METHOHEXITONE AND THIOPENTONE
Response to stimuli and incidence of some side effects

BY
C. T. BARRY, JOANNA GUY, VALERIE GOAT AND A. S. BUCHAN

SUMMARY
Over 600 patients were anaesthetized for minor urological procedures with either methohexitone or thiopentone, to compare the analgesic or antianalgesic effects of these drugs. Movement in response to preparation with a cold solution was more frequent after methohexitone. After 200 cases the dosage was increased by 20 per cent so as to reduce the incidence of this response, and this increased dose was given to the next 400 patients. This caused an increase in the proportion of patients responding to cold; there was also a marked increase in the incidence of respiratory depression and of hiccups; hiccups were linked with passive ventilation of the lungs. The incidence of arterial hypotension and respiratory depression was the same with both drugs. There was no significant difference in the incidence of movement during the passage of a cystoscope or bouginage, perhaps because by then the patient had received some inhalation anaesthesia.

A previous report (Barry, Lawson and Davison, 1967), in which methohexitone and thiopentone, followed by an inhalation supplement, were compared in anaesthesia for cystoscopy, confirmed the finding of other workers that consciousness returned sooner after methohexitone. It seemed during this work that there were fewer responses to peripheral stimuli after methohexitone, and a further investigation was undertaken to compare the analgesic (or antianalgesic) effect of these agents. Patients who have just lost consciousness after an intravenous barbiturate can still respond to peripheral stimuli, and we have compared the responses to two such stimuli: (1) the response to preparation of the external genitalia with a cold solution (this was assessed before the start of the inhalation anaesthetic); and (2) the response to cystoscopy or bouginage which took place after the start of the inhalation anaesthetic. It was also thought that if peripheral stimuli were less likely to cause responses after one or other of these agents, then that agent would be followed by a higher proportion of patients in whom anaesthesia could be satisfactorily maintained with nitrous oxide and oxygen only. All except a few patients were given this inhalation after their barbiturate induction and if the addition of halothane was required to produce satisfactory conditions this was noted. Observations were also made on the incidence of hiccups, respiratory depression and arterial hypotension.

PATIENTS AND METHODS
The drugs were given in a ratio of 1 unit of methohexitone to 3 units of thiopentone, these doses being found equivalent in the production of unconsciousness. Solutions were prepared as described by Green and associates (1963), containing 1 per cent methohexitone or 3 per cent thiopentone, and were brought to the same colour by the addition of riboflavine. The solutions were prepared by our pharmacy and designated by code letters, so that the anaesthetist did not know which agent he was giving.

The investigation was carried out on outpatients who were to undergo cystoscopy or bouginage. Some in-patients also attended and...
were included unless concurrent pathology made this inadvisable. Premedication consisted of atropine 0.6 mg alone. Patients on sedatives were excluded. Some of our categories may be affected by the fact that some 10 per cent of these patients had a high degree of bladder sensitivity; they attended every two, three or four months and, as this investigation lasted eighteen months, we have assumed that they have been evenly distributed between the drugs (see "Patients needing halothane", page 967).

The first solution to be given was chosen by tossing a coin; it was given to the first two patients, to one at a rate of 1 ml in 1 second, to the other at a rate of 1 ml in 3 seconds, the order being determined by tossing the coin again. The next two patients received the other solution in the same order of rates. This order was continued until the end of the list. As there was very little difference between the effects of the two rates of injection they will be considered together except where otherwise stated.

For the first 200 patients the dose of solution was 1 ml/stone (6.35 kg) body weight, corresponding to methohexitone 1.57 mg/kg and to thiopentone 4.72 mg/kg. The patients in the "rapid" group received methohexitone 10 mg or thiopentone 30 mg/sec; those in the "slow" group received methohexitone 3.3 mg or thiopentone 10 mg/sec. As soon as the patients became unconscious a large piece of cotton wool soaked in a cold aqueous solution of cetrimide or hexachlorophene was used to prepare the external genitalia for cystoscopy and some patients responded to this by movement. The usual response was a twitch of the adductor muscles or dorsiflexion of one or both feet; after this had been noted inhalation of nitrous oxide and oxygen was started. Sometimes the movement interfered with the procedure and it became necessary to add halothane to the gases (see next paragraph). Spontaneous movements were not looked for, as this study was concerned with movement in response to skin preparation or instrumentation. Movements were sometimes seen in response to putting a mask on the patient's face or to holding the chin up. These were not recorded unless they were sufficiently marked to require the addition of halothane to the nitrous oxide and oxygen mixture. The injections were give by one of three anaesthetists (J.G., V.G., or A.S.B.). The inhalation (nitrous oxide with 25 per cent oxygen) was given by the same anaesthetist (C.T.B.) to all patients except a few patients for bouginage early in the series; it was found that reasonable operating conditions could not be obtained without an inhalation supplement.

