

## Optimal Dose of Succinylcholine Revisited

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**Background:** The authors reappraised the conventional wisdom that the intubating dose of succinylcholine must be 1.0 mg/kg and attempted to define the lower range of succinylcholine doses that provide acceptable intubation conditions in 95% of patients within 60 s.

**Methods:** This prospective, randomized, double-blind study involved 200 patients. Anesthesia was induced with 2  $\mu$ g/kg fentanyl and 2 mg/kg propofol. After loss of consciousness, patients were randomly allocated to receive 0.3, 0.5, or 1.0 mg/kg succinylcholine or saline (control group). Tracheal intubation was performed 60 s later. A blinded investigator performed all laryngoscopies and also graded intubating conditions.

**Results:** Intubating conditions were acceptable (excellent plus good grade combined) in 30%, 92%, 94%, and 98% of patients after 0.0, 0.3, 0.5, and 1.0 mg/kg succinylcholine, respectively. The incidence of acceptable intubating conditions was significantly greater ( $P < 0.05$ ) in patients receiving succinylcholine compared with those in the control group but was not different among the different succinylcholine dose groups. The calculated doses of succinylcholine (and their 95% confidence intervals) that were required to achieve acceptable intubating conditions in 90% and 95% of patients at 60 s were 0.24 (0.19–0.31) mg/kg and 0.56 (0.43–0.73) mg/kg, respectively.

**Conclusions:** The use of 1.0 mg/kg of succinylcholine may be excessive if the goal is to achieve acceptable intubating conditions within 60 s. Comparable intubating conditions were achieved after 0.3, 0.5, or 1.0 mg/kg succinylcholine. In a rapid-sequence induction, 95% of patients with normal airway anatomy anesthetized with 2  $\mu$ g/kg fentanyl and 2 mg/kg propofol should have acceptable intubating conditions at 60 s after 0.56 mg/kg succinylcholine. Reducing the dose of succinylcholine should allow a more rapid return of spontaneous respiration and airway reflexes.

SUCCINYLCHOLINE remains the drug of choice during a rapid-sequence induction of anesthesia. However, it has been demonstrated that spontaneous recovery from 1.0

mg/kg succinylcholine-induced apnea may not occur rapidly enough to prevent hemoglobin desaturation in subjects whose ventilation is not assisted.<sup>1,2</sup> Possible clinical implications of this are that (1) significant to life-threatening hemoglobin desaturation is probable in patients with unanticipated difficult airways, and conversely, (2) smaller doses of succinylcholine may decrease this period of vulnerability.

It is not clear from the literature why 1.0 mg/kg dose of succinylcholine has been traditionally chosen for tracheal intubation. The ED<sub>95</sub> of succinylcholine is less than 0.30 mg/kg,<sup>3,4</sup> and a 1.0-mg/kg dose represents 3.5–4 times the ED<sub>95</sub>. With nondepolarizing neuromuscular blockers, doses equivalent to twice the ED<sub>95</sub> are generally considered to be the appropriate dose for intubation.

The clinical relevance of smaller doses of succinylcholine deserves to be reexamined. The purpose of this prospective, randomized, double-blind, placebo-controlled study was twofold: (1) to compare the intubating conditions during rapid-sequence induction after 0.3, 0.5, and 1.0 mg/kg succinylcholine or placebo and (2) to determine the optimal doses of succinylcholine required to achieve acceptable intubation conditions in 90% and 95% of patients within 60 s.

### Materials and Methods

After obtaining institutional approval (King Khalid University Hospital, Riyadh, Saudi Arabia) and informed consent, we studied 200 patients of both sexes with American Society of Anesthesiologists physical status I, aged 30 (29–32) yr (mean and 95% confidence interval) and weighing 67 (66–69) kg. All patients underwent elective procedures; had no neuromuscular, renal, or hepatic disease; and were not taking any drug known to interfere with neuromuscular function. Exclusion criteria included a history of drug or alcohol abuse, gastroesophageal reflux or hiatus hernia, cardiovascular disease, reactive airway disease, allergies to any of the study drugs, administration of sedative or narcotic drugs in the previous 24 h, renal or hepatic impairment, or anticipated difficult intubation. All patients received 2 mg oral lorazepam 90 min before operation. An infusion of lactated Ringer's solution was started before induction of anesthesia. Standard monitoring was used.

