THE EFFECT OF TWO DIFFERENT LEVELS OF POSITIVE END EXPIRATORY PRESSURE (PEEP) ON THE INCIDENCE RATE OF ATELECTASIS AND HEMODYNAMIC STATUS OF PATIENTS AFTER CORONARY ARTERY BYPASS SURGERY

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Abstract:
Background: Due to the high incidence of atelectasis following coronary artery bypass surgery and the effects of different levels of positive end expiratory pressure (PEEP) in preventing this condition, this study was designed aimed to investigate the effects of PEEP on the incidence of atelectasis after coronary artery bypass surgery

Material and methods: This study is a clinical trial with a control group conducted on 90 patients underwented coronary artery bypass surgery. After surgery and entering patients to the intensive care unit (ICU) the intervention group subjects were under PEEP = 10 cm H2O and the control group subjects were under PEEP = 5 cm H2O for 4 hours. For the final diagnosis of atelectasis, a chest radiograph was performed six hours after extubation and 5 days after surgery, saturation pulse oximetry was also examined.

Results: The observed difference in the incidence of atelectasis between the two groups 6 hours after extubation were statistically significant (P=0.003). There was also no statistical significant difference between the two groups 5 days after surgery (P=0.003). The difference between the two groups in terms of the average of saturation pulse oximetry was statistically significant (P=0.0025). There was no statistical significant difference between the two groups in terms of systolic (P = 0.25) and diastolic (P = 0.14) blood pressure before intervention. There also was no statistical significant difference between the two groups in terms of systolic (P = 0.62) and diastolic (P = 0.67) blood pressure after intervention.

Conclusion: this study indicated that applying PEEP=10 cmH2O after the Coronary Artery Bypass Surgery can lead to decrease the incidence rate of atelectasis following the surgery, and considering that applying of two levels of PEEP with 5 and 10 cm of water has no effect on the hemodynamic status of patients, so it is proposed that this technique be used at intensive care unit to reduce the incidence of atelectasis.

Keywords: positive end expiratory pressure (PEEP), coronary artery bypass graft surgery (CABG), atelectasis

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BACKGROUND:
Coronary Artery Disease is one of the most common chronic, progressive, and life-threatening diseases [1]. So that it is predicted that at least one in three deaths in developing countries will be due to cardiovascular diseases by 2020 [2]. Coronary artery bypass surgery is a common and successful way of coronary artery disease treatment [3]. Patients undergoing coronary artery bypass surgical treatment are at higher risk of pulmonary complications such as atelectasis [4]. Atelectasis due to hypoventilation, obstructive pulmonary diseases, deformation of the chest and diaphragm occur as a result of taking muscle relaxant drugs, cutting the sternum and cardiopulmonary bypass [5].

There is no agreement and consensus, at available resources, about the best rehabilitation intervention methods and improving the function of the respiratory system in patients undergoing CABG surgery [6]. Some of these methods are chest physiotherapy, incentive spirometry, training breathing exercises, deep cough and applying Positive End Expiratory Pressure (PEEP) [7]. Using PEEP causes to apply a pressure higher than barometric pressure at the end of expiration which reduces the incidence of atelectasis [8].

Different studies have investigated various levels of PEEP in order to improve pulmonary parameters and atelectasis incidence. In a study by Davoodi et al. patients who have received PEEP=5 cm/H2O during cardiopulmonary bypass compared to those who have not received any PEEP, showed higher levels of pulse oximetry pressure [9]. But in Gagnon et al. work, patients who have been ventilated with low tidal volume (3 cc/kg) and without applying PEEP have no higher Pao2 levels after cardiopulmonary bypass compared to those without above ventilation [10]. This difference in results obtained from Gagnon and Davoodi works has been likely due to the effects of the application of PEEP. In a study by Siliby et al. on patients underwent CABG surgery, the incidence rate of atelectasis was less in PEEP=20 cm/H2O group compared to the group with PEEP=5 cm/H2O [11].