The mask was applied as soon as the response to cold on the skin had been noted. If the patient was breathing spontaneously, this was allowed to continue. If the patient was apnoeic for longer than 3 seconds, passive ventilation was started. All patients being ventilated in this way were counted as having respiratory depression so that the incidence of this side effect is much higher than that found by other workers (Whitwam and Manners, 1962; Dundee, 1963). If it became clear at the start of the procedure that anaesthesia could not be managed on nitrous oxide and oxygen alone halothane was added and the patient classed under the heading "halothane late". In others a satisfactory start on nitrous oxide alone became unsatisfactory later, sometimes for no obvious reason, sometimes when the bladder was being distended. The patients in whom anaesthesia became too light at least 2 minutes after the start of the injection were classed under the heading "halothane late". In all cases the decision to give halothane was made by the anaesthetist giving the inhalation. The anaesthetist who had given the injection measured the blood pressure by palpation every minute for 5 minutes using a mercury sphygmomanometer and a cuff round the left arm; a reading had been taken before starting the intravenous injection.

After the first 200 patients an interim survey was made and it seemed that the incidence of movement after the cold solution on the skin was unacceptably high; it was decided to increase the doses by 20 per cent in the hope that fewer patients would respond in this way; this response to cold was not thought of as belonging to the mostly spontaneous "excitatory phenomena" first described by the Belfast school, and shown to have a higher incidence when the dose is increased (Dundee et al., 1961; Young and Whitwam, 1964; Barron and Dundee, 1967). The same solution, with two changes of coding, was used for the next 400 patients in a dose of 1.2 ml/stone (6.35 kg) body weight. This corresponded to
methohexitone 1.88 mg/kg or to thiopentone 5.66 mg/kg. The rates of administration were not changed: 1 ml in 1 or in 3 sec.

RESULTS

Table I shows that the patients receiving these different drugs and doses compared well in respect of age. The proportion of females was greater in the groups receiving the larger doses but this is not thought to affect the results reported except for the response to cold. This is shown in figure 1 where the sexes have been separated, as men respond more frequently than women. Table I also shows that the rates of injection have been evenly distributed between the different groups.

<table>
<thead>
<tr>
<th>Table I</th>
<th>Distribution of age, sex and rate of injection.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Methohexitone</td>
</tr>
<tr>
<td>Group totals</td>
<td>113</td>
</tr>
<tr>
<td>Doses (mg/kg)</td>
<td>1.57</td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>Under 60</td>
<td>62 (55)</td>
</tr>
<tr>
<td>Over 60</td>
<td>51 (45)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>86 (76)</td>
</tr>
<tr>
<td>Female</td>
<td>27 (24)</td>
</tr>
<tr>
<td>Rate</td>
<td></td>
</tr>
<tr>
<td>Fast</td>
<td>54 (48)</td>
</tr>
<tr>
<td>Slow</td>
<td>59 (52)</td>
</tr>
</tbody>
</table>

Figures in brackets are percentages of group totals.

Response to the application of a cold solution (fig. 1).

Small dose (1 ml/6.35 kg). After methohexitone, men responded more often than women; 28 of 86 men (32 per cent), against 7 of 27 women (26 per cent). The difference between proportions is 6, smaller than its standard error of 9, but the use of an angular transformation of the proportions with analysis of variance gives \( P < 0.05 \). The response was more frequent after methohexitone than after thiopentone; this is not significant.

Large dose (1.2 ml/6.35 kg). Response to cold was more frequent than with the small dose. This was especially marked in men receiving methohexitone, as with the small dose. 28 of 86 men (32 per cent) responded after the small dose, but 86 of 162 (53 per cent) responded to cold after the large dose of methohexitone. Although the difference between proportions (21) is nearly four times its standard error (5.3) it may not be justifiable to claim significance for this result because of lack of randomization in time (see Discussion). Response to cold was more frequent in men than in women. Considering both drugs together: 145 of 314 men (46 per cent) receiving the large doses moved after preparation, and 42 of 141 women (30 per cent). The difference between proportions is 16, three times its standard error of 4.8; angular transformation of the proportions as above gives \( P < 0.01 \).