Each patient then breathed 100% oxygen from the anesthesia circuit *via* a facemask (preoxygenation), and 2  $\mu$ g/kg fentanyl was administered intravenously. Pre-

This article is accompanied by an Editorial View. Please see: Donati F: The right dose of succinylcholine. ANESTHESIOLOGY 2003; 99:1037–8.

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Received from King Khalid University Hospital, Riyadh, Saudi Arabia. Submitted for publication February 24, 2003. Accepted for publication April 14, 2003. Support was provided solely from institutional and/or departmental sources. The results of this study were presented at the 16th Annual Meeting of the American Society of Anesthesiologists, San Francisco, California, October 11–15, 2003. Steven L. Shafer, M.D., served as acting Editor-in-Chief for this article.

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**Table 1. Intubation Conditions**

Variables	Excellent	Good	Poor
Vocal cords			
Position	Abducted	Intermediate	Closed
Movements	None	Moving	Closing
Reaction to intubation			
Movement of limbs	None	Slight	Vigorous
Coughing	None	Diaphragm	Sustained (> 10 s)

oxygenation was continued for 3 min and then 2 mg/kg propofol was administered intravenously. When the patient lost consciousness, one of the following doses was administered through a rapidly flowing intravenous line: 0.3, 0.5, or 1.0 mg/kg succinylcholine or saline (control group). Each patient was randomly assigned either to a particular dosage group or to the control group.

Because the observation of fasciculations would identify the drug administered as succinylcholine, the anesthesiologist performing and grading intubation was positioned with his back to the patient until just before beginning the intubation sequence. The tracheal intubation sequence was begun between 40 and 45 s after administration of the muscle relaxant. The patient's head was positioned, laryngoscopy was started at 50 s using a size 3 Macintosh blade, and tracheal intubation was subsequently performed 60 s after relaxant administration. Cuffed endotracheal tubes of 7- and 8-mm sizes were used in female and male patients, respectively. The scheme for grading conditions for tracheal intubation was based on the criteria of good clinical research practice (table 1).<sup>5</sup> Intubating conditions were excellent if all variables were excellent. If all the variables were not excellent, intubating conditions were good unless any variable was poor. If any variable was poor, the intubating conditions were poor. The investigator performing the intubation and grading intubation conditions was an experienced anesthesiologist, blinded as to which group the patient had been assigned. Intubation conditions

were classified as acceptable if they were graded as excellent or good and as unacceptable if they were graded as poor.

Before induction of anesthesia, surface electrodes were placed over the ulnar nerve at the wrist. Immediately after tracheal intubation, the ulnar nerve was stimulated at the wrist with square wave stimulus set at a current of 60 mA and a duration of 0.2 ms. Each stimulus was delivered in a train-of-four (TOF) sequence and repeated every 12 s using a Myotest peripheral nerve stimulator (Biometer International, Odense, Denmark). An investigator counted the number of tactile TOF responses immediately after tracheal intubation. Thereafter, the study was terminated, and anesthesia continued as appropriate for surgery. Each patient was followed up for any adverse affects.

### Statistical Analyses

Demographic data were analyzed with analysis of variance or chi-square test, where appropriate. If analyses of variance were significant, the Dunnett *post hoc* test was used to compare the study groups to the control group. Intubating conditions and TOF count were analyzed with a Kruskal-Wallis test for multiple comparisons using the Bonferroni adjustments. Statistical analyses were performed using the BMDP statistical package (release 7.01; University of California Press, Berkeley, CA; 1994) and StatXact for Windows (version 4.0.1; CYTEL Software Corporation, Cambridge, MA; 1999). The doses of succinylcholine that were required to achieve acceptable intubation conditions in 90% and 95% of patients at 60 s were calculated by probit analysis using pharmacologic software programs of Tallarida and Murray.<sup>6</sup> Unless otherwise specified, results were expressed as means and 95% confidence intervals or medians and interquartile ranges (25–75%) and were considered significant when *P* was less than 0.05.

