AN EVALUATION OF THE EFFECT OF METHOHEXITONE AND PROPANIDID ON BLOOD PRESSURE, PULSE RATE AND CARDIAC ARRHYTHMIA DURING ELECTROCONVULSIVE THERAPY

BY

W. N. ROLLASON, M. S. SUTHERLAND AND D. J. HALL

SUMMARY

The effects of methohexitone and propanidid on the cardiovascular system of patients undergoing electroconvulsive therapy were evaluated on thirty-five patients. The anaesthetic and electroconvulsive therapy practice included intubation as a routine and pulmonary ventilation with 100 per cent oxygen between the administration of the shock and the onset of spontaneous respiration. The electrocardiogram was monitored continuously and the blood pressure and pulse rate were recorded at seven points in time during the procedure. In the evaluation only the first two treatment occasions were taken into consideration, methohexitone being used on one and propanidid on the other, the order for any given patient being determined at random. The effect of the order of the drugs was allowed for in the calculation of the results. Compared with propanidid, methohexitone was associated with higher systolic and diastolic blood pressures during the earlier stages and with lower pressures during the later stages. The higher blood pressures were in general associated with lower pulse rates and the lower pressures with slightly higher pulse rates. The return of spontaneous respiration was slower when propanidid rather than methohexitone was used. There was no reason to suspect a difference in the incidence of cardiac arrhythmia produced by the drugs.

Since its inception in 1938 by Cerletti and Bini, electroconvulsive therapy has remained an important psychiatric treatment. The chief cause of mortality with drug-modified electroconvulsive therapy has been stated to be cardiovascular complications (Woodruff, Pitts and McClure, 1968).

Systematic evaluation of the use of two ultrashort-acting barbiturates, thiopentone and methohexitone, has been carried out by Pitts and associates (1965). In their study the electrocardiogram was used to evaluate the incidence of cardiac arrhythmias and it was shown that these were more frequent and more serious when thiopentone was the induction agent used. A subsequent study (Woodruff, Pitts and McClure, 1968) showed that the incidence of the arrhythmias using the same two induction agents was not altered by pre-oxygenation of the patients.

Propanidid and thiopentone have been compared as anaesthetic agents during electroconvulsive therapy in two reported studies. Naftalin, Haw and Blevans (1969) showed that when propanidid was used there was an absence of pains due to suxamethonium, apnoeic periods were longer, waking and talking times were shorter, and there was a marginal improvement of psychological performance. Finlayson, Burnheim and Boots (1970) demonstrated a faster rate of physical arousal and recovery of mental function when propanidid was used. A further study by Heifetz, Birkhan and Davidson (1969) compared propanidid with thiopentone and showed that the times to waking and walking were considerably shorter in patients who received propanidid.

This study was designed to evaluate the effects of methohexitone and propanidid used as induction agents on the cardiovascular system of patients undergoing electroconvulsive therapy. Because earlier studies (Pitts et al., 1965; Woodruff, Pitts and McClure, 1968) had indicated that arrhythmias were most common in the postcon-
vulsive phase, when hypoxia may be a factor, the patients in the study were intubated prior to the shock so that the lungs could be ventilated with 100 per cent oxygen during the period between the administration of the shock and the onset of spontaneous respiration. As propanidid is reputed to prolong the action of suxamethonium, the time to the onset of spontaneous respiration was recorded. The electrocardiogram was monitored continuously using the technique of radiotelemetry and the blood pressure and pulse rate were recorded at seven points in time.

METHOD

Patients who received electroconvulsive therapy at the Ross Clinic, Aberdeen, on Friday mornings over the period May 1969 to March 1970 were given either methohexitone or propanidid as part of the anaesthetic procedure. On the occasion of their first shock the choice of drug used was determined by convenience but on the occasion of their second shock the drug which was not used on the first occasion was used.

The anaesthetic and electroconvulsive therapy practice observed was as follows. Anaesthesia was induced using either 5 per cent propanidid 500 mg or 1 per cent methohexitone 100 mg, each solution containing atropine sulphate 1.2 mg. Each solution was injected intravenously very slowly at the rate of 1 ml per 15 sec and hypnotic suggestion was used.

Prior to the slow injection of either 1 per cent methohexitone or 5 per cent propanidid, the patient was asked to relax the whole body from the tips of the toes to the top of the head. During the slow injection the patient was asked, in a soporific voice, to relax feet, calves, thighs, "tummy", chest, both shoulders, both arms, the neck muscles and the face muscles. The patient was then asked to let the head sink into the pillow and told that the body was becoming heavy and warm and that the eyelids were getting heavier and heavier and he would soon be asleep.