Both doses and sexes together. Response to cold was more frequent after methohexitone: 148 of 353 patients responded (42 per cent), while after thiopentone 103 of 324 responded (32 per cent). Angular transformation of the proportions gives \( P < 0.01 \), confirmed by the difference between proportions (10) being nearly three times its standard error of 3.6.

Response to the passage of an instrument (tables II, III, IV).

The response recorded here was very similar to the response to cold. Usually the movement was slight but on occasion could interrupt the procedure. These marked responses were rare.
because (except for a few early cases: table IV, D) all these patients had at least 30 seconds of inhalation anaesthesia after the preparation and before instrumentation.

The only appreciable difference found in table II was that between men receiving large doses. Methohexitone 1.88 mg/kg was given to 162 (77 and 85) men of whom 52 (26 and 26) responded to passage of the instrument (32 per cent); 155 (77 and 78) men received the large dose of thiopentone, of whom 36 (18 and 18) responded (23 per cent). The difference between proportions is 9, less than twice the standard error of 5, and therefore just fails to achieve significance at the 5 per cent level.

<table>
<thead>
<tr>
<th>Dose</th>
<th>Methohexitone (1.57 mg/kg)</th>
<th>Thiopentone (4.72 mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Rate</td>
<td>Fast</td>
<td>Slow</td>
</tr>
<tr>
<td>Number</td>
<td>43</td>
<td>11</td>
</tr>
<tr>
<td>Respond</td>
<td>16 (37)</td>
<td>1 (10)</td>
</tr>
<tr>
<td>Total</td>
<td>113; responding 39 (34)</td>
<td></td>
</tr>
</tbody>
</table>

Figures in brackets are percentages of group totals. These results were obtained after the start of the inhalation anaesthetic.

These results suggested that women responded less frequently to instrumentation than did men, and that there were fewer responses after increasing the dose, but, perhaps because the groups considered were too small, the results were not significant. The groups have been brought together in table III, putting the two drugs and the two rates of injection together and comparing only (1) frequency of response to instrumentation after the two different dose levels and (2) frequency of response in men and in women. The results in table III were:

1. 37 per cent of the men responded after the small dose, 28 per cent after the large dose; while this difference is significant at the 5 per cent level, here again comparisons between the dose levels may be invalidated by inadequate randomization in time. If women are added the difference is no longer significant.

2. After the small dose 12 per cent of the women responded to the instrument, and 37 per cent of the men. The difference between proportions (25) is four times greater than its standard error (5.8) showing a high degree of significance. After the large dose more women responded than after the small dose, but there are still more men

<table>
<thead>
<tr>
<th>Patients needing halothane.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methohexitone</td>
</tr>
<tr>
<td>Group totals</td>
</tr>
<tr>
<td>Dose (mg/kg)</td>
</tr>
<tr>
<td>A. Not requiring halothane</td>
</tr>
<tr>
<td>(30)</td>
</tr>
<tr>
<td>B. Requiring halothane early</td>
</tr>
<tr>
<td>(24)</td>
</tr>
<tr>
<td>C. Requiring halothane late</td>
</tr>
<tr>
<td>(37)</td>
</tr>
<tr>
<td>D. No inhalation</td>
</tr>
<tr>
<td>(9)</td>
</tr>
</tbody>
</table>

Figures in brackets are percentages of group totals.
responding than women (28 and 18 per cent) and this is significant at the 5 per cent level.

Patients needing halothane (table IV).

As seen in Methods (page 964) a note was kept of whether the anaesthesia could be satisfactorily maintained using nitrous oxide alone, or whether halothane had to be added. These proportions are shown in table IV, and while none of these differences is significant, there may be a trend in favour of thiopentone, assuming that patients with high bladder sensitivity (see Patients and Methods, page 964) were evenly distributed. The time at which “halothane late” was given was noted, and it may be of interest that this time was very similar with both drugs, suggesting that they leave the brain at the same time (fig. 2). This survey of the proportions responding to the passage of the instrument leaves the impression that while none of the differences is significant there is a trend towards more frequent responses after methohexitone, and a more frequent need for halothane to provide smooth anaesthesia.

