PHENAZOCINE WITH NITROUS OXIDE ANAESTHESIA

BY

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SUMMARY

A blind trial was undertaken to compare phenazocine with pethidine. Both drugs were used to supplement nitrous oxide and oxygen anaesthesia in cases in which spontaneous respiration was possible during maintenance. Forty-six cases were given pethidine and forty-five cases phenazocine. There was no difference between the two drugs in their ability to provide satisfactory anaesthesia, or in the degree of respiratory depression, or in the effect upon the blood pressure. Recovery of reflexes following anaesthesia was more rapid in the phenazocine group but the results were not statistically significant. The literature upon phenazocine was discussed together with the results of the present trial.

Phenazocine (Narphen) is a synthetic analgesic drug which has a potency twenty times greater than that of morphine. It is claimed that despite this potency the incidence of side effects is low. Phenazocine has been used as an analgesic in patients with pain and postoperatively. It was thought that such a powerful analgesic with minimal side effects might be of use in anaesthesia as a supplement to nitrous oxide and oxygen and that it might replace pethidine, which cannot be said to be ideal for this purpose.

In a small group of cases phenazocine was used as an intravenous agent instead of pethidine to supplement nitrous oxide and oxygen anaesthesia and, except for some degree of respiratory depression, it seemed satisfactory. A blind trial was therefore undertaken to compare phenazocine with pethidine. One hundred patients were anaesthetized for this trial.

METHOD

Ampoules of pethidine 100 mg in 2 ml were used, which were exactly the same size and shape as ampoules containing phenazocine 2 mg in 2 ml; 100 mg of pethidine has been said to be approximately equal to 2 mg of phenazocine. The wording on the ampoules was obliterated with black adhesive tape. The ampoule containing one of the drugs was marked with a strip of green adhesive tape by an independent person. The identity of the marked drug was not known until after the trial. This marking was re-applied at about the fiftieth case.

Premedication consisted of either papaveretum 20 mg and hyoscine 0.44 mg or pethidine and atropine with dose graded to the size or medical fitness of the patient.

The author gave every anaesthetic personally. Selection of cases was at random. All were cases in which spontaneous respiration was permissible and in which muscular relaxation was not required (table III). A preponderance of hernia operations and dental procedures (mostly extractions of impacted wisdom teeth and clearances) were undertaken on purpose, principally because these seemed ideal cases for such a trial. Each ampoule was diluted with water so that 1 ml contained either pethidine 25 mg or phenazocine 0.5 mg. An effort was made to use pethidine or phenazocine as the sole analgesic supplement with nitrous oxide and oxygen. Induction of anaesthesia was always carried out with thiopentone 2½ per cent, and if intubation was required suxamethonium chloride was used, the trachea being sprayed with lignocaine 4 per cent. An exception to this technique was made with dental procedures in which a blind nasal intubation was performed using gallamine triethiodide 60 mg after thiopentone induction. This is the author's usual practice to avoid postoperative muscle pains and
TABLE I

Type of anaesthesia.

<table>
<thead>
<tr>
<th></th>
<th>Good</th>
<th>Satisfactory</th>
<th>Poor</th>
<th>Total number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pethidine</td>
<td>29 (63%)</td>
<td>10 (22%)</td>
<td>7 (15%)</td>
<td>46</td>
</tr>
<tr>
<td>Phenazocine</td>
<td>28 (63%)</td>
<td>11 (24%)</td>
<td>6 (13%)</td>
<td>45</td>
</tr>
</tbody>
</table>

TABLE II

Incidence of respiratory depression.

