

Neuromuscular Blocking Effects of Succinylcholine in Infants and Children

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The neuromuscular blocking effects and recovery times following two doses of succinylcholine on a weight basis were evaluated in 16 infants and 16 children. Infants had less profound neuromuscular blockade than children at both 0.5 and 1.0 mg/kg doses. Succinylcholine, 1 mg/kg, in infants produced blockade equal to that produced by 0.5 mg/kg in children; at these equipotent doses there was no statistically significant difference between the times to recover to 50 and 90 per cent neuromuscular transmission in the two groups. However, the rate of recovery from 50 per cent neuromuscular transmission to 90 per cent neuromuscular transmission was 69.1 per cent/min in children, as opposed to 46.4 per cent/min in infants. When dosage was calculated on a surface area basis, there was a linear relationship for infants and children as a single group between the log dose and the times to recover to 50 and 90 per cent neuromuscular transmission. Similarly, there was a linear relationship between the log dose (mg/m^2) and the maximum intensity of neuromuscular blockade. (Key words: Neuromuscular relaxants, succinylcholine; Anesthesia, pediatric, succinylcholine; Age factors, succinylcholine; Pharmacokinetics, succinylcholine.)

WHEN DOSAGE is calculated on a weight basis, infants and children require more succinylcholine to produce apnea or to depress respiration than adults do. This has been interpreted as relative resistance to succinylcholine.^{1,2} Nightingale *et al.* noted that the intensity and duration of the neuromuscular blockade following succinylcholine changed gradually throughout childhood from 1 to 8 years of age.³

A number of factors other than neuromuscular blockade may influence the amount of succinylcholine needed to maintain apnea or depress respiration. To exclude these other factors, we elected to measure the intensity

of neuromuscular blockades following succinylcholine in groups of infants and older children at two dose levels. We examined the maximum neuromuscular blockade following a single intravenous injection of succinylcholine, the duration of action as evidenced by the times to recover to 50 and 90 per cent neuromuscular transmission, and the rate of recovery from 50 to 90 per cent neuromuscular transmission.

Materials and Methods

Thirty-two infants or children having operations with general endotracheal anesthesia were studied. All patients were healthy, physical status 1, without fluid or electrolyte disturbance. Sixteen were infants 1-10 weeks of age (mean 4.6 weeks), weighing 3-5 kg (mean 3.9 kg), and 16 were children 5-7 years of age (mean 6.2 years), weighing 17-27 kg (mean 21.0 kg). The surface area of each patient was calculated from nomograms. Premedication, given intramuscularly about 1 hour prior to induction of anesthesia, consisted of atropine alone in infants (0.03 mg/kg). The older children received secobarbital (2 mg/kg), morphine (0.1 mg/kg), and scopolamine (0.01 mg/kg). Anesthesia was induced and maintained with nitrous oxide-oxygen-halothane in all cases. Respiration was assisted or controlled as necessary. All patients were euthermic at the time of the study. Neither alveolar level of halothane nor arterial blood gases were measured.

The neuromuscular blocking effects of succinylcholine were monitored in a standard way⁴; following induction of anesthesia, 25-gauge metal needles were inserted subcutaneously at and above the wrist over the ulnar nerve. The needles were connected to the electrodes of a Block-aid nerve stimulator. The stimulator provided supramaximal stimuli of 6 milliseconds duration at a rate of approximately 15/min. A force-displacement transducer connected to a string was secured to the thumb by means of a small wooden applicator. The electrical

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TABLE 1. Neuromuscular Blocking Effects of Succinylcholine and Recovery Times in Infants, Children, and Adults*

	Maximum Depression (Percentage of Control, Mean ± SD)	Recovery Times (Minutes, Mean ± SD)		
		T ₁₀	T ₅₀	T ₉₀
Infants				
0.5 mg/kg (n = 8)	69.0 ± 9.5	—	1.3 ± .4	2.3 ± .8
1.0 mg/kg (n = 8)	85.3 ± 12.0	—	3.0 ± 1.0	4.0 ± 1.0
Children				
0.5 mg/kg (n = 8)	83.6 ± 4.2	—	2.4 ± .8	3.0 ± 1.0
1.0 mg/kg (n = 8)	100.0 ± 0	3.4 ± .9	4.2 ± 1.0	4.8 ± 1.0
Adults (Waits and Dillon ⁴)				
0.5 mg/kg (n = 13)	100.0 ± 0	4.6 ± 1.4	5.9 ± 1.6	7.4 ± 2.0
1.0 mg/kg (n = 15)	100.0 ± 0	8.1 ± 3.0	10.1 ± 3.0	12.1 ± 3.0

* Maximal neuromuscular blockades following succinylcholine in infants and children compared with those in adults studied by Waits and Dillon⁴ at the same mg/kg dose. The times to recover to 10 (T₁₀), 50 (T₅₀), and 90 (T₉₀) per cent neuromuscular transmission are shown.

signal resulting from thumb adduction was recorded on a Grass Model #7 Polygraph. The chart speed was 0.5 mm/sec; an automatic time marker was used.

