INFLUENCE OF SUXAMETHONIUM ON THE ACTION OF SUBSEQUENTLY ADMINISTERED VECURONIUM OR PANCURONIUM

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Because of its rapid onset and short duration of action, suxamethonium is commonly used clinically to facilitate tracheal intubation. It is also common practice to follow a bolus injection of suxamethonium with a long-acting non-depolarizing neuromuscular blocking drug to maintain block during procedures of long duration. The interaction between suxamethonium and such subsequently administered agents has been documented frequently. However, no previous study has demonstrated if this interaction is clinically significant.

The present study was undertaken to determine the magnitude and duration of possible interactions between suxamethonium and subsequently administered non-depolarizing neuromuscular blocking drugs. Two steroids, vecuronium and pancuronium, were chosen—vecuronium for its reportedly unequivocal interaction with suxamethonium [1-4], and pancuronium, a bis-quaternary analogue of vecuronium, because there is controversy regarding its interaction with suxamethonium [1,5-6].

METHODS AND RESULTS
The study was approved by the local Ethics Committee. Informed consent was obtained from 45 adult patients (ASA class I or II), aged 16–65 yr, none of whom was taking medication or suffering from an illness known to affect neuromuscular function. They were allocated randomly to group A (25 patients who received suxamethonium) or group B (20 patients of comparable age and weight who did not receive suxamethonium). All patients were premedicated with a combination of pethidine and atropine i.m. 1 h before induction of anaesthesia by inhalation of 2% inspired halothane and 50% nitrous oxide in oxygen. Ventilation was assisted by mask.

As soon as the patient became unconscious, the ulnar nerve was stimulated electrically with supramaximal stimuli of 0.2 ms duration at 0.1 Hz, via surface electrodes on the wrist. The force of adduction of the thumb was measured with an FT-611 transducer (Nihon Kohden Inc., Japan) and recorded continuously on an RM = 6000 polygraph system (Nihon Kohden Inc., Japan). Approximately 15 min after induction of anaesthesia, when a stable twitch tension was obtained, the trachea was intubated, either following suxamethonium 1 mg kg⁻¹ i.v. (group A) or without this drug (group B). In group B, tracheal intubation was facilitated by tracheal administration of 4% lignocaine. Anaesthesia was maintained thereafter with nitrous oxide and 0.8–1%
SUXAMETHONIUM POTENTIATION

Table 1. Mean (SEM) onset time and duration of action of the intubating dose (0.08 mg kg⁻¹) and maintenance doses (0.02 mg kg⁻¹) of vecuronium or pancuronium with and without prior suxamethonium 1 mg kg⁻¹. Significantly different from values without suxamethonium (Student's t test): *P < 0.05; **P < 0.01

<table>
<thead>
<tr>
<th></th>
<th>Onset time of intubating dose (min)</th>
<th>Intubating dose</th>
<th>Maintenance doses</th>
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<tr>
<td></td>
<td>3.9 (0.3)</td>
<td>30.2 (0.3)</td>
<td>16.0 (0.8)</td>
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<td></td>
<td>(n = 10)</td>
<td>(n = 10)</td>
<td>(n = 10)</td>
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<tr>
<td>Vecuronium</td>
<td>6.6 (0.8)</td>
<td>68.3 (6.4)</td>
<td>45.9 (4.1)</td>
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<tr>
<td></td>
<td>(n = 10)</td>
<td>(n = 10)</td>
<td>(n = 10)</td>
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<tr>
<td>Suxamethonium +</td>
<td>2.2 (0.1)**</td>
<td>36.1 (1.5)**</td>
<td>21.7 (0.7)**</td>
</tr>
<tr>
<td>vecuronium</td>
<td>(n = 10)</td>
<td>(n = 10)</td>
<td>(n = 10)</td>
</tr>
<tr>
<td>Pancuronium</td>
<td>1.7 (0.2)**</td>
<td>92.0 (6.8)*</td>
<td>60.9 (4.1)*</td>
</tr>
<tr>
<td></td>
<td>(n = 10)</td>
<td>(n = 10)</td>
<td>(n = 8)</td>
</tr>
</tbody>
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inspired halothane, and ventilation was controlled to achieve normocapnia throughout the experiment. Rectal or oesophageal temperature was monitored and maintained at more than 35 °C.