Percentage of patients given halothane late

<table>
<thead>
<tr>
<th>Time in minutes from the start of the injection</th>
<th>Methohexitone</th>
<th>Thiopentone</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fig. 2

Time at which halothane was needed by patients in table IV, C. The two dose levels are considered together.

Side effects.

Hiccup (table V; figs. 3, 4). As reported by most previous workers this side effect was more frequent after methohexitone (table V); the higher frequency after methohexitone is highly significant both at low doses ($P=0.012$ exact test) and at high doses ($\chi^2 11.47$, $P<0.001$). The actual incidence was higher after the higher doses; table V shows 8 per cent with hiccup after the small dose of methohexitone, and 18 per cent after the large dose (difference between proportions: 9, SE 3.7, $P<0.05$).

Table V

<table>
<thead>
<tr>
<th>Doses and incidence of hiccup.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Group totals</td>
</tr>
<tr>
<td>Doses (mg/kg)</td>
</tr>
<tr>
<td>Hiccup</td>
</tr>
</tbody>
</table>

Figures in brackets are percentages of group totals.

Hiccup late and rate of injection

<table>
<thead>
<tr>
<th>Methohexitone</th>
<th>Thiopentone</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.57 mg/kg (113)</td>
<td>1.88 mg/kg (215)</td>
</tr>
<tr>
<td>4.72 mg/kg (109)</td>
<td>5.66 mg/kg (195)</td>
</tr>
</tbody>
</table>

Fig. 3

The dots represent patients with hiccup. This was more frequent after methohexitone and after larger doses but no significant difference was found between the two rates of injection.

Hiccup late and passive ventilation

<table>
<thead>
<tr>
<th>Methohexitone</th>
<th>Thiopentone</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.57 mg/kg (113)</td>
<td>1.88 mg/kg (215)</td>
</tr>
<tr>
<td>4.72 mg/kg (109)</td>
<td>5.66 mg/kg (195)</td>
</tr>
</tbody>
</table>

Fig. 4

Each dot represents a patient with hiccup, and this is more frequent among patients whose lungs were passively ventilated. Group totals are less than in other figures because some patients were managed without inhalation (table IV, D) and some records do not show whether the patient was ventilated or not; none of these had hiccup.
Barron (1968) and Lind and Roland (1969) stated that hiccup was more frequent in patients receiving methohexitone rapidly; this was not confirmed in this study (fig. 3), but another possible cause of hiccup was noted and seems worth reporting; it is passive ventilation (fig. 4).

The first column in figure 4 refers to 94 patients who were given the small dose of methohexitone. Forty-six of these breathed spontaneously and of these 3 had hiccup (6 per cent). The remaining 48 patients were ventilated and of these 6 (12 per cent) had hiccup. The difference between these proportions is not greater than its standard error.

The next shows the patients who were given the large dose of methohexitone. There were 228 with complete records, and of these 44 patients breathed spontaneously. None of these had hiccup. The remaining 184 patients were all ventilated and of these 45 (24 per cent) had hiccup. Hiccup was less frequent after thiopentone, even after passive ventilation, but figure 4 shows that after the large dose of thiopentone there was more hiccup in the ventilated patients; this difference is not significant.

Respiratory depression. The incidence of this side effect, which, as defined in this paper, signifies passive ventilation, is shown in table VI. Increasing the dose caused a significant increase in respiratory depression.

\[
\begin{array}{ccc}
\text{Methohexitone} & \text{Thiopentone} \\
\hline
\text{Doses (mg/kg)} & 1.57 & 1.88 & 4.72 & 5.66 \\
\text{Rate} & \text{Fast} & \text{Slow} & \text{Fast} & \text{Slow} \\
\text{Group totals} & 45 & 49 & 111 & 117 & 42 & 45 & 105 & 104 \\
\text{Respiratory depression} & 24 & 24 & 89 & 95 & 25 & 23 & 90 & 75 \\
\text{Figures in brackets are percentages of group totals.} \\
\end{array}
\]

Arterial hypotension. The maximum fall occurring during the period of observation (not more than 5 minutes) was noted and after comparison very little difference could be detected between the hypotensive effects of these agents (table VII). The only differences found were in the incidence of falls in blood pressure of from 10 to 20 mm Hg. These were more frequent after the small dose of thiopentone (20 per cent), but the difference between proportions (8.5) is less than twice its standard error (4.9) and is not significant.

