THE INFLUENCE OF KETAMINE INDUCTION ON POTASSIUM CHANGES AND FASCICULATIONS FOLLOWING SUXAMETHONIUM

T. J. GAL AND L. A. MALIT

SUMMARY

Plasma potassium levels were measured during induction with thiopentone or ketamine and subsequent administration of suxamethonium. The presence and magnitude of fasciculations following suxamethonium were noted. In addition arterial blood gases and glucose levels were measured. All patients displayed a small decrease in plasma potassium levels following the induction agents and a similar rise after the muscle relaxant. The rise occurred less rapidly after the thiopentone-suxamethonium sequence, but no other major differences with respect to potassium emerged in the two groups who received suxamethonium. In the third group, who received ketamine but no relaxant, potassium levels remained below the baseline values. The incidence and degree of fasciculations following suxamethonium 1 mg/kg appeared significantly less with the ketamine induction.

Present induction techniques utilize the familiar sequence of barbiturate-suxamethonium-endotracheal intubation, with occasional interposition of a potent inhalational agent. The fasciculations, which commonly herald the onset of relaxation, are followed by postoperative muscle pain (Paton, 1956), increased intraocular pressure (Schwartz and DeRoeth, 1958), increased intragastric pressure (Andersen, 1962), and an increase in levels of potassium. The last has long been recognized (Paton, 1956) but recently has been cause for concern in certain individuals (Cooperman, 1970). Measures directed at minimizing fasciculations and their untoward effects have included altering the dose and mode of administering the relaxant, pretreatment with non-depolarizing blockers (Weintraub, Heisterkamp and Cooperman, 1969), local anaesthetics (Wikinski, et al., 1965), and most recently magnesium sulphate (Aldrete, Zahler and Aikawa, 1970).

The dissociative agent ketamine has been used in lieu of barbiturate for induction of conventional general anaesthesia. Because of its effects on cardiovascular dynamics and the relative ease of airway management, it offers at least a theoretical advantage for some patients. Casual clinical observations suggested that patients who received ketamine for induction, displayed very little of the fasciculations anticipated on suxamethonium administration. We undertook to test this clinical impression and in addition to record any changes in potassium levels accompanying induction of anaesthesia with ketamine or thiopentone followed by suxamethonium.

METHODS

Plasma potassium levels were measured in 18 patients during induction of anaesthesia with ketamine or thiopenone. All patients were physical status I or II (ASA classification) with ages ranging from 16 to 75 with a mean of 46 (median 48) years. Presence of a hypertensive history, neuromuscular disease, or recent diuretic therapy were criteria for exclusion from the study.

All patients received pentobarbitone 1–2 mg/kg and atropine 0.4–0.6 mg intramuscularly about one hour prior to induction. Physiological saline was the sole intravenous fluid administered before and during the study; total volume never exceeded 150 ml and was limited to 50 ml during the period of measurement. Sampling of blood was accomplished via a radial artery cannula (20 gauge Medicut) inserted percutaneously with the aid of local anaesthesia. This was preceded in all cases by a test of adequate collateral ulnar flow. Verbal consent for the procedure was obtained during the pre-operative visit.

Baseline values for potassium were collected in heparinized glass tubes (Sample 1). Specimens for
glucose and blood gas determinations were obtained also. Patients were then randomly assigned to one of three groups based on the mode of induction:

Group I: 6 patients. Thiopentone 4-5 mg/kg followed in 3 min by suxamethonium 1 mg/kg

Group II: 6 patients. Ketamine 2.5 mg/kg (injected over 30 sec) followed in 3 min by suxamethonium 1 mg/kg

Group III: 6 patients. Ketamine 2.5 mg/kg with no muscle relaxant.

Additional measurements consisted of: sample taken 2-3 min after the induction agent but prior to suxamethonium, samples 3, 4, 5 taken 1, 3 and 5 min respectively after suxamethonium. (Samples in Group III were taken at the same intervals although no relaxant was given).

100 per cent oxygen was administered to all patients before and during the study. Following intubation (or collection of samples No. 4) a 5 l./min flow with 60 per cent nitrous oxide was used in a circle system. Spontaneous respiration was allowed prior to suxamethonium, but ventilation was controlled thereafter in patients who received the drug.

Fasciculations were graded by the same observer according to the following scale: 0—none observed; 1—small fine movements about face, neck, and fingers; 2—movement involving large muscle groups of the trunk; 3—gross movements of the extremities.

All samples for potassium were analyzed within 30 min of collection using a flame photometer (Instrumentation Laboratories 143). (Mean difference of duplicate samples 0.01 m.equiv/1.) Blood gas analysis was performed on the IL 127 analyzer.

Glucose concentrations were measured colorimetrically using the glucose oxidase method (mean difference of duplicate samples 2 mg/100ml). Statistical evaluation included analysis of variance and Student t test, with significance attached to the 5 per cent level (P<0.05).

