The Serum Potassium Response to Muscle Relaxants in Neural Injury


Twenty-three patients with peripheral-nerve injuries and muscle paralysis were studied to determine the changes in serum potassium following succinylcholine, gallamine, d-tubocurarine, and succinylcholine preceded by 6 mg d-tubocurarine. Potassium increased to 4.00 mEq/l above control in venous blood of the paralyzed limb, compared with only 0.7 mEq/l in the nonparalyzed limb. Neither gallamine nor d-tubocurarine provoked any significant change in serum potassium. d-Tubocurarine prior to succinylcholine reduced the potassium response but did not suppress it. The period of "sensitivity" to succinylcholine in neural injury is more than six months, but more precise limits are not yet defined. (Key words: Potassium; Muscle relaxants; Neural injury.)

HYPERKALEMIA following succinylcholine is a recognized danger in patients with severe burns, massive trauma, or central nervous system lesions with skeletal muscle paralysis.1–8 A few reports have indicated that nondepolarizing neuromuscular blocking agents are safe in burned or traumatized patients, but there are no data regarding changes in serum potassium in response to these agents in patients with neural injury.1–8 Furthermore, all reports of excessive potassium blood levels in neuromuscular diseases concern patients with upper motor neuron lesions only.

We elected to study patients in whom peripheral-nerve injuries had resulted in paralysis of skeletal muscle to determine whether hyperkalemia occurred after succinylcholine in these

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patients as well. We then studied the potassium and sodium responses following administration of d-tubocurarine, gallamine, and succinylcholine preceded by a small dose of d-
tubocurarine.

Method

Twenty-three young Marines with peripheral-nerve injuries resulting in skeletal muscle paralysis in one extremity were studied. Twenty-one had been wounded in Vietnam between 22 and 192 days before study and were scheduled for exploration and repair of injured nerves. One patient had paralysis secondary to a Volkman's contracture, and the other had paralysis secondary to radial-nerve compressions. All were otherwise well (A.S.A. Classification I), and most were ambulatory before study. Each patient gave his informed consent to participate in the study.

Patients were premedicated with meperidine (Demerol, 75–100 mg), pentobarbital (Nembutal, 100–150 mg), and atropine sulfate (0.4–0.8 mg) im, 60 to 90 minutes before anesthesia. Three venous catheters were inserted percutaneously: one for sampling blood draining a limb with atrophied muscles, a second for sampling blood from a normal limb, and a third elsewhere for administration of drugs. The catheter for sampling of blood from an arm was placed in either an antecubital vein or the cephalic vein; the one for sampling from the leg was placed in the femoral vein. Only 5 per cent dextrose in water was infused during the test period. Lead II of the ECG was monitored and recorded. After preanesthesia control blood samples had been obtained, anesthesia was induced with thiopental (Pentothal sodium, 4 mg/kg), followed by halothane, 1.0–2.0 per cent in oxygen. Respirations were assisted and/or controlled.

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TABLE 1. Time of Drug Administration and Mean Venous Blood Potassium Changes after Four Minutes in Each Test Period*

<table>
<thead>
<tr>
<th></th>
<th>Number of Patients</th>
<th>Test Period I</th>
<th></th>
<th>Test Period II</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Drug (min)</td>
<td>∆[K+] mEq/l (4-0)</td>
<td>SE</td>
</tr>
<tr>
<td>Group I</td>
<td>7</td>
<td>SCh (0-4)</td>
<td>P 3.97</td>
<td>0.68</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NP 0.70</td>
<td>0.27</td>
</tr>
<tr>
<td>Group II</td>
<td>9</td>
<td>SCh (0-4)</td>
<td>P 3.30</td>
<td>0.75</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NP 0.30</td>
<td>0.18</td>
</tr>
<tr>
<td>Group III</td>
<td>4</td>
<td>SCh (0-4)</td>
<td>P 2.63</td>
<td>0.72</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NP 0.73</td>
<td>0.46</td>
</tr>
<tr>
<td>Group IV</td>
<td>3</td>
<td>SCh (0-4)</td>
<td>P 1.90</td>
<td>0.35</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NP 0.10</td>
<td>0.70</td>
</tr>
</tbody>
</table>

* P = paralyzed limb; NP = nonparalyzed limb.

