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Succinylcholine-induced Hyperkalemia in Patients with Renal Failure?

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The effect of succinylcholine, 1 mg/kg, iv, on serum potassium was studied in ten patients without and ten patients with renal failure. Increases in serum potassium after succinylcholine in patients with renal failure were not significantly different from those in patients without renal failure. The largest increase was 0.7 mEq/l. Absence of myoglobinemia, myoglobinuria, and large increases in serum creatine phosphokinase activity suggest that there was no significant skeletal muscle damage. We conclude that succinylcholine in this dose is not contraindicated in patients with renal failure in the absence of uremic neuropathy. (Key words: Succinylcholine; Myoglobin; Hyperkalemia; Renal failure.)

TRANSIENT MILD HYPERKALEMIA is known to occur in man following administration of succinylcholine (SCh).[1,2] Larger increases in serum potassium leading to serious cardiac arrhythmias have occurred in patients with burns,[3] extensive soft-tissue trauma,[4] and some neuromuscular diseases.[5] Recently, Powell[6] and Roth *et al.*[7] stated that depolarizing muscle relaxants are absolutely contraindicated in the presence of renal failure even in patients with normal preoperative serum potassium levels. This opinion was based on experience with one patient with renal failure who developed several short runs of ventricular tachycardia and peaked T waves on the electrocardiogram following SCh administration.[6] Although laboratory confirmation was lacking, Roth *et al.* attributed these arrhythmias to hyperkalemia.[7]

We have administered SCh to more than 350 patients with renal failure severe enough to necessitate renal transplantation and have not observed serious cardiac arrhythmias. Since it is common practice for us to administer *d*-tubocurarine or gallamine before SCh, these agents might have prevented the hyperkalemia. The purpose of this study was to determine whether SCh increased serum potassium more in patients with renal failure than patients with normal kidney function. In addition, evidence of skeletal muscle damage was sought by measuring myoglobin levels in blood and urine and increases in blood creatine phosphokinase levels; all of these have been reported following SCh.[8,9] Myoglobin released from damaged skeletal muscle may be deposited in the convoluted tubules of the kidney and cause renal damage.[10,11] This would be particularly undesirable in a patient about to receive a kidney transplant. Our results indicate that SCh produces minimal changes in serum potassium levels, with no skeletal muscle damage, and that these changes are no greater in patients with renal failure than in those without renal failure.

Methods

Twenty patients undergoing general anesthesia were studied. Ten patients 21 to 59 years old had no history of renal disease and were scheduled for intra-abdominal operations. The remaining ten patients, 20 to 49 years old, had renal failure and were to undergo renal transplantation. The latter patients showed no evidence of uremic neuropathy. Despite recent dialysis, preoperative mean serum potas-

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TABLE 1. Serum Potassium (mEq/l) and Creatinine (mg/100 ml) of Patients with Renal Failure

	Preoperative Serum Creatinine	Pre-succinylcholine	Post-succinylcholine Minutes after Injection				Maximum Change (mEq/l)
			2	5	7	10	
Patient 1	9.1	4.4	4.9	4.9	—	4.9	+0.5
Patient 2	9.3	4.3	4.4	4.9	4.45	4.4	+0.6
Patient 3	9.7	4.6	4.6	—	4.4	4.6	−0.2
Patient 4	11.3	5.3	5.4	5.5	5.3	5.2	+0.2
Patient 5	15.6	5.6	5.9	5.8	5.8	5.8	+0.3
Patient 6	17.8	4.7	4.9	4.8	4.8	4.8	+0.2
Patient 7	10.1	4.6	4.4	4.2	4.2	4.2	−0.4
Patient 8	8.0	4.7	4.8	4.8	4.9	5.1	+0.4
Patient 9	20.8	6.6	6.0	6.8	6.5	6.1	+0.2
Patient 10	14.0	5.4	6.0	5.5	5.7	5.6	+0.6
Mean	12.6	5.0	5.0	5.2	5.1	5.1	+0.24
SD	4.29	0.71	0.59	0.76	0.77	0.62	0.45

TABLE 2. Serum Potassium Values (mEq/l) of Control Patients

	Pre-succinylcholine	Post-succinylcholine Minutes after Injection				Maximum Change (mEq/l)
		2	5	7	10	
Patient 1	4.0	4.0	4.2	4.2	4.1	+0.2
Patient 2	3.8	3.7	3.8	3.8	3.8	−0.1
Patient 3	4.1	4.4	4.3	4.2	3.9	+0.3
Patient 4	3.9	3.8	4.1	4.0	4.0	+0.2
Patient 5	3.3	3.5	3.5	3.4	3.9	+0.6
Patient 6	3.5	3.7	3.9	3.6	3.6	+0.4
Patient 7	2.8	3.0	—	3.1	2.9	+0.3
Patient 8	4.1	3.2	3.8	3.8	4.0	−0.9
Patient 9	4.0	4.0	4.1	3.9	4.0	+0.1
Patient 10	3.7	4.2	4.4	4.1	4.2	+0.7
Mean	3.7	3.6	4.0	3.8	3.8	+0.18
SD	0.42	0.43	0.28	0.36	0.37	0.50

sium level was 5.0 ± 0.71 (SD) mEq/l (range 4.3 to 6.6), and serum creatinine was 12.6 ± 4.29 mg/100 ml (range 8.0 to 20.8). All patients were premedicated with either barbiturate or opiate and atropine or scopolamine. Following preoxygenation and administration of thiopental, 3–5 mg/kg, and SCh, 1 mg/kg, iv, the trachea was intubated. Anesthesia was maintained with nitrous oxide (60–70 per cent) and fluroxene or halothane. No nondepolarizing muscle relaxants were given. No additional doses of SCh were necessary. All patients undergoing renal transplantation were monitored with an electrocardiograph. Two samples of venous blood were drawn before administration of SCh, and further samples were drawn 2, 5, 7, and 10 minutes after SCh administration. Serum potassium values were determined in duplicate with a flame photometer. Serum creatine phosphokinase (CPK) levels were determined [12] before and 24 and 48 hours after operation (normal range 5 to 60 IU/l). The plasma was tested for myoglobin before and 5, 10, and 15 minutes after

