Rocuronium pretreatment reduces suxamethonium-induced myalgia: comparison with vecuronium

G. P. FINDLAY and M. J. SPITTAL

Summary
We have studied, in 150 patients undergoing elective oral surgery, the effectiveness and sequelae of pretreatment with rocuronium for reducing myalgia after suxamethonium. Patients were allocated randomly to one of three groups: anaesthesia was induced with propofol and fentanyl, and group V received vecuronium 1 mg, group R rocuronium 6 mg and group P placebo pretreatment. Suxamethonium 1.5 mg kg\(^{-1}\) was given 60 s after the pretreatment agent. All patients received ketorolac 10 mg i.v. and morphine 10 mg i.m. for analgesia. The incidence of postoperative myalgia on day 1 after rocuronium (20 %) was significantly less than after vecuronium (42 %) (\(P < 0.05\)) or placebo (70 %) (\(P < 0.01\)). By day 4 the incidence of myalgia was 28.6 % in the rocuronium group, 46.3 % in the vecuronium group and 95 % in the placebo group. Intubating conditions were not affected adversely by any pretreatment regimen. (Br. J. Anaesth. 1996; 76: 526–529)

Key words

Despite the recent introduction of short-acting, non-depolarizing neuromuscular blockers, suxamethonium, with its rapid onset of action, short duration of effect, complete and predictable paralysis, remains unsurpassed in providing ideal intubating conditions for tracheal intubation. However, since its introduction into clinical practice it has been recognized that myalgia occurs frequently in the postoperative period [1, 2]. Several strategies have been advocated to decrease the incidence of myalgia, one of the most successful being the administration of a small dose of non-depolarizing neuromuscular blocking drug before administration of suxamethonium [3, 4]. Various factors influence the efficacy of pretreatment, including the choice of non-depolarizing agent [5, 7], degree of prejunctional receptor block, interval between administration of pretreatment agent and suxamethonium, and speed of onset of the non-depolarizing drug. Rocuronium, which has a more rapid onset of action compared with established non-depolarizing agents [8], providing good intubating conditions within 60 s, has not yet been evaluated for the purpose of reducing suxamethonium-induced myalgia. As the optimum time interval for pretreatment with pre-existing drugs is approximately 3 min, this property of rocuronium may be relevant to its use in the prophylaxis of myalgia after suxamethonium.

The aim of this prospective, randomized, double-blind study was to assess the effect of rocuronium pretreatment on the frequency of suxamethonium-induced myalgia and to compare it with probably the most effective current pretreatment agent [4, 5, 7].

Patients and methods
After approval by the Hospital Ethics Committee and completion of written, informed consent, we studied 150 patients, aged 16–65 yr, ASA I or II. All patients were undergoing elective oral surgery under general anaesthesia necessitating tracheal intubation. We excluded patients who were assessed as possibly posing difficulty with tracheal intubation, using a combination of Mallampati’s test and thyromental distance, and those considered unsuitable to receive the standard study anaesthetic technique.

All patients were premedicated with temazepam 0.3 mg kg\(^{-1}\), to the nearest 10 mg, 1 h before operation. Anaesthesia was induced with fentanyl 1 \(\mu\)g kg\(^{-1}\) and a sleep dose of propofol. Patients then received vecuronium 1 mg (group V), rocuronium 6 mg (group R) or normal saline (group P), each made up to 2 ml. Fifty patients were allocated randomly to each pretreatment group and 60 s after pretreatment, patients received suxamethonium 1.5 mg kg\(^{-1}\). Direct laryngoscopy was performed and the patient’s trachea was intubated via the nasal route using an appropriately sized Magill tracheal tube, 60 s after suxamethonium. Anaesthesia was maintained with 1–2 % isoflurane in oxygen-enriched air. Manual ventilation was adjusted to maintain normocapnia (Ohmeda 5200 carbon dioxide monitor) until commencement of spontaneous respiration. After induction of anaesthesia all patients received ketorolac 10 mg i.v. and morphine 10 mg i.m. for analgesia, and droperidol 500 \(\mu\)g i.v. as an antiemetic. The presence of fasciculations and their severity after suxamethonium were assessed on a four-point scale as: nil = no visible fasciculations, 1 = no visible fasciculations, 2 = slight fasciculations, 3 = moderate fasciculations, 4 = severe fasciculations.