Objectives
The overall goal of this study was to determine the effect of applying two different levels 5 and 10 cm of water of Positive End Expiratory Pressure (PEEP) on atelectasis incidence rate and on hemodynamic status of patients after coronary artery bypass surgery.

MATERIALS AND METHODS:
Setting
This study is a clinical trial with a control group conducted in KhoramAbad Shahid Madani Cardiovascular Specialist Hospital (affiliated with the Lorestan University of Medical Sciences) during 2013-2014. The trial protocol was approved by the research ethical committee of the university and also was registered in Iranian registry of clinical trial (IRCT) with the number of IRCT2013081714377N1.

Study Participants
The study population included all patients underwent coronary artery bypass surgery in Shahid Madani Hospital.

Inclusion Criteria
The age range of 30-80 years (EF>30%, BMI< 30 kg/m2), no history of Chronic Obstructive Pulmonary Diseases (COPD), Aortic clamp time less than 100 min., Cardiopulmonary Bypass time less than 120 min., anesthesia duration less than 8 hours, have surgery by median sternotomy method and not have surgery on an emergency basis.

Exclusion Criteria
using Intra-Aorta Balloon Pump (IABP) after surgery, experience mechanical ventilation more than 24 hrs., need for second surgery, need for mechanical ventilation out of ventilation protocol of the study and a drop in blood pressure greater than 10% of baseline blood pressure

Sample Size
The sampling method was consecutive convenient method so that, sampling was done from hospitalized eligible patients based on the study inclusion order and considering their consent. Based on the comparing the Pao2 average between the two groups of the same study, the obtained sample size was 45 subjects in reach group.

Randomization and Blinding
Patients were classified into two groups by stratified random blocking method and according to random table and in order of entering in groups, including the control group (PEEP=5 cm/H2O) and intervention group (PEEP= 10 cm/H2O). Samples were matched in both groups according to factors like age, gender, history of smoking and surgical method (on-pump or off-pump). Ventilatory parameters were standardized in both groups (SIMV, RP=12, -50%, TV=10 cc/kg FiO2) and then in case of having all the standard clinical criteria for extubation, they were extubated, and received it at a rate of 8-6 liters per minute for 24 hrs. using simple oxygen mask. However, the patients and investigator collecting the data were unaware of treatment assignment.

Intervention
After surgery and transferring to CSICU unit, patients were connected to mechanical ventilator,
and in the case of compliance of patients conditions with our ventilation protocol, they were included in the study and then interventions were applied by research assistant. Our intended variable was atelectasis occurrence six hours after extubation (removing the artificial endotracheal tube) and 5 days after surgery. The control group patients were subjected to PEEP=5 cm/H₂O upon entering the CSICU unit until extubation. On the other hand, intervention group subjects underwent PEEP=10 cm/H₂O upon entering CSICU unit for 4 hrs. and then underwent PEEP= 5 cm/H₂O until extubation. The patient's blood pressure was continently controlled immediately after transferring to CSICU unit through IBP, systolic and diastolic blood pressure were recorded 20 minutes after entering to unit and 2 hours after applying PEEP. Patient's SPo2 was measured every 2 hours for 5 days using NOVAMETRIX pulse oximetry. Measuring and recording systolic and diastolic blood pressure, Saturation Pulse Oximetry (SPo2) and applying PEEP performed by one of the nurses in ICU-OH unit (Research assistant) who was unaware of the two groups. Chest radiograph for antero-posterior Chest radiograph (A.P) was taken 6 hours after extubation and also 5 days after surgery. Atelectasis recurrence was diagnosed using Chest-X Ray evaluation by a radiologist who didn't know anything about random allocation of cases.