After stabilization of the twitch height, succinylcholine was administered intravenously. The maximum twitch depression following injection of succinylcholine and the times to recover to 10, 50, and 90 per cent neuromuscular transmission were noted from the recording. In calculating recovery times, the starting time (time zero) was taken from the point where twitch suppression began.

Eight infants were given 0.5 mg/kg succinylcholine and eight infants received 1.0 mg/kg. Likewise, eight children received 0.5 mg/kg and eight children received 1.0 mg/kg. Which dose a patient should receive was determined at random. Succinylcholine diluted in saline solution to 1.0 mg/ml was used for administration to the infants.

Results

The mean maximum twitch depressions following the two doses of succinylcholine and the mean times to recover to 10 (T₁₀), 50 (T₅₀), and 90 (T₉₀) per cent neuromuscular transmission are shown in table 1. All data are expressed in terms of percentage of the control twitch height. At each dose of succinylcholine infants had less intense neuromuscular blockade than did children.

In infants, 1.0 mg/kg succinylcholine pro-

duced about the same degree of neuromuscular blockade as did 0.5 mg/kg of succinylcholine in children. At these equipotent doses, there was no difference between the 50 and 90 per cent recovery times for infants and children (P < .20).

The rate of decline of neuromuscular blockade, i.e., rate of increase in neuromuscular transmission, from T₁₀ to T₅₀ averaged 46.

TABLE 2. Rates of Recovery from Succinylcholine in Infants, Children, and Adults*

	Rate of Recovery (Percent-Minute ⁻¹ , Mean ± SD)	
	T ₁₀ -T ₅₀	T ₅₀ -T ₉₀
Infants		
0.5 mg/kg	—	46.6 ± 17.7
1.0 mg/kg	—	46.2 ± 7.0
Children		
0.5 mg/kg	—	66.4 ± 29.9
1.0 mg/kg	59.4 ± 21.4	71.8 ± 39.1
Adults†		
0.5 mg/kg	30.7	26.6
1.0 mg/kg	20.0	20.0
Adults‡		
0.5 mg/kg	16.6	18.2
1.0 mg/kg	18.2	18.2

* Rates of recovery from 10 to 50 per cent neuromuscular transmission and from 50 to 90 per cent neuromuscular transmission (per cent min⁻¹) in infants, children, and adults.

† Estimated from data of Waits and Dillon.⁴

‡ Estimated from data of Katz and Ryan.⁵

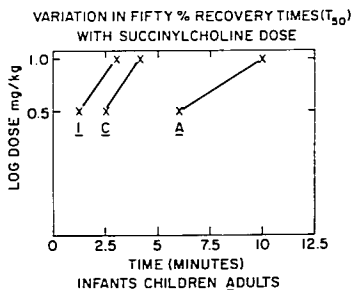


FIG. 1. Variation in times to 50 per cent neuromuscular transmission (T_{50}) as a function of the log dose in infants (I), children (C), and adults (A). Data for adults from Levy.⁶ The return of neuromuscular transmission follows linear first-order elimination kinetics. Standard deviations of the recovery times are shown in table 1.

per cent/min in infants and 69.1 per cent/min in children (table 2). The difference is significant ($P < .01$).

Discussion

This study demonstrates that the neuromuscular blocking effect of succinylcholine in infants is less profound than that in older children at the same dose on a weight basis. The intensity of neuromuscular blockade and times to recover to 50 (T_{50}) and 90 (T_{90}) per cent neuromuscular transmission in infants at 1.0 mg/kg succinylcholine were similar to those in children at 0.5 mg/kg.

Both infants and children had less profound neuromuscular blockade at equal mg/kg doses of succinylcholine than did adults studied by Walts and Dillon³ (table 1). At the 1.0 mg/kg dose of succinylcholine, although the apparent neuromuscular blockade is the same in children and adults, the 10, 50, and 90 per cent recovery times are significantly longer in adults ($P < .025$). Only 100 per cent twitch suppression can be determined; not, for example, 150 or 200 per cent. More profound blockade would be reflected, in large part, in prolongation of recovery times. Thus, the shorter recovery times in children suggest that they had less intense neuromuscular blockade than adults at the 1.0 mg/kg dose of succinylcholine.

