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Succinylcholine Dosage and Apnea-induced Hemoglobin Desaturation in Patients

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Background: **The authors examined the notion that a reduction in succinylcholine dose from 1 mg/kg to ≈0.6 mg/kg would allow a faster recovery of spontaneous ventilation and reduction in the incidence of hemoglobin desaturation during the period of apnea in simulated complete upper airway obstruction situations.**

Methods: **This prospective, randomized, double-blind study involved 60 patients. After preoxygenation to an end-tidal oxygen concentration >90%, patients were anesthetized with 2 μg/kg fentanyl and 2 mg/kg propofol. After loss of consciousness, patients were randomly allocated to receive 0.56 or 1.0 mg/kg succinylcholine or saline (control group). Oxygen saturation was monitored continuously at the index finger. When the patient became apneic, the face mask was removed and the patient's airway was left unsupported. If the oxygen saturation decreased to 90%, the face mask was reapplied, and ventilation was assisted until the patient was awake. Time from injection of the study drug to the first visible spontaneous diaphragmatic movements was noted.**

Results: **Oxygen saturation decreased <90% in 45%, 65%, and 85% of patients in the control, 0.56 mg/kg, and 1.0 mg/kg succinylcholine groups, respectively ($P = 0.03$). Corresponding times (mean ± SD) to spontaneous of diaphragmatic movements were 2.7 ± 1.2, 4.8 ± 2.5, and 4.7 ± 1.3 min, respectively. These times were longer ($P < 0.001$) after either dose of succinylcholine compared with controls.**

Conclusions: **Reduction in succinylcholine dose from 1.0 mg/kg to 0.56 mg/kg decreased the incidence of hemoglobin saturation <90% from 85% to 65% but did not shorten the time to spontaneous diaphragmatic movements. A significant fraction of patients would be at risk if there were failure to intubate and ventilate whether succinylcholine is administered or not and regardless of the dose of succinylcholine administered.**

BASED on a mathematical model of hemoglobin desaturation during apnea, Benumof *et al.*[1] predicted that in the large majority of patients with 1 mg/kg succinylcholine-induced apnea, significant to life-threatening hemoglobin desaturation will occur when ventilation is not assisted. This theoretical analysis prompted two studies. Heier *et al.*[2] reported that significant hemoglobin desaturation (Sa_{O_2} ≤80%) occurred in one third of volunteers during the period of apnea induced by 1 mg/kg succinylcholine. In another report, Hayes *et al.*[3] 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."

Consequently, the use of the 1.0 mg/kg dose of succinylcholine has been questioned, and it was proposed that a lower dose (≈0.6 mg/kg) of succinylcholine might be a preferable alternative.[4,5] The premises of this proposal are that intubating conditions[4] are not much different among patients who receive either 0.6 or 1.0 mg/kg, and decreasing the dose of succinylcholine to ≈0.6 mg/kg would allow a more rapid recovery of spontaneous ventilation. This, in turn, would decrease the incidence of life-threatening hypoxemia in patients with unanticipated difficult airways when ventilation cannot be assisted. In light of the aforementioned reports, we thought to determine the validity of the hypothesis that a lower dose of succinylcholine would allow for a greater margin of safety in airway management.

The aim of this prospective, randomized, double-blind, placebo-controlled study was to compare the duration of apnea and the incidence of hemoglobin desaturation after administration of 0.0, 0.56, and 1.0 mg/kg of succinylcholine in healthy patients. The 0.56 mg/kg succinylcholine is the calculated dose of succinylcholine that is required to achieve acceptable intubating conditions in 95% of patients at 60 s.[4]

This article is featured in "This Month in Anesthesiology." Please see this issue of ANESTHESIOLOGY, page 5A.

Materials and Methods

After obtaining institutional approval (King Khalid University Hospital, Riyadh, Saudi Arabia) and informed consent, we studied 60 nonsmoking patients of both sexes with American Society of Anesthesiologists physical status I, aged 31.2 ± 5.6 yr (mean ± SD) and weighing 74.4 ± 11.4 kg. All patients underwent elective procedures, had a normal airway anatomy, no neuromuscular, renal, or hepatic disease, and none were taking any drug known to interfere with neuromuscular function. No premedication was administered. An infusion of lactated Ringer's solution was started before induction of anesthesia. Standard monitoring was used. Hemoglobin satu-

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ration was monitored continuously at the index finger using a Nellcor pulse oximeter module incorporated into a Dräger Julian anesthesia machine (Dräger Medical AG & Co., Lübeck, Germany) with Nellcor sensor (Model DS100-A; Nellcor Durasensor, Pleasanton, CA) using beat-to-beat mode.

