PREVENTION OF SUXAMETHONIUM-INDUCED CHANGES IN SERUM POTASSIUM CONCENTRATION BY HEXAFLUORENIUM

Is their combined use justified?

P. A. RADNAY, R. P. BADOLA, A. DALSANIA, E. I. EL-GAWEET AND D. DUNCALF

SUMMARY

Sixty patients, none of whom was suffering from renal failure, received neurolept anaesthesia. They were divided into six groups of 10 patients each. Groups I and IV, II and V, and III and VI were given suxamethonium 0.2, 0.6 and 1.0 mg kg\(^{-1}\) respectively. Groups IV-VI were pretreated with hexafluorenium 0.3 mg kg\(^{-1}\). The serum potassium concentration decreased significantly after the induction of anaesthesia and also following the administration of hexafluorenium. Neither suxamethonium 0.2 mg nor 0.6 mg kg\(^{-1}\) with or without hexafluorenium restored the potassium concentration to the control value. Suxamethonium 1.0 mg kg\(^{-1}\) alone caused the serum potassium to increase to values greater than control; hexafluorenium attenuated this effect. The combination of hexafluorenium and suxamethonium may be of benefit in patients who are anephric or are in chronic renal failure.

While many authors find neurolept anaesthesia using droperidol and fentanyl suitable for patients in chronic renal failure (Trudnowski et al., 1971; Morgan and Lumley, 1975), the choice of neuromuscular blocking agent remains controversial.

Gallamine frequently (Churchill-Davidson, Way and de Jong, 1967; Abrams and Hornbein, 1975), pancuronium bromide and tubocurarine occasionally (Logan, Howie and Crawford, 1974; Abrams and Hornbein, 1975) have caused prolonged neuromuscular blockade, which has necessitated ventilatory support following surgery. Suxamethonium, when given rapidly i.v., is known to increase both the degree of fasciculation and the serum potassium concentration (Powell, 1970) and, when administered as a continuous infusion, the total dose may be high, leading to a phase II block (Foldes, 1966a).

The combination of hexafluorenium (Mylaxen) and suxamethonium decreases the amount of suxamethonium required (Foldes, 1960, 1966b; Figueroa, 1968; Campbell and Swerdlow, 1969; Cullen, 1971; Kleine and Moesker, 1976). This study was to determine if this combination would attenuate the effect of suxamethonium on the serum potassium concentration. Hexafluorenium causes histamine release (Selvin and Howland, 1959; Mostert and Kundig, 1964) and bronchospasm has been associated with its use. Fellini, Berstein and Zauder (1963) and Eustace (1967) described bronchospasm following suxamethonium also.

MATERIALS AND METHODS

Sixty patients (18–64 yr) who were not suffering from chronic renal failure and who were undergoing a variety of surgical procedures were studied. They were divided into six groups of 10 patients each.

All received diphenhydramine 75–100 mg, and pethidine 50–75 mg with atropine 0.4–0.6 mg i.m., 90 and 60 min respectively before the start of the study. The oropharynx was sprayed with 1% amethocaine HC\(\text{I}\) solution to facilitate the insertion of an oropharyngeal airway. Droperidol 150 \(\mu\)g kg\(^{-1}\) and fentanyl 1 \(\mu\)g kg\(^{-1}\) were given over 60 s, followed in 6 min by the inhalation of 75% nitrous oxide in oxygen. Increments of fentanyl 0.5 \(\mu\)g kg\(^{-1}\) were given as required.

The patients in groups I, II and III received suxamethonium 0.2, 0.6 and 1.0 mg kg\(^{-1}\) i.v., respectively, injected over 30 s. Those in groups IV, V and VI were given hexafluorenium 0.3 mg kg\(^{-1}\) i.v. followed after 5 min by suxamethonium in doses corresponding to groups I, II and III.

Fasciculations were classified as severe, moderate, mild and none. Heart rate, systolic and diastolic arterial pressures were recorded and the e.g. was observed.
Venous blood samples were taken from the arm which was not used for the infusion before and at the completion of the induction of anaesthesia and 1, 3, 5, 10 and 15 min after the completion of the injection of the suxamethonium in all groups; in a pilot study we had found that the change in the serum potassium concentration was maximal between 10 and 15 min. In groups IV–VI the serum potassium concentration was determined also 5 min after the administration of hexafluorenium. The serum potassium concentration was measured using an Orion Biochemical Sodium–Potassium Analyzer (Model SS-30).

