The effect of CPAP during preoxygenation and PEEP during induction upon the duration of non-hypoxic apnea and hemodynamic parameters

Genel anestezi sırasında preoksijenizasyonda CPAP uygulaması ile indüksiyonda PEEP uygulamanın non-hipoksidir apne süresine ve hemodinamik parametrelerine etkisi

Havva Esra Uyar Türkyılmaz 1, Asutay Göktuğ 2, Selçuk Tur 3, Hülya Başar 2

Aim: This study evaluated the effects of applying CPAP during preoxygenation and PEEP during mask ventilation upon the duration of non-hypoxic apnea and hemodynamic parameters.

Methods: This prospective randomized study included 100 patients allocated to 4 groups. In Groups I and III, preoxygenation was applied with CPAP mask without any pressure and during induction ventilation was performed with volume-controlled ventilation (CMV) in Group I and CMV + 6 cm H2O PEEP in Group III. In Groups II and IV, preoxygenation was applied with CPAP mask with 6 cmH2O pressure and during induction; ventilation was performed with CMV in Group II and CMV + 6 cm H2O PEEP in Group IV. After tracheal intubation, the tube was left open to air and the patient remained apneic until SpO2 reached 90%.

Results: The time for SpO2 to reach 90% is significantly longer in Group IV compared to the other groups. The durations were 412.50±97.37 sec in Group I, 443.52±88.84 sec in Group II, 415.20±117.45 sec in Group III, and 522.92±83.44 sec in Group IV. Using only CPAP during preoxygenation and only PEEP during mask ventilation had no significant effect on duration of non-hypoxic apnea.

Conclusion: Especially for patients with difficult intubation, application of CPAP during preoxygenation followed with PEEP during mask ventilation safe, simple and it prolongs non-hypoxic apnea period.

Keywords: CPAP, Non-hypoxic apnea, PEEP, Preoxygenation

Öz
Amaç: Bu çalışmada preoksijenizasyonda CPAP ve maske ile ventilasyon sırasında PEEP uygulamanın daha uzatmaktadır.

Yöntemler: Prospektif randomize çalışma 100 hasta 4 gruba ayrılmıştır. Grup I ve III‘te preoksijenizasyon PEEP maskesiyle uygulanmış ama hastaların başı açılmış, uygulananmış ve indüksiyon sırasında Grup I’de hücres kontrolü ventilasyon (CMV), Grup III’te ise CMV+6 cmH2O PEEP uygulanmıştır. Grup II ve IV’te ise preoksijenizasyon masası ile 6 cmH2O basınç uygulamış, indüksiyonu sırasında Grup II’de CMV ile ventilasyon sağlanması, Grup IV’te ise CMV+6 cmH2O PEEP uygulanmıştır. Trakeal entübasısondan sonra, tıbbi aycılın ve hasta SpO2 değeri %90’a düşene kadar apneik bırakılmıştır.


Anahtar kelimeler: CPAP, Non-hipoksidir apne, PEEP, Preoksijenizasyon

Abstract
Aim: This study evaluated the effects of applying CPAP during preoxygenation and PEEP during mask ventilation upon the duration of non-hypoxic apnea and hemodynamic parameters.

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Conclusion: Especially for patients with difficult intubation, application of CPAP during preoxygenation followed with PEEP during mask ventilation safe, simple and it prolongs non-hypoxic apnea period.

Keywords: CPAP, Non-hypoxic apnea, PEEP, Preoxygenation


**Introduction**

Using 100% oxygen during anesthesia induction is important in preventing hypoxia in the intubation period. The oxygen store in the body which is normally 1500 milliliters (mL) can rise to 3700 mL after preoxygenation with 100% oxygen [1]. When 100% oxygen is used in the induction period, the time for SpO2 to decrease to 90% is longer but using 100% oxygen is associated with atelectasis formation [2].

Atelectasis appears within minutes of induction of anesthesia in the lungs of 85–90% of healthy, non-obese patients [3,4]. Clinical studies have indicated that absorption atelectasis plays an important role in the genesis of anesthesia-related atelectasis and preoxygenation with 100% oxygen is the most important determinant in the formation of absorption atelectasis [5,6].

Formation of absorption atelectasis can be prevented by the application of positive end-expiratory pressure (PEEP) during the induction of anesthesia [7,8]. Herriger et al [9] reported that applying continuous positive airway pressure (CPAP) during preoxygenation and positive end-expiratory pressure (PEEP) during induction increases the duration of non-hypoxic apnea. Gender et al [10] had similar results in morbidly obese patients.

