Comparison of Arterial Oxygenation and Acid-Base Balance with the use of Transnasal Humidified Rapid-insufflation Ventilatory Exchange versus Tidal Volume Breathing with Continuous Positive Airway Pressure for Preoxygenation and Apneic Ventilation

Nandhini Joseph, Sunil Rajan, Pulak Tosh, Dilesh Kadapamannil, Lakshmi Kumar
Department of Anaesthesiology and Critical Care, Amrita Institute of Medical Sciences, Amrita Vishwa Vidyapeetham, Kochi, Kerala, India

Abstract

Background: Preoxygenation and apneic ventilation prolong apnea time without desaturation. Aims: The primary objective of this study is to compare arterial oxygenation during the periods of apnea following preoxygenation and apneic ventilation with tidal volume breathing for 3 min with continuous positive airway pressure (CPAP) versus with transnasal humidified rapid-insufflation ventilatory exchange (THRIVE). Settings and Designs: This prospective randomized study was conducted in 20 adult patients at a tertiary care institution. Subjects and Methods: Group C patients (n = 10) were preoxygenated with 100% oxygen using a face mask at a rate of 6 L/min for 3 min with CPAP of 15 cm of H₂O. In Group H, oxygen was administered using THRIVE at 30 L/min for 3 min. Apneic ventilation was given in Group C with 10 L/min oxygen with CPAP of 15 cm H₂O and in Group H with THRIVE at 60 L/min. The endpoint was desaturation to 90% or maximum duration of 12 min. Statistical Analysis Used: Chi-square test and Mann–Whitney test. Results: Both groups tolerated apnea for 12 min without desaturation. PaO₂ in Group C was significantly higher than Group H from 3 min of apnea to 12 min. The PaCO₂ was significantly lower in Group C from 6 min. The pH was comparable in both groups except at 12 min with Group H having significantly lower pH. Conclusion: Tidal volume breathing with CPAP resulted in significantly higher arterial oxygen levels than THRIVE, though both modalities were equally effective in prolonging apnea time without desaturation up to 12 min. Group C showed an added advantage of lower PaCO₂ with less acidemia.

Keywords: Apnea, humidified, oxygen, tidal, volume

Introduction

Airway critical incidents continue to be one of the most common scenarios an anesthetist comes across and “Cannot Intubate Cannot Ventilate situation” (CICV) can lead to significant patient morbidity due to hypoxic brain injury, if not properly managed. The time required to intubate can be more in patients with a difficult airway, and hence, they are at risk of development of hypoxic episodes unless adequately preoxygenated. Apneic oxygenation and a well-performed preoxygenation have been found to be very effective in prolonging the duration of apnea without desaturation.

Application of continuous positive airway pressure (CPAP) during this period will help to recruit the collapsed areas of the lung and thus improves oxygen reserve. Transnasal humidified rapid-insufflation ventilatory exchange (THRIVE) which provides high flow humidified nasal oxygen also has been used in this study.
found to be effective in prolonging apnea time.\textsuperscript{[5-8]} Hence in patients with anticipated difficult airway, delays during repeated intubation attempts might be better tolerated if preoxygenation was performed with either of the above-mentioned techniques.

**Aim of the study**

The primary objective of this study was to compare the arterial partial pressure of oxygen (PaO$_2$) during the periods of apnea following preoxygenation and apneic ventilation with tidal volume breathing for 3 min with the application of CPAP versus THRIVE. The secondary objectives of this study included the evaluation of time to desaturate to 90%, changes in arterial levels of carbon dioxide (PaCO$_2$), base excess, and lactate levels along with changes in blood pH and hemodynamic variables.

**Subjects and Methods**

This prospective randomized study was conducted during January 2017 to November 2017 after obtaining the Institutional Ethical Committee clearance and informed patients’ consent. As no similar studies have been conducted previously, a pilot study was conducted on 20 patients to calculate the sample size. Based on a primary objective of the PaO$_2$ at the end of the study, in Group C (415.30 ± 75.39 mm Hg) and Group H (187.70 ± 71.43 mm Hg), with a confidence interval of 95% and 99% power, a minimum sample size of three in each group was calculated to obtain a statistically significant result. During the study, another 20 patients were enrolled and assigned into two groups equally.

