Acute Effects of Continuous Positive Airway Pressure (CPAP) on Cardiovascular Responses in Healthy Subjects- A Single-Subject Experimental Design

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Introduction

There are significant correlation between the process of respiration and cardiovascular system. In the CNS, there are interactions between the respiratory pacemakers and efferent autonomic tone, which directly affect the HR and blood pressure. One factor that directly influences the cardiovascular response from the breathing process is the decrease in venous return during spontaneous inspiration, caused by increased intra-thoracic pressures, this phenomenon is called "respiratory pump", where the increase in venous return occurs due to an increase in the pressure gradient between the right heart chamber and leading into vessels. 

The breathing also causes changes in vagal tone, centrally mediated and related to breathing. These variations result in a decrease in vagal activity during inspiration and an increase in this activity during the expiratory phase. The utilization of Noninvasive ventilation (NIV) can modify these settings.

Objective: Thus the aim of the present study was to investigate the effects acute cardiovascular of Continuous Positive Airway Pressure (CPAP) utilization in healthy subjects. Materials and methods: On the third day, subjects rested the at the sitting position for 45 min, 15 min a respiratory frequency of 15 breath for minute without CPAP, and then 15 minutes with a positive pressure of 20 cmH2O and PEEP of 15 cmH2O with a face silicone mask. During the last 15 min volunteers rested quietly breathing again without CPAP. Blood pressure (BP) was measured by the auscultatory method every five minutes on the right arm and heart rate (HR) was obtained beat-by-beat by a R-R recorder (S810 Polar®, Finland). HR times series were processed by a specific algorithm developed in MATLAB® for time and frequency domain analysis. A two-way analysis of variance for repeated measures was used verify the effects of CPAP on BP and HR with or without positive pressure, and a Tukey test for post hoc comparisons. Statistical significance was accepted for p<0.05. Results: During the CPAP utilization there was a decrease in systolic blood pressure (SBP) and increased HR (p< 0.05), with a discrete but not significant fall in diastolic blood pressure (DBP) and rate pressure product (RPP). Spectral analysis showed an increase in the LF component and a decrease in the normalized HF component as measured in normalized units.

Conclusion: In healthy subjects the use of CPAP resulted in a drop in SBP, followed compensatory reflex mechanisms od HR when performed HRV analysis in time domain and frequency. We suggest further studies to investigate such mechanisms.

Key words: autonomic function, heart rate variability, continuous positive airway pressure, cardiopulmonary rehabilitation, cardiovascular effects.

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The NIV or of spontaneous ventilatory may be administered by some specific modalities such as continuous positive air pressure (CPAP), the Biphasic Air Pressure (BIPAP) and Proportional Pressure Assist Ventilatory.
The acute cardiovascular responses arising from the use of NIV are directly related to Positive Expiratory End Pressure (PEEP) was applied as technical resource for the treatment of acute cardiogenic pulmonary edema then in the mid 60, it was used as treatment technique in acute respiratory distress syndrome.5,6

Among the physiological effects of PEEP can be highlighted improvement of respiratory system compliance increased functional residual capacity (FRC), improved gas exchange decreased cardiac output, increased intrathoracic pressure, decreased venous return to the chest causing decrease in preload.7

There are few studies in the literature describing the acute cardiovascular responses arising from the use of NIV in any of its type in health subjects.6,8,9 Previous research showed that in resting conditions CPAP reduced the arterial blood pressure (BP) due to an increase in the spontaneous baroreflex sensitivity,8 or increased the baroreflex secondary to BP decline,9 possibly because of augmented intrathoracic pressure and reduced stroke volume.6,9 Thus the aim of the present study was to investigate the acute cardiovascular effects of CPAP utilization in healthy subjects.

Materials and methods

Subjects

Eleven healthy male subjects participated as subjects in the study. All subjects gave informed written consent to experimental procedures, which were approved by the Ethics Committee in Research of Universidade Salgado de Oliveira (process 61/2008) in accordance with Resolution 196/96 National Council of Health of Brazil. Subjects were not engaged in any exercise training program and had normal respiratory function defined by spirometry. Adaptation to CPAP was evaluated to exclude those who felt incapable to breathe using the device. Included in the study individuals were healthy volunteers, not practicing physical activity. Excluded from the study were individuals who showed changes in pulmonary function tests, acute diseases, cardiovascular and metabolic diseases known, the CPAP mask phobia, cognitive impairments that prevent the realization of the protocol.

