

Hemoglobin Desaturation after Succinylcholine-induced Apnea

A Study of the Recovery of Spontaneous Ventilation in Healthy Volunteers

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Background: Because of the rapid recovery of neuromuscular function after succinylcholine administration, there is a belief that patients will start breathing sufficiently rapidly to prevent significant oxygen desaturation. The authors tested whether this belief was valid.

Methods: Twelve healthy volunteers aged 18–45 yr participated in the study. After preoxygenation to an end-tidal oxygen concentration greater than 90%, each subject received 5 mg/kg thiopental and 1 mg/kg succinylcholine. Oxygen saturation (Sa_{O_2}) was measured at both a finger and an ear lobe (beat to beat). During the period of apnea and as they were recovering, the volunteers received continuous verbal reassurance by the investigators. If the Sa_{O_2} decreased below 80%, the volunteers received chin lift and, if necessary, assisted ventilation. The length of time the subject was apneic and level of desaturation were related by linear regression analysis. One hour after recovery and again 1 week later, subjects were asked a series of questions regarding their emotional experience.

Results: In six volunteers, Sa_{O_2} decreased below 95% during apnea; in four, Sa_{O_2} decreased below 80%, necessitating chin lift and assisted ventilation in three. Apnea time was significantly longer in volunteers who reached Sa_{O_2} less than 80% than in those who did not (7.0 ± 0.4 and 4.1 ± 0.3 min, respectively), and there was a significant correlation between the length of time the subject was apneic and the magnitude of desaturation.

Conclusions: Spontaneous recovery from succinylcholine-induced apnea may not occur sufficiently quickly to prevent hemoglobin desaturation in subjects whose ventilation is not assisted.

SUCCINYLCOLINE is the muscle relaxant with the fastest onset and recovery time.¹ Consequently, it is believed by many anesthesiologists that the recovery of muscle function after succinylcholine administration occurs sufficiently quickly to permit a safety margin in airway management during induction of anesthesia. This belief is based on a combination of facts; first, after preoxygenation for 3 min, oxygen saturation (Sa_{O_2}) will be greater than 98% after 5 min of apnea²; second, after 1 mg/kg succinylcholine, recovery of function of the

diaphragm and laryngeal muscles starts within 5 min.^{3,4} However, the validity of this belief has been challenged on the basis of a simulation suggesting that hemoglobin desaturation will occur before recovery of adequate spontaneous breathing after succinylcholine administration.⁵ This simulation has not been verified in humans.

The aim of this study was to investigate whether spontaneous respiration recovers in time to prevent significant hemoglobin desaturation after the administration of standard clinical doses of thiopental and succinylcholine in healthy volunteers.

Methods

This study was approved by our local institutional review board (University of California–San Francisco Committee on Human Research, Office of Research Administration, San Francisco, California), and 12 fasted healthy volunteers gave written informed consent to participate. As a part of the consent process, volunteers were specifically informed of the risks of hypoxia, such as brain damage and cardiac arrest. In addition, they were counseled as to the possibility of being aware and paralyzed and that they might feel a strong sense of panic because they could not breathe. Specific exclusion criteria were age less than 18 or greater than 45 yr, body mass index greater than 30, Malampatti airway grade 2–4, known allergy to thiopental or succinylcholine, family history of anesthesia-related complications, or alcohol or drug abuse. The volunteers were specifically informed about the nature of the drugs that would be administered and the possibility that they might recover consciousness before being able to breathe adequately.

For the study, subjects wore only shorts and a tee shirt and lay in the supine position on a gurney. Monitors were placed to measure noninvasive blood pressure (every minute for 12 min, then every 5 min for a further 20 min), continuous electrocardiography, capnography, and pulse oximetry. Hemoglobin saturation was measured (Nellcor Model N-200; Mallinckrodt Inc., St. Louis, MO) continuously at both an index finger (standard mode, averaging signals collected in 6-s epochs) and an earlobe (clinical research mode, for beat to beat monitoring). A 20-gauge intravenous catheter was placed for administration of fluid and drugs. Nerve stimulation was performed *via* surface electrodes placed over the sub-

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Received from the Department of Anesthesia and Perioperative Care, University of California, San Francisco, California. Submitted for publication July 5, 2000. Accepted for publication November 15, 2000. Support was provided solely from institutional and/or departmental sources.