The aim of this study is to examine the effects of applying CPAP during preoxygenation and PEEP during mask ventilation upon the duration of non-hypoxic apnea and hemodynamic parameters and consequently to determine which technique is more effective.

**Materials and methods**

Approval for the study was granted by the Local Ethics Committee (Ankara Training and Research Hospital Ethics Committee, Decision No: 0208/1408). A total of 100 patients, ASA I or II, aged 19-60 years, admitted for elective surgery were enrolled into the prospective randomized study. Exclusion criteria included SpO2 < 97% breathing room air, body mass index > 30 kg.m-2, smoking history, hospitalization for > 24 hours and all medical conditions that contraindicated even a short desaturation of oxygen or rise in PaCO2 such as coronary artery disease, cerebrovascular disease, intracranial hypertension, epilepsy and severe pulmonary disease. It was also planned to exclude patients who were not intubated at the first attempt. Written informed consent was received from all patients.

The patients were randomly allocated to one of 4 groups using a computer-generated random number sequence. For all groups, without any premedication, anesthesia was induced using thiopental 5-7 mg.kg-1; fentanyl 1.5 µgr.kg-1; vecuronium 0.1 mg.kg-1 and maintained using sevoflurane 2% in N2O 0% - O2 50%.

In Group I, preoxygenation was applied with CPAP mask but without any pressure for 5 minutes and then during induction, ventilation was performed with volume-controlled ventilation (6-8 mL.kg-1). In Group II, preoxygenation was applied with CPAP mask with 6 cmH2O pressure for 5 minutes and then during induction, ventilation was performed with volume-controlled ventilation (6-8 mL.kg-1). In Group III, preoxygenation was applied with CPAP mask but without any pressure for 5 minutes and then during induction, ventilation was performed with volume-controlled ventilation (6-8 mL.kg-1) + 6 cmH2O PEEP. In Group IV, preoxygenation was applied with CPAP mask with 6 cmH2O pressure for 5 minutes and then during induction, ventilation was performed with volume-controlled ventilation (6-8 mL.kg-1) + 6 cmH2O PEEP.

All the patients were tracheally intubated. Preoxygenation, mask ventilation and tracheal intubation of all the patients were applied by the same investigator who had four years experience in anesthesia. A blinded observer assessed the non-hypoxic apnea period and adverse effects after intubation period. Correct placement of the tracheal tube was confirmed once by auscultation and capnogram after ventilation. The tracheal tube was left open to air at atmospheric pressure and the patient remained apneic until SpO2 decreased to 90%. The time for SpO2 to decrease to 90% was recorded. Mean arterial pressure (MAP), heart rate (HR) and peripheral oxygen saturation (SpO2) was recorded when the patient arrived at the operating table (T1), at the end of preoxygenation (T2), at the end of induction (T3), after intubation (T4) and when SpO2 was 90% (T5). The hemodynamic side effects (hypotension, hypertension, bradycardia, tachycardia, and other arrhythmias) were recorded and the appropriate treatment was applied. Bradycardia was defined as heart rate <50 beats.min-1, tachycardia as heart rate > 100 beats.min-1, hypotension as a decrease in MAP <70 mmHg or a decrease >20% of baseline MAP, and hypertension as systolic arterial pressure>160 mmHg or diastolic arterial pressure>110 mmHg.

**Statistical analysis**

All statistical analyses were performed with SPSS 11.0 software (SPSS Inc. Chicago, IL, USA). The sample size of this study was calculated based on the sample size of previous studies, using a significance level of 5% (p=0.05) and power of 97.5%. Continuous values were stated as mean and standard deviation (SD), and categorical values as number and percentage. Normal distribution was determined using the Kolmogorov-Smirnov test for demographic data (age, weight, height and BMI) (mean ± SD). The difference between the groups was analyzed using One Way Variance Analysis (ANOVA). The Bonferroni post Hoc test was used to detect which group was different. As the distribution of the groups was normal, mean arterial pressure, peripheral oxygen saturation and heart rate values between the groups were analyzed with one way variance analysis and the Bonferroni test. Adverse effects were analyzed with the Chi square test. For all countable parameters, the Kolmogorov-Smirnov test was used. For the analysis inside the groups, the Friedman ANOVA test was used for dependent groups. A value of p<0.05 was accepted as statistically significant.

**Results**

The demographic characteristics of the study participants are given in Table 1. There were no significant differences between the groups in respect of age, weight, or BMI (p>0.05). There was a difference between Group II and Group III in height (p=0.035). A patient from Group I was excluded from the study because of severe arrhythmia. All the patients were
intubated at the first attempt so none of the patients was excluded from the study because of intubation difficulties.