After administration of suxamethonium, twitch tension returned to a level greater than control. In five patients in group A, the time course of change in the increased twitch tension was observed for 60 min. After complete recovery from suxamethonium-induced neuromuscular block in the remaining 20 patients in group A (19.6 (SEM 0.7) min after administration of suxamethonium), and after a comparable interval in group B, the patients received 0.08 mg kg⁻¹ of either vecuronium or pancuronium and thereafter received, as maintenance doses, 0.02 mg kg⁻¹ of the same drug each time the twitch tension recovered to 25% of the control value before administration of suxamethonium. Onset time (time from injection to development of the maximal twitch depression) of the intubating dose and clinical duration (time from injection to recovery of the twitch tension to 25% of control) of both the intubating dose and maintenance doses were noted for each patient. The changes in twitch tension after suxamethonium administration were tested for statistical significance compared with control using paired Student's t test. Comparisons of the changes in onset and recovery times between groups were by Student's t test. In both cases, P < 0.05 was considered significant.

After recovery from suxamethonium-induced neuromuscular block, mechanical twitch tension increased (P < 0.01) to 123.8 (2.5)% (mean (SEM); n = 25) of control. Twitch tension then decreased gradually, but remained increased (117.2 (2.7)%; n = 5) 60 min later. With prior administration of suxamethonium, the onset times of vecuronium and pancuronium were significantly shortened. The clinical durations were prolonged significantly except for that of the second maintenance dose of pancuronium (table I).

COMMENT

In common with previous studies [1,5–6], our data confirmed the potentiating effect of suxamethonium on the action of vecuronium administered subsequently. With prior administration of suxamethonium, the onset was accelerated and duration of action was prolonged significantly.

In contrast, controversy exists with regard to the effect on pancuronium. Katz [5] reported that the degree of partial neuromuscular block produced by a bolus injection of pancuronium 0.02 mg kg⁻¹ was potentiated by prior administration of suxamethonium, while Krieg, Crul and Booij [1] found no potentiation with pancuronium 0.016 mg kg⁻¹. Walts and Rusin [6] reported that time for recovery from complete neuromuscular block produced by a bolus injection of pancuronium 0.05 mg kg⁻¹ was not affected.

The difference between the previous results and ours may be explained as follows. First, the baseline of twitch depression changes after suxamethonium. It follows that the degree of neuromuscular block could be assessed differently according to the variation in control values. The
varying results with pancuronium may be attributed, in part, to the difference in the control values chosen. Second, in view of the long-acting nature of pancuronium and the larger dose given in this study, it is conceivable that a minor shift in potency may be associated with a clinically significant change in duration of action. Third, the neuromuscular effects of halothane may have affected our results. Although end-tidal concentration of halothane was not monitored in this study, inspired concentration and duration of halothane administration were almost identical between patients with and without prior administration of suxamethonium. It is unlikely, therefore, that there was a significant difference between groups, throughout the study, in the blood concentration of halothane.

d'Hollander and colleagues [3] reported that the action of vecuronium was potentiated 45 min after recovery from suxamethonium-induced neuromuscular block. d'Hollander's group has also shown [4], that the potentiation of vecuronium was not obtained 90 min later. Our finding that suxamethonium failed to potentiate the second maintenance dose of pancuronium suggests that the effect persists at least 2 h, but not more than 3 h.

The clinical implications of this study are that the clinician should be aware of the fact that suxamethonium does potentiate vecuronium and pancuronium. Using a nerve stimulator will allow the effect in individual patients to be monitored and add to patient safety. In addition, it may be inappropriate to use suxamethonium when the neuromuscular effects of new drugs are studied.

REFERENCES