

## Intubating conditions following rapid sequence induction with three doses of succinylcholine

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### ABSTRACT

**Background:** The aim of this prospective, randomized, double-blind study was to compare tracheal intubating conditions and the duration of apnoea following administration of 0.4, 0.6 and 1.0 mg/kg of succinylcholine during simulated rapid sequence induction of anaesthesia. **Methods:** Anaesthesia was induced with fentanyl 2 µg/kg and propofol 2 mg/kg followed by application of cricoid pressure. Patients were randomly allocated to three groups according to the dose of succinylcholine administered (0.4, 0.6 or 1.0 mg/kg). Intubating conditions were assessed at 60 s after succinylcholine administration. Time to first diaphragmatic contraction (apnoea time) and time to resumption of regular spontaneous breathing were noted. **Results:** Excellent intubating conditions were obtained in 52.4%, 95.7% and 100% of the patients after 0.4, 0.6 and 1.0 mg/kg succinylcholine, respectively;  $P < 0.001$ . Acceptable intubating conditions (excellent and good grade combined) were obtained in 66.7%, 100% and 100% of the patients after 0.4, 0.6 and 1.0 mg/kg succinylcholine, respectively;  $P < 0.001$ . Apnoea time and resumption of regular spontaneous breathing were dose-dependent. Apnoea time was  $3.8 \pm 1.1$  min,  $4.3 \pm 0.9$  min and  $8.2 \pm 3.4$  min in groups 0.4, 0.6 and 1.0 mg/kg, respectively;  $P < 0.001$ . Time to regular spontaneous breathing was  $5.3 \pm 1.2$  min,  $5.5 \pm 1.1$  min and  $8.9 \pm 3.5$  min in groups 0.4, 0.6 and 1.0 mg/kg, respectively;  $P < 0.001$ . **Conclusion:** A dose of 0.6 mg/kg succinylcholine can be used for rapid sequence induction of anaesthesia as it provides acceptable intubating conditions with a shorter apnoea time compared with a dose of 1 mg/kg.

**Key words:** Anaesthesia, intubating conditions, neuromuscular blockers, rapid sequence induction, succinylcholine

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### INTRODUCTION

Succinylcholine, a neuromuscular blocking agent (NMBA) with the fastest onset and recovery time,<sup>[1]</sup> is considered the drug of choice for rapid sequence induction of anaesthesia. Traditionally, the dose of succinylcholine recommended for this purpose is 1 mg/kg. The effective dose (ED) 95 of succinylcholine is less than 0.30 mg/kg.<sup>[2,3]</sup> Doses equivalent to twice the ED 95 are generally considered to be the appropriate dose of non-depolarizing NMBAs for intubation.<sup>[4]</sup> A 1.0 mg/kg dose represents 3.5-4-times the ED 95. Recovery of spontaneous respiration following 1.0 mg/kg

succinylcholine administration may not occur rapidly enough to prevent haemoglobin desaturation in patients whose ventilation is not assisted.<sup>[5,6]</sup> Based on a mathematical model of haemoglobin desaturation during apnoea, Benumof *et al.*<sup>[7]</sup> predicted that in the large majority of patients with 1 mg/kg succinylcholine-induced apnoea, significant to life-threatening haemoglobin desaturation will occur when ventilation is not assisted. Heier *et al.*<sup>[5]</sup> reported that significant haemoglobin desaturation ( $SpO_2 < 80\%$ ) occurred in one-third of the volunteers during the period of apnoea induced by 1 mg/kg succinylcholine. Decreasing the dose of succinylcholine would allow a more rapid

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recovery of spontaneous ventilation, thereby proving a greater margin of safety in airway management. The aim of this prospective, randomized, double-blind study was to compare tracheal intubating conditions and the duration of apnoea following administration of 0.4, 0.6 and 1.0 mg/kg of succinylcholine during simulated rapid sequence induction of anaesthesia.

