

INTUBATING CONDITIONS FOLLOWING RAPID SEQUENCE INDUCTION WITH THREE DOSES OF SUCCINYLCHOLINE

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ABSTRACT

BACKGROUND

Whenever rapid sequence induction is considered, succinylcholine is the neuromuscular blocking agent used because of its rapid onset and recovery time. In this study, we are studying the minimum dose required for this purpose.

This study consists of prospective, randomised, double-blind study to compare endotracheal intubating conditions and the apnoea duration after administration of 0.4, 0.6 and 0.8 mg/kg of succinylcholine in cases of rapid sequence induction of anaesthesia.

MATERIALS AND METHODS

Patients were randomly selected to 3 groups according to the dose of succinylcholine (0.4, 0.6 or 0.8 mg/kg). Anaesthesia was induced with fentanyl 2 µg/kg and propofol 2 mg/kg followed by application of cricoid pressure. Patients were intubated. Intubating conditions were assessed after 60 s of succinylcholine administration. Time of first diaphragmatic contraction (apnoea time) and time for resumption of regular spontaneous breathing were noted.

RESULTS

Intubating conditions were excellent for 0.4, 0.6 and 0.8 mg/kg succinylcholine; they were 52.4%, 95.7% and 100% respectively; $P < 0.001$. Acceptable intubating conditions (excellent and good grade combined) for 0.4, 0.6 and 0.8 mg/kg succinylcholine were 66.7%, 100% and 100% respectively; $P < 0.001$. Apnoea time for groups 0.4, 0.6 and 0.8 mg/kg was 3.8 ± 1.1 min, 4.3 ± 0.9 min and 8.2 ± 3.4 min respectively; $P < 0.001$. Time for regular spontaneous breathing for groups 0.4, 0.6 and 0.8 mg/kg were 5.3 ± 1.2 min, 5.5 ± 1.1 min and 8.9 ± 3.5 min 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 0.8 mg/kg.

KEY WORDS

Anaesthesia, Intubating Conditions, Neuromuscular Blockers, Rapid Sequence Induction, Succinylcholine.

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BACKGROUND

Succinylcholine, a Neuromuscular Blocking Agent (NMBA) with the fastest onset and recovery time,¹ is considered the drug of choice for rapid sequence induction of anaesthesia. Traditionally, 1 mg/kg of succinylcholine is used for this purpose. The Effective Dose (ED) 95 of succinylcholine is less than 0.30 mg/kg.^[2,3] Doses equivalent to twice the ED 95 are generally considered to be the appropriate dose of non-depolarising NMBAs for intubation.^[4] A 0.8 mg/kg dose was equivalent to 3.5 - 4 times the ED 95. Recovery of spontaneous respiration following 0.8 mg/kg succinylcholine administration may not occur rapidly enough to prevent haemoglobin desaturation in patients whose ventilation is not assisted.^[5,6] Based on a mathematical model of haemoglobin desaturation during apnoea, Benumof et al^[7] 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^[5] 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 recovery of spontaneous ventilation, thereby proving a greater margin of safety in airway management. This study consists of a prospective, randomised, double-blind study to compare endotracheal intubating conditions and the apnoea duration after administration of 0.4, 0.6 and 0.8 mg/kg of succinylcholine in cases of rapid sequence induction of anaesthesia.

MATERIALS AND METHODS

The study was approved by the Hospital Ethics Committee and written informed consent was obtained from all patients. Sixty-nine American Society of Anesthesiologists (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, renal impairment and those with body mass index > 28 kg/m² were excluded from the study, as were pregnant women. Patients with previous or family history of abnormal

