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Decamethonium and Serum Potassium in Man

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Decamethonium and succinylcholine were used to study the effects of depolarizing muscle relaxants on serum potassium in 60 patients, free of neuromuscular disease, during major orthopedic surgery. Significant increases in serum K^+ were found after administration of decamethonium or succinylcholine in the usual clinical doses. The abnormal elevations of serum K^+ found in patients with burns, massive trauma, or muscle denervation are thus accentuations of the process that occurs in normal man following use of these depolarizing drugs. The administration of any depolarizing agent to these abnormal patient groups would, therefore, appear contraindicated. (Key words: Neuromuscular relaxants, decamethonium; Neuromuscular relaxants, succinylcholine; Ions, serum potassium.)

PLASMA LEVELS of potassium have been shown to rise following administration of succinylcholine to burned[1,2] or injured patients[3–6] and following decamethonium in experimental animals.[7–9] No study to indicate the effect of decamethonium administration on serum potassium concentrations in patients without neuromuscular or heart disease is available.

The present study was designed to determine the incidence, magnitude, and timing of serum potassium changes after intravenous administration of decamethonium in patients undergoing total hip replacement. The anesthetic agents and adjuvant drugs used in this study were also investigated to determine their effects on serum potassium. We were interested in ascertaining whether the pathologic increases in serum potassium reported to occur in patients with burns, neurologic disease, massive tissue trauma, or various myopathies[1–6] represented a situation unique to succinylcholine or an accentuation of a normal process following depolarizing drugs. Decamethonium was used because it is devoid of actions on either autonomic ganglia[10] or the myocardium.[11]

Material and Methods

Sixty patients aged 22–87 years (mean 56.7 ± SE 4.65), scheduled for total hip replacement, were studied. The 26 female and 34 male subjects were free of neuromuscular, cardiovascular, acid–base and electrolyte disorders. Verbal consent for the investigation was obtained during the preoperative visit.

Premedication consisted of morphine sulfate, 0.1 mg/kg, and scopolamine, 0.4 mg/70 kg (reduced to 0.2 mg/70 kg in patients over 65 years), administered intramuscularly one hour prior to induction of anesthesia.

Anesthesia was induced while the electrocardiogram (ECG), central venous pressure (CVP), and radial arterial pressure were monitored directly and continuously.

Patients were divided into six groups of ten subjects according to the technique of induction. The various groups are summarized in table 1. Sodium thiopental (3–5 mg/kg) was administered to Groups I, III, IV, and VI. Decamethonium (0.1 mg/kg) was given to Groups I, II, and IV, and halothane (1–2 per cent inspired)–nitrous oxide–oxygen (3l:3l) to Groups II, III, and V. Group IV received *d*-tubocurarine (6 mg, 5 minutes prior to induction) as pretreatment before decamethonium. Group VI received succinylcholine (1 mg/kg). In Groups I, IV, and VI the depolarizing drug was administered 3

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TABLE 1. Summary of Techniques of Induction of Anesthesia and Endotracheal Intubation*

Patient Group (N = 10 per Group)	dTc Pretreatment (6 mg)	Sodium Thiopental (3–5 mg/kg)	Decamethonium (0.1 mg/kg)	Succinylcholine (1 mg/kg)	Halothane (1–2 Per Cent), N_2O–O_2 (3:1:3)	Age Range (Years) Mean ± SE
I		X	X			22–77 55.7 ± 4.94
II			X		X	41–84 59.6 ± 4.38
III		X			X	39–68 54.7 ± 3.16
IV	X	X	X			22–87 59.8 ± 5.21
V					X	42–84 59.7 ± 4.38
VI		X		X		28–72 50 ± 3.98

* See text for details of premedication and patient monitoring. Induction of anesthesia was accomplished with thiopental or halothane, nitrous oxide, and oxygen. Endotracheal intubation was performed in all patients, either with the aid of one of the above relaxants or using halothane, without a neuromuscular blocking drug.

minutes after thiopental induction, while in Group II it was given when surgical anesthesia was reached. The incidences of fasciculation, ECG changes, and muscle pains were recorded. Endotracheal intubation was performed in every case.

In all patients arterial P_{O_2}, P_{CO_2}, and pH, serum sodium, serum potassium, and hematocrit were measured. Samples were drawn into heparinized syringes immediately before induction of anesthesia and 3, 10, 15, 20, and 45 minutes thereafter in Groups III and V. In Groups I, II, IV, and VI blood samples were drawn before induction, after induction but prior to administration of decamethonium or succinylcholine, and 3, 10, 15, 20 and 45 minutes after the depolarizing drug.

