Journal of Clinical Anesthesia (2010) **22**, 164–168

ELSEVIER

Journal of Clinical Anesthesia

Original contribution

Apneic oxygenation during prolonged laryngoscopy in obese patients: a randomized, controlled trial of nasal oxygen administration

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Received 11 July 2008; revised 12 May 2009; accepted 27 May 2009

Keywords:
Difficult laryngoscopy;
Difficult mask ventilation;
Nasal oxygen administration;
Morbid obesity

Abstract

Study Objective: To evaluate the influence of nasal oxygen (O_2) administration on the duration of arterial oxygen saturation (SpO_2) ≥95% during simulated difficult laryngoscopy in obese patients.

Design: Prospective, randomized, controlled trial.

Setting: University hospital.

Patients: 30 obese men undergoing general anesthesia.

Interventions: After thorough preoxygenation, and using total intravenous anesthesia, simulated difficult laryngoscopy was performed, with half the patients receiving additional nasal O_2 during apnea.

Measurements: Duration of SpO_2 ≥95% was measured up to a maximum of 6 minutes. Lowest SpO_2 values and time to regain 100% SpO_2 (resaturation time) also were recorded.

Main Results: Nasal O_2 administration was associated with significant prolongation of SpO_2 ≥95% time (5.29 ± 1.02 vs. 3.49 ± 1.33 min, mean ± SD), a significant increase in patients with SpO_2 ≥95% apnea at 6 minutes (8 vs. one pt), and significantly higher minimum SpO_2 (94.3 ± 4.4% vs. 87.7 ± 9.3%). Resaturation times were no different between the groups.

Conclusions: Nasal O_2 administration is associated with significant increases in frequency and duration of SpO_2 ≥95%, and higher minimum SpO_2 during prolonged laryngoscopy in obese patients.

1. Introduction

Obesity is now recognized as an independent risk factor for difficult mask ventilation and increased risk of accelerated hemoglobin (Hb) desaturation during apnea [1,2]. Morbidity during prolonged laryngoscopy due to a difficult airway stems from two distinct and concurrent phenomena. There is an evolving pulmonary shunt due to atelectasis and the attendant loss of functional residual capacity during anesthesia. In addition, due to the constant uptake of oxygen (O_2) from the alveoli, ambient air is entrained into the lungs during laryngoscopy, contributing to Hb desaturation.

To reduce the frequency and severity of Hb desaturation, patients are commonly preoxygenated with 100% O_2 prior to induction of anesthesia. Although various preoxygenation

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0952-8180/$ – see front matter © 2010 Elsevier Inc. All rights reserved.
doi:10.1016/j.jclinane.2009.05.006

techniques have been evaluated, the quantal difference between techniques may be small. For example, the three-minute technique and the 8-deep-breaths technique uniformly prolong duration of normoxia [3]. Further benefit in morbidly obese individuals may accrue from the head up position [4] and application of continuous positive airway pressure [5] during preoxygenation. The best preoxygenation typically maintains O_2 saturation (SpO_2) ≥92% for a mean duration of 201 ± 55 seconds in morbidly obese individuals [4]. This "safe apnea" time is significantly shorter than the duration of apnea induced by a single dose of succinylcholine. Recovery of spontaneous ventilation after succinylcholine occurs between 4.1 and 7 minutes [6]. Therefore, preoxygenation techniques have limited clinical benefit in a difficult airway scenario, in which prolonged and multiple laryngoscopic attempts may engender precipitous Hb desaturation.

The concept of apneic oxygenation has been well established in the anesthesia literature for several years [7]. Teller et al. [8] and Taha et al. [9] separately showed that direct pharyngeal O_2 insufflation during apnea increases the duration of SpO_2 ≥95% for between 10 minutes and 6 minutes, respectively, during general anesthesia in non-obese, healthy patients. Although Baraka et al. went on to study the technique in morbidly obese patients [10], its value in obese patients during difficult laryngoscopy currently is unknown. We set out to evaluate the efficacy of O_2 administration through Salter type nasal prongs (Salter, Sevin, CA, USA) in prolonging the period of SpO_2 ≥95% during simulated difficult laryngoscopy in obese patients.

