HEPTABARBITONE AS A PRE-OPERATIVE SEDATIVE

BY

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SUMMARY

There are advantages to be gained from using an oral barbiturate as a pre-operative sedative. Heptabarbitone (Medomin) has been given in a dose of 400 mg to fifty healthy patients undergoing minor gynaecological operations. Using a scoring system, the sedative effects of this drug have been measured and found to be comparable with the sedation produced by papaveretum 20 mg and hyoscine 0.4 mg and significantly better than the sedation produced by pethidine in a dose of 100 mg. Nausea and vomiting did not occur pre-operatively after premedication with heptabarbitone and were seldom noted postoperatively, and in the cases studied postoperatively restlessness was rare.

Although there are many reasons for prescribing pre-anaesthetic medication, recent work has tended to re-emphasize that the main purpose of pre-medication is to sedate the patient. While the opiates provide good sedation, they also produce a high incidence of undesirable side effects such as nausea and vomiting (Riding, 1960; Feldman, 1963). The limitations of the barbiturates in premedication are well recognized and for this reason they have been employed less frequently in recent years. Following the work of Clutton-Brock, and Dundee and his colleagues, the antanalgesia which these drugs produce is now appreciated.

The barbiturates, however, provide excellent sedation and are widely used in medical practice for this purpose. If given by mouth they are active over a period of several hours, so that their effectiveness does not depend on the accurate timing of an intramuscular injection. They seldom cause nausea and vomiting and are not usually associated with major cardiovascular or respiratory changes. The antanalgesic effects of the drugs can be countered by the use of analgesics in the postoperative period. If a short-acting barbiturate is used the postoperative antanalgesic effect may be minimized. Heptabarbitone is claimed to be a short-acting barbiturate with no hangover effect and this paper reports a comparative study of its use in premedication.

Heptabarbitone (Medomin) is 5-ethyl-5-cyclohept-1-enylbarbituric acid (fig. 1) and is claimed to have a wider safety margin than other barbiturates (Lienert, 1954; Weithaler and Biedermann, 1955). The cycloheptenyl ring is rapidly and easily oxidized, forming the cycloheptenonyl derivatives which have no hypnotic action and are much less toxic than the original substance. Because the drug is rapidly metabolized and is not retained in the fat depots (Bernhard and Bickel, 1957), when its effects wear off they do so rapidly and for this reason it may be more suited for use in the immediate pre-operative period than other barbiturates.

![Fig. 1](cycloheptenylethyl barbituric acid (heptabarbitone-Medomin))
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METHOD

The sedative properties of heptabarbitone were studied using the scoring system described by Nisbet and Norris (1963). Fifty otherwise healthy gynaecological patients from the one ward unit were studied, excluding those patients at the extremes of age. Each patient was premedicated for a theatre list starting at 9.15 a.m. with an oral dose of 400 mg of heptabarbitone given at 8 a.m. No other sedative drug was given. These patients formed part of a larger group in whom the effects of standard premedicant drugs were being studied and heptabarbitone was given in a random fashion along with the other drugs, so that the anaesthetist was unaware what premedication the patient had received. No atropine was given. Measurements were made in the ward; and in the anaesthetic room before and after the application of a stimulus as previously described (Nisbet and Norris, 1963).

RESULTS

The distribution of scores in the patients receiving heptabarbitone is shown in figure 2. The mean score in the series was 6.72 ± 2.27. Using the previous classification, thirty-two patients were considered to show good sedation, eleven to show fair sedation, while seven were considered to be poorly sedated. In tables I and II the results obtained with heptabarbitone are compared with papaveretum 20 mg and hyoscine 0.4 mg and with pethidine 100 mg. Using a “t” test, the mean score obtained with heptabarbitone was indistinguishable from that obtained with papaveretum and hyoscine, but compared with pethidine alone the mean score was significantly higher. When a chi-squared test was applied to the results shown in table II, the sedative effects of heptabarbitone were found to be indistinguishable from those of papaveretum 20 mg and hyoscine 0.4 mg, and significantly more “good” results were obtained than with pethidine 100 mg.

