The Neuromuscular Effects and Tracheal Intubation Conditions After Small Doses of Succinylcholine

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Succinylcholine 1.0 mg/kg usually produces excellent tracheal intubation conditions in 60 s. Recovery of respiratory muscle function after this dose, however, is not fast enough to forestall oxyhemoglobin desaturation when ventilation cannot be assisted. In this study, we investigated whether smaller doses of succinylcholine can produce satisfactory intubation conditions fast enough to allow rapid sequence induction with a shorter recovery time. Anesthesia was induced with fentanyl/propofol and maintained by propofol infusion and N_2O in O_2. After the induction, 115 patients were randomly allocated to five groups according to the dose of succinylcholine (0.3 mg/kg, 0.4 mg/kg, 0.5 mg/kg, 0.6 mg/kg, or 1.0 mg/kg). Evoked adductor pollicis responses to continuous 1-Hz supramaximal ulnar nerve stimulation were recorded using acceleromyography. Tracheal intubation conditions were graded 60 s after succinylcholine administration. Onset time, maximal twitch depression, time to initial twitch detection after paralysis, and to 10%, 25%, 50%, and 90% twitch height recovery were recorded. Time to initial diaphragmatic movement as well as time to resumption of regular spontaneous respiratory movements were calculated. Onset times ranged between 82 s and 52 s, decreasing with increasing doses of succinylcholine but not differing between 0.6 and 1 mg/kg. Maximum twitch depression was similar after 0.5, 0.6, and 1 mg/kg (98.2%–100%). Recoveries of twitch height and apnea time were dose-dependent. Intubation conditions were often unacceptable after 0.3- and 0.4-mg/kg doses. Acceptable intubation conditions were achieved in all patients receiving a 0.5, 0.6, and 1 mg/kg dose of succinylcholine. Intubation conditions in patients receiving 0.6 and 1 mg/kg were identical, whereas times to $T_1 = 50\%$ and 90% and time to regular spontaneous reservoir bag movements were significantly shorter in the 0.6-mg/kg dose group (5.78, 7.25, and 4.0 min, respectively) versus patients receiving 1 mg/kg (8.55, 10.54, and 6.16 min, respectively). The use of 0.5 to 0.6 mg/kg of succinylcholine can produce acceptable intubation conditions 60 s after administration. The conditions achieved after 0.6 mg/kg are similar to those after 1.0 mg/kg. These smaller doses are associated with faster twitch recovery and shorter apnea time.

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Satisfactory tracheal intubation conditions can be quickly achieved in nearly all patients after the IV administration of succinylcholine. The traditionally recommended "intubating dose" of 1.0 mg/kg can establish an intense neuromuscular block in less than a minute, allowing rapid sequence tracheal intubation to proceed in a timely manner (1). Despite the brief duration of the neuromuscular block, functional recovery of respiratory activity after this dose does not occur fast enough to prevent critical oxyhemoglobin desaturation if ventilation is not assisted (2). Using the same dose in humans, further studies revealed that dangerous oxyhemoglobin desaturation levels can occur before spontaneous resumption of respiratory efforts if a "cannot intubate, cannot ventilate" situation was encountered (3,4).

In view of these findings, and in an effort to shorten the apnea time, the practice of using 1.0 mg/kg as an intubating dose has been questioned (5). Because the ED95 of succinylcholine is approximately 0.3 mg/kg, 1.0 mg/kg constitutes more than three times ED95 of succinylcholine (6). Furthermore, smaller doses of succinylcholine have been successfully used for tracheal intubation (7,8).

The objective of this study was to investigate whether smaller doses of succinylcholine can produce satisfactory intubation conditions fast enough to allow rapid sequence tracheal intubation and in the same

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time be associated with a shorter recovery time that might avoid critical oxyhemoglobin desaturation if ventilation cannot be assisted after anesthesia induction in healthy adult patients.