\(P\) values were calculated by the use of a \(\chi^2\) test or Fisher’s exact test. Data are expressed as mean ± SD, or \(\%\) and \(95\%\) confidence interval (CI).

After this study, in 422 patients undergoing general anaesthesia necessitating laryngeal intubation, we observed an incidence of suxamethonium-induced myalgia of 52.6 %.

Acknowledgements
We wish to thank our patients for their co-operation, and Mr H. M. Hidayat of the Medical Statistics Unit for his help and advice. We would also like to thank Mrs M. J. Harman for her secretarial assistance in the preparation of this paper.

G. P. FINDLAY*, MB, CHB, FRCA, M. J. SPITTAL†, MB, BS, FRCA, Department of Anaesthesia, Princess Alexandra’s Hospital, Royal Air Force Wroughton, Swindon, Wiltshire SN40QJ. Accepted for publication: December 5, 1995. Present addresses: *Intensive Therapy Unit, University Hospital Wales, Heath Park, Cardiff CF4 4XW. †Department of Anaesthesia, Princess Mary’s Hospital, Royal Air Force Akrotiri, BFPO 57, Cyprus.
mild = very fine fingertip or facial muscle movements, moderate = minimal fasciculations on trunk and extremities, severe = vigorous fasciculations on trunk and extremities [9]. Overall intubating conditions were assessed as: excellent = intubation easy, no reaction from the patient, good = intubation resulting in slight coughing or bucking, poor = intubation possible, but resulting in more marked patient response [10]. The time taken to resumption of spontaneous respiration and duration of anaesthesia were noted.

Patients were visited on the first postoperative morning before discharge from hospital and interviewed by an investigator, blind to the pretreatment agent used, according to a structured questionnaire, as described by Erkola [5]. The presence and severity of myalgia were noted. Myalgia was graded on a four-point scale using the system described by White [11] (table 1). At the end of the interview, patients were given a second questionnaire, which was to be completed on day 4 after operation, and was designed to evaluate the incidence and severity of myalgia after discharge.

Patient characteristics and operative details were analysed using the independent samples t test. The incidence of myalgia and fasciculations was analysed using Fisher’s exact test. Intubating conditions, severity of myalgia and severity of fasciculations were analysed initially using the Kruskal–Wallis test. If the Kruskal–Wallis test showed that significant differences existed between the groups then Dunn’s multiple comparisons were performed to demonstrate which groups differed. P < 0.05 was considered significant.

Results

There were no significant differences in patient characteristics or operative details between the three groups (table 2).

The incidence of fasciculations in group R was significantly less than that in groups V and P (P < 0.01) (table 3). Analysis of the severity of fasciculations revealed highly significant differences (Kruskal–Wallis statistic $H = 81.91$, $P < 0.001$) between the three groups. This test was logically followed by Dunn’s multiple comparisons which showed significant differences in the severity of fasciculations between groups V and R ($P < 0.01$) and between groups R and P ($P < 0.01$), but no significant difference between groups V and P.

There were no significant differences in intubating conditions between the three groups (table 4). Analysis of the incidence of myalgia on the first postoperative day (table 5) revealed significant differences between groups V and R ($P < 0.05$), groups V and P ($P < 0.01$) and groups R and P ($P < 0.0001$). There were highly significant differences in the severity of myalgia on the first postoperative day between the three groups (Kruskal–Wallis statistic $H = 18.11$, $P < 0.001$) and therefore Dunn’s multiple comparisons were performed which showed that only the difference between groups R and P was statistically significant ($P < 0.01$).

