CHLORALHYDRATE AS A PREMEDICATION
FOR ANÆSTHESIA

BY

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HISTORICAL AND PHARMACOLOGICAL INTRODUCTION

PREVIOUS experience with chloralhydrate as a premedication for toxic thyroid cases and with cases for operation under local analgesia led us to believe that chloralhydrate might be usefully employed as a premedication with atropine before general anaesthesia. This belief was reinforced by a verbal account by E. S. Rawbotham of his experience with the drug.

Chloralhydrate was the first synthetic hypnotic to be used in medicine (Liebreich, 1869). For some years it was the only alternative hypnotic to opium and its derivatives apart from alcohol. It was also the first drug to be used as an intravenous anaesthetic (Oré, 1872'), and was used to prepare patients for operation as long ago as 1874 by Forné.

Lately it has been widely used, especially in midwifery, in combination with nembutal.³ ¹ Little use, however, has been made of chloral in recent years as far as general anaesthesia is concerned, and no reference to it is found in the current British textbooks on anaesthetics except in connection with thyroid surgery and midwifery. The use of chloralhydrate has been neglected of late years because attention has been focused more on the modern hypnotics such as the barbiturates.
Chloral in dosages of 10 to 30 grains produces a natural type of sleep lasting 6 to 8 hours. This sleep is prevented by pain and lesser disturbances and there is no diminution of normal reflexes. These effects are due to a depression of the C.N.S. which first shows itself by a general diminution of objective perception, a diminished consciousness and so a tendency to sleep. Small doses diminish the normal movements produced by electrical excitation of the motor area of the brain, and large doses prevent any response to such stimulation. The medulla is the last part of the C.N.S. to be attacked. In moderate doses respiration is not more depressed than in normal sleep. There is some depression of the vasomotor centre which produces vasodilation. This is said to result in some cases in skin eruptions which, however, are not common. Chloral produces a fall of temperature partly by increased heat loss due to vasodilatation and partly by diminished heat production. Chloral in large doses has been shown in animals to have a direct action on the heart muscle which lessens the power of automatic contraction of the muscle. Death from chloral poisoning, however, almost always results from respiratory failure, though marked cardiac depression occurs as well.

While other effects of chloralhydrate have been investigated before, our attention has been drawn to its effect on the blood-pressure, especially as there is a widespread prejudice amongst the medical profession as to bad effects of chloralhydrate on the heart. Even amongst pharmacologists, however, opinion has turned in favour of chloralhydrate. H. H. Meyer mentions the effect of small doses of chloralhydrate on hypertension. Gunn states that the therapeutic dose is considerably less than the depressant dose. Clinically chloralhydrate has found an application even in the treatment of cardio-vascular diseases. J. MacKenzie recommended chloralhydrate as a hypnotic in circulatory disorders. Alstead used it for producing prolonged periods of rest (7 to 10 days with two doses of 10 grs. in daytime and one night dose of 20 grs.) in heart cases and reports favourably on his results. Jaquet and Glaus treated sleeplessness in circulatory diseases with chloralhydrate with favourable results particularly in hypertensive cases.
EXPERIMENTAL PART

The blood-pressure was taken in 125 soldier patients all of whom were E.N.T. cases admitted for operation. As premedication they were given chloralhydrate XXX grs. (ad. ¼ oz. water) twice, the first dose being given in the evening before the operation, the second dose in the morning about 4 hours before the operation, leaving an interval of at least 8 hours between the two doses. Besides chloralhydrate per os they were given an injection of 1/100 or 3/200 gr. (in the later stage of the investigation) of atropine. Readings of the blood-pressure were taken at least twice: the first time soon after arrival in hospital, that is to say before any medication, the second time 3 hours after the second dose of chloralhydrate. A proportion of the cases was subjected to four blood-pressure readings: the first two being performed as mentioned above, the third 1 hour after the atropine injection and the fourth on the day after the operation.

Each blood-pressure reading consisted itself of three measurements by stethoscope according to American usage,\(^\text{12}\) the first measurement being the point where the pulse sound reappears (systolic blood-pressure), the second one the point where the sound changes from a loud one to a weaker one and the third one the point where the sound disappears entirely. The judgment on rise or fall of the blood-pressure, however, has been based on the systolic blood-pressure only as experience has shown that this reading is the most reliable of the three, that is to say, the one which is almost free from subjective factors.

The main object of investigation was the comparison between blood-pressure reading 1 (before chloral) and blood-pressure reading 2 (after chloral). The distribution of the results is shown in Table I.

<table>
<thead>
<tr>
<th>TABLE I.</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Effect of Chloral on the Blood-pressure (our results)</td>
</tr>
<tr>
<td>Mm. Hg.</td>
</tr>
<tr>
<td>5 10 15 20 25 30 35 40 45 50</td>
</tr>
<tr>
<td>Number of patients</td>
</tr>
<tr>
<td>Percentage of series</td>
</tr>
</tbody>
</table>
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It is interesting to compare our results with those obtained by Alstead (1936) who investigated 55 cases (33 of whom had heart disorders).

