Journal of Critical Care 36 (2016) 8–12

Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: www.jccjournal.org

Pulmonary

Preoxygenation and apneic oxygenation using Transnasal Humidified Rapid-Insufflation Ventilatory Exchange for emergency intubation☆,☆☆

Alexander J. Doyle, MDRes [a,b], Daniel Stolady, MBBS [c], Maryanne Mariyaselvam, MBBS [c], Gayathri Wijewardena, MD [c], Emma Gent, MBBS [c], Mark Blunt, MBBS, FRCA [c], Peter Young, MD, FRCA [c,*]

[a] Barts and the London School of Anaesthesia, The Royal London Hospital, Whitechapel, London, UK
[b] William Harvey Research Institute, Barts and The London School of Medicine, Queen Mary University of London, London, UK
[c] Department of Anaesthesia and Critical Care, Queen Elizabeth Hospital, King's Lynn, UK

ARTICLE INFO

Keywords:
Hypoxia
Preoxygenation
Apneic oxygenation
Emergency intubation
Complications
Patient safety

ABSTRACT

Purpose: Hypoxia is one of the leading causes of anesthesia-related injury. In response to the limitations of conventional preoxygenation, Transnasal Humidified Rapid-Insufflation Ventilatory Exchange (THRIVE) has been used as a method of providing both preoxygenation and apneic oxygenation during intubation.
Materials and methods: In this prospective, observational study, THRIVE was introduced in a critical care unit (CCU), operating room (OR), and emergency department (ED) during emergency intubation of patients at high risk of hypoxia. Linear regression analysis tested for correlation between apnea time or body mass index and hemoglobin saturation (Spo_2).
Results: Across 71 sequential patients, the interquartile range for apnea time and decrease in Spo_2 were 60 to 125 seconds and 0% to 3%, respectively. Significant desaturation occurred in 5 (7%) patients. There was no evidence of correlation between apnea time or body mass index and Spo_2 ($R^2 = 0.04$ and 0.08 for CCU/ED and OR and 0.01 and 0.04 CCU/ED and OR, respectively). There were no complications reported from using THRIVE.
Conclusions: This study demonstrated that preoxygenation and apneic oxygenation using THRIVE were associated with a low incidence of desaturation during emergency intubation of patients at high risk of hypoxia in the CCU, OR, and ED. THRIVE has the potential to minimize the risk of hypoxia in these patient groups.

1. Introduction

Hypoxia is one of the leading causes of anesthesia-related injury in the United Kingdom [1]. It is particularly common during the emergency intubation of patients outside the operating theater environment and associated with severe adverse harm in this patient group [2,3]. The techniques of preoxygenation and rapid sequence induction (RSI) have developed to minimize the risk of hypoxia during intubation.

Preoxygenation describes the process of maximizing the amount of oxygen stored in the body before induction of anesthesia. The most important store of oxygen is the functional residual capacity (FRC), the volume of gas present at the end of passive expiration. The amount of oxygen contained in the FRC can be improved by (1) increasing the inspired Fio_2 to denitrogenate the FRC, (2) applying continuous positive airway pressure (CPAP) to minimize airway atelectasis, and (3) positioning the patient in a head up (25°-35°) to increase the available volume of the FRC.

Rapid sequence induction describes the sequential process of (1) preoxygenation, (2) administration of a predetermined dose of induction agent, (3) administration of a predetermined dose of muscle relaxant, (4) avoidance of positive pressure ventilation, and (5) confirmation of tracheal intubation. It is thought that this approach minimizes the duration of time the airway is unprotected and avoids gastric insufflation, thereby reducing the risk of aspiration.

Adequate preoxygenation and RSI have become cornerstones of safe anesthetic practice. These techniques are considered to be particularly useful for patients with high metabolic rates, respiratory pathology, or a reduced FRC, who have either a higher oxygen requirement or a

Abbreviations: THRIVE, Transnasal Humidified Rapid-Insufflation Ventilatory Exchange; CCU, critical care unit; OR, operating room; ED, emergency department; RSI, rapid sequence induction; FRC, functional residual capacity; CPAP, continuous positive airway pressure; BMI, body mass index; Spo_2, hemoglobin saturation; NO-DESAT, nasal oxygen during efforts securing a tube.

☆ Conflict of interest: Dr Young has received honoraria for UK presentations from Fisher and Paykel Healthcare.