Experimental Protocol

The experimental protocol was conducted on two days separated by 48 hours, at the same time of the day (13:00-18:00h). Volunteers abstained from caffeine for 6 hours prior to protocol and physical exercise for 24 hours prior to protocol and fasted for 2 h before the protocol. During all sessions, environment temperature was controlled and adjusted to 21 to 23°C. In the first day subjects underwent anthropometric and body composition evaluation, pulmonary function testing (PFT) and adaptation to CPAP (Rem Reset® – 1999, Model C1001, USA) with 10 cmH2O.

Anthropometry (first day)

The body mass (Welmy® 2006, Brazil), height (American Medical do Brasil, Brazil), and three skinfolds (pectoral, abdominal and thigh) (Lange, Skinfold Caliper – 2001, CA, EUA) were assessed to calculate body density, body fat, and body mass index (BMI).

Pulmonary Function Testing and Adaptation to CPAP (first day)

Pulmonary Function Testing (PFT) were measure the total lung capacity (TLC) and to strongly exhale into the spirometer’s mouthpiece to measure the residual volume (RV).executed three times and the best result was computed for forced vital capacity (FVC), forced expiratory volume in one second (FEV1), peak flow (PF) and FEV1/FVC (EasyOne®, Model 2001, Switzerland).10

Maximum inspiratory pressure (MIP) and maximum expiratory pressure (MEP) were measured with manuvacuometers (M120 healthcare; 2001; São Paulo, Brazil) to verify static respiratory pressure. The manuvacuometer mouthpiece has 2-mm holes that dissipate the pressures generated by the facial muscles and the oropharynx. To measure the MIP, individuals were instructed to exhale up to the RV, inhale deeply with the manuvacuometer’s mouthpiece (Müller’s maneuver) in place and maintain the strain with their
respiratory muscles for 3 seconds.\textsuperscript{11}

The subjects underwent a 15 minute adaptation protocol to CPAP breathing at a respiratory frequency of 15 breath for minute with a positive pressure of 20 cmH\textsubscript{2}O and end expiratory pressure (PEEP) of 10 cmH\textsubscript{2}O.\textsuperscript{5}

\textit{CPAP to utilization and cardiovascular measurement(second day)}

On the third day, subjects rested the at the sitting position for 45 min, 15 min a respiratory frequency of 15 breath for minute without CPAP, and then 15 minutes with a positive pressure of 20 cmH\textsubscript{2}O and PEEP of 15 cmH\textsubscript{2}O with a face silicone mask. During the last 15 min volunteers rested quietly breathing again without CPAP.\textsuperscript{2}

Blood pressure was measured by the auscultatory method every five minutes on the right arm using a mercury column (Oxigel\textsuperscript{®}, Brasil) and HR was obtained beat-by-beat by a R-R recorder (S810 Polar\textsuperscript{®}, Finland).\textsuperscript{12} HR times series were processed by a specific algorithm developed in MATLAB (Mathworks\textsuperscript{®}, Massachusetts, USA) for time and frequency domain analysis.\textsuperscript{13} The time domain analysis variables were: mean R-R intervals, standard deviation of R-R intervals (SDNN), the number of pairs of adjacent R-R intervals differing by more than 50 ms from de previous ones (NN50), the percentage of NN50 from the whole time series and the squared root of the mean squared successive differences of R-R intervals (rMSSD). Spectral analysis was obtained by means of a Fast Fourier Transformation with the Welch’s periodogram and a Hanning window with 50\% overlapping, and the spectral power calculated by integration of the power spectrum density function in the whole spectrum (Total power), very low (< 0.04 Hz), low (LF; 0.04-0.15 Hz) and high frequency (HF; 0.15-0.4 Hz) bands. The LF and HF powers were also computed in normalized units dividing the respective power by the total power subtrated the VLF power.\textsuperscript{14}

\textbf{Statistical analysis}

The appropriate sample size was calculated by adjusting the power of statistical tests and error \( \alpha \) to 0.8 to 0.05. To analyze the results and preparation of the chart, we used the program SigmaStat 3.1 (Jandel Scientific, San Rafael, CA, USA) and SigmaPlot 9.01 (Jandel Scientific, San Rafael, CA, USA), respectively. Data distribution was checked by Kolmogorov-Smirnov test (with Lilliefors correction) and homogeneity of variances (Levene’s test).

A two-way analysis of variance (ANOVA) measures was used verify the effects of CPAP on BP and HR with or without positive pressure, and a Tukey test for post hoc comparisons. Statistical significance was accepted for \( p < 0.05 \) (Graphpad Prism\textsuperscript{®} 4.0, CA, USA).

\textbf{Results}

From the initial eleven volunteers two were rejected for reporting phobia to the facial mask during CPAP adaptation. The anthropometric data and PFT results of the remaining nine subjects are presented in Table 1.

