

Failure of "Self-taming" Doses of Succinylcholine to Inhibit Increases in Postoperative Serum Creatine Kinase Activity in Children

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The combined use of halothane and succinylcholine leads to an increased serum creatine kinase (CK) activity^{1,2} which reaches its peak on the day of surgery.³ Succinylcholine probably triggers,^{1,2} and halothane amplifies² the muscle cell damage with subsequent outflow of the muscle-specific enzyme into the plasma.¹ The cell lesion in skeletal muscle which composes 45 per cent of the body mass⁴ can lead to the release of further cell components such as myoglobin⁵ and even possibly cause kidney damage.^{6,7} The muscle fasciculations induced by succinylcholine have been claimed to be partly responsible for the damage to the cell.⁸ The fasciculations can be attenuated (self-taming) by prior injection of a small dose of succinylcholine (10 mg for adults) one minute before the subsequent larger dose (1 mg/kg).⁹

The object of the present study was the question whether the self-taming method inhibits an increased serum CK activity in the postoperative period.

METHOD

The subjects were children, ages 7 to 11 years of both sexes, scheduled for urological surgery inflicting no skeletal muscle trauma. They received no drugs outside of the study. Anesthesia was induced with 66 per cent nitrous oxide and halothane in increasing concentrations up to an inspired concentration of 1.5 per cent and maintained with halothane 0.8-1.2 per cent. After induction

of anesthesia (disappearance of lid reflex and tolerance of the oropharyngeal airway), an indwelling catheter was inserted into the dorsum of each hand or forearm for the withdrawal of blood and the rapid injection of succinylcholine which was done in two portions: 0.125 mg/kg followed one minute later with 1 mg/kg. Ventilation was controlled.

Venous blood samples for determining serum CK activity were taken on the day of operation following induction of anesthesia and prior to injection of succinylcholine (CK₁), postoperatively at 6 P.M. (CK₂) and on the first day after surgery at 10 A.M. (CK₃). The activity of the serum CK was determined with the test combination "CK-NAC-activated" (Boehringer Mannheim) on a LBK reaction rate analyzer.¹⁰ The upper normal level is considered to be 70 IU/l. Previous studies of a comparable group of patients showed a CK₁ of 39.4 IU/l (SEM \pm 2.7; n = 52). One of the authors (J.P.) estimated whether muscle fasciculations were present on a yes or no basis; no attempt was made to estimate their intensity. For control purposes the findings in two further groups of 24 children, the results of which had already been reported,³ and one additional group of 10 children from an unpublished study were used. The anesthetics were identical except for muscle relaxants: 10 children received one single dose of succinylcholine 1.0 mg/kg (control 1), and 14 children received no succinylcholine (control 2); 10 additional children received a single dose of succinylcholine 1.5 mg/kg (control 3).

RESULTS (TABLE 1)

The ten children who received the "self-taming" dose of succinylcholine did not have an inhibition of the mean postoperative CK activity in comparison to control group 1 either on the day of operation or the first postoperative day. To the contrary, the mean postoperative CK activity was higher in the "self-taming" group than in the control group on the first postoperative day. The frequency of visible fasciculations was reduced in the "self-taming" group of children.

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TABLE 1. Serum CK Activities (IU/l; Mean Values \pm SEM and Range) before (CK₁) and after Succinylcholine and Visible Fasciculations Following the Paralyzing Dose of Succinylcholine

	n	Age (Years)	Body Weight (kg)	Sex (m/f)	CK ₁	CK ₂ *	CK ₃ †	Fasciculations (Number of Patients)
Present study ("Self-taming")	10	9.4 \pm 0.7	32.3 \pm 2.8	9/1	40.4 \pm 4.3 19-58	408.1 \pm 104.4 95-982	226.2 \pm 56.3 55-527	2
Control studies								
1 (succinylcholine 1.0 mg/kg)	10	7.6 \pm 1.3	28.8 \pm 4.9	8/2	32.6 \pm 2.7 19-51	240.2 \pm 119.1 33-1,244	99.4 \pm 33.8 30-371	9
2 (no succinylcholine)	12-14	8.0 \pm 2.6	25.5 \pm 6.7	13/1	42.7 \pm 11.4 22-140	57.2 \pm 13.2 20-57	63.3 \pm 20.0 20-249	—
3 (succinylcholine 1.5 mg/kg)	10	9.3 \pm 1.0	33.6 \pm 3.4	9/1	34.0 \pm 5.0 12-69	445.5 \pm 189.3 70-2,105	353.4 \pm 104.1 49-1,197	8
Significance of difference§ P < 0.05						NS	S	S

* Determined at 6 P.M. the day of surgery.