<table>
<thead>
<tr>
<th></th>
<th>Mild respiratory depression</th>
<th>Severe respiratory depression</th>
<th>Total number of cases of respiratory depression</th>
<th>Total number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pethidine</td>
<td>7 (15%)</td>
<td>7 (15%)</td>
<td>14 (30%)</td>
<td>46</td>
</tr>
<tr>
<td>Phenazocine</td>
<td>5 (10%)</td>
<td>6 (13%)</td>
<td>11 (24%)</td>
<td>45</td>
</tr>
</tbody>
</table>

was continued in this series in view of the larger number of cases. It is appreciated that gallamine causes respiratory depression and respiration had often to be aided during the early part of the operation.

For simplicity the criteria used were the analgesic power of the drug as its ability to suppress reflexes, the degree of respiratory depression, the speed of recovery, and the level of arterial blood pressure. On finally checking the records, four cases in the pethidine group and five cases in the phenazocine group were rejected because of insufficient data or for some other reason which cast doubt on the results. This left forty-six cases in the pethidine group and forty-five in the phenazocine group.

Criteria.

Analgesia. An assessment of "good", "satisfactory", or "poor" was made. The criteria for these gradings was made as follows:

"Good analgesia": the patient's reflexes were adequately suppressed; there was no movement of the extremities and no "bucking" on the endotracheal tube.

"Satisfactory": some involuntary movement of hand or foot was made or there was slight "bucking" on the endotracheal tube. This was sometimes, it is felt, the fault of the anaesthetist rather than of the drug, and resulted from a determined effort to employ only pethidine or phenazocine as a means of suppressing reflexes in very robust patients. In this group such movement was abolished by a further dose of pethidine or phenazocine.

"Poor": anaesthesia could not be maintained with the sole use of pethidine or phenazocine, and the addition of thiopentone or trichloroethylene was required to allow the operation to continue. In practice the groups "good" and "satisfactory" could be put together in the results but the group "poor" was characteristic.

Respiratory depression was considered to occur when the respiratory rate, which was counted every 5 minutes, fell below 8 per minute. A further subdivision was made into a mild degree of depression that required aided respiration for less than 10 minutes and where apnoea did not occur, and a severe degree of depression needing aid for more than 10 minutes or control of respiration. In three cases nalorphine was used before the patients were returned to the wards.

Recovery was classified into two groups: patients who awoke in the theatre at the end of the operation, rejected their airway and opened their eyes; and patients who were asleep on return to the ward.

Arterial blood pressure was measured and observed closely in the first fifty patients. There appeared to be no significant fall in any of these
Table III
Description of operations in the two series.

<table>
<thead>
<tr>
<th>Type of operation</th>
<th>Pethidine</th>
<th>Phenazocine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herniorrhaphy</td>
<td>14</td>
<td>11</td>
</tr>
<tr>
<td>Dental</td>
<td>13</td>
<td>13</td>
</tr>
<tr>
<td>Varicose veins</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Orthopaedic</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Excision sub-mandibular gland</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Radical mastectomy</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Cystodiathermy</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Skin tumours</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Rectal</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Biopsy of breast</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Orchidopexy</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Ophthalmic</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Vaginal repair</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Radiological investigation</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>46</strong></td>
<td><strong>45</strong></td>
</tr>
</tbody>
</table>

cases and careful study failed to show any difference in the two groups. An exception might be case 3 described later in whom there was a marked fall in the blood pressure. This was associated, however, with blood loss in a hypertensive patient and it would be impossible to draw any conclusions from this case with regard to the blood pressure.

**RESULTS**

**Analgesia** (table I). In the pethidine group analgesia was judged “good” or “satisfactory” in 39 cases, and in 7 cases it was judged “poor”. In the phenazocine group 39 cases were judged “good” or “satisfactory” and 6 “poor”. This gives a very striking picture of no difference whatsoever in a blind trial. The reasons noted on the record cards for judging the anaesthesia as “poor” were similar for each drug.

