OXYPERTINE (INTEGRIN): A STUDY OF ITS USE IN PREMEDICATION

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SUMMARY

In 100 otherwise healthy gynaecological patients the sedative effects of oxypertine 20 mg given orally before operation have been studied using a standard scoring system. In the patients studied, oxypertine 20 mg provided relief of anxiety (sedation) comparable to that obtained after the administration of a tablet of Mandrax used as comparison. Side effects were minimal and after oral administration oxypertine provided adequate preoperative sedation over a period of 5 hours.

Preanaesthetic medication is used to relieve anxiety, abolish or reduce parasympathetic activity and reduce postoperative vomiting. Of these, the relief of anxiety, or psychic sedation, is probably the most important function and this is not always satisfactorily achieved by the conventional injection given shortly before the operation. The use of anxiolytic drugs which can be given orally and have a longer duration of action may allow better preanaesthetic preparation of the patient.

Oxypertine (Integrin) is a member of a series of indole-piperazine derivatives first described by Archer et al. in 1962. Its structural formula is shown in figure 1. It was synthesized following interest in the "indole theory" of schizophrenia (Osmond and Smythies, 1952) by adding phenylpiperazine to a 5-hydroxytryptamine nucleus.

CH₃

CH₃

N

CH₃

CH₃

OXYPERTINE

FIG. 1

Penn (1972) has reviewed the basic pharmacology of oxypertine which appears to act by selectively reducing the levels of adrenaline and noradrenaline in the brain. Animal studies have indicated that some of the actions of oxypertine resemble those of chlorpromazine (Wylie and Archer, 1962) and subsequent clinical trials have shown that in low doses oxypertine has anxiolytic and tranquilizing effects (Tyson, 1970) and in higher doses (about 200 mg) a neuroleptic effect (Mises, 1967). Oxypertine has been favourably compared with the phenothiazines and benzodiazepines in the treatment of anxiety (Bonn, Salkind and Rees, 1971) and psychoses (Wadzisz, 1969). Side effects are uncommon and the drug is active approximately 40 minutes after oral administration (Ashton et al., 1972).

In this study we have compared oxypertine with Mandrax* for preanaesthetic medication. Mandrax has been the subject of several previous studies in this department.

METHOD

The method of study has been described previously by Nisbet and Norris (1963) and Norris and Wallace (1971). All measurements were made on patients scheduled for minor gynaecological procedures who were otherwise healthy and were from one ward unit. Of the total 100 patients studied, 50 were given Mandrax (1 tablet) and the remainder oxypertine (20 mg). The drugs were given in random order 1 hour before the operating list was due to start. In order to have a double-blind trial with dissimilar drug formulations the double-placebo technique was used. Thus one group of patients received a Mandrax tablet and 2 lactose capsules identical to oxypertine and the other group received 2 capsules of oxypertine and a lactose tablet indistinguishable from Mandrax.

Assessments. Combined subjective and objective estimates were made of the degree of sedation, using a standard scoring system. The patients were seen in the ward on the day before operation and an assessment was made of the degree of anxiety

*Mandrax (Roussel): each tablet consists of methaqualone 250 mg and diphenhydramine 25 mg.
The blood pressure and pulse rate were recorded. The patients were reassessed in the anaesthetic room prior to induction of anaesthesia, when the three measurements were repeated. A stimulus in the form of the application of an anaesthetic face mask was applied and the blood pressure and pulse were recorded again. Points were given to patients who appeared drowsy and relaxed in the anaesthetic room and who showed either a slight fall in blood pressure or heart rate or, at least, no rise in these measurements. Further points were awarded if the patient did not react to the specific stimulus in the anaesthetic room. Points were lost when the patient appeared apprehensive or showed a rise in blood pressure or heart rate on arrival in the anaesthetic room, or after application of the stimulus. The scoring system gave a possible maximum score of 10. Patients scoring 0–4 were considered to be poorly sedated, those scoring 5 and 6 fairly well sedated and those scoring 7–10 well sedated.