There was a statistically significant difference between Group II and IV in respect of mean arterial pressure (MAP) measured when the patient came to the operating room (T1) \(p=0.026\). There was no statistically significant difference within the groups or between the groups in respect of MAP at other measurement times (Table 2). A statistically significant difference was determined between Groups II and IV in respect of heart rate (HR) at the end of the preoxygenation period (T2) \(p=0.012\). There was no statistically significant difference within the groups or between the groups in HR at other measurement times (Table 3). At the end of the mask ventilation (T3), the peripheral saturation of oxygen (SpO\(_2\)) values of patients in Group I were significantly lower than those of Group III \(p=0.038\) and Group IV \(p=0.038\). There was no statically significant difference within the groups or between the groups in SpO\(_2\); at other measurement times (Table 4, p>0.05). The time for SpO\(_2\) to decrease to 90% (non-hypoxic apnea period) was statistically significantly longer in Group IV compared to the other groups. \(p=0.001\) Groups I-IV; \(p=0.030\) Groups II-IV; \(p=0.001\) Groups III-IV (Table 5, Figure 1). No statistically significant difference was found between the groups in respect of adverse effects (Table 6). The detected adverse effects were bradycardia, tachycardia, hypotension, and arrhythmia.

Table 1: The demographic characteristics of the study participants

<table>
<thead>
<tr>
<th>N</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>Group IV</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>25</td>
<td>25</td>
<td>25</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Age (year±SD)</td>
<td>34.16±11.19</td>
<td>30.88±11.09</td>
<td>34.96±11.96</td>
<td>33.36±11.59</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Height(cm±SD)</td>
<td>166.60±9.91</td>
<td>170.36±10.29</td>
<td>162.46±7.14</td>
<td>169.76±11.77</td>
<td>0.035*</td>
</tr>
<tr>
<td>Weight(kg±SD)</td>
<td>66.84±9.22</td>
<td>67.64±8.59</td>
<td>63.36±8.65</td>
<td>66.44±11.69</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>BMI(kg/m(^2)+SD)</td>
<td>23.99±2.32</td>
<td>23.26±2.99</td>
<td>23.97±3.07</td>
<td>22.96±3.38</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Table 2: The changes in mean arterial pressure (MAP)(mmHg±SD)

<table>
<thead>
<tr>
<th>T1</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>Group IV</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>96.64±13.24</td>
<td>91.76±9.35*</td>
<td>94.64±14.02</td>
<td>101.56±11.18*</td>
<td>0.026*</td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>95.88±9.84</td>
<td>93.28±8.51</td>
<td>94.04±12.12</td>
<td>95.96±11.63</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>T3</td>
<td>88.24±11.59</td>
<td>84.24±10.17</td>
<td>81.28±10.95</td>
<td>91.08±15.58</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>T4</td>
<td>110.32±15.50</td>
<td>111.92±9.99</td>
<td>113.48±13.70</td>
<td>117.60±19.92</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>T5</td>
<td>114.33±13.70</td>
<td>111.44±16.38</td>
<td>114.12±20.22</td>
<td>110.44±14.76</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

\(p<0.05\): T1: when the patient arrived at the operating table, T2: at the end of the preoxygenation period, T3: at the end of mask ventilation, T4: after intubation, T5: when SpO\(_2\) was 90%.

Table 3: The changes in heart rate (beats.min\(^{-1}\)+SD)

<table>
<thead>
<tr>
<th>T1</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>Group IV</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>84.84±17.43</td>
<td>77.08±19.87</td>
<td>82.36±16.87</td>
<td>88.72±17.42</td>
<td>&gt;0.05</td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>84.88±16.01</td>
<td>78.36±17.97*</td>
<td>84.08±15.76</td>
<td>92.56±13.25*</td>
<td>P=0.012*</td>
</tr>
<tr>
<td>T3</td>
<td>87.30±11.70</td>
<td>81.52±12.12</td>
<td>88.04±15.10</td>
<td>91.20±16.73</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>T4</td>
<td>97.64±13.41</td>
<td>94.72±9.92</td>
<td>102.48±11.96</td>
<td>98.60±12.85</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>T5</td>
<td>99.83±17.94</td>
<td>91.08±21.21</td>
<td>97.76±20.90</td>
<td>98.64±19.30</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

\(p<0.05\): T1: when the patient arrived at the operating table, T2: at the end of the preoxygenation period, T3: at the end of mask ventilation, T4: after intubation, T5: when SpO\(_2\) was 90%.