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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, 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 the three groups (23 patients each) according to the dose of succinylcholine to be administered intravenously (0.4, 0.6 or 0.8 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 0.8 received 0.8 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^[8] score of laryngoscopy was recorded: Grade 1= full view of epiglottis, Grade 2a= partial view of glottis, Grade 2b= only posterior extremity of glottis seen, Grade 3= only epiglottis seen, Grade 4= neither glottis nor epiglottis seen. Qualitative score system by Viby-Mogensen et al^[9] employed for evaluation of intubating conditions. This include ease of laryngoscopy, position and movement of vocal cords, coughing and movement of the limbs [Table 1]. If jaw is relaxed (no resistance to laryngoscopic blade), it is considered as easy. If jaw is not fully relaxed (slight resistance to blade), it is considered as fair. If there is poor jaw relaxation (active resistance of patient to laryngoscopic blade), it is considered as difficult. 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 considered as clinically acceptable; poor intubating conditions considered as clinically not acceptable.^[9] Time taken to do the laryngoscopy has been noted. Blood pressure heart rate (HR) and SpO₂ were recorded just before starting of anaesthesia (pre-induction), and after starting (post-induction) and then after every 1 min of tracheal intubation for 5 min (time 1 - 5). If bradycardia occurs while doing laryngoscopy (HR < 50 beats per min), atropine 0.6 mg was given. If there is decrease in mean arterial pressure (MAP) > 25%, ephedrine 6 mg was given in increments. Adverse events such as laryngospasm, bronchospasm, masseter spasm or muscle rigidity were recorded.

After tracheal intubation, ventilation (0.6% isoflurane and 66% nitrous oxide in oxygen using carbon dioxide absorption) was gently assisted manually to maintain an EtCO₂ 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 for 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 for regular reservoir bag movements that produced a well-formed end-tidal CO₂ 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.

Study Design

It is a prospective, randomised, double-blind, hospital-based controlled study.

Sample Size

It was calculated by taking the previous study results on rapid sequence intubation accepting a 2-tailed alpha error of 5% and a beta error of 20%. Power analysis was performed for apnoea time and time for resumption of regular spontaneous breathing. A sample of 23 patients were obtained in each group.

Patient Allocation

By a computer-generated random number, patients were randomly allocated to 3 groups.

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 0.8 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 0.8 mg/kg succinylcholine, respectively; P < 0.001. The 0.6 and 0.8 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 0.8 mg/kg succinylcholine, respectively. This difference was statistically significant ($P < 0.001$) [Table 3]. Comparable intubating conditions were achieved after 0.6 and 0.8 mg/kg succinylcholine; $P > 0.05$. Patients receiving 0.4 mg/kg succinylcholine had a frequent incidence (33.3%) of poor tracheal intubating conditions.

Variables	Intubating Conditions		
	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 limbs	None	Slight	Vigorous

Table 1. Assessment of Intubating Conditions

	Group 0.4 (n=21)	Group 0.6 (n=23)	Group 0.8 (n=20)	P value
Age (yrs.)	33.4±9.5	34.8± 13.2	34.9 ±10.6	
Gender (M:F)	09:12	07:16	03:17	
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				
Class 1	20(95.2)	19(82.6)	17(85)	0.18
Class 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	0.1

Table 2. Patient Data

Intubating Conditions	Group 0.4 (n=21)	Group 0.6 (n=23)	Group 0.8 (n=20)	P value
Excellent	11(52.4)	22(95.7)	20(100)	0
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
Clinically unacceptable	7(33.3)	0(0)	0(0)	
Rocuronium requirement	0(0)	0(0)	0(0)	

Table 3. Intubating Conditions and Requirement for Rocuronium

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 0.8 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].

	Group 0.4 (n=21)	Group 0.6 (n=23)	Group 0.8 (n=20)	P value
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 movements (none/moving/closing)	21/0/0	23/0/0	20/0/0	-
Coughing (none/diaphragm/sustained > 10s)	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

Table 4. Details of Intubating Conditions

Apnoea time and the time for regular spontaneous breathing (end-tidal CO₂ waveform) were dose-dependent and are presented in Table 5.