Table I shows the mean ages, weights and the times from administration of the drugs until the readings were taken. It can be seen that each group of 50 patients was similar.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mean age (years)</th>
<th>Mean weight (kg)</th>
<th>Mean interval between administration of drug and test (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mandrax</td>
<td>32</td>
<td>55.9</td>
<td>210</td>
</tr>
<tr>
<td>Oxypertine</td>
<td>30</td>
<td>58.1</td>
<td>212</td>
</tr>
</tbody>
</table>

**RESULTS**

**Relief of anxiety (sedation).** Table II shows the scores obtained in the study. The mean scores are similar in each group, there being no statistically significant difference in the numbers tested. The study indicated that oxypertine 20 mg produced almost identical sedation to that obtained with 1 tablet of Mandrax.

**Circulatory side effects** are shown in table III. The mean changes in blood pressure and heart rate taken from the day before operation to the immediate preoperative reading are shown in table IV: both drugs produced adequate sedation for about 5 hours.

**Duration of action.** Although the mean time from administration of the medication to the time of testing was the same in each group the individual patients were studied at widely different times after administration of the drugs. The relief of anxiety or sedation in each hour after administration of the drugs is shown in table V: both drugs produced adequate sedation for about 5 hours.

**DISCUSSION**

We have once again used Mandrax as our "standard" drug for comparison since we have considerable data about this drug from previous trials. Table VI shows that the scoring system has...
TABLE V. Patients scoring 7 to 10 ("good sedation") in each hour after administration of drug.

<table>
<thead>
<tr>
<th>Year of study</th>
<th>Mean score (±1SD)</th>
<th>Good (7-10)</th>
<th>Fair (5-6)</th>
<th>Poor (0-4)</th>
<th>Total studied</th>
</tr>
</thead>
<tbody>
<tr>
<td>1965¹</td>
<td>6.94±2.27</td>
<td>31</td>
<td>9</td>
<td>8</td>
<td>48</td>
</tr>
<tr>
<td>1967/68²</td>
<td>6.90±2.11</td>
<td>33</td>
<td>8</td>
<td>9</td>
<td>50</td>
</tr>
<tr>
<td>1969²</td>
<td>6.48±2.27</td>
<td>28</td>
<td>10</td>
<td>12</td>
<td>50</td>
</tr>
<tr>
<td>1970/71³</td>
<td>6.92±2.08</td>
<td>34</td>
<td>7</td>
<td>9</td>
<td>50</td>
</tr>
<tr>
<td>1972²</td>
<td>7.24±1.90</td>
<td>33</td>
<td>13</td>
<td>9</td>
<td>50</td>
</tr>
</tbody>
</table>


Provided reproducible results with Mandrax over a period of 8 years and this confirms the reproducibility of results using the scoring system with morphine 10 mg (Norris, 1969).

The results of the present study suggest that oxypertine 20 mg produces sedation or relief of anxiety comparable to that produced by 1 tablet of Mandrax.

Side effects were minimal. In each group 6 patients underwent laparoscopy after administration of gallamine 120 mg. All patients were intubated and ventilation was controlled. In each of these subgroups, 1 patient subsequently proceeded to laparotomy and in these two cases analgesia was maintained with intravenous Cyclimorph 6 mg. The incidence of emetic sequelae was unaffected by this and no interaction between oxypertine and gallamine was clinically evident.

ACKNOWLEDGEMENTS

We are grateful to Dr R. A. P. Burt and Winthrop Laboratories who supplied the drugs in double-blind form, also to Roussel who supplied the Mandrax tablets used. We are also grateful to Professor M. C. Macnaughton and the medical and nursing staff of his unit for their continued co-operation in these studies.

REFERENCES


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L’OXYPERTINE (INTEGRINE): ETUDE DE SON EMPLOI EN TANT QUE PREMEDICATION

SOMMAIRE

En recourant à un système d’évaluation standard, les effets sédatifs de l’oxypertine, administrée avant une intervention à raison de 20 mg par voie orale, ont été étudiés chez 100 malades ressortissant de la gynécologie et par ailleurs en bonne santé. Chez les malades ainsi étudiés, à la dose de 20 mg, l’oxypertine a engendré une séduction de l’anxiété comparable à celle obtenue à la suite de l’administration d’un comprimé de Mandrax, substance ayant servi de base de comparaison. Les effets secondaires ont été minimes, et administrée par voie orale, l’oxypertine a permis d’obtenir une séduction préopératoire adéquate pendant un laps de temps de cinq heures.