## METHODS

The study was approved by the hospital ethics committee and written informed consent was obtained from all patients. Sixty-nine American society of anaesthesiologist (ASA) physical status I and II adult patients, aged 18-60 years, scheduled for elective surgery requiring general anaesthesia and tracheal intubation, were included in this study. Patients with cardiac, pulmonary, neuromuscular disease, hepatic or renal impairment, and those with body mass index >28 kg/m<sup>2</sup> were excluded from the study, as were pregnant women. Patients with previous or family history of abnormal response to succinylcholine were also excluded. The airway was clinically assessed (mouth opening, Mallampati class, thyromental distance, range of neck movement, any obvious head or neck pathology) to exclude those in whom difficulty with intubation was anticipated. No premedication was administered.

In the operating room, standard monitoring was established [electrocardiogram (ECG), non-invasive blood pressure, pulse oximetry and capnography] and baseline (pre-induction) measurements were recorded. Intravenous access was secured and fentanyl 2 µg/kg IV was administered. Patients were randomly allocated to one of three groups (23 patients each) according to the dose of succinylcholine to be administered intravenously (0.4, 0.6 or 1.0 mg/kg) using a computer-generated random number table (sealed envelopes): Group 0.4 received 0.4 mg/kg of succinylcholine; group 0.6 received 0.6 mg/kg of succinylcholine; and group 1.0 received 1.0 mg/kg of succinylcholine. Succinylcholine was taken in a 2 mL syringe and saline 0.9% was added to make a volume of 2 mL. All drugs were prepared by an anaesthetist not involved with the study to keep the study investigator blinded.

Pre-oxygenation using a tight-fitting mask was performed for 3 min with 100% oxygen. Anaesthesia was induced with propofol 2 mg/kg followed by application of cricoid pressure and administration of the designated dose of succinylcholine. Laryngoscopy

was performed 50 s after the administration of succinylcholine (size 3 Macintosh blade), aiming to intubate the trachea at 60 s. Cuffed tracheal tubes of 7 and 8 mm size were used in female and male patients, respectively. Tracheal intubation and grading of the intubating conditions was performed by an experienced anaesthetist unaware of the dose of succinylcholine given. The Cormack and Lehane<sup>[8]</sup> grade of laryngoscopy was recorded: Grade 1=complete visualization of the vocal cords; grade 2=visualization of the inferior portion of the glottis; grade 3=visualization of only the epiglottis; grade 4=non-visualized epiglottis. Intubating conditions were evaluated by a qualitative scoring system described by Viby-Mogensen *et al.*<sup>[9]</sup> which includes ease of laryngoscopy, position and movement of vocal cords, coughing and movement of the limbs [Table 1]. Laryngoscopy was considered as easy (jaw relaxed, no resistance to laryngoscope blade), fair (jaw not fully relaxed, slight resistance to blade) or difficult (poor jaw relaxation, active resistance of the patient to laryngoscopy). Intubating conditions were considered as excellent (all variables were excellent), good (all variables were either excellent or good) or poor (the presence of a single variable listed under poor). Excellent or good intubating conditions were regarded as clinically acceptable; poor intubating conditions were regarded as clinically not acceptable.<sup>[9]</sup> Duration of laryngoscopy (time from start of laryngoscopy until tracheal intubation and removal of laryngoscope blade from the mouth) was noted. Blood pressure heart rate (HR) and SpO<sub>2</sub> were recorded before induction of anaesthesia (pre-induction), after induction (post-induction) and then every 1 min after tracheal intubation for 5 min (time 1-5). In the event of bradycardia (HR < 50 beats per min), atropine 0.6 mg was administered. In the event of a decrease in mean arterial pressure (MAP) >25%, ephedrine was administered in 6 mg increments. Adverse events such as laryngospasm, bronchospasm, masseter spasm or muscle rigidity were recorded.