2. Materials and methods

The University Hospital, University of Michigan Medical Center, institutional review board (IRB) approved this study, and informed consent was obtained from all patients. This prospective, randomized trial was performed in 30 obese men, who were scheduled for elective surgery with general anesthesia, and whose obesity was defined by a body mass index (BMI) of between 30 and 35 kg/m^2. Each subject received general anesthesia with endotracheal intubation. Exclusion criteria are listed in Table 1.

A total of 36 eligible patients were approached in the preoperative holding room on the day of their surgery. Three patients declined to enter the study, two patients were excluded from the study, one due to a malfunctioning pulse oximeter probe and the other for inadvertent removal of the pulse oximeter from his digit. An additional patient was excluded due to upper respiratory illness; thus, 30 patients consented and participated in the study. Patients were randomly allocated by a computer-generated table of random numbers to receive nasal O_2 (O_{nas} group) or not to receive it (NO_{nas} group). The study investigators were blinded to patient group allocation until the time of preoxygenation in the operating room (OR). As the hiss of the nasal O_2 was audible to the study investigators, any further blinding was considered impossible. In the preoperative holding room, baseline heart rate (HR), blood pressure (BP), and SpO_2 on room air were obtained.

Table 1 Study exclusion criteria

Female gender
BMI < 30 or > 35 kg/m^2
Smoker
Chronic respiratory disease
Uncontrolled hypertension
Congestive heart failure
Nasal obstruction
Gastroesophageal reflux disease
Elevated intracranial pressure
Unable to give informed consent
SpO_2 ≤ 97% on 100% via face mask
Grade 3 or 4 mask ventilation: current or past
Grade 3 or 4 laryngoscopic view: current or past

BMI=body mass index, SpO_2=oxygen saturation as measured by pulse oximeter.

Subjects were premedicated with intravenous (IV) midazolam two mg prior to transfer to the operating room. On patient arrival at the OR, standard monitoring was instituted, including continuous electrocardiogram, automated BP monitor, and pulse oximeter (Masimo SET; Masimo, Irvine, CA, incorporated in GE Marquette, General Electric Marquette Services, Jupiter, FL, USA). The default signal averaging time for all pulse oximeters in this study was 8 seconds. An adult Salter style nasal prong set was placed on each of the patients and attached to the auxiliary O_2 outlet of the anesthesia machine (Aisys; General Electric Healthcare, Madison, WI, USA). Side-stream respiratory gases were sampled with a three-meter sample line from between the facemask and the Y-piece of the anesthetic circuit. Calibration of the airway module (Aisys) was automatically performed, as is routine practice, before the start of each case. A device warm-up time of at least 30 minutes was permitted before all procedures in the study to ensure that the airway module functioned at full specification. Response time of the airway module was 2.5 seconds.

The 15 subjects assigned to the O_{nas} group received 5 L/min of O_2 via nasal prongs, while the other 15 subjects (NO_{nas} group) received no O_2 via the nasal prongs. Patency of the nasal passages was assured by capnography through the nasal prongs. Preoxygenation was then performed using a tight-fitting face mask and having each subject breathe 100% O_2 at 12 to 15 L/min, to improve the efficacy of preoxygenation [9]. Preoxygenation was deemed adequate when the end-tidal oxygen percentage (ETO_2) was either >90% or + ≤10% of inspired oxygen concentration (FIO_2) during normal tidal ventilation. To achieve this level, reverse Trendelenburg position (with head up 25°) and at least 8 vital capacity breaths were used in all patients.

Once adequate preoxygenation was achieved, anesthetic induction was performed using a bolus consisting of propofol two mg/kg and remifentanil 0.75 μg/kg. After