\[
\begin{array}{ccc}
\text{Fall of systolic pressure} & \text{Between 10 and 40 mm Hg} & \\
\hline
\text{Methohexitone} & 113 & 240 & 109 & 215 \\
\text{Thiopentone} & 1.57 & 1.88 & 4.72 & 5.66 \\
\text{Doses (mg/kg)} & 10-20 & 13 (11.5) & 49 (20.4) & 22 (20) & 47 (22) \\
\text{Fall of systolic pressure} & 20-40 & 29 (25.6) & 49 (20.4) & 25 (23) & 56 (26) \\
\text{Fall of systolic pressure} & >40 & 14 (12.4) & 30 (12.5) & 12 (11) & 26 (12) \\
\end{array}
\]

Falls of blood pressure between 10 and 20 mm Hg were also more frequent after large doses of methohexitone (20 per cent) than after the small doses (11 per cent). The differences between proportions (9) is more than twice its standard error (4) and P<0.05. As with all comparisons between the two dose levels in this study, this can be criticized on the grounds of inadequate randomization in time.

The similarity between the hypotensive effect of the two drugs is especially striking when the incidence of falls in blood pressure of more than 40 mm Hg is considered (table VII; fig. 5). The chi-square test confirms this, both chi-squares being virtually zero with a continuity correction.

\[
\begin{array}{ccc}
\text{Patients with a fall in blood pressure \geq 40 mm Hg} & \\
\hline
\text{Methohexitone} & 113 & 240 & 109 & 215 \\
\text{Thiopentone} & 1.57 & 1.88 & 4.72 & 5.66 \\
\end{array}
\]

Incidence of arterial hypotension was not influenced by drug or by dose.
Halothane, when it was given, had no effect on the blood pressure, thus confirming the finding of Whitwam and Young (1964), and the only effect noted after surgical stimuli was a rise in blood pressure. 

**Figure 6**

Laryngeal spasm was more frequent after thiopentone.

**Laryngeal spasm** (fig. 6). This was more frequent after thiopentone and with the larger doses the difference with methohexitone is significant. With small frequencies in some cells as in this case it is better to calculate exact probabilities; at the low dose level the difference between the drugs is not significant (P = 0.31). At high doses the difference is significant (P = 0.0096).

**DISCUSSION**

*Are the doses equivalent?*

This question is important in the assessment of the more frequent response to cold after methohexitone. If the doses are equivalent then methohexitone is less effective than thiopentone at blocking certain peripheral stimuli, for instance cold. If the doses are not equivalent then the difference reported may be due to the patients being given relatively more thiopentone than methohexitone. The ratio of equivalent dosage has been given by some workers as 1:3 and by others as 1:2.5. Dundee (1963) states that the amount of thiopentone equivalent to 1 unit of methohexitone is between 2.5 and 4 units; Green and Jolly (1960) give a range of between 2 and 4.

A ratio of 1:3 was chosen for this investigation because in this ratio these drugs cause very similar effects on the respiration and blood pressure and this seems a reliable indication of equivalence. With this ratio there was more frequent response to cold after methohexitone. Would reducing the amount of thiopentone produce an equal incidence of response to cold? This can be found by comparing the response to cold after methohexitone 1.88 mg/kg and after thiopentone 4.72 mg/kg. This is a ratio of 1:2.5, and it can be seen (fig. 1) that the difference in the response to cold is even greater than with a ratio of 1:3 (53:28 per cent). As will be seen, this marked difference can be criticized on the grounds of inadequate randomization in time; it may also be objected that a large dose (frequent response) of methohexitone is being compared with a low dose (less frequent response) of thiopentone, nevertheless it remains that when the thiopentone is reduced to 2.5 units instead of 3 to each unit of methohexitone the higher incidence of response to cold after methohexitone is more marked. On the other hand, with this ratio of 1:2.5 there is a marked difference in the incidence of respiratory depression: 80 per cent after methohexitone 1.88 mg/kg, 55 per cent after thiopentone 4.72 mg/kg. This gives an example of the difficulties of working out equivalent doses of these drugs. It can be stated, however, that in doses having the same effect on the breathing and the blood pressure, methohexitone was less effective than thiopentone at blocking the sensation of cold and, by this standard, did not give deeper anaesthesia, as some authors had thought it did (Green and Jolly, 1960).