There were no significant differences in the response rate to the questionnaire on day 4 after operation with 41, 42 and 40 patients from groups V, R and P, respectively, returning completed questionnaires. Analysis of the incidence of myalgia by day 4, using pooled information from questionnaires on days 1 and 4 (table 5), revealed significant differences between groups V and P ($P < 0.0001$) and groups R and P ($P < 0.0001$). The difference between groups V and R was not significant. The Kruskal–Wallis test indicated highly significant differences in the severity of myalgia by day 4 between the three groups (Kruskal–Wallis statistic $H = 25.8$, $P < 0.001$) and therefore Dunn’s multiple comparisons were performed which revealed that only the differences between groups V and P ($P < 0.025$) and groups R and P ($P < 0.001$) were statistically significant.

---

**Table 1** Grading system for postoperative myalgia (after White [11])

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nil</td>
<td>No muscle pains or stiffness</td>
</tr>
<tr>
<td>Mild</td>
<td>Muscle pains or stiffness at one site but not causing disability or limiting activities</td>
</tr>
<tr>
<td>Moderate</td>
<td>Muscle pains or stiffness at more than one site but not causing disability or limiting activities</td>
</tr>
<tr>
<td>Severe</td>
<td>Muscle pains or stiffness at one or more sites and causing disability or limiting activities, e.g. difficulty getting out of bed or turning head</td>
</tr>
</tbody>
</table>

---

**Table 2** Patient data and operative details (mean (range of SD) or number). No significant differences (independent samples t test)

<table>
<thead>
<tr>
<th>Group</th>
<th>(n = 50)</th>
<th>Group R</th>
<th>(n = 50)</th>
<th>Group P</th>
<th>(n = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>24.9 (17–46)</td>
<td>25.1 (19–40)</td>
<td>24.6 (17–48)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>76.7 (11.6)</td>
<td>75.6 (12.2)</td>
<td>78.8 (13.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex (M : F)</td>
<td>39 : 11</td>
<td>38 : 12</td>
<td>40 : 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propofol induction dose (mg)</td>
<td>194 (26)</td>
<td>198 (28)</td>
<td>203 (30)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>26 (9)</td>
<td>28 (7)</td>
<td>25 (8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of apnoea (min)</td>
<td>7.1 (1.9)</td>
<td>7.1 (2.9)</td>
<td>7.3 (2.1)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

**Table 3** Incidence and severity of fasciculations. **P < 0.01 vs groups V and P (Fisher’s exact test)

<table>
<thead>
<tr>
<th>Group</th>
<th>(n = 50)</th>
<th>Group R</th>
<th>(n = 50)</th>
<th>Group P</th>
<th>(n = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>8</td>
<td>46</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>11</td>
<td>4</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>13</td>
<td>0</td>
<td>21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>18</td>
<td>0</td>
<td>19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total incidence (%)</td>
<td>84</td>
<td>8**</td>
<td>100</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

**Table 4** Intubating conditions. No significant differences (Kruskal–Wallis test)

<table>
<thead>
<tr>
<th>Group</th>
<th>(n = 50)</th>
<th>Group R</th>
<th>(n = 50)</th>
<th>Group P</th>
<th>(n = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good</td>
<td>47</td>
<td>47</td>
<td>49</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adequate</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Discussion

Suxamethonium is the best drug for rapidly providing ideal intubating conditions for short procedures. However, the usefulness of suxamethonium is limited by the frequent occurrence of postoperative myalgia. This is often listed as a minor side effect of the drug but it may be one of the most distressing consequences of minor surgery for the patient. The incidence of myalgia varies from 20% to 85% [12, 13]. This is undoubtedly a reflection of the many factors which influence the occurrence of pain.

