Academic Sciences International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 5, Suppl 4, 2013

Research Article

A STUDY TO REEXAMINE THE DOSE OF SUCCINYLCHOLINE TO PROVIDE OPTIMAL INTUBATING CONDITIONS

[1]DR SUSHEELA TAXAK, [1*]DR TARANDEEP SINGH, [1]DR ASHA ANAND, [2]DR KULDEEP LALLAR

[1]Dept. of Anesthesiology & Critical Care, Dept of Cardiology, Post graduate Institute of Medical Sciences Rohtak - 124001 India. Email: dr_taran@yahoo.co.in.

Received: 23 Sep 2013, Revised and Accepted: 15 Oct 2013

ABSTRACT

Introduction: Succinylcholine remains the conventional choice for muscle relaxant for rapid sequence induction because of its ultra short duration of action. The most commonly used intubating dose of succinylcholine is 1 $mgkg^{-1}$. Lower doses of succinylcholine can provide acceptable intubation conditions with considerable decrease in apnea time. This study was undertaken in an attempt to reexamine the optimal dose of SCh for facilitating endotracheal intubation in Indian population.

Method and materials: After preoxygenation for 3 minutes, anaesthesia was induced with injection propofol 2$mgkg^{-1}$ and injection pethidine 1$mgkg^{-1}$ given intravenously. Following this, the evoked response of the adductor pollicis muscle to ulnar nerve stimulation at the wrist was recorded. Supramaximal stimulus was provided at 10s. Patients received 1.0, 0.8, 0.6 and 0.4 $mgkg^{-1}$ of SCh and twitch height was monitored till its ninety percent return.

Results: Intubation conditions were excellent in 100%, 88%, 76% and 32 % of patients after 1.0, 0.8, 0.6 and 0.4 $mgkg^{-1}$ of SCh. The mean onset time was 51.72±10.38s, 54.72±9.71s, 60.80±11.40s and 69.40±10.76s after 1.0, 0.8, 0.6 and 0.4 $mgkg^{-1}$ of SCh. The increase in onset time after 0.4 $mgkg^{-1}$ is statistically significant as compared to 0.6 $mgkg^{-1}$ ($p < 0.01$). The corresponding time for ninety percent return in twitch height for same doses was 501.80±41.53s, 422.20±58.21s, 358.80±65.82s and 244.00±61.07s. Mean apnoea time after 1.0, 0.8, 0.6 and 0.4 $mgkg^{-1}$ of SCh was 333.40±68.11s , 272.40±43.31s ,228.20±65.79s and 113.60±32.18s respectively. With decreasing dose, apnea time of patient is also decreased. Apnea time following 0.6 $mgkg^{-1}$of SCh is significantly lower as compared to 1 $mgkg^{-1}$ ($p<0.01$). Lower doses of Sch provide acceptable intubation conditions and at the same time decreases the apnea time.

Conclusions: Succinylcholine in dose of 0.6 $mgkg^{-1}$ provide clinically acceptable conditions for tracheal intubation when combined with a standard anaesthetic sequence and at the same time will allow a more rapid return of spontaneous respiration before life threatening haemoglobin desaturation occur in previously preoxygenated individual. Use of 1.0 $mgkg^{-1}$ of SCh for tracheal intubation is excessive if the goal is to achieve acceptable intubating conditions within 60 s. We recommend a dose of 0.6 $mgkg^{-1}$of SCh for RSI of anaesthesia.

Keywords: Succinylcholine, Intubation conditions, Apnoea time.