The study was performed in 20 adult patients of the American Society of Anesthesiologists (ASA) physical status classes I and II, coming for major head and neck surgeries with free flap reconstruction, under general anesthesia with endotracheal intubation. Patients with carcinoma maxilla, alveolus, tongue, tonsils, ameloblastoma, and osteoradionecrosis of mandible without anticipated difficult intubation, were included in the study. Whereas patients with chronic obstructive pulmonary disease, obesity, pregnancy, thyrotoxicosis, pheochromocytoma, hyperkalemia, the presence of significant cardiac illness with pulmonary hypertension, raised intracranial pressure, and Cormack–Lehane Grade 3 or more were excluded from the study.

For this study, patients were allocated to either Group H or Group C randomly based on computer-generated random sequence of numbers. The allocation concealment was ensured using sequentially numbered opaque sealed envelopes. Once monitors were attached and an intravenous (i.v.) line secured, glycopyrrolate 0.2 mg and midazolam 1 mg were administered. The patient’s airway was then topicalized by nebulization with 5 ml of 4% lignocaine. This was followed by a quick and gentle laryngoscopy to confirm that the grade of glottic view was Cormack–Lehane 1 or 2. Any grade higher than this was excluded from the study at this point. A baseline arterial blood gas (ABG) was then taken after securing an arterial cannula in the radial artery under local anesthesia.

In Group C, the patients were preoxygenated with 100% oxygen using a tight-fitting face mask at a rate of 6 L/min for 3 min with the application of CPAP. The CPAP of 15 cm of H$_2$O was ensured by adjusting the adjustable pressure limiting (APL) valve. If the patient complained of discomfort or difficulty, the CPAP was reduced until patient comfort was attained. In Group H, warmed (37°C) and humidified oxygen was delivered through nasal cannula using AIRVO™ 2 (Fisher and Paykel Healthcare Ltd, New Zealand) at the rate of 30 L/min for 3 min. AIRVO™ 2 is a humidifier with an integrated flow generator that delivers a high flow of warmed and humidified oxygen up to 60 L/min [Figure 1]. In both groups, patients were asked to perform tidal volume breathing.

After this period, patients in both groups received general anesthesia as per a standardized protocol. Induction was done with i.v. midazolam 1 mg, fentanyl 2 µg/kg, and propofol 2 mg/kg. Neuromuscular blockade was attained with atracurium 0.5 mg/kg. Once the patient became apneic, oxygenation was ensured using apneic oxygenation. In Group C, while ensuring the tight face mask seal the oxygen flow was increased to 10 L/min with APL valve closed at 15 cm H$_2$O. It was ensured that the airway pressures never exceeded 15 cm H$_2$O. In Group H, the flow in the high flow nasal cannula was increased to 60 L/min. This apneic oxygenation continued until the patient desaturated to 90% or a maximum duration of 12 min. The study was also terminated if the patient became hemodynamically unstable due to hypotension or arrhythmias which was treated according to the standard guidelines. After the study, ventilation was established for 1 min if there was no desaturation, or till pulse oximetry showed 100% saturation in case of desaturation before the patient was intubated. The rest of the surgery proceeded as per protocol.

ABG samples were taken before preoxygenation (baseline), end of preoxygenation, every 3 min once the patient became apneic until saturation dropped to 90% or to a maximum of 12 min. During these time periods, hemodynamic parameters such as heart rate (HR) and mean arterial pressure (MAP) were...
also recorded. ABG values of oxygen, carbon dioxide, base excess, lactate, pH, and time to desaturate to 90% were noted. The depth of anesthesia was ensured throughout the intervention with i.v. Propofol boluses of 20–30 mg at an interval of 3 min. Any increase in HR or MAP to more than 20% of the baseline was also treated similarly.

Chi-square test was used for analysis of nonparametric data and Mann–Whitney test was used for parametric data. The statistical analysis was performed using SPSS software Version 20.0 for Windows (IBM Corporation ARMONK, NY, USA).

**RESULTS**

The demographic characteristics (age, weight, height, gender, and ASA physical status) of the patients were found to be comparable in both groups [Table 1]. All patients in both groups were able to tolerate an apnea time of 12 min without desaturation and had comparable saturations at the end of this time frame. However, the PaO$_2$ in Group C (410.40 ± 116.09 mm Hg) was significantly higher than Group H (211.80 ± 107.50 mm Hg) at the end of 12 min [Figure 2].