During the CPAP utilization there was a decrease in systolic blood pressure (SBP) and increased HR (\( p < 0.05 \)), with a discrete but not significant fall in DBP and RPP (Figure 1). Spectral analysis showed an increase in the LF component and a decrease in the normalised HF component as measured in normalized units (Table 2).

\textbf{Discussion}

The present study determined the effects of positive airway pressure was to investigate the effects acute cardiovascular of CPAP utilization in healthy subjects. The PFP used as part of an exclusion criterion indicates that no components of the sample showed a change in origin restrictive or obstructive, as well as MIP MEP and which allows us to state that none of the results obtained with the use of NIV are influenced by lung disorder.

Second, our data showed that CPAP has distinct effects on HR and BP from rest to high intensity sustained exercise. At rest, positive ventilation reduced BP and produced reflex tachycardia, however during heavy sustained exercise BP and HR were similar to free breathing. Third, during heavy exercise both central and peripheral RPE were lower in CPAP condition to a greater period of time as compared to control.
Table 1: Anthropometric characteristics and pulmonary function of the participants.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>25.2±4.4</td>
</tr>
<tr>
<td>Body mass (kg)</td>
<td>72.6±5.8</td>
</tr>
<tr>
<td>Stature (cm)</td>
<td>172.9±5.9</td>
</tr>
<tr>
<td>Body fat (kg)</td>
<td>13.4±6.5</td>
</tr>
<tr>
<td>Lean body mass (kg)</td>
<td>58.7±3.3</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>24.8±3.2</td>
</tr>
<tr>
<td>Abdominal Circumference (cm)</td>
<td>82.4±8.2</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>19.6±7.7</td>
</tr>
<tr>
<td>FVC (L)</td>
<td>4.7±0.6</td>
</tr>
<tr>
<td>FEV₁ (L)</td>
<td>3.9±0.4</td>
</tr>
<tr>
<td>PF (L·seg⁻¹)</td>
<td>594.11±93.7</td>
</tr>
<tr>
<td>FEV₁/CVF (%)</td>
<td>0.84±0.07</td>
</tr>
<tr>
<td>MIP (cmH₂O)</td>
<td>118.2±5.3</td>
</tr>
<tr>
<td>MEP (cmH₂O)</td>
<td>117.5±3.9</td>
</tr>
</tbody>
</table>

FVC = forced vital capacity; FEV₁ = forced expiratory volume at the first second; PF = peak flow; MIP = maximal inspiratory pressure; MEP = maximal expiratory pressure; MVV = maximal voluntary ventilation. Data are means ± DP

Table 2: Spectral and time domain analysis heart rate variability pre CPAP, CPAP and post CPAP

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre CPAP</th>
<th>CPAP</th>
<th>Post CPAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>NN</td>
<td>821.49±71.21</td>
<td>807.43±56.60*</td>
<td>859.10±68.81</td>
</tr>
<tr>
<td>SDNN (ms)</td>
<td>60.64±20.81</td>
<td>62.45±10.31</td>
<td>68.50±4.88</td>
</tr>
<tr>
<td>NN50 (ms)</td>
<td>117.25±54.74</td>
<td>153±86.01†</td>
<td>134±78.84</td>
</tr>
<tr>
<td>pNN50 (%)</td>
<td>15.92±7.10</td>
<td>19.32±9.61</td>
<td>18.63±10.45</td>
</tr>
<tr>
<td>rMSSD (ms)</td>
<td>37.08±6.10</td>
<td>39.86±8.69</td>
<td>39.22±9.16</td>
</tr>
<tr>
<td>Total power (ms²)</td>
<td>3496.59±2464.68</td>
<td>2670.53±1459.10*</td>
<td>5960.86±2922.24</td>
</tr>
<tr>
<td>VLF (ms²)</td>
<td>1357.56±1065.62</td>
<td>1331.60±803.14</td>
<td>3094.62±2799.52</td>
</tr>
<tr>
<td>LF (ms²)</td>
<td>666.61±593.30</td>
<td>1010.15±500.47†</td>
<td>1420.44±995.45†</td>
</tr>
<tr>
<td>LF normalized</td>
<td>25.34±14.23</td>
<td>51.12±12.81</td>
<td>45.87±26.80</td>
</tr>
<tr>
<td>HF (ms²)</td>
<td>525.78±402.54</td>
<td>421.22±308.49</td>
<td>1154.06±1110.24*</td>
</tr>
<tr>
<td>HF normalized</td>
<td>30.82±17.75</td>
<td>20.56±9.30</td>
<td>30.86±16.25</td>
</tr>
<tr>
<td>LF/HF</td>
<td>1.73±1.40</td>
<td>3.74±3.31†</td>
<td>1.91±1.77</td>
</tr>
</tbody>
</table>