Blood glucose levels were determined in an additional group of ten patients treated in a manner similar to the patients in Group I. Samples were drawn before induction and at 15-minute intervals after induction for a period of 45 minutes.

Anesthesia was maintained with halothane (0.5–1.5 per cent, inspired concentration) in 50 per cent nitrous oxide and oxygen in a semiclosed system with a CO_2 absorber. The halothane vaporizer (Fluotec Mark II) was placed outside the circle. Pulmonary ventilation was assisted or controlled as necessary to keep arterial P_{CO_2} and pH as near to normal values as possible (P_{CO_2} 36–46 torr; pH 7.35–7.44).[12] Physiologic saline solution was the sole intravenous fluid administered before and during the sampling period; total volume was limited to 50 ml during the period of measurement. Surgical intervention did not take place until after termination of the study.

Serum electrolytes were determined using an Instrumentation Laboratories Flame Photometer, Model 143; the laboratory errors for the method used are ±0.1 mEq/l for potassium and ±2 mEq/l for sodium. P_{O_2}, P_{CO_2} and pH were measured using a Radiometer Digital Acid–Base Analyzer, type PHM72, with the P_{O_2} Module, type PHA932, and the P_{CO_2} Module, type PHA933. Hematocrit was determined using the micropillary method. Blood glucose concentrations were estimated colorimetrically using the Technicon AutoAnalyzer.

Statistical comparisons were made using Student's t test. Significance was attached to a probability of 5 per cent or less ($P < 0.05$).

Results

Table 2 shows the statistical analysis, and figure 1 is a graphic analysis of the data.

A marked decrease in serum potassium was observed 3 minutes after thiopental induction (table 2, fig. 1). This was statistically significant in Groups I ($P < 0.02$), III ($P < 0.001$), and VI ($P < 0.001$). The mean changes were between −6 and −12.6 per cent.

After decamethonium administration (Groups I, II, and IV), a significant increase in serum potassium occurred ($P < 0.001$). One patient showed an increase in potassium of over 0.8 mEq/l, a magnitude that could by itself produce electrocardiographic changes.[13] In 25 patients, potassium levels increased between 0.4 and 0.8 mEq/l, an increase less likely to alter cardiac rate or rhythm. Four patients had potassium changes of less than 0.4 mEq/l. The mean increase in the 30 patients who received decamethonium was +8.02 per cent; in Group I it was +10.85 per cent; in Group II, +6.30 per cent; in Group IV, +6.90 per cent. No statistically significant difference between Groups II and IV was found, but a significant difference ($P < 0.01$) could be seen when Groups II and IV were compared with Group I following decamethonium administration. It is postulated that thiopental reduced the increase in serum potassium that would otherwise occur following decamethonium.

The timing of the increases in serum potassium levels was not uniform in the groups in which decamethonium was used. In patients pretreated with 6 mg *d*-tubocurarine, a highly significant elevation ($P < 0.005$) occurred 10 minutes after decamethonium administration; it was sustained for the duration of the study (45 minutes). A significant increase ($P < 0.05$) in serum potassium was also observed in Group I 15 minutes after decamethonium administration; it persisted for 45 minutes. When decamethonium was given after halothane–nitrous oxide–oxygen induction, a highly

TABLE 2. Serum Potassium (mEq/l, Mean ± SE) before and after Induction of Anesthesia

	Before Induction	After Induction, before Depolarizing Agent	Minutes after Induction (Groups III and V), or after Depolarizing Agent (Groups I, II, IV, and VI)				
			5	10	15	20	45
Group I N = 10 Thiopental Decamethonium*	3.80 ± 0.094	3.50 ± 0.126 $P < 0.02$	3.50 ± 0.139 N.S.†	3.78 ± 0.13 N.S.	3.98 ± 0.109 $P < 0.05$	4.07 ± 0.118 $P < 0.01$	4.15 ± 0.151 $P < 0.005$
Group II N = 10 Halothane, N_2O–O_2 Decamethonium*	3.92 ± 0.031	3.98 ± 0.031 N.S.	4.16 ± 0.054 $P < 0.001$	4.35 ± 0.063 $P < 0.001$	4.4 ± 0.044 $P < 0.001$	4.51 ± 0.031 $P < 0.001$	4.54 ± 0.033 $P < 0.001$
Group III N = 10 Thiopental Halothane N_2O–O_2	3.86 ± 0.077		3.46 ± 0.109 $P < 0.001$	3.63 ± 0.083 $P < 0.001$	3.85 ± 0.077 N.S.	3.87 ± 0.077 N.S.	3.91 ± 0.089 N.S.
Group IV N = 10 d-Tubocurarine Thiopental Decamethonium*	3.73 ± 0.083	3.67 ± 0.089 N.S.	3.71 ± 0.077 N.S.	3.89 ± 0.063 $P < 0.005$	4.01 ± 0.054 $P < 0.001$	4.05 ± 0.054 $P < 0.001$	4.27 ± 0.063 $P < 0.001$
Group V N = 10 Halothane, N_2O–O_2	3.79 ± 0.054		3.85 ± 0.063 $P < 0.025$	3.96 ± 0.077 $P < 0.001$	3.95 ± 0.063 $P < 0.005$	4.07 ± 0.112 $P < 0.005$	3.88 ± 0.083 N.S.
Group VI N = 10 Thiopental Succinylcholine*	3.91 ± 0.070	3.64 ± 0.077 $P < 0.001$	3.92 ± 0.077 $P < 0.001$	3.99 ± 0.077 $P < 0.001$	4.25 ± 0.282 $P < 0.001$	3.88 ± 0.063 $P < 0.005$	3.85 ± 0.054 $P < 0.01$

