EFFECT OF SALBUTAMOL AND SUXAMETHONIUM ON THE PLASMA POTASSIUM CONCENTRATION

R. M. SLATER AND I. D. MCLAREN

Suxamethonium given i.v. may lead to an increase, (0.3-0.5 mmol litre\(^{-1}\)) in plasma potassium concentration (Paton, 1956). Weintraub, Heisterkamp and Cooperman (1969) noted that the hyperkalaemia immediately followed the injection of the depolarizing neuromuscular blocker, and reached its peak between 1 and 7 min after the i.v. injection. After denervation injuries or severe burns, the increase in plasma potassium concentration may be of sufficient magnitude to threaten life (Allan, Cullen and Gillies, 1961; Belin and Karleen, 1966; Tolmie and Joyce, 1967).

Extracellular potassium concentrations may be influenced by the state of the adrenergic nervous system. Stimulation of the beta-2 adrenoceptor results in a decrease in extracellular potassium concentration (Smith and Thompson, 1977; Hurlbert, Edelman and David, 1981). Beta-adrenoceptor blockade, on the other hand, has been shown to augment and prolong the increase in potassium concentration after acute potassium loading (Carlsson and Fellenius, 1978). Salbutamol, a beta-2 adrenoceptor stimulant, has been used successfully to alleviate hyperkalaemic attacks in patients suffering from hyperkalaemic familial periodic paralysis (Wang and Clausen, 1976). It was noted that salbutamol also abolished the symptoms of myalgia and weakness in these patients. The present study has been designed to examine the hypothesis that pretreatment with salbutamol might reduce both the increase in potassium concentration and the myalgia often associated with the administration of suxamethonium.

**SUMMARY**

In a double-blind randomized study, patients received premedication with lorazepam 0.04 mg kg\(^{-1}\) and salbutamol 0.1 mg kg\(^{-1}\) or lorazepam 0.04 mg kg\(^{-1}\) and placebo given orally 2.5-3 h before anaesthesia. The plasma potassium concentration was measured at the time of premedication, before the induction of anaesthesia and at selected intervals after suxamethonium 1 mg kg\(^{-1}\) i.v. The plasma potassium concentration was lower in those patients who received salbutamol than in those given placebo, and remained lower at all the subsequent sample times. Oral salbutamol did not appear to affect the incidence of suxamethonium related muscle pain.

**PATIENTS AND METHODS**

Forty patients (ASA I or II, aged 16-65 yr) gave written consent to participation in the study which had been approved by the Hospital Ethical Committee. Patients taking beta-adrenoceptor agonists or antagonists, digoxin, calcium antagonists or potassium supplements were excluded from the study. Patients were to undergo minor ENT or dental procedures for which intubation of the trachea would be required.

Immediately before premedication, 10 ml of venous blood was taken from each patient (for the measurement of plasma potassium concentration) via a 21-gauge cannula sited in a vein in the antecubital fossa. The same cannula was used for all sampling and drug administration, and was flushed with saline after use.

Patients were allocated to one of two groups using a randomized, double-blind design. Patients in group A were given salbutamol 0.1 mg kg\(^{-1}\) and lorazepam 0.04 mg kg\(^{-1}\) by mouth, and those in group B received lorazepam 0.04 mg kg\(^{-1}\) and...
placebo tablets, 2.5–3 h before induction. Heart rate and arterial pressure were recorded at this time and again immediately before the induction of anaesthesia with thiopentone 4–6 mg kg⁻¹. Suxamethonium 1 mg kg⁻¹ was administered i.v., the presence or absence of fasciculation noted and the trachea intubated. Blood samples were taken at the time of premedication, immediately before the induction of anaesthesia and at 1, 3, 5, 7, 15 and, where possible, 20 min after the suxamethonium. Anaesthesia was maintained using a spontaneous breathing technique with 66% nitrous oxide and 2–5% enflurane in oxygen via a Magill system. Arterial pressure and heart rate were recorded at intervals throughout the procedure using an automatic device (Dinamap) and the ECG was monitored throughout. During the sampling period, no i.v. fluids were given. The 10-ml aliquots of blood were taken without a tourniquet over 1 min and centrifuged within 5 min of collection. Potassium concentration was measured using a Corning 435 Flame Photometer. A Corning 800 automatic dilutor was used to dilute 0.1 ml of the plasma or standard using lithium 15 mmol litre⁻¹ in deionized water. Data represent the means of two readings on each of two aliquots of blood. No haemolysis was noted in any sample.