Methods

After IRB approval, written informed consent to participate in the study was obtained from 115 ASA physical status I and II adult patients aged 18–65 yr scheduled for elective surgical procedures requiring general anesthesia and tracheal intubation. Patients with hepatic, renal, cardiac, pulmonary, or neuromuscular disease, or those taking medications known or suspected to interfere with neuromuscular transmission were excluded. Pregnant women, patients with body mass indices more than 28 kg/m^2, patients with a documented or family history of abnormal response to succinylcholine, and patients with a history of difficult intubation or abnormal airway examination were also excluded from the study.

Patients were randomly allocated to 1 of 5 groups (23 patients each) according to the dose of succinylcholine to be administered (0.3 mg/kg [1 × ED95], 0.4 mg/kg, 0.5 mg/kg, 0.6 mg/kg [2 × ED95] and 1.0 mg/kg). Random assignment was assured by asking subjects to pick an opaque, sealed envelope containing cards specifying the dose to be given. All patients were premedicated with IV midazolam 1–2 mg. The administration of O_2 with a tight-fitting mask was performed for at least 3 min and until the end-tidal O_2 concentration exceeded 90%. Anesthesia was induced with fentanyl 1.5 $\mu g/kg$ and propofol 2 mg/kg and maintained with a propofol infusion 100–200 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and 60% N_2O in O_2.

Continuous supramaximal 1-Hz single-twitch stimuli were applied to the ulnar nerve at the wrist, and the resultant adductor pollicis evoked responses were detected, displayed, and recorded for later analysis using acceleromyography (TOF-Watch SX, Organon-Teknika, Durham, NC). Because of the fast onset and short duration of block associated with succinylcholine, the 1-Hz rate was selected to more precisely determine onset and recovery.

After loss of verbal contact and eyelash reflex, a 5-s, 50-Hz tetanic stimulus was applied to the ulnar nerve at the wrist followed by repeated 1-Hz stimuli until the response stabilized over 20 consecutive stimuli and calibration was performed. During this period, typically lasting 2 to 5 min, the patients were manually ventilated by a tight-fitting face mask to maintain an end-tidal CO_2 between 35–40 mm Hg. The designated dose of succinylcholine was then administered via the freely running IV infusion on the contralateral arm. Refrigerated vials of succinylcholine were used for all patients. Lag time (time to initial decrease in twitch height), maximum twitch depression attained (peak effect), and onset time (time to maximal twitch depression) were recorded. One minute after succinylcholine administration, tracheal intubation was attempted by an experienced anesthesiologist unaware of the dose of succinylcholine given, and the intubation conditions were graded using the Copenhagen Consensus Conference criteria (Table 1) (9). If tracheal intubation proved impossible because of inadequate relaxation, patients were ventilated by face mask and given a supplemental dose of 0.5 mg/kg of succinylcholine, and another attempt was made 1 min later. After tracheal intubation, ventilation was gently assisted manually to maintain an end-tidal CO_2 between 35–40 mm Hg. The abdomen was inspected, and the time to first visible diaphragmatic contraction that coincided with reservoir bag movement (apnea time) was recorded. The time to the first reservoir bag movement followed by regular movements producing a well-formed end-tidal CO_2 waveform indicated the time to resumption of spontaneous breathing.

Neuromuscular recovery was also simultaneously monitored, and the time to initial twitch recovery and the time to 10%, 25%, 50%, and 90% of twitch height recovery were recorded and later analyzed for every group, excluding the patients in whom an additional dose of succinylcholine had to be administered. If, despite adequate stabilization, full T_1 recovery exceeded 100%, the recovery data were normalized according to the final maximum T_1 achieved.

Sample size was determined by using an *a priori* power analysis as to provide an 80% chance of detecting a 12-s difference in lag, onset, and twitch recovery times between any two groups assuming a SD of 20 s. A one-way analysis of variance and Student-Newman-Keuls (for continuous variables) and the Kruskal-Wallis (for discrete variables) tests were used to identify statistically significant differences among the five groups. The Kruskal-Wallis test was used to identify significant differences between intubation conditions by succinylcholine dose. Statistical significance was accepted when $P < 0.05$.

