COMPARISON OF THE NEUROMUSCULAR BLOCKING PROPERTIES
OF ORG NC 45 AND PANCURONIUM IN THE RAT, CAT AND
RHESUS MONKEY

N. N. DURANT, M. C. HOUWERTJES AND J. F. CRUL

SUMMARY

The neuromuscular and cardiovascular activities of pancuronium were compared with those of its
16(3 monoquaternary congener, Org NC 45, in the anaesthetized rat, cat and rhesus monkey.
In the rat Org NC 45 was 3.4 times less potent as a neuromuscular blocking agent than was pan-
curonium. In the cat, both drugs were found to be approximately equally eliminated by the liver,
whereas renal elimination was observed only with pancuronium. In the rhesus monkey,
Org NC 45 was about 1.5 times less potent than pancuronium as a neuromuscular blocking agent.
At doses approximately eight times that producing 80% twitch block, the neuromuscular block
produced by Org NC 45 was significantly shorter in duration and recovery than that produced by
pancuronium. In addition, these high doses of Org NC 45 did not produce the tachycardia which
is seen with pancuronium. Org NC 45 showed less tendency than pancuronium to produce
cumulative effects on repeated administration in the monkey. Both Org NC 45 and
pancuronium were antagonized by anti-cholinesterases and aminopyridines. It is suggested that
the lack of tachycardia with Org NC 45 may be related to the low cardio-selective anti-muscarinic
potency of Org NC 45 previously reported in the cat and, together with its low renal elimination
and lack of cumulative effects, Org NC 45 may be a clinically useful non-depolarizing muscle
relaxant free of cardiovascular side-effects.

Many non-depolarizing neuromuscular blocking
agents in clinical use cause tachycardia in man
(Kennedy and Kelman, 1970; Coleman et al., 1972;
Stoelting, 1972). These agents are known to block
cardiac muscarinic receptors in experimental animals
(Saxena and Bonta, 1970, 1971; Hughes and Chapple,
1976; Lee-Son and Waud, 1978); in addition
pancuronium can also cause sympathetically-mediated
activity in animals (Nana, Cardan and Domokas,
1973; Ivankovitch et al., 1975; Domenech et al.,
1976; Docherty and McGrath, 1977, 1978). Thus,
the exact mechanism by which non-depolarizing
neuromuscular blocking agents produce tachycardia
in man is not clear. Durant and others (1979)
demonstrated that Org NC 45 (fig. 1), a monoquat-
erinary homologue of pancuronium which is similar
in neuromuscular blocking potency to pancuronium,
blocks the cardiac muscarinic receptors in the cat

Only at doses many times greater than those produc-
ing submaximal neuromuscular block.

We compared Org NC 45 and pancuronium in the
rat, cat and rhesus monkey. Particular attention has
been paid to the effect of Org NC 45 on the heart
rate in the rhesus monkey and to the elimination of
Org NC 45 in the cat, since both these factors are of
clinical importance.

Some of this work was communicated at the Vth
European Congress of Anesthesiology, Paris, Sept-
ember 1978 (Durant, 1978) and the American Society
of Anesthetists meeting, San Francisco, October
1979 (Durant, Houwertjes and Agoston, 1979a, b).

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METHODS

Anaesthetized rat sciatic nerve–tibialis anterior muscle preparation

Male rats (300–600 g) were anaesthetized with pentobarbitone sodium 60 mg kg\(^{-1}\) i.p. and the lungs were artificially ventilated with air at a rate of 100 b.p.m. and a tidal volume of 7 ml kg\(^{-1}\). Body temperature was maintained at 37–38 °C and drugs were administered through a polythene cannula placed in a jugular vein. Arterial pressure was recorded via a polythene cannula placed in a carotid artery. The sciatic nerve was stimulated by rectangular pulses of 0.2 ms duration, a frequency of 0.1 Hz and at sufficient stimulus strength to elicit maximal twitch responses of the tibialis anterior muscle.

Anaesthetized cat sciatic nerve–tibialis anterior muscle preparation

Cats of either sex (2.4–4.5 kg) were anaesthetized with pentobarbitone sodium 40 mg kg\(^{-1}\) i.p. and were artificially ventilated with air at a rate of 26 b.p.m. and a tidal volume of 18 ml kg\(^{-1}\). Body temperature was maintained at 36–38 °C and drugs were administered through a polythene cannula placed in a jugular vein. Arterial pressure was recorded via a polythene cannula placed in a carotid artery. The sciatic nerve in the popliteal space was stimulated with rectangular pulses of the same parameters as described above to elicit maximal twitch responses of the tibialis anterior muscle.