The PaCO$_2$ at the end of 12 min was also significantly lower in Group C (66.08 ± 7.22 mm Hg) as opposed to Group H (87.24 ± 9.97 mm Hg) [Figure 3]. This significant difference in arterial partial pressure of oxygen started from 3 min of apnea. The PaCO$_2$ became significantly higher in Group H than Group C from 6 min of apnea. The pH was comparable in both groups up to 12 min of apnea. At 12 min, Group H (7.13 ± 0.03) had significantly lower pH as compared to Group C (7.21 ± 0.06) [Figure 4]. The lactate and base excess were comparable in both groups throughout the study period [Table 2]. The hemodynamic parameters (HR and MAP) were comparable in both groups during the study [Figures 5 and 6].

**DISCUSSION**

Duration of apnea without desaturation was prolonged in both groups. Hence, both techniques were found to be equally effective in ensuring a well-performed preoxygenation and apneic oxygenation. However, the PaO$_2$ was significantly higher in Group C than Group H at the end of 12 min. This was further supported by a lower PaCO$_2$ in Group C than Group H.

### Table 1: Demographic characteristics of patients

| Variables       | Group C | Group H | P     |
|-----------------|---------|---------|-------|
| ASA 1, n (%)    | 1 (20)  | 3 (60)  | 0.524 |
| ASA 2, n (%)    | 4 (80)  | 2 (40)  |       |
| Male, n (%)     | 2 (40)  | 3 (60)  | 1.000 |
| Female, n (%)   | 3 (60)  | 2 (40)  |       |
| Age in years    | 57.80±10.80 | 49.80±26.82 | 0.600 |
| (mean±SD)       |         |         |       |
| Weight in kg    | 65.24±10.65 | 54.40±15.90 | 0.209 |
| (mean±SD)       |         |         |       |
| Height in cm    | 161.20±9.37 | 155.80±9.55 | 0.295 |
| (mean±SD)       |         |         |       |

SD=Standard deviation, ASA=American Society of Anesthesiologists
Joseph, et al.: CPAP provides better oxygenation

This indicates that the apneic ventilation was more effective in Group C as opposed to Group P.

Apneic oxygenation is a technique where oxygen flow continues to take place without any lung movement due to the mass flow of gases as a result of the gradient created by the continuous uptake of oxygen by the alveoli. This will take place as long as the patency of the airway has been maintained.[9,10] THRIVE provides a high flow of oxygen and creates airway pressures of a maximum of 7 cm H$_2$O.[5] The better oxygenation observed in Group C could be due to the augmented recruitment of the alveoli resulting in reduced ventilation-perfusion mismatch as CPAP of 15 cm of H$_2$O was used.

Absorption atelectasis due to oxygenation with 100% oxygen can be prevented by the application of a continuous positive pressure to keep the alveoli patent. The application of positive pressure and positive pressure ventilation has been found to be effective in prolonging apnea time in high-risk populations such as obesity, pregnancy, and critically ill.[11-13] A number of studies in emergency situations have found that an effective preoxygenation with positive pressure in critically ill patients leads to a better arterial partial pressure of oxygen levels.[14,15] The preoxygenation with bag and mask ventilation and THRIVE were found to be equally effective in crash sequence induction in emergency situations.[16]

The studies using CPAP have applied positive pressure ranging from 10 to 25 cm H$_2$O. There is enough evidence available that the pressures should be kept below 15 cm H$_2$O to prevent gastric insufflation of air. It was found that lung ventilation was insufficient with an inspiratory pressure of 10 cm H$_2$O. The inspiratory pressure of 15 cm H$_2$O was recommended for reducing gastric insufflation with proper lung ventilation during induction of anesthesia in nonparalyzed and nonobese patients.[17] Due to these reasons, we chose to use CPAP of 15 cm H$_2$O. There are reports of the usefulness of CPAP of 20 cm of H$_2$O in non-intubated patients for prolonging safe apnea time. However, evidence of gastric insufflation with the use of CPAP at this level was not assessed.[18] In the present study, all our patients underwent Ryle’s tube insertion soon after intubation as demanded by the surgical procedure for postoperative feeding. We did not notice gastric insufflation as evidenced by either visible epigastric distension or escape of air through Ryle’s tube after insertion in any of our patients.

Although THRIVE ensures apneic oxygenation, its high cost and limited availability is a restraining factor in its widespread use. Traditional preoxygenation with the application of CPAP was found to be equally effective and in fact, a better method of apneic oxygenation in comparison to THRIVE. Hence in a CICV situation, this can ensure a safer patient till help arrives.