The patients were given questionnaires to be completed 24 and 48 h after surgery. These contained four main questions with subheadings, all related to postoperative problems. The only question relevant to the study asked, “Since your operation have you noticed any aches or pains in your muscles? If so, please specify whereabouts.”

Results were analysed using the Student’s t test, Chi-squared test and by a two-way analysis of variance.

RESULTS

Nineteen patients received salbutamol and 21 received placebo. The characteristics of the two groups were similar (table I). One patient who had received salbutamol vomited during the injection of thiopentone and was withdrawn from the study. The time from injection to intubation and quality of relaxation for intubation, as assessed by one of the authors (I.D.McL.), was similar in both groups. One patient in the placebo group developed prolonged apnoea (over 3 h) after suxamethonium and was subsequently found to be homozygous for atypical cholinesterase with a dibucaine number of 17.

There were no significant differences in the mean plasma potassium concentrations at the time of premedication (baseline value) (table II). The plasma potassium concentration in the salbutamol group was reduced immediately before the administration of suxamethonium, in relation to both the baseline value and the pre-suxamethonium value in the placebo group (P < 0.001). At 1, 3, 5, 7 and 15 min after the administration of suxamethonium, the plasma potassium concentration was significantly lower in the salbutamol group (P < 0.001 in all cases). Blood samples were taken 20 min after induction in six patients in the placebo group and nine patients in the salbutamol group. The difference between the values obtained in the two groups was significant (P < 0.001) (fig. 1). In the placebo group, the change in plasma potassium concentration was +0.367 ± 0.063 mmol litre⁻¹, whereas the change in the salbutamol group was −0.257 ± 0.064 mmol litre⁻¹. The maximum re-

### Table I. Demographic data

<table>
<thead>
<tr>
<th>Group</th>
<th>Sex (M : F)</th>
<th>Age (yr) (Mean (SD) range)</th>
<th>Weight (kg) (Mean (SD) range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salbutamol</td>
<td>10 : 9</td>
<td>39 (15)</td>
<td>67 (9)</td>
</tr>
<tr>
<td>(n = 19)</td>
<td></td>
<td>17–60</td>
<td>60–90</td>
</tr>
<tr>
<td>Placebo</td>
<td>9 : 12</td>
<td>36 (14)</td>
<td>70 (11.5)</td>
</tr>
<tr>
<td>(n = 21)</td>
<td></td>
<td>18–65</td>
<td>55–100</td>
</tr>
</tbody>
</table>

### Table II. Baseline plasma potassium concentration and mean changes (±SEM) before and after suxamethonium

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline (Mean (SD))</th>
<th>Time after suxamethonium (min)</th>
<th>1</th>
<th>3</th>
<th>5</th>
<th>7</th>
<th>15</th>
<th>20</th>
</tr>
</thead>
<tbody>
<tr>
<td>placebo</td>
<td>3.89 (0.055)</td>
<td>+0.02 (0.063)</td>
<td>+0.03 (0.07)</td>
<td>+0.11 (0.08)</td>
<td>+0.13 (0.063)</td>
<td>+0.29 (0.082)</td>
<td>-0.33</td>
<td></td>
</tr>
<tr>
<td>salbutamol</td>
<td>3.97 (0.056)</td>
<td>-0.62 (0.069)</td>
<td>-0.45 (0.069)</td>
<td>-0.55 (0.07)</td>
<td>-0.58 (0.076)</td>
<td>-0.48 (0.085)</td>
<td>-0.30</td>
<td></td>
</tr>
</tbody>
</table>
The increase in plasma potassium concentration associated with the administration of suxamethonium is thought to be related to the depolarization of excitable membranes with consequent loss of potassium from skeletal muscle. While this effect is generally small, it becomes significant when there has been muscle injury or when the preoperative plasma potassium concentration is increased (Weintraub, Heisterkamp and Cooperman, 1969). It has been shown, in animals, that the increase in plasma potassium concentration induced by suxamethonium is further increased in the presence of propranolol-induced beta-adrenoceptor blockade (McCammon and Stoelting, 1984). In the present study, salbutamol given in approximately twice the normal oral dose produced a consistent decrease in plasma potassium concentration. The mechanism for this hypokalaemic response seems to be a cellular shift mediated via beta-2 receptors linked to membrane sodium-potassium ATPase, which causes an influx of potassium to the cell (Smith and Kendall, 1984). Salbutamol did not, however, appear to prevent the release of potassium after the administration of suxamethonium. However, the peak potassium concentrations following salbutamol and suxamethonium were lower than those which followed the injection of suxamethonium alone.