To exclude the liver from the general circulation, the method described by Agoston, Houwertjes and Salt (1980) was used. Initially, a control dose of antagonist sufficient to produce an 80–90% reduction of twitch tension was administered via the jugular vein. The same dose was then used throughout the experiment. The second administration was made whilst the kidneys were temporarily excluded for 10 min. The third administration was made whilst the kidneys were permanently excluded.

The time between administrations was 2 h for pancuronium and 1 h for Org NC 45; initial studies indicated that these two time intervals resulted in the minimum cumulative effect.

Anaesthetized rhesus monkey ulnar nerve–adductor pollicis muscle preparation

Rhesus monkeys of either sex (4.7–11.5 kg) were anaesthetized with ketamine hydrochloride 10 mg kg\(^{-1}\) i.m. and pentobarbitone sodium 30 mg total dose and were artificially ventilated with 67% nitrous oxide in oxygen at a rate of 20 b.p.m. and tidal volume of 12 ml kg\(^{-1}\). Drugs were administered i.v. through an indwelling polyethylene cannula placed in the saphenous vein. E.c.g. was recorded (heart rate).

The ulnar nerve was stimulated via two polar subcutaneous needle electrodes with rectangular pulses of the same parameters as those described above. The twitch responses of the adductor pollicis muscle were recorded via a Statham UC3 transducer attached by a wire to a small U-clamp which could be fixed firmly to the basal phalanx of the thumb.

Drug and solutions

Drugs used were: 3,4-diaminopyridine, atropine sulphate, heparin, ketamine hydrochloride, neostigmine methylsulphate, pancuronium bromide, Org NC 45 bromide and pentobarbitone sodium. Org NC 45 was dissolved at a concentration of 1 mg ml\(^{-1}\) in 2.1 mg ml\(^{-1}\) of citric acid to prevent alkaline hydrolysis; a fresh solution was used for each experiment. Other drugs were dissolved in 0.9% saline. Doses are expressed as weight in terms of the salt when appropriate.

Statistics

Neuromuscular blockade during a drug effect was measured as the percentage depression of twitch tension relative to the height of the control twitch responses. Onset of neuromuscular blockade was measured as the time from injection to maximum depression of twitch tension, duration time as the time from injection to either 50% or 90% recovery of twitch height and recovery time as the time from 25% to 75% recovery of twitch height. Results are presented as the mean ± SEM of at least four observations.
except when indicated. The dose which produced a 50% inhibition of twitch tension was determined by regression analysis of the log-dose–effect curve. Comparisons of paired data were made with Wilcoxon's test and comparisons of unpaired data with the Mann–Whitney U-test. Probability values of less than 0.05 were regarded as significant.

RESULTS

Neuromuscular blockade

In the rat and rhesus monkey Org NC 45 was 3.4 and 1.5 times less potent respectively than pancuronium as a neuromuscular blocking agent (table I), but at submaximal blocking doses the time courses of the blocks produced by the two compounds were not significantly different (fig. 2, table II). At doses which produced submaximal neuromuscular block in the anaesthetized rhesus monkey there was no evidence of any change in heart rate with either pancuronium or Org NC 45 (fig. 3).

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Dose (μg kg⁻¹)</th>
<th>% Block</th>
<th>Onset (min)</th>
<th>Duration to 50% (min)</th>
<th>Recovery time (min)</th>
<th>Heart rate (%Δ)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pancuronium</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rat tibialis anterior</td>
<td>69.0</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Monkey adductor pollicis</td>
<td>5.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Org NC 45</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rat tibialis</td>
<td>237.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monkey adductor pollicis</td>
<td>8.1</td>
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</tbody>
</table>

Neuromuscular block produced by pancuronium and Org NC 45 was reversed in significantly faster time than control recovery by neostigmine 35 μg kg⁻¹ and 3,4-diaminopyridine 1 mg kg⁻¹ when injected at maximal block. At the doses used, 3,4-diaminopyridine caused marked bradycardia which was antagonized by a total dose of atropine 0.5 mg.

