ANAESTHESIA WITH HYDROXYDIONE (PRESUREN)

BY

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Steroids were first introduced as an anaesthetic by Murphy and his colleagues (1955) and in the published reports of several thousand administrations, which have been admirably summarized by Ditzler and Dumke (1957), many advantages have been claimed. However real these may be, the disadvantages of early preparations (Viadril) which caused a high incidence of venous thrombosis, produced anaesthesia slowly, and had to be given in the form of an intravenous drip, discouraged the widespread use of the agent. More recently 21-hydroxy-pregnane-3, 20-dione, as the water soluble sodium hemisuccinate, has become available under the name of Presuren.* It may be given as a single intravenous injection (Stedtfeld, 1957), and with a lower incidence of vein complications, allows steroids to be employed as a practical and convenient form of anaesthesia.

In an attempt to assess the value of the claims which have been made, I have used Presuren on more than 200 occasions during which particular attention was paid to the effects on respiration, blood pressure, and the immediate postoperative period.

Presuren is available as a white crystalline powder in vials containing 0.5 and 1 gram, which dissolves readily in warm, normal saline. One gram may be regarded as an average dose, but less may be necessary in the aged or the gravely ill (Opderbeke, 1957). Repeated injections may be made, but since there is a time lag before the full effect is produced, there may be difficulty in judging the dose accurately.

Concentrations of 2.5, 5, and 10 per cent have been used. Clinically there seems to be little to choose between these different concentrations, but 5 per cent proved the most convenient for general use, and was the one most commonly used in this series.

OBSERVATIONS

Induction.

Induction with Presuren is usually smooth and pleasant for the patient, with unconsciousness supervening about 4 minutes after the injection. The maximal effect appears to be reached after a further 2-3 minutes. Unfortunately, as with other steroids, Presuren is an irritant and the injection may cause pain. This is usually in the upper arm, aching in character, and often spreads along the venous distribution. It rarely occurs at the site of injection unless the solution has been deposited inadvertently outside the vein. Pain occurred in about 35 per cent of the cases, but in addition, thrombophlebitis and venous spasm were also seen (table I).

<table>
<thead>
<tr>
<th>Vein complications in 200 cases</th>
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<tr>
<td>Pain</td>
</tr>
<tr>
<td>------</td>
</tr>
<tr>
<td>Number of cases</td>
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<td>Incidence in cases</td>
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The venous spasm resolved after about 2 hours without any residual signs or symptoms, and the thrombophlebitis responded quickly to conservative measures. Pain at the time of injection can be relieved by a variety of means, of which vigorous massage proved most effective. Injections of saline or a weak local analgesic solution may be helpful, and it has been suggested that

* Registered trade name of A. G. Schering, Berlin. Chemically this substance is identical to Viadril, but certain physical properties are different. To distinguish the form of hydroxydione used in this investigation, the trade name Presuren has been used throughout.
the latter may avoid pain and irritation altogether if it is injected at the same time as the steroid (Galley and Lerman, 1959).

Venous complications are reduced considerably if large veins only are chosen (those in the antecubital fossa being most suitable), and the injection made as fast as possible through a No. 1 hypodermic needle.* The concentration of hydroxydione seems to play no part in the incidence of these complications and the suggestion by Harbut (1957) that cold solutions cause more pain than those which are warm was not borne out in practice.

An excitement stage was not seen although movements of different parts of the body, most frequently the upper limbs, were not uncommon. Such movements were often athetoid in character, and while not necessarily related to painful stimuli they could be provoked during light anaesthesia by external stimulation (Taylor and Shearer, 1956).

Effect on Respiration.

All respiratory studies were made with a low resistance dry gas meter. This was attached to a face mask which incorporated a unidirectional expiratory valve. The volume of air inspired in 1 minute was measured, and the respiratory rate counted. Thus the estimation of tidal volume was based on an average reading.

Within 5 minutes of receiving Presuren there was an average fall in the tidal volume of about 150 ml. This represents a fall of about 30 per cent on the pre-anaesthetic value. During the next 5 minutes, a further slight fall may be expected, but thereafter little change occurs until the respiratory exchange increases again as the result of lightening anaesthesia or painful stimulation (Taylor and Shearer, 1956).

The type of premedication used (papaveretum 21.6 mg and scopolamine 0.40 mg, or pethidine 50 mg and atropine 0.65 mg, or atropine alone) had little effect on these readings, although the mechanism by which the alteration in tidal exchange was brought about differed. In those who had received the first, "heavy", premedication, a fall in minute volume might be seen, but a rise in respiratory rate was characteristic (table II), and has been already noted by Hohmann (1958).