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ject's ulnar nerve at the wrist. The current was increased until the subject's thumb started to twitch, the purpose being to alert the investigators to the possibility of a subject having plasma cholinesterase deficiency.

The volunteers breathed 100% oxygen through a tight-fitting face mask for a minimum of 3 min and until expired oxygen concentration was greater than 90%. While still awake, subjects were asked to relax and stop breathing while the anesthesiologist applied positive airway pressure to ensure that investigators could ventilate each subject's lungs. The time needed to obtain an end-tidal oxygen concentration greater than 90% was recorded.

When preoxygenation was complete, anesthesia was induced with 5 mg/kg intravenous thiopental. Immediately after loss of consciousness, 1.0 mg/kg succinylcholine was administered. When the subject ceased making respiratory efforts (apnea), the face mask was removed and the patient's airway left unsupported. During the subsequent period of observation, the face mask was reapplied, and chin lift or assisted ventilation commenced only if the hemoglobin saturation decreased to 80%. This level of hypoxia was chosen based on the SaO_2 tolerated by subjects in studies of pulse oximeter accuracy⁶ and hypoxic ventilatory responsiveness.⁷ The face mask was once again removed when SaO_2 increased to greater than 98% and if the patient was awake, able to talk, and had regained a firm hand grip. SaO_2 was continuously measured until values were stable at greater than 95% for more than 10 min while the volunteer was breathing room air. The need for additional airway support (chin lift or assisted ventilation) was noted.

Throughout the period from loss of consciousness until the subject had fully recovered, the investigators talked gently to the subject, reassuring them that all was well and that everything was under control. Every 30 s they were asked to open their eyes and squeeze the observer's hand. The subject's abdomen was continuously observed for respiratory movements. Duration of apnea as measured by time to spontaneous diaphragm movement, and eye opening and hand squeeze on command were measured from injection of drugs until the first sign of recovery of each modality.

The subjects were observed for an hour after recovery from anesthesia. At this time they were asked to answer a questionnaire designed to explore their experience from participation in the study (table 1). Special emphasis was placed on detecting awareness and to relieve the emotional distress that the subject might have experienced from being aware but unable to breathe. The questionnaire was repeated in a follow-up telephone conversation with each subject 1 week after the study. The presence of awareness of paralysis, breathlessness, and emotional distress was recorded.

The subjects were discharged home after the study, accompanied by a friend, a significant other, or one of

Table 1. Questionnaire Presented to Volunteers 1 h after Conclusion of the Experiment and Repeated in a Follow-up Telephone Interview 1 Week after the Study

Order of Questions Asked
What is the last thing you remember before going to sleep?
What was the first thing that came to your mind after going to sleep?
Were you awake without being able to signal consciousness?
Did you have a strong desire to breathe?
If you were aware without the ability to breathe, how would you describe your emotional response?
Calm? Why?
Worried? Why?
Frightened? Why?
How do you feel now before going home?
Relaxed?
Worried?
Would you do the experiment again?
Do you have any muscle pain?

the investigators. Volunteers were counseled that they should not drive or operate hazardous equipment until the next day.

Statistical Analysis

The difference between recovery times (apnea duration *vs.* eye opening *vs.* hand squeeze) was tested using the Dunnett test (analysis of variance). The difference in apnea duration between groups with and without significant oxyhemoglobin desaturation ($SaO_2 > 95\%$ *vs.* $< 80\%$) was tested using an unpaired *t* test, and the relation between apnea duration and the lowest attained SaO_2 value was analyzed by least squares linear regression analysis. A *P* value < 0.05 was considered statistically significant.

Results

Two female and 10 male volunteers were studied. Mean age, weight, and height were 27 ± 6 yr (range, 18–36 yr), 70 ± 13 kg (range, 51–88 kg), and 173 ± 9 cm (range, 158–188 cm), respectively. The size of our volunteer population was not sufficiently large to analyze the data for possible gender differences.