INTRODUCTION

Succinylcholine (SCh) has been a mainstay of anaesthetic practice for about 60 years now and remains the conventional choice of muscle relaxant for rapid sequence induction (RSI) till today.[1]The main reason for SCh to still enjoy such a popularity despite a long list of undesirable side effects has been its unique onset and offset profile.[2] Its ultra rapid onset of action reduces the time from induction of anaesthesia to endotracheal intubation which minimizes the time during which trachea is unprotected from aspirated fluid during anaesthesia. This has been its main advocate for SCh to be used in RSI. Its ultra short duration of action may allow neuromuscular recovery before oxygen desaturation in the event of failure to intubate the trachea. Despite its short duration of action, SCh when given in its usual dose of 1 $mgkg^{-1}$ can produce apnoea of duration that may lead to significant haemoglobin desaturation before recovery of neuromuscular blockade in those whose ventilation is not assisted.[3-6] This fact assumes a great significance in cases of difficult airway which may land up in cannot intubate and cannot ventilate situation. We, therefore, have an obligation to keep trying to improve the safety of SCh and the possibility of an earlier return of neuromuscular function following its low dose has much to recommend it. Therefore we in this prospective, randomized, double blind study attempted to reexamine the optimal dose of SCh for facilitating endotracheal intubation in Indian population.

METHODS AND MATERIALS

This prospective, randomized, double blind study was approved by ethical committee of the Pt.B.D.Sharma PGIMS, Rohtak. Two hundred patients in age group of 20-60 years of either sex having physical status of ASA grade I or II scheduled for any kind surgery under general anaesthesia requiring endotracheal intubation were included in the study. All patients who had reactive airway disease, anticipated difficult airway, known neuromuscular disorder, body mass index (BMI) more than 35, history of drug therapy known to interact with SCh for e.g. lithium, magnesium sulphate, kanamycin, cimetidine, oral contraceptive pills, Gastroesophageal reflux disease or hiatus hernia were excluded from the study.

After written informed consent patient were kept fasting for six hours prior to scheduled time for surgery and were premedicated with tablet alprazolam orally 0.5 mg on the night before and two hours prior to surgery. After arrival in the operating room, routine monitoring for pulse rate, noninvasive blood pressure, pulse oximetry and electrocardiography were set up. Patients were randomly allocated to one of the four groups of equal size (n=50) by drawing coded slips from an envelope. Group I, II, III and IV received 1$mgkg^{-1}$, 0.8$mgkg^{-1}$,and 0.6$mgkg^{-1}$ and 0.4$mgkg^{-1}$ body weight of SCh. After preoxygenating the patient for 3 minutes, anaesthesia was induced with injection propofol 2$mgkg^{-1}$ and injection meperidine 1$mgkg^{-1}$ given intravenously. Following this, the evoked response of the adductor pollicis muscle to ulnar nerve stimulation at the wrist was recorded using the TOF-watch SX monitor (organon teknika). Single supramaximal stimulus was provided at 10s interval and baseline twitch height was noted. This was followed by the stipulated dose of SCh made to 2 ml solution by adding normal saline as per the group allocation. Patient received 8 litre $minute^{-1}$ oxygen through Bain's circuit via anatomical facemask till intubation but no intermittent positive pressure ventilation was done. If the SpO_2 dropped to less than 90%, two positive pressure breaths were delivered. Tracheal intubation was subsequently done at 60 seconds. The intubating conditions were graded using criteria of good clinical research practice (table- 1).[7]

Intubating conditions were graded as excellent if all the variables were excellent. They were graded as good if any of the variables was good but none was poor and were graded poor if any of the variables was poor. Intubating conditions were classified as acceptable if they

were graded excellent or good and as unacceptable if they were poor. Inability to open the jaw or to introduce the laryngoscope, were considered as failure. In patients with unacceptable or failed intubating conditions additional dose of SCh 1mgkg^{-1} was given to facilitate endotracheal intubation. The neuromuscular monitoring was followed till 90% return of twitch height. Lag time was referred to as the time from administration of SCh to first depression in twitch height. Onset time was the time from administration of SCh to maximal depression in twitch height and twitch recovery time was referred to as the time from first depressed twitch height to 90% return of twitch height. Apnoea time was measured from injection of SCh until time to spontaneous diaphragmatic movement.

