The effect of desflurane on rocuronium onset, clinical duration and maintenance requirements

R. G. STOUT (*), T. J. GAN (**), P. S. A. GLASS (**), D. G. SILVERMAN (*) and S. J. BRULL (****)

Abstract: Volatile anesthetics potentiate the effects of non-depolarizing agents. This study investigated the interaction between the inhalational anesthetic desflurane and rocuronium. Forty ASA I and II patients randomly received desflurane/N₂O/fentanyl, or propofol/N₂O/fentanyl anesthesia, and rocuronium 0.6 mg/kg. Neuromuscular block was assessed at the adductor pollicis muscle. Block onset and clinical duration times were measured; a rocuronium infusion was started when the first twitch on train-of-four returned to 10% of control (T₁₀%). Maintenance infusion requirements and recovery profiles (spontaneous and after reversal) were recorded until recovery of twitch to 90% of control (T₉₀%). Rocuronium onset was prolonged by 67% (p = 0.034), clinical duration by 30% (p = NS), and infusion requirements were lower in the desflurane group (4.5 vs. 7.1 mg/kg/min, p = 0.003). Recovery times were not statistically different. Desflurane significantly delays the onset of neuromuscular block, potentiates rocuronium during maintenance infusion, but does not affect clinical duration or recovery.

Key words: Inhalational anesthetics, desflurane; muscle relaxants, rocuronium; neuromuscular block, monitoring.

INTRODUCTION

All volatile anesthetic agents are known to alter the pharmacodynamics of nondepolarizing neuromuscular blocking drugs. This study was undertaken to compare the effects of desflurane to those of propofol on rocuronium pharmacodynamics. Anesthesiologists seeking a relatively rapid onset of neuromuscular block, facile maintenance of neuromuscular relaxation, and fast emergence from general anesthesia and reversal of neuromuscular block use the desflurane/rocuronium drug combination frequently. It is important, therefore, to determine the extent to which desflurane affects rocuronium’s onset, duration, maintenance and recovery profiles.
given intermittent iv boluses of fentanyl at the discretion of the anesthesiologist to maintain hemodynamic stability. End-tidal CO₂ was maintained between 30 and 40 mmHg and core body temperature was kept above 35°C by active warming. Neuromuscular function was monitored with a Datex 221 NMT device (Datex, Shrewsbury, MA) that measured the evoked electromyographic (EMG) response to serial train-of-four (TOF) stimulation of the adductor pollicis muscle. Superficial stimulation of the ulnar nerve was achieved via skin electrodes placed on the volar surface of the wrist. Neuromuscular monitoring was then allowed to stabilize for approximately 3 minutes, while serial single-twitch monitoring at 1 Hz was delivered. Following baseline stabilization, neuromuscular stimulation was continued with four supramaximal square-wave, 2-Hz pulses (TOF) at 20-second intervals while anesthesia was maintained with either propofol infusion or desflurane, and rocuronium (0.6 mg/kg) was then administered by rapid iv bolus into a port close to the iv insertion site. Mask ventilation was continued until the first twitch of the TOF (T₁) declined to 10% of the pre-relaxant baseline (Tc). At this point (defined as onset), the patient’s trachea was intubated, and ease of intubation was assessed by a blinded investigator. Intubation scores were recorded as excellent (easy, vocal cords open, no patient movement), good (easy, cords open, coughing or bucking), fair (not easy and/or cord closed and/or excessive patient movement), or poor (unable to intubate). Neuromuscular monitoring and maintenance anesthesia were continued in the same fashion throughout the anesthetic. The neuromuscular block was allowed to recover until T₁ reached 10% of Tₙ (defined as time until recovery), at which point an iv infusion of rocuronium, 10-12 µg/kg/min was begun. The rocuronium infusion rate was titrated to keep T₁ at 10% (± 5%) of Tₙ. Infusion rates were recorded every 5 minutes, and whenever the rate was changed. Approximately 30 minutes prior to the end of surgery the infusion was discontinued and spontaneous neuromuscular recovery was recorded as long as possible. When clinically indicated (e.g., once surgery was complete and Tₕ/Tₙ ratio was still less than 0.75), the patient received pharmacologic-induced reversal with iv neostigmine (2-3 mg) and glycopyrrolate (0.5 mg) and EMG neuromuscular recovery was recorded for the next 10 minutes. Desflurane and propofol were discontinued after T₁ recovered to 90% of baseline.

Data comparisons between rocuronium with and without desflurane included onset, clinical duration times, and recovery times, as well as infusion dosing requirements. Data are expressed as mean ± SD (range). Groups were compared using ANOVA, and p < 0.05 was considered statistically significant.

RESULTS
Forty patients completed the protocol. Nineteen received propofol, and twenty-one received desflurane. There were no differences between groups with respect to patient demographics (Table 1). All patients demonstrated complete neuromuscular block (T₁ = 0) and “good” or “excellent” intubating conditions in response to 0.6 mg/kg of rocuronium (Table 2).