NN = number of NN intervals; SDNN = Standard deviation of all NN intervals; rMSSD = Square root of the mean of the sum of the squares of differences between adjacent NN intervals; pNN50 = NN50 count divided by the total number of all NN intervals; VLF = Power in very low frequency range; LF = Power in low frequency range; HF = Power in high frequency range; LF/HF = HF/(Total Power-VLF) x 100 Ratio LF [ms²]/HF [ms²].

*statistical difference (p<0.05) † (p < 0.01).

Data are means ± SD.

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Figure 1: Behavior of blood pressure, heart rate and rate pressure product during use of CPAP at home.

Values expressed in mean±sd of eleven subjects in our sample. p <0.05. SBP = systolic blood pressure; DBP = diastolic blood pressure; HR = heart rate

The most common effects of CPAP is the increase of residual functional capacity and lung complacence, increase in arterial oxygen partial pressure, intrathoracic pressure and reduction of preload.15-18 Cassidy et al19 described the cardiovascular effects of PEEP set at 10cmH₂O in healthy subjects, showing a fall in BP using intraarterial catheter, and changes in transmural pressure and CO reductions.

The findings of Cassidy et al19 are similar to those who conducted an experiment using two-dimensional echocardiography for evaluation of the hemodynamic effects of NIV in CPAP mode with PEEP of 15cmH₂O compared with control period. The sample group consisted of 15 healthy subjects, which evidenced a change in the diameter of the vena cava and reduced end systolic volume equivalent to 15% and 21% diastolic volume, thus demonstrating a reduction in preload. But there was no evidence any statistically significant change observed when the ejection period.

The results obtained by Leech & Ascah21 differ from those described above, which evaluated the effects of NIV by echocardiography, with PEEP values ranging from 5 to 15 cmH₂O in 19 healthy volunteers and 6 patients with sleep apnea, not being statistically significant alterations in pulmonary artery pressure, ventricular blood volume and cardiac index. But it is noteworthy that this experiment the data from healthy subjects were compared to patients with sleep apnea (which were the
control group. Since the cardiovascular responses are directly related to the value of PEEP, the variation of these values may have influenced the results.

In the present study there was a marked fall in BP during CPAP as compared to pre- and post-CPAP adjusted for 15 cm H_2O of PEEP at a breathing frequency of 15 bpm, similar to others. There is scarce data in literature regarding CPAP application to healthy and young subjects. Valipour et al described stroke volume reductions up to 38% and and 28% in CO relative to control without CPAP, for all studied PEEP values, strongly suggesting baroreflex-induced vagal withdrawal. On the other hand, the low PEEP pressure utilized by Fietze et al produced augments in BP pressure and possible baroreflex-induced increases in vagal modulation of HR as shown by the higher values for the index in the HF band. Our results are in line with those of Valipour et al with BP reductions and increased LF power and reduced spectral HF power of HR, suggesting a reflex mediated by the baroreceptors. In our study volunteers were in the sitting position that may have influenced the results as compared to those at supine with the head elevated 30°.

In another study, Fietze et al investigated 55 healthy subjects from both sexes, 47±11 years old, applying CPAP in the supine position with the head elevated 45°. Volunteers underwent CPAP adaptation for ten minutes with a PEEP of 5 mbar that is equivalent to 5.1 cm H_2O, breathing at 12 bpm. Differently form the present study and others, there was an increase in both systolic and diastolic BP with augmented spontaneous baroreflex as evaluated by the HF component of the respiratory sinus arrhythmia (RSA). This means that both the process of inspiration and expiration, at first we find a rise in HR, followed by a decrease of the same, differing from the two phases of the respiratory cycle only on the time of appearance of larger and smaller values of FC. However it is believed that increasing the CPAP using gives rise to new adjustment mechanisms as observed in our study and in described by other authors.

In healthy subjects the use of CPAP resulted in a progressive reduction in parasympathetic modulation of HR correlated to increases in PEEP values, strongly suggesting baroreflex-induced vagal withdrawal. The major limitation of this study was to measuring blood pressure by auscultation, but the study by Polito et al demonstrated that since the examiner is properly trained, there are no significant differences between the values found by the method auscultarório when compared to the gold standard for verification of noninvasive blood pressure (photoplethysmographic), validating the results obtained by our group.

Study limitations

None identified and/or declared.

References:


