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The "Intubating Dose" of Succinylcholine

The Effect of Decreasing Doses on Recovery Time

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Background: **The usually cited "intubation dose" of succinylcholine is 1.0 mg/kg. In the majority of patients, this dose will produce apnea of sufficient duration that significant hemoglobin desaturation may occur before neuromuscular recovery takes place in those whose ventilation is not assisted. This study was undertaken to examine the extent to which reducing this dose would decrease the duration of action of succinylcholine.**

Methods: **During stable desflurane/oxygen/opioid anesthesia and after adequate twitch stabilization, neuromuscular function was recorded with an acceleromyographic monitor. Supramaximal stimuli were delivered at 0.10 Hz. Patients received 0.40, 0.60, or 1.0 mg/kg succinylcholine, and twitch height was monitored for at least 20 min thereafter.**

Results: **The onset times to maximal effect were 105 ± 23 s, 81 ± 19 s, and 71 ± 22 s, respectively. The lowest dose (0.40 mg/kg) did not reliably produce 100% twitch depression. The times to 90% twitch recovery at the adductor pollicis in the three groups were 6.6 ± 1.5 min, 7.6 ± 1.6 min, and 9.3 ± 1.2 min, respectively.**

Conclusions: **Reducing the dose of succinylcholine from 1.0 mg/kg to 0.60 mg/kg shortens the duration of effect at the adductor pollicis by more than 90 s. The authors believe that even this modest decrease in the duration of drug-induced paralysis is often worth pursuing.**

THE utility of succinylcholine as a tool in facilitating tracheal intubation was first described 50 yr ago.[1,2] In these early reports, doses averaging less than 0.50 mg/kg were usually employed (range, 10–50 mg). One of the advantages seen for succinylcholine was a "short duration of respiratory arrest even when an overdosage is administered as a result of error in judgment." However, Foldes noted that a problem with doses of this magnitude was that they ". . .allow only 60–90 s for [intubation] when a single intravenous dose is administered."[2] Perhaps as a consequence, doses of 1.0 mg/kg or greater have come to be accepted as usual and customary for succinylcholine-abetted intubation.[3]

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Recently, second thoughts about the margin of safety associated with succinylcholine in doses ≥ 1.0 mg/kg have been expressed. Based on theoretical considerations, Benumof *et al.* suggested that ". . .in the large majority of patients with 1 mg/kg of succinylcholine-induced apnea, significant life threatening hemoglobin desaturation will occur before functional recovery" in subjects whose ventilation is not assisted.[4] Heir *et al.*, in a study of adult volunteers, were able to demonstrate the validity of this position.[5] They remarked that "a smaller dose of succinylcholine would have decreased the duration of muscle paralysis. . .but the results would have been less clinically relevant."

Nevertheless, the clinical utility of succinylcholine in doses of less than 1.0 mg/kg deserves to be reexamined. With nondepolarizing neuromuscular blockers of low potency (and, hence, fast onset), satisfactory conditions for tracheal intubation can be achieved with doses approximating only 1.5 times the ED_{95}.[6] Because the ED_{95} of succinylcholine is less than 0.30 mg/kg,[7] doses as small as 0.40 mg/kg might also provide clinically acceptable conditions for intubation in the majority of individuals. An article in the current issue of the Journal by Naguib *et al.* strongly supports this hypothesis.[8] These authors found that 0.60 mg/kg succinylcholine was sufficient to achieve acceptable intubating conditions at 60 s in 95% of patients anesthetized with 2 μg/kg fentanyl and 2 mg/kg propofol. Even doses as low as 0.30 mg/kg produced good or excellent conditions for intubation in 92% of patients, as compared to only 30% of individuals receiving a saline placebo.

The possibility of an earlier return of neuromuscular function following low-dose succinylcholine has much to recommend it, especially in situations in which the anesthesiologist is less than certain of complete control of a patient's airway. Unfortunately, only a limited amount of objective information is available to document the extent to which recovery is expedited by using doses of succinylcholine of less than 1.0 mg/kg. We undertook this study to determine the degree to which smaller than conventional doses of succinylcholine reduced the duration of neuromuscular block.