Cumulation studies

The cumulative effects of pancuronium and Org NC 45 were tested in the anaesthetized rhesus monkey by recording the depth and duration of neuromuscular block produced by six administrations of one of three different doses of either drug. Each

![Dose-inhibition plots for pancuronium (squares) and Org NC 45 (circles) on the rat tibialis anterior muscle preparation (open symbols) and monkey adductor pollicis muscle preparation (closed symbols).](http://bja.oxfordjournals.org/DownloadedFrom/)

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**TABLE I. Doses of pancuronium and Org NC 45 which produced a 50% reduction of twitch tension in the anaesthetized rat and rhesus monkey**

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Dose (μg kg⁻¹)</th>
<th>% Block</th>
<th>Onset (min)</th>
<th>Duration to 50% (min)</th>
<th>Recovery time (min)</th>
<th>Heart rate (%Δ)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pancuronium</strong></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rat tibialis anterior</td>
<td>69.0</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Monkey adductor pollicis</td>
<td>5.4</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>Org NC 45</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rat tibialis</td>
<td>237.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monkey adductor pollicis</td>
<td>8.1</td>
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</tbody>
</table>

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**TABLE II. Comparison of the time-course of neuromuscular block produced by pancuronium and Org NC 45 in anaesthetized rats, cats and monkeys (n = 4 minimum). *Significantly different from pancuronium (P < 0.05)**

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Dose (μg kg⁻¹)</th>
<th>% Block</th>
<th>Onset (min)</th>
<th>Duration to 50% (min)</th>
<th>Recovery time (min)</th>
<th>Heart rate (%Δ)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pancuronium</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rat tibialis</td>
<td>100</td>
<td>92 ± 2</td>
<td>2 ± 0.3</td>
<td>4 ± 0.4</td>
<td>1 ± 0.2</td>
<td>—</td>
</tr>
<tr>
<td>Cat tibialis</td>
<td>22</td>
<td>88 ± 5</td>
<td>7 ± 1</td>
<td>14 ± 2</td>
<td>5 ± 0.8</td>
<td>—</td>
</tr>
<tr>
<td>Monkey adductor pollicis</td>
<td>7</td>
<td>90 ± 3</td>
<td>7 ± 1</td>
<td>15 ± 3</td>
<td>9 ± 3</td>
<td>1 ± 6</td>
</tr>
<tr>
<td><strong>Org NC 45</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rat tibialis</td>
<td>450</td>
<td>90 ± 3</td>
<td>2 ± 0.1</td>
<td>4 ± 1.0</td>
<td>1 ± 0.4</td>
<td>—</td>
</tr>
<tr>
<td>Cat tibialis</td>
<td>25–40</td>
<td>81 ± 6</td>
<td>5 ± 0.5</td>
<td>9 ± 1</td>
<td>5 ± 1.0</td>
<td>—</td>
</tr>
<tr>
<td>Monkey adductor pollicis</td>
<td>55</td>
<td>100</td>
<td>3 ± 0.6</td>
<td>111 ± 7</td>
<td>81 ± 4</td>
<td>+6 ± 2</td>
</tr>
</tbody>
</table>
administration was made when recovery of twitch height from the previous administration had reached 90% of control height. Both pancuronium and Org NC 45 produced a greater depth of neuromuscular blockade with the second compared with the first administration (fig. 4). However, pancuronium exhibited a dose-dependent increase in duration of action up to the third administration, whereas Org NC 45 exhibited increase in duration only between the first and second administration (fig. 5). This suggests a slight difference between the pharmacokinetics of Org NC 45 and pancuronium in the rhesus monkey. Bolus administrations of the same multiple of equi-active neuromuscular blocking doses of pancuronium 55 μg kg⁻¹ resulted in a 6 ± 2% increase in heart rate, but Org NC 45 81 μg kg⁻¹ was without effect. At these high doses, Org NC 45 was significantly more rapid in onset, shorter in duration and faster in recovery than pancuronium (table II).

Effect of exclusion of the liver
Temporary (10-min) exclusion of the liver in the cat resulted in a significant increase in the depth and duration of the neuromuscular block produced by both pancuronium and Org NC 45 compared with the first control doses of the drugs. Permanent exclusion of the liver also produced a significant increase in the depth and duration of the block produced by both drugs. Intra-portal vein administra-
COMPARISON OF PANCURONIUM AND ORG NC 45

Fig. 5. The duration to 90% of recovery of twitch tension of the anaesthetized rhesus monkey ulnar nerve–adductor pollicis muscle produced by six successive administrations of three different doses of pancuronium (left, □) 4.5, 5.5 and 7.0 µg kg\(^{-1}\), and Org NC 45 (right ○) 7, 8.5 and 10 µg kg\(^{-1}\).