<table>
<thead>
<tr>
<th>Table II</th>
<th>The effect of premedication on minute volume and respiratory rate.</th>
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<tbody>
<tr>
<td></td>
<td>Rise</td>
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<tr>
<td>&quot;Light&quot; premedication (50 patients)</td>
<td>Rate</td>
</tr>
<tr>
<td>Min. vol.</td>
<td>7</td>
</tr>
<tr>
<td>&quot;Heavy&quot; premedication (50 patients)</td>
<td>Rate</td>
</tr>
<tr>
<td>Min. vol.</td>
<td>7</td>
</tr>
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The average tidal volume after premedication and before anaesthesia was about 400 ml in both groups, but a few exceptionally high readings were encountered. These can be explained on the basis of emotional factors, and, as might be expected, were slightly more common in lightly premedicated patients. The administration of recognized antidotes to respiratory depression had no effect. However, nalorphine given to patients in whom depression was due primarily to premedication, was found to improve the respiratory exchange.

Presuren was administered to three patients who had previously suffered from poliomyelitis. In two, the disease had been contracted in childhood more than 20 years previously, leaving residual symptoms in the legs only. The third patient had suffered a more recent attack with extensive bulbo-spinal involvement, but with good return of respiratory function. In all three, marked respiratory depression was seen soon after the injection of Presuren, and in two this proceeded to apnoea. No adequate explanation can be offered for this dramatic occurrence, but recovery after artificial respiration was uneventful.

Case History.

Housewife, aged 35, for tonsillectomy. History of poliomyelitis when 7 years old, leaving residual weakness of left leg only, but able to lead a normal active life. Premedication, pethidine 50 mg and atropine 0.65 mg. Before induction with 750 mg Presuren the tidal exchange was 360 ml and the respiratory rate 18 per
Histograms showing the effect on respiration of 1 gram of Presuren. The results were obtained from fifty patients who received pethidine 50 mg and atropine 0.65 mg and fifty more who received papaveretum 21.6 mg and scopolamine 0.40 mg, as premedication. The basal tidal volume was recorded in the anaesthetic room approximately 1 hour after premedication, but before the induction of anaesthesia.

minute. The patient fell asleep within 3 minutes and 2 minutes later the tidal exchange had fallen to 70 ml and the respiratory rate had increased to 28. Complete apnoea supervened and during this time the patient was intubated and artificial respiration performed with oxygen. The operation was performed and no additional drugs were needed. The apnoea lasted for 30 minutes and within 5 minutes of restarting spontaneous respiration the tidal exchange was 150 ml and the respiratory rate 24. One hour after the induction the patient had recovered consciousness and the respiratory exchange had returned to normal.

Only two other cases of prolonged apnoea during steroid anaesthesia appear to have been recorded (Howland et al., 1956; Schwarz, 1958).

**Effect on the Cardiovascular System.**

Five minutes after the injection of Presuren, there is usually an average fall in the blood pressure of about 20 mm Hg systolic. Thereafter there may be a slight fall of about 10 mm Hg (fig. 2). In many instances, however, there is no further reduction, and often indeed a slight rise.

The pulse rate is variable, but such changes as do occur rarely exceed a rise or fall of 10 per minute and can therefore be ignored (table III). Neither the effects on the blood pressure nor the pulse rate appear to be affected significantly by the type of premedication received by the patient. No cardiac arrhythmias were observed.

Dilatation of superficial veins occurred soon after consciousness was lost and although this may be a typical response to the release of sympathetic tone to be expected under general anaes-
Anaesthesia with Hydroxydione (Presuren)

Histograms showing the effect of Presuren on the systolic blood pressure. 1 gram of Presuren was administered to fifty patients who received pethidine 50 mg and atropine 0.65 mg, and fifty more who received papaveretum 21.6 mg and scopolamine 0.40 mg as premedication. The differences between the two groups are small, but a slightly greater, and a slightly more prolonged fall in those who had received the heavier premedication can be noted.

Other Observations.

Presuren has been used in association with a variety of other anaesthetic agents and muscle relaxants. Although adequate relaxation may be obtained using smaller doses of relaxants than usual, such an observation can only be regarded as a clinical impression. Variables such as the depth of anaesthesia and physical state of the patient are important factors in influencing the degree of muscular relaxation and it is possible that they may not have been fully taken into account in some reports (Just and Ibe, 1956).

When followed by halothane, marked respiratory depression and hypotension were observed. A return to normal levels occurred after discontinuing the halothane.
TABLE III

The effect of Presuren on pulse rate

<table>
<thead>
<tr>
<th>Premedication</th>
<th>Rise</th>
<th>Fall</th>
<th>No change</th>
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</thead>
<tbody>
<tr>
<td>&quot;Light&quot;</td>
<td>21</td>
<td>22</td>
<td>7</td>
</tr>
<tr>
<td>&quot;Heavy&quot;</td>
<td>24</td>
<td>17</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>45</td>
<td>39</td>
<td>16</td>
</tr>
<tr>
<td>Total</td>
<td></td>
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<td>100</td>
</tr>
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"No change" was recorded where the pulse rate remained within a range of ± 4 per minute. Numbers refer to patients.

Case History.

Female, aged 36, for removal of thyroid adenoma. Premedication with papaveretum and scopolamine 1 hour before induction with 1 gram Presuren. Ten minutes later, during which time no further drugs were administered, the blood pressure had fallen from 130 mm Hg systolic to 120, and the tidal exchange from 390 ml to 360 ml. Five minutes after breathing 1 per cent halothane in air, the blood pressure fell to 80 mm Hg, and the tidal exchange to 200 ml. These values returned to their normal level within a few minutes of stopping the halothane.

