HEXAFLUORENIUM-SUXAMETHONIUM RELAXATION FOR ABDOMINAL SURGERY

BY
F. N. CAMPBELL AND M. SWERDLOW

SUMMARY
Hexafluorenium was used to potentiate suxamethonium in 93 patients undergoing abdominal surgery of up to 60 minutes duration. Anaesthesia consisted of thiopentone-nitrous oxide-oxygen, usually with pethidine supplementation, and ventilation was controlled. In one group hexafluorenium was administered before induction, the intubating dose of suxamethonium then providing relaxation for surgery. In a second group of patients hexafluorenium followed by suxamethonium was given after the intubating dose of suxamethonium had worn off. No bronchospasm or cardiovascular side effects were noted. It is considered that this drug combination provides excellent relaxation for abdominal surgery but is particularly suitable in cases which last 30 minutes or longer.

Hexafluorenium was first investigated as a neuromuscular blocking agent by Cavallito, Gray and Spinner (1954) and was introduced into clinical anaesthesia by Cordaro and Arrowood (1955), who observed that muscular relaxation was marked during anaesthesia but was not apparent in the conscious patient.

Arrowood and Kaplan (1956) noted that hexafluorenium potentiated and prolonged the action of small doses of suxamethonium. They used this combination of drugs to provide muscular relaxation in preference to hexafluorenium on its own. Foldes and others (1958, 1960a, b) studied the neuromuscular and anticholinesterase actions of hexafluorenium. Hexafluorenium has a weak non-depolarizing action at the neuromuscular junction and a marked anticholinesterase activity. It has been used by a number of workers—notably by Rizzi (1956), Foldes (1960) and Kok, Sher and Kruger (1962)—to potentiate suxamethonium for muscular relaxation, mainly in prolonged operations. There have been some reports of the occurrence of bronchospasm (Selvin and Howland, 1959), as well as of cardiac arrhythmias and histamine release (Mostert and Kündig, 1964), but the liability of hexafluorenium to produce these side effects has been strongly refuted by a number of workers (Foldes, 1960; Duncalf et al., 1965; van Hemert and Pearce, 1965). The present investigation was undertaken to see if the hexafluorenium-suxamethonium combination would be useful in abdominal operations of short duration.

METHOD
Any patient over 14 years of age undergoing abdominal surgery of an anticipated duration of less than 30 minutes was included in the study. However, operations which should have been short were sometimes rather protracted and such cases were included unless they exceeded a duration of 1 hour. In all a total of 93 cases was studied including elective and emergency operations, and patients of varied physical fitness. The operations included a wide range of general surgical procedures and Caesarean section. Premedication varied according to the fitness of the patient and the anaesthetist's preference but generally an opiate plus a belladonna preparation were administered.

Two different techniques were employed in the course of the trial.

Group I. In 35 cases hexafluorenium 0.3—0.5 mg/kg was given intravenously 3 minutes before induction of anaesthesia with thiopentone; suxamethonium 0.25—0.3 mg/kg was then given and the patient intubated when conditions became...
adequate. Anaesthesia was maintained with nitrous oxide and oxygen supplemented usually with pethidine, the ventilation being controlled. When the operation outlasted the relaxation produced by the suxamethonium a second dose of suxamethonium was administered; the size of this second dose depended on the response to the first dose and on the likely duration of surgery; the dose was usually 5–10 mg.

**Group II.** In the remaining 58 patients induction was with thiopentone, and a dose of suxamethonium (usually 50 mg) was then given to facilitate intubation. After the effects of this initial dose of suxamethonium had worn off 0.3–0.5 mg/kg hexafluorenium was administered and 1½–2 minutes later a dose of 0.25–0.3 mg/kg of suxamethonium; anaesthesia was maintained as above. In 14 of these patients an additional dose of suxamethonium was required, the amount depending on the likely duration of relaxation and the size and effect of the preceding dose.

In earlier cases the quality and duration of relaxation was estimated clinically by observation of the wound, watching for return of respiratory effort, palpation of the reservoir bag and comment from the surgeon. In later cases a peripheral nerve stimulator, as described by Cohen (1963), was applied to the facial nerve to observe the degree of paralysis. Observations were visual and were charted at 5-minute intervals. The response was graded as:

- + first noticeable twitch;
- ++ small but more definite response;
- +++ a vigorous response;
- ++++ a very vigorous response equal to that of the non-paralyzed patient.

The response to single, tetanic and post-tetanic stimulation was noted.

Returning muscle tone was carefully observed at the end of the operation and thereafter. The time from the end of the operation to the patient being able to raise his head off the pillow on request was noted. In addition pulse rate and blood pressure were followed throughout surgery and in the immediate postoperative period.