Results

Table 2 compares demographic data, including age, sex, height, weight, and ASA physical status. There were no significant differences in the demographic data among the five groups.

A comparison of the lag time, onset time, and maximum twitch depression among the five groups is displayed in Table 3. There was no significant difference in the lag time among the five groups. Increasing the dose of succinylcholine from 0.3 mg/kg to 0.6 mg/kg shortened the onset time; however, there was no difference in onset time between 0.6 mg/kg

Table 1. Assessment of Intubation Conditions

	Intubation conditions[a]		
	Clinically acceptable		Clinically unacceptable
Criteria	Excellent	Good	Poor
Ease of laryngoscopy (jaw relaxation)	Easy	Fair	Difficult
Vocal cord position	Abducted	Intermediate	Closed
Vocal cord movement	None	Moving	Closing
Airway reaction	None	Diaphragm	Sustained
Movement of limbs	None	Slight	Vigorous

[a] Intubation conditions: Excellent = all criterion are excellent; Good = all criterion are either excellent or good; Poor = the presence of a single criterion graded as poor.

Table 2. Comparison of Demographic Data in 115 Patients Receiving 0.3, 0.4, 0.5, 0.6, or 1.0 mg/kg of Succinylcholine Before Orotracheal Intubation

	Succinylcholine dose (mg/kg)				
	0.3	0.4	0.5	0.6	1.0
Age	42 ± 13	41 ± 12	42 ± 12	41 ± 13	45 ± 11
Sex					
men	10	12	11	10	12
women	13	11	12	13	11
Height (cm)	165.8 ± 7.9	167.0 ± 9.1	161.0 ± 12.3	164.4 ± 8.1	163.7 ± 7.7
Weight (kg)	68.5 ± 10.6	69.6 ± 13.4	71.4 ± 14.6	70.5 ± 12.8	67.6 ± 15.1
ASA PS					
I	15	14	12	14	15
II	8	9	11	9	8

Data appear as mean ± SD or as counts.

and 1.0 mg/kg. Regarding the magnitude of the block, marked variability in response was found in the 0.3 and 0.4 mg/kg groups (maximum twitch height depressions ranged between 40% and 95%). There was no significant difference in the maximum twitch depression (peak effect) in the 0.5, 0.6, and 1.0 mg/kg groups.

Intubation conditions, graded 60 s after succinylcholine administration, are displayed in Table 4. Patients receiving 0.3 and 0.4 mg/kg doses of succinylcholine had a frequent incidence of poor or impossible tracheal intubation conditions. Tracheal intubation was impossible at 1 min after succinylcholine in seven patients in the 0.3 mg/kg group and in two patients in 0.4 mg/kg group because of the very poor relaxation. All nine patients were easily tracheally intubated 1 min later, after administering a supplemental dose of succinylcholine (0.5 mg/kg) and ventilation. Neuromuscular and respiratory recovery variables were not considered in these patients. Tracheal intubation could be accomplished successfully in all other patients after administering the allocated dose of succinylcholine. Clinically satisfactory intubation conditions (good to excellent) 1 min after succinylcholine injections were similar in the 0.5, 0.6, and 1.0 mg/kg groups. The 0.6 and 1.0 mg/kg groups were identical with regards to the frequency of excellent conditions, whereas half the patients in 0.5 mg/kg group had a slight diaphragmatic reaction upon tracheal tube placement, although other criteria such as jaw muscle relaxation and vocal cord paralysis were similar.

Table 5 compares the times to return of twitch, T_1 = 10%, T_1 = 25%, T_1 = 50%, T_1 = 90%, first diaphragmatic movement (apnea time), and resumption of spontaneous breathing (regular capnographic waveform). Increasing the dose of succinylcholine from 0.3 mg/kg to 1.0 mg/kg results in a progressive increase in values for the above measures of return of neuromuscular function.

