NEUROMUSCULAR BLOCKING EFFECTS OF VECURONIUM AND PANCURONIUM DURING HALOTHANE ANAESTHESIA

J. ENGBÆK, H. ØRDING AND J. VIBY-MOGENSEN

SUMMARY

The neuromuscular blocking properties of vecuronium (Org NC 45) and pancuronium were compared in 40 patients during halothane anaesthesia. Onset time was found to be dose-dependent, but no significant difference was found between the two drugs. The duration of action of vecuronium was significantly shorter than pancuronium. Times to 90% recovery of twitch height following vecuronium 0.03 mg kg⁻¹ and 0.057 mg kg⁻¹ were 32.0 min and 44.9 min, respectively, compared with 72.9 min and 124.7 min following equipotent doses of pancuronium (0.042 mg kg⁻¹ and 0.08 mg kg⁻¹). Recovery indices following both doses of vecuronium (10.0 min and 11.8 min) were significantly shorter than after pancuronium (31.0 min and 46.9 min). The reversal times of vecuronium (times from 10% to 90% twitch height recovery) were significantly shorter than those of pancuronium (7.9 min and 7.3 min, respectively, compared with 17.1 min and 17.7 min).

The ideal neuromuscular blocking drug should have a brief, non-cumulative non-depolarizing action, and a rapid onset and recovery. It should be readily reversible by an antagonist and have minimal cardiovascular side-effects (Savarese, 1975). Vecuronium (Org NC 45), a monoquaternary analogue of pancuronium appears to possess several of these ideal properties (Marshall and Ojewole, 1979; Agoston et al., 1980; Booij et al., 1980; Durant, Houwertjes, and Crul, 1980; Krieg, Crul and Booij, 1980; Krieg et al., 1980; Marshall et al., 1980).

This study compared the neuromuscular blocking properties of equipotent doses of vecuronium and pancuronium during halothane anaesthesia.

PATIENTS AND METHODS

Forty adult female patients (ASA I) scheduled for elective gynaecological operations gave informed consent to the investigation. The programme of the study was approved by the Ethics Committee. All patients were free from neuromuscular disease and did not receive any drug that might alter neuromuscular function. Diazepam 0.2 mg kg⁻¹ was given orally 60 min before the induction of anaesthesia. Anaesthesia was induced with thiopentone 4–5 mg kg⁻¹ i.v. and suxamethonium 1 mg kg⁻¹ was administered i.v. to facilitate tracheal intubation. Anaesthesia was maintained with 66% nitrous oxide and 0.5–2.0% halothane in oxygen. The lungs were ventilated using a Monaghan ventilator delivering a minute volume of 100–120 ml kg⁻¹ min⁻¹. Ventilation was altered, as necessary, to maintain arterial PCO₂ within the normal range. Using a Myotest nerve stimulator (Viby-Mogensen et al., 1980), the ulnar nerve was stimulated at the wrist through percutaneous electrodes. The adduction force of the resultant thumb twitch was measured by a displacement transducer (Statham UC 3, gold cell) and recorded on a Gould Brush 220 recorder. A series of four supramaximal single stimuli (rectangular pulses of 0.2 ms duration) were applied to the nerve at 2 Hz for 2 s every 12 s (train-of-four (TOF)) (Ali, Utting and Gray, 1970). When stable halothane anaesthesia was established and the response to TOF nerve stimulation was constant, at least 20 min after the injection of suxamethonium, the height of the first twitch of the train was taken as the standard control (control twitch height).

The patients were randomly allocated to one of four groups with 10 patients in each group. In groups I and II, the patients received vecuronium 0.03 mg kg⁻¹ (ED₉₀) and 0.057 mg kg⁻¹ (1.2 times the EDₙ₀), respectively (Ørding and Viby-Mogensen, 1981). In groups III and IV, the patients received the equipotent doses of pancuronium, 0.042 and 0.08 mg kg⁻¹, respectively. All injections were given over a period of 10 s in a fast flowing i.v. infusion. At 10% recovery of twitch height, five patients in each group received neostigmine 0.02 mg kg⁻¹ preceded by atropine 0.01 mg kg⁻¹.