The patients were divided into four groups and tested during two periods (table 1). Test period I for all groups was from 0 to 18 minutes after induction, during which time 1 mg/kg of 0.1 per cent succinylcholine was infused at a constant rate during a 4-minute period. Blood samples were obtained at 0, 2, 4, 6, 12, and 18 minutes from both paralyzed and nonparalyzed limbs, with 0 minutes being the start of the succinylcholine infusion.

Test period II was from 18 to 36 or 41 minutes after the beginning of the succinylcholine infusion of period I, depending on the drugs administered. Group I consisted of seven patients who were given a second infusion of 1 mg/kg succinylcholine 18 to 22 minutes after the initial infusion. Blood samples were obtained at 20, 22, 24, 30, and 36 minutes. Nine patients (Group II) were given 6 mg d-tubocurarine at 18 minutes and then 1 mg/kg succinylcholine at between 23 and 27 minutes. Blood samples were obtained at 23, 25, 27, 29, 35, and 41 minutes. Four patients (Group III) were given gallamine, 1.5 mg/kg, and three patients (Group IV) were given d-tubocurarine, 0.3 mg/kg, as an intravenous bolus at 18 minutes; blood samples were obtained as in Group I.

Tracheal intubation was accomplished in all patients using topical anesthesia (lidocaine, 4 per cent) in the time between the last two blood samples of period II.

Blood was analyzed for potassium and sodium by a flame photometer (Instrumentation Laboratories, Waltham, Massachusetts). Means were statistically compared by Student’s t test.

Results

Mean changes from control of serum potassium 4 minutes after administration of the test drug are summarized in table 1 and figures 1 through 4.

Potassium in venous blood draining the paralyzed limbs increased after succinylcholine, but not after gallamine or d-tubocurarine. The mean difference at 4 minutes in period I was 4.0 mEq/l in the paralyzed limb, compared with 0.70 mEq/l in the nonparalyzed limb, in Group I patients (P < 0.005). During period II, succinylcholine evoked an increase of 1.93 mEq/l in the paralyzed extremity 4 minutes after infusion; this was significantly less than the increase after the first infusion (P < 0.02).

Neither gallamine nor d-tubocurarine altered potassium concentration in the paralyzed or nonparalyzed limb.

Preceding succinylcholine with 6 mg d-tubocurarine reduced the hyperkalemic response in the paralyzed limb. The mean increase in se-
Fig. 1. Mean venous blood potassium concentrations in paralyzed and nonparalyzed limbs of patients in Group I.

Fig. 2. Mean venous blood potassium concentrations in paralyzed and nonparalyzed limbs of patients in Group II.
Fig. 3. Mean venous blood potassium concentrations in paralyzed and nonparalyzed limbs of patients in Group III.

Fig. 4. Mean venous blood potassium concentrations in paralyzed and nonparalyzed limbs of patients in Group IV.
rum potassium was only 0.62 mEq/l at 27 minutes, significantly less than the response without d-tubocurarine.

Serum sodium decreased to 129 mEq/l in some patients, but no consistent change could be identified.

Although tachycardia to 120/min occurred in some patients, arrhythmias were not observed.

Discussion

Previous reports of hyperkalemia associated with neuromuscular disease have concerned patients with upper motor neuron lesions. We describe here the occurrence of the same phenomenon in patients with lower motor neuron lesions. Since elevated potassium levels were found in the venous blood of the paralyzed muscle only, the source of the potassium must be the abnormal muscle distal to the neural lesion. Similar findings in experiments with dogs whose sciatic nerves or spinal cord were sectioned were reported by Stone et al. It is commonly thought that the administration of a small dose of d-tubocurarine before succinylcholine is a safe means of preventing a dangerous increase in potassium in susceptible patients. The data presented above confirm that the mean potassium increase is reduced by d-tubocurarine, but for an individual patient, the increase in potassium may be enough to produce serious arrhythmias. For example, one of the nine patients tested in this manner had an elevation in potassium to 2.0 mEq/l above control. Weintraub et al. also observed that the mean increase in potassium was suppressed when d-tubocurarine was given before succinylcholine to trauma patients, but one of ten patients in their report had an increase to 2.8 mEq/l above control. An alternative method which does not provoke an increase in potassium is the use of gallamine or d-tubocurarine alone.

