METHOHEXITONE 5 PER CENT: EVALUATION USING AN EXPERIMENTAL PAIN GENERATOR

BY

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SUMMARY

Doses of methohexitone (Brietal) of 50 or 75 mg were administered intravenously to 125 healthy volunteers of both sexes. The duration of unconsciousness and the time until there was a response to painful and then verbal stimuli were recorded. The lower dose level was insufficient to allow the performance of any surgical procedure. The higher dose produced anaesthesia for a clinically useful period of time in some volunteers but this occurred at the expense of significant airway obstruction or other respiratory complication in 24 of the 50 volunteers.

There are many minor outpatient therapeutic and diagnostic procedures productive of considerable discomfort for a brief period of time. Examples of these are incision and drainage of superficial abscesses, single tooth extractions, myringotomies, closed fracture reduction or electroshock therapy. It would be desirable to have available a drug that could be administered intravenously and which would be capable of producing transient but profound anaesthesia for a brief period of time. Methohexitone is an ultrashort-acting, oxybarbiturate which was introduced as an induction agent in 1957 (Stoelting, 1957) and is currently used in a 1 per cent concentration. A mean induction dose of 1.2 mg/kg has been recommended for this purpose (Barron and Dundee, 1962).

It was proposed to make methohexitone available in a prepackage unit containing 1 ml of a 5 per cent solution. It was proposed that this prepackaged unit be made available to physicians and dentists for use in ambulatory patients for outpatient procedures.

The purpose of this study is to evaluate the ability of methohexitone in this concentration and dosage range to produce anaesthesia of such duration and depth that brief surgical and diagnostic manipulations may be possible.

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METHOD

Methohexitone 5 per cent (50 mg and 75 mg) was studied in two groups of volunteers (table I). The procedure was identical in both groups and at both dose levels.

To eliminate variables such as length of surgical procedure and degree of surgical stimulation, an experimental electrical pain generator was used to provide a reproducible stimulus. This pain generator consisted of an inductorium with the secondary coil mounted on an electrically driven worm gear. Interrupted direct current was produced through the circuit breakers of the inductorium. This was adjusted to produce a faradic current of 60 pulses/sec. This current was directed across the earlobe of the subject by means of an earpiece (Siker, Wolfson and Stewart, 1966). Volunteers were unpremedicated and had fasted for at least 3 hours. Following measurements of blood pressure, pulse and respirations, the electrical stimulator was applied to the ear, and the instrument turned on. The volunteer was given a hand switch and told to stop the machine when the painful stimulus became intolerable. The same level of electrical stimulation was then used following the administration of the drug.

At this time each volunteer received either 50 or 75 mg of methohexitone 5 per cent intravenously. Injection was made through a 20-gauge needle as rapidly as the lumen of this needle would allow. The time at which the subject failed
to respond to verbal command was noted. After 15 seconds, the electrical stimulus was again applied for 2 seconds. This stimulation was repeated every 15 seconds until a response was obtained. This interval is listed in table I as "First response".

Following this, again at intervals of 15 seconds, each volunteer was asked a question that required a verbal response, such as "What is your name?", "What is your address?" etc. The time at which they first made a correct coherent verbal reply was recorded. This interval is referred to in table I as "First verbal".

The subject was then encouraged, at 15-second intervals, to sit up. The time at which he was able to do this without assistance was noted. This interval is referred to as "Sitting" in table I.

The duration of unconsciousness was taken as the interval between the loss of verbal response and the time at which the response could again be obtained.

Blood pressure, pulse and respirations were monitored throughout the test period.

RESULTS

Male group—50 mg.
There were 24 volunteers in this group with an average age of 22 years and average weight of 74 kg. In this group 23 did not lose consciousness at any time following injection of 1 ml of 5 per cent methohexitone. The one volunteer who did go to sleep first responded at 1.5 minutes, first responded verbally at 3 minutes and sat without assistance at 4.25 minutes. The remaining 23 volunteers were aware that they had been given a hypnotic drug, became drowsy, but never lost contact and were able to sit within an average of 3 minutes. No attempt was made to demonstrate analgesia to electrical stimulation in those volunteers who did not lose consciousness. Five of this group noted pain on injection, which was probably due to venous irritation. In one volunteer there was a pronounced local erythematosus reaction.

Male group—75 mg.
There were 26 volunteers in this group with an average age of 24 and average weight of 80 kg. Seven did not lose consciousness. The remainder were unconscious for an average of 1 minute. The average time until the first response to painful stimulus was 28 seconds and the average time until they were first able to answer a question coherently was 1.4 minutes. The average time

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### Table I

Results of injection of methohexitone in doses of 50 or 75 mg in 125 volunteers.