The very slow injection seemed to allow time to take the patient to the hypnoidal plane and made induction of anaesthesia a pleasant experience for these anxious and depressed patients.

Suxamethonium 50 mg was then administered and the lungs ventilated with 100 per cent oxygen using an Oxford oxygen inflator. After the fibrillary twitchings had ceased the trachea was intubated and ventilation with 100 per cent oxygen continued via the endotracheal tube which remained in situ until spontaneous respiration had returned. The shock was administered immediately after the intubation. A mouth gag was placed in position and a current of 8 joules passed for 3 sec using bifrontal leads. The patient was observed for evidence of generalized cortical stimulation. If there was no such evidence a second current of 9 joules was passed for 4 sec. This invariably produced evidence of generalized cortical stimulation.

The blood pressure and pulse rate were monitored and their values recorded at seven points in time. These were: pre-induction, post-induction, post-suxamethonium, post-intubation, post-shock, post-extubation, and finally when respiration had returned to normal. The time to the return of spontaneous respiration was also recorded. This was taken to be the onset of regular diaphragmatic movement which was quickly followed by intercostal movement and straining on the endotracheal tube. The blood pressure was recorded by a new von Recklinghausen Scala Altera oscillotonometer which was retained in its own special carrying case. The same instrument was used throughout the investigation and the same observer (W.N.R.) made all the measurements using the orthodox technique for this type of instrument. It was not considered ethical to use intra-arterial manometry in this investigation.

The electrocardiogram was monitored continuously from before induction of anaesthesia to the resumption of normal spontaneous respiration. The method of radiotelemetry was employed (Rollason, 1969). Standard lead 1 was used in conjunction with an oscilloscope, a Telefunken 85 tape recorder and a Mingograph direct writer.

RESULTS

From the total of shocks administered and monitored in this way only a certain subgroup were included in this evaluation. For each patient involved, only his first two treatments were considered and only when the time that had elapsed between them was one week and when the anaesthetic and electroconvulsive therapy practice was standard (i.e. no extra drugs had been given and
intubation had been successfully undertaken). If the recordings of blood pressure or pulse were absent at more than two points of time on any one treatment the patient was not included.

Thirty-five patients satisfied these criteria. Five were males each of whom received the drugs in the order (i) propanidid (ii) methohexitone. Thirty were females, of whom eighteen received the drugs in the order (i) propanidid (ii) methohexitone, and twelve received them in the opposite order.

Because of the possible effect that order and sex might have on the results, data concerning the five males who received propanidid the first week and methohexitone the second, and for whom there was no group of the same sex who received the treatments in the opposite order for comparison, were omitted from statistical consideration.

The mean age of the group that received methohexitone first was 46 years and their mean weight was 59 kg. For the group that received propanidid first the means were 52 years and 58 kg. Of the women, fifteen patients were concurrently receiving antidepressant medication, and six were receiving phenothiazine derivatives. There were no statistically significant differences between the results from the patients receiving antidepressants and the others. The patients receiving phenothiazine derivatives did not form a large enough group for tests of significance but there is no evidence to suggest that the psychotropic medication in any way influenced the results.

The mean blood pressures and pulse rates were calculated for each drug for each of the seven stages of the procedure. In order to average the possible effect of order the mean of the two group means was obtained. The results for the patients when they were given propanidid are shown in table I. The typical systolic pattern was a large fall in pressure from pre-induction to post-induction stages, followed by a compensating rise up to the post-suxamethonium stage. The pressure continued to rise and reached a maximum at the post-shock stage and then decreased to end at the final reading 12 beats/min faster than at pre-induction.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Systolic</th>
<th>Diastolic</th>
<th>Pulse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-induction</td>
<td>136.5</td>
<td>77.9</td>
<td>83.2</td>
</tr>
<tr>
<td>Post-induction</td>
<td>106.7</td>
<td>67.6</td>
<td>108.6</td>
</tr>
<tr>
<td>Post-suxamethonium</td>
<td>137.0</td>
<td>83.2</td>
<td>114.2</td>
</tr>
<tr>
<td>Post-intubation</td>
<td>185.8</td>
<td>103.5</td>
<td>122.5</td>
</tr>
<tr>
<td>Post-shock</td>
<td>193.5</td>
<td>98.9</td>
<td>126.9</td>
</tr>
<tr>
<td>Post-extubation</td>
<td>170.5</td>
<td>89.2</td>
<td>108.4</td>
</tr>
<tr>
<td>Final</td>
<td>145.1</td>
<td>81.8</td>
<td>95.6</td>
</tr>
</tbody>
</table>

* One group contained 18 female patients who received propanidid first. The other contained 12 female patients who received methohexitone first.