**Respiratory depression** (table II). Respiratory depression was observed in 14 cases of the pethidine series and 11 cases in the phenazocine series. On subdividing the depression into “severe” and “mild”, it was found that with pethidine 7 cases fell into each subdivision and with phenazocine 6 fell into the “severe” and 5 into the “mild” subdivision. In 2 patients in the phenazocine group a respiratory rate below 8 per minute was observed for a considerable time (over 1 hour). Prolonged respiratory depression of this degree occurred once in the pethidine group. These cases are briefly described as follows:

**Case 1.** Phenazocine. A healthy woman, 68 years old, underwent a radical mastectomy. After administration of 2 mg in six divided doses the respiratory rate fell to between 5 and 6 per minute. Respiration was aided for 1 hour and nalorphine was given at the end of operation. Blood loss was replaced with 500 ml of blood. Her systolic blood pressure fell from 120 to 100 mm Hg during the procedure and she was in good condition and awake at the end of the operation.

**Case 2.** Phenazocine. A 34-year-old woman underwent an aortogram. She was grossly obese with a blood pressure of 220/140 mm Hg. After phenazocine 1 mg had been given in two doses the respiratory rate fell to between 2 and 7 per minute for 1½ hours. This case was complicated further by some degree of blood loss and a fall of the systolic blood pressure to 100 mm Hg. Nalorphine reversed the slow respiratory rate at the end of operation.

**Case 3.** Pethidine. A fit man aged 42 underwent excision of submandibular gland. After pethidine 50 mg had been given in two doses the respiratory rate dropped to 6 per minute and remained between 3 and 7 per minute for 1 hour. Respiration was aided and nalorphine given at the end of operation restored a normal rate of respiration.

**Recovery** of reflexes in the operating theatre occurred in 9 patients in the pethidine series and 17 in the phenazocine series. Despite this apparently more rapid recovery after pethidine anaesthesia, the difference is not statistically significant (P<0.2).

**DISCUSSION**

Phenazocine has been used in the United States for the control of postoperative pain and for obstetric patients. All reports speak favourably of its analgesic power but most of the reports give impressions and there are no controlled trials using phenazocine in anaesthesia.

When phenazocine was given intravenously in obstetrics (Sadove et al., 1960) 82 per cent of patients were said to have had excellent or good pain relief. No mention was made of respiratory depression in the mothers. Depression occurred in 22 out of 205 of the infants though this was said to be related to phenazocine in only 7 infants.
Phenazocine was given as a supplement to nitrous oxide and oxygen by Stephen and Macmillan (1960) but in only two instances. Other cases mentioned were complicated by the varying types of anaesthesia or else the phenazocine was given as a supplement to a regional block. The authors thought that phenazocine depressed the respiration as much as pethidine but tended to cause less fall in blood pressure.

Berkowitz, Rodman and Close (1961) found that phenazocine depressed respiration more than morphine but they used 4 mg of phenazocine and compared it with 16 mg of morphine. This is a very large dose of phenazocine and respiratory depression would certainly be expected.

In Britain phenazocine has been used as a supplement to inhalation anaesthesia by several workers. Thomas (1961) wrote favourably of the drug but Jenkins (1961), Shaw (1961), and McEwan (1961) thought that respiratory depression limited the usefulness of phenazocine in this field. Deacock (1961), in a carefully controlled trial, found no significant difference between the incidence of respiratory depression with pethidine and phenazocine.

When trying to assess such a drug many factors have to be taken into account. Different kinds of premedication may affect the degree of respiratory depression and the use of different anaesthetics with phenazocine will certainly obscure the picture. In addition it is difficult to assess the value of a drug of this kind except by a comparison with a similar and familiar drug such as pethidine. For example, use of a new drug may produce respiratory depression in 24 per cent of patients but this becomes of more practical importance when it is found that pethidine causes respiratory depression in 30 per cent of patients in similar conditions.

Bias will occur either for or against the new drug, depending on the anaesthetist's personality, unless the trial is blind. In this instance the author used phenazocine in several cases before the trial and his impression was that respiratory depression was more frequent than with pethidine.