Table 1: Assessment of intubation conditions

Variables	Intubation conditions		
	Excellent	**Good**	**Poor**
Vocal cord			
• Position	Abducted	Intermediate	Close
• Movement	None	Moving	Closing
Reaction to intubation			
• Movement of limbs	None	Slight	Vigorous
• Coughing	None	Diaphragm	Sustained

[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.

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. Demographic data were analyzed with analysis of variance. Intubating conditions were analyzed with a Kruskal-Wallis test for multiple comparisons using the Bonferroni adjustments. Statistical analyses were performed using StatXaxt for Windows (version 4.0.1; CYTEL Software Corporation, Cambridge, MA; 1999). Statistical significance was accepted when $P< 0.05$.

RESULTS

Table 2 compares the demographic profile of patients. There were no significant differences in the demographic data among the four groups.

Table 2: Distribution of mean age, weight, height in 4 groups

Group (SCh in mgkg^{-1})	Age (in years)	Mean weight (in kg)	Height (in centimetres)
I (1.0)	41.24±13.00	54.76±9.87	156.26±7.84
II (0.8)	41.74±10.03	57.20±9.09	159.20±9.09
III (0.6)	37.94±10.93	55.50±9.41	156.60±8.26
IV (0.4)	38.48±11.55	53.06±8.09	155.56±7.39

Data are means ± SD

Table 3 shows the number of patients having different variables of intubation conditions in different groups.

Table 3: Variables of intubation conditions in patients of different groups

Intubating conditions			Group I (1.0 mg/kg)	Group II (0.8 mg/kg)	Group III (0.6 mg/kg)	Group IV (0.4 mg/kg)
Vocal Cord	Position	Abducted	50	49	46	46
		Intermediate	-	1	4	4
		Close	-	-	-	-
		None	50	50	48	48
	Movement	Moving	-	-	2	2
		Closing	-	-	-	-
		None	50	45	43	31
Reaction to intubation	Movement of limbs	Slight	-	5	7	15
		Vigorous	-	-	-	4
		None	50	44	38	18
	Coughing	Diaphragm	-	6	12	24
		Sustained	-	-	-	8

Intubation conditions, graded 60 s after SCh administration, are displayed in Table 4 and figure 1.

Table 4: Intubation conditions in different groups

Intubation Conditions	Group I (1.0 mg/kg)	Group II (0.8 mg/kg)	Group III (0.6 mg/kg)	Group IV (0.4 mg/kg)
Excellent	50	44	38	16
Good	-	6	12	24
Poor	-	-	-	10*

*p < 0.01 compared to group I,II,III. Statistical significance accepted when P < 0 .05.

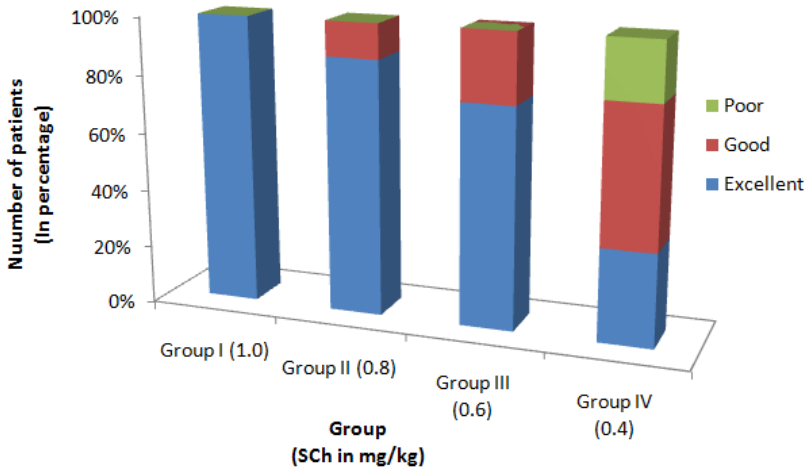

Fig. I: Intubation conditions in different groups.

Number of patients having acceptable intubating conditions (either excellent or good) are depicted in table 5.