Venous pH and \( P_{\text{CO}_2} \) were measured before the induction of anaesthesia and 15 min after the administration of suxamethonium.

**RESULTS**

The characteristics of the patients are presented in table I.

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Sex</th>
<th>Weight (kg)</th>
<th>Physical status (ASA classification)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>Range</td>
<td>M</td>
<td>F</td>
</tr>
<tr>
<td>40.4</td>
<td>18–64</td>
<td>25</td>
<td>35</td>
</tr>
</tbody>
</table>

No severe fasciculations were observed; the number of moderate fasciculations increased with increasing doses of suxamethonium. The patients who received hexafluorenium did not exhibit fasciculations (table II).

There were no significant changes in either arterial pressure or heart rate (table III) and no arrhythmia was noted in any patient.

**Table II. Fasciculations following the administration of suxamethonium i.v.**

<table>
<thead>
<tr>
<th>Group</th>
<th>Severe</th>
<th>Moderate</th>
<th>Mild</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>—</td>
<td>1</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>II</td>
<td>—</td>
<td>6</td>
<td>4</td>
<td>—</td>
</tr>
<tr>
<td>III</td>
<td>—</td>
<td>9</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>IV</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>10</td>
</tr>
<tr>
<td>V</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>10</td>
</tr>
<tr>
<td>VI</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>10</td>
</tr>
</tbody>
</table>

**Table III. Haemodynamic changes (mean ± SEM) during the induction of neuroleptanaesthesia in 30 patients who received hexafluorenium**

<table>
<thead>
<tr>
<th>Arterial pressure (mm Hg)</th>
<th>Heart rate (beat min(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic</td>
<td>Diastolic</td>
</tr>
<tr>
<td>Before induction</td>
<td>127.3 ± 4.7</td>
</tr>
<tr>
<td>5 min after hexafluorenium</td>
<td>131.8 ± 4.0</td>
</tr>
</tbody>
</table>

Although we did not measure blood histamine concentration, we did not observe any signs or symptoms of histamine release, such as wealing along the course of the vein or bronchospasm. The venous pH and \( P_{\text{CO}_2} \) values obtained 15 min after the administration of suxamethonium were not significantly different from the values noted before induction.

The serum potassium concentrations at various times throughout the study are detailed in table IV. Following the induction of anaesthesia a decrease in the serum potassium concentration was observed in each group. The mean (± SEM) serum potassium concentration (\( n = 60 \)) following the induction of

<table>
<thead>
<tr>
<th>Suxamethonium (mg kg(^{-1}))</th>
<th>Hexafluorenium 0.3 mg kg(^{-1}) followed in 5 min by suxamethonium (mg kg(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.2</td>
<td>0.6</td>
</tr>
<tr>
<td>Control</td>
<td>4.07 ± 0.19</td>
</tr>
<tr>
<td>After induction</td>
<td>3.74 ± 0.14</td>
</tr>
<tr>
<td>5 min after hexafluorenium</td>
<td>—</td>
</tr>
<tr>
<td>After i.v. injection of suxamethonium (min)</td>
<td>1 3.53 ± 0.10</td>
</tr>
<tr>
<td>3 3.46 ± 0.07</td>
<td>3.94 ± 0.14</td>
</tr>
<tr>
<td>5 3.56 ± 0.10</td>
<td>3.94 ± 0.12</td>
</tr>
<tr>
<td>10 3.50 ± 0.06</td>
<td>3.81 ± 0.09</td>
</tr>
<tr>
<td>15 3.58 ± 0.08</td>
<td>3.77 ± 0.09</td>
</tr>
</tbody>
</table>
HEXAFLUORENIUM AND SUXAMETHONIUM

Anaesthesia (3.60 mmol litre\(^{-1} \pm 0.07\)) was significantly less (\(P<0.001\)) than the mean value before induction (3.98 mmol litre\(^{-1} \pm 0.07\)). In the patients in groups V and VI there were further decreases in serum potassium concentration 5 min after the administration of hexafluorenium 0.3 mg kg\(^{-1}\).

