CARDIOVASCULAR EFFECTS OF PANCURONIUM IN MAN

BY

G. R. KELMAN AND B. R. KENNEDY

SUMMARY

We have investigated the effects of pancuronium bromide (0.07 mg/kg body weight) on heart rate, mean arterial blood pressure, cardiac output and calculated total peripheral resistance in ten artificially ventilated patients, anaesthetized with 60 per cent nitrous oxide in oxygen plus phenoperidine (1 mg/15 kg body weight). End-tidal Pco₂ was maintained constant at 30 ± 2 mm Hg. There was a marked and statistically significant increase of heart rate of about 25 per cent, accompanied by lesser, but still statistically significant, increases of cardiac output and mean arterial blood pressure. Total peripheral resistance was unchanged, suggesting that pancuronium has little ganglion-blocking activity.

Pancuronium bromide, a bisquaternary amino- steroid described by Buckett, Hewett and Savage (1967), has been shown to be a potent neuromuscular blocking agent with only minimal ganglion-blocking and histamine-releasing properties (Buckett et al., 1968). These qualities make it a valuable drug, particularly in poor-risk patients and in patients with an allergic diathesis (McDowell and Clarke, 1969; Stojanov, 1969).

In the present study we have investigated the effects of pancuronium bromide on the human cardiovascular system. The dose used (0.07 mg/kg body weight) was selected as being intermediate between that needed to produce muscular relaxation sufficient for tracheal intubation and that required to maintain muscular relaxation after intubation with suxamethonium.

METHOD

The fifteen patients studied were adult in-patients undergoing routine surgery under general anaesthesia. All were free from cardiorespiratory disease. The age, weight and sex of each patient, together with the dose of premedicant and induction agent used are shown in Table I. All patients had consented to the investigation.

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Wt (kg)</th>
<th>Premedication (P/H mg)</th>
<th>Thiopentone (mg/kg)</th>
<th>Suxamethonium (mg)</th>
<th>Phenoperidine (mg)</th>
<th>Pancuronium (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>33</td>
<td>M</td>
<td>65</td>
<td>15/0.4</td>
<td>4.6</td>
<td>50</td>
<td>4.5</td>
<td>~</td>
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<tr>
<td>2</td>
<td>52</td>
<td>M</td>
<td>68</td>
<td>15/0.4</td>
<td>3.7</td>
<td>50</td>
<td>4.0</td>
<td>~</td>
</tr>
<tr>
<td>3</td>
<td>50</td>
<td>M</td>
<td>60</td>
<td>15/0.4</td>
<td>5.8</td>
<td>50</td>
<td>4.0</td>
<td>~</td>
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<tr>
<td>4</td>
<td>69</td>
<td>M</td>
<td>76</td>
<td>20/0.4</td>
<td>3.9</td>
<td>50</td>
<td>5.0</td>
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<tr>
<td>5</td>
<td>38</td>
<td>M</td>
<td>75</td>
<td>20/0.4</td>
<td>5.3</td>
<td>50</td>
<td>5.0</td>
<td>~</td>
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<tr>
<td>6</td>
<td>44</td>
<td>M</td>
<td>78</td>
<td>20/0.4</td>
<td>4.5</td>
<td>50</td>
<td>5.0</td>
<td>0.07</td>
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<tr>
<td>7</td>
<td>54</td>
<td>M</td>
<td>66</td>
<td>20/0.4</td>
<td>5.3</td>
<td>50</td>
<td>4.0</td>
<td>0.07</td>
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<tr>
<td>8</td>
<td>48</td>
<td>F</td>
<td>83</td>
<td>20/0.4</td>
<td>5.3</td>
<td>50</td>
<td>5.0</td>
<td>0.07</td>
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<tr>
<td>9</td>
<td>55</td>
<td>M</td>
<td>82</td>
<td>20/0.4</td>
<td>4.3</td>
<td>50</td>
<td>5.5</td>
<td>0.07</td>
</tr>
<tr>
<td>10</td>
<td>55</td>
<td>M</td>
<td>93</td>
<td>20/0.4</td>
<td>4.8</td>
<td>50</td>
<td>6.0</td>
<td>0.07</td>
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<tr>
<td>11</td>
<td>21</td>
<td>M</td>
<td>60</td>
<td>15/0.4</td>
<td>5.8</td>
<td>50</td>
<td>4.0</td>
<td>0.07</td>
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<td>12</td>
<td>21</td>
<td>M</td>
<td>68</td>
<td>15/0.4</td>
<td>5.1</td>
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<td>13</td>
<td>39</td>
<td>F</td>
<td>58</td>
<td>10/0.2</td>
<td>4.3</td>
<td>50</td>
<td>4.0</td>
<td>0.07</td>
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<tr>
<td>14</td>
<td>30</td>
<td>M</td>
<td>75</td>
<td>15/0.4</td>
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<td>5.0</td>
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<tr>
<td>15</td>
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<td>F</td>
<td>50</td>
<td>10/0.4</td>
<td>5.0</td>
<td>50</td>
<td>3.5</td>
<td>0.07</td>
</tr>
</tbody>
</table>