The differences between the mean values at each stage of the systolic and diastolic pressures and pulse rates, compared with the succeeding stage, were, with the exception of the difference post-intubation to post-shock, each significant (P<0.01).

For each of the thirty female patients the differences between the systolic blood pressures, the diastolic blood pressures and the pulse rates on the two treatment occasions at each of the seven recorded points of time were calculated. The means and variances of these differences were computed for the group of women who received the drugs in the order (i) propanidid (ii) methohexitone and for the group who received them in the opposite order. The values of the mean differences and their standard deviations are shown in table II. It is seen that the differences (methohexitone minus propanidid) when propanidid was the first treatment were positive for the first four stages and negative for the last three. The standard deviation was similar for all stages apart from pre-induction when it was a little lower. The findings were consistent when methohexitone was the first treatment. The pattern of results for the diastolic pressure was similar to the systolic but both the mean values and the standard deviations were, in general, lower. No pattern is immediately discernible from the results for the pulse rates.

The effect of the order in which the treatments were given was eliminated by using half the difference of the means of the two groups as a
measure of the difference of the drugs for each of the seven points in time.

It was seen from table III that the use of methohexitone was associated with higher blood pressure at the pre-induction stage. The largest positive difference, propanidid minus methohexitone,

| TABLE III |
|------------------|------------------|------------------|
| **Means and standard deviations of differences of blood pressure (mm Hg) and pulse rate (beats/min) by order of anaesthetic practice in 30 females.** |
|                  | **Systolic**     |                  | **Diastolic** |                  | **Pulse** |
|                  | **Mean**| **SD** | **Mean**| **SD** | **Mean**| **SD** |
| **Pre-induction**| +6.4 | -2.1 | 16.0 | 11.1 | +1.1 | -2.5 | -1.8 | +0.5 | -9.0 | 19.1 |
| **Post-induction**| +26.4 | -11.2 | 27.7 | 14.6 | +9.7 | -8.8 | 10.2 | 6.5 | -0.4 | +3.9 | 13.4 | 14.7 |
| **Post-suxamethonium**| +6.5 | -7.9 | 18.3 | 17.4 | 0 | -2 | 10.7 | 13.9 | -1.8 | +6.0 | 11.1 | 14.1 |
| **Post-intubation**| +6.9 | -1.7 | 22.1 | 25.8 | +0.8 | +1.2 | 13.4 | 11.6 | -0.2 | +8.5 | 10.6 | 8.8 |
| **Post-shock**| -3.9 | +16.8 | 21.8 | 12.8 | -6.9 | +6.8 | 13.6 | 9.6 | -2.7 | +2.7 | 14.4 | 16.6 |
| **Post-extubation**| -2.5 | +15.8 | 24.6 | 22.4 | -1.7 | +5.8 | 10.0 | 10.8 | +4.8 | +3.5 | 14.3 | 10.3 |
| **Final**  | -7.2 | +2.3 | 21.6 | 14.2 | -6.2 | +3.2 | 7.2 | 9.8 | +4.9 | +0.7 | 9.2 | 10.9 |

* PM means the order was first propanidid, second methohexitone; the value given in the column is the mean increase, methohexitone minus propanidid. This group contains 18 patients.

MP means the order was first methohexitone, second propanidid; the value given in the column is the mean increase, propanidid minus methohexitone. This group contains 12 patients.

The mean difference between the times to the return of spontaneous respiration with the two drugs was 1.0 minute, methohexitone having the lower mean. This difference was significant ($t = 3.321$, $P < 0.01$, d.f. = 27).

The effect of the difference in the order with which the drugs were given on the two occasions upon the results was obtained as half the sum of the means of the two orders of anaesthetic practice, shown in table II. These effects are sum-

marized in table IV. Both systolic and diastolic blood pressures gave some positive and some negative results, none was statistically significant. The mean effect of order upon pulse gave higher values for the second occasion at each of the seven points of measurement, only one was individually significant, post-intubation $P<0.05$. The probability of the seven readings being either all positive or all negative on the basis of random chance was 0.016. It was concluded that the order in which the drugs were given had little effect upon blood pressure but that an effect on pulse rate could not be excluded. There was no significant order effect on the time to spontaneous respirations.