The ability to ventilate the patient's lungs was tested before induction of anesthesia by applying positive airway pressure *via* a tightly fitting mask. Thereafter, all patients inhaled 100% oxygen from the anesthesia circuit *via* a face mask for a minimum of 3 min and until the expired oxygen concentration was >90%. After preoxygenation, anesthesia was induced with 2 μg/kg fentanyl and 2 mg/kg propofol. When the patient lost consciousness, one of the following doses was administered in a rapidly flowing intravenous: 0.56, or 1.0 mg/kg succinylcholine, or saline (control group). Succinylcholine and placebo (saline) were prepared in coded syringes to achieve double blinding. The coded syringes were prepared by a pharmacist using a randomization schedule provided in sealed envelopes according to a computer-generated list. All other personnel were blinded as to the patient's treatment group. Each patient was randomly assigned to a particular dosage group or to the control group (n = 20 in each group). When the patient became apneic, the face mask was removed and the patient's airway left unsupported. If the hemoglobin saturation decreased to 90%, the face mask was reapplied, and ventilation was assisted until the patient was awake. Throughout the study period, an investigator reassured patients that everything was under control. The patient's abdomen was continuously observed for respiratory movements. Times from injection of the study drug to the first visible spontaneous diaphragmatic movements (or the duration of apnea) and to spontaneous eye opening were noted. Thereafter, the study was terminated and anesthesia continued as appropriate for surgery.

The patient's experience from participation in the study was assessed twice by an investigator blinded as to the group assignment using a questionnaire originally developed by Heier *et al.*[2] The first assessment was done in the recovery room and before discharge and repeated 1 week later when the patient was contacted by the same investigator in a follow-up telephone interview.

Statistical Analysis

Data were analyzed with analysis of variance or chi-square test, where appropriate. If analyses of variance were significant, then the Dunnett *post hoc* test was used to compare the study groups to the control group. Comparisons among the three groups were carried out using the Tukey Studentized range method. The relation between apnea duration and lowest oxygen saturation (Spo_2) was estimated by least squares linear regression analysis. Stepwise discriminant analysis was performed to test the influence of body mass index (BMI), time to spontaneous diaphragmatic movements, age, and gender as predictors for oxygen desaturation to less than 90%. Statistical analyses were carried out using the BMDP statistical package (release 7.01, University of California Press, Berkeley, CA, 1994) and StatXaxt for Windows (version 6.0, CYTEL Software Corporation, Cambridge, MA). Unless otherwise specified, results were expressed as mean and SD and were considered significant at $P < 0.05$.

Table 1. Demographic Data

	Succinylcholine (mg/kg)		
	0.56 (n = 20)	1.0 (n = 20)	Control 20
Age (yr)	31.8 ± 3.9	31.3 ± 7.7	30.5 ± 5.6
Weight (kg)	73.3 ± 10.6	78.4 ± 11.7	71.5 ± 11.3
Sex (Male/Female)	18/2	17/3	13/7
Height (cm)	170 ± 7.9	170 ± 8.1	165 ± 8.9
Body mass index (kg/m^2)	25.4 ± 3.6	26.9 ± 2.9	26.1 ± 3.2

Data are mean ± SD. No significant differences were noted.

Results

There were no significant differences among the three groups regarding baseline demographic values (table 1). In all patients, end-tidal oxygen concentration was >90% and the preinduction values for Spo_2 were between 98% and 100% except for two patients (one in the control group and the other in the succinylcholine 0.56 mg/kg group) in whom it was 95% and 96%, respectively.