**Table 2: Comparison of arterial pH, partial pressures of oxygen & carbon dioxide, levels of lactate & base excess between two groups**

| Time       | Group C | Group H | $P$   |
|------------|---------|---------|------|
|            | $n$     | Mean±SD | $n$  | Mean±SD |
| **Comparison of pH** |         |         |      |         |
| Baseline   | 5       | 7.39±0.04 | 5   | 7.39±0.02 | 0.917 |
| After preoxygenation |         |         |      |         |
| 3 min      | 5       | 7.30±0.08 | 5   | 7.26±0.05 | 0.251 |
| 6 min      | 5       | 7.27±0.05 | 5   | 7.21±0.03 | 0.094 |
| 9 min      | 5       | 7.23±0.05 | 5   | 7.17±0.02 | 0.059 |
| 12 min     | 5       | 7.21±0.06 | 5   | 7.13±0.03 | 0.028 |
| **Comparison of PO$_2$ (mm Hg)** |         |         |      |         |
| Baseline   | 5       | 48.40±15.37 | 5   | 48.60±62.99 | 0.917 |
| After preoxygenation |         |         |      |         |
| 3 min      | 5       | 490.20±64.94 | 5   | 353.40±119.77 | 0.047 |
| 6 min      | 5       | 468.40±50.44 | 5   | 291.80±119.52 | 0.028 |
| 9 min      | 5       | 456.20±34.85 | 5   | 277.20±119.63 | 0.009 |
| 12 min     | 5       | 410.40±116.09 | 5   | 211.80±107.50 | 0.047 |
| **Comparison of lactate (mmol/L)** |         |         |      |         |
| Baseline   | 5       | 38.36±2.67 | 5   | 40.40±1.26 | 0.251 |
| After preoxygenation |         |         |      |         |
| 3 min      | 5       | 51.12±11.04 | 5   | 60.94±7.20 | 0.076 |
| 6 min      | 5       | 56.24±5.74 | 5   | 69.46±7.15 | 0.009 |
| 9 min      | 5       | 62.24±6.19 | 5   | 76.48±7.29 | 0.028 |
| 12 min     | 5       | 66.08±7.22 | 5   | 87.24±9.97 | 0.009 |
| **Comparison of PCO$_2$ (mm Hg)** |         |         |      |         |
| Baseline   | 5       | 1.78±0.75 | 5   | 1.04±0.31 | 0.071 |
| After preoxygenation |         |         |      |         |
| 3 min      | 5       | 1.76±0.72 | 5   | 1.26±0.33 | 0.236 |
| 6 min      | 5       | 1.84±0.65 | 5   | 1.26±0.28 | 0.092 |
| 9 min      | 5       | 1.62±0.72 | 5   | 1.26±0.32 | 0.530 |
| 12 min     | 5       | 1.58±0.65 | 5   | 1.28±0.30 | 0.459 |
| **Comparison of base excess (mmol/L)** |         |         |      |         |
| Baseline   | 5       | −1.3±1.80 | 5   | −0.28±1.42 | 0.209 |
| After preoxygenation |         |         |      |         |
| 3 min      | 5       | −1.6±1.57 | 5   | −0.50±1.84 | 0.347 |
| 6 min      | 5       | −1.16±1.57 | 5   | −0.40±1.80 | 0.402 |
| 9 min      | 5       | −1.16±1.64 | 5   | −0.48±2.14 | 0.465 |
| 12 min     | 5       | −1.28±1.67 | 5   | −0.76±2.23 | 0.463 |

SD=Standard deviation

Figure 6: Changes in mean arterial pressure

![Figure 6](image-url)
The major drawback in our study is that we did not compare the effectiveness of preoxygenation alone with either method. This would have enabled us to assess its usefulness in high-risk population. Apneic oxygenation with a tight-fitting mask and CPAP, though more effective, will not be practically useful in a situation where efforts in securing an airway are being attempted. The depth of anesthesia should have been observed with a more objective monitor like Bispectral Index monitoring rather than using less accurate indices like hemodynamics.

We considered any hemodynamic compromise not responding to fluids and vasopressors during the study as an indication of increased intrathoracic volume, and the study intervention was supposed to be stopped. However, none of our patients in either group had such complications. If the intrathoracic pressures were recorded, it would have given a better preview into the effects of such high gas flows and pressures on the cardiopulmonary system.

**Conclusion**

Tidal volume breathing with CPAP resulted in a significantly higher arterial oxygen levels as compared to THRIVE though both modalities were equally effective in prolonging apnea time without desaturation up to 12 min. Tidal volume breathing with CPAP showed an added advantage of lower arterial carbon dioxide levels with less acidemia.

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**Conflicts of interest**

There are no conflicts of interest.

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