**TABLE IV**

*Mean effect of order of anaesthetic practice upon blood pressure (mm Hg) and pulse rate (beats/min) of 30 female patients. The effects of the propanidid and methohexitone have been eliminated.*

<table>
<thead>
<tr>
<th>Time to spontaneous respiration (min)</th>
<th>Systolic</th>
<th>Diastolic</th>
<th>Pulse</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+2.3</td>
<td>−0.7</td>
<td>+0.9</td>
</tr>
<tr>
<td>Pre-induction</td>
<td>+7.6</td>
<td>+0.5</td>
<td>+1.7</td>
</tr>
<tr>
<td>Post-induction</td>
<td>−0.7</td>
<td>−1.0</td>
<td>+2.1</td>
</tr>
<tr>
<td>Post-suaxamethonium</td>
<td>+2.7</td>
<td>−1.0</td>
<td>+4.4</td>
</tr>
<tr>
<td>Post-shock</td>
<td>+6.5</td>
<td>−0.1</td>
<td>+0.0</td>
</tr>
<tr>
<td>Post-extubation</td>
<td>+6.7</td>
<td>+2.1</td>
<td>+4.2</td>
</tr>
<tr>
<td>Final</td>
<td>−2.5</td>
<td>−1.5</td>
<td>+2.8</td>
</tr>
</tbody>
</table>

Note: A positive value indicates a higher mean value on the second occasion; a negative value indicates a higher mean value on the first occasion.

A comparison of the male group that received the drugs in the order (i) propanidid (ii) methohexitone with the corresponding female group gave no indication of major differences between the sexes.

Of the thirty female patients eight showed evidence of cardiac arrhythmia. Four showed ventricular ectopics, one post-shock when propanidid had been administered, and one post-intubation, one post-shock and one post-extubation each when methohexitone had been used. Four patients exhibited a tachycardia exceeding 160 beats/min during the procedure. This occurred on each of the drugs for three of them and only when propanidid was used for the fourth. One of the five male patients experienced tachycardia with each of the drugs. On the basis of these results there was no reason to suspect a difference of adverse cardiac effect between the drugs.

**DISCUSSION**

The slow injection of either 1 per cent methohexitone or 5 per cent propanidid, coupled with hypnotic suggestion, ensures a smooth and pleasant induction of anaesthesia without any side effects such as hiccup or convulsive movements being observed. Atropine 1.2 mg was added to each induction agent to prevent the profuse secretion in the upper respiratory tract and the marked bradycardia that has occurred after unmodified electroconvulsive therapy and which has been ascribed to vagal over-activity. The absence of secretions and the increase in pulse rate seen in all cases would suggest that this dosage of atropine could be drastically reduced and the dosage of 1.0 to 2.5 mg atropine recommended by Rich and associates (1969) is too high.

The slight prolongation of the effect of suxa-methonium by propanidid provided consistently ideal conditions for intubation and modified the subsequent convulsion more effectively.

The reduction in blood pressure and increase in pulse rate was more marked after induction with propanidid than methohexitone, although this was transient.

A slightly increased blood pressure and pulse rate was subsequently seen with propanidid relative to methohexitone up until the post-convulsive phase but after this phase this trend was reversed.

The incidence of electrocardiographic changes was not significantly greater with one agent than the other. Such changes tended to be more frequent during the peak of cardiovascular stress in the immediate post-convulsive phase. On occasion this stress, although transient, was marked. This has been observed by others (Yamashita, Matsuba and Tominaga, 1970).

There was no instance of bed-wetting during the recovery phase with either agent.

Under the conditions of this study, propanidid and methohexitone were equally satisfactory as induction agents but intubation was more consistently smooth and the subsequent shock more consistently modified after propanidid. Blood pressure and pulse rate changes, however, were somewhat more marked when this agent was used,
although there was no significant increase in the incidence of cardiac arrhythmia as reflected by the technique of radiotelemetry using standard lead 1. During the administration of the shock the tracing was temporarily obliterated for approximately 5 sec.

The use of an endotracheal tube, 100 per cent oxygen and adequate ventilation eliminated the possibility of hypoxia or carbon dioxide retention occurring between the administration of the shock and the onset of adequate spontaneous respiration. On the other hand, intubation itself produced a marked pressor response and prolonged the duration of the period of peak cardiovascular stress. Its routine use in electroconvulsive therapy is probably not justified.

