Effects of Preoxygenation with Tidal Volume Breathing Followed by Apneic Oxygenation with and without Continuous Positive Airway Pressure on Duration of Safe Apnea Time and Arterial Blood Gases

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Abstract

Background: Application of continuous positive airway pressure (CPAP) helps to recruit collapsed areas of the lung, which improves the oxygen reserve. Aim of the Study: To compare the time to desaturate to 90% during apnea following preoxygenation and apneic ventilation with tidal volume breathing for 3 min with and without the application of CPAP. Settings and Design: This prospective randomized study was conducted in a tertiary care institution. Subjects and Methods: Twenty adult surgical patients were allocated into two groups. Group C patients were preoxygenated with 100% oxygen with CPAP of 20 cm H\textsubscript{2}O for 3 min. Group P patients were preoxygenated for 3 min without CPAP. In Group C, apneic oxygenation was initiated following induction and neuromuscular blockade with CPAP of 20 cm H\textsubscript{2}O. In Group P, no CPAP was applied. The study was terminated when the patient desaturated to 90%. Statistical Analysis Used: Chi-square test and Mann–Whitney test. Results: Group C had a significantly longer apnea time as compared to Group P (816.00 ± 30.98 vs. 348.00 ± 122.64 s). Three patients in Group P desaturated to <90% by 3 min and the remaining soon after 6 min. No patient in Group C desaturated till 12 min of apnea. PaO\textsubscript{2} was significantly higher in Group C at 3 and 6 min of apnea. At 3 and 6 min, Group P had significantly lower saturation as compared to Group C. Conclusion: Preoxygenation with CPAP significantly delayed desaturation during apnea with significantly higher arterial partial pressure of oxygen as compared to preoxygenation without CPAP.

Keywords: Apneic ventilation, continuous positive airway pressure, oxygenation, PaO\textsubscript{2}, tidal volume breathing

Introduction

Anesthetists frequently come across patients who may require more than the usual time for securing the airway such as those with anticipated difficult airway. The safety of the patient during the extended periods of apnea is usually ensured with a proper preoxygenation, which provides added oxygen reserves by denitrogenating the functional residual capacity. Desaturation during attempts at intubation can be further delayed by apneic oxygenation. Apneic oxygenation results in increased peri-intubation oxygen saturation, decreased rates of hypoxemia, and increased intubation success in the first attempt.\(^1\)

Application of continuous positive airway pressure (CPAP) helps to recruit the collapsed alveoli\(^2\) and thereby reduces the ventilation–perfusion mismatch. As more alveoli are recruited, the rate of desaturation during apnea presumably will be slower. We hypothesized that patients who received CPAP during preoxygenation and apneic oxygenation would be able to tolerate apnea for a longer time in contrast to those who did not receive CPAP.

Aim of the study

The primary objective of this study was to compare the time to desaturate to 90% during apnea following preoxygenation...
and apneic ventilation with tidal volume breathing for 3 min with and without the application of CPAP. The secondary objectives included evaluation of changes in arterial oxygen, carbon dioxide, bicarbonate and lactate levels, pH, and the hemodynamics following these two techniques.

**Subjects and Methods**

This study was a prospective randomized single-blinded one conducted during the period January 2017 to November 2017 after obtaining the Institutional Ethical Committee clearance and informed consent from patients. The study was performed in 20 adult American Society of Anesthesiologists (ASA) Physical Status 1 and II patients with Cormack-Lehane Grade 1 or 2 coming for free-flap surgeries under general anesthesia with endotracheal intubation. Exclusion criteria included anticipated difficult airway, chronic obstructive pulmonary disease, obesity, pregnancy, thyrotoxicosis, pheochromocytoma, hyperkalemia, significant cardiac illness with pulmonary hypertension, and raised intracranial tension.

Patients were randomly allocated to either Group C or Group P based on computer-generated random sequence of numbers, and concealment of allocation was ensured using sequentially numbered opaque-sealed envelopes. All patients received a generalized anesthesia protocol and were premedicated with intravenous (IV) glycopyrrolate 0.2 mg and midazolam 1 mg followed by topicalization of the airway by nebulizing with 5 ml of 4% lignocaine. A quick and gentle laryngoscopy was then performed to assess the grade of glottic view, and only those with Cormack-Lehane Grade 1 or 2 were recruited into the study.