☆☆ Sources of financial support: Funding was awarded from Queen Elizabeth Hospital King's Lynn Research Fund, Kings Lynn, UK.Equipment and consumables for Optiflow oxygenation system supplied by Fisher and Paykel Healthcare Limited, Panmure, Auckland, New Zealand.Each funding source had no involvement in study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the article for publication.

* Corresponding author.
E-mail addresses: ajdoyle@gmail.com (A.J. Doyle), danielstolady@gmail.com (D. Stolady), maryannemariyaselvam@gmail.com (M. Mariyaselvam), gwijewardena@hotmail.com (G. Wijewardena), emma_gent@doctors.org.uk (E. Gent), markblunt@me.com (M. Blunt), peteryoung101@googlemail.com (P. Young).

http://dx.doi.org/10.1016/j.jcrc.2016.06.011
0883-9441/

lower oxygen storage capacity and are therefore likely to develop hypoxia (desaturate) more rapidly. However, despite apparent adequate preoxygenation and RSI, desaturation can still occur within 60 seconds in susceptible patients [4]. This limitation of conventional preoxygenation and RSI has led to renewed interest in the use of apneic oxygenation to extend the period of time that a patient maintains adequate oxygenation after induction of anesthesia, but before intubation.

Apneic oxygenation occurs in response to differences in solubility of oxygen and carbon dioxide. After the onset of apnea, oxygen continues to diffuse from the alveolar air space into the blood at a rate of approximately 250 mL/min. At the same time, carbon dioxide continues to diffuse from the blood into the alveolar air space at a rate of approximately 200 mL/min. This results in an initial volume deficit of 50 mL/min in the alveolar air space. In the absence of ventilation, carbon dioxide accumulates in the alveolar air space and approaches equilibrium with carbon dioxide in the blood. As a consequence, carbon dioxide diffusion falls to approximately 10 mL/min after approximately 45 seconds and the difference between the volume of oxygen leaving and the volume of carbon dioxide entering the alveolar air space is approximately 240 mL/min [5]. This discrepancy generates a negative pressure gradient between the alveolus and the upper airway, promoting the flow of gas from the pharynx to the alveolus, provided that the upper airway is patent. If the upper airway is insufflated with 100% oxygen, apneic oxygenation provides a mechanism to replenish the oxygen stored in the FRC at a rate approximately equal to rate oxygen diffuses across the alveolar membrane and so extend the duration of adequate oxygenation during periods of apnea [6,7].

Recently, humidified high-flow nasal oxygenation, known as Transnasal Humidified Rapid-Insufflation Ventilatory Exchange (THRIVE), has been investigated as a mechanism of providing both preoxygenation and apneic oxygenation in elective surgical patients, and reported to extend oxygen saturations during laryngoscopy and highly specialized airway surgery from a few minutes to more than 1 hour in some cases with relatively modest rises in carbon dioxide [7]. The beneficial effects of THRIVE in maintaining hemoglobin saturation (Spo_2) have also been demonstrated during the emergency intubation of critical care patients [8].

We hypothesized that preoxygenation and apneic oxygenation using THRIVE would be associated with a low incidence of desaturation during the emergency intubation of patients at high risk of hypoxia in our hospital. We report the findings of our pilot study, demonstrating the practicalities and results of implementing a THRIVE protocol in our critical care unit (CCU), operating room (OR), and emergency department (ED).

2. Material and methods

This prospective, observational study was conducted at the Queen Elizabeth Hospital, Norfolk, UK. As the data were collected as part of delivering routine care after a change of practice at the institution for audit, service surveillance, and improvement purposes, and anonymized, formal ethical committee approval was not sought. However, the Chair of the Research Governance Committee and Caldicott Guardian were consulted for approval to report data from routine practice and for publication of anonymized data. All equipment was used according to the manufacturers' instructions. Each patient was more than 18 years of age and required intubation as part of his or her routine care.

