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Desaturation following rapid sequence induction using succinylcholine vs. rocuronium in overweight patients

L. TANG[1], S. LI[1], S. HUANG[1], H. MA[1] and Z. WANG[2]
Departments of [1]Anesthesiology and [2]Pain Management, Shanghai First People's Hospital, Shanghai Jiaotong University, Shanghai, China

Background: Rapid sequence induction may be associated with hypoxemia. The purpose of this study was to investigate the possible difference in desaturation during rapid sequence induction in overweight patients using either succinylcholine or rocuronium.
Methods: Sixty patients with a body mass index (BMI) between 25 and 30 kg/m^2, American Society of Anesthesiologists class I or II, undergoing general anesthesia were randomly divided into a succinylcholine group and a rocuronium group. After a 3-min preoxygenation, patients received rapid sequence induction of general anesthesia with midazolum–fentanyl–propofol and succinylcholine (1.5 mg/kg) or rocuronium (0.9 mg/kg). Ventilation was not initiated until oxygen saturation declined to 92%. We measured the times when oxygen saturation reached 98%, 96%, 94% and 92%. Safe Apnea Time was defined as the time from administration of neuromuscular blocking drugs to oxygen saturation fell to 92%. The recovery period was defined as the time from initiation of ventilation until oxygen saturation was 97%. Arterial blood gases were taken at baseline, after preoxygenation and at 92% oxygen saturation.
Results: The mean Safe Apnea Time (95% CI) was 283 (257–309) s in succinylcholine vs. 329 (303–356) s in rocuronium ($P = 0.01$). The mean recovery period (95% CI) was 43 (39–48) s in succinylcholine vs. 36 (33–38) s in rocuronium ($P = 0.002$). Blood gas analysis showed no difference between the two groups.
Conclusions: Succinylcholine was associated with a significantly more rapid desaturation and longer recovery of oxygen saturation than rocuronium during rapid sequence induction in overweight patients.

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APNEA is always present during rapid sequence induction of general anesthesia. It is potentially life-threatening or organ-injuring if it is inadequately managed, particularly in obese patients. These patients might have an increased risk of hypoxia due to the diminished oxygen reserve during induction of general anesthesia.[1] A body mass index (BMI) >26 kg/m^2 is a predictor of a higher risk of difficult ventilation with a facemask.[2] Therefore, it is extremely important for anesthesiologists to maintain the balance between oxygen supply and consumption for overweight patients during anesthesia induction.

Current studies have been focused on maximizing the intrapulmonary oxygen reserve to prolong non-hypoxic apnea duration. Various techniques of 'preoxygenation' including deep breathing with a high fresh gas flow of oxygen,[3] application of positive airway pressure during preoxygenation [4,5] and nasopharyngeal oxygen insufflation following preoxygenation[6,7] can delay the onset of arterial hemoglobin desaturation during apnea. The head-up position has been recommended to optimize preoxygenation in non-obese patients,[8] in overweight patients[9] and in morbidly obese patients.[10,11]

How can we decrease oxygen consumption during anesthesia induction? Succinylcholine is the most commonly used depolarizing neuromuscular blocking drug in rapid sequence induction of general anesthesia because of its fast onset and short duration. Unfortunately, it increases muscle oxygen consumption as a result of skeletal muscle fasciculation[12] and it can cause serious side effects such as malignant hyperthermia. Rocuronium, a non-depolarizing muscle relaxant, has an onset of action that is more rapid than other available non-depolarizing neuromuscular blocking agents. It is a well-documented alternative to succinylcholine for intubation in rapid sequence induction.[13,14]

The purpose of this study was to investigate the possible difference in desaturation during rapid sequence induction in overweight patients using

either succinylcholine or rocuronium. We hypothesized that succinylcholine would be associated with a shorter time from administration until oxygen saturation was 92%.