TABLE I

Comparison of mean scores with different forms of sedation.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mean score</th>
<th>Standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heptabarbitone 400 mg</td>
<td>6.72</td>
<td>± 2.27</td>
</tr>
<tr>
<td>Papaveretum 20 mg</td>
<td>6.6</td>
<td>± 1.84</td>
</tr>
<tr>
<td>Hyoscine 0.4 mg</td>
<td>5.8</td>
<td>± 2.28</td>
</tr>
<tr>
<td>Pethidine 100 mg</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TABLE II

Results obtained with three types of sedatives.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Degree of sedation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Papaveretum 20 mg</td>
<td>Good 33 Fair 13 Poor 4</td>
</tr>
<tr>
<td>Hyoscine 0.4 mg</td>
<td></td>
</tr>
<tr>
<td>Heptabarbitone 400 mg</td>
<td></td>
</tr>
<tr>
<td>Pethidine 100 mg</td>
<td></td>
</tr>
</tbody>
</table>

Side effects.

After heptabarbitone no patient complained of nausea in the anaesthetic room. Several patients were euphoric before the induction of anaesthesia but restlessness was not noted at this stage. In the postoperative period only one patient was
restless, but this patient had developed abdominal pain suggestive of dysmenorrhoea before she was given premedication. As the majority of these patients were undergoing dilatation and curettage, postoperative pain was normally minimal.

DISCUSSION

The results suggest that the sedative effects of heptabarbitone are comparable with those of papaveretum and hyoscine, and superior to those of pethidine in the dosage used. It was convenient to administer the drug to all the theatre patients at the one time, and by mouth, and the results suggest that in the majority of cases the drug was effectively absorbed. Nausea and vomiting were considerably less common in the postoperative period in those patients premedicated with heptabarbitone than in those given papaveretum and hyoscine, morphine or pethidine. While barbiturate premedication is perhaps most useful in patients in whom postoperative pain is likely to be minimal the addition of an opiate or pethidine to the barbiturate in premedication will tend to prevent postoperative restlessness. Thus a mixture of quinalbarbitone, morphine and atropine has been found useful in paediatric anaesthesia.

It has been claimed that the lack of hangover effect makes heptabarbitone an ideal hypnotic to be given on the night before operation. We feel, however, that some hangover effect may be useful on the morning of operation and that it is possible and desirable to superimpose a further degree of sedation on that which already exists. As the current practice is to give thiopentone in a dosage sufficient only to produce sleep it is unlikely that the effects of the barbiturates will summate in a manner such as to produce marked circulatory or respiratory depression. A more important benefit from the rapid breakdown of the drug will be obtained in the postoperative phase if it reduces the period of antinociception.

CONCLUSION

Heptabarbitone given orally in a dose of 400 mg provided good sedation with minimal side effects in the majority of patients undergoing minor gynaecological operations in whom postoperative pain was not a marked feature. The sedation provided was comparable to that which followed the use of papaveretum 20 mg and hyoscine 0.4 mg and better than that provided by pethidine 100 mg. There was less postoperative nausea and vomiting with the barbiturate than after the other drugs. It was an advantage to be able to give oral premedication to all the patients on the theatre list at the same time.

Where postoperative pain is not anticipated a short-acting barbiturate should be considered in prescribing pre-operative sedation. These drugs may be usefully combined with a narcotic analgesic with weak sedative action (for example pethidine) where postoperative analgesia is desired.

ACKNOWLEDGMENTS

We continue to be grateful to Professor D. Fyfe Anderson and the medical and nursing staff of his unit in Glasgow Royal Infirmary for their patient cooperation in this work; to our colleagues, Dr. Gordon Hendry and Dr. William Martin, for their help with some of the cases; and to Mrs. Milliken for secretarial assistance.