**Table II.**

<table>
<thead>
<tr>
<th>EFFECT OF CHLORAL ON THE BLOOD-PRESSURE</th>
<th>FALL</th>
<th>UNCHANGED</th>
<th>RISE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mm. Hg.</td>
<td>5</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>Number of patients</td>
<td>14</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Percentage of series</td>
<td>15.9</td>
<td>9.1</td>
<td>3.6</td>
</tr>
<tr>
<td>Mm. Hg.</td>
<td>20</td>
<td>25</td>
<td>30</td>
</tr>
<tr>
<td>Number of patients</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Percentage of series</td>
<td>3.6</td>
<td>1.8</td>
<td>1.8</td>
</tr>
<tr>
<td>Mm. Hg.</td>
<td>35</td>
<td>40</td>
<td>-</td>
</tr>
<tr>
<td>Number of patients</td>
<td>4</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Percentage of series</td>
<td>7.3</td>
<td>5.3</td>
<td>1.1</td>
</tr>
</tbody>
</table>

If we consider our series as a whole, chloral produces an average fall of the blood-pressure of 15.4 mm. Hg. (-4.0 mm. Hg. with Alstead). This average figure, however, is a bit misleading, as the group distribution shows a bigger effect in the direction of a fall of the blood-pressure. In 54 cases e.g. the fall amounts to 20 mm. Hg. or more. There is always a small percentage of cases (8.8 in our series, 23.7 in Alstead’s) which respond to chloral with a rise of the blood-pressure, the cause of this individual reaction being unknown.

Our blood-pressure readings after the atropine injection led us to think that atropine counteracts the effect of the chloral to a certain degree by raising the blood-pressure again. In 45 cases in which the blood-pressure had been taken after atropine there was an average rise of the blood-pressure of 5.7 mm. Hg. The distribution of the cases, however, shows that 26 responded with a rise and 12 with a fall while 7 remained unchanged. If we take the 26 plus cases alone, the average rise amounted to 14.8 mm. Hg. In the later stages of the investigation (30 cases) we increased the amount of atropine to 3/200 gr., but the average rise of the blood-pressure was not greater than after 1/100 gr. of atropine. A control experiment was made with 8 soldiers outside our series who were given 3/200 gr. of atropine without any chloral. Only 4 of these cases showed a rise of the blood-pressure after 30 minutes. According to pharmacological experience atropine causes a slight rise of the blood-pressure.*
Blood-pressure readings on the day after operation were taken in 38 cases. In the majority (22 cases) the blood-pressure did not return to the level before the operation. It did return in 7 cases and went even higher in 9 cases.

The question can be raised whether the decrease in the blood-pressure is really due to the drug or to a night's rest or to other oscillations of the blood-pressure which usually occur even under normal circumstances, e.g. after mental stress. (An interesting experiment has recently been made in which civil defence workers were conditioned to air raid noises by producing them on records. Their blood-pressure rose by 15 mm. Hg. in the average.) Four soldiers outside our series in whom a control reading of the blood-pressure was taken after a night's rest in hospital showed the following figures: -5, -10, +5, +0, -5, this indicates an average fall of 3 mm. Hg. It is, therefore, obvious that the effect of chloral exceeds the usual oscillations of the blood-pressure.

A further question was whether the decrease in the blood-pressure is accompanied by a fall in the pulse rate. Sixteen cases in whom the pulse rate was noted two hours after the second dose of chloral showed an average fall of the pulse rate of 6 beats. It could be questioned, finally, whether or not the slight increase in the blood-pressure produced by atropine was due to the fading out of the effect of the chloral. Some control experiments, however, showed that the effect of chloral on the blood-pressure is still traceable after many hours (6 to 8).

**Clinical Observations**

Our clinical observations were based on the study of a series of 162 soldiers undergoing general anaesthesia for ear, nose and throat operations controlled by a series of 132 soldiers undergoing operations of the same type by the same team in the previous four months who were given $\frac{1}{2}$ gr. of morphia and $\frac{1}{100}$ gr. of atropine as premedication. The bulk of the operations were either submucous resections of the septum nasi or removals of tonsils by dissection. Chloral-hydrate causes the patients to fall asleep in about half an hour. The sleep is sound but the patients are easily roused and usually arrive awake in the anaesthetic room being then well
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orientated and not at all anxious. The patients are more sensible and co-operative than after omnopon and scopolamine.

During the induction of anaesthesia (NO, and O2 or open Ethylchloride) no respiratory depression was noticed so that induction was quick. Maintenance of anaesthesia was by intratracheal N2O, O2 and ether. Less ether was required than with morphia and atropine premedication. The pupils were larger at every stage of anaesthesia. The cough reflex returned promptly after operation but there was a tendency to restlessness which was controlled in the later cases by morphine gr. ½ given immediately after operation.

As to postoperative complications there occurred a few cases (3 to 5 per cent) of bronchitis, local sepsis and secondary haemorrhage in both series, their number was slightly less in the chloral series. There were no cardiovascular complications at all and none of the other complications was serious.

CONCLUSIONS

Chloralhydrate premedication has the advantage of allaying anxiety without depressing respiration or delaying the return of the cough reflex; furthermore, it is reliable in its clinical effects. It reduces the amount of ether required, is cheap and easily obtainable.

As disadvantages must be mentioned its nasty taste (which can be mitigated by dilution and flavouring with synthetic lemon) and the occasional postoperative restlessness which can be controlled by a small injection of morphine (gr. ½) immediately after the operation. This is the more advisable as chloral is not an analgesic.

Our experience with chloralhydrate leads us to believe that it deserves to be used more widely as a premedication.

SUMMARY

In about 160 cases chloralhydrate with atropine proved to be a safe and satisfactory preoperative medication. Its main advantage is that it reduces fear without depressing the respiration or cough reflex. The effect of chloralhydrate on the
blood-pressure has been more closely studied and found to be far short of the danger line.

We wish to express our thanks to Dr. F. Pygott, Acting Medical Superintendent, for the helpful interest he has shown in this work.

REFERENCES