Times to spontaneous diaphragmatic movements were significantly longer ($P < 0.001$) in patients who received succinylcholine (0.56 mg/kg or 1.0 mg/kg) compared with the control group (fig. 1). Times to the return of diaphragmatic movements were 2.7 ± 1.2, 4.8 ± 2.5, and 4.7 ± 1.3 min in the control, succinyl-

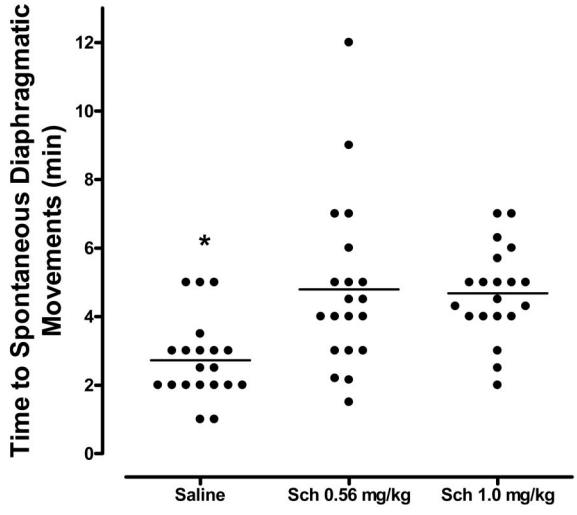

Fig. 1. Time to spontaneous diaphragmatic movements (or the duration of apnea) in different groups. *Horizontal lines* present the mean values. *$P < 0.001$ *versus* succinylcholine (Sch) groups.

choline 0.56 mg/kg, and succinylcholine 1.0 mg/kg groups, respectively.

The changes in Spo_2 *versus* times are shown in figure 2. Oxygen saturation (Spo_2) decreased to less than 90% in nine (45%), 13 (65%), and 17 (85%) patients in the control, succinylcholine 0.56 mg/kg, and succinylcholine 1.0 mg/kg groups, respectively ($P = 0.03$). A chi-square analysis disclosed a highly significant linear trend ($P = 0.009$) for doses (0.0, 0.56, and 1.0 mg/kg), indicating a dose-response relationship, although the difference between the 0.56 and 1.0 mg/kg doses was not significant ($P = 0.3$). These patients required airway support and assisted ventilation. Times to spontaneous diaphragmatic movements did not significantly ($P = 0.08$) correlate with the lowest Spo_2 reached (fig. 3).

Stepwise discriminant analysis revealed that both BMI ($P = 0.024$) and times to spontaneous diaphragmatic movements ($P = 0.037$) were significant predictors for the frequency of desaturation to less than 90%. The relation between BMI and Spo_2 in different groups is presented in table 2.

Times to spontaneous eye opening were 6.2 ± 2.5, 7.3 ± 2.2, and 7.4 ± 1.6 min in the control, succinylcholine 0.56 mg/kg, and succinylcholine 1.0 mg/kg groups, respectively (not significant). The anesthetic procedure was uneventful in all patients. No patient experienced awareness in this study. Two patients (one in the control group and the other in the succinylcholine 1.0 mg/kg group) reported that they were anxious before induction of anesthesia. However, no patient reported any manifestations of distress 1 week later. All patients reported that they were prepared to participate in a second study. Postoperative myalgia of varying intensity was reported in four patients who received succinylcholine (two in each of the succinylcholine groups) and lasted for 1–3 days.

Discussion

In this study, we simulated the inability to intubate or ventilate situations in anesthetized patients during succinylcholine-induced apnea. We noted a 45% incidence of hemoglobin desaturation (Spo_2 <90%) in the control group. Compared with the traditional intubating dose of 1.0 mg/kg succinylcholine, we found that 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 hemoglobin desaturation (Spo_2 <90%) in American Society of Anesthesiologists physical status I patients anesthetized with 2 μg/kg fentanyl and 2 mg/kg propofol. The difference in the incidence of hemoglobin desaturation between the 1.0 mg/kg succinylcholine group and the control group was 40% (85% *versus* 45% incidence, respectively). On the other hand, the difference in the incidence of hemoglobin desaturation be-

