SERUM POTASSIUM CHANGES AFTER SUCCINYLCHOLINE IN SWINE WITH THERMAL TRAUMA OR SCIATIC NERVE SECTION*

GERALD A. GRONERT, M.D. AND RICHARD A. THEYE, M.D.

HYPERKALAEMIA after succinylcholine (SCh) administration has been observed in patients with burns,[1] trauma,[2,3] or neuromuscular disease.[4] The basis for this response has not been fully explained, nor have the means for prevention been totally clarified.[2,3,5] Additional studies in man are limited, however, by the associated risk of cardiovascular collapse.[2,4] Furthermore, animal experimentation is complicated since the response develops several weeks after trauma, and effective long-term nursing care is difficult to provide. This study explores the feasibility of using swine with either thermal injury or sciatic nerve division as an appropriate model. Swine are hardy, have a blood volume great enough to permit multiple sampling, and have serum and blood levels of potassium (K) similar to those of humans.[6]

MATERIALS AND METHODS

Thermal Trauma. Six unpremedicated, weanling swine were given thiopental (10 to 15 mg/kg) and atropine (0.06 mg/kg) intravenously, intubated, and ventilated by a Harvard pump with a mixture of 0.5 to 1.5 per cent halothane and oxygen. The saphenous artery was cannulated, with provision for sampling and pressure determinations. When $Paco_2$ was stable at 40 ± 2 torr, a control arterial sample was drawn and SCh (3 mg/kg) was injected intravenously. Additional arterial samples were then obtained at 1, 3, 5, 10, 15, and 20 minutes and all were analyzed for blood and serum K (IL flame photometer) and for pH, Pco_2, and Po_2 (IL electrodes).

Three of the pigs were then subjected to thermal trauma, accomplished by immersing the dorsal body surface and flanks into 95°C water for 20 seconds.[7] Thereafter, anaesthesia was discontinued, and lactated Ringer's solution† (150 ml/kg) was infused during the next 1 to 2 hours.[8] Care after thermal injury included individual pens, supplemental feedings, daily wound cleansing, and application of mafenide‡ twice daily.[9] Between 2 and 6 weeks after the initial studies and under similar conditions, weekly determinations of the response of serum and blood K to SCh were made in all six pigs, with successive studies alternating injections of SCh and lactated Ringer's solution (blank).

Denervation. In six other weanling swine, unilateral sciatic nerve section was performed during anaesthesia with intramuscularly administered phencyclidine

*Mayo Clinic and Mayo Foundation: Department of Anesthesiology, Rochester, Minnesota.

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†Courtesy of Baxter Laboratories, Morton Grove, Ill.

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(1 to 2 mg/kg) supplemented with intravenously administered pentobarbital (5 mg/kg). Three to 4 weeks later, under conditions similar to those described in Thermal Trauma, and after control samples from the carotid artery and both femoral veins, SCh (3 mg/kg) was injected intravenously and repeated at 10 minutes, with repetitive sampling from all sites. Venous and arterial samples were analyzed for blood and serum K; arterial samples were analyzed in addition for pH, Pco_2, and Po_2. In all, statistical significance was tested by application of Student's *t*-test for paired or unpaired data, with $p < 0.05$ considered significant.

Results

The responses of the control and thermal trauma groups to SCh were not significantly different (Figure 1) and were characterized by an increase of approximately 0.5 mEq/liter of serum K at 1 minute, with continued elevated levels throughout the period of observation. The response in the thermal trauma group did not vary during the 2- to 6-week period of study, and the data have been pooled in Figure 1. Serum K levels did not change initially after the blank injection, but did gradually increase during the period of observation (Figure 2). The increases were small, 0.2 to 0.4 mEq/liter, and were significant at 10 minutes. No changes were detected in blood K levels in any of these situations, most likely because of the magnitude of error (± 0.8 mEq/liter) in the method of analysis. Burn size ranged

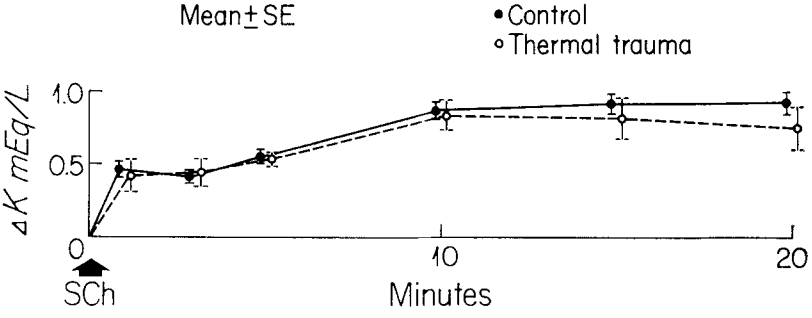

FIGURE 1. Changes of serum potassium after succinylcholine administration in the absence (solid line) and presence (dotted line) of previous thermal trauma.