The patients in Group C were preoxygenated with 100% oxygen using a tight-fitting face mask at a rate of 6 L/min with CPAP of 20 cm H2O. CPAP was maintained at 20 cm H2O by adjusting the adjustable pressure limiting (APL) valve. Anytime during preoxygenation, if the patient complained of discomfort, the CPAP was reduced to a level at which patient comfort was adequate. Group P patients were preoxygenated for 3 min with an oxygen flow of 6 L/min using face mask without application of CPAP. In both the groups, patients were asked to perform tidal volume breathing.

Following preoxygenation, patients in both the groups were induced with IV midazolam 1 mg, fentanyl 2 µg/kg, and propofol 2 mg/kg till there was loss of response to verbal commands. Neuromuscular blockade was attained with IV atracurium 0.5 mg/kg. Once the patient became apneic, as evidenced by cessation of bag movement or a flat line in capnography, apneic oxygenation was initiated. In Group C, the oxygen flow was increased to 10 L/min with APL valve closed at 20 cm H2O. It was ensured that at no point, the airway pressures went above 20 cm H2O. In Group P, oxygen was delivered using face mask with a flow rate of 6 L/min without CPAP.

The study was terminated when the patient desaturated to 90% or became hemodynamically unstable due to hypotension or arrhythmias which were treated according to the standard guidelines. In those with hypotension not responding to fluid bolus or vasopressors, CPAP was discontinued. If there was no desaturation, the study was extended up to a maximum period of 14 min. At the end of the study, the patients were mask ventilated for few minutes (if saturation remained at 100%) or till saturation became 100% (if there was desaturation), before intubation and initiation of mechanical ventilation.

Samples for arterial blood gas (ABG) analysis were obtained before preoxygenation (baseline), at the end of preoxygenation, and then every 3 min since the patient became apneic till saturation dropped to 90% or to a maximum of 12 min. At these time periods, hemodynamic parameters such as heart rate (HR) and mean arterial pressure (MAP) were also recorded. ABG values of partial pressures of oxygen, carbon dioxide, base excess, pH, and time to desaturate to 90% were also noted.

The depth of anesthesia was ensured during apnea by administration of propofol boluses of 20–30 mg at 3-min interval. Any increase in HR or MAP to more than 20% of the baseline was also treated in a similar fashion.

As there was no similar study published, a pilot study was conducted in 20 patients to calculate the sample size. Considering the time to desaturate to 90% as primary objective in Group C (843 ± 27.0 s) and Group P (290.7 ± 25.7 s) with a confidence interval of 95% and 99% power, the minimum required sample size to obtain statistically significant result was calculated to be one patient in each group. However, we recruited 20 new cases who were equally allocated to Group C and Group P. Chi-square test was used to compare gender and ASA physical status, and Mann–Whitney test was used to compare continuous variables among the groups. Statistical analyses were conducted using SPSS Version 20.0 for Windows (IBM Corporation, Armonk, NY, USA).

**Results**

Both the groups did not show any significant difference while comparing age, sex, weight, height, and ASA physical status [Table 1]. Group C had a significantly longer apnea time as compared to Group P (816.00 ± 30.98 vs. 348.00 ± 122.64 s,

| Variables                  | Group C | Group P | P       |
|----------------------------|---------|---------|---------|
| ASA 1, n (%)               | 2 (20)  | 2 (20)  | 1.000   |
| ASA 2, n (%)               | 8 (80)  | 8 (80)  |         |
| Male, n (%)                | 4 (40)  | 8 (80)  | 1.028   |
| Female, n (%)              | 6 (60)  | 2 (20)  |         |
| Age (mean±SD)              | 57.80±10.19 | 52.20±11.79 | 0.446   |
| Weight (mean±SD)           | 65.24±10.04 | 69.20±12.10 | 0.286   |
| Height (mean±SD)           | 161.50±8.83 | 160.50±7.69 | 0.879   |

SD=Standard deviation, ASA=American Society of Anesthesiologists
Three patients in Group P desaturated to <90% by 3 min and the remaining seven patients soon after 6 min. No patient in Group C desaturated till 12 min of apnea.

Baseline ABG parameters were comparable between groups. PaO_2 was comparable after preoxygenation in both groups. However, at 3 and 6 min, Group C had significantly higher PaO_2 than Group P (P < 0.001). Although Group P patients were more acidic than Group C till 6 min, the difference was not statistically significant. PaCO_2, lactate, base excess, and bicarbonate were similar in both groups till 6 min [Table 2]. Figures 2–4 depict the changes in PaO_2, PaCO_2, and pH throughout the study period in both the groups.