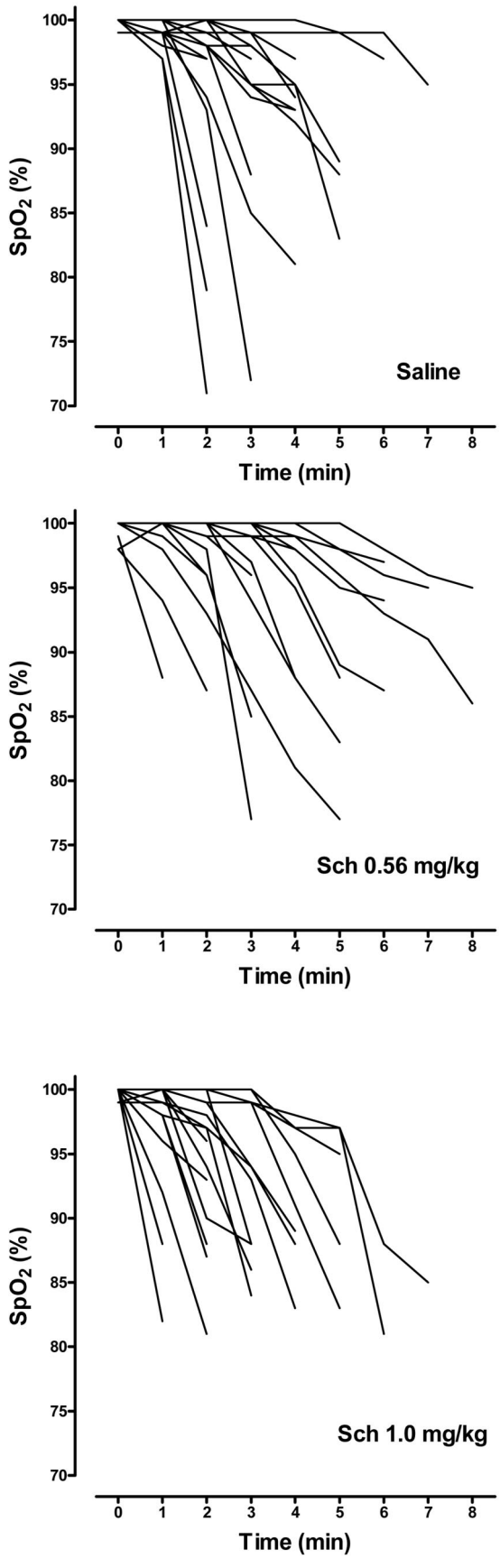

Fig. 2. Oxygen saturation (Spo_2) *versus* time in different groups.

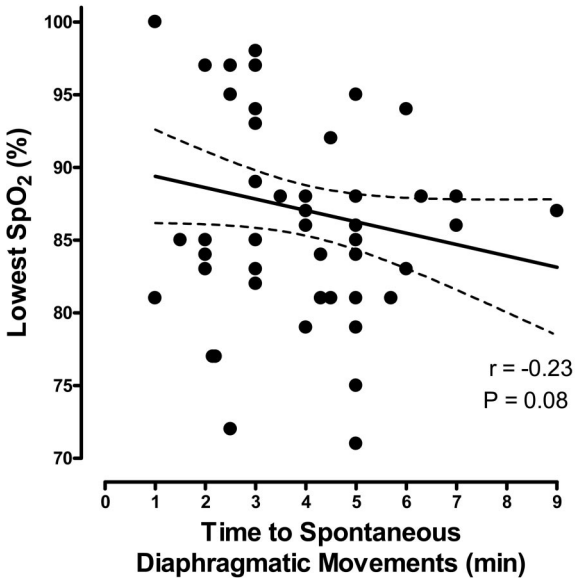

Fig. 3. The relation between apnea duration and lowest oxygen saturation (Spo_2).

tween the 0.56 mg/kg succinylcholine group and the controls is 20% (65% *versus* 45% incidence, respectively). Therefore, the reduction in the incidence of hemoglobin desaturation noted with the 0.56 mg/kg group represents a 50% improvement over that seen with the 1.0 mg/kg group (20% compared with 40%, respectively).