Table 4: The changes in spO\(_2\) (%±SD)

<table>
<thead>
<tr>
<th>T1</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>Group IV</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>99.16±1.06</td>
<td>98.68±1.06</td>
<td>98.64±1.11</td>
<td>99.24±0.87</td>
<td>&gt;0.05</td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>99.38±0.33</td>
<td>99.24±3.19</td>
<td>99.96±0.20</td>
<td>99.16±3.59</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>T3</td>
<td>99.44±0.50*</td>
<td>99.64±0.49</td>
<td>99.80±0.40*</td>
<td>99.80±0.40*</td>
<td>0.035*</td>
</tr>
<tr>
<td>T4</td>
<td>99.92±0.27</td>
<td>100.00±0.00</td>
<td>99.96±0.20</td>
<td>100.00±0.00</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>T5</td>
<td>99.00±0.00</td>
<td>99.00±0.00</td>
<td>100.00±0.00</td>
<td>99.00±0.00</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

\(p<0.05\): T1: when the patient arrived at the operating table, T2: at the end of the preoxygenation period, T3: at the end of mask ventilation, T4: after intubation, T5: when SpO\(_2\) was 90%.

Table 5: The time for SpO\(_2\) to decrease to 90% (sec±SD)

<table>
<thead>
<tr>
<th>SpO(_2)</th>
<th>Group I (n=24)</th>
<th>Group II (n=25)</th>
<th>Group III (n=25)</th>
<th>Group IV (n=25)</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>99%</td>
<td>412.50±79.37</td>
<td>443.52±88.84</td>
<td>415.20±117.45</td>
<td>522.92±83.44</td>
<td>&gt;0.001*</td>
</tr>
</tbody>
</table>

* \(p=0.001\) Group I-IV; \(p=0.030\) Group II-IV; ** \(p=0.001\) Group III-IV

Discussion

During general anesthesia, atelectasis formation with the use of 100% oxygen is of high importance in the intrapulmonary shunts primarily caused by atelectasis occurs during general anesthesia. The formation of atelectasis in patients during general anesthesia was demonstrated on computed tomography imaging in the 1980s. An increase in density in dependent regions of the lungs five minutes after the induction of anesthesia was reported. In animal researches, these densities have been reported as atelectatic lung regions.

The most dramatic effect of atelectasis is the impairment of systemic oxygenation. There is a correlation between the impaired gas exchange and atelectasis. A high concentration of inspired oxygen has been found to be related to atelectasis formation. It has been demonstrated that preoxygenation with 100% oxygen is the most important determinant in atelectasis formation. Previous studies have shown that when FiO\(_2\) is decreased or no preoxygenation is performed, atelectasis formation can be minimized. In this situation, the safe apnea period shortens. Preoxygenation before anesthesia induction is recommended to increase total body oxygen stores and delay oxyhemoglobin desaturation in the state of apnea. In patients at risk of rapid desaturation in particular or in those with no tolerance to a decrease in oxygen content, body oxygen stores must be filled.

It has been shown that applying CPAP during preoxygenation and PEEP during induction prevents atelectasis formation and improves oxygenation in patients who have been preoxygenated with 100% oxygen. Applying CPAP during preoxygenation and PEEP during mask ventilation has been reported to prolong the duration of non-hypoxic apnea by approximately 2 minutes. Applying 10 cmH\(_2\)O CPAP during preoxygenation and 10 cmH\(_2\)O PEEP during mask ventilation in...
morbidly obese patients has been reported to decrease the amount of atelectasis, improve arterial oxygenation and prolong the duration of the non-hypoxic apnea period [19]. In those studies, CPAP and PEEP were used together and therefore it could not be determined which was effective. In the current study, 4 groups were established to examine which method was more effective on the non-hypoxic apnea period, the application of CPAP during preoxygenation or PEEP during mask ventilation.

The main finding in this study was that using only CPAP during preoxygenation and only PEEP during mask ventilation had no effect on the duration of non-hypoxic apnea, but when CPAP and PEEP were used together, the non-hypoxic apnea period was significantly prolonged.