Discussion

The current study demonstrates that satisfactory tracheal intubation conditions could be achieved one minute after succinylcholine administration with doses much less than the traditionally recommended dose of 1.0 mg/kg. Doses of 0.3 and 0.4 mg/kg did not often result in satisfactory conditions at 60 s and therefore cannot be recommended for rapid tracheal intubation. The conditions after 0.5 mg/kg were clinically acceptable, although not ideal, whereas the intubation conditions after 0.6 mg/kg were identical to those obtained using the traditional 1.0-mg/kg dose. The effectiveness of small doses in achieving adequate

Table 3. Comparison of Lag Time, Onset Time, and Maximum Twitch Depression in 115 Patients Receiving 0.3, 0.4, 0.5, 0.6, or 1.0 mg/kg of Succinylcholine Before Orotracheal Intubation

	Succinylcholine dose (mg/kg)				
	0.3	0.4	0.5	0.6	1.0
Lag time (s)	30.3 ± 8.7	29.8 ± 11.2	27.8 ± 6.3	26.4 ± 6.7	24.9 ± 4.4
Onset time (s)	82.1 ± 8.9*	73.4 ± 12.9*	67.3 ± 9.6*	54.9 ± 10.8	51.8 ± 4.9
Median max twitch ↓ (range)	100 (40)	100 (20)	100 (15)	100 (3)	100 (0)

Data displayed as mean ± SD.
Statistical significance accepted when $P < .05$; * significantly different from all other values.

Table 4. Intubation Conditions 60 s After Succinylcholine Administration During Laryngoscopy by an Experienced Anesthesiologist Unaware of the Dose of Succinylcholine Given. Grading was Performed Using the Copenhagen Consensus Conference Criteria

	Succinylcholine dose (mg/kg)					
	0.3	0.4	0.5	0.6	1.0	Total
Intubation conditions						
Impossible	7	2	0	0	0	9
Poor	9	9	0	0	0	18
Good	7	10	11	2	2	32
Excellent	0	2	12	21	21	56
Total	23	23	23	23	23	115
Significance	$P < 0.001$	$P < 0.001$	$P < 0.001$	NS	NS	

Statistical significance accepted when $P < .05$.

Table 5. Comparison Recovery from Neuromuscular Blockade in 106 Patients Receiving 0.3, 0.4, 0.5, 0.6, or 1.0 mg/kg of Succinylcholine before Orotracheal Intubation

	Succinylcholine dose (mg/kg)				
	0.3	0.4	0.5	0.6	1.0
Time to initial twitch	1.9 ± 0.8	3.0 ± 0.5*	3.0 ± 0.7*	3.6 ± 0.6*	5.3 ± 0.8*†‡§
Time to T_1 = 10%	2.8 ± 0.8	3.7 ± 0.7*	3.2 ± 1.2	4.1 ± 0.8*‡	6.1 ± 0.9*†‡§
Time to T_1 = 25%	3.3 ± 0.8	4.0 ± 1.1	3.9 ± 1.0	4.8 ± 0.8*†‡	6.9 ± 1.2*†‡§
Time to T_1 = 50%	4.1 ± 0.9	5.0 ± 1.0*	5.1 ± 1.0*	5.8 ± 0.9*†‡	8.6 ± 0.5*†‡§
Time to T_1 = 90%	5.3 ± 0.8	6.2 ± 1.1*	6.5 ± 1.0*	7.25 ± 1.0*†‡	10.5 ± 1.3*†‡§
Time to initial diaphragm movement	2.0 ± 0.8	2.7 ± 1.2*	3.00 ± 0.7*	3.41 ± 0.6*†	5.3 ± 0.8*†‡§
Time to resumption of spontaneous breathing	2.7 ± 0.7	3.3 ± 1.4*	3.5 ± 0.7*	4.0 ± 0.5*†	6.2 ± 0.8*†‡§

Data displayed as mean ± SD.
Statistical significance accepted when $P < .05$; * significantly different from 0.3-mg/kg dose; † significantly different from 0.4-mg/kg dose; ‡ significantly different from 0.5-mg/kg dose; § significantly different from 0.6-mg/kg dose.

tracheal intubation conditions 60 s after succinylcholine administration has been reported (7,8). We believe that these previous studies went unappreciated, largely for two reasons. First, before Benumof et al. (2) drew attention to the popular misconception that respiratory recovery occurs fast enough to save the patient in whom ventilation cannot be assisted, there was no clear reason to reduce the dose of succinylcholine. Second, the traditional dose has a highly reliable and consistent effect, so there was a fear that smaller doses might prove less reliable.