Methods

A total of 45 patients (aged 20–64 yr, American Society of Anesthesiologist's physical status I and II) undergoing elective surgical procedures were included in the study. All patients were free from neuromuscular disease

Table 1. Patient Demographics

Group	0.4 mg/kg	0.6 mg/kg	1.0 mg/kg
Age (yr)	39 ± 14	41 ± 10	40 ± 13
Weight (kg)	74 ± 16	71 ± 12	65 ± 11
Height (cm)	171 ± 9	168 ± 10	171 ± 13
Gender (M/F)	8/6	6/9	4/12

and had a body mass index ≤ 30. The protocol was approved by our hospital's Human Subject Review Committee, and consent was obtained. Anesthesia was induced with alfentanil 15–40 μg/kg plus propofol 2.0–2.5 mg/kg intravenous, and laryngeal mask placement or tracheal intubation was accomplished without the use of neuromuscular blocking drugs. Anesthesia was maintained with desflurane in oxygen (4.0–5.0%, end-tidal) and intermittent doses of fentanyl as required. Ventilation was controlled, and end-tidal partial pressure of carbon dioxide was maintained between 34 and 40 mmHg.

Following induction of anesthesia, the evoked response of the adductor pollicis muscle to ulnar nerve stimulation at the wrist was recorded in all subjects. The monitor/stimulator used was the TOF-Watch SX® acceleromyograph (Organon Teknika B.V.; Boxtel, The Netherlands). The study arm was immobilized, and the thumb was placed under a small preload with a single strand of an elastic rubber band.[9] All data were transferred to a personal computer using a TOF-Link® fiber-optic cable and were saved using TOF-Watch SX Monitor® software. Just before calibration of the TOF-Watch® unit, a 5-s 50-Hz supramaximal tetanic stimulus was administered at the ulnar nerve. Previous work in our department has demonstrated that the period required for baseline stabilization is shortened considerably by this procedure.[10]

Immediately thereafter, the acceleration transducer was taped to the volar aspect of the thumb at the interpharyngeal joint, and calibration of T1 was performed. Single stimuli were then administered at 10-s intervals. After initial T1 calibration, an additional 5 min of stimulation (0.10 Hz) was allowed for baseline stabilization. A second T1 calibration was performed, and a single dose of succinylcholine was administered as a rapid intravenous bolus. One of three doses was given: 0.40, 0.60, or 1.0 mg/kg. No further neuromuscular blocking agents were administered. Twitch height was then followed for not less than 20 min. In accordance with the recommendations of the Copenhagen Consensus Conference, all twitch height data recorded during recovery from neuromuscular block were "normalized" to the final T1 value.[11]

Statistics

All summary data are presented as mean ± SD. The recovery intervals from bolus to 10%, 25%, and 90% twitch recovery were calculated and compared using an unpaired Student *t* test. Demographic data were examined using chi-square analysis and Fisher exact *P* value. The Bonferroni inequality correction was applied. Observed differences were considered significant if $P < 0.05$.

Results

Although the male/female sex distribution between the three groups was not perfectly balanced (Table 1), these differences did not reach statistical significance. It should be noted that in the 1.0-mg/kg group in which female patients outnumbered male patients by 3 to 1, the 90% recovery times were essentially the same regardless of sex (9.3 *vs.* 9.2 min, on average).

Table 2 and figure 1 summarize our neuromuscular observations. Although we demonstrate that reducing the dose of succinylcholine from 1.0 to 0.6 mg/kg results in a statistically significant average reduction in duration of action (T1 times to 90% recovery of 9.3 ± 1.2 min *vs.* 7.6 ± 1.6 min, $P < 0.01$), there was considerable overlap in individual recovery times between these groups. It should be noted that the duration of action of even a modest dose of succinylcholine (0.60 mg/kg) might still be longer than is generally appreciated. In 4 of 15 patients in this group, the time to 10% twitch height recovery took 6 min or longer.