Tools
Data collection tools included three parts; the first part related to collect basic demographic information about patient. The second part consisted of two main question evaluating the incidence of atelectasis 6 hrs. after extubation and 5 days after surgery. The third part was a questionnaire related to check the patient's vital signs including systolic and diastolic blood pressure before applying PEEP and 2 hrs. after applying PEEP and also, saturation pulse oximetry 6 hrs. after extubation. The tools content validity reviewed and approved by 10 faculty members of Lorestan University of Medical Sciences.

Statistical Analysis
Software SPSS version 18 and also descriptive and inferential tests were used to analysis data. Descriptive statistics (frequency distribution tables) were used to describe demographic characteristics, Chi-square test was used to compare qualitative data between the two groups. In order to compare quantitative data between the two groups, independent T-test was applied. P<0.05 was considered significant in all tests.

RESULTS:
According to obtained results, in each group, 25 subjects (55.6%) were male and 20 subjects (44.4%) were female. 3 subjects in each group (6.7%) were in the age range 30-44 years, 16 subjects (35.6%) were 45-59 years and 26 subjects (57.8) were 60 or more than 60. 15 patients underwent off-pump surgery (33.3%) and 30 (66.7%) patients had on-pump surgery. The history of smoking equaled to 31.1% in each group. Body Mass Index (BMI) in PEEP=5 group was 24.6±3.7 kg/m² and in PEEP=10 group it was 23.4±3.6 kg/m², among which there was no statistical significant differences (P=0.82). No statistical significant differences were observed in terms of risk of high blood pressure, diabetes and hyperlipidemia (table 1).

Studied groups showed no significant differences statistically in terms of the mean duration of anesthesia, surgery duration, aortic clamp time, cardiopulmonary bypass time, the number of arterial and venous grafts and left ventricular ejection fraction (table 2).

<table>
<thead>
<tr>
<th>Variable</th>
<th>control group</th>
<th>Intervention group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>with</td>
<td>33 (73.3%)</td>
<td>27 (60%)</td>
<td>0.18</td>
</tr>
<tr>
<td>without</td>
<td>12 (26.7%)</td>
<td>18 (40%)</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>with</td>
<td>18 (40%)</td>
<td>15 (33.3%)</td>
<td>0.51</td>
</tr>
<tr>
<td>without</td>
<td>27 (60%)</td>
<td>30 (66.7%)</td>
<td></td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>with</td>
<td>31 (68.9%)</td>
<td>34 (75.6%)</td>
<td>0.48</td>
</tr>
<tr>
<td>without</td>
<td>14 (31.1%)</td>
<td>11 (24.4%)</td>
<td></td>
</tr>
</tbody>
</table>

The type of statistical test = Chi Square
Table 2: Mean and standard deviation of variables divided according to experimental groups

<table>
<thead>
<tr>
<th>variable</th>
<th>Group PEEP:10 Mean ± SD</th>
<th>Group PEEP:10 Mean ± SD</th>
<th>T-statics</th>
<th>df</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anesthesia duration (hrs.)</td>
<td>4.1±0.59</td>
<td>4.05±0.57</td>
<td>0.35</td>
<td>88</td>
<td>0.72</td>
</tr>
<tr>
<td>surgery duration, (hrs.)</td>
<td>3.62±0.58</td>
<td>3.55±0.58</td>
<td>0.54</td>
<td>88</td>
<td>0.59</td>
</tr>
<tr>
<td>aortic clamp time (hrs.)</td>
<td>45.23±7.68</td>
<td>49.23±8.72</td>
<td>-1.88</td>
<td>58</td>
<td>0.06</td>
</tr>
<tr>
<td>cardiopulmonary bypass time (hrs.)</td>
<td>52.46±11.41</td>
<td>55.5±10.11</td>
<td>-1.08</td>
<td>57</td>
<td>0.28</td>
</tr>
<tr>
<td>Arterial graft (No.)</td>
<td>1.02±0.15</td>
<td>1±0</td>
<td>1.01</td>
<td>87</td>
<td>0.31</td>
</tr>
<tr>
<td>Venous graft (No.)</td>
<td>2.33±0.7</td>
<td>2.28±0.95</td>
<td>0.23</td>
<td>75</td>
<td>0.81</td>
</tr>
<tr>
<td>left ventricular ejection fraction (%)</td>
<td>46±5.39</td>
<td>46.1±5.92</td>
<td>-0.093</td>
<td>88</td>
<td>0.92</td>
</tr>
</tbody>
</table>