Although the onset time was dose-dependent, there was no difference between the 0.6 mg/kg and 1.0 mg/kg groups. This suggests that doses larger than 0.6 mg/kg may not produce any faster onset and that 50 seconds is about the minimal time required for any dose of succinylcholine to produce its maximal effect on the adductor pollicis muscle, although onset could be faster at other muscles groups, such as the laryngeal muscles (10) or the diaphragm (11).

Much variation in block intensity was noted with the smaller two doses (twitch height suppression ranged from 40% to 95% in the 0.3 mg/kg group) (12,13). Doses of 0.5 mg/kg and larger, however, reliably produced near complete ablation of the twitch in all the patients. The ability of doses as small as 0.5 mg/kg to completely abolish the twitch was reported by others (13–15).

The apnea time and the time to regular reservoir bag movement (end-tidal CO_2 waveform) were also, as expected, dose-dependent. Both initial respiratory attempts and regular spontaneous respiratory movements occurred much earlier than the 50% twitch recovery time as monitored at the adductor pollicis. In agreement with our results, Viby-Mogensen (16) reported an apnea time of 5.8 minutes after 1.0 mg/kg of succinylcholine in 41 patients with normal enzymatic activity, and Stewart et al. (8) reported a 3.7-minute apnea time after 0.5 mg/kg.

Regarding the relationship between the adductor pollicis evoked responses and the resumption of respiratory activity, the results from our study show that the apnea time is approximately the time required for initial twitch detection after paralysis, and the time to regular respiratory movements is approximately the time required for T_1 to return to 10% of the control value. Walts and Dillon (17) noticed that respiration began in most of their patients, even before any demonstrable activity at the thumb, and Pansard et al. (11) demonstrated that diaphragmatic recovery occurs two minutes earlier than adductor pollicis recovery at all levels of twitch height recovery. However, Benumof et al. (2) defined the time to functional recovery as the time required for the adductor pollicis twitch to recover to 50% of the control value. Although initial spontaneous and regular breathing may not reflect full functional recovery, this may still prevent oxyhemoglobin desaturation that would ensue if the patient remained apneic.

The duration to the different levels of twitch-height recovery (Fig. 1) was dose-dependent and in agreement with published values (13,15,17). To illustrate the significance of our recovery data, we applied our measures of apnea time to the oxyhemoglobin desaturation data by Heier et al. (3) that were obtained in young, healthy volunteers. If we assume that functional recovery corresponds to return of regular reservoir bag movement or alternately to time to 50% adductor pollicis twitch height recovery, as suggested by Benumof et al. (2), we see from Figure 2 that recovery occurs much earlier when 0.5 or 0.6 mg/kg doses are used instead of 1.0 mg/kg. Thus, critical oxyhemoglobin desaturation might not occur with the use of 0.5 to 0.6 mg/kg doses, especially in the healthy adult. However, because we did not allow our patients to desaturate, we cannot fully appreciate the effect of these doses in a "cannot intubate, cannot ventilate" scenario. Thus, rescue options should be considered when the larger doses (0.5, 0.6, or 1.0 mg/kg) of succinylcholine are administered. In addition, the administration of O_2 should be adequately performed, and all other factors that can affect oxyhemoglobin saturation should remain constant. Alternately, the more rapid return of neuromuscular function after smaller