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This was repeated after 6–8 min. In 20 patients the block was allowed to wear off spontaneously.

In assessing the neuromuscular effects of the two drugs, the following indices were measured from TOF recordings:
- **Onset time** (time from end of injection of neuromuscular blocker to total disappearance or maximal depression of the twitch response);
- **Duration of action** (time from end of the injection to 10% and 90% twitch recovery);
- **Recovery time** (time from 25% to 75% twitch recovery (recovery index));
- **Reversal time** (time from 10% twitch height to either 90% twitch height recovery or a TOF ratio of 0.70 following reversal with neostigmine).

The Mann–Whitney rank sum test for unpaired data was used for analysis of results. Significance was assigned at a level of 0.05 or less.

**RESULTS**

No statistically significant differences were found between the mean ages, weights or heights in the four groups of patients.

There were no statistically significant differences in the onset times between vecuronium and pancuronium with either dose (table I). However, when the larger doses of both drugs were compared with the smaller doses the onset times were decreased significantly. The twitch response was not completely abolished in one patient receiving the smaller dose of vecuronium (group I) and in three patients receiving the smaller dose of pancuronium (group III). Twitch height depression was always 100% following the larger doses (groups II and IV).

The duration of action and the recovery time (recovery index) following vecuronium were significantly shorter than after equipotent doses of pancuronium. The statistically insignificant differences in duration of action were obtained with both drugs. Although the recovery times increased with the larger dose of each drug this difference was not statistically significant.

The neuromuscular blockade following vecuronium was easily antagonized with neostigmine. At either dose the reversal time to both 90% twitch height and a TOF ratio 0.70 was significantly shorter than after pancuronium. The reversal times of both drugs were not dependent on the doses of drug administered (table II).

**DISCUSSION**

In any comparison of the effects of different neuromuscular blocking agents, equipotent doses must be used. However, since opinions differ as to the relative potency of vecuronium and pancuronium (Krieg, Crul and Booij, 1980; Fahey et al., 1981), the doses used in this study were based upon results from our own dose–response studies indicating that vecuronium is 1.4–1.5 times as potent as pancuronium during halothane anaesthesia (Ørding and Viby-Mogensen, 1981).

In this study, no significant difference was found in onset time between the two drugs and these results are in agreement with those of Krieg, Crul and Booij (1980) and Fahey and colleagues (1981).

It has been found that the previous administration of suxamethonium may enhance the neuromuscular blocking effect of both vecuronium (Krieg, Hendrickx and Crul, 1981) and pancuronium (Katz, 1971). This may explain why the depression of twitch height following both vecuronium and pancuronium in our study was greater than would be expected from the doses administered.

With vecuronium, both the duration of action and the recovery time were two to three times shorter than those of pancuronium. Similar results have been reported by Krieg, Crul and Booij (1980) and Crul and Booij (1980). The statistically insig-

### Table I. Neuromuscular blockade and time-course of action of equipotent doses of vecuronium and pancuronium during halothane anaesthesia (mean ± SD).