Table 5: Comparison of acceptable and non acceptable intubation conditions in different groups

Group (SCh in mgkg^{-1})	Acceptable	Non - Acceptable	Significance
I (1.0)	50	Nil	NS#
II (0.8)	50	Nil	NS#
III (0.6)	50	Nil	NS#
IV (0.4)	40	10	P<0.001*

between group I, II and II, NS= non significant p>0.05

*Group IV compared to groupI,II& III. Statistical significance accepted when P < 0 .05.

Patients receiving 0.4 mgkg^{-1} doses of SCh had a frequent incidence of poor tracheal intubation conditions. All patients receiving 1.0, 0.8 and 0.6 mgkg^{-1} of SCh had acceptable intubating conditions. Ten patients out of fifty receiving 0.4 mgkg^{-1}SCh had non acceptable intubating conditions. Table 6 and figure 2 compares the lag time, onset time, time to ninety percent return in twitch height and resumption of spontaneous breathing.

Table 6: Neuromuscular parameters in different groups

Time	Group 1 (1.0 mg/kg)	Group 2 (0.8 mg/kg)	Group 3 (0.6 mg/kg)	Group 4 (0.4 mg/kg)
Lag time	23.20±6.20s	24.80±5.79s	29.20±7.23s	32.80±9.58s
Onset time	51.72±10.38s	54.72±9.71s	60.80±11.40s	69.40±10.76s#
Twitch recovery time	501.80±41.53s	422.20±58.21s	358.80±65.82s*	244.00±61.07s
Apnoea time	333.40±68.11s	272.40±43.31s	228.20±65.79s*	113.60±32.18s

Time in seconds (s) Data are means ± SD

*p< 0.01 versus SCh 1.0 mgkg-1 groups; #p < 0.01 versus SCh 0.6 mgkg-1 group.

Statistical significance accepted when P < 0 .05.

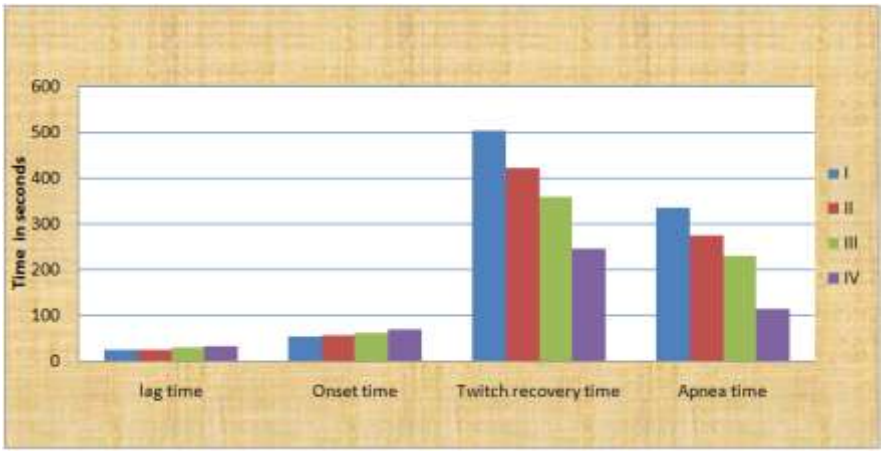

Fig. 2: Neuromuscular parameters in different groups

Decreasing the dose of SCh from 1.0 mgkg^{-1} to 0.4 mgkg^{-1} results in a progressive decrease in values for the return of neuromuscular function. Duration of action of SCh was dose dependent.

DISCUSSION

Our study demonstrates that satisfactory intubation conditions can be achieved after one minute of SCh administration with doses much less than the traditionally recommended dose of 1.0mgkg^{-1}, which at the same time considerably reduces the duration of paralyses by SCh. Intubation conditions after 0.6 mgkg^{-1} were clinically acceptable which came out to be the lower limit of dose for clinical use. Doses of 0.4 mgkg^{-1} did not often result in satisfactory conditions at 60 s. Laryngoscopy was not a problem even in such a low dose, both the position of vocal cords and its movement after laryngoscopy was acceptable. The main reason for unacceptable intubation condition was reaction to intubation with many patients showing vigorous movement of limbs and sustained coughing after intubation (Table III). Therefore this dose cannot be recommended for rapid tracheal intubation.