TABLE 3. Pre- and Postoperative Creatine Phosphokinase (CPK) Levels (IU/l)

	Number of Patients Studied	Preoperative	Hours Postoperative	
			24	48
Patients without renal failure	10	41.2 ± 35.2* 5 to 105†	203.1 ± 158.3 40 to 567	101.1 ± 55.6 40 to 210
Patients with renal failure	10	68.5 ± 103.4 15 to 330	202.9 ± 100.1 45 to 404	155.6 ± 101.7 40 to 270

* ± SD. † Range.

SCh administration. The first urines voided after surgery were examined for the presence of myoglobin. If the serum or urine was Hemastix-positive, a two-dimensional precipitation test with Ouchterlony's method was performed on an agar gel plate using specific antiserum to purified human myoglobin.[13] The Hemastix test could detect myoglobin in a concentration as low as 5 μg/ml, while the antiserum gave a positive reaction with as little as 1.5 μg/ml myoglobin.

Results

The largest increase in serum potassium in patients both with (table 1) and without (table 2) renal failure was 0.7 mEq/l. There was no significant difference between the serum potassium elevations in patients with and without renal failure. Both groups showed similar significant increases in CPK levels 24 and 48 hours after operation ($P < 0.01$, table 3). Myoglobin was absent from the plasma of all 20 patients. Myoglobin could not be detected in the urine of seven of ten control patients or four of ten renal-failure patients. The presence of myoglobinuria was not determined in the other cases because the patients were anuric or otherwise unable to provide urine specimens.

Discussion

This study substantiates our previous clinical experience that patients who have renal failure are not susceptible to marked hyperkalemia and severe arrhythmias as a result of receiving SCh. Elevated CPK (an enzyme released from muscle cells with skeletal muscle damage) levels in both groups suggested muscle damage which might be accountable for by surgery and SCh. The CPK levels were equally elevated in both groups suggests that the patients with renal failure were no more prone than the control patients to suffer significant skeletal muscle damage from SCh. In addition, SCh did not induce significant skeletal muscle damage, as judged by the absence of myoglobin from plasma and urine. Thus there is little risk of renal damage from myoglobinuria in patients with renal failure are given SCh.

Our findings are similar to those of Katz *et al.* and Jacobsen *et al.*, who reported no difficulties associated with the use of SCh in 24 [14] and 58 [15] patients with renal failure, respectively. Roth had two cases of cardiac arrest following intubation, all in patients with renal failure.[2] However, SCh-induced hyperkalemia was not confirmed in one patient by serum potassium levels or electrocardiographic evidence of hyperkalemia. In Powell's case electrocardiographic evidence of hyperkalemia did not appear until 6 minutes after the *third* dose of SCh, which was given at least 30 minutes after the first dose. Serum potassium remained elevated for at least 24 hours postoperatively in this patient. SCh-induced hyperkalemia, however, usually returns to the pre-SCh level within 15 minutes of administration of SCh to patients without renal failure.[1-3] Because of the lack of significant hyperkalemia in our study, and the lack of confirmed diagnosis in the reports of Powell and Roth *et al.*, we believe that administration of 1 mg/kg SCh to patients who have renal failure is not contraindicated. It should be noted that we did not study the effect of re-

peated doses of SCh, which might have been involved in the case reported by Powell,[6] and which have been reported to cause myoglobinuria and elevation of serum creatinine phosphokinase in normal patients.[8]

Patients with various neuromuscular diseases such as multiple sclerosis, muscular dystrophy, and Parkinson's disease are particularly susceptible to marked hyperkalemia and cardiac arrhythmias after administration of SCh. It may be that marked hyperkalemia following SCh occurs in renal-failure patients only when they have uremic neuropathy. Even though all our patients had elevated preoperative serum creatinine and potassium levels, they had no uremic neuropathy. Additionally, all of our patients had renal transplantation and hemodialysis, which alleviates uremic neuropathy.[16] The safety of SCh may not apply to patients with uremic neuropathy.

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Metabolism

PSEUDOCHOLINESTERASE STRUCTURE Human serum cholinesterases were separated into two groups, one of mol wt 86,000, the other of mol wt approximately 438,000. This suggests that active cholinesterase is a tetramer aggregate of smaller units, with intermediate molecular forms representing other multiples of the subunit being possible. The authors speculate that pseudocholinesterase variants might represent tetramers in which one or more subunits are genetically altered. Thus, genetic defects of all four subunits would result in the formation of the homozygous (atypical) variant, whereas defects of 1, 2 or 3 subunits would yield enzymes corresponding to various heterozygous (intermediate) types. (*Boutin, D., and Brodeur, J.: Human Serum Pseudocholinesterases: Molecular Weight Estimation of a Subunit Structure, Canad. J. Physiol. Pharmacol. 49:777, 1971.*)