RESULTS

All groups displayed a small fall in plasma potassium following induction of anaesthesia (table I). Although the largest mean decrease (—0.17 m.equiv/l.) occurred in the thiopentone group (1), only the decrease in the ketamine controls (Group III) was statistically significant when compared to the baseline (P<0.05). Values in this group remained below the baseline throughout the study. This is similar to observations with other anaesthetics (List 1967).

Following suxamethonium potassium levels rose

<table>
<thead>
<tr>
<th>Sample</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Fasciculations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I (K+)</td>
<td>3.47 ± 0.01</td>
<td>3.30 ± 0.12</td>
<td>3.40 ± 0.09</td>
<td>3.42 ± 0.11</td>
<td>3.53 ± 0.12</td>
<td>Total scores 13</td>
</tr>
<tr>
<td>change from baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(mean 2.16)</td>
</tr>
<tr>
<td>Group II (K+)</td>
<td>3.67 ± 0.09</td>
<td>3.56 ± 0.07</td>
<td>3.69 ± 0.07</td>
<td>3.81 ± 0.10</td>
<td>3.76 ± 0.11</td>
<td>Total scores 5</td>
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<tr>
<td>change from baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(mean 0.83)</td>
</tr>
<tr>
<td>Group III (K+)</td>
<td>3.72 ± 0.04</td>
<td>3.61 ± 0.03</td>
<td>3.58 ± 0.03</td>
<td>3.56 ± 0.04</td>
<td>3.55 ± 0.03</td>
<td></td>
</tr>
<tr>
<td>change from baseline</td>
<td></td>
<td></td>
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</tbody>
</table>

Values are expressed in m.equiv/l. as mean ± SE

Group I: thiopentone + suxamethonium Sample 1 = baseline value
Group II: ketamine + suxamethonium Sample 2 = 3 min after induction of anaesthesia
Group III: ketamine Samples 3, 4, 5 = 1, 3 and 5 min after suxamethonium
TABLE II. Blood gas changes.

<table>
<thead>
<tr>
<th>Sample</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.45 ± 0.01</td>
<td>7.39 ± 0.02</td>
<td>7.44 ± 0.02</td>
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<td></td>
</tr>
<tr>
<td>Pco₂</td>
<td>33.9 ± 0.8</td>
<td>40.9 ± 3.6</td>
<td>34.6 ± 1.3</td>
<td></td>
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</tr>
<tr>
<td>pH</td>
<td>7.44 ± 0.01</td>
<td>7.37 ± 0.03</td>
<td>7.39 ± 0.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pco₂</td>
<td>35.2 ± 0.7</td>
<td>43.6 ± 3.4</td>
<td>39.4 ± 2.3</td>
<td></td>
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</tr>
<tr>
<td>pH</td>
<td>7.48 ± 0.03</td>
<td>7.38 ± 0.02</td>
<td>7.37 ± 0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pco₂</td>
<td>31.8 ± 3.2</td>
<td>43.0 ± 3.8</td>
<td>42.2 ± 2.8</td>
<td></td>
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</tr>
</tbody>
</table>

Values expressed as mean ± SE

modestly in 3 to 5 minutes. The ketamine group (II) reached +0.14 m.equiv/l. above baseline at 3 minutes while the thiopentone group reached +0.06 m.equiv/l. at 5 min. Variance analysis indicated a significant difference (P<0.05) at the 3 minute sample (No. 4). This appears to support List’s (1967) contention that the suxamethonium-induced potassium elevation occurs less rapidly after thiopentone than other anaesthetic inductions, ketamine now included. In contrast to the relatively similar effects on potassium changes, clinical assessment of fasciculations revealed a difference between the two groups who received suxamethonium. The incidence and degree of fasciculations were significantly less (P<0.025) in the ketamine patients (total score 5) than the thiopentone patients (total score 13).

The ketamine dose, when injected in the manner described, resulted in transient periods (20-30 sec) of apnoea in several patients; this was less common in the thiopentone group. Blood gases (table II) showed a fall in pH accompanied by increased Pa₀₂ following induction and the relaxant administration in groups I and II. Values returned toward the baseline at the end of the study. Group III (without relaxant) exhibited minimal carbon dioxide retention. Glucose values rose slightly during the period: thiopentone group from 96 ± 5.2 mg/100ml to 100 ± 5.2 mg/100ml and the ketamine groups from 98 ± 7.3 mg/100ml to 111 ± 6.6 mg/100ml. Neither rise was statistically significant.

DISCUSSION

Decreases in potassium levels during induction of anaesthesia was first noted with thiopentone-nitrous oxide anaesthesia in dogs (Stevenson, 1960) and were attributed to metabolic factors causing potassium to enter the cells. They include alkalosis and an insulin-mediated decrease in blood sugar. Our patients displayed neither; the blood glucose level rose slightly during the period of observation, and a mild degree of respiratory acidosis was noted. Another group suggests that the drug induced "sensory deprivation" causes movement of plasma potassium into tissues (Dobkin, Byles and Neville, 1966). Still others ascribe the net decrease in potassium to a reduced number of depolarizations occurring with induction of anaesthesia (List, 1967).