Recovery of neuromuscular transmission

following succinylcholine is related to several factors, primary of which are redistribution of succinylcholine away from the motor endplate and subsequent metabolism by pseudocholinesterase. The rate of recovery from succinylcholine from one depth of block to another reflects these two factors. The rates of recovery of both infants and children from T_{10} to T_{50} and from T_{50} to T_{90} are faster than the estimated recovery rates of adults^{4,5} (table 2). Rates of recovery from one point to another are independent of the time to reach the first point and hence independent of the dose.

Levy has suggested that in adult man the duration of action of succinylcholine is dose-related and follows linear first-order elimination kinetics over a 0.5 to 4 mg/kg dose range.⁶ When we plotted the 50 and 90 per cent recovery times as a function of the log dose (mg/kg) for infants, children, and adults, we obtained three families of curves (fig. 1). The recovery-time plots of infants and children to the same endpoint, 50 per cent recovery, were parallel but different. The plot for 50 per cent recovery in adults has a different slope (fig. 1).

Walts and Dillon found no difference between infants and adults in the times to recover to 10, 50, and 90 per cent neuromus-

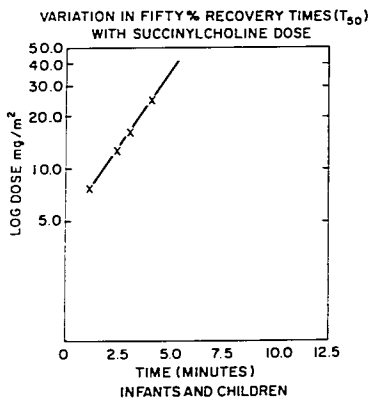


FIG. 2. Linear regression line, $r = .92$, showing the relationship of the log dose (mg/m²) to 50 per cent recovery times (T_{50}) for infants and children as a single group.

cular transmission when succinylcholine was given in equal doses on a surface-area basis (40 mg/m^2).⁷ We found a linear relationship, with a correlation coefficient of 0.92, between the logarithm of the dose on a milligram per surface area basis and the 50 and 90 per cent recovery times for infants and children as a combined single group (fig. 2). Since extracellular fluid and surface area bear a constant relationship throughout life, this suggests that the volume of distribution is important in defining the duration of the neuromuscular blockade following succinylcholine.

It is tempting to ascribe the difference in maximal intensity of neuromuscular blockade also to a larger volume of initial distribution for succinylcholine in the infant than in the older child. There was a linear relationship, with a correlation coefficient of 0.78, between the log dose on a mg/m^2 basis and the maximum intensity of neuromuscular blockade for infants and children as a combined single group (fig. 3). The blood volume and extracellular fluid volume of the infant are significantly greater than the child's on a weight basis. There is a much smaller muscle mass in the infant than in the adult. If succinylcholine were preferentially distributed to muscle one would expect the infant to have a more intense neuromuscular blockade than adults. As noted, this is not so.

That the infant's rate of recovery is slower than the child's is not surprising if one considers that the infant's level of pseudocholinesterase is about half the older child's.⁸ However, volume of distribution must be more important if pseudocholinesterase levels are normal or near normal, since the infant's rate of recovery is closer to that of an adult than it is to that of a child. The small muscle mass, high muscle blood flow, and larger extracellular fluid volume into which succinylcholine may be redistributed appear to compensate well for the infant's lower pseudocholinesterase levels.

It appears that the magnitude of the initial response to succinylcholine is determined by the volume (blood and extracellular fluid volume) into which it is distributed, the time to recover is determined also in large part by redistribution volume if pseudocholinesterase levels are adequate. The infant more

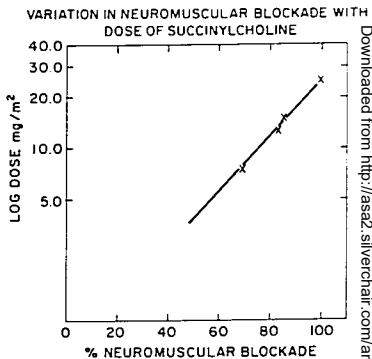


FIG. 3. Linear regression line, $r = .78$, showing the relationship of the log dose (mg/m^2) to the maximum neuromuscular blockades for infants and children as a single group.

than the child does require more succinylcholine on a weight basis to produce similar neuromuscular blockade, compared with the adult. This, combined with their faster rate of recovery, makes infants and children appear resistant to succinylcholine.

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