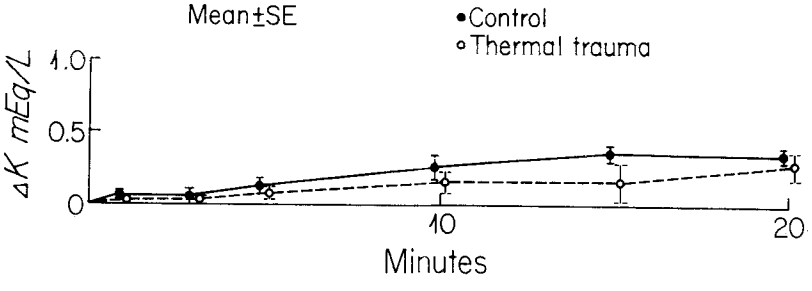

FIGURE 2. Changes of serum potassium after injection of blank solution in the absence (solid line) and presence (dotted line) of previous thermal trauma.

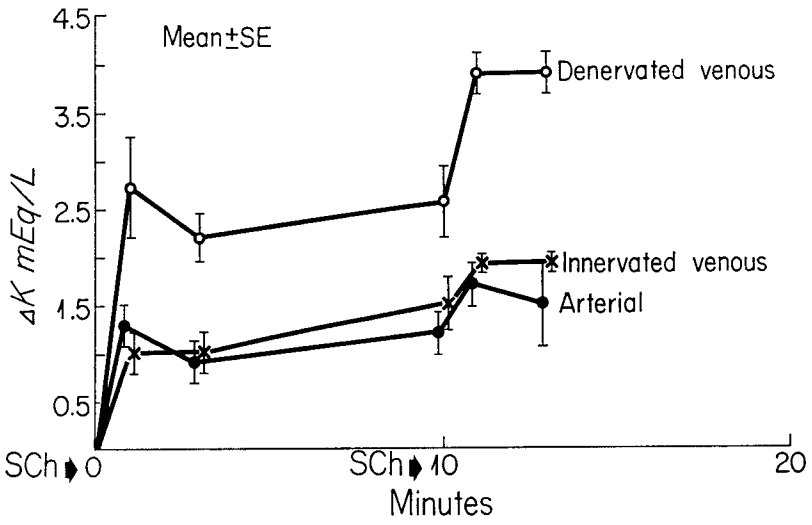

FIGURE 3. Serum potassium changes in arterial blood and in femoral venous blood from denervated and innervated limbs after succinylcholine administration.

from 23 to 30 per cent of body surface area (mean 27 per cent). Burn depth varied from full thickness, just into the subcutaneous fat, to deep dermal. The thermal wounds were sharply demarcated and did not appear to be painful. The pigs in this group were active and did not develop wound infections, but gained weight more slowly than did the control pigs. There were no deaths.

After denervation, the increase in arterial serum K levels at 1 minute after SCh administration (Figure 3) was greater ($p < 0.01$) than that seen in control and thermally traumatized pigs (Figure 1). Furthermore, the increase in femoral venous serum K level in the denervated limb was twice that in either the femoral vein of the innervated limb or the carotid artery. These differences were maintained for the initial 10 minutes of observation and were augmented with the second injection of SCh. Changes of blood K were similar to those of serum K.

DISCUSSION

In the present studies, normal swine had a modest increase of serum K after SCh administration, similar to that seen in normal man.[1-3] However, in contrast to thermally injured man, swine did not develop a hyperkalaemic response to SCh in the 2- to 6-week period after the burn. This difference in response is considered to be based not on direct species-related differences but on direct and indirect differences in the effects of thermal injury on skeletal muscle in swine and man. In the present study, swine subjected to thermal trauma did not have direct, gross injury to the underlying muscle, continued to have a good appetite and to gain weight, were not immobilized, engaged in vigorous generalized muscular activity, and did not display disuse atrophy. By contrast, patients studied after thermal trauma[1] had various degrees of direct muscle injury, loss of appetite, inanition, loss of weight,

immobility, disuse atrophy, and lessened physical activity. Although it is not presently possible to ascertain the relative influence of each of these various factors, future studies are indicated, in addition to those involving direct muscle injury.

In the denervation studies, serum K levels increased in the venous effluent from the denervated limb by several times that observed in the venous blood flow from the innervated limb. The arteriovenous difference in serum K was large for the denervated limb and insignificant for the innervated limb. This is consistent with the presumption that the primary source of the K was the muscles of the denervated limb. These findings are qualitatively similar to those of Stone *et al.*[10] and Birch *et al.*,[2] who determined the serum K response to SCh after spinal cord transection or sciatic nerve section in the dog. In these studies, either form of nervous system injury and paralysis resulted in an increase in the level of serum K with SCh. As suggested by these investigators, the likely explanation for their findings and ours involves an alteration in the response of the muscle cell membrane to drugs, which occurs with denervation and which also has been reported with disuse atrophy.[11] This alteration has been characterized by Thesleff[12] to consist of a nonselective increase in sensitivity of the entire muscle membrane to chemical depolarization by either acetylcholine or SCh. Presumably, this increase in sensitivity (or decrease in threshold) is accompanied by a greater loss of K during depolarization.