We noted that after 1.0 mg/kg of succinylcholine, the time to spontaneous diaphragmatic function was 4.8 ± 2.5 min and was not different from 4.7 ± 1.3 min noted after 0.6 mg/kg. El-Orbany *et al.*[6] noted that the mean times (± SD) to spontaneous diaphragmatic movements after 0.6 mg/kg and 1.0 mg/kg succinylcholine were 3.41 ± 0.6 and 5.3 ± 8.0 min, respectively ($P < 0.05$). Previous studies have shown that a reduction of succinylcholine dosage from 1.0 mg/kg to 0.5 mg/kg reduced the duration of succinylcholine by more than 3 min (as measured by time to 10% recovery of twitch tension).[7–9] Recently, Kopman *et al.*[5] demonstrated that this difference is <90 s (6.2 *versus* 5.1 min, respectively) after a 40% reduction in dose to 0.6 mg/kg succinylcholine. Doubling the dose would not double the duration of action but it would increase the duration by one half-life. Kopman *et al.*[5] also demonstrated that although time to 90% recovery of twitch tension of 0.6 mg/kg *versus* 1.0 mg/kg succinylcholine is 1.7 min different (on average), this difference is <60 s at 10–25% recovery of twitch tension. At this level, the diaphragm should have a greater degree of recovery than the adductor pollicis muscle. It is widely recognized that the centrally located muscles of respiration, including the diaphragm, recover faster than the adductor pollicis from a neuromuscular block.[10,11] The aforementioned discussion might explain why we did not observe any difference in the time to spontaneous diaphragmatic function between the two doses of succinylcholine. It should be noted, however, that the return of diaphragmatic movements should not be equated with the adequate functional recovery of muscles necessary to maintain airway patency.[12]

Benumof *et al.*[1] assumed that the time to 50% recovery of twitch tension from 1 mg/kg succinylcholine block (≈8.5 min) is the time to functional recovery (defined as "life-sustaining spontaneous ventilation"). Our results, however, do not support this contention. We noted that the mean time for the return of diaphragmatic movements in the control group was 2.7 min, which was increased by 170% (to ≈4.7 min) after administration of either dose of succinylcholine. In fact, the time to spontaneous eye opening in our patients was <8.5 min. Consistent with our results, Hayes *et al.*[3] reported that recovery of diaphragmatic movements occurred 4.7 (SD ± 1.5–2.0) min after administration of 1 mg/kg succinylcholine in patients anesthetized with 1 μg/kg fentanyl and 3–7 mg/kg thiopental. Similarly, in volunteers who received 5 mg/kg thiopental and 1 mg/kg succinylcholine, Heier *et al.*[2] noted diaphragmatic activity 5.2 (SD ± 1.5–2.0) min after drug injection.

In this study, hemoglobin desaturation (Spo_2 <90%) occurred in 65% and 85% of patients who received 0.56 mg/kg and 1.0 mg/kg succinylcholine, respectively, compared to 45% in the control group. There is a linear trend for dose (0.0, 0.56, and 1.0 mg/kg succinylcholine) indicating a dose-response. However, the incidence of hemoglobin desaturation was not significantly different between the two doses of succinylcholine studied, likely owing to an insufficient number of patients studied. Perhaps increasing the number of patients would reveal such difference. We did not perform *a priori* power analysis because preliminary data were not available for such an analysis. Nevertheless, the fact that there was a

Table 2. Body Mass Index and Hemoglobin Saturation

	Patients with Spo_2 < 90%			Patients with Spo_2 > 90%		
Group	No.	BMI	Spo_2	No.	BMI	Spo_2
Control	9	26.7 ± 2.5	82.8 ± 7.2	11	25.5 ± 3.9	96.5 ± 2.0*
Succinylcholine 0.56 mg/kg	13	26.2 ± 3.5	84.4 ± 4.4	7	23.8 ± 3.3	95.9 ± 1.3*
Succinylcholine 1.0 mg/kg	17	27.3 ± 2.7	85.3 ± 2.9	3	25.2 ± 4.3	94.7 ± 1.5*

Data are mean ± SD.

BMI = body mass index; Spo_2 = hemoglobin saturation.

* $P < 0.0001$ compared to the other group.