† Determined at 10 A.M. the day following surgery.

‡ Control data are from Plötz, Braun, and Stallenberger³ and from an unpublished study (control 3).§ Student's *t* test (CK) and chi-square analysis (fasciculations) for present study and control study 1.NS = not significant, S = statistically significant (*P* < 0.05).

DISCUSSION

Self-taming proved to be ineffective in inhibiting the increased postoperative serum CK activity. The mean CK activities were even higher when the "self-taming" dose was used than after a single injection of succinylcholine. Since the entire amount of succinylcholine in self-taming was 10 per cent greater than after a single injection (control 1) this could be a dose-dependent effect. This supposition is supported by the largest dose leading to highest mean activity (control 3). Self-taming did, however, prove effective in reducing visible fasciculations. These are the earliest signs commonly observed indicating the onset of the neuromuscular blockade following a single injection of succinylcholine.¹¹ When administered by infusion, a direct correlation was observed between the rate of infusion and the degree of visible fasciculations showing nearly elimination with the smallest infusion rate.¹¹ Dividing the bolus into two portions may result in similar plasma concentrations as in an infusion and lead to similarities in the visible fasciculations.

The discrepant effects of succinylcholine on CK and fasciculations oppose the opinion that fasciculations are responsible for rupture of the muscle cell and outflow of the enzyme.¹ Evidence contrary to cell injury as the *conditio sine qua non* for the efflux of cell components is delivered by clinical reports of myoglobinuria without previous injury.¹² Limitations in respect to the validity of this concept have resulted from the fact that a constant direct relation between CK activity and fasciculations could not be established.^{1,8} Efforts trying to show morphologic lesions have also been to no avail.^{13,14} Even if functional damage existed, small molecules should reach

the plasma more rapidly than larger ones; this would possibly be reflected in the sequence of their maximal concentrations. Actually the peak of serum myoglobin (molecular weight: 17,500) was observed as soon as 30 min after succinylcholine (1 mg/kg, iv) and the highest activity of serum CK (70,000) no earlier than 8 hours afterward.¹⁵ The reservations facing the existing concept are strengthened by our study. We propose that not the fasciculations but other events in connection with the neuromuscular blockade after succinylcholine produce the cell damage which is responsible for the outflow of cell components. This proposal is consistent with the findings which show that pretreatment with small amounts of *d*-tubocurarine^{1,8} or dantrolene³ exerts a moderating effect on both CK activity and fasciculations. *d*-Tubocurarine is a direct antagonist of succinylcholine.⁸ Dantrolene has little or no relation to the depolarizing or nondepolarizing neuromuscular blockers but rather develops its muscle-relaxing effect within the muscle cell without influencing the neuromuscular transmission or transmembrane potentials.¹⁶ The effect on the CK activity can be explained again in the case of *d*-tubocurarine by its antagonism of succinylcholine; in the case of dantrolene³ by an interruption of the neuromuscular blocking events induced by succinylcholine taking place in the cell interior and preventing the onset of damage.

Halothane led to significantly greater changes in CK and myoglobinemia in comparison to thiopental, diethylether, propanidid, and althesin.^{2,8,15} In children, myoglobinuria has been observed significantly more frequently than in adults.¹⁷ Inagaki *et al.*,¹⁵ using a radioimmunoassay technique sensitive to 1 ng/ml, reported a maximal rise of the mean level for serum myoglobin from 14.3 ng/ml prior to preanesthetic medication to

nearly 100 times this in children, but only 15 times more in adults. Juvenile patients and the use of halothane and succinylcholine are the common characteristics of several reports concerning patients who exhibited myoglobinuria and an increase of CK activity.^{7,18-22} Isoenzyme typing showed an overwhelming share (89.6 ± 2 per cent; $n = 7$) of the total CK activity belonging to the skeletal muscle.²² Thus, by using halothane, our study was designed to maximally test the efficacy of the self-taming approach to the use of succinylcholine.

In earlier studies self-taming was found to be ineffective in preventing the sudden increase in intraocular pressure²³ and myalgia²⁴ after succinylcholine. In our study, we found that the self-taming approach does not protect from the increase in CK activity. Self-taming apparently is unsuitable in preventing various clinically significant problems arising in connection with succinylcholine.

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