The clinical implications of these studies deserve a brief comment. A hyperkalaemic response to SCh has been observed in various clinical circumstances having in common direct and indirect changes in skeletal muscle: thermal injury, massive trauma, denervation, and central nervous lesions with motor involvement. Certain other conditions resulting, per se, in immobilization, inanition, and disuse atrophy probably will also eventually be added to this list. The hyperkalaemic response at times results in elevations of serum K sufficient to result in altered myocardial function, including arrhythmias, and consequent deterioration of haemodynamics, progressing in some instances to circulatory arrest. Although some information suggests that the hyperkalaemic response to SCh may be moderated by prior administration of curare,[2,3] the use of SCh probably should be avoided in all of the previously mentioned situations.[3,5]

Summary

Study of swine indicates that post-traumatic SCh-induced hyperkalaemia is related not to the type of trauma per se but to trauma-induced abnormalities in muscle. Three groups of swine were studied: normal controls, thermal-trauma swine, and sciatic-section swine. The normal control and the thermal-trauma swine reacted similarly to SCh, with an immediate increase in arterial serum K of approximately 0.5 mEq/liter. Denervated swine responded to SCh with a significantly greater increase; simultaneous femoral venous samples indicated that the source of the K was the denervated leg. These findings are discussed in terms of the responses of human burn and trauma patients to SCh.

RÉSUMÉ

Une étude sur des truies nous démontre que l'hyperkalémie produite par l'injection de succinylcholine chez l'animal traumatisé ne dépend pas du traumatisme lui-même mais des anomalies produites dans le muscle par le traumatisme. Nous avons étudié trois groupes de truies: un groupe de contrôle: truies normales, un autre groupe avec un traumatisme par la chaleur et un autre, avec section du nerf sciatique. Les animaux du groupe de contrôle et du groupe traumatisme thermique ont réagi de la même façon à l'injection de la succinylcholine, c'est-à-dire une augmentation immédiate du taux sérique de potassium de 0.5 mEq/litre. Les animaux du groupe au sciatique sectionné ont répondu à l'injection de succinylcholine par une augmentation beaucoup plus grande du taux de potassium; le prélèvement simultané d'échantillons dans les veines fémorales nous a permis de découvrir que la source de potassium venait du membre au nerf sectionné. Nous discutons ces résultats en songeant aux réponses à la succinylcholine chez les brûlés et les traumatisés humains.

REFERENCES

1. SCHANER, P. J.; BROWN, R. L.; KIRKSEY, T. D.; GUNTHER, R. C.; RITCHEY, C. R.; & GRONERT, G. A. Succinylcholine-Induced Hyperkalemia in Burned Patients – 1. Anesth. & Analg. (Cleveland), *48*: 764 (1969).
2. BIRCH, A. A.; MITCHELL, G. D.; PLAYFORD, G. A.; & LANG, C. A. Changes in Serum Potassium Response to Succinylcholine Following Trauma. J.A.M.A., *210*: 490 (1969).
3. WEINTRAUB, H. D.; HEISTERKAMP, D. V.; & COOPERMAN, L. H. Change in Plasma Potassium Concentration After Depolarizing Blockers in Anaesthetized Man. Brit. J. Anaesth., *41*: 1048 (1969).
4. TOBEY, R. E. Paraplegia, Succinylcholine and Cardiac Arrest. Anesthesiology, *32*: 359 (1970).
5. GRONERT, G. A. Potassium Response to Succinylcholine. (Letter to the Editor.) J.A.M.A., *211*: 300 (1970).
6. CHARBON, G. A. & HOEKSTRA, M. H. Mineral Content in Plasma and Blood Cells of Various Species. Acta Physiol. Pharmacol, Neerl., *10*: 209 (1962).
7. FOX, C. L., JR., & BAER, H. Redistribution of Potassium, Sodium and Water in Burns and Trauma, and Its Relation to the Phenomenon of Shock. Amer. J. Physiol., *151*: 155 (1947).
8. MOYER, C. A.; MARGRAF, H. W.; & MONAFO, W. W., JR. Burn Shock and Extravascular Sodium Deficiency – Treatment With Ringer's Solution With Lactate. Arch. Surg. (Chicago), *90*: 799 (1965).
9. ARTZ, C. P. & MONCRIEF, J. A. The Treatment of Burns, 2nd Ed., p. 305. Philadelphia: W. B. Saunders Company (1969).
10. STONE, W. A.; BEACH, T. P.; & HAMELBERG, W. Succinylcholine-Induced Hyperkalemia in Dogs With Transected Sciatic Nerves or Spinal Cords. Anesthesiology, *32*: 515 (1970).
11. SOLANDT, D. Y.; PARTRIDGE, R. C.; & HUNTER, J. The Effect of Skeletal Fixation on Skeletal Muscle. J. Neurophysiol., *6*: 17 (1943).
12. THESLEFF, S. Effects of Motor Innervation on the Chemical Sensitivity of Skeletal Muscle. Physiol-Rev., *40*: 734 (1960).