Nitrous oxide, trichloroethylene and ether were used after induction with Presuren uneventfully.

Laryngeal and pharyngeal reflexes tend to be depressed to such an extent that laryngoscopy is nearly always, and intubation frequently, possible without the addition of other anaesthetic drugs or muscle relaxants. Even if the patient responds to laryngeal stimulation by coughing or closure of the glottis, spasm is unusual (laryngeal spasm was provoked in one case only).

INDICATIONS

The indications for steroid anaesthesia may be difficult to define accurately. Presuren appears to be well tolerated in the aged, and although it is broken down in the liver (Jakoby and Tomkins, 1956) and excreted rapidly by the kidneys (Gardocki et al., 1956), recovery was not delayed after using the drug in patients with gross cirrhosis of the liver and hepatic failure (10 cases), and in others with a high blood urea (8 cases).

The high incidence of pain following injection may be regarded as a contra-indication to its use in young children, although Landau (1958) suggests that it is well tolerated even by the young.

A more uniform level of anaesthesia can be obtained with Presuren than with thiopentone, so that with added nitrous oxide it may prove convenient in operations requiring a relatively light level of anaesthesia. By itself, Presuren provides good sedation during operations performed under local analgesia.

Although most indications and contra-indications for the use of a drug are relative, a very real case can be made for anaesthesia with Presuren in two instances:

1. In the chronic alcoholic with a history of being "anaesthetic resistant". In three such patients Presuren gave a smooth trouble-free induction of anaesthesia.

Case History.

Ex-guardsman, aged 68, weighing 250 lb., a known alcoholic, for dilatation of urethral stricture. On previous occasions this man had required about 1 gram of thiopentone and a muscle relaxant to allow the operation to be performed. With thiopentone alone, a violent excitement stage was usual. After premedication with papaveretum 21.6 mg and scopolamine 0.4 mg, 1 gram of Presuren produced a peaceful unconsciousness in 6 minutes. With the addition of nitrous oxide and oxygen, bouginage was performed without difficulty. The patient recovered consciousness after about 30 minutes.

2. In laryngoscopy and bronchoscopy where it is desirable that the patient should continue breathing spontaneously during the examination. As a rule, this can be performed under 1 gram of Presuren only, but cocainization of the larynx as well is recommended.

Postoperative Course.

The impression that patients recovering from steroid anaesthesia exhibited a sense of well-being in the immediate postoperative period was confirmed (Galley and Rooms, 1956; Lerman, 1956). A state of euphoria was not unusual. The incidence of nausea and vomiting was about 10 per cent, being slightly more common in those who had received morphine for premedication than in those who received pethidine or atropine only.

Since the majority of the patients in this series received supplementary anaesthesia, it was difficult to estimate the duration of effect of Presuren by itself. Although this may be of the order of 30-40 minutes, the period of unconsciousness will be prolonged for several hours by the use of additional drugs. Had thiopentone been used in similar circumstances, a much quicker recovery would have been expected.
Summary of ten cases who received 1 gram of Presuren after "light" premedication (pethidine 50 mg, atropine 0.65 mg) and ten cases after "heavy" premedication (papaveretum 21.6 mg, scopolamine 0.40 mg). The initial recordings were taken before induction, and further readings were made at 5-minute intervals after the injection of Presuren. No other drugs were administered during the period of observation and the patients received no operative stimulation.

1) Systolic blood pressure. There is a slight fall in both groups which tends to be prolonged into the second 5 minutes in the "heavy" premedication group.

2) A fall in minute volume occurs in the first 5 minutes, being most obvious in the "heavy" premedication group. After 10 minutes the recordings remain unchanged or tend to rise.

3) While there is no obvious change of pattern in the respiratory rate in the "heavy" premedication group, in those who had received the "light" premedication, the rate rises. This rise occurs throughout the first 10 minutes after administration of Presuren.
This prolonged recovery period, which may often be due to a combination of drugs, is usually associated with depressed respiration and a low blood pressure. In these circumstances, a potentially dangerous situation arises. Six patients were encountered in this series who behaved in this manner and required careful supervision during the postoperative period.

SUMMARY

Presuren is a further stage in the development of steroid anaesthesia, with convenience, speed of action, and reduced incidence of vein complications as advantages over its predecessors.

It may cause a slight fall in systolic pressure and some respiratory depression, though rarely to a significant extent (fig. 3).

It is often difficult to judge the dose of Presuren sufficiently accurately to allow it to be used as a sole anaesthetic. The addition of premedication or supplementary anaesthesia can alter the response to this agent and tend to delay recovery.

The incidence of pain on injection and venous thrombosis cannot be ignored and contra-indicate the use of Presuren in the young. It is, however, well tolerated by the aged and the sick, and the sense of well-being in the postoperative period is impressive.

REFERENCES