The blood pressure tended to be higher during the second treatment and the pulse rate consistently so and may be related to increasing apprehension.

ACKNOWLEDGEMENTS
Our thanks are due to Mr Gordon Bowie for his assistance with the electrocardiographic monitoring and to Dr Eleanor Walker for her co-operation in the study.

REFERENCES


UNE ANALYSE DE L'EFFET DE METHOHEXITONE ET PROPANIDID SUR LA PRESSION SANGUINE, LE POULS ET L'ARRHYTHMIE CARDIAQUE AU COURS DE LA THERAPIE ELECTROCONVULSIVE

SOMMAIRE
Les effets de methohexitone et propanidid sur le systéme cardiovasculaire de malades soumis à l'électrochock, ont été analysés chez trente cinq patients. La pratique de l'anesthésie et de la thérapie electroconvulsive comprenait l'intubation de routine, ainsi que la ventilation pulmonaire avec de l’oxygen à 100 pour cent, sous l'administration du choc et le début de la respiration spontanée. L'electrocardiogramme a été enregistré sans interruption et la pression sanguine et le pouls ont été notés à sept reprises durant la procédure. Pour l'évaluation on ne prit en considération que les deux premiers traitements, avec pour l’un des deux, administration de methohexitone, pour l’autre de propanidid; l’ordre d’administration fut établi au hasard pour chacun des patients. On a tenu compte dans le calcul des résultats de l'effet de l'ordre des médicaments. Le methohexitone, comparativement au propanidid, s'accompagne d'une pression sanguine systolique et diastolique plus élevée aux premiers stades et d'une pression moins élevée au cours des stades ultérieurs. La pression sanguine plus élevée d’association en général à un pouls plus lent et la pression plus basse à un pouls légèrement accéléré. Le retour à la respiration spontanée fut retardé lorsqu’on avait utilisé propanidid plutôt que methohexitone. Il n’y eut aucune raison de croire en une différence de la fréquence des arrhythmies cardiaques, produites par les deux médicaments.

BEWERTUNG DER WIRKUNG VON METHOHEXITONE UND PROPANIDID AUF BLUTDRUCK, PULSFREQUENZ UND HERZARRHYTHMEN WÄHREND ELEKTROSHOCK-BEHANDLUNG

ZUSAMMENFASSUNG
BOOK REVIEW


Thirteen years have elapsed since the publication of Professor Campbell’s classic monograph on the respiratory muscles. The second edition is transformed by a threefold expansion of length, extension of scope and the addition of two more authors. In fact, they make free use of additional authors where this seems necessary and Professor Milk-Emili makes a particularly important contribution. The result is a magnificent work of unquestioned authority covering in great detail a most difficult and relatively neglected field. It traces the act of breathing from the origin of rhythmicity in the medulla, through spinal control, to the action of the individual respiratory muscles and thence moves to a consideration of chest movements and the expenditure of work overcoming the various forms of impedance to breathing. Curiously this sequence is presented in the reverse order. The work ends with a rather short section on pathological states.

The core of the first edition was the account of the action of the respiratory muscles: this is largely unchanged in the new edition, although a new chapter on the diaphragm has been written by Agostoni and Sant’Ambrogio. It is comforting to find that theories of the role of the respiratory muscles do not appear to have undergone fundamental changes in recent years although new information is available on their control. Important new sections deal with the part played by muscle spindles in the control of the respiratory muscles and it will be remembered that the subject first came to attention largely as a result of Professor Campbell’s studies. It is unfortunate that spindles should have been omitted from the index.

The book contains many references to the influence of anaesthesia on the respiratory muscles and the mechanics and control of breathing. These are scattered widely through the text but the index gives three useful leads. The now well-known effects of curarization and vagal block on the sensation of breathing are well covered and the whole difficult subject is brought together in an admirable chapter presenting the complex model of respiratory sensation first proposed by Godfrey and Campbell in 1968. It is also pleasing to find the number of anaesthetists who have made contributions to the original work on which the book is based. For example, at least nine anaesthetists feature in the reference list of the chapter on supraspinal control.

Once more it must be said that this is a book for the serious student. The difficult subject material does not make this an easy book to read after a busy day in the operating theatre, although there is wonderful uniformity of style for a multi-author book. The book seems likely to become an essential reference work for study and research in the fields of the respiratory muscles and the mechanics and control of breathing. No department of anaesthesia should be without a copy.

J. F. Nunn