In the desflurane group, the onset of relaxation was significantly prolonged as compared with the propofol group: 198 ± 147 (21-614) and 118 ± 78 (24-333) seconds, in the desflurane and propofol groups, respectively (p = 0.034). The clinical duration of rocuronium tended to be prolonged in the desflurane group as compared with the propofol group: 39.0 ± 25 (7.2-134) and 29.3 ± 13 (10.7-61.8) minutes, respectively; p = NS (Table 3). Rocuronium infusions were started at the same T₁ percent recovery in each group, but the infusion requirements were significantly lower in the desflurane group (Table 4). All measured spontaneous recovery indexes (T₁₀%, T₂₅%, T₅₀% and T₇₅%) were prolonged in the desflurane group, but failed to achieve

### Table 1

<table>
<thead>
<tr>
<th>Patient Demographics</th>
<th>Desflurane Group</th>
<th>Propofol Group</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years, mean ± SD)</td>
<td>40.8 ± 12.9</td>
<td>43.8 ± 12.2</td>
<td>0.442</td>
</tr>
<tr>
<td>Height (cm, mean ± SD)</td>
<td>165 ± 9</td>
<td>195 ± 9</td>
<td>0.920</td>
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<tr>
<td>Weight (kg, mean ± SD)</td>
<td>71 ± 11</td>
<td>73 ± 14</td>
<td>0.581</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>5 / 16</td>
<td>5 / 14</td>
<td>0.855</td>
</tr>
<tr>
<td>Race (Caucasian/other)</td>
<td>17 / 4</td>
<td>18 / 1</td>
<td>0.188</td>
</tr>
<tr>
<td>ASA PS Class (I/II)</td>
<td>6 / 15</td>
<td>10 / 9</td>
<td>0.121</td>
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statistical significance (Table 5). Patients who received pharmacologic reversal with neostigmine after discontinuation of relaxant infusion (the majority of the study subjects), exhibited a slower rate of recovery in the desflurane group, but these differences also did not reach statistical significance. Percent recovery at the time of reversal was similar in both groups.

**DISCUSSION**

It is well known that volatile anesthetic agents tend to potentiate the effects of all commercially available non-depolarizing neuromuscular blocking agents, including rocuronium (1, 2, 4-8, 10-13, 15).

This study was designed to specifically investigate the extent to which desflurane (compared with an equipotent non-volatile anesthetic) affected rocuronium onset, maintenance, and recovery pharmacodynamics. We hypothesized that we could minimize the accumulation typically observed with steroidal relaxants by administering it in patients anesthetized with desflurane, thereby decreasing dosing requirements necessary to maintain intraoperative surgical relaxation. Further, since desflurane is relatively insoluble, its potentiating effect should be extremely short-lived and have minimal influence on neuromuscular recovery (either spontaneous or pharmacologic), soon after it is discontinued.

In this study, $2\times ED_{95}$ of rocuronium administered by rapid iv bolus resulted in complete block in all patients in both groups. Intubating conditions for all patients were either excellent or good, with no significant differences observed between groups.

Onset times were significantly different between groups. We initially postulated that the onset time in the desflurane group would be significantly shorter than that in the propofol group because of desflurane’s ability to potentiate neuromuscular block. Interestingly, we found that onset

<table>
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<th>Table 2</th>
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<tr>
<td><strong>Ease of Intubation Rating</strong></td>
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<tr>
<td>Score</td>
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<tr>
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<tr>
<td>Excellent</td>
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<tr>
<td>Good</td>
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<tr>
<td>Total</td>
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* Data not recorded for one subject.
time in the desflurane group was, in fact, an average of 67% longer (80 seconds, p = 0.034) than in the propofol group. The range of onset times in the desflurane group was also much greater than in the propofol group (21-614 seconds vs. 24-333 seconds). The variable onset of rocuronium-induced neuromuscular block was magnified (nearly doubled) in the group receiving desflurane, making this regimen appear less reliable in situations where rapid and/or predictable block onset is desirable. For rapid sequence intubation situations, however, desflurane’s effect on onset is immaterial, since patients would not be exposed to an inhalation anesthetic prior to intubation. The prolonged onset time in the desflurane group might be explained by the increase in sympathetic tone known to occur in patients after exposure to the inhalational agent, especially if the inhaled concentration is increased rapidly (3, 9). This increased tone would cause superficial vasoconstriction and delay delivery of rocuronium to the stimulated muscle group (in this case, the adductor pollicis muscle), especially as the vasodilating effect of propofol used for induction is antagonized. Whether this same postulated mechanism of vasoconstriction also affects the axial (diaphragmatic, laryngeal) musculature is yet unknown.

Clinical duration was prolonged by about 30% in the desflurane group, but the difference did not reach statistical significance. Again, the ranges of clinical duration were much greater in patients receiving desflurane. Relaxant infusion rates titrated to maintain a T1/Tc ratio of 10% were 67% less in the desflurane group, but the differences did not reach statistical significance. Again, the ranges of onset times and infusion duration in the desflurane group might be explained by the increase in sympathetic tone known to occur in patients after exposure to the inhalational agent, especially if the inhaled concentration is increased rapidly (3, 9). This increased tone would cause superficial vasoconstriction and delay delivery of rocuronium to the stimulated muscle group (in this case, the adductor pollicis muscle), especially as the vasodilating effect of propofol used for induction is antagonized. Whether this same postulated mechanism of vasoconstriction also affects the axial (diaphragmatic, laryngeal) musculature is yet unknown.

In summary, our data indicate that desflurane significantly potentiates rocuronium-induced neuromuscular block as compared with iv propofol, and significantly delays the onset of neuromuscular block at the adductor pollicis muscle.

Acknowledgements

Supported, in part, by a grant from Organon, Inc.

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