* Agent given after induction.
† N.S. = not significant.

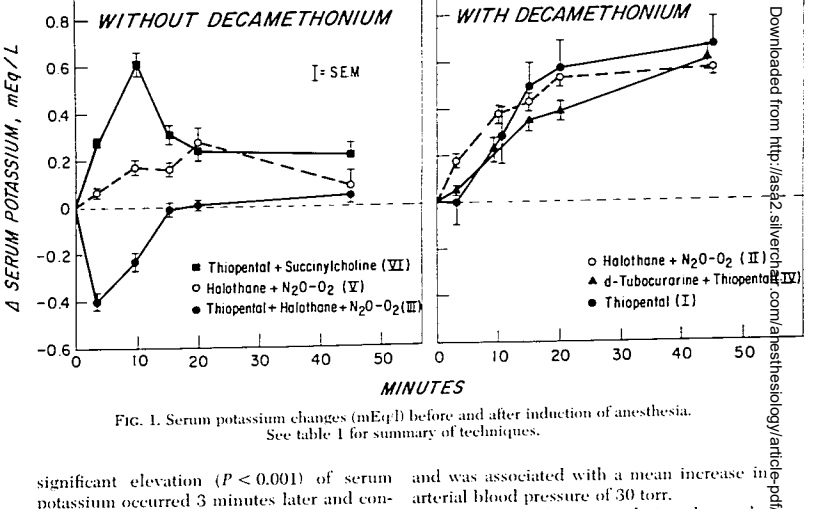

FIG. 1. Serum potassium changes (mEq/l) before and after induction of anesthesia. See table 1 for summary of techniques.

significant elevation ($P < 0.001$) of serum potassium occurred 3 minutes later and continued until the end of the study period.

Succinylcholine was similarly associated with a significant increase in serum potassium 3 minutes after its administration; the increase was sustained throughout the period of observation. The increases ranged from 0.2 to 0.6 mEq/l.

In Group V, in which a mixture of halothane–nitrous oxide–oxygen was used for induction and no relaxant drug was given, there were highly significant ($P < 0.025$ and < 0.005) elevations of serum potassium between the 3- and 20-minute intervals. Insignificant changes occurred thereafter.

Moderate fasciculation was observed in only two of the 30 patients who received decamethonium, and in these two patients serum potassium levels increased significantly from the start. Only three of the 30 patients complained of postoperative muscle stiffness. No change in cardiac rate or rhythm was detected in the ECG's and no important blood pressure fluctuation occurred. Fasciculation developed in all ten patients who received succinylcholine; postoperative muscle pains occurred in six of them. Sinus tachycardia was observed on three occasions and was associated with a mean increase in arterial blood pressure of 30 torr.

Pa_{O_2}'s averaged 187 torr during the study, Pa_{CO_2}'s 38 torr, pH values 7.38, hematocrits 38 per cent, and serum sodium concentrations 142 mEq/l. There was no significant change in blood gases during any phase of the study. Blood glucose levels in ten patients averaged 71 mg/100 ml before induction of anesthesia and 73, 74, and 75 mg/100 ml 15, 30, and 45 minutes after induction, respectively. These changes were not significant.

Discussion

Serum levels of potassium, principally an intracellular cation, represent a dynamic balance between the rate at which potassium enters serum (from cells, from alimentation by way of intestinal absorption, and from parenteral infusion) and the rate at which it leaves serum (into cells, into alimentary juices, and into urine). Changes in serum potassium concentration reflect very small alterations in this dynamic equilibrium, and serum concentration thus provides a useful clinical guide to disturbances in potassium balance. A relatively small percentage change in intracellular potassium concent-

tration may result in a marked reciprocal change in the serum potassium level. Furthermore, relatively small absolute changes in extracellular concentration, by producing large differences in the ratio of intracellular to extracellular potassium, may have important effects on neuromuscular and cardiac physiology.