P = papaveretum  
H = hyoscine

Premedication in all patients was with papa-
veretum, 15 or 20 mg depending on body weight,
together with hyoscine 0.4 mg, given intramus-
cularly 60 minutes before induction of anaesthesia
with thiopentone (250-400 mg). Tracheal intuba-
tion was performed under suxamethonium-indu-
ced muscular relaxation. Continued apnoea was
then produced with phenoperidine (1 mg/15 kg),
and controlled ventilation maintained (60 per cent
nitrous oxide in oxygen) with a Manley ventilator
and non-rebreathing circuit. End-tidal Pco₂ was
monitored continuously with an infra-red carbon
dioxide analyzer (URAS 3, Hartmann and Braun).
The ventilatory minute volume was adjusted to
maintain the end-expired Pco₂ at 30 ± 2 mm Hg.

All measurements of heart rate, arterial blood
pressure and cardiac output were made before the
start of surgery. Control measurements were made
at 17 and 19 minutes after induction of anaes-
thesia. The patients were then given either no
drug (5 patients) or (10 patients) pancuronium
bromide, 0.07 mg/kg body weight intravenously.
The cardiovascular measurements were then re-
peated after 2, 5 and 10 minutes.

Heart rate was measured from an e.c.g. tracing,
which was also scrutinized for the occurrence of
arrhythmias. Arterial blood pressure (systolic and
diastolic) was measured with a sphygomanometer;
the mean pressure was assumed to be diastolic
pressure plus one-third pulse pressure. Changes in
cardiac output were estimated by the indicator
dilution technique with indocyanine green and a
Waters XE 302 photoelectric earpiece and associ-
ated electronic equipment. The dye curves were
not calibrated. The object was to measure the
changes of cardiac output induced by pancuron-
iun; non-calibrated dye curves are sufficient for
this purpose (Gabe, Tuckman and Shillingford,
1962) and avoid the necessity for arterial puncture.

**RESULTS**

The initial values of mean arterial blood pressure
and heart rate were comparable for the patients
who received pancuronium and for those who
received no drug (table II).

The effects of pancuronium on heart rate, car-
diac output, cardiac stroke volume, mean arterial
blood pressure and total peripheral resistance (cal-
culated by dividing mean arterial blood pressure
by cardiac output) are shown in table III. All
results are expressed as percentage change from
the pre-drug value, i.e. the state 20 minutes after
induction of anaesthesia.

**Table II**

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Mean arterial pressure (mm Hg)</th>
<th>Heart rate (beats/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>90</td>
<td>72</td>
</tr>
<tr>
<td>2</td>
<td>85</td>
<td>56</td>
</tr>
<tr>
<td>3</td>
<td>55</td>
<td>39</td>
</tr>
<tr>
<td>4</td>
<td>85</td>
<td>70</td>
</tr>
<tr>
<td>5</td>
<td>70</td>
<td>43</td>
</tr>
<tr>
<td>Mean ± SEM</td>
<td>77.0 ± 6.4</td>
<td>56.0 ± 6.7</td>
</tr>
</tbody>
</table>

**Table III**

<table>
<thead>
<tr>
<th>Cardiac output changes in five control patients and ten patients who received pancuronium.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td>Heart rate</td>
</tr>
<tr>
<td>Cardiac output</td>
</tr>
<tr>
<td>Stroke volume</td>
</tr>
<tr>
<td>Mean arterial pressure</td>
</tr>
<tr>
<td>Total peripheral resistance</td>
</tr>
</tbody>
</table>

All results (mean ± SEM) are expressed as percentages of values obtained before injection of
pancuronium (0.07 mg/kg body weight) or no drug.

**P<0.01. *0.01<P<0.05. n.s. = not statistically significant. All comparisons are with 100 per cent.**
Pancuronium caused a marked increase of heart rate (22–26 per cent), accompanied by lesser increases of cardiac output (6–9 per cent) and of mean arterial blood pressure (8–9 per cent). These changes were all statistically significant, although the effect on cardiac output was only just so (P<0.05 at 2 min). Calculated total peripheral resistance was unchanged from its value before the administration of pancuronium. There was no physiologically important change of any cardiovascular parameter in the five patients who received no drug, although there was, in fact, a small, statistically significant decrease of heart rate at 5 and 10 minutes.