**Table 2. Demographics, Intubating Conditions, and Train-of-four Count**

	Succinylcholine, mg/kg			
	0.3	0.5	1.0	Control
n	50	50	50	50
Age, yr	30.9 (27.9–33.8)	30.5 (27.2–33.7)	30 (27.7–32.3)	29.5 (26.9–32)
Weight, kg	66.6 (63.5–69.7)	67.4 (64.1–70.7)	67.8 (64.6–71)	67.4 (63.9–70.9)
Sex (M/F)	25/25	27/23	22/28	27/23
Height, cm	164 (161–167)	164 (161–167)	164 (161–166)	164 (160–167)
Intubating conditions*				
Acceptable	46 (92%)‡	47 (94%)‡	49 (98%)‡	15 (30%)
Unacceptable	4 (8%)	3 (6%)	1 (2%)	35 (70%)
TOF count†	4 (3.75–4)§	4 (2–4)‡§	0.0 (0–2)‡	4 (4–4)

Data are mean (95% CI), number (%)\*, or median and interquartile range (25–75%).

\* Intubation conditions were classified as acceptable if they were graded excellent or good and as unacceptable if they were graded poor. † TOF count = the number of tactile train-of-four responses immediately after tracheal intubation. ‡ *P* < 0.05 versus the control group (Kruskal-Wallis test for multiple comparisons). § *P* < 0.05 versus the 1.0 mg/kg succinylcholine group (Kruskal-Wallis test for multiple comparisons).

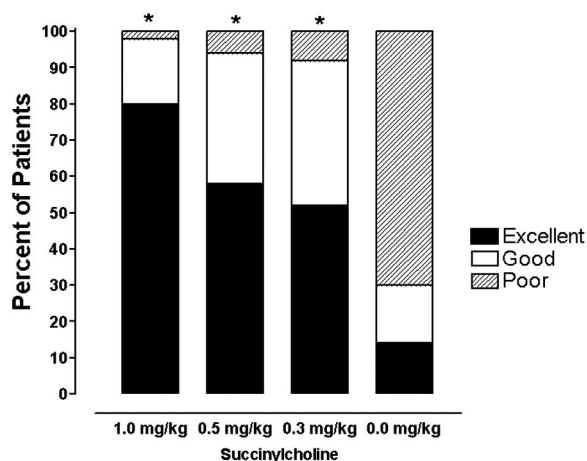


Fig. 1. Intubating conditions with different doses of succinylcholine ( $n = 50$  in each group). \* $P < 0.05$  versus the control group (Kruskal-Wallis test for multiple comparisons).

## Results

There were no significant differences among the four groups regarding baseline demographics (table 2). Tracheal intubation was successful in all patients. The grading of intubations noted in different groups is depicted in figure 1. The incidence of acceptable (excellent plus good grade combined) intubating conditions was significantly greater ( $P < 0.05$ ) in patients receiving all three doses of succinylcholine compared with those in the control group (fig. 1 and table 2). In contrast, there was no significant difference in intubating conditions among the groups receiving succinylcholine.

The calculated doses of succinylcholine (and their 95% confidence intervals) that were required to achieve acceptable intubating conditions in 90% and 95% of pa-

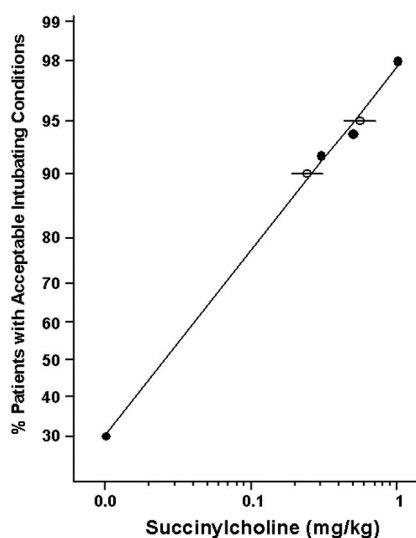


Fig. 2. Percent of patients with acceptable intubating conditions in each group is represented by filled circles. The calculated doses giving 90% and 95% of acceptable intubation at 60 s are the open circles, and the error bars are the 95% confidence intervals.

tients at 60 s were 0.24 (0.19–0.31) mg/kg and 0.56 (0.43–0.73) mg/kg, respectively (fig. 2). Table 2 shows the TOF count observed immediately after tracheal intubation. The number of tactile TOF responses decreased significantly with the increasing dose of succinylcholine.