	Group 0.4 (n=21)	Group 0.6 (n=23)	Group 0.8 (n=20)	P value
Apnoea time (min)	3.8± 1.1	4.3± 0.9	8.2± 3.4	0.00
Time for regular spontaneous breathing (min)	5.3± 1.2	5.5± 1.1	8.9± 3.5	0.00

Table 5. Apnoea Time and Time for Resumption of Regular Spontaneous Breathing

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

Time Point	Heart Rate (Beat/Min)			
	Group 0.4 (n=21)	Group 0.6 (n=23)	Group 0.8 (n=20)	P value
Pre-induction	75± 13	80± 11	84± 9	0.072
Post-induction	87± 14	83± 12	93± 19	0.078
p/i 1 min	98± 18	97 ±16	94 ±14	0.8
p/i 2 min	95 ±18	92± 15	91± 14	0.663
p/i 3 min	84± 11	87± 15	85± 13	0.724
p/i 4 min	82± 10	85± 15	81± 15	0.689
p/i 5 min	79± 10	81± 13	79 ±13	0.738

Table 6. Heart Rate response to Induction and Intubation

Time Point	Mean Arterial Blood Pressure (mmHg)			
	Group 0.4 (n=21)	Group 0.6 (n=23)	Group 0.8 (n=20)	P value
Pre-induction	89± 6	92 ±11	93± 12	0.421
Post-induction	77± 12	77± 12	83± 15	0.21
p/i 1 min	86± 12	90± 12	83± 15	0.23
p/i 2 min	88 ±13	87± 11	84± 14	0.621
p/i 3 min	82± 10	83± 12	79± 14	0.608
p/i 4 min	78± 8	80± 11	80± 13	0.656
p/i 5 min	76± 8	79± 10	78 ±12	0.718

Table 7. Mean Arterial Pressure response to Induction and Intubation

Oxygen saturation before and following induction of anaesthesia and endotracheal intubation ranged between 97% and 100%. There were no episodes of bronchospasm, laryngospasm, masseter spasm or generalised rigidity observed.

DISCUSSION

This study demonstrates that satisfactory tracheal intubating conditions can be achieved in 1 min after succinylcholine administration with doses much less than the usually recommended dose of 0.8 mg/kg. The intubating conditions following 0.6 mg/kg succinylcholine were similar to those obtained after the 0.8 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.^[4,10-12] Stewart et al^[11] 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 0.8 and 0.6 mg/kg succinylcholine was associated with 100% and 95.7% incidence of excellent tracheal intubating conditions. In contrast Stewart et al 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^[12] 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, 0.8, 1.5 and 2.0 mg/kg succinylcholine, respectively. Our results indicate that apnoea time and time for resumption of regular spontaneous breathing (End-tidal CO₂ 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 ± 0.9 min versus 8.2 ± 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 ± 1.1 min and 8.9 ± 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 apnoeic. Thus, critical haemoglobin desaturation may not occur with the use of 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^[13] found that compared with the traditional intubating dose of 0.8 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 (SpO₂ < 90%) in ASA physical status I patients anaesthetised with 2 µg/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^[14] noted that the mean time (±SD) to spontaneous diaphragmatic movements after 0.6 mg/kg and 0.8 mg/kg succinylcholine were 3.41 ± 0.6 and 5.3 ± 8.0 min, respectively (P < 0.05). Hayes et al^[6] reported that the recovery of diaphragmatic movements occurred 4.7 (SD ± 1.5-2.0) min after the administration of 1 mg/kg succinylcholine in patients with 1 µg/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^[5] noted diaphragmatic activity of 5.2 (±1.5 - 2.0) min after succinylcholine and Stewart et al^[11] 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^[15] reported that the neuromuscular blocking effect of succinylcholine (1 mg/kg) in adults was shorter in London (9.1 ± 2.9 min) than in New York (14.6 ± 3.6 min). Houghton et al^[16] reported that the recovery of spontaneous ventilation after succinylcholine was 35% slower in Asian patients than in European patients. Hosseini et al^[17] showed that Irish subjects (7.82 ± 0.14 U/mL) had more serum cholinesterase activity than Iranian subjects (4.22 ± 0.90 U/mL). These inter-racial differences in drug response could be due to differences in drug kinetics or sensitivity.^[17] 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. Evaluation of neuromuscular block at the laryngeal, diaphragm and masseter muscles^[4] is done by monitoring adductor pollicis, but it was not useful as the diaphragm recovers faster than hand muscles after succinylcholine.^[2] Pansard et al^[18] 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 0.6 mg/kg dose increases the margin of safety in the event of a "Cannot Intubate, Cannot Ventilate" situation compared with 0.8 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 for regular spontaneous breathing.

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