CPAP causes an increase in thoracic lung volume and functional residual capacity and a decrease in total airway resistance [20], lung compliance [21] and work of breathe [21]. CPAP prevents the collapse of alveoli of borderline stability as the effect is greater in the early period, when the alveoli are already open [22]. Some authors have reported the potential benefits of preoxygenating the patient with CPAP before intubation [23,24]. In contrast, it has been reported that no statistically significant difference was found in the safe apnea period between a group in which CPAP was used in the preoxygenation period and a control group [25]. Using CPAP during the preoxygenation period in morbidly obese patients has been reported to have no effect on the non-hypoxic apnea period. The mechanism of ineffectiveness of CPAP is explained as the regression of FRC to pre-CPAP levels within 1 min once the CPAP mask is removed or an increased activation of expiratory muscles to maintain lung volumes at previous values.

In the current study, no difference was found in the non-hypoxic apnea period between the group to which preoxygenation was administered with CPAP and mask ventilation was applied without PEEP (Group II) and the control group (Group I). This can be explained as the regression of FRC to pre-CPAP levels within 1 min once the CPAP mask was removed and after occurrence of this atelectatic areas as the mask ventilation was applied with 100% oxygen without PEEP.

The application of 10 cmH2O PEEP has been examined in many studies and has been reported to be successful in re-opening collapsed lung tissue. However, in some patients, small atelectatic areas persist. When PEEP level is increased, shunts do not always decrease and arterial oxygenation is not always improved. It can be explained as the redistribution of blood to the dependent regions of the lung because of the increased intrathoracic pressure. In this case, applying PEEP causes atelectatic lung regions to receive more blood from the pulmonary circulation [27].

To re-open all collapsed lung regions an inflation pressure of 40 cmH2O must be applied for 15 seconds [28]. This pressure is equal to vital capacity inflation and is therefore called the vital capacity maneuver (VCM). A previous study reported that arterial oxygenation improved in the group to which VCM was applied but showed no difference from the control group of 5cmH2O PEEP with no VCM [29]. The PEEP applied just after the VCM has been shown to be efficient in the prevention of atelectasis formation despite the use of 100% oxygen [30]. As a result, it has been demonstrated that to correct anesthesia-induced collapse, a pressure higher than the pressure of collapsed alveoli is needed.

In the current study, no difference was found in the non-hypoxic apnea period between the group to which preoxygenation was applied without CPAP and mask ventilation was performed with PEEP (Group III) and the control group (Group I). This situation can be explained by the inadequacy of the level of PEEP applied during the mask ventilation (6 cm H2O) to re-open the alveoli which had already collapsed during the preoxygenation without CPAP.

When CPAP is applied during the preoxygenation period and PEEP is applied during mask ventilation (Group IV), alveolar collapse is prevented beginning from the preoxygenation period and thus the level of PEEP used in the current study could be enough to keep the alveoli open despite the use of 100% oxygen. In this way the impairment in oxygenation is prevented and the duration of the non-hypoxic apnea period is prolonged.

A potential risk of mechanical ventilation by mask with PEEP is to expose a sedated, paralyzed patient to insufflation of the stomach, thereby, increasing the risk of regurgitation and bronchoaspiration. This risk exists with an insufflation pressure higher than 25 mm Hg. To avoid this complication, the alarm limits of the ventilator are set at 20mmHg, which will prevent the use of higher pressure via the facemask.

Adverse cardiovascular effects have been reported with the use of CPAP and PEEP. In the current study, no significant cardiovascular depressant effects of CPAP were observed in any group in respect of systolic, diastolic and mean arterial pressure. The mean heart rate was lower in Group II compared with Group IV, although in both groups CPAP was used at the end of the pre-oxygenation period. However, the difference was not evaluated as statistically significant. The CPAP mask may not be tolerated by conscious patients but in the current study it was well-tolerated by all patients. No adverse effects or impairment in cognitive functions developed in any patient throughout the follow-up period.

One limitation of the study is the absence of arterial blood gas analysis. Some studies measured paO2 values of the patients after intubation before lifting the tube at air at atmospheric pressure. In this study paO2 value at this time was not measured because further focus on the practical result - the safe apnea period is aimed.

The time for SpO2 to decrease to 90% was statistically significantly longer in the group for which preoxygenation was applied with CPAP and mask ventilation was applied with PEEP. Using only CPAP during preoxygenation and only PEEP during mask ventilation had no significant effect on the duration of non-hypoxic apnea. Therefore, especially for patients with difficult intubation, the application of CPAP during preoxygenation followed by PEEP during mask ventilation is a safe and simple method, which is well accepted by patients.

References
2. Edmark L, Enlund M, Kostova-Aherdan K, Hedenstierna G. Atelectasis formation and apnoea tolerance after pre-oxygenation with 100%, 80%, or 60% oxygen. Anesthesiology. 2001;95:A1330.