subjects were unconscious, they received succinylcholine one mg/kg. Concurrent with induction drugs, IV infusions of propofol at 100 to 150 μg/kg/min and remifentanil at 0.075 μg/kg/min were commenced. Dosing was based on 120% ideal body weight and titrated to clinical effect. At exactly 60 seconds from injection of succinylcholine, laryngoscopy was performed to evaluate the airway. If the laryngoscopic view was Cormack and Lehane grade 3 or grade 4 [11], the subject was excluded from the study and tracheal intubation was performed. If the laryngoscopic view was better, the force on the laryngoscope blade was reduced to simulate and maintain a grade 4 view (simulated difficult laryngoscopy). Additional remifentanil, propofol, and vecuronium 0.5 to 0.1 mg/kg was given to the patient as needed to ensure adequate depth of anesthesia and muscle relaxation. Blood pressure and HR were maintained within 20% of preoperative value with boluses of ephedrine, phenylephrine, or glycopyrrolate, as indicated. At precisely 6 minutes after injection of succinylcholine or when SpO_2 decreased to 95%, the simulated difficult laryngoscopy was terminated and tracheal intubation was performed. Once successful tracheal intubation was confirmed based on capnography, the time to achieve an SpO_2 of 100% (resaturation time) was recorded. Ventilation via the endotracheal tube was performed with fixed tidal volumes of 750 mL at 10 breaths/min and 5 cm H_2O of positive end-expiratory pressure. The end-tidal carbon dioxide ($ETCO_2$) value on commencing ventilation was noted, as was the lowest SpO_2. The remainder of the case was managed as routinely planned.

Postoperatively, subjects were followed up for possibility of awareness using the modified Brice questionnaire [12] (Appendix) and screened for incidental dental damage. Subjects were interviewed in the postanesthesia care unit and at 24 hours postoperatively.

2.1. Statistical analysis

A power analysis was performed to determine the number of subjects required for the study. We expected a minimum of 60 seconds' difference between the SpO_2 ≥95% times of the two groups. Based on this assumption and Type I and Type II errors of 5% and 20%, respectively, 15 patients per group were required to prove the hypothesis. Statistical analysis was performed using SPSS version 15 software (SPSS Inc., Chicago, IL, USA). All continuous data were identified as nonparametric, and the Mann Whitney U test was used to determine statistical significance of any differences between groups. Pearson's chi-squared test and Fisher's exact test were used to show significant differences between the two groups in frequency data.

3. Results

The subjects in the two groups had similar demographics (Table 2). The average BMI and resting vital signs (HR, BP, and SpO_2 on room air) between the groups did not differ significantly. After preoxygenation with 100% oxygen via face mask, there were no differences in FIO_2 or ETO_2 between the two study groups.

Table 2 Study group demographics

Variable	O_{nas} (n=15)	NO_{nas} (n=15)
Age (yrs)	53.4 (8.7)	52.9 (7.3)
BMI (kg/m^2)	31.2 (1.1)	31.2 (1.1)
Baseline MAP (mmHg)	98.7 (11.1)	98.8 (13.7)
Baseline heart rate (bpm)	71.8 (8.2)	73 (8.7)
Baseline SpO_2 on room air (%)	97.1 (1.9)	96.7 (1.8)

Results are means (standard deviations). There were no significant differences between any of the baseline variables. O_{nas}=nasal oxygen administration group, NO_{nas}=group who did not receive nasal oxygen, BMI=body mass index, MAP=mean arterial pressure, SpO_2=oxygen saturation as measured by pulse oximeter.

The study results are described in Table 3. The SpO_2 ≥95% apnea time in the NO_{nas} group was significantly shorter than the O_{nas} group (3.49 ± 1.33 vs. 5.29 ± 1.02 min, means ± SD; Fig. 1). Significantly more patients in the O_{nas} group (n = 8, 53.3%) had persistent SpO_2 ≥95% at 6 minutes compared with one patient in the NO_{nas} group ($P = 0.001$, by Fisher's exact test). The lowest SpO_2 obtained in the O_{nas} group was significantly greater than that seen in the NO_{nas} group (94.3 ± 4.4% vs. 87.7 ± 9.3%, means ± SD). Six patients did not regain 100% SpO_2 after tracheal intubation: 4 NO_{nas} group patients and two from the O_{nas} group ($P = 0.34$).

As the resaturation time to 99% was not recorded precisely to the last second, those data were excluded from the resaturation time analysis. Although there was a trend to faster resaturation times in the O_{nas} group (0.7 ± 0.4 vs. 1.5 ± 1.5 min, means ± SD), this difference was not statistically significant ($P = 0.42$). No patient from either group required ephedrine, phenylephrine, or glycopyrrolate during the study period. In the postoperative interviews, no dental damage was noted and no patients reported awareness either on recovery from anesthesia or during the 24-hour follow-up interview.