Table 2. Onset and Duration of Succinylcholine at 0.40, 0.60, and 1.0 mg/kg (Present Study)

	Sux 0.40 mg/kg* (n = 14)				Sux 0.60 mg/kg (n = 15)				Sux 1.0 mg/kg (n = 16)			
	Average	SD	Min	Max	Average	SD	Min	Max	Average	SD	Min	Max
Onset												
Time to max block (s)	105	23	80	150	81	19	60	110	71	22	40	120
Max block (% control)	93.2	8.8	68	100	100	—	—	—	100	—	—	—
Offset												
Time to T1 = 10% (min)	—	—	—	—	5.1	1.4	3.2	8.0	6.2	0.8	4.6	7.0
Time to T1 = 25% (min)	4.4	0.8	3.2	6.3	5.5	1.4	3.6	8.4	6.6	0.9	5.0	7.7
Time to T1 = 50% (min)	5.0	1.1	2.5	7.3	6.1	1.5	4.0	9.0	7.4	1.0	5.5	8.9
Time to T1 = 75% (min)	5.8	1.3	3.3	9.0	6.8	1.6	4.6	9.7	8.3	1.1	6.1	10.0
Time to T1 = 90% (min)	6.6	1.5	3.8	10.0	7.6	1.6	5.5	10.5	9.3	1.2	6.8	11.0

* Time to 10% recovery not calculated. Time to 25% recovery based on the 13 of 14 patients in whom peak effect exceeded 75% T1 depression.
Sux = succinylcholine.

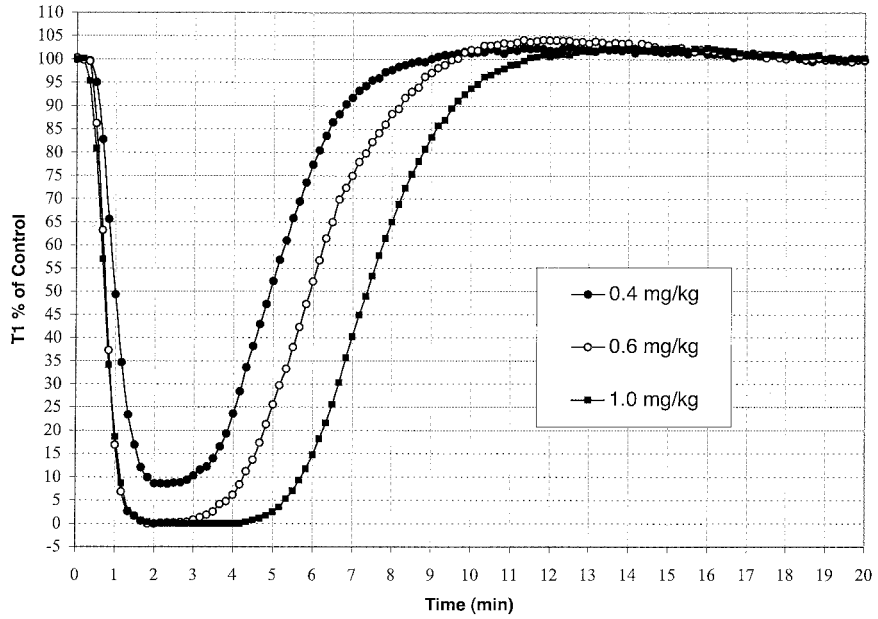

Fig. 1. Twitch height (*T1*) as a percent of control at the adductor pollicis *versus* time from initial drug bolus for three different doses of succinylcholine.

Discussion

The duration of action (at the adductor pollicis) of succinylcholine-induced block that we report is virtually identical to the observations of Viby-Mogensen[12] and is quite similar to the observations of other investigators[13–15] (Table 3).