REFERENCES


L'HEPTABARBITONE COMME SÉDATIF PRÉOPÉRATOIRE

SOMMAIRE

On peut obtenir des avantages en utilisant un barbiturique par voie perorale comme sédatif avant une intervention chirurgicale. Des doses de 400 mg de Heptabarbitone (Médédomine) ont été administrées à 50 patients sains, tous de sexe féminin, avant de petites interventions gynécologiques. Par un système de points l'effet sédatif de ce médicament a été mesuré. Il en résulte que l'effet est comparable à la sédation obtenue par 20 mg de papaveretum et 0.4 mg d'hyoscine et notablement meilleur que celui obtenu par 100 mg de Pethidine. L'administration préopératoire de heptabarbitone ne provoque ni nausées ni vomissements avant l'intervention et elle les provoque rarement après cette dernière. Dans les cas étudiés l'agitation post-opératoire était rare.
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ZUSAMMENFASSUNG

Die Verwendung eines oralen Barbiturates zur präoperativen Sedierung kann Vorteile mit sich bringen. Heptabarbitursäure (Medomin) wurde in Dosen von 400 mg 50 gesunden Patientinnen, bei denen kleinere gynäkologische Eingriffe vorgenommen werden sollten, gegeben. Unter Benutzung einer Bewertungsskala wurden die sedativen Eigenschaften dieser Droge gemessen, wir fanden, daß sie vergleichbar waren mit dem Sedierungseffekt von 20 mg Papaverin und 0.4 mg Skopolamin und erheblich besser als die Sedierung mit 100 mg Pethidine. Nach einer Prä-Medikation mit Heptabarbitursäure trat prä-operativ kein Brechreiz und Erbrechen auf und wurde nur selten postoperativ beobachtet, und bei den untersuchten Fällen trat eine postoperative Unruhe nur ganz gelegentlich auf.

BOOK REVIEWS


Here are two books practically identical in title and size. One is the result of a joint British authorship of a Professor of Surgery and an artist: the other is by an American anaesthetist.

Ellis clearly draws his sympathies and outlook from the Oxford school of anaesthesia (a foreword by Sir Robert Macintosh introduces the volume) while Miss McLarty is well known to all anaesthetists for her illustrations in other books in their field. These two have combined excellently in a well selected and excellently illustrated survey of anatomy aimed particularly at the Primary F.F.A. candidate. Whether anatomy, to the exclusion of perhaps other more important basic sciences for the anaesthetist, deserves a separate place in the Primary rather than in the Final part of that examination is another question. So long as anatomy remains, only the good sense of examiners and of books like this maintain the relevance of the examination to the work of the anaesthetist. Neither examiners nor candidates will go far wrong if this book gives them guidance on this point. Until all the former have read it and agree with its message, candidates may have to read a little more here and there to be quite sure of success.

The American volume is utterly different. Dornette sets out to show the importance of sound anatomical knowledge as a proper basis for practically everything the anaesthetist does, from preparation of the patient for general anaesthesia to the care of the unconscious patient, and from conduction anaesthesia to electro-anaesthesia. The reader will find buried here a mine of information, pharmacological, clinical and pathological with additional and valuable snippets about hypnotism, electrophysiology, physics and monitoring devices, the whole forming an interesting and readable conglomeration. The author is dedicated to the idea of stereoscopy as an aid to teaching anatomy. He may well be, for the method has proved its value in teaching this subject. This book, however, could have provided a better advertisement. Most of the illustrations consist of pairs of stereoscopic photographs; plastic spectacles for viewing them are included. The photographs, however, are in the main either of poor quality or their message does not seem to need the help of stereo. This is more than offset by an excellent chapter on the method in which the principles are clearly explained. In the next edition, which is bound to be called for, the collaboration of an expert professional photographer and of someone with "visual aid" expertise will enormously improve the arrangement of the models and the labelling. In this edition they have an amateur look that does not match the excellent text. It is a pity that these comments have to be made, for Dornette has written a highly interesting and somewhat unique book. The text alone will repay reading in its own right, and the stereoscopes are not without merit. The whole book is an important experiment in anaesthetic teaching.

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