Table III. Neuromuscular blockade of the sciatic nerve–tibialis anterior muscle preparation of the anaesthetized cat produced by pancuronium 22 µg kg\(^{-1}\) and Org NC 45 25–40 µg kg\(^{-1}\) with the liver temporarily and permanently excluded from the general circulation. The responses to intraportal vein (IPV) administration are also shown. (n = 5; *significantly different from control)

<table>
<thead>
<tr>
<th>Drug and procedure</th>
<th>% Blockade</th>
<th>Onset time (min)</th>
<th>Duration to 50% (min)</th>
<th>Recovery time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancuronium</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>92 ± 7</td>
<td>6 ± 2</td>
<td>15 ± 4</td>
<td>5 ± 1</td>
</tr>
<tr>
<td>10 min exclusion</td>
<td>100</td>
<td>3 ± 1</td>
<td>26 ± 2*</td>
<td>5 ± 1</td>
</tr>
<tr>
<td>IPV</td>
<td>99 ± 1</td>
<td>4 ± 2</td>
<td>17 ± 1</td>
<td>5 ± 1</td>
</tr>
<tr>
<td>Control</td>
<td>98 ± 2</td>
<td>4 ± 1</td>
<td>17 ± 2</td>
<td>4 ± 1</td>
</tr>
<tr>
<td>Permanent exclusion</td>
<td>100*</td>
<td>2 ± 0.2</td>
<td>No recovery at less than 45 min*</td>
<td></td>
</tr>
<tr>
<td>Org NC 45</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>82 ± 7</td>
<td>5 ± 1</td>
<td>10 ± 2</td>
<td>5 ± 2</td>
</tr>
<tr>
<td>10 min exclusion</td>
<td>100*</td>
<td>3 ± 0.3</td>
<td>19 ± 1*</td>
<td>6 ± 1</td>
</tr>
<tr>
<td>IPV</td>
<td>63 ± 12</td>
<td>5 ± 0.3</td>
<td>10 ± 1</td>
<td>6 ± 2</td>
</tr>
<tr>
<td>Control</td>
<td>98 ± 1</td>
<td>4 ± 1</td>
<td>12 ± 1</td>
<td>6 ± 1</td>
</tr>
<tr>
<td>Permanent exclusion</td>
<td>100*</td>
<td>2 ± 1</td>
<td>28 ± 9*</td>
<td>10 ± 1*</td>
</tr>
</tbody>
</table>

Effect of exclusion of the kidneys

Temporary (10-min) exclusion of the kidneys did not have a significant effect on either the depth or duration of the neuromuscular block produced by either pancuronium or Org NC 45. Permanent kidney exclusion only significantly increased the duration (to 50% recovery) and decreased the onset time of the neuromuscular block produced by pancuronium, whereas the neuromuscular block produced by Org NC 45 was unaffected (Table IV).

Table IV. Neuromuscular blockade of the sciatic nerve–tibialis anterior muscle preparation of the anaesthetized cat produced by pancuronium 22 µg kg\(^{-1}\) and Org NC 45 25–40 µg kg\(^{-1}\) with both kidneys temporarily and permanently excluded from the general circulation. (n = 5; *significantly different from control)

<table>
<thead>
<tr>
<th>Drug and procedure</th>
<th>% Blockade</th>
<th>Onset time (min)</th>
<th>Duration to 50% (min)</th>
<th>Recovery time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancuronium</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>85 ± 7</td>
<td>9 ± 1</td>
<td>15 ± 3</td>
<td>6 ± 1</td>
</tr>
<tr>
<td>10 min exclusion</td>
<td>98 ± 1</td>
<td>7 ± 2</td>
<td>17 ± 1</td>
<td>6 ± 1</td>
</tr>
<tr>
<td>IPV</td>
<td>96 ± 2</td>
<td>6 ± 1</td>
<td>17 ± 3</td>
<td>6 ± 1</td>
</tr>
<tr>
<td>Control</td>
<td>100*</td>
<td>3 ± 1*</td>
<td>27 ± 6*</td>
<td>8 ± 2</td>
</tr>
<tr>
<td>Permanent exclusion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Org NC 45</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>79 ± 8</td>
<td>4 ± 1</td>
<td>10 ± 2</td>
<td>5 ± 2</td>
</tr>
<tr>
<td>10 min exclusion</td>
<td>86 ± 8</td>
<td>4 ± 0.2</td>
<td>9 ± 2</td>
<td>6 ± 2</td>
</tr>
<tr>
<td>IPV</td>
<td>78 ± 11</td>
<td>4 ± 1</td>
<td>10 ± 2</td>
<td>5 ± 1</td>
</tr>
<tr>
<td>Control</td>
<td>85 ± 8</td>
<td>4 ± 0.7</td>
<td>8 ± 2</td>
<td>4 ± 1</td>
</tr>
<tr>
<td>Permanent exclusion</td>
<td></td>
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</tbody>
</table>