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (yr)</th>
<th>Weight (kg)</th>
<th>Duration of unconsciousness</th>
<th>First response</th>
<th>First verbal</th>
<th>Sitting</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MALE</strong> 50 mg N=24</td>
<td>Average 22</td>
<td>74</td>
<td>2.5*</td>
<td>1.5*</td>
<td>3*</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Range 21–28</td>
<td>55–109</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>75 mg N=26</td>
<td>Average 24</td>
<td>80</td>
<td>1</td>
<td>0.46</td>
<td>1.36</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Range 21–29</td>
<td>68–109</td>
<td>0–2.75</td>
<td>0–1.75</td>
<td>0–3</td>
<td>2.45</td>
</tr>
<tr>
<td><strong>FEMALE</strong> 50 mg N=25</td>
<td>Average 25.6</td>
<td>58</td>
<td>0.9</td>
<td>0.6</td>
<td>1.44</td>
<td>4.4</td>
</tr>
<tr>
<td></td>
<td>Range 21–43</td>
<td>44–82</td>
<td>0–2.5</td>
<td>0–2.5</td>
<td>0–4.75</td>
<td>1.5–6.5</td>
</tr>
<tr>
<td>75 mg N=24</td>
<td>Average 27.4</td>
<td>55</td>
<td>2.75</td>
<td>1.36</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Range 21–43</td>
<td>44–82</td>
<td>0–10</td>
<td>0–3.25</td>
<td>0–10</td>
<td>2.5–25</td>
</tr>
</tbody>
</table>

* Only one volunteer in this group lost consciousness and the figures refer to this individual. Range and average do not apply in this case.

*Note.* All times are given in minutes.
for sitting without assistance was 3 minutes. Seven of those who lost consciousness were apnoeic for periods of 15 to 45 seconds. Six complained of pain on injection and a local erythematous reaction appeared in three. Four patients exhibited pronounced muscle tremors during induction (not related to painful stimulation) and in one patient there was an episode of coughing during induction.

**Female group—50 mg.**

There were 25 volunteers in this group with an average age of 25.6 years and average weight of 58 kg. Six volunteers did not lose consciousness. In the other 19 the average duration of unconsciousness was 56 seconds. The first response to painful stimulus was at 36 seconds on average and the first coherent verbalization was at 1.4 minutes on average. Average sitting time for this group was 4.4 minutes. One patient was apnoeic for a brief period of time. Two experienced pain on injection. There were two volunteers who experienced muscle tremors on induction.

**Female group—75 mg.**

There were 24 volunteers in this group with an average age of 27.4 years and average weight of 55 kg. In this group there was only one who did not lose consciousness. The remainder were unconscious an average of 2.75 minutes. The average time until first response to painful stimulus was 1.4 minutes. The average time to first coherent verbalization was 3 minutes and time to sitting without assistance was 5 minutes. Of this group, eight had sufficient airway obstruction to require airway support (holding chin forward). An additional eight were apnoeic from 15 to 45 seconds. Nine were aware of pain on injection and three had noticeable muscle tremors not related to painful stimuli. There was one episode of coughing on induction.

**DISCUSSION**

There have been several reports in the literature regarding the use of different agents in single or multiple dose forms, for brief surgical procedures or for electroconvulsive therapy. It has been reported by Ayd (1961) that 6 ml of 1 per cent methohexitone (60 mg) was the average dose for electroconvulsive therapy. In outpatient dental anaesthesia, however, an operating time of 18 to 20 minutes was required and this necessitated methohexitone in doses of from 700 to 1000 mg (Christensen, Hebert and Driscoll, 1961).

It is apparent from the data presented in this study that 50 mg is a grossly inadequate dose in both the male and female groups. Twenty-three of the 24 males were not even asleep and the average duration of unconsciousness of 56 seconds in the female group is too short to be of any clinical usefulness. A dose of 75 mg produced only 60 seconds of anaesthesia in 19 of the 26 volunteers in the male group and this was done at the expense of a transitory apnoea in 7 of the 26 volunteers. In the female group the duration of unconsciousness produced by 75 mg (2 minutes 45 seconds) is approaching a useful range but at the expense of considerable respiratory complications—either transitory apnoea or airway obstruction—requiring support in 16 of the 24 (table II).

<table>
<thead>
<tr>
<th>Complications.</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>Apnoea</th>
<th>Respiratory obstruction</th>
<th>Local reaction</th>
<th>Others*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>50 mg</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>N=24</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>75 mg</td>
<td>7</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>N=26</td>
<td></td>
<td></td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Female</td>
<td>50 mg</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>N=25</td>
<td></td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Female</td>
<td>75 mg</td>
<td>8</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>N=24</td>
<td></td>
<td></td>
<td></td>
<td>12</td>
</tr>
</tbody>
</table>

* Cough, tremor, pain on injection.

It is our feeling that whilst it is not possible to produce clinically useful anaesthesia with 50-mg doses of methohexitone, a dose of 75 mg might be useful if it did not cause respiratory complications in almost 50 per cent of the volunteers. It would therefore be inadvisable to administer this drug in an outpatient setting without trained anaesthetic personnel being available.

This study also corroborates previous reports that it is not possible to perform surgical procedures of more than the briefest duration with...
methohexitone without supplementation and without the use of doses which result in either respiratory complications or undue delay in the recovery of consciousness (Swerdlow, 1964).

REFERENCES


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REFRESHER COURSE IN ANAESTHESIA

for General Practitioners and part-time Anaesthetists

APRIL 24 TO 27, 1968.

Particulars from Dr. R. A. FISHER,
Consultant Anaesthetist, Postgraduate Medical Centre,
Royal Victoria Hospital, Bournemouth, Hampshire.