In a recent letter in the Journal, we suggested that the usually cited 1.0-mg/kg "intubation dose" of succinylcholine was unnecessarily large.[16] It was hypothesized that a smaller dose (0.50–0.60 mg/kg) might enhance overall patient safety if this reduced dose resulted in a significant reduction in the duration of succinylcholine-induced apnea. Previously published data (Table 3) suggested that reducing the dose of succinylcholine from 1.0 to 0.5 mg/kg should decrease the duration of neuromuscular block by more than 4 min.[17–19] Although all recovery intervals (T_{10} through T_{90}) that we measured were shorter after 0.60 mg/kg succinylcholine compared to the 1.0 mg/kg dose, the magnitude of these differences was less than we anticipated. A 40% decrease in dose does not result in a comparable reduction in the drug's duration of effect.

Only limited information is available on how the twitch response at the adductor pollicis following suc-

Table 3. Offset Characteristics of Succinylcholine 0.50, and 1.0 mg/kg (Historic Controls)

		Duration					
Dose (mg/kg)	n	T10	T25	T50	T75	T90	Reference
0.5	13	4.6 ± 1.4		5.9 ± 1.6		7.4 ± 2.1	17
1.0	15	8.1 ± 3.0		10.1 ± 3.0		12.1 ± 3.4	
0.5	12	4.8 ± 1.3 (3.3 –7.5)		6.3 ± 1.6 (4.3 –10)		8.3 ± 2.5 (5.2 –13.5)	18
1.0	12	8.5 ± 2.2 (5.8 –11.7)		10.6 ± 2.5 (7.1 –13.9)		13.2 ± 3.2 (8.1 –17.7)	
0.5	20	5.5 (1.5 –9.4)	6.7 (2.0 –10.6)	7.9 (2.7 –12.2)		10.1 (1.2 –16)	19
1.0	20	10.2 (4.1 –15.4)	11.3 (5.1 –16.9)	12.4 (6.2 –18.1)		14.6 (8.3 –21)	
1.0	41	5.6 ± 2.1 (4.0 –8.0)	7.0 ± 2.7 (4.5 –10.0)		8.7 ± 3.1 (6.0 –12.0)	9.3 ± 3.3 (6.0 –13.0)	12
1.0	31		9 ± 3			11.5 ± 3	13
1.0	15		8 ± 2.5			10.6 ± 3.3	14
1.0	15		7.6 (5.7 –11.3)			10.5 (7.8 –13.8)	15

Durations T10, T25, T50, *etc.*, are the times (min) from succinylcholine bolus administration to 10%, 25%, 50%, *etc.*, recovery of twitch height compared to initial control values. Data are expressed as mean ± SD (range). T10 duration for reference 12 is time to first detectable twitch.

cinylcholine relates to diaphragmatic and laryngeal function. Smith *et al.* reported that the diaphragm may require more than 1.5 times as much succinylcholine as the adductor pollicis for a comparable degree of neuromuscular block.[20] Dhonneur *et al.* provide what appears to be the only comparative duration data available at the adductor pollicis *versus* the diaphragm (n = 8).[21] Following succinylcholine 1.0 mg/kg, they report T_{25}, T_{75}, and T_{90} recovery intervals at the respective adductor pollicis of 6.9 ± 2.6, 8.3 ± 2.9, and 9.1 ± 3.0 min, values very similar to those in the present study. At the diaphragm these values were 3.7 ± 1.5, 6.5 ± 3.0, and 7.2 min. Thus, return of diaphragmatic function seems to precede that seen at the hand by about 2 min. However, in this small series at least one individual still required 14 min for 90% twitch recovery at the diaphragm.