Table 3 Study results

Study variable	O_{nas} (n=15)	NO_{nas} (n=15)
Pre-induction ETO_2 (mmHg)	88.3 (1.9)	88.7 (2.6)
Pre-induction FIO_2 (%)	97.4 (1.7)	97.6 (1.9)
Initial $ETCO_2$ (mmHg)	45.3 (4.6)	43.8 (3.9)
Lowest SpO_2 (%)	94.3 (4.4) *	87.7 (9.3)
SpO_2 ≥95% time (min)	5.29 (1.02) *	3.49 (1.33)
Resaturation time (min)	0.69 (0.4)	1.57 (1.49)

Results are means (SD). O_{nas}=nasal oxygen administration group, NO_{nas}=the group who did not receive nasal oxygen, ETO_2=end-tidal oxygen, FIO_2=inspired oxygen concentration, $ETCO_2$=end-tidal carbon dioxide, SpO_2=oxygen saturation as measured by pulse oximetery. Resaturation time=time to regain SpO_2 100% after tracheal intubation.
* Statistically significant difference.

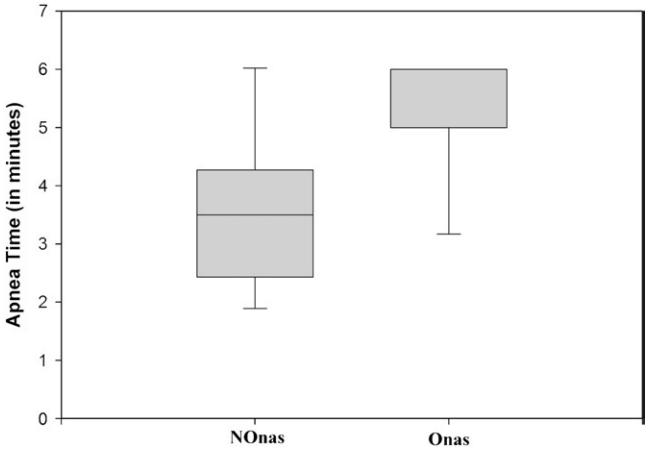

Fig. 1 Box and whisker plot comparison of oxygen saturation (SpO_2) ≥95% time in the nasal oxygen administration (O_{nas}) and non-nasal oxygen (NO_{nas}) groups. Boxes=means and standard deviations of the data for each group. Whiskers=range of data.

4. Discussion

The main finding of this study is that nasal O_2 via Salter type nasal prongs significantly increased the duration of SpO_2 ≥95% during simulated difficult laryngoscopy in obese patients. In addition, patients who received nasal O_2 were more likely to have SpO_2 ≥95% for at least 6 minutes and maintain higher minimum SpO_2 during laryngoscopy than those patients who did not receive it.

The adult human body typically consumes approximately 250 mL of O_2 and produces 200 mL of carbon dioxide (CO_2) every minute. During apnea, the body continues to consume O_2 and produce CO_2 at the same rate. Since CO_2 elimination is critically linked to alveolar ventilation, the vast majority of it is retained in the circulation, resulting in progressive, uncompensated respiratory acidosis. On the other hand, O_2 is continually extracted from the alveoli, resulting in a net loss of lung volume [7]. The resulting pressure differential is thought to cause mass movement of gas from the upper airways into the alveoli. Increasing FIO_2 either externally or at the level of the trachea or the pharynx provides a higher amount of O_2 to the alveoli. The prerequisite for this phenomenon is the presence of a patent upper airway [13]. If there is no patent airway, alveolar collapse and rapid progression of pulmonary shunting cause an exponential decline in arterial oxygen tension. This Hb desaturation can be delayed for a few minutes by preoxygenating patients before anesthetic induction. Obesity independently increases the risks of difficult intubation [14] and Hb desaturation [1] during apnea. Thus, we chose this high-risk group as our study population.