DISCUSSION

In all three species tested, Org NC 45 was slightly less potent than pancuronium as a neuromuscular...
blocking agent. At submaximal blocking doses both compounds had similar time-courses of action. The potencies of Org NC 45 and pancuronium in the cat in the present study are slightly greater than previously reported (Durant et al., 1979); this is most probably because of the different anaesthetics used. With large doses in the monkey the time-course of the neuromuscular block produced by Org NC 45 was shorter than that of pancuronium and the increase in heart rate associated with pancuronium was not seen. Org NC 45 has been demonstrated to have only a very weak blocking action at the cardiac vagus neuroeffector junction (Durant et al., 1979; Marshall and Ojewole, 1979) and no evidence has been found that Org NC 45 enhances noradrenergic transmission (Marshall and Ojewole, 1979). It is likely that this lack of autonomic effect at doses many times those blocking neuromuscular transmission explains the lack of cardiovascular side-effects reported by Booij and others (1980), and the absence of tachycardia in the present study.

The neuromuscular block produced by Org NC 45 was antagonized by anticholinesterases as easily as was the block produced by pancuronium, an essential requirement of any non-depolarizing muscle relaxant of potential clinical use. The neuromuscular blocks produced by both pancuronium and Org NC 45 were also antagonized by 3,4-diaminopyridine, a compound that is known to increase the evoked release of acetylcholine (Durant and Marshall, 1978). Based on neuromuscular block in the rhesus monkey, pancuronium and Org NC 45 exhibited similar cumulation characteristics in that both agents produced a greater depth of blockade with the second administration than with the first. This suggests, as previously demonstrated by Paton and Waud (1967) and Waud and Waud (1972), that considerable occupation of the receptors occurs when twitch responses have returned to control height after neuromuscular block. However, pancuronium produced a more pronounced increased duration of blockade with successive doses than did Org NC 45. This suggests that the pharmacokinetics of Org NC 45 are different from those of pancuronium in the rhesus monkey. The lower cumulative effects of Org NC 45 may be of some potential clinical benefit, as prediction of additional dosage should be straightforward.

Pancuronium is eliminated mainly by the kidneys in man (Agoston et al., 1973; Tanaka, Hioki and Shindo, 1974; Buzello, 1975) and has been shown to exhibit a prolonged action in patients with impaired renal function (Popescu, 1972; Miller, Stevens and Way, 1973; McLeod, Watson and Rawlins, 1976; Hull et al., 1978). Similarly, biliary obstruction can double the plasma half-life of pancuronium in man (Somogyi, Shanks and Triggs, 1977). The neuromuscular block produced by pancuronium administered via the intraportal vein was not significantly different from control in the present study, confirming that the liver uptake of pancuronium is small in the cat (Agoston et al., 1977). The biliary excretion of pancuronium, reported by Agoston and others (1977) and Miller and others (1978), was confirmed in the present study by the marked increase of the duration of the neuromuscular block when the liver was excluded.

The importance of the renal route of elimination of pancuronium in the cat is illustrated by the increase in the duration of neuromuscular blockade which accompanies renal occlusion of the circulation to the kidneys. However, neuromuscular blockade induced by Org NC 45 was not significantly altered by occlusion of the circulation to the kidneys. This observation may be explained in two different ways. First, the renal elimination of Org NC 45 is small; second, Org NC 45 is subject to rapid breakdown into non-active metabolites. In either case renal excretion of the intact molecule will be small.

The actions of Org NC 45 described, if observed in man, would make the drug a significant advance in the search for a more selective, shorter-acting muscle relaxant.

ACKNOWLEDGEMENTS
We acknowledge gratefully the help of Drs I. G. Marshall, S. Agoston and D. S. Savage with the organization of this project and preparation of the manuscript. We also wish to acknowledge the help of Dr C. Lee with the manuscript and Dr N. Krieg and Ms F. Van der Pol for assistance with some of the monkey experiments. One of us (N. N. D.) was the recipient of a Science Research Council C.A.S.E. award.