Following the administration of suxamethonium the serum potassium concentration was noted to decrease further in group I, to increase to less than the control in group II and to exceed the control in group III. In the patients who received the combination of hexafluorenium and suxamethonium the changes in the serum potassium concentration were less marked. In group IV the results were similar to those obtained in group I. The serum potassium concentration increased in groups V and VI, but in neither group did it reach the control value during the first 15 min after administration of suxamethonium.

**DISCUSSION**

Stoelting and Peterson (1975) observed that suxamethonium 1–2 mg kg\(^{-1}\) preceded by tubocurarine 0.4 mg kg\(^{-1}\) caused changes in the serum potassium concentration, slowing of the heart and junctional rhythm. The latter was also observed by Duncalf and others (1965) with the use of hexafluorenium 0.4 mg kg\(^{-1}\). Those who have shown that hexafluorenium can cause bronchospasm used larger doses and different agents (Selvin and Howland, 1959; Mostert and Kundig 1964) and anxiety about the histamine releasing effect of larger doses of suxamethonium (Fellini, Berstein and Zauser, 1963; Eustace, 1967; Bele-Binda and Valeri, 1971) was not confirmed in our study.

No arrhythmias occurred in this series, in contrast to observations by Duncalf and others (1965) and Stoelting and Peterson (1975). Droperidol may have played a role in their prevention (Schotz and Geigler, 1967; Goodman and Gilman, 1975), while diphenhydramine as part of the premedication may have helped to prevent the release of histamine.

Several authors have reported significant, but transient decreases in serum potassium concentration after the administration of halothane, thiopentone, methohexitone, ketamine and diazepam (List, 1967; Logan, Howie and Crawford, 1974; Ball, Dundee and Assaf, 1973; Konchigeri and Tay, 1975). We observed a substantial decrease after induction with neuroleptic agents. This decrease in serum potassium concentration was augmented in many of the patients given hexafluorenium 0.3 mg kg\(^{-1}\). However, the reduction in the serum potassium concentration was not transient, for it persisted through the entire period of observation in groups I and IV (i.e. patients who received suxamethonium 0.2 mg kg\(^{-1}\)). In all the patients who received hexafluorenium the serum potassium concentration remained less than the control values during the period of observation. Since acidosis and alkalosis did not occur it is unlikely that the changes played a role in the changes in potassium concentration (Wong et al., 1973). The cause of the sustained decrease in serum potassium concentration is not clear.

The addition of hexafluorenium prevents the rapid hydrolysis of suxamethonium, thus both the intensity and duration of its block are increased markedly (Foldes, 1960). However, the neuromuscular blockade produced by the combination wears off within a reasonable time without the use of an antagonist and its duration may be adjusted by altering the hexafluorenium–suxamethonium ratio.

We recommend 0.2-mg kg\(^{-1}\) increments of suxamethonium. As soon as the interval between two doses of suxamethonium decreases to 10–15 min, we repeat the hexafluorenium in a 0.1–0.15 mg kg\(^{-1}\) dose and follow it in 2 min by suxamethonium 0.2 mg. With proper management the patient should breathe spontaneously at the end of surgery. It is rarely necessary to assist the respiration for short periods, as the total amount of suxamethonium used during surgery is small (Foldes, 1966), making this method safe even in patients with abnormal cholinesterase activity. The mixture will eliminate the undesirable side-effects of suxamethonium such as fasciculation, increased intraocular pressure (Dillon et al., 1957) and the increases in serum potassium concentration.

The technique might be safe for anephric patients and for those in chronic renal failure.

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thiopental and halothane with or without respiratory

PREVENTION DES VARIATIONS PROVOQUEES
PAR LE SUXAMETHONIUM SUR LA
CONCENTRATION DE POTASSIUM DANS LE
SERUM APRES ADMINISTRATION
D'HEXAFLUORENIUM
Leur usage conjoint est-il justifie?

