) compared with the suxamethonium group (25.3 (4.6) min vs 4.2 (1.4) min, respectively). In addition, a much larger SD for onset times was noted in the mivacurium–rocuronium combination groups compared with that after suxamethonium.

In part 1 of this study, we followed the strict clinical procedure of rapid sequence induction. Drugs that influence intubating conditions, such as volatile anaesthetics, opioids or hypnotics, were not given to our patients after administration of the neuromuscular blocking drug or drug combination. In our patients, anaesthesia was induced with propofol. Although it has been suggested that propofol produces greater depression of pharyngeal and laryngeal reactivity than thiopentone, this finding has not been substantiated by others. In our study, the tracheas of all children were intubated successfully within 60 s after administration of the neuromuscular blocking drug or drug combination, and intubating conditions did not differ in patients who received either suxamethonium, rocuronium 0.9 mg kg⁻¹ or the higher dose of the combination groups (table 1). Rocuronium 0.6 mg kg⁻¹ did not produce as good intubating conditions as suxamethonium 1.0 mg kg⁻¹ after 60 s. We noted also that mivacurium 0.2 mg kg⁻¹ was not suitable for rapid tracheal intubation in children (table 1). Similar observations were reported by others even when doses up to mivacurium 0.3 mg kg⁻¹ were administered in children. Our results are in accordance with those reported by Fuchs-Buder and Tassonyi in children in whom tracheal intubation was carried out by mimicking rapid sequence induction. They noted excellent intubating conditions in 83% and 94% of patients, 60 s after rocuronium 0.6 mg kg⁻¹ and 0.9 mg kg⁻¹, respectively. Woelfel and colleagues found that intubating conditions 60 s after rocuronium in 12 children during steady state halothane anaesthesia were excellent in nine and good in three patients.

We found that complete neuromuscular block at the adductor pollicis muscle was not a prerequisite for optimal intubating conditions. In our study tracheal intubation was performed 60 s after administration of the neuromuscular blocking drug or drug combination, regardless of the degree of neuromuscular block. In adults, faster onset at the
laryngeal compared with the peripheral muscles has been reported with suxamethonium, rocuronium and mivacurium. However, the onset of action of rocuronium at the laryngeal adductor muscles is slower than that after suxamethonium, and the degree of block is less intense. In this study, onset time in the rocuronium 0.9 mg kg\(^{-1}\) group was similar to that in the suxamethonium group (table 2). As the dose of rocuronium increased from 0.6 to 0.9 mg kg\(^{-1}\), onset time for neuromuscular block decreased by 28% (from 97.9 to 70.5 s; \(P<0.05\)) and duration of action increased by 55% (from 23.7 to 36.4 min; \(P<0.05\)) (table 2). This was associated with a concomitant increase in the recovery index (table 2). Using electromyography (Relaxograph) during isoflurane anaesthesia, Fuchs-Buder and Tassonyi demonstrated that increasing the dose of rocuronium from 0.6 to 0.9 mg kg\(^{-1}\) in children significantly decreased onset time (193 (47) vs 118 (23) s) and prolonged clinical duration (21 (4) vs 34 (11) min). In the latter study, however, the investigators re-calibrated the Relaxograph after administration of rocuronium when steady state concentrations of the volatile anaesthetic were achieved.

The results of our study confirm our previously published data in adults that combinations of rocuronium and mivacurium produced a shorter onset time comparable with that of suxamethonium.14 In this study, time to maximal neuro-muscular block decreased from 97.9 to 67 s (\(P<0.05\)) and both clinical duration and recovery index decreased from 23.7 and 9.2 min to 15.2 (\(P<0.05\)) and 7.3 min, respectively, when rocuronium 0.3 mg kg\(^{-1}\) together with mivacurium 0.1 mg kg\(^{-1}\) were given instead of rocuronium 0.6 mg kg\(^{-1}\) alone. The clinical profile of this combination was similar to that reported with equipotent doses in adults (rocuronium 0.3 mg kg\(^{-1}\) and mivacurium 0.075 mg kg\(^{-1}\)) with respect to onset time (69 s) and recovery index (7.5 min). However, the clinical duration was different—15.2 min in children (this study) vs 34 min in adults.14 There may be pharmacokinetic reasons for the differences between adults and children. The pharmacokinetics of rocuronium in children aged 4–11 yr revealed an age-dependent increase in plasma clearance27 that contributed to the shorter duration of action compared with infants or adults.28 The increased cardiac output in children may also contribute to the shortened duration of action by removing the drug from the neuromuscular junction more rapidly than in adults.29 These pharmacokinetic differences could explain the longer clinical duration of the rocuronium–mivacurium combination observed in adults compared with children.

We also noted that increasing the dose of the components in the combination—as in the rocuronium 0.45 mg kg\(^{-1}\)-mivacurium 0.15 mg kg\(^{-1}\) combination—resulted in a 44% and 22% shorter onset time than that produced by rocuronium 0.6 and 0.9 mg kg\(^{-1}\), respectively (55 vs 97.9 and 70.5 s, respectively). The clinical duration observed with the latter combination (25.3 min) was similar to that seen with rocuronium 0.6 mg kg\(^{-1}\) (23.7 min), but was 30% shorter (\(P<0.05\)) than that noted with rocuronium 0.9 mg kg\(^{-1}\) (36.4 min) (table 2).

References