DISCUSSION

The advantages of our technique for studying the cardiovascular effects of muscle relaxants have been discussed in a previous paper (Kennedy and Kelman, 1970). In the present study, as in previous investigations, we have avoided the effects of surgical stimulation, and have maintained the arterial Pco₂ constant at a level typically found during artificial ventilation of anaesthetized patients.

The present investigation is, to our knowledge, the only study of the effects of pancuronium on cardiac output in man, although this has been investigated in dogs by Smith, Proctor and Spence (1970).

Previous studies of the effects of pancuronium on heart rate and arterial blood pressure in man have been conflicting. Baird and Reid (1967) found that it had little effect on arterial blood pressure and heart rate; McDowell and Clarke (1969) showed that it had little effect on heart rate before the injection of pancuronium was 82 beats/min (cf. 58 beats/min in the present study). The increase of heart rate in these patients was only 8 per cent, while the increases of mean arterial blood pressure and of cardiac output were only 3 per cent and 5 per cent, respectively. This finding strongly supports the hypothesis outlined in the previous paragraph.

The fact that pancuronium has no significant effect on the calculated total peripheral resistance suggests that this drug has little or no ganglion-blocking activity. This is in keeping with the finding of Buckett and associates (1968) that the ganglion-blocking activity of pancuronium on the guineapig ileum and on the cat nictitating membrane is much less marked than that of hexamethonium.

ACKNOWLEDGEMENTS

We are indebted to Organon Laboratories Ltd for a supply of pancuronium bromide. We also thank Mr D. W. Blair, Mr N. A. Matheson, Mr G. E. Mavor and Mr W. Michie for permission to study patients under their care.

REFERENCES


**EFFETS CARDIO-VASCULAIRES DU PANCURONIUM CHEZ L’HOMME**

**SOMMAIRE**

Nous avons étudié les effets du bromure de pancuronium (administre à la dose de 0.07 mg/kg de poids corporel) sur la fréquence cardiaque, la pression artérielle moyenne, le débit cardiaque et la résistance périphérique totale (évaluée indirectement par calcul) chez dix malades soumis à une inspiration assistée et anesthésiés à l’aide de protoxyde d’azote à 60%, dans de l’oxygène, avec administration de phénopéridine (à raison de 1 mg/15 kg de poids corporel) en plus. La tension en gaz carbonique Pco₂ à la fin de l’onde respiratoire a été maintenue constante à un niveau de 30 ± 2 mm Hg. On a noté un accroissement marqué et statistiquement significatif de la fréquence cardiaque de 25%, environ, accompagné d’une élévation moindre, mais encore statistiquement significative, du débit cardiaque et de pression artérielle moyenne. La résistance périphérique totale est demeurée inchangée, ce qui indique que le pancuronium ne possède qu’une faible activité ganglionnaire.

**WIRKUNG VON PANCURONIUM AUF DAS KARDIOVASKULÄRE SYSTEM DES MENSCHEN**

**ZUSAMMENFASSUNG**

Wir untersuchten die Wirkungen des Pancuronium-Bromids bei zehn künstlich beatmeten Patienten; die Narkose wurde mit 60% Lachgas in Sauerstoff plus Phenoperidin (in einer Dosis von 1 mg/kg Körpergewicht) durchgeführt. Das Pco₂ zum Zeitpunkt des Ausatmungs endes wurde mit 30 ± 2 mm Hg konstant gehalten. Es fand sich ein deutlicher und statistisch signifikanter Ansteig der Herzfrequenz um etwa 25 Prozent, begleitet von einem geringeren, jedoch immer noch statistisch signifikanten Anstieg des Herzschlagvolumens und mittlerem arteriellen Blutdruck. Der periphere Gesamtwiderstand blieb unverändert. Woraus geschlossen wird, daß Pancuronium kaum eine Ganglion blockierende Wirkung hat.

**EFECTOS CARDIOVASCULARES DEL PANCURONIO EN EL HOMBRE**

**RESUMEN**

Hemos investigado los efectos del bromuro de pancuronio (0.07 mg/kg peso corporal) sobre la frecuencia cardíaca, presión sanguínea arterial media, rendimiento cardíaco y resistencia periférica total calculada en diez pacientes ventilados artificialmente, anestesiados con óxido nitroso al 60% en oxígeno más fenoperidina (1 mg/15 kg peso corporal). La Pco₂ ventilatoria final fue mantenida constante a 30 ± 2 mm Hg. Hubo un marcado incremento estadísticamente significativo de la frecuencia cardíaca de aproximadamente el 25 por ciento, acompañado por incrementos menores, pero todavía estadísticamente significativos, del rendimiento cardíaco y presión sanguínea arterial media. La resistencia periférica total no fue modificada, lo cual indica que el pancuronio tiene poca actividad bloqueadora ganglionar.