After tracheal intubation, ventilation (0.6% isoflurane

Table 1: Assessment of intubating conditions<sup>[9]</sup>

Variables	Intubating conditions		
	Clinically acceptable		Not acceptable
	Excellent	Good	Poor
Laryngoscopy	Easy	Fair	Difficult
Vocal cords			
Position	Abducted	Intermediate	Closed
Movement	None	Moving	Closing
Coughing (>10 s)	None	Diaphragm	Sustained
Movement of the limbs	None	Slight	Vigorous

and 66% nitrous oxide in oxygen using carbon dioxide absorption) was gently assisted manually to maintain an EtCO<sub>2</sub> between 35 and 40 mmHg. The patient's abdomen was continuously observed for respiratory movements. Apnoea time was defined as the time from IV succinylcholine administration to the time to first visible diaphragmatic contraction that coincided with reservoir bag movement. Time to resumption of spontaneous breathing was taken as the time from IV succinylcholine administration to the time to regular reservoir bag movements that produced a well-formed end-tidal CO<sub>2</sub> waveform. When the trachea could not be intubated because of inadequate relaxation, the lungs were ventilated by face mask, and rocuronium 0.6 mg/kg was administered IV and another attempt was made 1 min later. The study end-point was resumption of spontaneous breathing. Thereafter, anaesthesia was continued as appropriate for surgery.

### Statistical analysis

Descriptive statistics in the form of mean, standard deviation, frequency and percentages have been calculated for interval and categorical variables, respectively. To see a significant difference among the groups, one way analysis of variance (ANOVA) with post-hoc Bonferroni test has been applied to interval variables and chi-square tests for categorical variables. *P* value=0.05 (two tailed) has been considered as the statistically significant level. Statistical Package for Social Sciences (SPSS) 18.0 statistical software has been used for the analysis.

## RESULTS

Sixty-nine eligible patients were enrolled in the study, 23 in each group. Two patients in group 0.4 mg/kg and three patients in group 1.0 mg/kg were excluded from the study due to protocol violation.

There were no significant differences in patient characteristics among the three groups [Table 2]. The modified Mallampati class of pharyngeal structures, Cormack grade of laryngoscopy and the duration of laryngoscopy in the three groups was comparable. Intubation was completed successfully in all (100%) patients. No patient required rocuronium administration.

Excellent intubating conditions were obtained in 52.4%, 95.7% and 100% of the patients after 0.4, 0.6 and 1.0 mg/kg succinylcholine, respectively; *P*<0.001. The 0.6 and 1.0 mg/kg groups were similar with regard to the incidence of excellent intubating conditions;

*P*>0.05. Overall intubating conditions were regarded as acceptable (excellent and good grade combined) in 66.7%, 100% and 100% of the patients after 0.4, 0.6 and 1.0 mg/kg succinylcholine, respectively. This difference was statistically significant (*P*<0.001) [Table 3]. Comparable intubating conditions were achieved after 0.6 and 1.0 mg/kg succinylcholine; *P*>0.05. Patients receiving 0.4 mg/kg succinylcholine had a frequent incidence (33.3%) of poor tracheal intubating conditions.

Laryngoscopy was easy in all patients except one patient in group 0.6 mg/kg succinylcholine. No patient had closed or closing vocal cords requiring administration of rocuronium before successful intubation. A greater number of patients (four of 21 patients) had sustained coughing in the group receiving 0.4 mg/kg succinylcholine compared with patients receiving 0.6 and 1.0 mg/kg succinylcholine, *P*=0.04). Five patients in group 0.4 mg/kg succinylcholine had vigorous limb movement compared with none in the other two groups; *P*<0.001 [Table 4].