The effectiveness of small doses of SCh in achieving adequate intubation conditions after 60 s has been reported. Naguib et al concluded that in RSI, 95 % of patients with normal airway anatomy anaesthetized with 2μgkg^{-1} fentanyl and 2 mgkg^{-1} propofol should have acceptable intubation after 0.56 mgkg^{-1}SCh.[8] El orbany et al recommended that SCh in doses of 0.5-0.6 mgkg^{-1} produces clinically satisfactory intubation conditions after IV administration.[9]

Onset time of SCh was dose dependent. It increased as dose of SCh was decreased (Table VI). Onset time after 1.0 mgkg^{-1} and 0.6 mgkg^{-1} of SCh was 51.72 s and 60.80 s respectively whereas onset time after 0.4 mgkg^{-1} was 69.40 s. Since 60s is the time after which intubation is done during RSI, SCh in dose of 0.6 mgkg^{-1} can be used during RSI but not in dose of 0.4 mgkg^{-1} due to delayed onset, although onset time could be fast at other muscle group, such as laryngeal muscle or the diaphragm as compared to adductor pollices.[10-12]

Duration of action of SCh induced block as noted by recovery to ninety percent twitch height was also dose dependent (Table VI). It ranged from 244.0 s after 0.4 mgkg $^{-1}$ to 501.80s after 1.0 mgkg^{-1} of SCh. Recovery time for 0.6 mgkg $^{-1}$ of SCh was 358.8 s. These results are consistent with previously published results of other investigators. Katz and Ryan using mechanomyographic monitoring, found in patients anaesthetized with 150-500 mg thiamyal, the median time for ninety percent return in twitch height for doses of 1.0 mgkg^{-1} of SCh was 14.6 minutes.[13] Corresponding times reported by naguib et al was 7.2 minutes.[10] El-Orbany et al reported the mean time for ninety percent return in twitch height in minutes after 1.0, 0.6 and 0.4 mgkg^{-1} of SCh as 10.5, 7.25 and 6.2 minutes respectively.[9] Kopman et al reported the mean time for ninety percent return in twitch height in minutes after 1.0, 0.6 and 0.4 mgkg^{-1} of SCh as 9.3, 7.6 and 6.6 minutes respectively.[14]

Apnoea time as measured from time to spontaneous diaphragmatic movement was also, as expected, dose dependent. The mean apnoea time was 333.40±68.11s after 1mgkg^{-1}and 228.20±65.79s after 0.6 mgkg^{-1}of SCh .El-Orbany reported mean apnoea time after doses 1.0, 0.6 and 0.4 mgkg^{-1} of SCh was 5.3±0.8, 3.41±0.6, 2.7±1.2. [9] Naguib et noted that the mean apnoea time after 1 mgkg^{-1} of SCh was 4.7 minutes.[3]

The fact that lowering the dose of SCh considerably decreases the duration of paralyses and at the same time provide acceptable intubation conditions assumes a great significance. Few studies in the past drew attention to the misconception that respiratory recovery occur fast enough to save the patient in whom ventilation cannot be assisted after receiving 1mg/kg SCh. Benumof et al analyzed the published data on desaturation following apnoea and apnoea time following IV SCh to show that critical haemoglobin desaturation occurs before the functional recovery for various patients receiving 1 mgkg^{-1}of IV SCh.[4]Hayes et al concluded that the use of 1 mgkg^{-1} of SCh may not always prevent desaturation if there is a failure to intubate and ventilate during a RSI of anaesthesia.[5] Heier et al also observed that significant haemoglobin desaturation can occur after 1mgkg^{-1} SCh. In his study on SCh induced apnoea on haemoglobin desaturation on 12 healthy volunteers aged 18-45 years, one third of healthy volunteers desaturated during the period of apnoea following 1 mgkg^{-1}SCh given intravenously.[6]