## Discussion

Compared to the traditional intubating dose of 1.0 mg/kg succinylcholine, we found that a reduction in succinylcholine dose to 0.3 mg/kg or 0.5 mg/kg provided equally acceptable intubating conditions within 60 s. We estimated that 0.56 mg/kg succinylcholine (95% confidence interval, 0.43–0.73 mg/kg) is required to achieve acceptable intubating conditions at 60 s in 95% of patients anesthetized with 2  $\mu$ g/kg fentanyl and 2 mg/kg propofol. This dose represents approximately  $2 \times \text{ED}_{95}$  of succinylcholine.<sup>3,4</sup>

The duration of action of succinylcholine is dose dependent.<sup>7</sup> Thus, reducing the dose of succinylcholine allows a more rapid return of spontaneous respiration and airway reflexes. After intravenous administration of 1.0 mg/kg succinylcholine, recovery of the control single-twitch height (T1) to 10% and 90% ranged from 5.5–8.5 to 10.1–13.2 min, respectively.<sup>7,8</sup> Corresponding recovery times after 0.5 mg/kg succinylcholine were from 4.8 to 8.3 min, respectively.<sup>8</sup> Similarly, we noted with a mechanomyographic recording that the mean times to 10% recovery of T1 after 0.3 mg/kg, 0.5 mg/kg, and 1.0 mg/kg succinylcholine during propofol-fentanyl-nitrous oxide-oxygen anesthesia were 3.7 (2.7–4.7), 4.9 (4.4–5.5), and 8 (7.1–9), respectively (unpublished data, Mohamed Naguib, M.D., 2002–2003). Meistelman *et al.*<sup>9</sup> also reported that the mean time to 25% recovery of T1 was 3.1 min. In patients anesthetized with 15  $\mu$ g/kg alfentanil and 2.5 mg/kg propofol, Nimmo *et al.*<sup>10</sup> reported that the mean durations (ranges) of apnea after 0.0, 0.25, and 0.5 mg/kg succinylcholine were 4.6 (0.5–9.0), 3.6 (1.0–8.0), and 4.5 (2.0–10.0) min, respectively. After 1.0 mg/kg succinylcholine, the mean durations of apnea were 5.2 min and 5.5 min in volunteers<sup>1</sup> and patients,<sup>2</sup> respectively.

Based on the aforementioned data and on the calculations of Benumof *et al.*,<sup>11</sup> it is predicted that for a healthy 70-kg adult and a moderately ill 70-kg adult, arterial oxygen saturation will not decrease below 90%, on average, during the period of apnea induced by 0.5 mg/kg succinylcholine when ventilation is not assisted. In contrast, the same calculations predicted that in the majority of patients with 1 mg/kg succinylcholine-induced apnea, significant to life-threatening hemoglobin desaturation will occur when ventilation is not assisted.<sup>11</sup> However, it should be noted that monitoring the adductor pollicis is not a very useful measure for evaluating the neuromuscular block at the laryngeal, diaphragm, and masseter muscles. The diaphragm recovers faster than



hand muscles after succinylcholine.<sup>12,13</sup> Nevertheless, the calculations of Benumof *et al.*<sup>11</sup> have been substantiated in both volunteers and patients.<sup>1,2</sup> Hayes *et al.*<sup>2</sup> concluded that the use of 1.0 mg/kg succinylcholine “may not always prevent desaturation if there is a failure to intubate and ventilate during a rapid-sequence induction of anesthesia.” Decreasing the dose of succinylcholine (from 1.5 mg/kg to 0.5 mg/kg) has additional clinical advantages by reducing the incidence of succinylcholine-induced myalgia and hemodynamic changes.<sup>14</sup>

The reported range of acceptable intubating conditions after the administration of 1.0 mg/kg succinylcholine varies from 91.8% to 97%.<sup>15–18</sup> Consistent with our results, there is ample evidence in the literature suggesting that acceptable intubating conditions can be achieved with lower doses of succinylcholine. Similarly, Stewart *et al.*<sup>14</sup> reported that 26 (96%) out of 27 patients receiving 1.5 mg/kg succinylcholine and 30 (94%) out of 32 patients receiving 0.5 mg/kg had acceptable intubating conditions.