A recent article by Hayes *et al.* provides highly relevant data.[22] They studied 100 patients who, following preoxygenation, received an anesthetic induction consisting of fentanyl 1 μg/kg, a sleep dose of thiopental (3–7 mg/kg), and succinylcholine 1.0 mg/kg. Ventilation was not assisted unless the oxygen saturation decreased below 90%. They noted that the first movement of the reservoir bag appeared, on average, at 4.7 (± 1.5–2.0) min and that the first recordable end-tidal carbon dioxide reading did not appear for 5.5 (± 1.5–2.0) min. Hayes *et al.* found that only 11% patients developed arterial desaturation, a figure much lower than that reported by Heir *et al.*[5] However, in Hayes *et al.*'s study the anesthesia mask with oxygen running was kept on the patient's face. Heir *et al.* removed the facemask and provided no support to the airway. The effect on the diaphragm of succinylcholine in doses of less than 1.0 mg/kg has not been studied. Current evidence suggests that the duration of action of succinylcholine at the laryngeal adductors does not appear to be significantly shorter than that at the adductor pollicis.[21,23]

It is not clear how the decreased duration in action as the dose of succinylcholine is reduced should be calculated. Benumof *et al.* defined the time to 50% T1 recovery as the time to functional recovery and used this point for comparisons in their hemoglobin desaturation model.[4] They reasoned that this degree of recovery should permit adequate spontaneous ventilation if the airway was patent. By this standard, we estimate that succinylcholine 0.60 mg/kg decreases the duration of block by less than 90 s, compared to a dose of 1.0 mg/kg. However, Benumof *et al.*'s analysis does not really reflect the problem that concerns the clinical anesthesiologist, because if the patient has a patent airway then the need for *spontaneous* ventilation may be of little importance. The more pressing question seems to be, At what level of neuromuscular recovery is the patient able to spontaneously maintain a patent airway? Certainly, with nondepolarizing relaxants, 50% return of twitch height is still associated with profound weakness in the muscles of the upper airway. However, even if the time to 90% return of twitch height is used as the criterion by which recovery is measured, reducing the "standard" intubation dose of succinylcholine to 0.60 mg/kg still results in less than a 2-min decrease in the drug's duration of action (at the adductor pollicis).

Decreasing the dose of succinylcholine even further (to < 0.50 mg/kg) results, as expected, in additional reductions in the drug's duration of action (Table 2). In only 6 of the 14 patients who received succinylcholine 0.40 mg/kg was complete twitch depression at the adductor pollicis achieved. The average peak effect for the group as a whole was 93%. This is a little surprising, because previous work from our department estimated that the ED_{95} for succinylcholine under N_2O/propofol anesthesia was only 0.27 mg/kg.[7] However, our current data do not imply that the ED_{95} of succinylcholine approximates 0.40 mg/kg. In those patients in whom twitch was abolished, all that can be said is that the ED_{95} was obviously less than 0.40 mg/kg. Therefore, the average ED_{95} value of succinylcholine cannot be estimated from the data in Table 2. Doses of this magnitude still facilitate ease of tracheal intubation compared to placebo administration.[8] However, administration of low-dose succinylcholine mandates certain trade-offs that not all clinicians may accept. In Naguib *et al.*'s series, these doses produced "excellent conditions" for intubation in only half of their patients. In situations in which complete patient immobility is required, even doses of 1.0 mg/kg may occasionally prove unsatisfactory.

In summary, reducing the dose of succinylcholine from 1.0 to 0.60 mg/kg will shorten the duration of neuromuscular effect at the adductor pollicis by 1.5 to 2 min. The extent to which this will reduce the period of profound neuromuscular block at the diaphragm, laryngeal adductors, and muscles of the upper airway remains largely untested. In the vast majority of patients, this reduced dose of succinylcholine will provide perfectly acceptable conditions for tracheal intubation when combined with a standard anesthetic induction sequence.[8] We believe that even this modest decrease in the duration of drug-induced paralysis will often be worth pursuing. Nevertheless, when complete neuromuscular block is critical, doses of 1.0 to 1.5 mg/kg may still be appropriate. Thus, there does not appear to be a single ideal "intubating dose" of succinylcholine.

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