The type of statistical test = independent T-test

Table 3: Mean and standard deviation of saturation pulse oximetry mean 6 hours after extubation

<table>
<thead>
<tr>
<th>Study groups</th>
<th>saturation pulse oximetry</th>
<th>T statistics</th>
<th>df</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEEP: 5</td>
<td>93.66 ± 1.16</td>
<td>-2.28</td>
<td>88</td>
<td>0.025</td>
</tr>
<tr>
<td>PEEP: 10</td>
<td>94.31 ± 1.48</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The type of statistical test = independent T-test

Independent t-test demonstrated that saturation pulse oximetry mean 6 hours after extubation in intervention group was more than the control group (94/31±1/48 vs. 93/66±1/16), this difference was significant statistically (P=0/025) (table 3).

The incidence rate of atelectasis 6 hours after extubation based on the Chest-X Ray changes were equal to 16 subjects (35/6%) in control group and 7 subjects (15/6%) in intervention group. This difference was significant statistically (P=0/03).

The incidence of atelectasis 5 days after surgery extubation based on the Chest-X Ray changes were equal to 3 subjects (6/7%) in control group and 1 subject (2/2%) in intervention group, this difference was not statistically significant (P=0/3) (table 4).

Based on the results of the independent t-test, before the intervention, there was no statistical significant difference regarding the mean systolic blood pressure (P=0/25). Also, no statistical significant difference was observed between the two groups in terms of diastolic blood pressure (P=0/14) (table 5).

Table 4: Frequency of atelectasis 6 hours after extubation and five days after surgery.

<table>
<thead>
<tr>
<th>5 days after surgery</th>
<th>6 hours after extubation</th>
<th>variable</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 (6.7%)</td>
<td>16 (35.6%)</td>
<td>64.4%</td>
</tr>
<tr>
<td>1 (2.2%)</td>
<td>7 (15.6%)</td>
<td>84.4%</td>
</tr>
</tbody>
</table>

Statistical test: Chi-square

Table 5: comparing the mean and standard deviation of systolic and diastolic blood pressure in study groups before intervention

<table>
<thead>
<tr>
<th>Study groups</th>
<th>PEEP:5</th>
<th>PEEP:10</th>
<th>Pressure(p)</th>
<th>T</th>
<th>Df</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic pressure</td>
<td>117.9 ± 21.4</td>
<td>112.6 ± 21.6</td>
<td>0.25</td>
<td>1.15</td>
<td>88</td>
</tr>
<tr>
<td>Diastolic pressure</td>
<td>73.5 ± 10.5</td>
<td>69.9 ± 12.5</td>
<td>0.14</td>
<td>1.47</td>
<td>88</td>
</tr>
</tbody>
</table>

Statistical test: independent T-test
Table 6: comparing the mean and standard deviation of systolic and diastolic blood pressure in study groups after intervention

<table>
<thead>
<tr>
<th>Study groups</th>
<th>PEEP:5</th>
<th>PEEP:10</th>
<th>P value</th>
<th>T</th>
<th>DF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic pressure</td>
<td>112.8 ± 18.1</td>
<td>111.02 ± 16.7</td>
<td>0.62</td>
<td>0.49</td>
<td>88</td>
</tr>
<tr>
<td>Diastolic pressure</td>
<td>70.5 ± 9.3</td>
<td>69.5 ± 10.8</td>
<td>0.67</td>
<td>0.42</td>
<td>88</td>
</tr>
</tbody>
</table>

Statistical test: independent T-test
Based on the results of the independent t-test, after the intervention, there was no statistical significant difference regarding the mean systolic blood pressure (P=0.62). Also, no statistical significant difference was observed between the two groups in terms of diastolic blood pressure (P=0.67) (table 6).