The THRIVE protocol was introduced to the CCU, OR, and ED as part of routine care for patients at high risk of hypoxia during intubation. The THRIVE protocol consisted of preoxygenation for 3 minutes using a simplified Optiflow system (Fisher and Paykel, New Zealand), incorporating of a high-flow rotameter, a reusable humidifier, reusable circuit, and a disposable nasal interface. The rotameter was set at 60 L/min during preoxygenation and a disposable bacterial filter was applied between the breathing circuit and nasal interface. Anesthesia and neuromuscular blockade were achieved using either a predetermined dose of thiopental (4-5 mg/kg) and succinylcholine (1-2 mg/kg) (OR and ED) or propofol (1-2 mg/kg) and rocuronium (1 mg/kg) (CCU). Approximately 30 N of cricoid pressure was applied to the cricoid cartilage at the time of loss of consciousness until tracheal intubation had been confirmed, in accordance with established practice in the United Kingdom. A face mask was not used as part of the THRIVE protocol and therefore manual ventilation was absent during the apneic period; however, airway patency was maintained using head tilt, chin lift, and/or jaw thrust. Finally, tracheal intubation was performed with a cuffed endotracheal tube. Patients at high risk of hypoxia during intubation were identified as those requiring intubation on the CCU or ED, or those patients presenting to the OR with a high metabolic rate, acute respiratory disease, predicted difficult airway, body mass index (BMI) >30, patients with chronic respiratory disease, and/or pathology reducing their FRC.

The data collected included the patient age, gender, BMI and known comorbidities, the location and reason for intubation, risk factors for desaturation, the grade of larynx according to the Cormack-Lehane system, the number of attempts at laryngoscopy, the use of difficult intubation equipment (equipment other than a direct laryngoscope and appropriately sized Macintosh blade), pre- and postintubation Spo_2, *apnea time* (defined as time from administration of neuromuscular blockade to confirmed placement of endotracheal tube), and any complications from the use of the THRIVE protocol. *Significant desaturation* was defined as a reduction in Spo_2 >10% after induction of anesthesia. Data were entered into a spreadsheet and analyzed using Excel (Microsoft, CA). Statistical analysis was performed using linear regression analysis to test for correlation between apnea time or BMI and Spo_2.

3. Results

Data were collected from 71 sequential patients. The demographic details and patient comorbidities are shown in Table 1. The location and reason for intubation are shown in Table 2. The risk factors for desaturation are shown in Table 3. The grade at laryngoscopy ranged from 1 to 4 (grade 1, 59%; grade 2, 27%; grade 3, 13%; grade 4, 1%). Thirteen cases required ≥2 attempts at laryngoscopy before successful intubation (3 (23%) of which underwent significant desaturation). Difficult airway equipment was used for 36 patients.

Overall, the median apnea time was 80 seconds (interquartile range [IQR], 60-125 seconds; range, 30-480 seconds) and the median decrease in Spo_2 was 1% (IQR, 0%-3%; range, 0%-33%). Significant desaturation occurred in 5 (7%) patients.

In the CCU/ED, the median apnea time was 115 seconds (IQR, 60-175 seconds; range, 30-480 seconds) and the median decrease in Spo_2 was 1% (IQR, 0%-4%; range, 0%-33%). Seven patients had a preinduction Spo_2 <90% (range, 67%-89%) secondary to acute respiratory failure. In these 7 patients, the median decrease in Spo_2 was 3% (IQR, 1.5%-3.5%;

Table 1
The demographic details and comorbidities of patients at high risk of hypoxia during intubation in CCU, OR, and ED

Variable	CCU/ED (IQR)	OR (IQR)
No. of patients	34	36
Median age	65 (60-70)	56 (44-75)
Gender (male/female)	12/22	16/20
Median BMI	27 (23-32)	31 (26-38)
Asthma	4	4
Chronic obstructive pulmonary disease	6	6
Obstructive sleep apnea	2	1
Hypertension	14	12
Ischaemic heart disease	5	7
Chronic heart failure	4	1
Cerebrovascular disease	3	1
Peripheral vascular disease	4	0
Atrial fibrillation	2	2
Diabetes mellitus	10	6
Chronic liver disease	5	0
Cancer	5	3

Table 2
The indications for tracheal intubation for patients at high risk of hypoxia during intubation in CCU, OR, and ED

Indication	Value
CCU/ED	
Acute respiratory failure	19
Postcardiac arrest	2
Airway protection	
GCS <8	7
Status epilepticus	1
Upper GI hemorrhage	1
Change of endotracheal tube	4
OR	
Emergency abdominal surgery	24
Emergency surgery other	6
Elective surgery	6

GCS indicates Glasgow Coma Scale; GI, gastrointestinal.

range, 0%-13%), with significant desaturation occurring in 1 patient. The apnea time for this patient was 60 seconds. In those patients (n = 27) with a preinduction Spo_2 >90%, significant desaturation also occurred in 1 patient, who was also intubated for acute respiratory failure. In this patient (in whom Spo_2 decreased 33%), the apnea time was 146 seconds and difficulty maintaining airway patency during the apneic period was reported.