Although various preoxygenation techniques reduce the incidence of Hb desaturation during tracheal intubation in obese patients, they are of limited value in the scenario of prolonged difficult laryngoscopy. Return of spontaneous respiratory efforts after succinylcholine often helps a patient recover from this scenario, but the duration of apnea following succinylcholine is significantly greater than that of SpO_2 ≥95% [6] after all preoxygenation techniques. Recent work by Taha et al. [9] on supplemental nasal O_2 administration during apnea suggests that it can prolong the duration of SpO_2 ≥95% for at least 6 minutes in healthy, non-obese patients. Taha et al.'s findings cannot be extrapolated automatically to all patients for two reasons: the non-obese study population and the irrelevance of the study protocol in a difficult intubation scenario. Although Baraka et al. [10] subsequently validated this technique during laryngoscopy in morbidly obese patients, two aspects of their study warranted further investigation. One, does the use of nasal prongs offer the same clinical benefit? Two, does the technique work during difficult laryngoscopy? We therefore sought to explore the benefit of O_2 delivered through nasal prongs during simulated difficult laryngoscopy in obese patients.

Although our study findings are important in improving patient safety during anesthetic induction and laryngoscopy, there are some limitations of the study. First, we accepted the working theory that nasal O_2 administration would result in pharyngeal O_2 enrichment, which in turn would supply additional O_2 to the lungs during apnea by mass movement, as described above. The benefits of nasal O_2 were apparent in the majority of patients who received this technique. These benefits were similar to results of previous investigations but were of smaller magnitude, either in duration (in non-obese patients [8,9]) or in number of patients with maximum response [15]. Nasal O_2 administration may not always deliver the set flows to the posterior pharynx, and thus it is less effective than direct pharyngeal O_2 administration. Increasing the flow rates beyond 5 L/min may overcome this shortcoming.

Second, some of the non-responders may have had occluded airways during sham difficult laryngoscopy, either at the retropalatal level or the glottic level. This lack of clinical response in some patients is a unique finding of our study and we believe it reflects an important shortcoming of nasal O_2 administration in a real-life cannot-intubate scenario. Third, Baraka et al.'s study protocol stopped short at 4 minutes [10], which means that we could not compare the desaturation rates at 6 minutes in morbidly obese patients. Finally, the duration of effect of succinylcholine was not measured in this study, as it has been studied already in multiple trials of similar populations.

Several steps were taken to reduce the number of confounding variables. Only men were included in the study because men have a higher prevalence of sleep apnea than women [16]. Due to the small sample size, we thought that a variation in the fraction of patients with airway closure prior to laryngoscopy could adversely affect the quality of the outcome data. The study included only subjects with good cardiovascular and pulmonary function. Each subject was adequately preoxygenated in the same manner. The strict end points for preoxygenation were chosen to differentiate between the effects of improved preoxygenation and apneic oxygenation. The duration of preoxygenation was

not measured in this study, and some patients needed preoxygenation in excess of 5 minutes to achieve this end point, a finding that strongly suggests the risks of mask leak with nasal prongs. Nasal air was not administered to a control group –which would have created a true double-blind study – for two reasons: one, it would not reflect actual clinical practice; and two, it would have required the use of a separate air cylinder, which would have reduced significantly the efficacy of the blinding process.

The study patients comprise a truly high-risk population for severe hypoxemia during anesthetic induction. The described technique complements the benefits of various other techniques of preoxygenation, several of which were employed in this study. Second, the severity of Hb saturation is significantly improved by concurrent nasal O_2 administration, with a definite trend towards faster resaturation times. The finding of minimum SpO_2 values of 87.7 ± 9.3% in the control group, in spite of immediate tracheal intubation at 95% SpO_2, shows the rapid progression of desaturation in this high-risk population. Similarly, although all patients had baseline SpO_2 after 100% preoxygenation, a trend towards faster and more complete resaturation back to 100% SpO_2 was noted with O_2 administration. The noninvasive nasal prongs provide comparable benefit to direct pharyngeal oxygen administration.

In summary, we have shown that O_2 administration via nasal prongs is associated with significant prolongation of $SpO_2 \geq 95\%$ during anesthesia. Although more patients may benefit from more invasive methods of pharyngeal O_2 administration, they are at greater risk of epistaxis related to nasal trauma. Nasal O_2 administration during preoxygenation and simulated difficult laryngoscopy prevents desaturation in the majority of patients, making it a significant addition to the safety of airway management in the obese patient.

Appendix A. Modified Brice Interview

1. What is the last thing you remember before surgery?
2. What is the first thing you remember after surgery?
3. Do you remember anything happening during surgery?
4. Did you have any dreams during surgery?
5. What was the worst thing about your surgery?

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