Even after 50 year of use and despite dramatic advances in anaesthesia, a replacement for SCh does not appear to be eminent. We, therefore, have an obligation to keep trying to improve the safety of SCh. Hence minimal effective doses of SCh are recommended because they result in a shorter apnoea time that may avoid critical oxyhaemoglobin desaturation in healthy adult patients in whom ventilation cannot be assisted. SCh in dose of 0.6 mgkg^{-1} provide clinically acceptable conditions for tracheal intubation when combined with a standard anaesthetic sequence and at the same time will allow a more rapid return of spontaneous respiration. Use of 1.0 mgkg^{-1} of SCh for tracheal intubation is excessive if the goal is to achieve acceptable intubating conditions within 60 s. Therefore using larger doses of SCh does not produce more favorable intubation conditions and is associated with longer recovery time. We believe that even a modest decrease in the duration of drug induced paralyses will often be worth pursuing. Hence to facilitate endotracheal intubation, we recommend SCh in dose of 0.6 mgkg^{-1}.

REFERENCES

1. Hampton L J, Little D M, Fuller E M: The use of succinylcholine to facilitate endotracheal intubation. Anesthesiology 1953;14:382-9.
2. Miller RD. Miller's anesthesia. 7thed. Philadelphia: Churchill Livingstone; 2009.p.862-7.
3. Naguib M, Samarkandi AH, Khaled A, Riad W, Saleh W. Alharby SW. Succinylcholine dosage and apnea-induced hemoglobin desaturation in patients. Anesthesiology 2005;102: 35-40.
4. Benumof J L, Dagg R, Benumof R. Critical hemoglobin desaturation will occur before return to an unparalysed state following 1 mgkg^{-1} intravenous succinylcholine. Anesthesiology 1997;87:979-82.
5. Hayes AH, Breslin DS, Mirakhur RK, Reid JE, O'Hare RA: Frequency of haemoglobin desaturation with the use of succinylcholine during rapid sequence induction of anaesthesia. Acta Anaesthesiol Scand 2001; 45:746-9.
6. Heier T., Feiner J R, Lin J, Brown R, Caldwell J E. Hemoglobin desaturation after succinylcholine-induced apnea: A study of the recovery of spontaneous ventilation in healthy volunteers. Anesthesiology 2001;94:754-9.
7. Viby-Mogensen J, Engbrek J, Erikson L I, Gramstad I, Jensen E, Jensen F S et al. Good clinical research practice (GCRP) in pharmacodynamic studies of neuromuscular blocking agents. Acta Anaesthesiol Scand 1996; 40: 59-74.
8. Naguib M, Samarkandi A, Riad W, Alharby SW. Optimal dose of succinylcholine revisited. Anesthesiology 2003; 99: 1045–9.
9. El-Orbany MI, Joseph NJ, Salem MR, Klowden AJ: The neuromuscular effects and tracheal intubation conditions after small doses of succinylcholine. Anesth Analg 2004; 98:1680-5.
10. Pansard JL, Chauvin M, Lebrault C, Gauneau P, Duvaldestin P: Effect of an intubating dose of succinylcholine and atracurium on the diaphragm and the adductor pollicis muscle in humans. Anesthesiology 1987; 67:326-30.
11. Smith CE, Donati F, Bevan DR: Potency of succinylcholine at the diaphragm and at the adductor pollicis muscle. Anesth Analg 1988; 67: 625-30.
12. Meistelman C, Plaud B, Donati F: Neuromuscular effects of succinylcholine on the vocal cords and adductor pollicis muscles. Anesth Analg 1991; 73: 278-82.
13. Katz RL, Ryan JF. The neuromuscular effects of suxamethonium in man. Br J Anaesth 1969;41: 381-90.
14. Kopman A F , Zhaku B, Lai K S. The intubating dose of succinylcholine. Anesthesiology 2003;99:1050-4.