In the OR, the median apnea time was 70 seconds (IQR, 30-120 seconds; range, 30-300 seconds) and the median decrease in Spo_2 was 0% (IQR, 0%-3%; range, 0%-16%). Significant desaturation occurred in 3 patients (in whom Spo_2 decreased 16%, 12%, and 13%, respectively). The apnea times for these 3 patients were 60, 30, and 30 seconds, respectively. Each patient had a BMI >35. In 2 of these patients, difficulty maintaining airway patency during the apneic period was also reported.

There was no evidence of correlation between apnea time and Spo_2 ($R^2 = 0.04$ and 0.08 for CCU/ED and OR, respectively) (Fig. 1), nor BMI and Spo_2 ($R^2 = 0.01$ and 0.04 CCU/ED and OR, respectively). There were no complications resulting from the use of the THRIVE protocol.

4. Discussion

Hypoxia is one of the most common and serious risks of tracheal intubation [1-3]. There is a growing body of evidence that apneic oxygenation has the potential to minimize the risk of hypoxia in patients requiring intubation. In 2, small, randomized controlled studies in healthy patients, insufflating oxygen at a flow rate of 3 to 5 L/min via a nasal catheter in apneic individuals extended the period of time that adequate oxygenation was maintained from 6 to 10 minutes in contrast to control groups, who desaturated to the study safety thresholds of 95% and 92% in 3 to 6 minutes, respectively [9,10]. In another small, randomized controlled study in obese patients, insufflating oxygen at a flow rate of 5 L/min via a nasal cannula extended the period of time that adequate oxygenation was maintained by almost 2 minutes compared with control patients [11]. More recently, preoxygenation using a nonrebreather face mask followed by apneic oxygenation by insufflating oxygen at a flow rate of 15 L/min via nasal cannula (nasal oxygen during efforts securing a tube [NO-DESAT]) and the continuous delivery of THRIVE have been reported as methods to reduce desaturation in high-risk intubations, with the latter having been shown to extend the safe apnea time between 5 and 65 minutes [6,7]. Nasal oxygen during efforts securing a tube has demonstrated effectiveness in both ED and out of hospital settings [6,12] and THRIVE has been shown to be useful in elective surgical and critical care patients [7,8]. Although both NO-DESAT and THRIVE provide apneic oxygenation, NO-DESAT is reliant on preoxygenation with either a nonrebreather or anesthetic face mask and does not provide CPAP. In contrast, THRIVE does not require preoxygenation using a mask because it is able to deliver significantly increased Fio_2 compared with nasal cannula and nonrebreather face masks as well as provide CPAP sufficient for lung recruitment [13,14].

Table 3
The risk factors for desaturation

Risk factor	Value
CCU/ED	
Respiratory failure	23
Aspiration	3
Predicted difficult airway	1
Hypermetabolic state	1
OR	
Sepsis	13
Pneumonia	4
Predicted difficult airway	21
BMI >30	22
Chronic respiratory disease	6
Surgical pathology reducing FRC	10

In line with these previous efforts, our study demonstrated that preoxygenation and apneic oxygenation using THRIVE were associated with a low incidence of desaturation during emergency intubation of patients at high risk of hypoxia in the CCU, but also suggested that THRIVE may provide a safe method of oxygenating patients during intubation in the OR and ED. Contrary to what would be anticipated, desaturation did not correlate with either the duration of apnea or increased BMI, highlighting the effectiveness of the THRIVE protocol in our patient population [15,16]. There were no complications resulting from the use of the THRIVE protocol.

We designed the simplified Optiflow system to be convenient and easy to use. In the OR, the system was permanently fixed to the anesthetic machine, and in the CCU and ED, it was fixed to a wheeled stand. The high-flow rotameter was marked with red tape displaying the prescribed flow rate (60 L/min) and the Schrader pipeline and connector were preattached. The humidifier was permanently switched on and so it was ready for use pro re nata. In the CCU and ED, the system simply had to be brought to the patient, connected to an oxygen source and an electrical socket, and the flow rotameter turned on. The system was intuitive and simple to use with minimal training.

Potential ancillary benefits of the THRIVE protocol included the ability to provide hands-free preoxygenation as soon as the patient entered the CCU, OR, or resuscitation area. This enabled staff to perform other essential functions, such as cannulation or preparation of drugs and equipment while preoxygenation was ongoing and meant that patients received an extended period of preoxygenation as it occurred concurrently with administrative and preparatory procedures. In addition, THRIVE appeared to be at least as comfortable and less stimulating to patients, who reported claustrophobia from conventional anesthetic face masks. In particularly anxious patients, a staged increase in flow rates up to 60 L/min may be even more tolerable.

