Precurarisation in infants and children less than three years of age

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Sixty patients less than three years of age about to undergo adenoidectomy or endoscopy were divided into three groups of 20 each according to age (0–11 months, 12–23 months, 24–35 months). Before the induction of anaesthesia with thiopentone, either tubocurarine 0.05 mg·kg⁻¹ or normal saline was given at random in a double-blind fashion. Three minutes later, the children received succinylcholine 1.5 or 1.0 mg·kg⁻¹, respectively. Muscle movements were graded according to a four-point scale. Blood was sampled for creatine kinase (CK) activity before anaesthesia and on the following morning. When all age groups were combined, there was a significant reduction of muscle movements in patients who had received tubocurarine pretreatment. Serum CK activity rose significantly when saline pretreatment was used in children over the age of one year but not in the infants, despite the presence of muscle movements following succinylcholine administration.

The response of muscle to an intravenous injection of succinylcholine is an evanescent stimulation of some muscle fibres. Generally, this muscle activity, which is referred to as fasciculation, begins with the muscles of the eyelids and spreads quickly over the face and neck to the trunk. Finally, gross movements of one or more of the limbs may take place before flaccid paralysis and blockade of myoneural conduction occurs.

Mayrhofer¹ showed that if a dose of 0.05 mg·kg⁻¹ of tubocurarine is administered before succinylcholine, the fasciculations are controlled. Tammisto and Airaksinen²

reported that the fasciculations provoked by the depolarising relaxant produced an elevation of serum creatine kinase (CK) activity. Miller³ noted that if tubocurarine is given before succinylcholine, the elevation of CK is reduced or eliminated.

All the above reports pertain to individuals over the age of three years. In younger patients, fasciculations are not normally seen following intravenously administered succinylcholine. Instead, only gross movements of the limbs are usually seen. Salem *et al.*⁴ described fasciculations from succinylcholine 1.1 mg·kg⁻¹ as being absent or minimal in infants who had been premedicated with hyoscine and in children up to three years of age who had received hyoscine and morphine before anaesthesia was induced with either thiopentone or halothane.

The effect of a small dose of tubocurarine before succinylcholine in children less than three years of age has not been examined and neither therefore in this context have the levels of serum CK. We decided to examine the effect of "precurarisation" on succinylcholine-induced muscle movements and its effect, if any, on levels of serum CK in patients aged less than three years.

Methods

Sixty caucasian infants and children (ASA physical status 1) scheduled to undergo adenoidectomy or endoscopy were studied. The protocol had been approved by the ethics committees of both the Children's Hospital and the Otolaryngological Hospital. The patients had not been receiving any drug therapy and had not had an intramuscular injection for at least one month before the anaesthetic. They were divided into three groups of twenty each according to their ages: (1) 0–11 months, (2) 12–23 months and (3) 24–35 months. In the morning, oral premedication given about 60 minutes before the start of anaesthesia consisted of Triclos Liquid (sodium salt of trichloroethyl phosphate, Merrell Dow) 0.7 ml·kg⁻¹ and atropine 0.03 mg·kg⁻¹ given together in 7 ml of fruit juice.

In the operating theatre, ECG electrodes were applied and a sphygmomanometer was used for blood pressure measurement. A peripheral vein was then cannulated and

Key words

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TABLE I Demographic and CK data

Treatment	Age group (months)	Sex M/F	Age mean $\pm$ SD (months)	Weight mean $\pm$ SD (kg)	CK ₁ median (range) (IU·L ⁻¹)	CK ₂ median (range) (IU·L ⁻¹)
Tubocurarine	0-11	6/4	9.1 $\pm$ 1.59	8.5 $\pm$ 1.43	119 (72-429)	110 (48-806)
	12-23	8/2	19.5 $\pm$ 2.99	12.9 $\pm$ 2.02	95 (52-186)	86 (63-136)
	24-35	5/5	27.7 $\pm$ 3.23	13.5 $\pm$ 1.51	88 (54-176)	81 (48-163)
Saline	0-11	9/1	8.3 $\pm$ 1.23	8.8 $\pm$ 1.23	198 (55-684)	211 (49-472)
	12-23	8/2	18.1 $\pm$ 3.57	11.4 $\pm$ 1.58	132 (71-426)	273* (105-4405)
	24-35	4/6	28.4 $\pm$ 3.27	13.2 $\pm$ 1.32	99 (42-147)	121† (63-592)

*p < 0.05.