Of the many regimens which have been proposed as a means of reducing the incidence of myalgia [9, 14–19], the most effective and widely used method is pretreatment with a small dose of non-depolarizing neuromuscular blocker [20]. A review of the literature revealed that vecuronium was probably the best agent in this respect [4, 5, 7] and for this reason we chose to compare rocuronium with vecuronium. Previous studies have used vecuronium 1 mg [7]. We therefore accepted that dose and, based on potency ratios, calculated a rocuronium dose of 6 mg. Administration of pretreatment agents both on a weight-related basis [21] and on a fixed-dose regimen [6, 7] has been recommended, but we chose a fixed-dose regimen for ease of routine administration.

One of the main concerns regarding pretreatment with non-depolarizing agents is that intubating conditions may be affected adversely. It is therefore recommended that a larger dose of suxamethonium be given to those who are pretreated [22]. In this study we used suxamethonium 1.5 mg kg\(^{-1}\) and found that pretreatment had no effect on intubating conditions. It has been suggested that increasing the dose of suxamethonium is not associated with accentuation of its adverse effects [23] but recent work has refuted this [24]. We therefore acknowledge that the use of such a dose of suxamethonium in the placebo group may be responsible for the high incidence of myalgia.

Rocuronium pretreatment is particularly effective in reducing fasciculations after suxamethonium. In 92% of patients, fasciculations were absent and in this respect rocuronium was superior to vecuronium [24]. We therefore acknowledged that the use of its adverse effects [23] but recent work has refuted this [24]. We therefore acknowledge that the use of such a dose of suxamethonium in the placebo group may be responsible for the high incidence of myalgia.

Rocuronium pretreatment is particularly effective in reducing fasciculations after suxamethonium. In 92% of patients, fasciculations were absent and in this respect rocuronium was superior to vecuronium [24]. We therefore acknowledged that the use of its adverse effects [23] but recent work has refuted this [24]. We therefore acknowledge that the use of such a dose of suxamethonium in the placebo group may be responsible for the high incidence of myalgia.

There has been much discussion about the interval between administration of the pretreatment agent and suxamethonium. Intervals of 2, 3 and 4 min, or longer, have been recommended [11, 23, 25]. Obviously such lengthy intervals, required by slow onset drugs, are impractical on busy operating lists. Our hypothesis that rocuronium, because of its rapid onset of action, would be effective at reducing myalgia when only a short interval was allowed appears to have been substantiated.

Rocuronium pretreated decreased the incidence of myalgia to 20% on the first postoperative day and to 28.6% by day 4. Compared with vecuronium this was significant on day 1 but not by day 4 (\(P < 0.05, P = 0.15\), respectively). This may be a reflection of the small sample size as a reduction in myalgia from 46.3% with vecuronium pretreatment to 28.6% with rocuronium pretreatment may be considered clinically significant. A larger sample size may clarify this issue.

Using reduced doses of suxamethonium alone can decrease the incidence of myalgia. Using suxamethonium 0.5 mg kg\(^{-1}\), Stewart, Hopkins and Dean [24] reported that 41% of patients complained of myalgia while Nimmo and colleagues [26], using suxamethonium 0.25 mg kg\(^{-1}\), reported an incidence of 20%. Intubating conditions in both studies were good. It may be seen that the use of rocuronium pretreatment and suxamethonium 0.25 mg kg\(^{-1}\) alone produce very similar incidences of myalgia while providing satisfactory intubating conditions. We plan a future prospective study to evaluate which strategy is superior. It is interesting to note that the study by Nimmo and colleagues [26] included a group in which no neuromuscular blocking drugs were used and who experienced an incidence of myalgia of 28%. It may be that, no matter which strategy is used to reduce suxamethonium myalgia, significant reductions below this value are unlikely. Against this background the results obtained in our rocuronium group appear to be excellent.

Acknowledgement

We thank Mr P. Strike, Principal Statistician, Institute of Pathology and Tropical Medicine, Royal Air Force Halton, for statistical advice.

References

Prevention of suxamethonium myalgia