Oxygen saturation was comparable in both the groups after preoxygenation. However, at 3 and 6 min, Group P had significantly lower saturation as compared to Group C. Lowest saturation recorded was 84.90 ± 9.20 in Group P versus 100.00 ± 0.00 in Group C (P < 0.001). HR and MAP were comparable in both the groups till 6 min of apnea [Table 3].

**DISCUSSION**

In the present study, preoxygenation and apneic ventilation with application of CPAP had resulted in significantly high PaO_2 which had led to a prolonged time to desaturate to 90% as compared to preoxygenation and apneic ventilation without CPAP. Although these patients did not desaturate till 12 min of apnea, there was significant carbon dioxide retention with acidemia.

Preoxygenation provides an extended safe period by delaying desaturation when patients remain apneic. Tidal volume breathing of 100% oxygen for 3 min or 3–8 vital capacity breaths is the standard recommendation for preoxygenation in general population. This allows achieving a 90% end-tidal oxygen level by replacing the nitrogen content of the atmospheric air. Eight vital capacity breaths in 1 min has shown to result in a significantly high PaO_2 with an almost doubled apnea-induced desaturation time as compared to vital capacity breaths for 3 min.

Application of positive pressure ventilation with and without positive end-expiratory pressure (PEEP) has shown to shorten preoxygenation time (time to achieve expired O_2 fraction of 90%) as compared to spontaneous breathing. During positive pressure ventilation, alveoli which were perfused but not ventilated get recruited and take part in gas exchange. This will result in diminished shunt fraction. The application of PEEP to the dependent lung, CPAP to the nondependent lung, and the combination of PEEP and CPAP has shown to improve oxygenation and decrease shunt fraction during one-lung ventilation.
Table 2: Comparison of arterial blood gas analysis variables

| Time          | Group C          | Group P          | P     |
|---------------|------------------|------------------|-------|
|               | n    | Mean±SD | n    | Mean±SD |       |
| Comparison of pH |      |         |      |         |       |
| Baseline      | 10   | 7.39±0.04 | 10   | 7.38±0.04 | 0.401 |
| After preoxygenation | 10   | 7.39±0.07 | 10   | 7.38±0.06 | 0.448 |
| 3 min         | 10   | 7.30±0.07 | 10   | 7.27±0.03 | 0.224 |
| 6 min         | 10   | 7.27±0.04 | 7     | 7.22±0.04 | 0.095 |
| 9 min         | 10   | 7.24±0.05 | -     | -        |       |
| 12 min        | 10   | 7.22±0.05 | -     | -        |       |
| Comparison of PO₂ |      |         |      |         |       |
| Baseline      | 10   | 88.94±4.12 | 10   | 84.41±21.58 | 0.879 |
| After preoxygenation | 10   | 498.40±14.50 | 10   | 468.70±69.82 | 0.879 |
| 3 min         | 10   | 490.20±61.23 | 10   | 225.70±135.22 | <0.001 |
| 6 min         | 10   | 468.40±47.55 | 7     | 144.01±113.49 | 0.001 |
| 9 min         | 10   | 456.20±32.86 | -     | -        |       |
| 12 min        | 10   | 410.40±109.45 | -    | -        |       |
| Comparison of CO₂ |      |         |      |         |       |
| Baseline      | 10   | 38.36±2.51 | 10   | 39.01±5.93 | 0.649 |
| After preoxygenation | 10   | 38.46±7.85 | 10   | 37.33±5.45 | 0.879 |
| 3 min         | 10   | 51.12±10.41 | 10   | 55.21±6.66 | 0.095 |
| 6 min         | 10   | 56.24±5.40 | 7     | 58.51±4.40 | 0.278 |
| 9 min         | 10   | 62.24±5.83 | -     | -        |       |
| 12 min        | 10   | 66.08±6.81 | -     | -        |       |
| Comparison of lactate |      |         |      |         |       |
| Baseline      | 10   | 1.78±0.70 | 10   | 1.28±0.49 | 0.067 |
| After preoxygenation | 10   | 1.62±0.61 | 10   | 1.26±0.45 | 0.108 |
| 3 min         | 10   | 1.76±0.68 | 10   | 1.46±0.40 | 0.347 |
| 6 min         | 10   | 1.84±0.61 | 7     | 1.34±0.51 | 0.094 |
| 9 min         | 10   | 1.60±0.68 | -     | -        |       |
| 12 min        | 10   | 1.58±0.62 | 0     | -        |       |
| Comparison of HCO₃⁻ |      |         |      |         |       |
| Baseline      | 10   | 23.12±1.26 | 10   | 22.73±4.59 | 0.223 |
| After preoxygenation | 10   | 22.84±1.28 | 10   | 21.81±3.68 | 0.648 |
| 3 min         | 10   | 23.86±1.40 | 10   | 24.64±3.89 | 0.172 |
| 6 min         | 10   | 24.58±1.55 | 7     | 22.57±3.69 | 0.281 |
| 9 min         | 10   | 24.88±1.60 | 0     | -        |       |
| 12 min        | 10   | 24.98±1.79 | 0     | -        |       |
| Comparison of BE |      |         |      |         |       |
| Baseline      | 10   | -1.34±1.70 | 10   | -1.83±4.81 | 0.323 |
| After preoxygenation | 10   | -1.68±1.49 | 10   | -2.72±4.06 | 0.288 |
| 3 min         | 10   | -1.56±1.48 | 10   | -0.97±3.99 | 0.129 |
| 6 min         | 10   | -1.16±1.48 | 7     | -3.10±3.96 | 0.624 |
| 9 min         | 10   | -1.16±1.55 | -     | -        |       |
| 12 min        | 10   | -1.28±1.58 | -     | -        |       |