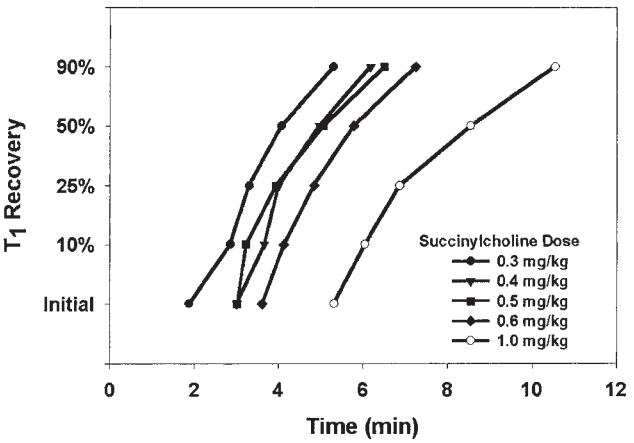

Figure 1. Adductor pollicis T_1 twitch-height recovery after different doses of succinylcholine for tracheal intubation.

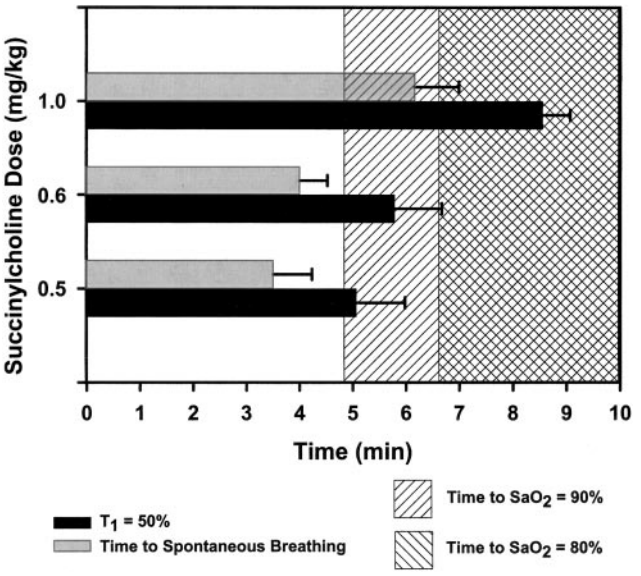

Figure 2. Onset of regular spontaneous respiratory activity and time to T_1 twitch-height 50% recovery after 0.5, 0.6, and 1.0 mg/kg of succinylcholine in healthy adults. Shaded areas correspond to time to oxyhemoglobin desaturation to 90% and 80% in healthy 70-kg adults based upon data from Heier et al. (3).

doses of succinylcholine could negatively affect intubation conditions by narrowing the window of opportunity for successful tracheal intubation.

Several compromises were made when preparing our research protocol. For example, no control group was studied. We felt that the small doses of opioid and induction drugs we used would undoubtedly have led to failed intubations in nearly all patients not receiving a neuromuscular blocking drug. Second, neuromuscular monitoring required a two- to five-minute period after the induction to stabilize the response before the administration of succinylcholine. Thus, our induction sequence did not simulate the actual clinical picture in which succinylcholine would be given immediately after

the induction drug. This is the reason most studies have addressed either the onset/recovery of neuromuscular block or the intubating conditions separately and not in the same patients. We chose to study both in the same patient, however, to establish the relationship between twitch height during onset/recovery of the block with the resultant intubating conditions. We felt that this deviation would not negatively impact on our results.

Succinylcholine, in doses of 0.5 to 0.6 mg/kg, produces clinically satisfactory intubation conditions one minute after IV administration. The latter dose is similar to the traditional 1.0-mg/kg dose in onset time, neuromuscular block intensity, and intubation conditions. These minimum effective doses are recommended because they result in a shorter apnea time that may avoid critical oxyhemoglobin desaturation in healthy adult patients in whom ventilation cannot be assisted. Using doses larger than 0.6 mg/kg does not produce a faster onset, a more intense neuromuscular block, or a more favorable intubation condition, and it is associated with a longer recovery time. Additional studies are required to examine the effectiveness of these smaller doses of succinylcholine after different induction drugs and techniques and also for different patient populations, including obese, pregnant, pediatric, and critically ill patients.

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