End-tidal oxygen concentration was between 90 and 95% in all volunteers at the time of drug administration. Only one subject had end-tidal oxygen concentration less than 90% after 3 min of preoxygenation (84%) and needed an additional 1 min for end-tidal SaO_2 to increase above 90%.

In six volunteers, SaO_2 decreased below 95% during the apnea time. In four volunteers SaO_2 decreased below 80% (fig. 1 and table 2), necessitating chin lift alone in one and both chin lift and assisted ventilation for 1–2 min in three (table 2). An open airway was easily maintained in all four of these volunteers. Apnea duration was significantly longer in volunteers who reached

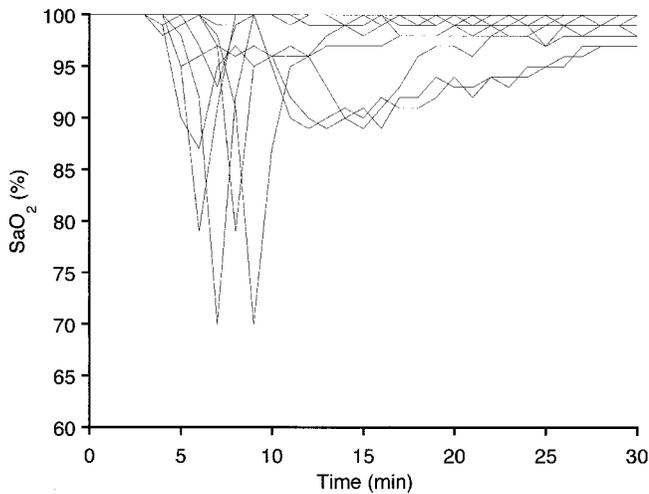


Fig. 1. Changes in oxygen saturation (SaO_2) with time in all 12 volunteers.

SaO_2 less than 80% than in those who did not (7.0 ± 0.4 and 4.1 ± 0.3 min, respectively), and there was a significant correlation between apnea duration and the lowest SaO_2 reached ($R^2 = 0.78$; fig. 2).

Mean values for apnea duration, eye opening on command, and hand squeeze were 5.2, 5.7, and 7.7 min, respectively. Recovery times of spontaneous breathing and eye opening to command were not different, and both were significantly shorter than commencement of the recovery of the ability to hand squeeze (table 2). In two volunteers, the recovery time of eye opening to command was shorter than the apnea duration (by 2 and 2.5 min; table 2).

Figure 1 shows the changes in SaO_2 with time in all 12 volunteers. After restoration of adequate spontaneous ventilation and SaO_2 greater than 98%, a second phase occurred in four volunteers, characterized by a moderate decrease in SaO_2 with a duration of approximately 15 min. Twenty-five minutes after drug administration, all volunteers had SaO_2 values greater than 95%. This secondary decrease in SaO_2 was accentuated in the three volunteers who needed assisted ventilation (fig. 1) and was associated with significant coughing.

The recordings of heart rate, blood pressure, and SaO_2 in volunteer 9 are shown in figure 3. The apnea period was associated with significant increases in blood pressure and heart rate in all volunteers.

Seven volunteers experienced awareness during the period of apnea and reported either recall of specific words spoken to them by the observers or that they were unable to breathe or move certain parts of their body (table 3). Five of these seven volunteers reported emotional distress, which was partially relieved by the observer talking to them. For all five, the distress was because they had a strong urge to breathe but were unable to do so. The awareness of muscle paralysis by itself was not reported as causing distress (table 3). None

of the volunteers reported any symptoms of emotional distress at 1 week after the study.

Six volunteers had myalgia of varying severity the day after the study, and for one the myalgia persisted for 3 days. All of the volunteers stated that they would participate in a second similar study if asked to do so.