In light of these theories it is somewhat surprising that induction with ketamine should produce the same sustained decrease in potassium as other anaesthetics (List, 1967). Its effect is not one of relaxation but rather of heightened skeletal muscle tone and deep tendon reflexes (Domino, Chodoff and Corssen, 1965). Furthermore the association with signs of increased sympathetic activity would suggest that phenomena such as increased blood sugar and potassium might occur (O’Brien et al., 1954).

Patients given suxamethonium displayed a small, clinically insignificant rise in plasma potassium levels. The peak levels are considerably less than those reported in other healthy patients (Weintraub, Heisterkamp and Cooperman, 1969). However, in most of the previous studies baseline values for potassium were measured following induction of anaesthesia, when they would presumably be reduced below true baseline values, thus causing the net rise following suxamethonium to appear larger.

Nevertheless, it is not likely that one could avoid hyperkalemia in susceptible patients by using ketamine, despite the apparent reduction of fasciculations. This underscores the lack of overall correlation between fasciculations and potassium changes, a phenomenon demonstrated so well by decamethonium. Thus any efforts to prevent fasciculations, including pretreatment with tubocurarine, do not guarantee protection against increases in plasma potassium levels (Weintraub, Heisterkamp and Cooperman, 1969).

It is sometimes suggested that ketamine should be used for emergency induction of anaesthesia in the hypovolaemic or dehydrated patient with a precarious haemodynamic status because it lacks the capacity to cause cardiovascular depression to the same degree as that which accompanies barbiturate administration (Corssen et al., 1970). The apparent dampening of suxamethonium-induced fasciculations may provide an additional advantage because many of these patients present with a "full stomach", thus posing the threat of regurgitation and aspiration. The danger of increased intragastric pressure has been related directly to the intensity of fasciculations (Miller and Way, 1971). However,
before ketamine is advocated in these situations, the nature and extent of its effect on muscle tone need clarification. It is possible that increased muscle tone attributable to ketamine can mask the appreciation of fasciculations and at the same time cause a rise in intragastric pressure, thus failing to offer any real protection against the dangers of regurgitation and aspiration.

ACKNOWLEDGEMENTS
The authors wish to express thanks to Dr Lee H. Cooperman for assistance in preparing the manuscript.

REFERENCES

L'EFFET DE L'INDUCTION PAR KETAMINE SUR LES MODIFICATIONS DU POTASSIUM ET LES FASCICULATIONS APRES SUXAMETHONIUM

SOMMAIRE
Les taux plasmatiques de potassium ont été mesurés pendant l'induction par thiopentone ou ketamine et l'administration ultérieure de suxamethonium. La présence et la magnitude des fasciculations consécutives au suxamethonium ont été notées. On a en outre mesuré les gaz artériels et les taux de glucose. Tous les patients ont manifesté une légère réduction des taux plasmatiques de potassium après l'emploi des agents d'induction et une augmentation similaire après le relâchement musculaire. L'augmentation était moins rapide après la séquence thiopentone-suxamethonium, mais aucune autre différence majeure du potassium ne s'est manifestée dans les deux groupes, qui avaient reçu suxamethonium. Dans le troisième groupe, qui avait reçu ketamine mais pas de relâchant, les taux de potassium sont demeurés inférieurs aux valeurs initiales. L'incidence et le degré des fasciculations après suxamethonium 1 mg/kg paraissaient significativement moindres avec l'induction par ketamine.

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DER EINFLUSS VON KETAMIN AUF DIE KALIUMVERÄNDERUNGEN UND MUSKELZUCKUNGEN NACH GABE VON SUXAMETHONIUM

ZUSAMMENFASSUNG

LA INFLUENCIA DE LA INDUCCIÓN CON CETAMINA SOBRE LOS CAMBIOS DEL POTASIO Y FASCICULACIONES DESPUÉS DE SUXAMETONIO

RESUMEN
Los niveles plasmáticos de potasio fueron medidos durante la inducción con tiopentona o cetamina y la administración subsiguiente de suxamethonio. Fue registrada la presencia y magnitud de las fasciculaciones después del suxamethonio. También fueron medidos los gases y niveles de glucosa de la sangre arterial. Todos los pacientes mostraron una pequeña disminución de los niveles de potasio en el plasma después de los agentes de inducción y una elevación semejante después del relajante muscular. El aumento fue menos rápido después de la secuencia thiopentona-suxamethonio, pero no hubo otras diferencias importantes en relación con el potasio en los dos grupos que recibieron suxamethonio. En el tercer grupo, el cual recibió cetamina sin relajante, los niveles de potasio permanecieron inferiores a los valores basales. La frecuencia y la intensidad de las fasciculaciones después de 1 mg/kg de suxamethonio fueron significativamente menores con la inducción por cetamina.