**RESULTS**

It was found that good relaxation could always be obtained with the combination of hexafluorenium and suxamethonium. The results are detailed according to the two groups:

**Group I. Cases who received hexafluorenium before the induction of anaesthesia.**

These patients soon became apnoeic when suxamethonium was given following induction of anaesthesia, but conditions for laryngoscopy and intubation were not good until 1½ minutes later and even then the cords were usually mobile. There were no muscular fasciculations, but increased salivation was noted. In 2 patients bradycardia occurred following administration of the suxamethonium. In the short time between injection of hexafluorenium and induction of anaesthesia 8 patients complained of nausea and 4 vomited.

Eight of the 35 cases in this group lasted less than 30 minutes; the remainder were of up to an hour's duration. In 14 patients, only one dose of suxamethonium was necessary; the duration of action of this dose is analyzed in table I. At the end of anaesthesia there was return of adequate muscle tone within 5 minutes in 12 of these 14 patients.

Twenty-one patients required more than one dose of suxamethonium; the duration of surgery was more than 30 minutes in all but 2 of these 21 patients. The duration of relaxation produced by the first dose of suxamethonium was from 15 to 30 minutes in 19 of the patients. At the end of anaesthesia adequate muscle tone returned within 5 minutes in 15 cases and within 15 minutes in the remaining 6.

Six cases in Group I were tested with a nerve stimulator. Of these, 5 showed phase I block and 1 phase II.

**TABLE I**

<table>
<thead>
<tr>
<th>Duration of action of suxamethonium (min)</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>10–20</td>
<td>0</td>
</tr>
<tr>
<td>21–30</td>
<td>4</td>
</tr>
<tr>
<td>31–40</td>
<td>6</td>
</tr>
<tr>
<td>41–50</td>
<td>3</td>
</tr>
<tr>
<td>51–60</td>
<td>0</td>
</tr>
<tr>
<td>&gt;60</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>14</strong></td>
</tr>
</tbody>
</table>
Group II. Cases given hexafluorenium after the intubating dose of suxamethonium had worn off.

Of the 58 cases in this group 42 required only a single dose of suxamethonium to provide relaxation for the surgery. In 36 of these 42 patients the operation lasted less than 30 minutes. The duration of action of the potentiated suxamethonium is shown in table II.

<table>
<thead>
<tr>
<th>Duration of action of suxamethonium (min)</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-20</td>
<td>6</td>
</tr>
<tr>
<td>21-30</td>
<td>19</td>
</tr>
<tr>
<td>31-40</td>
<td>17</td>
</tr>
<tr>
<td><strong>Total 42</strong></td>
<td></td>
</tr>
</tbody>
</table>

The time from end of operation to return of adequate muscle tone is detailed in table III.

<table>
<thead>
<tr>
<th>Time from end of anaesthesia to return of adequate muscle tone (min)</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5</td>
<td>25</td>
</tr>
<tr>
<td>6-10</td>
<td>7</td>
</tr>
<tr>
<td>11-15</td>
<td>8</td>
</tr>
<tr>
<td>16-20</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total 42</strong></td>
<td></td>
</tr>
</tbody>
</table>

Sixteen patients in Group II required a second dose of suxamethonium in order to achieve an adequate duration of muscular relaxation. The duration of surgical relaxation provided in these patients by the first dose of suxamethonium is detailed in table IV.

<table>
<thead>
<tr>
<th>Duration of relaxation from first dose suxamethonium (min)</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>21-25</td>
<td>1</td>
</tr>
<tr>
<td>26-30</td>
<td>11</td>
</tr>
<tr>
<td>31-35</td>
<td>2</td>
</tr>
<tr>
<td>36-40</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total 16</strong></td>
<td></td>
</tr>
</tbody>
</table>

In all these 16 patients adequate muscle tone had returned within 5 minutes of discontinuance of anaesthesia. Of the 58 cases in Group II, 15 were tested with a nerve stimulator. Phase I block was found in 14 patients, and phase II block in 1 patient.

**DISCUSSION**

At the beginning of this study it seemed that it might be advantageous to administer hexafluorenium before the induction of anaesthesia. A small dose of suxamethonium would then be adequate for intubation and for the surgical relaxation. In addition it seemed probable that postoperative muscle pains from suxamethonium would be avoided (Kok, Sher and Kruger, 1962; McCaul and Robinson, 1962). Because of the high incidence of nausea and vomiting in the 3 minutes between administration of hexafluorenium and the induction of anaesthesia, this method was discontinued. (The sequence of thiopentone-hexafluorenium-suxamethonium was not tried as vomiting after hexafluorenium was thought to be possible, especially in emergency cases, although this sequence is recommended by Foldes (1968, personal communication) for elective surgery.)

For the remaining cases in the study it was decided to give a dose of suxamethonium for intubation and allow this to wear off before giving hexafluorenium.