Table 2: Patient data

	Group 0.4 (n=21)	Group 0.6 (n=23)	Group 1.0 (n=20)	<i>P</i>
Age (years)	33.4±9.5	34.8±13.2	34.9±10.6	
Gender (M:F)	9:12	7:16	3:17	
Weight (kg)	53.2±7.7	52.8±7.2	52.6±11.6	
Height (cm)	158.0±5.3	156.7±6.0	155.6±7.9	
Mallampati class				
1	20 (95.2)	19 (82.6)	17 (85)	0.180
2	1 (4.8)	4 (17.4)	3 (15)	
Cormack laryngoscopic view				
Grade 1	21 (100)	23 (100)	20 (100)	–
Grade 2	0 (0)	0 (0)	0 (0)	
Duration of laryngoscopy(s)	9.8±1.9	10.1±2.1	11.2±2.5	0.100

Values are mean±SD or numbers (%), where appropriate

Table 3: Intubating conditions and requirement for rocuronium

Intubating conditions	Group 0.4 (n=21)	Group 0.6 (n=23)	Group 1.0 (n=20)	<i>P</i>
Excellent	11 (52.4)	22 (95.7)	20 (100)	0.000
Good	3 (14.3)	1 (4.3)	0 (0)	
Poor	7 (33.3)	0 (0)	0 (0)	
Overall intubating conditions				
Clinically acceptable	14 (66.7)	23 (100)	20 (100)	0.000
Clinically unacceptable	7 (33.3)	0 (0)	0 (0)	
Rocuronium requirement	0 (0)	0 (0)	0 (0)	–

Values are number (%)

Apnoea time and the time to regular spontaneous breathing (end tidal CO<sub>2</sub> waveform) were dose-dependent, and are presented in Table 5.

Haemodynamic responses to induction and intubation are shown in Tables 6 and 7. Pre-induction HR and MAP were comparable in the three groups. There was no statistically significant difference in mean HR and MAP between the three groups at any time point.

Oxygen saturation before as well as following induction of anaesthesia and tracheal intubation ranged between 97% and 100%. No episodes of laryngospasm, bronchospasm, masseter spasm, or generalized rigidity were observed.

## DISCUSSION

This study demonstrates that satisfactory tracheal intubating conditions can be achieved 1 min after succinylcholine administration, with doses much less than the traditionally recommended dose of 1.0 mg/kg. The intubating conditions following 0.6 mg/kg succinylcholine were similar to those obtained after the 1.0 mg/kg dose. Doses of 0.4 mg/kg did not often result in acceptable intubating conditions and therefore cannot be recommended for rapid sequence tracheal intubation.

The effectiveness of small doses of succinylcholine in achieving satisfactory intubating conditions has been previously described.<sup>[4,10-12]</sup> Stewart *et al.*<sup>[11]</sup> reported that 26 (96%) of 27 patients receiving 1.5 mg/kg succinylcholine and 30 (94%) of 32 patients receiving 0.5 mg/kg had acceptable intubating conditions. However, in patients with a full stomach or in those with raised intracranial pressure, excellent intubating conditions are warranted. In our study the administration of 1.0 and 0.6 mg/kg succinylcholine was associated with 100% and 95.7% incidence of excellent tracheal intubating conditions. In contrast, Stewart *et al.*<sup>[11]</sup> reported that, after induction of anaesthesia with 5 mg/kg thiopental, 23 (85%) of 27 patients receiving 1.5 mg/kg succinylcholine, and 18 (56%) of 32 patients receiving 0.5 mg/kg succinylcholine had excellent intubating conditions at 60 s. Naguib *et al.*<sup>[12]</sup> also found the incidence of excellent intubating conditions following induction with 2 µg/kg fentanyl and 2 mg/kg propofol to be 0.0%, 43.3%, 60.0%, 63.3%, 80.0% and 86.7% of patients after 0.0, 0.3, 0.5, 1.0, 1.5, and 2.0 mg/kg succinylcholine, respectively.