RESUME
Soixante patients, dont aucun ne souffrait d'insuffisance
renale, ont ete soumis a une neuroleptanesthesie. On les a
divise en six groupes de 10 patients: Groupes I et IV, II et
V, et II et VI auxquels on a administr£ respectivement du
suxamethonium a raison de 0,2, 0,6 et 1,0 mg kg$^{-1}$. Les
Groupes IV et VI ont ete pretrait£s a l'hexafluorouium sur
la base de 0,3 mg kg$^{-1}$. La concentration de potassium dans
le £rum a dimin£ d'une maniere significative apres l'
induction de l'anesthesie et a£galement apres l'admin-
istration d'hexafluorouium. Ni le suxamethonium a
0,2 mg kg$^{-1}$, ni ce meme produit mais a 0,6 mg kg$^{-1}$,
avec ou sans hexafluorouium, n'ont pu ramener la concentration
de potassium a la valeur temoin. Le suxamethonium seul
a raison de 1 mg kg$^{-1}$ a fait augmenter le potassium du
£rum a une valeur superieure a la valeur temoin. L'hexa-
fluorouium a att£nu£ cet effet. La combinaison d'hexa-
fluorouium et de suxamethonium peut etre benefique pour
les malades qui souffrent d'anephrite ou d'insuffisance
renale chronique.

VERHÜTUNG VON DURCH
SUXAMETHONIUM INDIUEREFEN
VERÄNDERUNGEN IN DER SERUM-
KALIUMKONZENTRATION DURCH HEXA-
FLUORENIUM
Ist ihre gemeinsame Anwendung gerechtfertigt?

ZUSAMMENFASSUNG
Sechzig Patienten, von denen keiner an einem Versagen der
Nieren litt, erhielten neuroleptische Narkose. Sie wurden
in sechs Gruppen von je 10 Patienten aufgeteilt. Den
Gruppen I und IV, II und V, und II und VI wurden 0,2,
0,6 bzw. 1,0 mg kg$^{-1}$ Suxamethonium gegeben. Gruppen
IV—VII wurden mit 0,3 mg kg$^{-1}$ Hexafluorenium vorbe-
handelt. Die Serum-Kaliumkonzentration nahm nach
Narkoseinduktion und auch der Verabreichung von Hexa-
fluorenium bedeutend ab. Weder 0,2 mg noch 0,6 mg kg$^{-1}$
Suxamethonium mit oder ohne Hexafluorenium brachten
die Kaliumkonzentration auf den Kontrollwert zur£ck.
Allein 1,0 mg kg$^{-1}$ Suxamethonium verursachte eine
Zunahme im Serum-Kalium auf Werte, die ^ber den
Kontrollwerten lagen; Hexafluorenium schwachte diese
Wirkung ab. Die Hexafluorenium-Suxamethonium-Kom-
bination kann bei solchen Patienten von Nutzen sein, die
anephrizisch sind oder an chronischem Nierenversagen
leiden.
PREVENCION DE CAMBIOS INDUCIDOS POR SUXAMETONIO EN LA CONCENTRACION DE POTASIO EN EL SUERO MEDIANTE HEXAFLUORENIO
¿Se justifica su empleo combinado?

SUMARIO
Sesenta pacientes, ninguno de los cuales sufría de deficiencia de los riñones, recibieron anestesia neuroléptica. Se dividieron en seis grupos de diez pacientes cada uno. Los Grupos I y IV, II y V, y III y VI recibieron 0,2, 0,6 y 1,0 mg kg⁻¹ de suxametonio, respectivamente. Los Grupos IV a VI fueron pretratados con 0,3 mg kg⁻¹ de hexafluorenio. La concentración de potasio en el suero disminuyó significativamente después de la inducción de anestesia y también siguiendo la administración de hexafluorenio. Ni 0,2 mg kg⁻¹ ni 0,6 mg kg⁻¹ de suxametonio con o sin hexafluorenio pudieron recobrar la concentración de potasio al valor de control; 1,0 mg kg⁻¹ de suxametonio solo hizo que el potasio en el suero aumentara a valores superiores a los de control—el hexafluorenio atenuó este efecto. La combinación de hexafluorenio y suxametonio puede ser beneficiosa en pacientes anéfricos o que sufren de deficiencia crónica de los riñones.