Discussion

We found that significant hemoglobin desaturation occurred in one third of our subjects during the period of apnea after administration of 1 mg/kg succinylcholine. Because we removed the face mask after onset of paralysis, our study design represents the worst case scenario of complete upper airway obstruction, where not even apneic oxygenation is occurring. It is likely that our results underestimate the incidence of desaturation that would occur with patients given a similar dose of succinylcholine and whose lungs could not be ventilated or their trachea intubated. There are several differences between our healthy subjects and patients in the clinical setting that would predispose the latter to greater risk of desaturation. All of our volunteers were young, healthy, and slim and had optimal preoxygenation. Increasing age is associated with decreasing functional residual capacity, which is the reservoir for oxygen during apnea.^{8,9} Thus, patients older than our group of volunteers would be expected to undergo more rapid desaturation than our subjects. Our volunteers were of normal weight, but many patients have some degree of obesity, a disease that decreases functional residual capacity and predisposes the patient to desaturation.^{8,10} In contrast to our volunteers, a proportion of patients have preexisting disease processes that compromise lung function and that would predispose to desaturation.⁸

It is not only physical characteristics as described that suggest that the incidence of desaturation would be greater in patients than in our volunteers. For all of our subjects, preoxygenation was optimized by ensuring a good mask seal and taking the time to achieve an end-tidal oxygen concentration greater than 90%. This may not always be possible in the clinical setting, for instance, if the patient is uncooperative or a good mask seal cannot be obtained. It is obvious that the less good the preoxygenation the greater the risk of desaturation. Finally, our volunteers received only 5 mg/kg thiopental and no other drugs with respiratory depressant effects. In the clinical situation, patients often receive benzodiazepines or opioids, which can prolong the period of apnea by direct respiratory depression, and thus increase the likelihood of desaturation.

Our results confirm the simulation of Benumof *et al.*⁵ and suggest very strongly that there is no margin of safety conferred by the use of succinylcholine in patients for whom manual ventilation of the lungs cannot be

Table 2. Recovery Times from Drug Injection until Spontaneous Breathing, Eye Opening, and Hand Squeeze, Lowest Oxygen Saturation, and Duration of Airway Support in 12 Volunteers

Volunteer No.	Spontaneous Breathing	Eye Opening	Hand Squeeze	Sa _o ₂ Low (Ear)	Sa _o ₂ Low (Finger)	Airway Support (min)
1	4.0	5.0	5.0	99	99	none
2	5.0	7.0	8.0	79	100	CL (1)
3	4.3	4.5	5.5	100	96	none
4	4.0	6.0	7.0	100	100	none
5	3.5	6.0	7.0	95	96	none
6	4.3	5.0	7.5	98	99	none
7	8.0	6.0	12.0	70	99	AV (1)
8	9.0	6.5	11.0	79	73	AV (2)
9	7.0	7.3	9.0	70	72	AV (1)
10	4.5	5.0	5.5	93	93	none
11	5.0	5.0	7.8	87	82	none
12	3.5	4.8	7.5	100	99	none
Mean	5.2	5.7	7.7	89	92	
SD	1.8	0.9	2.1	12	11	

Sa_o₂ = oxygen saturation; CL = chin lift; AV = assisted ventilation.

achieved. The American Society of Anesthesiologists' algorithm for the management of the difficult airway suggests that the anesthesiologist should consider allowing the patient to emerge from anesthesia if initial attempts of tracheal intubation are unsuccessful.¹¹ Our results suggest that if the patients lungs cannot be manually ventilated during this time, there is likely to be a high incidence of significant desaturation before the patient emerges from anesthesia and supports their own respiration.

As we expected, we found that the incidence of hemoglobin desaturation correlates with the duration of apnea (fig. 2), and volunteers who did not desaturate had significantly shorter apnea duration than those who attained Sa_o₂ less than 80%. It appears that significant desaturation (Sa_o₂ < 80%) is caused by the duration of succinylcholine block, not by the ventilatory depressant effect of thiopental, because all four volunteers with

significant desaturation were aware at the time the lowest Sa_o₂ value was attained.