**Effect of increasing the dose.**

Previous workers have shown that increasing the dose of methohexitone increased the incidence of some side effects (Dundee et al., 1961; Young and Whitwam, 1964; Barron and Dundee, 1967). Our patients receiving larger doses responded more frequently to cold, had more respiratory depression and had more hiccup. All these differences are statistically significant; it appears, however, that significance should not be claimed for these results, because of insufficient randomization in time. The small doses were given at the early part of the trial, during the winter 1966/67; the larger doses were given later, during the summer 1967 and the following winter; variables may have been introduced. The patient population
did not seem to change. It is difficult to imagine a variable factor causing an increase in the response to cold from 32 to 53 per cent, and at the same time causing an increase in respiratory depression from 50 to 80 per cent; the intervention of two variable factors does not seem very likely, especially as the workers quoted at the beginning of this section have all reported an increase in some side effects when the dose of methohexitone is increased. As the increase in response to certain stimuli when the dose is increased is of practical importance, and as the same can be said of the increase in respiratory depression, as we believe that this is followed by an increase in hiccup, we felt that these findings should be reported and that the reader can judge their significance.

Hiccup and passive ventilation.

Hiccup has often been described as a side effect of methohexitone anaesthesia. The incidence reported varies. Wyant and Chang (1959) reported 12 per cent after thiopentone and 41 per cent after methohexitone. They gave no details about ventilation but indicated a high incidence of apnoea. Wyant and Barr (1960) found no hiccup. They injected slowly but gave no details about ventilation. Taylor and Stoelting (1960) found hiccup in 2.5 per cent of their patients; they reported apnoea in 17 per cent, who needed ventilation for not more than 3 minutes. Dundee and others (1961) made the interesting observation that the incidence of hiccup (and other side effects) increased when the dose was increased; this was confirmed by Young and Whitwam (1964). Dundee and his colleagues gave no details about passive ventilation; Young and Whitwam ventilated all their patients and found up to 38 per cent hiccup in men given 2.2 mg/kg.

In this study the incidence of hiccup increased when the dose was increased. A possible explanation for this could be passive ventilation. Increasing the dose caused a marked increase in respiratory depression which as defined in this paper means a marked increase in passive ventilation, and this is accompanied by a marked increase in hiccup. It is noteworthy that where there was no passive ventilation, increasing the dose did not increase the hiccup. Perhaps this factor explains the variations in the reports quoted above.

Another factor has been suggested. Barron (1968) studied the effect of different rates of administration. Methohexitone was given in a dose of 1.6 mg/kg at rates of 1 ml/10 sec, 1 ml/5 sec, 1 ml/3 sec and 1 ml/1 sec, to 50, 35, 30 and 50 patients respectively. A highly significant difference in the incidence of cough and hiccup (no separate figures are given for these two side effects) was found in the very fast (1 ml/sec) and the very slow (1 ml/10 sec) groups. The incidence of marked respiratory depression, needing respiratory assistance, was the same (4 per cent) in these two groups, so that our finding of a relationship between passive ventilation and hiccup is not apparent in Barron's results. Lind and Roland (1969) observed a significant rise in the incidence of hiccup when the rate of injection was increased. They gave a dose of 2 mg/kg and their fast rate of injection was 4 mg/sec, producing a 50 per cent incidence of hiccup; our fast rate for methohexitone was 10 mg/sec and produced 9 per cent hiccup for the small dose and 21 per cent for the large dose. The slow rate used by Lind and Roland was 1 mg/sec and produced 20 per cent incidence of hiccup; ours was 3.3 mg/sec and gave 7 per cent hiccup for the small dose, 16 per cent for the large dose. It would be interesting to know how often these workers found it necessary to assist ventilation in their patients, but it may be supposed that their slow rate, which was slower than ours, would cause less respiratory depression. This should imply a lesser need for respiratory assistance, and therefore less hiccup.

It seems reasonable to conclude that the best results with these drugs are obtained by giving them very slowly, aiming at a rate of 1-2 mg/sec for methohexitone and avoiding passive ventilation. This will mean the use of smaller doses with fewer responses to instrumentation, and less respiratory depression with less hiccup. None of the factors considered here suggests any strong evidence that one of these agents should be preferred to the other. Thiopentone may be slightly more potent and preferable for resistant patients. There remains an important reason for choosing methohexitone, namely that it is more rapidly removed from the plasma (Brand et al., 1963) and this should reduce the prolonged post-operative antanalgesia which has been predicted.
and demonstrated after thiopentone (Clutton-Brock, 1960, 1961; Dundee, 1960). Whilst this may not matter for the type of case considered in this study, the use of methohexitone could be expected to reduce the severity of postoperative pain and the need for analgesics after major surgery.