†p < 0.01.

2 ml blood was withdrawn for total serum creatine kinase (CK) activity, measured within four hours according to the Recommendation of the Scandinavian Committee on Enzymes.⁵ The normal upper limits (95th percentile) in the laboratory are: 170 IU·L⁻¹ for infant (<one year of age) boys and girls and respectively, 109 and 100 IU·L⁻¹ for boys and girls from one to four years of age. Within each age group, in random order and in a double-blind fashion, half of the patients were given tubocurarine (Tubarine, Wellcome) 0.05 mg·kg⁻¹ IV. This tubocurarine preparation is free of pain on injection.⁶ The remaining children received an equal volume of normal saline solution. At 0 min, either tubocurarine or saline was given. Thiopentone 5 mg·kg⁻¹ IV was injected and when the loss of the eyelash reflex occurred, the patient was ventilated with 100 per cent oxygen through a modified Jackson-Rees circuit. At 3 min (the optimal time interval for precurarisation)⁷ and without the anaesthetist knowing which dose was being used, succinylcholine 1.5 or 1.0 mg·kg⁻¹ was given, depending on whether tubocurarine or saline, respectively, had been earlier administered. All drugs were given into the intravenous cannula and immediately flushed with saline.

Muscle movements were graded by the "blinded" anaesthetist as follows: 0 = absent, 1 = some movement but without limb flexion, 2 = movement accompanied with flexion of either upper or lower limb(s), 3 = exaggerated limb flexion. The trachea was intubated and the patient was ventilated with halothane 1-2 per cent in a mixture of nitrous oxide and oxygen (2:1). A slow drip of glucose five per cent was started and the planned operative procedure was carried out. Postoperative analgesia was provided in the Recovery Room with either IV meperidine

or with a paracetamol suppository, the latter being used exclusively later on the ward. On the following morning (21 to 24 hours later) a second blood sample was taken for total creatine kinase determination (CK₂).

Statistical analysis of the non-parametric data was with Fisher's exact probability test, the chi-square test, and Wilcoxon signed-ranks test. A one-way analysis of variance was used for parametric data. The level of statistical significance was taken at p < 0.05.

Results

Demographic and CK data of the patients studied are given in Table I. Regarding sex, age, and weight, there were no significant differences between the groups.

Statistically, because of the small number of patients in the age groups, a dichotomous classification was used *a priori* indicating the treatment for the muscle responses as being "effective" if graded 0 or 1 and "ineffective" when graded 2 or 3. Table II suggests that tubocurarine provided more effective treatment than did saline, although the differences did not reach statistical significance. When, however, the three age groups were combined, a significant difference in favour of the tubocurarine treatment was found.

Mean CK activity immediately before the start of anaesthesia (CK₁) was, in the case of males, 160 IU·L⁻¹ and in females, 112 IU·L⁻¹, p = 0.10. Due to the skewed distribution of the enzyme values, particularly for the second sample (CK₂) (Table II) the medians rather than the means were employed in the analysis of the data. When the levels of the CK₁ and CK₂ samples were compared, there was no significant difference for any of the age groups which had received tubocurarine. When

TABLE II The effect of tubocurarine or saline before succinylcholine on muscle movements in the three age groups and all age groups combined.