The lowest recommended dose of succinylcholine in an emergency situation is 1 mg/kg.¹ With this dose, complete muscle paralysis is obtained within 60 s in most patients.^{4,12,13} To simulate a clinical situation, we decided to administer 1 mg/kg succinylcholine together with a standard dose of thiopental (5 mg/kg). A smaller dose of succinylcholine would have decreased the duration of muscle paralysis^{14,15} and increased the probability of restoration of spontaneous ventilation in time to prevent hemoglobin desaturation, but the results would have been less clinically relevant. We did not find any significant difference in recovery time between spontaneous breathing and eye opening on command. This relation has not been studied previously for succinylcholine. However, a similar response relation between the

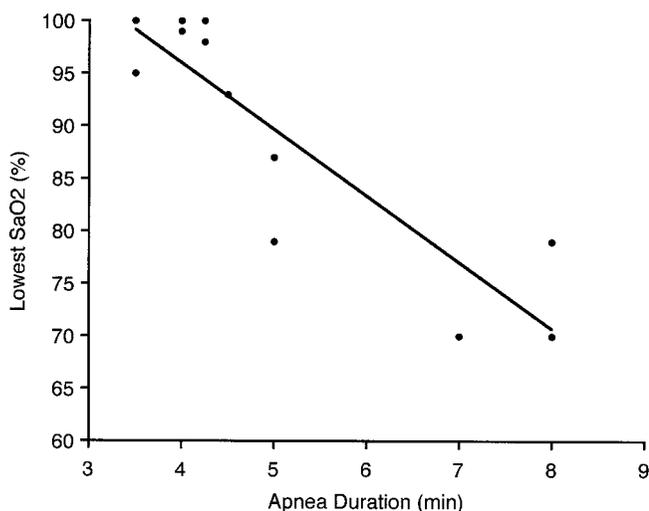


Fig. 2. The relation between the lowest recorded oxygen saturation (Sa_o₂) and duration of apnea in 12 volunteers.

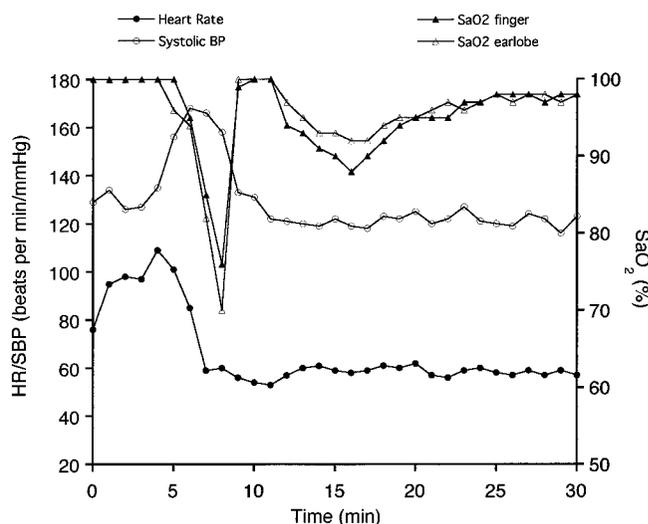


Fig. 3. Changes with time in heart rate (HR), systolic blood pressure (SBP), and oxygen saturation (Sa_o₂) recorded at finger tip and earlobe in one volunteer (No. 9).

Table 3. Objective Signs and Symptoms of Awareness and Occurrence of Emotional Distress While Paralyzed: Recall of Spoken Words (R), Paralysis (P), and Breathlessness (B) in Seven Volunteers

Volunteer No.	Objective Signs and Symptoms of Awareness			Emotional Distress		
	Recall Spoken Words	Paralysis	Breathlessness	R	P	B
2	Yes	Yes	Yes	No	No	Yes
5	Yes	Yes	No	No	No	No
6	Yes	Yes	No	No	No	No
7	Yes	Yes	Yes	No	No	Yes
8	Yes	Yes	Yes	No	No	Yes
9	Yes	Yes	Yes	No	No	Yes
12	Yes	Yes	Yes	No	No	Yes

two muscle groups involved was found when a single dose of vecuronium was administered to surgical patients.¹⁶ In two of our volunteers, eye opening to command occurred before spontaneous breathing. This was surprising, because the diaphragm is believed to be the muscle most resistant to the action of muscle relaxants.¹⁷ It is possible that in these two volunteers the diaphragm was, in fact, more sensitive than the circumorbital muscles to the effect of succinylcholine. Alternatively, differences in blood flow to the two muscles may have resulted in greater delivery of succinylcholine to the diaphragm. However, neither of these possibilities was studied, and we cannot speculate further on the cause of the earlier recovery of eye opening in these two volunteers.