Contraindications to the use of THRIVE include blocked nasal passages and fractures to the midface. From our experience, 3 further points require special mention. Firstly, THRIVE is intended for use as an open system. Concurrent application of an anesthetic face mask will close the system, provide very high flow rates, and lead to a rapid increase in pharyngeal pressure. This may cause gastric insufflation, injury to the inner ear, and patient discomfort. The use of THRIVE should not be combined with the concurrent use of a face mask. Secondly, intravenous anesthesia requirements should be carefully addressed during prolonged attempts at intubation. Finally, the airway must be patent after inducing anesthesia for THRIVE to work. This should be stressed at the time of introducing the technique, particularly if there is a risk of obstructive sleep apnea or in those patients with a raised BMI. Airway obstruction will prevent apneic oxygenation and so substantial desaturation may occur rapidly as occurred in 3 of our patient group. It may be possible to prevent airway obstruction in vulnerable patients by the early placement of an airway adjunct or by siting a nasopharyngeal airway before inducing anesthesia.

An important limitation of this study was that the incidence of desaturation before introducing the THRIVE protocol was unknown.

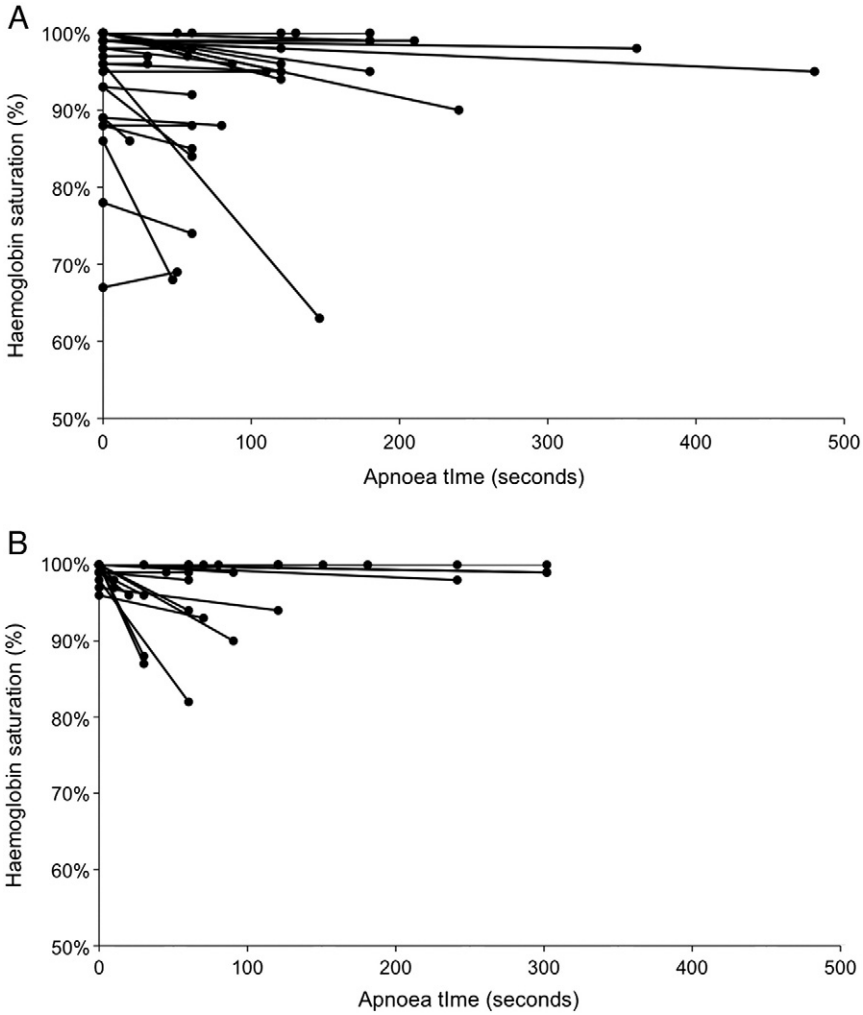

Fig. 1. Hemoglobin saturation vs apnea time in patients intubated in the CCU and ED (A) or OR (B).

