Serum creatine kinase levels after succinylcholine in children with "muscle, eye and brain disease"

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Four boys belonging to a group of children affected by a rare form of muscular dystrophy with eye and brain involvment, termed the "muscle, eye and brain disease" (MEB), were anaesthetized for various eye examinations and surgery. On some occasions succinylcholine was used during anaesthesia and the initially elevated serum creatine kinase (CK) values increased from a range of 122 to 1200 units·L^{-1} to a range of 4350 to 9690 units·L^{-1} 22 hours after anaesthesia. CK values after anaesthesia without succinylcholine remained at the initially elevated levels. Rectal temperatures of the children were normal. These findings suggest that succinylcholine should be avoided in patients with MEB disease.

From 1974 to 1977, four mentally retarded boys who also suffered from severe muscular dystrophy underwent general anaesthesia for diagnostic eye examinations and surgery for glaucoma, or muscle biopsy. In 1977, Santavuori *et al.* included these patients in a report of children with the rare condition termed "muscle, eye and brain disease" (MEB).[1] The aetiology of this condition remains unknown and in order to determine the degree of muscle damage, serum creatine kinase (CK) activity of the children had been repeatedly analyzed in the paediatric unit and found to be increased. Recent interest in MEB disease[2] prompted the presentation of this report to determine whether anaesthesia and surgery had influenced the initially elevated serum CK levels of these patients.

Key words

ENZYMES: creatine kinase; MUSCULAR DYSTROPHY: muscle, eye and brain disease; NEUROMUSCULAR RELAXANTS: succinylcholine.

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Case reports

Four boys aged 2 to 44 months and weighing 5.3 to 13.0 kg were anaesthetized 9, 7, 4 and 3 times for various ophthalmological procedures or muscle biopsy. The children were mentally retarded and suffered from severe muscle weakness; they were bedridden, able to sit when supported and although they could swallow food, retained their secretions. Examinations revealed large corneal diameters and myopia. Three of the patients had developmental glaucoma which required goniopuncture or trabeculectomy.

Serum CK values were measured variably on the first postoperative day. Possible correlation between these values and the mode of anaesthesia with and without succinylcholine administration, as well as to other CK values of the same children was sought. Rectal temperatures had been measured one hour after some of the anaesthestics: the CK activity was measured at 25° C with test sets (Boehringer, Mannheim). Normal values for adults were 0 to 50 units·L^{-1}.

Serum CK determinations were made on eight occasions 20–24 hours after anaesthesia. These values, along with the mode of anaesthesia and the patient's rectal temperatures one hour following anaesthesia, are shown in the Table. High CK values of 5200, 5500, 9690 and 4350 units·L^{-1} were noted following anaesthesia which included intravenously administered succinylcholine for trabeculectomy or eye examinations. Anaesthesia without use of succinylcholine, for muscle biopsy or trabeculectomy, was associated with CK values of 149, 395, 920 and 223 units·L^{-1}. These results were compared to the control baseline CK values for the four children: patient 1: mean 486 units·L^{-1} (range 127–1200, n = 7); patient 2: mean 339 units·L^{-1} (range 157–590, n = 4); patient 3: mean 319 units·L^{-1} (range 197–480, n = 3) and patient 4: mean 223 units·L^{-1} (range 122–440, n = 6). These results are summarized in the Figure.

TABLE Age, mode of anaesthesia, postoperative creatine kinase activities and body temperatures of children with "muscle, eye and brain disease" undergoing anaesthesia with or without succinylcholine

Patient	*Age (months)*	*Premedication IM atropine dose (mg)*	*Induction IV thiopentone dose (mg)*	*Succinylcholine IV dose (mg)*	*Halothane*	*Tracheal intubation*	*Postoperative creatine kinase units·L⁻¹*	*Recial temperature (°C)*
1	7	0.1	—	—	+	−	149	—
2	2	0.1	25	—	+	+	395	35.8
2	4	0.1	30	10	+	+	5200	36.1
2	10	0.1	37	10	+	+	5500	36.7
2	13	0.2	—	—	+	−	920	—
3	17	0.2	50	15+100	−	+	9690	36.8
4	12	0.1	50	10	+	+	4350	36.7
4	19	0.1	40	—	+	+	223	37.2

Discussion

Succinylcholine is known to transiently increase intraocular pressure. Three of the children in the present series had developmental glaucoma which was surgically treated. The succinylcholine-induced increase in intraocular pressure was not considered a risk for nerve fibre damage.