<table>
<thead>
<tr>
<th>Group</th>
<th>Drug</th>
<th>Dose (mg kg⁻¹)</th>
<th>Onset time (min)</th>
<th>Block (%)</th>
<th>10% twitch height</th>
<th>90% twitch height</th>
<th>Recovery index (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Vecuronium</td>
<td>0.030</td>
<td>3.3 ± 0.6</td>
<td>99.8 ± 0.6</td>
<td>13.2 ± 4.5</td>
<td>32.0 ± 4.7</td>
<td>10.0 ± 2.1</td>
</tr>
<tr>
<td>II</td>
<td>Vecuronium</td>
<td>0.057</td>
<td>1.7 ± 0.3</td>
<td>100</td>
<td>23.1 ± 3.7</td>
<td>44.9 ± 4.5</td>
<td>11.8 ± 2.0</td>
</tr>
<tr>
<td>III</td>
<td>Pancuronium</td>
<td>0.042</td>
<td>2.9 ± 0.9</td>
<td>99.6 ± 0.7</td>
<td>24.7 ± 8.3</td>
<td>72.9 ± 18.9</td>
<td>31.0 ± 13.9</td>
</tr>
<tr>
<td>IV</td>
<td>Pancuronium</td>
<td>0.080</td>
<td>1.6 ± 0.4</td>
<td>100</td>
<td>60.7 ± 16.7</td>
<td>124.7 ± 15.2</td>
<td>46.9 ± 12.7</td>
</tr>
</tbody>
</table>
significant increases in recovery time following the larger dose of both drugs are in agreement with the findings of Agoston and co-workers (1980). Fahey and colleagues (1981) found an almost five-fold increase in recovery time when the dose of vecuronium was increased from 0.07 mg kg\(^{-1}\) to 0.28 mg kg\(^{-1}\). However, most studies indicate that the recovery time is constant from 0.03 mg kg\(^{-1}\) to 0.1 mg kg\(^{-1}\) (Agoston et al., 1980; Buzello et al., 1980; Fahey et al., 1981). The duration of action found in this study was longer than that reported during neurolept anaesthesia (Agoston et al., 1980; Buzello et al., 1980; Crul and Booij, 1980). However, results obtained by Fahey and colleagues (1981), during halothane anaesthesia, were similar. As the neuromuscular blocking effect of both vecuronium and pancuronium is potentiated by halothane (Katz, 1971; Foldes, Bencini and Newton, 1980), these differences may be explained by the different anaesthetic agents used.

The neuromuscular block resulting from vecuronium was easy to antagonize with neostigmine. Reversal time to 90% twitch height and a TOF ratio of 0.70 (which is normally taken to reflect adequate recovery) (Brand et al., 1977) was two to three times shorter than that of pancuronium—findings which are consistent with those of Krieg and co-workers (1980). Recently, however, Gencarelli and Miller (1982) demonstrated that vecuronium and pancuronium were antagonized equally by neostigmine. Thus, the more rapid reversal of neuromuscular blockade following vecuronium found in this study may be a result of the more rapid spontaneous recovery of vecuronium compared with pancuronium.

In conclusion, we found that the onset time of vecuronium was not different from that of pancuronium. The time courses of action (duration of action, recovery time and reversal time) following a single dose of vecuronium were two to three times shorter than that of an equipotent dose of pancuronium. These data, together with previous reports of minimal cardiovascular side effects (Booij et al., 1980; Engbæk et al., 1983), indicate that vecuronium possesses distinct advantages over presently used non-depolarizing neuromuscular blocking drugs.

### Table II. Neostigmine-induced reversal of neuromuscular blockade from equipotent doses of vecuronium and pancuronium during halothane anaesthesia. Mean ± SD of reversal time from 10% twitch height to either 90% twitch height or train-of-four ratio of 0.70 are given. *Statistically significant difference between the two drugs.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>90% twitch height (min)</th>
<th>TOF ratio (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>5</td>
<td>7.9 ± 1.5</td>
<td>7.6 ± 1.8</td>
</tr>
<tr>
<td>II</td>
<td>5</td>
<td>7.3 ± 0.9</td>
<td>7.5 ± 1.1</td>
</tr>
<tr>
<td>III</td>
<td>5</td>
<td>17.1 ± 7.3*</td>
<td>20.6 ± 7.9*</td>
</tr>
<tr>
<td>IV</td>
<td>5</td>
<td>17.7 ± 5.0*</td>
<td>19.4 ± 7.7*</td>
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</table>