Table 4: Details of intubating conditions

	Group 0.4 (n=21)	Group 0.6 (n=23)	Group 1.0 (n=20)	P
Laryngoscopy (easy/ fair/difficult)	21/0/0	22/1/0	20/1/0	0.404
Vocal cords position (abducted/ intermediate/closed)	21/0/0	23/0/0	20/0/0	–
Vocal cords movement (none/moving/closing)	21/0/0	23/0/0	20/0/0	–
Coughing (none/ diaphragm/sustained >10 s)	11/6/4	14/8/1	20/0/0	0.004
Movement of the limbs (none/slight/vigorous)	14/2/5	19/4/0	19/1/0	0.012

Values are numbers

Table 5: Apnoea time and time to resumption of regular spontaneous breathing

	Group 0.4 (n=21)	Group 0.6 (n=23)	Group 1.0 (n=20)	P
Apnoea time (min)	3.8±1.1	4.3±0.9	8.2±3.4	0.000
Time to regular spontaneous breathing (min)	5.3±1.2	5.5±1.1	8.9±3.5	0.000

Values are mean±SD

Table 6: Heart rate response to induction and intubation

Time point	Heart rate (beat/min)			P
	Group 0.4 (n=21)	Group 0.6 (n=23)	Group 1.0 (n=20)	
Pre-induction	75±13	80±11	84±9	0.072
Post-induction	87±14	83±12	93±19	0.078
Post-intubation				
1 min	98±18	97±16	94±14	0.800
2 min	95±18	92±15	91±14	0.663
3 min	84±11	87±15	85±13	0.724
4 min	82±10	85±15	81±15	0.689
5 min	79±10	81±13	79±13	0.738

Values are mean±SD

Table 7: Mean arterial pressure response to induction and intubation

Time point	Mean arterial pressure (mmHg)			P
	Group 0.4	Group 0.6	Group 1.0	
Pre-induction	89±6	92±11	93±12	0.421
Post-induction	77±12	77±12	83±15	0.210
Post-intubation				
1 min	86±12	90±12	83±15	0.230
2 min	88±13	87±11	84±14	0.621
3 min	82±10	83±12	79±14	0.608
4 min	78±8	80±11	80±13	0.656
5 min	76±8	79±10	78±12	0.718

Values are mean±SD

Our results indicate that apnoea time and time to resumption of regular spontaneous breathing (end tidal CO<sub>2</sub> waveform) were dose-dependent. In all the three groups, start of regular spontaneous breathing occurred approximately 1 min after the detection

of the first diaphragmatic movement. There was a statistically and clinically significant difference in apnoea time between 0.6 mg/kg and 1 mg/kg dose of succinylcholine ( $4.3 \pm 0.9$  min versus  $8.2 \pm 3.4$  min, respectively). Return of regular spontaneous breathing occurred significantly earlier when the 0.6 mg/kg dose of succinylcholine was used compared with the 1 mg/kg ( $5.5 \pm 1.1$  min and  $8.9 \pm 3.5$  min, respectively) dose. Although initial spontaneous and regular breathing may not reflect complete functional recovery, this may still prevent haemoglobin desaturation that would ensue if the patient remained apneic. Thus, critical haemoglobin desaturation may not occur with the use of the 0.6 mg/kg dose, especially in healthy adults. Because we did not allow our patients to desaturate, we cannot comment on the effect of these doses in a “Cannot Ventilate, Cannot Intubate” situation. However, Naguib *et al.*<sup>[13]</sup> found that, compared with the traditional intubating dose of 1.0 mg/kg succinylcholine, a reduction in succinylcholine dose to 0.56 mg/kg was associated with a 20% absolute decrease and a 50% relative decrease in the incidence of haemoglobin desaturation ( $\text{SpO}_2 < 90\%$ ) in ASA physical status I patients anaesthetized with 2  $\mu\text{g}/\text{kg}$  fentanyl and 2 mg/kg succinylcholine.