Intermittent bolus doses of succinylcholine during halothane anaesthesia provoked an increase in serum CK levels which was not observed when the patients received an infusion of succinylcholine after a bolus dose.[3] In the present report, the child who received an infusion of succinylcholine following an initial intravenous dose, showed the highest postoperative CK value (9690 units·L^{-1} – Table).

Succinylcholine given during halothane anaesthesia in children aged 2 to 17 years produced a tenfold increase in CK levels. However, when induction was achieved with thiopentone, followed by succinylcholine, the increase, although statistically significant, was only twofold.[4]

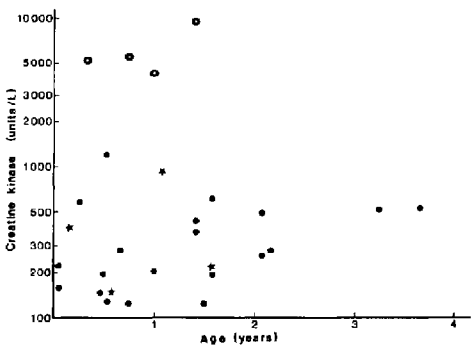

FIGURE Logarithm of serum creatine kinase (units·L^{-1}) of four boys affected by "muscle, eye and brain disease." ● = baseline values; ★ = values determined 20–24 hours after anaesthesia without succinylcholine; ○ = values after anaesthesia with succinylcholine.

Although the children included in the present study all received thiopentone before succinylcholine their CK levels showed a tenfold increase.

Cozanitis *et al.* reported that in children one to three years of age gross muscle movements and increases in CK produced by succinylcholine were controlled by d-tubocurarine pretreatment.[5] They stressed that in normal infants CK values remained unchanged irrespective of whether pretreatment with d-tubocurarine was or was not used. Three of the four boys in the present study were aged one year or less at the time of anaesthesia, and they presented a tenfold rise in CK activity after intravenous succinylcholine administration, without d-tubocurarine pretreatment.

High baseline levels of CK have been reported in patients with neuromuscular dystrophy and other forms of neuromuscular disease,[6] as well as in neonates with MEB disease.[2,7] Succinylcholine produces high levels of serum CK in patients with strabismus and/or with Duchenne's muscular dystrophy.[8,9] The increase in the serum CK activity apparently results from skeletal muscle where most of the enzyme is located. Increased levels of CK indicates either an acute muscle necrosis or a sudden change in the permeability of the sarcolemma. It is interesting that histological changes of the muscle of the children affected by MEB disease are compatible with the muscular dystrophies.[2] In light of this, these individuals may indeed be suspectible to malignant hyperthermia. In progressive muscular dystrophies, such as Duchenne's dystrophy, various abnormalities have been described in the plasma membranes and in sarcolemma.[10] Several enzyme activities are constantly elevated in the early stage of Duchenne's muscular dystrophy, to levels even higher than detected in this study.[11] Had other enzymes or myoglobin been estimated in the present study, they too would have been elevated, although not to the same extent as CK which is the most sensitive indicator of muscle damage. There is no indication whatsoever that increased muscle enzyme activities in themselves are harmful for

the body, unless the critical threshold for myoglobinuria is exceeded which could occur only at much higher levels of CK activity.[12]

It is possible that pretreatment with certain non-depolarizing neuromuscular blocking drugs prior to succinylcholine administration would decrease the outflow of CK from the muscle fibres of children with MEB disease,[5,13–15] but a prospective study to examine such a hypothesis is considered ethically questionable. Although the clinical course of the patients of this study was uneventful, it is concluded that succinylcholine should be avoided in patients with MEB disease.

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Résumé

Quatre garçons atteints d'une maladie rare comprenant une dystrophie musculaire avec atteinte oculaire et cérébrale "muscle, eye and brain disease" ont été anesthésiés pour des biopsies musculaires, divers examens diagnostiques et des interventions ophtalmologiques. A quatre reprises la succinylcholine fut utilisée lors de l'anesthésie et le taux sérique de la créatine kinase déjà élevé chez ces malades (valeur de 122 à 1200 unités·L^{-1}) a décuplé 22 heures après l'anesthésie (valeur de 4350 à 9690 unités·L^{-1}). Après anesthésie sans succinylcholine le taux de créatine kinase sérique est demeuré inchangé. La température rectale des enfants demeurait normale. L'augmentation importante du taux de la créatine kinase sérique indique que la succinylcholine devrait être évitée chez ces malades.