Age group (months)	Treatment	Grading		<i>p</i> =
		0 or 1 <i>n</i>	2 or 3 <i>R</i>	
0-11	Tubocurarine	9	1	0.057
	Saline	4	6	
12-23	Tubocurarine	5	5	0.14
	Saline	1	9	
24-35	Tubocurarine	6	4	0.057
	Saline	1	9	
Combined	Tubocurarine	20	10	0.007
	Saline	6	24	

saline had been given, the 12-23-month-old group and the 24-35-month-old group, but not the infants, had significant changes in their median CK values (Table I).

Discussion

This study demonstrates that the gross muscle movements which follow the intravenous injection of succinylcholine in children aged less than three years can be controlled by the prior administration of tubocurarine. In children over one year of age, the muscle movements were accompanied by a rise in serum CK activity, indicating some change in the skeletal muscle biochemistry. This increase in the enzyme activity was inhibited by the pretreatment with tubocurarine. The infants in the study, however, behaved differently. Regardless of whether or not pretreatment with tubocurarine was used, serum CK activity remained unchanged in both groups even when muscle movements had been clearly evident in those patients who had received saline pretreatment. It is likely that in infants a degree of immaturity of neuromuscular transmission exists. In any case, it should be borne in mind that the study population was reasonably small and therefore for example, the lack of statistical significance of muscle movements in the infant and 24-35-month-age groups (Table II) may be attributed to small numbers.

Why gross muscle movements rather than fasciculations are manifested in infants and children less than three years of age is unknown. Cook and Fischer⁸ believe that it is related to the dilution of succinylcholine in a large extracellular fluid volume before it is distributed to a relatively small muscle mass. Mastaglia* (personal communication) suggests the relative immaturity of the neuromuscular junction to be a factor of relevance. If

excitation occurs simultaneously at the majority of end plates of a particular muscle, then one could envisage that grosser movements, such as flexion or extension of limbs could be produced rather than fasciculations, which represent fractional activation of muscle.

Race, sex, age, seasonal influence, diurnal variation, physical activity, intramuscular injections and genetic factors may account for the wide variation of CK activity within individuals. The level of this enzyme is elevated in certain conditions, such as Duchenne muscular dystrophy, as it is in acute states such as myocardial infarction, burns and trauma, including surgery involving skeletal muscle.⁹⁻¹¹ In the present study, the mean CK activity was higher in boys than girls but this difference did not reach statistical significance. This is in accordance with some reports^{12,13} although other authors observed that CK activity in boys was significantly higher than in girls.^{9,11} In agreement with the finding of Lane and Roses¹⁴ regarding age, the infants in the present study had higher CK levels than the children in the two older age groups, before anaesthesia.

While this study was underway, Plötz¹⁵ reported that the maximum serum CK concentration occurs at about six hours after the injection of succinylcholine. Thus, in the present study where sampling was carried out 21 to 24 hours after succinylcholine administration the CK values might have been found to be more elevated, had the blood been taken earlier.

In conclusion, children between the ages of one and three years were shown to be as prone to succinylcholine-induced elevations in serum CK levels as older patients. Prior treatment with tubocurarine was effective in curtailing this increase.

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Résumé

Soixante patients tous âgés de moins de trois ans et devant subir une adénoïdectomie ou une endoscopie, ont été divisés selon l'âge en trois groupes de 20. Avant l'induction de l'anesthésie avec thiopentone, soit de la DTC 0.05 mg·kg⁻¹ ou du salin physiologique a été administré au hasard et à double insu. Trois minutes plus tard les enfants ont reçu respectivement de la succinylcholine 1.5 ou 1.0 mg·kg⁻¹. Les mouvements musculaires ont été gradés d'après une échelle à quatre points. Du sang a été retiré pour l'activité de la créatinine kinase (CK) avant l'anesthésie et le lendemain matin. Quand tous les groupes ont été combinés on a noté une diminution significative des mouvements musculaires avec le pré-traitement à la DTC. L'activité sérique de la CK s'éleva significativement quand le pré-traitement au salin physiologique était utilisé pour les enfants dont l'âge est supérieur à un an et non chez ceux âgés de moins d'un an malgré les fasciculations musculaires.