20% absolute decrease in the incidence of hemoglobin desaturation (or a 50% relative improvement) after 0.56 mg/kg compared with 1.0 mg/kg should not detract the clinician from a 45% incidence of hemoglobin desaturation seen in the absence of a neuromuscular blocker in our controls. One, therefore, could extrapolate that a significant fraction of patients would not be able to maintain adequate hemoglobin saturation if there were to be a failure to intubate and ventilate after induction of anesthesia. It is known that propofol is associated with a higher incidence of apnea compared with thiopental (77% [23 of 30] *versus* 53% [16 of 30], respectively)[13] and this might be a factor contributing to our results. The influence of anesthetics *per se* on duration of apnea and hemoglobin desaturation was not addressed in previous studies.[2,3]

Based on Benumof *et al.*'s calculations,[1] it is predicted that for a healthy 70-kg adult with 1 mg/kg succinylcholine-induced apnea, Sao_2 will start to decrease to less than 90% after 8.0 min. Our data do not support this prediction. In this study, times to spontaneous diaphragmatic movements were 2.7 ± 1.2, 4.8 ± 2.5, and 4.7 ± 1.3 min in the control, succinylcholine 0.56 mg/kg, and succinylcholine 1.0 mg/kg groups, respectively. Despite this duration of apnea shorter than that predicted by Benumof *et al.*,[1] a significant fraction of our patients had Spo_2 <90% during the period of apnea (fig. 1).

Of note, a high percentage of healthy patients started to desaturate after relatively short periods of time (fig. 2). At 2 min, a significant minority of our patients (13% of all patients) had Spo_2 < 90%. Hayes *et al.*[3] noted that after preoxygenation for 3 min, 8% (2 of 25) of their patients had Spo_2 <90 after 2.9 min (range, 1.7–4.0 min). However, Gambee *et al.*[14] reported that after preoxygenation for 3 min, time to Spo_2 = 90% ranged from 8.2 to 11 min. Alveolar gas exchange during apnea (with patent airway) entails both oxygen uptake and linear increase in mixed venous (and hence the alveolar) carbon dioxide tension.[15] If the airway is occluded, the lung volume decreases by the difference between the oxygen uptake and the carbon dioxide output. However, this difference in the lung volume is replaced by mass movement of the ambient gas down the trachea if the airway is patent.[16] In this study, with an approximately 2000 ml of oxygen available after preoxygenation (assuming a functional residual capacity of 2000 ml), and assuming an oxygen uptake of 250 ml/min from the lung and an initial alveolar fraction of oxygen (FAo_2) of 0.8, decreased oxygen saturation in less than 4–5 min are surprising. After preoxygenation, the rate of hemoglobin desaturation during apnea depends on several factors: reduced functional residual capacity (this will result in an increase in shunt fraction because of collapse of alveoli) and increased oxygen consumption and, to a lesser degree, hemoglobin concentration and respiratory quotient.[17] Hemoglobin desaturation with apnea probably occurs with the onset of shunting. The more rapid desaturation noted in this study than that simulated by Benumof *et al.*,[1] which was independent of time, strongly implies that early onset of shunting plays an important role in our observations. In accordance with our data (fig. 2), Heier *et al.*[2] demonstrated that hemoglobin desaturation persists some time afterward. In this study, stepwise discriminant analysis disclosed that that both BMI (P = 0.024) and times to spontaneous diaphragmatic movements (P = 0.037) were significant predictors for the frequency of desaturation to less than 90%. Increases in BMI are associated with reductions in functional residual capacity, oxygenation, and respiratory compliance and increases in total respiratory resistance and work of breathing.[18]

Heier *et al.*[2] noted that hemoglobin desaturation (Spo_2 <90%) occurred in 42% (5 of 12) of their volunteers after administration of 5 mg/kg thiopental and 1 mg/kg succinylcholine. Compared to our results, Heier *et al.*[2] reported a similar duration of apnea but a less frequent incidence of hemoglobin desaturation. This could be explained by the fact that the subject population was intentionally thin (an average BMI of 23.4) in Heier *et al.*'s study compared with our patient population with an average BMI of 26.1 (SD ± 3.3).

In this study, the induction sequence (2 μg/kg fentanyl and 2 mg/kg propofol) was chosen to mimic normal anesthetic practice. One may extrapolate from this study that the incidence and magnitude of hemoglobin desaturation likely would be greater in the patients who have some degree of pulmonary dysfunction or decreased functional residual capacity if ventilation cannot be assisted. Reductions in the functional residual capacity and closing capacity (the oxygen reserves in the lungs) by ≈20% occur shortly after induction of anesthesia in almost all patients.[19,20] Greater reductions are seen during pregnancy, in obese and elderly persons, and in patients with chronic obstructive airway disease.[20–23]

In this study we used beat-to-beat mode of pulse oximetry. The commonly used mode in clinical practice is the "normal mode" that has a 10-s averaging time. This means that there is a delay after the actual hemoglobin saturation starts to decrease because the signal is averaged over 10 s. However, beat-to-beat mode allows precise determination of the degree of hemoglobin saturation on a beat-to-beat basis.

