ALTERATIONS IN RESPONSE TO SOMATIC PAIN ASSOCIATED WITH ANAESTHESIA
XVI: METHOHEXITONE

BY

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SUMMARY

Subanaesthetic doses of methohexitone were found to produce increased sensitivity to somatic pain in a manner qualitatively similar to thiopentone. However, the duration of antanalgesia after recovery from large doses was much shorter than after comparable doses of thiopentone.

Apart from the work of Keats and Beecher (1950), who found that hypnotic doses of pentobarbitone sodium intravenously relieved postoperative pain in about half of a series of surgical patients, it was felt for many years that clinical doses of barbiturates had little or no analgesic action. In 1960 Clutton-Brock showed that not only was thiopentone without analgesic action in subnarcotic dosage, but is capable of antagonizing the analgesic action of nitrous oxide or pethidine in adults when given in quantities of 25–100 mg. This antanalgesic action is also possessed by phenobarbitone and pentobarbitone. Dundee (1960) extended Clutton-Brock's studies on a more quantitative basis and from comparisons of the effects of thiopentone and pentobarbitone (which penetrate the brain at different rates) he postulated that antanalgesia was associated with a low cerebral concentration of barbiturate. More important from the clinical viewpoint he found that the antanalgesic action persisted for up to 5 hours after large doses of thiopentone.

In recent years great interest has been shown in the use of the methylated barbiturate, methohexitone, as an alternative to thiopentone under certain conditions. In view of the findings with the three compounds referred to above, it was thought to be of interest to know whether it also can antagonize analgesia. Such a finding would suggest that this property applies to all barbiturates.

This paper reports a study of the effect of subanaesthetic and clinical doses of methohexitone on the patient's appreciation of somatic pain. The findings are compared with those obtained by Dundee (1960) with thiopentone.

METHOD

Observations were carried out on fit female subjects admitted for minor gynaecological operations. When observations were carried out during the first minute after injection of the drug only, premedication was varied and consisted of atropine 0.6 mg alone or with pethidine 100 mg. When studies were carried out for some time after recovery from anaesthesia, premedication was limited to atropine.

The patient's sensitivity to somatic pain was studied by the application of a variable measurable degree of pressure to the anterior surface of the tibia. Patients were asked to tell (a) when the sensation of pressure changed to pain (threshold reading) and (b) when the pain became intolerable (response reading). When patients were very drowsy, the observations were limited to the latter readings. Details of this method of analgesimetry, its applications and limits of error have been described by Dundee and Moore (1960). Duplicate readings were made prior to injection of the drug, and with small doses single observations were made 30 and 60 seconds later. With larger doses duplicate readings were carried out at intervals after return of consciousness.

The findings are reported either as changes in readings from the pre-injection control or as percentage incidence of significant increases or decreases in threshold, response, and threshold plus response readings.
ALTERATIONS IN RESPONSE TO SOMATIC PAIN—XVI

TABLE I

Average effects of subanaesthetic doses of methohexitone and thiopentone on pain threshold and response readings and the percentage of post-injection readings which differ significantly from the controls. Observations were made at half a minute and one minute after injection.

<table>
<thead>
<tr>
<th></th>
<th>Number of cases</th>
<th>Half-minute</th>
<th>One minute</th>
<th>Half-minute</th>
<th>One minute</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Average change in readings</td>
<td></td>
<td></td>
<td>Percentage frequency of changes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Threshold Response</td>
<td>Increase Decrease</td>
<td>Increase Decrease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methohexitone</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 mg</td>
<td>5</td>
<td>-2.2</td>
<td>-3.8</td>
<td>-2.0</td>
<td>-3.7</td>
</tr>
<tr>
<td>20 mg</td>
<td>10</td>
<td>-2.6</td>
<td>-2.9</td>
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<tr>
<td>Thiopentone</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>50 mg</td>
<td>32</td>
<td>-2.1</td>
<td>-1.7</td>
<td>-2.1</td>
<td>-1.8</td>
</tr>
<tr>
<td>100 mg</td>
<td>15</td>
<td>-0.8</td>
<td>-0.7</td>
<td>-2.3</td>
<td>-1.2</td>
</tr>
</tbody>
</table>

RESULTS

Table I shows that small doses of methohexitone cause an immediate degree of antanalgesia which is comparable with that resulting from equivalent doses of thiopentone.

A small number of observations were made after the use of large doses injected over a period of 5 to 10 minutes. These demonstrate a brief period of antanalgesia during recovery (fig. 1), but this was much shorter than after equivalent doses of thiopentone. With 4 mg/kg of the latter drug antanalgesia was frequently found for the first hour and a half, while with 2.5-4 mg/kg methohexitone this was not found for longer than 50 minutes after injection.

DISCUSSION

This study shows the similarity between the actions of methohexitone and thiopentone on the patient’s appreciation of somatic pain. The findings are summarized in figure 2 and reveal that the difference in the immediate effects of the two drugs is one of potency. In view of the claims for the shorter action of methohexitone, as compared with equivalent doses of thiopentone, the shorter antanalgesic action of the former is not unexpected.

Increased sensitivity to somatic pain has now been demonstrated after two barbiturates (pentobarbitone and phenobarbitone), a thiobarbiturate (thiopentone) and a methylated barbiturate (methohexitone). The author has also found (unpublished observations) that this occurs after subanaesthetic doses of Inactin and hexobarbitone. Thus, it seems unlikely that this property is associated with any particular side chains, but is rather an effect of all types of barbiturates.

ACKNOWLEDGMENTS

Thanks are due to the gynaecological staff at Musgrave Park Hospital, Balmoral, for providing facilities for this study and to Eli Lilly & Company Limited, for providing the methohexitone.
Changes in pain response reading found half a minute after varying doses of methohexitone and thiopentone.

Individual cases given methohexitone. —— Average effects of thiopentone as found by Dundee (1960).

REFERENCES


VARIATIONS DES REPONSES A LA DOULEUR SOMATIQUE EN ASSOCIATION AVEC L'ANESTHESIE. XVI: METHOHEXITONE

SOMMAIRE

Des doses sous-anesthésiques de méthohexitone provoquent une sensibilité accrue à la douleur somatique d'une façon analogue à ce qui se produit avec la thiopentone. Toutefois la durée de l'antanalgésie après rétablissement de doses importantes était considérablement plus courte qu'avec des doses comparables de thiopentone.

VERÄNDERUNGEN DER REAKTION AUF SOMATISCHEN SCHMERZ IN VERBINDUNG MIT ANÄSTHESIE

ZUSAMMENFASSUNG

Es wurde festgestellt, daß subanästhetische Dosen von Methohexitone eine gesteigerte Empfindlichkeit auf somatischen Schmerz-qualitativ ähnlich der bei Thiopentone- verursachen. Im Anschluß an das Erwachen nach hohen Dosen war die Dauer der Schmerzüberempfindlichkeit jedoch viel kürzer als bei vergleichbaren Dosen Thiopentone.