The dose of succinylcholine must be individualized depending on the clinical situation. There are clinical situations in which “acceptable” conditions for tracheal intubation may not be ideal. For example, in a patient with increased intracranial pressure or in a patient with a full stomach, decreasing the dose of succinylcholine to less than 1.0 mg/kg might increase morbidity. In these situations, anything short of excellent intubating conditions may not be suitable. Our data indicate that 1.0 mg/kg succinylcholine is associated with an 80% incidence of excellent intubating conditions. The reported range of excellent intubating conditions after the administration of 1.0 mg/kg succinylcholine in a simulated rapid-sequence induction varies from 63% to 74%.<sup>15,17,18</sup> However, it seems that doses greater than 1.0 mg/kg succinylcholine will not guarantee excellent intubating conditions in 95% of patients. Stewart *et al.*<sup>14</sup> reported that increasing the succinylcholine dose from 0.5 to 1.5 mg/kg was associated with both a higher incidence of excellent intubating conditions (from 56% to 85%, respectively) and a significantly longer duration of apnea (from 3.8 to 5.6 min, respectively). In another study, excellent intubating conditions were noted in 55% of patients (33 of 60) after 1.5 mg/kg succinylcholine in a simulated rapid-sequence induction.<sup>19</sup>

The reported intubating scores in patients who received no neuromuscular blockers also vary. Pino *et al.*<sup>20</sup> could not intubate any of 10 patients who received a placebo relaxant after 2  $\mu$ g/kg fentanyl and 2 mg/kg propofol induction. Their results are quite different from those we report in this study and could be attributed to time taken to stabilize their mechanomyographic monitoring system before performing laryngoscopy. Similarly, Kahwaji *et al.*<sup>21</sup> reported that intubating conditions were poor or impossible in 19 of 20 subjects when neuromuscular blockers were not administered. In the current

study, we noted a 70% incidence of poor intubating conditions in the control group. We suspect that this was due to the modest doses of fentanyl and propofol used in this study. Increasing the doses of propofol and opioids has been shown to improve intubating conditions without the use of neuromuscular blockers.<sup>22–25</sup> It should also be noted that the interpretation of published intubation protocols is extremely difficult. Kopman *et al.*<sup>26</sup> have reviewed some of these problems. In many reports, anesthetic regimens are not described clearly, and this makes it difficult to interpret the findings. Also, intubation scoring systems still have not been standardized. There is also great variability in the intubation intervals that are reported, and many investigators never specify whether this refers to the onset of laryngoscopy or to actual tube placement.

Frequently, investigators induce anesthesia and take time to stabilize neuromuscular monitoring before giving the relaxant. The intubation data reported in such studies cannot be applied to the clinical situation when intubation is performed soon after induction of anesthesia. Hence, we did not attempt to determine the onset and recovery times of different doses of succinylcholine used in this study. We started the peripheral nerve stimulation immediately after tracheal intubation. The stimulation current used in this study (60 mA) was of a sufficient magnitude to provide supramaximal stimulation. Kopman and Lawson<sup>27</sup> reported that a current of 50–60 mA provides supramaximal stimulation in all patients during anesthesia.

It should be noted that at doses of 0.30 and 0.50 mg/kg succinylcholine, one should not expect to see complete twitch abolition in 60 s at the thumb (table 2). When 0.3- to 0.35-mg/kg doses of succinylcholine are administered, it may take approximately  $\approx$ 2 min for the maximum effect of succinylcholine to manifest.<sup>28,29</sup> Even after 1.0 mg/kg succinylcholine, the time to peak effect at the thumb averages almost 70 s.<sup>28,30</sup> Therefore, one might argue that the conditions for intubation might have improved beyond those reported in this study if laryngoscopy had been delayed by an additional 15 s. There are no data available about the risk of aspiration if the tube is introduced into the trachea at 60–90 s instead of the usually advocated 60 s. It should be noted that intubating conditions depend on several factors, including the type of anesthetic used, the depth of anesthesia, the interval between drug administration and laryngoscopy, the dose of the neuromuscular blocker given, the anatomy of the airways, and the experience of the intubationist.

In conclusion, our study highlights the role of the lower dose of succinylcholine as an alternative to a 1.0-mg/kg dose for tracheal intubation performed within 60 s. In a rapid-sequence induction, we recommend using 0.5–0.6 mg/kg succinylcholine to facilitate tracheal intubation in patients anesthetized with 2  $\mu$ g/kg fentanyl and 2 mg/kg propofol. This technique should be

effective in achieving acceptable intubating conditions at 60 s in 95% of patients. This technique should also allow a rapid return of spontaneous respiration and airway reflexes, thereby decreasing the window of vulnerability in airway management during induction of anesthesia.

The authors thank Michael M. Todd, M.D. (Department of Anesthesia, University of Iowa College of Medicine, Iowa), for suggesting the idea of this study and for his comments on the manuscript.

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