**DISCUSSION:**
The results of this study showed that the incidence of atelectasis six hours after extubation was different statistically between the two group, but 5 days after surgery this difference was not significant. The average of saturation pulse oximetry was not significant statistically. The difference in systolic and diastolic blood pressure between the two groups was not statistically significant. Based on the research findings, it seems that variables such as saturation pulse oximetry are not considered as atelectasis specific symptoms, so that in the present study, no clear and significant changes was observed in these symptoms. Although, the average of saturation pulse oximetry 6 hours after extubation in intervention group was more compared to control group (94.31±1.48 vs. 93.68±1.61) and this was a significant statistical difference (P=0.025). However, clinically, this difference was not statistically significant because saturation pulse oximetry less than 90% was not observed in none of the patients; but, according to the radiologist diagnosis, Chest x-ray results suggested changes caused by the collapse that were observed as proportional and in linear form, that is, the extent of atelectasis was limited. Perhaps the reason for the lack of saturation pulse oximetry less than 90% is that atelectasis has not been complete in these patients, but also it was linear and proportional.

Therefore, in this study it was shown that in order to diagnosis of postoperative atelectasis or to evaluate this complication between hospitalized patients caused by secretions accumulation due to respiratory muscle weakness, reducing the activity of the respiratory center due to consumption of narcotic drugs, reducing the number of sighing, reducing surfactant and so on, one should not expect to see very apparent signs, because atelectasis is not extensive in these patients, but it is in moderate to mild levels. Postoperative atelectasis is very important because it does not cause very sever clinical representations, so does not draw the attention of medical staff, but due to its progressive course can cause to develop side effects such as hospital pneumonia, postoperative breathing problems, increased length of hospital stay and increased therapeutic costs. Atelectasis, whether severe or mild, can cause infection and damaging to lungs tissue. So it must be diagnosed and appropriate remedial measures be taken prior to progress and develop clinical symptoms. According to the obtained results it was found that the incidence of atelectasis six hours after extubation in intervention group was less than the control group. Perhaps, we can say that higher levels of PEEP are affective in opening the lungs and removing atelectasis, because applying PEEP inhibits the small airways collapse, increases Functional Residual Capacity (FRC), improves pulmonary alveolar function, decreases the intra-pulmonary shunt and also improves the oxygenation. All of these impacts reduce the incidence of atelectasis in patients who have higher levels of PEEP after CABG surgery. Increased Functional Residual Capacity is the main consequence of PEEP which can cause fluid displacement in interstitial space, improve oxygenation and help to eliminate micro atelectasis alveoli [12]. According to the results, in addition to that the incidence of atelectasis five days after surgery was not statistically significant between the two groups (P=0.03), its incidence was reduced in both groups compared to six hours after extubation, and this reduction may be due to the fact that atelectasis in these patients is non-extensive, proportional and linear and also, occurred atelectasis can be removed through appropriate medical interventions during 5 days after surgery.