Reports in the literature vary considerably in their opinion of hexafluorenium. On the one hand, Foldes and his associates (1960b), Kok, Sher and Kruger (1962), Rizzi (1956), Brazy, Schmidt and Fick (1962) produced favourable reports. On the other hand, Selvin and Howland (1959) reported several cases of bronchospasm with one case of cardiac arrest and Mostert and Kündig (1964) demonstrated that the drug caused severe arrhythmias and warned against its use. Foldes et al. (1960a) have pointed out that in the 6 cases of severe bronchospasm encountered by Selvin and Howland, the difficulty was caused by the administration of too large a dose of suxamethonium. The case described by Mostert and Kündig (1964) appears from its description to have been similar. It would seem inadvisable to administer too large a dose of suxamethonium after hexafluorenium. Mostert and Kündig (1964) put forward the hypothesis of hexafluorenium causing histamine
release to explain their own and other cases of severe bronchospasm. Van Hemert and Pearce (1965) were unable to confirm the findings of Mostert and Kündig concerning histamine release and, in common with Duncalf et al. (1965), were unable to confirm any adverse circulatory effects of hexafluorenium. Histamine release is possibly due to a high dosage of suxamethonium (Paton, 1959).

There has been much discussion of the mode of action of hexafluorenium. Foldes (Torda et al., 1967) demonstrated a weak non-depolarizing action as well as a marked anticholinesterase action.

The present findings are in accord with the more favourable reports. A good quality of relaxation was always achieved and with the return of respiration there was a fairly rapid recovery of good muscle tone. In view of the incidence of increased salivation with hexafluorenium it is recommended that a routine pre-operative dose of atropine should be given. Bronchospasm, however, was not observed and no arrhythmias were noted on routine palpation of the pulse. With regard to recovery of adequate muscle tone, a delay of up to 5 minutes from the end of the operation was considered good and up to 10 minutes not unreasonable. Longer delays are inconvenient and can disrupt an operating list, and for this reason the method is considered less suitable for cases of less than 30 minutes duration.

In the more prolonged operations reported by American workers, repeated doses of both suxamethonium and hexafluorenium were administered. None of the patients in the present series required a second dose of hexafluorenium.

REFERENCES


RELACHEMENT PAR L'HEXAFLUORENIUM-SUXAMETHONIUM DANS LA CHIRURGIE ABDOMINALE

SOMMAIRE

L'hexafluorene a été utilisé pour potentialiser le suxaméthion chez quatre-vingt-dix-neuf patients subissant une intervention de chirurgie abdominale de plus de 60 minutes de durée. L'anesthésie a été conduite par un mélangé de thiopentone-protoxyde d'azote-oxygène, en général avec un supplément de pétidine et la ventilation a été contrôlée. Dans un groupe l'hexafluorene a été administré avant l'intubation, la dose d'intubation du suxaméthion assurant le relâchement nécessaire à la chirurgie. Dans un second
Groupes de patients l’hexafluorene suivi par le suxaméthonium était administré au moment où la dose d’intubation du suxaméthonium cessa d’agir. On n’a noté aucun bronchospasme ni aucun effet secondaire cardiovasculaire. On pense que cette association médicamenteuse assure un relâchement excellent pour la chirurgie abdominale, mais qu’elle convient particulièrement aux cas dont l’intervention dure 30 minutes ou plus.

HEXAFLUORENIUM-SUXAMETHONIUM ALS RELAXANTIEN IN DER BAUCH-CHIRURGIE

ZUSAMMENFASSUNG

Bei dreiviertausend Patienten, die sich einer bis 60 Minuten dauernden Bauchoperation zu unterziehen hatten, wurde Hexafluoreniun zur Potenzierung der Suxamethonium-Wirkung angewendet. Die Narkose wurde mit Thiopenton-Lachgas-Sauerstoff und meist einer Zugabe von Pethidin bei kontrollierter Atmung durchgeführt. In einer Patientengruppe wurde Hexafluoreniun vor der Induktion appliziert, wonach die zur Intubation erforderliche Suxamethonium-Dosis eine ausreichende Relaxation für die Operation bewirkte. Einer zweiten Patientengruppe wurde Hexafluoreniun und danach Suxamethonium verabreicht, nachdem die Wirkung der zur Intubation gegebenen Suxamethonium-Dosis abgeklungen war. Man ist der Ansicht, daß mit dieser Wirkstoffkombination eine ausgezeichnete Relaxation für abdominelle Operationen erzielt wird; besonders empfohlen wird die kombinierte Anwendung der beiden Substanzen in solchen Fällen, in denen die Operation länger als 30 Minuten dauert.

REGISTRARS PRIZE (ANAESTHETICS)

Applications are invited by the Royal Society of Medicine, Section of Anaesthetics, for a prize of £50 provided by Messrs. May & Baker Ltd., for a paper written by a medical practitioner of Senior Registrar or Registrar status, holding an appointment in anaesthesia in a department or hospital, or in the armed forces of the Commonwealth or of the Republic of South Africa or Eire. Fellowship of the Royal Society of Medicine is not necessary for entry. The subject will be of the author’s choice, but must be connected with anaesthesia. All papers for the 1970 award must be submitted in triplicate by 1 January, 1970.

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