ACKNOWLEDGMENTS

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REFERENCES


METHOHEXITONE ET THIOPENTONE:

REACTION AUX STIMULATIONS ET INCIDENCE DE CERTAINS EFFETS SECONDAIRES

SOMMAIRE

Plus de six cent patients ont été anesthésiés au méthohexitone ou thiopentone pour des interventions urologiques mineures et on compara l'effet analgésique ou anti-analgésique de ces médicaments. Des mouvements en réaction à la stimulation avec une solution froide furent plus fréquents après méthohexitone. On décida après deux cent cas d'augmenter la posologie de 20% pour réduire la fréquence de cette réaction, et cette dose plus élevée fut administrée aux quatre cent patients suivants. Ce qui causa une augmentation de la proportion de patients réagissant au froid; il y eut également une augmentation marquée de la fréquence de dépression respiratoire et hoquet; ce dernier s'associa à une ventilation passive des poumons. L'incidence d'hypotension artérielle et dépression respiratoire fut identique avec les deux médicaments. Il n'y eut pas de différence significative dans la fréquence des mouvements lors du passage d'un cystoscope ou du bouginage, peut-être en raison du fait que les malades avaient à ce moment déjà reçu une certaine dose d'anesthésique par inhalation.

METHOHEXITAL UND THIOPENTAL:

REAKTION AUF STIMULI UND AUFGETRETENE NEBENWIRKUNGEN

ZUSAMMENFASSUNG

METOHEXITONA Y TIOPENTONA:
RESPUESTA A ESTIMULOS Y FRECUENCIA
DE ALGUNOS EFECTOS SECUNDARIOS

RESUMEN
Más de seiscientos pacientes fueron anestesiados para intervenciones urológicas menores con metohexitona o tiopentona para comparar los efectos analgésicos o anti-analgésicos de estos medicamentos. El movimiento en respuesta a la preparación con una solución fría fue más frecuente después de metohexitona. Después de doscientos casos, la dosificación fue incrementada en un 20 por ciento para reducir la frecuencia de esta respuesta y esta dosis incrementada fue administrada a los cuatrocientos pacientes siguientes. Esto causó un incremento en la proporción de pacientes que responden al frío; también hubo un acusado incremento en la frecuencia de depresión respiratoria e hipo; el hipo estaba relacionado con la ventilación pasiva de los pulmones. La frecuencia de hipotensión arterial y depresión respiratoria fue igual para ambos medicamentos. No hubo diferencia significativa en la frecuencia de movimiento durante el paso de un cistoscopio o dilatación con bujía, tal vez porque para entonces el paciente había recibido alguna anestesia por inhalación.

SECTION OF ANAESTHETICS, MANCHESTER MEDICAL SOCIETY

Meetings during the coming session of the Section will be held at 8.15 p.m. in the University Refectory.

1971
October 14  Presidential Address: Dr M. W. Johnstone, “Anaesthetics Today”
November 11  Professor J. A. Thornton, “The Pre-operative Visit”
December 1  Professor J. G. Robson, Dr P. J. Tomlin, “A College of Anaesthetists?—A Debate”

1972
January 13  Professor A. M. Barrett (subject to be announced later)
February 10  Professor J. Parkhouse (subject to be announced later)
March 9  Registrars’ Papers (see below)
April 13  Joint Meeting with the Liverpool Society of Anaesthetists, to be held in Manchester. Dr M. Swerdlow, “A Clinical Trial of a new Intravenous Anaesthetic, CT1341”. Dr J. E. Utting (subject to be announced later)

REGISTRAR’S PRIZE. The Section of Anaesthetics of the Manchester Medical Society will award a prize of £50 annually, donated by ICI Limited, for a paper reporting research undertaken mainly during employment as an anaesthetist at a hospital in the area. Selected entries will be read to the Section at a meeting in March 1972 and must be submitted to the Secretary of the Section by January 1, 1972. Details may be obtained from the Secretary, Manchester Medical Society, The University, Manchester M13 9PL.