Methods

The study was approval by the Research Ethics Committee of Shanghai First People's Hospital). Written informed consent was obtained from 60 patients from August 2007 to February 2009. All 60 patients with BMI 25–30 kg/m^2 were either American Society of Anesthesiologists (ASA) class I or II, age 23–64 years, and undergoing elective surgery requiring rapid sequence induction. Exclusion criteria included the following: contraindication for receiving succinylcholine (serum potassium concentration above 5.5 mml/l, a family history of malignant hyperthermia) or rocuronium, hemoglobin concentration <6.8 mmol/l, pregnancy, a history of significant cardiorespiratory disease or difficult intubation or those who had a phobia to facemasks. If any difficulty was encountered with the patient during induction, the anesthesiologist would take all appropriate action to optimize patient care, and the patient would be excluded from the study.

Participants were randomly allocated (sealed envelopes) to receive either 1.5 mg/kg of succinylcholine (Suxamethonium Chloride Injection, Shanghai Xudong Haipu, Pudong, Shanghai, China) or 0.9 mg/kg of rocuronium (Esmeron™, Organon, Pukou, Nanjing, China) as the neuromuscular blocking drug. The study drugs were administered in a double-blind fashion. To minimize bias, we assigned an independent investigator to record data and take arterial blood samples. To prevent the investigator from noting the muscle fasciculation induced by succinylcholine, she or he was called to enter the study room 60 s after the administration of the neuromuscular blocking drugs.

No premedication was given. Upon arrival in the operating room, standard monitoring was applied (Datex S/5, Helsinki, Finland) and 10 ml/kg Lactated Ringer's solution was given through a forearm vein. All patients received 0.02 mg/kg midazolam i.v. 10 min before induction, and then an arterial catheter was inserted into the left radial artery for arterial blood gas (ABG) analysis (ABBOTT i-STAT, East Windsor, NJ), and a baseline ABG was performed at this time. The anesthesiologist held a clear facemask in position to achieve an airtight seal. Preoxygenation with 100% oxygen in the supine position (10 l/min fresh gas flow) was conducted for 3 min via a circle system prefilled with oxygen (Datex-Ohmeda 7900, Madison, WI, USA), and all patients were asked to breathe normally. A second arterial blood sample was taken immediately after the period of preoxygenation. Anesthesia was induced using propofol via a target-controlled infusion device (Veryark TCI-I, Guangxi, China) at a target serum concentration of 5 μg/ml, accompanied by midazolam (0.02 mg/kg) and fentanyl (1.5 μg/kg). Succinylcholine (1.5 mg/kg) or rocuronium (0.9 mg/kg) was given on loss of eyelash reflex. The facemask was removed after the administration of a neuromuscular blocking drug. Tracheal intubation was performed 60 s[15,16] after the administration of succinylcholine or rocuronium with a laryngoscope. The correct placement of the tracheal tube was confirmed by a fiber bronchoscope, without ventilation. The tracheal tube was left open to air until oxygen saturation declined to 92% (oxygen saturation was monitored continuously at the left index finger) and anesthesia was maintained with vecuronium bromide (0.1 mg/kg) and propofol at a target of 3 μg/ml. Once oxygen saturation declined to 92%, the third arterial blood sample was taken and the patient was reconnected to the breathing system. Ventilation was initiated with 100% inspired oxygen (ventilation parameter: tidal volume 8 ml/kg, frequency 12 min^{-1}, inspiratory/expiratory 1 : 2, with a fresh flow rate of 1 l/min of oxygen) (Fig. 1).

Comprehensive routine monitoring, including noninvasive blood pressure (recorded at 1-min intervals), pulse oximetry, electrocardiography and heart rate, was performed throughout the procedure. If heart rate was >110 bpm or <45 bpm and systolic blood pressure was >170 mmHg or <80 mmHg, the patient was treated and excluded from the study.