We allowed SaO_2 to decrease to 80% before assisting the subject's ventilation. This is a conservative cutoff point because lower SaO_2 values have been used in previous studies without significant complications.^{6,7} However, in that previous study,⁷ the level of saturation was maintained at a steady state level, whereas in our study saturation was decreasing. The rate of hemoglobin desaturation during apnea is dependent on several factors. First, the subject's oxygen consumption is a major determinant. All of our volunteers had significant increases in heart rate and blood pressure (fig. 2), which presumably increased their oxygen consumption. We believe that similar autonomic changes would also have occurred during a prolonged apnea period in the clinical setting. Second, the functional residual capacity of the lungs gradually decreases during prolonged apnea, and consequently the degree of shunting of blood in the pulmonary capillaries increases because of collapse of alveoli.¹⁸ Third, the steep slope of the oxygen hemoglobin dissociation curve may influence the speed of desaturation. As long as SaO_2 is more than 90%, changes in arterial oxygen partial pressure will cause small changes in SaO_2 . However, at values below 80%, the curve enters the steep part, and SaO_2 changes rapidly with small changes in arterial oxygen partial pressure. For the aforementioned reasons, we expected that the rate of decline of the SaO_2 would increase rapidly once significant desaturation commenced. Therefore, to minimize further desaturation, we decided to intervene once an SaO_2 level

of 80% was reached. As illustrated in figure 1, it took 5–8 min for the SaO_2 to decrease to 95%, but the subsequent decline to 70% occurred over less than 1 min. We also attempted to minimize the delay in detecting desaturation by our technique of measuring the SaO_2 . We monitored saturation on a finger, which is the usual site used in clinical practice, and also used an earlobe oximeter. Because of shorter circulation time, the earlobe oximeter should record changes in saturation faster than one placed on a finger.⁶ In addition, the earlobe recording was also set to the fast mode, which means that SaO_2 values were recorded beat to beat rather than averaged over 6 s. Consequently, we were able to prevent profound decreases in SaO_2 . Spontaneous ventilation was judged to be adequate when the volunteer was awake, able to talk, had regained a firm hand grip, and SaO_2 was greater than 98% while breathing oxygen *via* the mask without chin lift. At this point, the face mask was removed, and the patient breathed room air. Subsequently, the three volunteers who previously had required assisted ventilation showed a second decrease in SaO_2 of moderate degree, which lasted for another 15–20 min (fig. 1). We speculate that this second decrease in SaO_2 , which was associated with coughing, was caused by atelectasis as a result of partial and temporary alveolar collapse.¹⁹ After 15–20 min, SaO_2 remained stable at greater than 95% on room air, presumably because of reexpansion of alveoli.

Seven of the volunteers experienced awareness while paralyzed. Temporary or permanent emotional distress has been associated with awareness episodes during surgery, especially if the patient experiences pain or severe panic because of the feeling of being left unattended or that an anesthetic mishap has occurred.^{20–22} However, if a knowledgeable individual is informed of a planned awakening during anesthesia, the experience is well tolerated.²³ This is in agreement with our findings in volunteers who were thoroughly informed before signing the consent to participate in the study. None of the volunteers reported unpleasant feelings related to being paralyzed while aware, as long as the observers provided reassuring verbal information. This observation suggests that the anesthesiologist should verbally communicate with a patient during surgery whenever the

anesthesia depth is judged to be inadequate to secure unconsciousness. All five volunteers who experienced emotional distress while aware and paralyzed related this experience to their strong desire to breathe, a phenomenon that may be caused by both hypercapnia and hypoxemia.⁷ This is in agreement with the study by Topulos *et al.*,²³ which showed that even a small increase in arterial carbon dioxide partial pressure is associated with a very unpleasant feeling. The subjects described this sensation as “an urge to breathe,” “air hunger,” and “like holding your breath at breaking point.”

In summary, our results show that significant hemoglobin desaturation occurs in one third of healthy volunteers during the period of apnea after the induction of anesthesia with 5 mg/kg thiopental and 1 mg/kg succinylcholine. It is our belief that the incidence of desaturation is likely to be greater than this in the clinical situation. We conclude that there is a significant risk of desaturation if a patient's lungs cannot be ventilated during the period of succinylcholine-induced apnea.

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