Our results with regard to duration of apnoea are in contradistinction with that reported by others. El-Orbamy *et al.*<sup>[14]</sup> noted that the mean time ( $\pm\text{SD}$ ) to spontaneous diaphragmatic movements after 0.6 mg/kg and 1.0 mg/kg succinylcholine were  $3.41 \pm 0.6$  and  $5.3 \pm 8.0$  min, respectively ( $P < 0.05$ ). Hayes *et al.*<sup>[6]</sup> reported that the recovery of diaphragmatic movements occurred 4.7 (SD  $\pm 1.5$ -2.0) min after the administration of 1 mg/kg succinylcholine in patients with 1  $\mu\text{g}/\text{kg}$  fentanyl and 3-7 mg/kg thiopentone. Similarly in volunteers who received 5 mg/kg thiopentone and 1 mg/kg succinylcholine, Heier *et al.*<sup>[5]</sup> noted diaphragmatic activity 5.2 ( $\pm 1.5$ -2.0) min after succinylcholine and Stewart *et al.*<sup>[11]</sup> reported a 3.8 min apnoea time after 0.5 mg/kg.

An interesting finding of our study is the striking dissimilarity in the intubating conditions (better) obtained and the duration of apnoea (longer) observed following administration of three doses of succinylcholine compared with that reported previously in the literature. We are unable to explain this. Geographic location and ethnic background influence the potency and duration of action of drugs. Previous studies have shown that the response to muscle relaxants differs between geographical

areas. Katz *et al.*<sup>[15]</sup> reported that the neuromuscular blocking effect of succinylcholine (1 mg/kg) in adults was shorter in London ( $9.1 \pm 2.9$  min) than in New York ( $14.6 \pm 3.6$  min). Houghton *et al.*<sup>[16]</sup> reported that the recovery of spontaneous ventilation after succinylcholine was 35% slower in Asian patients than in European patients. Hosseini *et al.*<sup>[17]</sup> showed that Irish subjects ( $7.82 \pm 0.14$  U/mL) had more serum cholinesterase activity than Iranian subjects ( $4.22 \pm 0.90$  U/mL). These inter-racial differences in drug response could be due to differences in drug kinetics or sensitivity.<sup>[17]</sup> Thus, ethnic and geographic differences could possibly explain the differences found in our results in the Indian population.

Our study has several limitations. First, no control group was studied. The quality of intubating conditions without NMBAs is less predictable and the incidence of failed tracheal intubations is higher. We felt that intubation without NMBA is unlikely to be used in a rapid sequence induction scenario. Second, we did not study the onset and recovery times of different doses of succinylcholine by neuromuscular monitoring. In studies assessing the neuromuscular effects, succinylcholine is administered after calibration of the response to stimuli after induction of anaesthesia, and the results of intubating conditions so obtained cannot be applied to the clinical situation of rapid sequence induction. Moreover, monitoring the adductor pollicis is not a useful measure for evaluating the neuromuscular block at the laryngeal, diaphragm, and masseter muscles<sup>[4]</sup> as the diaphragm recovers faster than hand muscles after succinylcholine.<sup>[2]</sup> Pansard *et al.*<sup>[18]</sup> demonstrated that diaphragm recovery occurs 2 min earlier than adductor pollicis recovery at all levels of twitch height recovery. Third, our results were obtained in young, healthy and normal weight patients. Increasing age, obesity and pre-existing lung disease would make patients more vulnerable to desaturation. There are clinical situations in which “acceptable” conditions for tracheal intubation may not be ideal, e.g. a patient with increased intracranial pressure and a full stomach. In such patients, decreasing the dose of succinylcholine to less than 1 mg/kg might increase morbidity.

Our findings have clinical relevance in patients with unanticipated difficult airway. The faster return to spontaneous ventilation with the 0.6 mg/kg dose increases the margin of safety in the event of a “Cannot Intubate, Cannot Ventilate” situation compared with the 1.0 mg/kg dose.

## CONCLUSION

To conclude, a reduction in succinylcholine dose to 0.6 mg/kg provided equally acceptable intubating conditions at 60 s compared with the use of 1 mg/kg succinylcholine during rapid sequence induction of anaesthesia, with the advantage of a shorter apnoea time and time to regular spontaneous breathing.

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## Announcement

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