We recorded the times when oxygen saturation reached 98%, 96%, 94% and 92%, respectively. The Safe Apnea Time was defined as the time from the administration of neuromuscular blocking drugs to the time when oxygen saturation declined to 92%. The recovery period was defined as the time from the initiation of ventilation to the time when the oxygen saturation returned to 97%.[10]

The primary end point was the Safe Apnea Time and a 30-s difference was considered clinically relevant. In a previous pilot study, we determined that the standard deviation was 41 s. A sample size of 30 patients in each group was predicted to have 80% power, using a two-group *t*-test with a 0.05 significance level. Student's *t*-test was used for

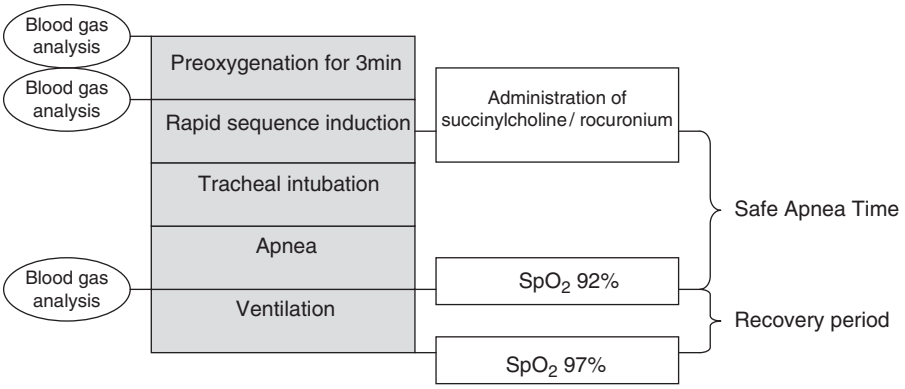

Fig. 1. Trial profile.

statistical analysis (SPSS 11.0 for Windows Software). A P value of <0.05 was considered significant.

Results

A total of 60 patients were recruited. There were no exclusions for adverse events during the study. Patient characteristics were similar in both groups (Table 1).

The mean Safe Apnea Time was 283 (257–309) s after succinylcholine vs. 329 (303-356) s after rocuronium ($P = 0.01$) (Fig. 2, Table 2). The mean recovery period was 43 (39–48) s in succinylcholine vs. 36 (33–38) s in rocuronium ($P = 0.002$).

When ventilation with 100% O_2 was started, there was a further decline in oxygen saturation. The lowest oxygen saturation was $87 \pm 2\%$ in the succinylcholine group vs. $88 \pm 2\%$ in the rocuronium group ($P = 0.04$).

No patient reported any episodes of awareness. Nine patients' blood gas samples (five allocated to the succinylcholine group and four allocated to the rocuronium group) could not be analyzed due to technical factors.

Blood gas analysis at baseline, after preoxygenation and at 92% oxygen saturation showed that oxygen, carbon dioxide and pH did not differ significantly between the two groups. In addition, no significant accumulation of carbon dioxide was observed (Table 3). The blood pressure and heart rate of all patients remained within 20% of the baseline values during the apneic period.

Table 1

Characteristics of patients receiving succinylcholine or rocuronium.

	Succinylcholine ($n = 30$)	Rocuronium ($n = 30$)
Age (year)	52 ± 8	52 ± 10
Sex (male/female)	11/19	9/21
ASA Status (I/II)	20/10	17/13
BMI (kg/m^2)	27.2 ± 1.4	27.7 ± 1.4
S_pO_2 base (%)	98 ± 1	97 ± 1
Hb (mmol/l)	8.4 ± 0.6	8.4 ± 0.7
Hct (%)	39.5 ± 3.6	39.5 ± 3.6

Values are mean $\pm$ SD.
BMI, body mass index; Hb, hemoglobin concentration; Hct, hematocrit; S_pO_2 base, pulse oxygen saturation breathing air.