References

1. Benumof JL, Dagg R, Benumof R: Critical hemoglobin desaturation will occur before return to an unparalyzed state following 1 mg/kg intravenous succinylcholine. Anesthesiology 1997; 87:979–82

2. Heier T, Feiner JR, Lin J, Brown R, Caldwell JE: Hemoglobin desaturation after succinylcholine-induced apnea: A study of the recovery of spontaneous ventilation in healthy volunteers. Anesthesiology 2001; 94:754–9

3. 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

4. Naguib M, Samarkandi A, Riad W, Alharby SW: Optimal dose of succinylcholine revisited. ANESTHESIOLOGY 2003; 99:1045–9

5. Kopman AF, Zhaku B, Lai KS: The "intubating dose" of succinylcholine: the effect of decreasing doses on recovery time. ANESTHESIOLOGY 2003; 99:1050–4

6. 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

7. Viby-Mogensen J: Correlation of succinylcholine duration of action with plasma cholinesterase activity in subjects with the genotypically normal enzyme. ANESTHESIOLOGY 1980; 53:517–20

8. Miguel R, Witkowski T, Nagashima H, Fragen R, Bartkowski R, Foldes FF, Shanks C: Evaluation of neuromuscular and cardiovascular effects of two doses of rapacuronium (ORG 9487) versus mivacurium and succinylcholine. ANESTHESIOLOGY 1999; 91:1648–54

9. Hayes A, Breslin D, Reid J, Mirakhur RK: Comparison of recovery following rapacuronium, with and without neostigmine, and succinylcholine. Anaesthesia 2000; 55:859–63

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. Donati F, Meistelman C, Plaud B: Vecuronium neuromuscular blockade at the adductor muscles of the larynx and adductor pollicis. ANESTHESIOLOGY 1991; 74:833–7

12. Pavlin EG, Holle RH, Schoene RB: Recovery of airway protection compared with ventilation in humans after paralysis with curare. ANESTHESIOLOGY 1989; 70:381–5

13. Kim DW, Kil HY, White PF: Relationship between clinical endpoints for induction of anesthesia and bispectral index and effect-site concentration values. J Clin Anesth 2002; 14:241–5

14. Gambee AM, Hertzka RE, Fisher DM: Preoxygenation techniques: Comparison of three minutes and four breaths. Anesth Analg 1987; 66:468–70

15. Cherniack NS, Longobardo GS: Oxygen and carbon dioxide gas stores of the body. Physiol Rev 1970; 50:196–243

16. Nunn's Applied Respiratory Physiology, Fifth Edition. Edited by Lumb AB. Oxford, Butterworth-Heinemann, 2000, pp 239–241

17. Hardman JG, Wills JS, Aitkenhead AR: Factors determining the onset and course of hypoxemia during apnea: An investigation using physiological modelling. Anesth Analg 2000; 90:619–24

18. Pelosi P, Croci M, Ravagnan I, Tredici S, Pedoto A, Lissoni A, Gattinoni L: The effects of body mass on lung volumes, respiratory mechanics, and gas exchange during general anesthesia. Anesth Analg 1998; 87:654–60

19. Juno J, Marsh HM, Knopp TJ, Rehder K: Closing capacity in awake and anesthetized-paralyzed man. J Appl Physiol 1978; 44:238–44

20. Wahba RW: Perioperative functional residual capacity. Can J Anaesth 1991; 38:384–400

21. Baraka AS, Hanna MT, Jabbour SI, Nawfal MF, Sibai AA, Yazbeck VG, Khoury NI, Karam KS: Preoxygenation of pregnant and nonpregnant women in the head-up versus supine position. Anesth Analg 1992; 75:757–9

22. Wahba WM: Influence of aging on lung function: Clinical significance of changes from age twenty. Anesth Analg 1983; 62:764–76

23. Damia G, Mascheroni D, Croci M, Tarenzi L: Perioperative changes in functional residual capacity in morbidly obese patients. Br J Anaesth 1988; 60:574–8