Pancuronium and Org NC 45 were supplied by Organon Scientific Development Group.

REFERENCES


COMPARAISON DES PROPRIETES DE BLOCAGE NEUROMUSCULAIRE D’ORG NC 45 ET DE CELLES DU PANCURONIUM CHEZ LE RAT, LE CHAT ET LE SINGE RHESUS

**Résumé**

On a comparé les activités neuromusculaires et cardiovasculaires du pancuronium à celles de son congénère monoquaternaire 16 β: Org NC 45, sur le rat, le chat et le singe rhésus anesthésiés. Org NC 45 a été 3,4 fois moins efficace sur le rat, en tant qu’agent de blocage neuromusculaire, que le pancuronium. Sur le chat, ces deux produits ont été trouvés à peu près équivalents du point de vue elimination par le foie, alors que leur elimination rénale n’a été observée qu’avec le pancuronium. En ce qui concerne le singe rhésus, Org NC 45 a été environ 1,5 fois moins efficace que le pancuronium en tant qu’agent de blocage neuromusculaire. A des doses à peu près huit fois supérieures à celles produisant un blocage à 80% de la...
crispation, le blocage neuromusculaire produit par Org NC 45 a été nettement plus court du point de vue durée et récupération que celui occasionné par le pancuronium. De plus, ces fortes doses d'Org NC 45 n'ont pas produit la tachycardie que l'on constate avec le pancuronium. Org NC 45 a moins eu tendance que le pancuronium à produire des effets cumulatifs lors de l'administration répétée sur le singe. Org NC 45 tout comme le pancuronium ont été contrariés par les anticholinestérase et les aminopyridines. On pense que le fait qu'il n'y ait pas eu de tachycardie avec Org NC 45 peut être lié à la faible efficacité antimuscarinique cardio-sélective d'Org NC 45 que l'on avait précédemment constatée sur le chat, de même que par suite de sa faible élimination par voie rénale et de son manque d'effets cumulatifs. Org NC 45 peut être utile du point de vue clinique en tant que décontractant musculaire non dépolarisant n'ayant aucun effet secondaire cardiovasculaire.

VERGLEICH DER NEUROMUSKULÄREN BLOCKIERUNGSEIGENSCHAFTEN VON ORG NC 45 UND PANCURONIUM BEI RATTEN, KATZEN UND RHEUSAFFEN

ZUSAMMENFASSUNG


COMPARACION DE LAS PROPIEDADES DE BLOQUEO NEUROMUSCULAR DEL ORG NC 45 Y DEL PANCURONIUM EN LA RATA, GATO Y EN EL MONO RHEUS

SUMARIO

Se compararon las actividades neuromusculares y cardiovasculares del pancuronium con las de su congénere monoquaternario 16g, el Org NC 45, en la rata, gato y en mono rhesus anestesiado. El Org NC 45 fue 3,4 veces menos potente en la rata, cuál un agente de bloqueo neuromuscular, que el pancuronium. Se encontró que, en el caso del gato, el hígado eliminó ambas drogas por igual, aproximadamente, mientras que sólo se observó eliminación renal cuando se usó pancuronium. En el caso del mono rhesus, el Org NC 45 fue 1,5 veces menos potente, aproximadamente, que el pancuronium, a guisa de agente de bloqueo neuromuscular. Para dosis 8 veces superiores, aproximadamente, que las que producen un bloqueo de sustención del 80%, el bloqueo neuromuscular producido por el Org NC 45 fue significativamente más corto en lo que respecta a su acción y recuperación, que el producido por el pancuronium. Además, estas altas dosis de Org NC 45 no produjeron la taquicardia característica del pancuronium. El Org NC 45 mostró menor tendencia que el pancuronium, a producir efectos acumulativos bajo administraciones sucesivas en el mono. Tanto el Org NC 45 como el pancuronium fueron contrarrestados mediante anticholinesterases y aminopyridinas. Se ha sugerido que la ausencia de taquicardia asociada con el Org NC 45 puede estar relacionada con la baja potencia cardioseletiva y antimuscarínica del Org NC 45, de la que se informó anteriormente para el gato y, junto con su baja eliminación renal y la ausencia de efectos acumulativos, el Org NC 45 puede que sea un relajante muscular no despolarizante de utilidad clínica que no presenta efectos secundarios cardiovasculares.