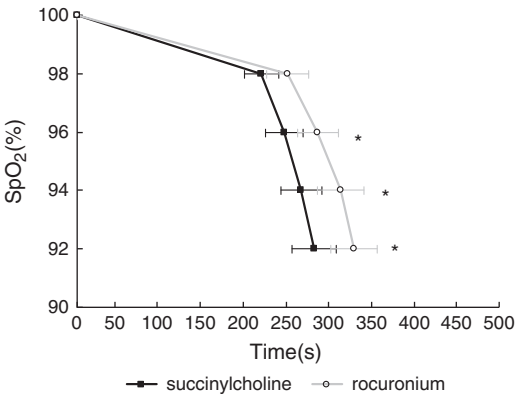

*Fig. 2. Changes in oxygen saturation (S_pO_2) with time during non-hypoxic apnea in the succinylcholine or the rocuronium group. Mean values (points) for both groups are shown. The vertical lines indicate 95% CI. The curves show smooth before S_pO_2 reach 98%, but afterward fall straightly to 92% S_pO_2. *P <0.05 compared with succinylcholin.*

Discussion

The present study investigated the non-hypoxic apnea duration during induction of general anesthesia. According to previous studies,[4,10,11,17] we constructed a desaturation model and ensured that the procedures were under control and safe.

Succinylcholine 1.5 or 1.0 mg/kg is traditionally used for rapid sequence induction in healthy adults

Table 2

Desaturation time after succinylcholine or rocuronium.

	Succinylcholine ($n = 30$)	Rocuronium ($n = 30$)	*P* value
T_{98}	221 ± 55	252 ± 65	0.06
T_{96}	248 ± 58	287 ± 65*	0.02
T_{94}	268 ± 64	314 ± 72*	0.01
T_{92}	283 ± 70	329 ± 71*	0.01

Values are mean ± SD.
*$P < 0.05$ compared with succinylcholin (between-group comparison).
T_{98}, time to S_pO_2 of 98%; T_{96}, time to S_pO_2 of 96%; T_{94}, time to S_pO_2 of 94%; T_{92}, time to S_pO_2 of 92%.

Table 3

Comparison of arterial blood gas results (oxygen, carbon dioxide and pH) for patients assigned to the succinylcholine and rocuronium.

	Succinylcholine ($n = 25$)	Rocuronium ($n = 26$)	*P* value
Baseline			
P_aO_2 (kPa)	10.4 ± 0.9	10.0 ± 1.1	0.13
P_aCO_2 (kPa)	4.9 ± 0.4	4.9 ± 0.4	0.84
pH	7.415 ± 0.025	7.425 ± 0.027	0.21
After 3 min of preoxygenation			
P_aO_2 (kPa)	58.9 ± 9.1	56.7 ± 9.2	0.37
P_aCO_2 (kPa)	5.2 ± 0.8	5.5 ± 0.5	0.16
pH	7.407 ± 0.034	7.426 ± 0.036	0.05
At 92% pulse oxygen saturation			
P_aO_2 (kPa)	8.7 ± 0.9	8.7 ± 0.8	0.85
P_aCO_2 (kPa)	7.1 ± 0.9	7.3 ± 0.6	0.21
pH	7.307 ± 0.037	7.301 ± 0.027	0.532

Values are mean ± SD. There was no statistically significant difference between the groups.
pH, power of hydrogen; P_aCO_2, arterial carbon dioxide tension; P_aO_2, arterial oxygen tension.

in Asia, but recent reports suggest that succinylcholine 0.6 mg/kg produces as satisfactory tracheal intubation conditions as succinylcholine 1.0 mg/kg,[16,18–20] and decreased the incidence of hemoglobin desaturation.[21] To minimize oxygen consumption, we could have chosen a smaller dose of succinylcholine that may have also provided good intubation conditions. Andrews et al.[15] concluded that rocuronium 1.0 mg/kg in a rapid sequence induction of anesthesia is clinically equivalent to succinylcholine 1.0 mg/kg. However, it has been proved that succinylcholine creates better intubation conditions than rocuronium in a large meta-analysis comparing intubation conditions.[22] We think that it is important to make intubation easier and faster for patients at risk for hypoxemia during anesthesia induction. Therefore, in our study, we finally decided to use succinylcholine 1.5 mg/kg to achieve excellent intubation conditions and investigated the desaturation time using this large dose.