SD=Standard deviation, BE=Base excess

Effective preoxygenation with positive pressure results in better arterial partial pressure of oxygen. The better oxygenation observed in Group C in our study could be due to the recruitment of the nonventilated alveoli which had resulted in a reduced ventilation–perfusion mismatch. A disadvantage of preoxygenation is absorption atelectasis due to the presence of 100% oxygen in the alveoli. This can be prevented by application of a continuous positive pressure which keeps the alveoli patent. The application of positive pressure has shown to be advantageous in high-risk patients such as obesity, pregnancy, and critically ill as desaturation during apnea gets delayed. The effects of alveolar recruitment on oxygenation last as long as the trachea is intubated, and lungs are ventilated with high PEEP. During apneic oxygenation, oxygen flow continues to take place without any lung movement due to mass flow of gases because of the gradient created by the continuous uptake of oxygen. This results in prolongation of safe apnea time. Hence, it is considered mandatory to maintain airway patency during apneic oxygenation for its beneficiary effects to manifest to the maximum.

It has been shown that administration of low fraction of inspired oxygen (0.5) with CPAP of 5 cm H₂O provides better arterial oxygenation with lower pulmonary shunt during one-lung ventilation as compared to high inspired fractions of oxygen (1.0) without CPAP. Earlier studies using CPAP have used a positive pressure ranging from 5 to 10 cm H₂O, whereas we used a positive pressure of 20 cm H₂O which was similar to airway pressure release ventilation (APRV) being used in ventilated patients. Safety of use of CPAP of this level could be justified with the fact that lung injury caused by APRV was found to be much lesser as compared to other controlled modes of ventilation. The rationale being that majority of the lung injury is caused by repeated opening and closing of alveoli (atelectrauma) as opposed to barotrauma. The ARDS protocol in this regard encourages the use of ventilatory modes ensuring airway plateau pressures <30 cm H₂O.

In our study, when patients were preoxygenated, CPAP was adjusted to ensure patient comfort, and during apnea, continuous positive pressure was maintained at 20 cm H₂O with vigilant monitoring to identify signs of increased intrathoracic volume. Development of hypotension not responding to fluid bolus or vasopressors was considered as a reflection of increased intrathoracic volume necessitating discontinuation of CPAP. However, during the present study, none of our patients had such complications.

Tolerable apnea time or safe apnea time is defined as the delay until the oxygen saturation reaches 90% which can be extended up to almost 10 min after 3 min of classic preoxygenation. However, maximizing benefits of preoxygenation with application of CPAP may be of an additional advantage in situations where apneic period needs to be prolonged. It may have application in surgeries such as direct laryngoscopies with biopsy from vocal cords or subglottic region where it is sometimes mandatory to keep patient apneic without intubation. Prolonging safe apnea time with preoxygenation with CPAP significantly increases patient safety in these situations. Moreover, this technique has application in managing patients with anticipated difficult airway.

The major drawback in our study was that we depended only on clinical signs to identify development of awareness, if any. Although the depth of anesthesia was ensured with
There are no conflicts of interest.