Peak plasma concentrations of salbutamol are seen 2.5–3 h after an oral dose. A similar time scale is seen after inhalation of the drug, although changes in FEV₁ occur before the maximum blood concentrations are achieved. Salbutamol given orally undergoes extensive metabolism on first pass through the liver and, at peak plasma concentration, the ratio of salbutamol to its metabolite is 1:4 (Walker et al., 1972). An i.v. infusion of salbutamol 10 μg min⁻¹ in human volunteers produced a reduction in plasma potassium concentration of 0.8 mmol litre⁻¹ in 1 h (Leitch et al., 1976).

The increase in potassium concentration following suxamethonium can be reduced by pretreatment with a small dose of tubocurarine

FIG. 1. Change in plasma potassium concentration (±SEM) from baseline and following suxamethonium. • = Placebo group; ○ = salbutamol group.

FIG. 2. Frequency of muscle pain following suxamethonium 24 and 48 h after surgery in patients pretreated with salbutamol or placebo. ■ = Pain; □ = no pain.

corded increase in the placebo group was +0.8 mmol litre⁻¹ and in the salbutamol group +0.1 mmol litre⁻¹. However, measured from the time of injection of suxamethonium the increase in potassium concentration in the two groups was similar at all times.

The mean heart rate was increased from baseline both before and 5 min after induction in both groups. However, there was a significantly greater increase in these variables in the salbutamol group before induction. The maximum recorded increase in rate in the placebo group was +18 ± 3 beat min⁻¹ and in the salbutamol group was +32 ± 4 beat min⁻¹. There were no significant differences in arterial pressure in either group. Fasciculations were noted in all but three patients; there was no difference between the groups.

All patients were ambulant within 12 h of their operation. Twelve patients in the salbutamol group and 14 in the placebo group returned the questionnaires. The overall frequency of pain was 54% after 24 h and 53% after 48 h, and was similar in both groups (fig. 2).

DISCUSSION

The increase in plasma potassium concentration associated with the administration of suxamethonium is thought to be related to the depolarization of excitable membranes with consequent loss of potassium from skeletal muscle. While this effect is generally small, it becomes significant when there has been muscle injury or when the preoperative plasma potassium concentration is increased (Weintraub, Heisterkamp and Cooperman, 1969). It has been shown, in animals, that the increase in plasma potassium concentration induced by suxamethonium is further increased in the presence of propranolol-induced beta-adrenoceptor blockade (McCammon and Stoelting, 1984). In the present study, salbutamol given in approximately twice the normal oral dose produced a consistent decrease in plasma potassium concentration. The mechanism for this hypokalaemic response seems to be a cellular shift mediated via beta-2 receptors linked to membrane sodium-potassium ATPase, which causes an influx of potassium to the cell (Smith and Kendall, 1984). Salbutamol did not, however, appear to prevent the release of potassium after the administration of suxamethonium. However, the peak potassium concentrations following salbutamol and suxamethonium were lower than those which followed the injection of suxamethonium alone.

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The increase in potassium concentration following suxamethonium can be reduced by pretreatment with a small dose of tubocurarine
(Weintraub, Heisterkamp and Cooperman, 1969). Other methods which may be used to reduce increased potassium concentrations are, however, often associated with marked side-effects such as the potential for hypoglycaemia with insulin and dextrose regimens and the alkalosis and sodium loading with i.v. bicarbonate. Beta-2 stimulation, apart from providing potentially beneficial bronchodilatation, may also produce unwanted effects which include tremor, tachycardia and metabolic effects—such as an increase in circulating glucose and insulin concentrations. In the present study, no patient complained of tremor, but the heart rate was increased significantly. Salbutamol given orally did not alter the incidence of related myalgia.

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REFERENCES