The main finding of this study was that succinylcholine made the Safe Apnea Time shorter and the recovery period of time to saturation to 97% longer than rocuronium. This is primarily the result of increasing muscle oxygen consumption by succinylcholine-related skeletal muscle fasciculations.[23] We considered that this phenomenon would be much more pronounced in overweight patients, who have a larger body surface area but smaller oxygen reserve due to a lower functional residual capacity than lean patients. The amount of oxygen consumption is related to the succinylcholine dose. Previous studies showed that 0.25 mg/kg succinylcholine doubles oxygen consumption in normal muscle,[24] and oxygen consumption increases as much as 150% with 2 mg/kg succinylcholine.[12] A previous study demonstrated that 1 min after the administration of succinylcholine, as opposed to rocuronium, the saturation of blood oxygen was similar but the levels of blood lactic acid were significantly higher in the right atrium.[25] In our study, we also observed a further decline in oxygen saturation after ventilation. Thus, we considered that the main effect of succinylcholine-induced fasciculations was an insufficient oxygen supply in skeletal muscles. This is probably why the recovery period was longer in the succinylcholine group after establishing ventilation in our study.

Figure 2 shows that oxygen saturation decreases slowly before reaching 98%, and afterwards, the curves immediately decline to to 92%. We inferred that it would be better to re-ventilate at 98% oxygen saturation in patients who have a high risk of hypoxemia. But for normal cases, 92% oxygen saturation was a safe endpoint, because at that time, arterial oxygen tension was acceptable and there was no significant accumulation of carbon dioxide (Table 3).

There is no unified definition for desaturation duration in non-hypoxic apnea. The starting point could be during anesthesia induction, after the administration of neuromuscular blocking drugs, when the muscles are completely relaxed, or as soon as $P_{ET}CO_2$ becomes a straight line. Irrespective of the starting point we use, it is hard to estimate the decline of breath before apnea during anesthesia induction. Although we arbitrarily set the starting point as 'from administration of succinylcholine or rocuronium,' it is pragmatic for clinical work. But the limitation of this definition

is that the different desaturation durations between the two neuromuscular blocking drugs may lead to different times for the onset of paralysis and perhaps the rocuronium patients continued to breathe for longer. This is one of the limitations in our study. However, the differences in the recovery time and further decline in pulse oximetry after reventilation between the two groups reveal that succinylcholine leads to further oxygen consumption in non-hypoxic apnea than rocuronium. Another limitation in our study is that we did not assess the degree, onset and duration of fasciculations. Taha et al.[17] reported that fentanyl administered at induction may reduce the intensity and duration of fasciculations. The 46-s difference in Safe Apnea Time in our study was statistically significant, but it may not be clinically relevant, and smaller differences could be seen when less succinylcholine was used. Compared with overweight people, patients with normal BMI and subsequently normal oxygen consumption have a longer time to desaturation.[17] Therefore, minimizing oxygen consumption during apnea is more important for patients with a high BMI, and especially for morbidly obese patients.

In conclusion, succinylcholine (1.5 mg/kg) was associated with a significantly more rapid desaturation and longer recovery of oxygen saturation than rocuronium during rapid sequence induction in overweight patients. Rocuronium may be superior to succinylcholine in patients at risk for hypoxemia at anesthesia induction.

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Address:
Dr *Zhengping Wang*
Department of Pain Management
Shanghai First People's Hospital
Shanghai Jiaotong University
100 Haining Road
Hongkou District
Shanghai 200080
China
e-mail: Wangzpli@hotmail.com