Therefore, the impact of introducing THRIVE could not be quantified. The small number of patients included in our analysis and the fact that the data were collected at a single institution also represented weaknesses of our study. However, all the reported cases were selected on the basis of a clinical expectation of desaturation during intubation after conventional preoxygenation. Despite this, only 5 (7%) cases showed significant desaturation >10%. In light of this, a prospective, multicenter study with larger patient groups and in independent centers is warranted. In those patients who did desaturate >10%, acute respiratory failure preintubation in 2 CCU patients and lack of airway patency during apnea in 3 patients (1 CCU patient and 2 OR patients) were identified as the potential cause of the desaturation.

5. Conclusions

In conclusion, our study demonstrated that preoxygenation and apneic oxygenation using THRIVE were associated with a low incidence of desaturation during emergency intubation of patients at high risk of hypoxia in the CCU, OR, and ED. Transnasal Humidified Rapid-Insufflation Ventilatory Exchange has the potential to minimize the risk of hypoxia in these patient groups.

Acknowledgments

None.

References

[1] Cook T, Woodall N, Frerk C. *major* Complications of airway management in the UK: results of the fourth National Audit Project of the Royal College of Anaesthetists and the difficult airway society. Part 1: anaesthesia. Br J Anaesth 2011;106:617–31.
[2] Reid C, Chan L, Tweeddale M. The who, where, and what of rapid sequence intubation: prospective observational study of emergency RSI outside the operating theatre. Emerg Med J 2004;21:296–301.
[3] Cook T, Woodall N, Harper J, Benger J. *major* Complications of airway management in the UK: results of the fourth National Audit Project of the Royal College of Anaesthetists and the difficult airway society. Part 2: intensive care and emergency departments. Br J Anaesth 2011;106:632–42.
[4] Farmery AD, Roe PG. A model to describe the rate of oxyhaemoglobin desaturation during apnoea. Br J Anaesth 1996;76:284–91.
[5] Eger EI, Severinghaus JW. The rate of rise of PACO2 in the apneic anesthetized patient. Anesthesiology 1961;22:419–25.
[6] Weingart SD, Levitan RM. Preoxygenation and prevention of desaturation during emergency airway management. Ann Emerg Med 2012;59:165–75.
[7] Patel A, Nouraei SA. Transnasal Humidified Rapid-Insufflation Ventilatory Exchange (THRIVE): a physiological method of increasing apnoea time in patients with difficult airways. Anaesthesia 2015;70:323–9.
[8] Miguel-Montanes R, Hajage D, Messika J, Bertrand F, Gaudry S, Rafat C, et al. Use of high-flow nasal cannula oxygen therapy to prevent desaturation during tracheal intubation of intensive care patients with mild-to-moderate hypoxemia. Crit Care Med 2015;43:574–83.
[9] Teller LE, Alexander CM, Frumin MJ, Gross JB. Pharyngeal insufflation of oxygen prevents arterial desaturation during apnea. Anesthesiology 1988;69:980–2.
[10] Taha SK, Siddik-Sayyid SM, El-Khatib MF, Dagher CM, Hakki MA, Baraka AS. Nasopharyngeal oxygen insufflation following pre-oxygenation using the four deep breath technique. Anaesthesia 2006;61:427–30.
[11] Ramachandran SK, Cosnowski A, Shanks A, Turner CR. Apneic oxygenation during prolonged laryngoscopy in obese patients: a randomized, controlled trial of nasal oxygen administration. J Clin Anesth 2010;22:164–8.
[12] Wimalasena Y, Burns B, Reid C, Ware S, Habig K. Apneic oxygenation was associated with decreased desaturation rates during rapid sequence intubation by an Australian helicopter emergency medicine service. Ann Emerg Med 2015;65(4):371–6.

[13] Wagstaff TA, Soni N. Performance of six types of oxygen delivery devices at varying respiratory rates. Anaesthesia 2007;62:886–90.
[14] Corley A, Caruana LR, Barnett AG, Tronstad O, Fraser JF. Oxygen delivery through high-flow nasal cannulae increase end-expiratory lung volume and reduce respiratory rate in post-cardiac surgical patients. Br J Anaesth 2011;107:998–1004.
[15] Jense HG, Dubin SA, Silverstein PI, O'Leary-Escolas U. Effect of obesity on safe duration of apnea in anesthetized humans. Anesth Analg 1991;72: 89–93.
[16] Berthoud MC, Peacock JE, Reilly CS. Effectiveness of preoxygenation in morbidly obese patients. Br J Anaesth 1991;67:464–6.