In this trial the power of 2 mg of phenazocine to depress sensory reflexes during anaesthesia appears to be approximately equal to the power of 100 mg of pethidine. The degree of respiratory depression is similar with both drugs. The incidence of depression is high but it is emphasized that an effort was made in this investigation to use only phenazocine or pethidine as an adjuvant to nitrous oxide and oxygen anaesthesia. This often meant that a large dose needed to be given to provide satisfactory anaesthesia in what were often robust and healthy patients. In normal practice the author would not be so single-minded in his choice of anaesthetic technique. Similarly there is, for the same reason, a high incidence of poor anaesthesia.

Recovery from phenazocine supplementation of anaesthesia was more rapid than after pethidine supplementation though the results are not statistically significant and may be due to chance. The assessment of recovery was crude in this trial and a more detailed study is in progress. The rapid recovery of reflexes is an extremely important factor in anaesthesia especially in hospitals in which there is no recovery ward.

This blind trial is only intended as a brief guide to the efficiency of phenazocine. Many analgesic drugs are appearing on the market and such preliminary trials are of use as an indication of the need for future work.

REFERENCES


SOMMAIRE
Une expérience “aveugle” fut faite pour comparer phenazocine et pethidine. Les deux furent employés pour servir de supplément à l’anesthésie par oxyle nitreux et oxygène dans les cas dans lesquels la respiration spontanée était possible pendant le maintien.
46 patients reçurent de la pethidine et 45 de la phenazocine.
La capacité des deux produits de donner une anesthésie satisfaisante était le même, comme le fut le degré de dépression respiratoire ou l’action sur la tension sanguine. Le retour des réflexes après anesthésie était plus rapide dans le groupe des patients ayant reçu de la phénazocine, mais la différence n’atteignit pas des proportions statistiquement significatives. L’auteur discute la littérature concernant la phénazocine ainsi que les résultats de son expérience.

ZUSAMMENFASSUNG
In einem Blindversuch wurde Phenazocine mit Pethidine verglichen. Beide Medikamente wurden ange-wendet, um die Lachgas-Sauerstoffnarkose in Fällen zu ergänzen, bei denen während der Erhaltungszeit eine Spontanatmung möglich war.
46 Fälle erhielten Pethidine und 45 Fälle Phenazocine.
Es bestand kein Unterschied zwischen den beiden Medikamenten hinsichtlich der Erzielung einer ausreichenden Narkose oder im Ausmass der Atemdepression oder in der Wirkung auf den Blutdruck.
Bei der Phenazocine-Gruppe war die Erholungszeit der Reflexe nach der Narkose kürzer, doch waren die Ergebnisse statistisch nicht signifikant.
Die Literatur über Phenazocine wurde zusammen mit den Ergebnissen dieser Untersuchung besprochen.

BOOK REVIEW
This book is better described by its sub-title, for it does not contain a mere description of elementary anaesthetic techniques; for example, there is an account of the management of coma and a chapter on pulmonary function tests. On the other hand, no comprehensive attempt has been made to deal with the problems associated with special types of operation though there are chapters on paediatric and obstetrical anaesthesia, and on anaesthesia for ambulant patients.
There has been a considerable expansion from the first edition, and the book is well up to date; the section on external cardiac massage is a particularly useful summary of a subject which is now making its first appearance in the textbooks. Indeed there are several excellent chapters—for example, the one on arterial hypotension during anaesthesia—and some subjects are covered which are usually given less prominence than they deserve; for example, a chapter is included on asepsis in anaesthesia.
The narrative is vague in places; the reader might well like to know the differences between neostigmine and edrophonium if both drugs be mentioned. Some of the chapters are too short to give an adequate and really useful account of their subjects and they tend to suffer somewhat in clarity.
Inevitably in a foreign textbook there are very wide differences in emphasis from current British anaesthetic practice, but despite this, candidates for the diploma in anaesthesia will find much of value on the basic principles of the specialty.
J. E. Utting