Although it is believed that increased positive end expiratory pressure can lead to reduce the cardiac output and to disrupt the hemodynamic status of patients, but according to our findings, the hemodynamic status of patients in both groups before and after intervention has no significant difference statistically, so it can be concluded that applying 5 and 10 cm /H2O PEEP cannot lead to a disruption of the patient’s hemodynamic status. Therefore, it can be concluded that research hypothesis that is “the incidence of atelectasis after coronary artery bypass surgery is different between intervention and control groups” is approved. In this regard, Zupancich et al. have reported that 40 patients underwent coronary artery bypass surgery...
after cardiopulmonary bypass were divided into two groups and were ventilated by two different methods. The first group, was ventilated with high tidal volume (10 to 12 cc per kilogram of body weight) and low positive end expiratory pressure (PEEP = 2-3 cm/H2O) and the second group with low tidal volume (8 cc per kilogram of body weight) and high positive end expiratory pressure (PEEP = 10 cm/H2O), then, IL-6 and IL-8 were measured in Broncho alveolar Lavage fluid and plasma. IL-6 and IL-8 in Broncho alveolar Lavage fluid and plasma in both groups have increased immediately after cardiopulmonary bypass. But 6 hours after mechanical ventilation, it was increased only in patients ventilated with low tidal volume and high PEEP. So we can say that applying mechanical ventilation using PEEP as a cofactor can influence inflammatory response after cardiac surgery [13]. According to this study, it may be said that high levels of PEEP decreases inflammatory responses in patients subjected to mechanical ventilation and reducing the inflammatory processes in the lungs may be one of the PEEP mechanisms which improves arterial oxygenation and respiratory condition. By the same token, Dave et al. have examined 120 patients (in one RCT) with coronary artery bypass surgery in two equal groups of PEEP=5 cm/H2O receivers and PEEP=10 cm/H2O receivers, among which the difference in arterial oxygenation was statistically significant so that arterial oxygenation levels were higher in PEEP=10 group. The results of this study were in accordance with the results of our study [14]. Lakinger and colleagues also reported that applying PEEP= 10 cm/H2O during cardiopulmonary bypass have had positive effects on postoperative respiratory parameters, so that final results indicated improved arterial oxygenation by 20% and reduced shunting in the lungs by 50% [15]. Along with the results of this study, in a research by Niazi et al. on the effects of PEEP=0,5-10 cm/H2O on the incidence of atelectasis in patients undergoing coronary artery bypass surgery, it was revealed that the incidence of atelectasis in group receiving PEEP=5-10 cm/H2O was less than group receiving PEEP=0 cm/H2O and this difference was significant statistically (P<0/02). But, there was no significant difference statistically in terms of saturation pulse oximetry (SpO2). Therefore, as stated in the results of the Niazi study, criteria such as saturation pulse oximetry cannot be considered as final diagnostic factor of atelectasis; this finding has been confirmed in our study [16]. Moreover, in a meta-analysis study, 388 patients have been evaluated in the form of 8 clinical trials divided in two groups PEEP recipients PEEP non-recipients. In this research, the Pressure arterial O2 / Friction Inspiratory O2 (Pao2/Fio2) ratio on the first day after surgery was higher and atelectasis incidence was less in PEEP recipient group. There were no significant differences between the two groups regarding mortality rates, barotrauma (pneumothorax) and reducing the cardiac output [17]. Despite the useful positive effects of PEEP in improving the arterial oxygenation and reducing atelectasis incidence, its applications in clinical conditions is restricted due to the risk of complications such as barotrauma (pneumothorax) and reducing the cardiac output. Although, based on the findings of this meta-analysis and results obtained from other similar studies, we can say that applying PEEP will not cause to such complications within the physiological and medical range. Therefore, it can be used to reform and improve oxygenation conditions in patients subjected to mechanical ventilation under medical supervision.

In general, according to the results of this study it can be concluded that applying 10 cm/H2O of positive end expiratory pressure can cause to decrease the atelectasis incidence and can be effective on enhancing the abilities of the patient; also using 5 and 10 cm/H2O of PEEP does not disrupt the hemodynamic status of patients. The main role of chest radiography for the detection of atelectasis after coronary artery bypass surgery is another critical finding of this study. It is highly recommended to follow up in the next days or even weeks after surgery in order to evaluate respiratory complications, especially atelectasis in CABG patients, however, because of certain limitations this process didn’t carry out in our study. It is suggested that considering positive significant effects of different levels of PEEP in reducing postoperative atelectasis, further investigation be carried out regarding evaluation of PEEP application during surgery and/or after surgery in patients undergoing valve surgery and long-term surgeries such as thoracic and upper abdominal surgeries which require postoperative ventilator.

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