Not only reports of cases of patients with neural injuries but also those of patients with burns and trauma have documented elevated potassium for as long as 85 days after injury. In this study, hyperkalemia occurred in several patients as late as 112, 134, and 192 days after injury. The limit of sensitivity in patients with neural injury is more than six months, but still has not been clearly defined. It is also important to note that almost all of these patients had recovered from their wounds and many were ambulatory at the time of study. The trauma patients who had hyperkalemia following succinylcholine reported by Mazze et al. often had fever, infection, and open wounds, and were generally in a catabolic state.

It has long been known that denervation produces many changes in muscle membrane. Axelsson and Thesleff have demonstrated the enlargement of the pharmacologic receptor area of the endplate in denervated skeletal muscle so that the entire fiber membrane is finally encompassed. Then the sensitivity to depolarizing agents is increased to 10,000–100,000 times normal at any point on the muscle fiber membrane. This process of "denervation sensitivity" develops over a period of time, usually several weeks. Also, a decrease in re-entry permeability to potassium of denervated muscle has been reported. It may be that in man the membrane of the entire muscle fiber becomes as sensitive to depolarizing agents as the endplate and, coupled with an altered potassium permeability, accounts for the hyperkalemia observed clinically.

Further investigations must be done to explain the hyperkalemia phenomenon, not only in patients with neural injuries but also in those with burns and trauma.

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References

Transfusion

BLOOD TRANSFUSION AND HEPATITIS A prospective study of post-transfusion viral hepatitis was undertaken in 5,142 patients who underwent cardiovascular surgery at 14 university hospital centers. Selection was limited to patients more than 15 years old who received at least two units of blood and who did not have histories of hepatitis or had received transfusions within six months before operation. Preoperative liver function tests were done in 72 per cent of the patients. All patients were followed for at least three months, and nearly 97 per cent, for six months. Follow-up histories were obtained from the patients by questionnaire; SGPT or SGOT measurements of 494 patients were obtained. In 60 cases liver biopsy or autopsy specimens were reviewed by three hepatologists. Only patients with onset of symptoms between 16 and 180 days after operation were considered to satisfy the criteria of viral hepatitis. Four patients developed hepatitis within 15 days of operation, and one died. Three were exposed to halothane and the fourth to methoxyflurane. Of 4,984 patients who received an average of 7.7 units of blood, 157 (3.2 per cent) developed viral hepatitis. Five died of hepatitis, a death rate of approximately 1/1,000 patients or 1/7,700 donor exposures. Of 158 other patients who also received fibrinogen (22) and pooled plasma (136), 31 developed viral hepatitis. The corrected incidence of hepatitis in the fibrinogen group was 19 per cent, with a mortality rate of 4 per cent, and in the pooled plasma group 12 per cent, without mortality. The incidence of hepatitis was not related to age or sex, but all patients who died of hepatitis were men more than 60 years old. Increasing risk with increasing number of transfusions was not established by the study. Among patients who received only known-volunteer-donor blood, the incidence of hepatitis was 1.5 per cent, contrasted to the incidence of 5.3 per cent when blood was obtained commercially from paid donors. The risk of hepatitis correlated well with the rate of detection of HB antigen. Prophylactic injections of immune serum globulin not only failed to reduce the incidence or severity of hepatitis, but adverse reactions to globulin injections occurred in 1 per cent of the recipients. (Grady, G. F., and others: Risk of Posttransfusion Hepatitis in the United States, J.A.M.A. 220: 692–701, 1972.) ABSTRACTER'S COMMENT: It is interesting to compare the incidence of hepatitis and the mortality after halothane with the incidence of hepatitis and mortality following transfusion of blood products in this group.