The results of the present investigation indicate that decamethonium administration was associated with an increase in serum potassium (range 0.1–0.9 mEq/l). This was observed following thiopental or halothane induction, with or without pretreatment with 6 mg *d*-tubocurarine. Succinylcholine administration was similarly associated with an elevation in serum potassium, which ranged between 0.2 to 0.6 mEq/l. A significant decrease in serum potassium was found following thiopental administration, while with halothane, a significant increase was observed from 3 until 20 minutes after the start of anesthesia.

Depolarizing muscle relaxants, such as decamethonium and succinylcholine, reduce the transmembrane potential of the motor endplate and, in doing so, alter the permeability of the membrane to sodium. This is followed by the exit of intracellular potassium ions. Zaimis[14] has shown (using ^{42}K) an increase (as much as 30 per cent) in the flux of potassium from perfused muscle under the influence of decamethonium. Paton,[8] in 1956, working with the isolated perfused gastrocnemius muscle of the cat, found that the release of potassium amounted to about 1 per cent of the potassium content in the muscle and confirmed that the source of potassium was the muscle itself. In the whole animal, overall release was sufficient to increase plasma potassium substantially (as much as 30 per cent). Klupp *et al.*,[7] working with dogs, found that decamethonium, succinylcholine, and other depolarizing drugs increased plasma potassium by as much as 30 per cent. The latter authors also showed that pretreatment of animals with *d*-tubocurarine prevented liberation of potassium caused by depolarizing muscle relaxants. More recently, Wong and associates[15] confirmed this observation, also in dogs. This finding, however, could not be duplicated in the present clinical study. On the contrary, serum potassium levels were elevated in all patients (Group IV) pretreated with *d*-tubocurarine prior to decamethonium administration. This discrepancy might be explained by species variation.

The increase in serum potassium outlasted the neuromuscular block. Resumption of spontaneous ventilation in patients who received decamethonium (excluding those pretreated with *d*-tubocurarine) occurred after 13–25 minutes (mean 17), yet serum potassium remained elevated for 45 minutes.

Several workers have described a decrease in serum potassium following administration of barbiturates in man and in experimental animals.[16–19] In the present study a significant decrease was observed 3 minutes after induction of anesthesia with sodium thiopental. The serum potassium values of patients anesthetized with a mixture of halothane, nitrous oxide, and oxygen showed significant increases at the 3-, 10-, 15-, and 20-minute intervals without a preliminary decrease. As present, no satisfactory explanation can be given for the changes in serum potassium that attend the use of thiopental or halothane.

Results of arterial blood–gas and *p*H studies were within normal limits in all patients. Thus, acidosis or alkalosis, factors that can alter serum potassium,[20,21] did not influence serum potassium in this study. The insignificant changes in blood glucose levels had no effect on serum potassium, a finding also documented by List[16] and by Gal and Malit.[17]

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Monitoring

ARTERIAL PUNCTURE AND TRAUMA

Monitoring arterial blood gases, intra-arterial blood pressure, and cardiac output has become common practice in recent years and has, on occasion, caused complications such as injuries to radial and other arteries. Two patients who developed partial and complete ischemia of the hand secondary to arterial cannulation are described. In the face of rapidly developing ischemia, intra-arterial injection of a lidocaine–papaverine "cocktail" and early removal of the arterial catheter could prevent loss of the thumb and one or more fingers. Teflon catheters with an outer diameter of 1 mm and an inner diameter of 0.6 mm are recommended. Patency of the ulnar artery is mandatory and should be established before puncture of the radial artery is attempted. Factors that may favor occurrence of complications are extremes of age, shock, and repeated attempts at cannulation, particularly with disregard to aseptic technique, too strong or prolonged compression of the wrist after removal of the catheter, too weak and too short compression, subintimal or intramural injection, prolonged use of indwelling catheters, tendency toward thrombosis, diabetes, and pre-existing arteriosclerotic or ischemic disease of the extremity. (*Schwander, D., and Schwander, A.: Arterial Trauma in Anesthesia and in the Intensive Care Unit—Surgical Treatment. Z. Gefaesskrkh 2:330, 1973.*) ABSTRACTER'S COMMENT: The incidence of complications is, in the author's words "not as frequent as one might anticipate." An incidence of two in impressive cases, beautifully illustrated in color photographs, in approximately 600 procedures seems to be high indeed.