### References


DIE NEUROMUSKULARE RELAXATIONSWIRKUNG VON VECURONIUM UND PANCURONIUM WÄHREND HALOTHANNARKOSE

ZUSAMMENFASSUNG

Bei 40 Patienten wurden während Halothannarkose die neuromuskulären Relaxationsleistungen von Vecuronium (Org NC 45) und Pancuronium miteinander verglichen. Die Zeit bis zum Wirkungseintritt war dosisabhängig, doch wurde zwischen den beiden Präparaten kein signifikanter Unterschied gefunden. Die Wirkungsdauer von Vecuronium war signifikant kürzer als die von Pancuronium. Nach Gabe von 0,03 mg kg⁻¹ und 0,057 mg kg⁻¹ Vecuronium betrug die 90%ige Erholungszeit der Einzelreizantwort 32,0 Minuten bzw. 44,9 Minuten im Gegensatz zu 72,9 Minuten bzw. 124,7 Minuten nach equispezifischen Dosen von Pancuronium (0,042 mg kg⁻¹ und 0,08 mg kg⁻¹). Der Erholungsindex war nach beiden Dosen von Vecuronium mit 10,0 Minuten bzw. 11,8 Minuten signifikant kürzer als nach Pancuronium (31,0 Minuten bzw. 46,9 Minuten). Die Umkehrzeit (Zeit von 10%iger bis 90%iger Erholung der Einzelreizantwort) war bei Vecuronium signifikant kürzer als bei Pancuronium (7,9 und 7,3 Minuten verglichen mit 17,1 und 17,7 Minuten).

EFFETS DE BLOC NEUROMUSCULAIRE DU VECURONIUM ET DU PANCURONIUM AU COURS DE L'ANESTHESIE A L'HALOTHANE

RESUME

Les propriétés de bloc neuromusculaire du vecuronium (Org NC 45) ont été comparées à celles du pancuronium chez 40 patients au cours d'une anesthésie à l'halothane. On a trouvé que le délai d'action était dose-dépendant mais sans qu'il y ait de différences significatives entre les deux agents. La durée d'action du vecuronium était significativement plus brève que celle du pancuronium. Les délais de récupération de 90% de hauteur du twitch après 0,03 mg kg⁻¹ et après 0,057 mg kg⁻¹ de vecuronium étaient respectivement de 32 min et de 44,9 min contre 72,9 min et 124,7 min après des doses équipedientes de pancuronium (0,042 mg kg⁻¹ et 0,08 mg kg⁻¹). Les débuts de récupération (10 min et 11,8 min) étaient, après l'une et l'autre dose de vecuronium, significativement plus brefs qu'après pancuronium (31 min et 46,9 min). Les durées de récupération après vecuronium (temps compris entre 10% et 90% de récupération de hauteur du twitch) étaient significativement plus courtes que celles du pancuronium (7,9 min et 7,3 min respectivement, contre 17,1 min et 17,7 min).

EFECTOS DE BLOQUEO NEUROMUSCULAR DEL VECURONIO Y DEL PANCURONIO DURANTE LA ANESTESIA CON HALOTANO

SUMARIO

Se compararon las propiedades bloqueantes del vecuronio (Org NC 45) y del pancuronio en 40 pacientes, durante la anestesia con halotano. Se observó que el tiempo de comienzo de la actividad iba en función de la dosis, pero no se observó diferencia estadísticamente significativa en la actividad de los dos agentes. La actividad del vecuronio fue significativamente más corta que la del pancuronio. Los períodos de tiempo hasta una recuperación del 90% de la altura de crispación, después de 0,03 mg kg⁻¹ y 0,057 mg kg⁻¹ de vecuronio, fueron de 32,0 min y de 44,9 min respectivamente, en comparación con 72,9 min y 124,7 min para dosis equipotentes de 0,042 mg kg⁻¹ y 0,08 mg kg⁻¹ de pancuronio. Los índices de recuperación a razón de ambas dosis de vecuronio (10,0 min y 11,8 min) fueron significativamente más cortos que los correspondientes al pancuronio (31,0 min y 46,9 min). Los periodos de tiempo de inversión correspondientes al vecuronio (tiempos desde el 10% al 90% de la recuperación de la altura de crispación) fueron significativamente más cortos que los correspondientes al pancuronio (7,9 y 7,3 min respectivamente, en comparación con 17,1 y 17,7 min).