Analysis of heart rate variability in individuals subjected to different positive end expiratory pressure levels using expiratory positive airway pressure

Thiago Lorentz Pinto1, Luciana Maria Malosá Sampaio1, Ivan Peres Costa1, Leandro Yukio Alves Kawaguchi1, Flávio Aimbire Soares de Carvalho2, Regiane Albertini de Carvalho1

Abstract

Introduction: The increase in the number of studies has led to greater security in the application of this method and the determination of its effectiveness in adults. The purpose of the present study was to evaluate heart rate variability in healthy individuals subjected to different levels of positive expiratory pressure using an expiratory positive airway pressure (EPAP) device.

Material and methods: The study involved 27 healthy male individuals ranging in age from 20 to 35 years. Patient histories were taken and the subjects were submitted to a physical examination. The volunteers were monitored using the Polar 810s® and submitted to the EPAP experiment. Analyses were performed on variables of the frequency domain. Sympathetic and parasympathetic bands and their relationship with sympathovagal response were also analyzed.

Results: The mean value of this variable was 526.89 (55.50) ms² in the first period, 2811.0 (721.10) ms² in the fourth period and 726.52 (123.41) ms² in the fifth period. Regarding the parasympathetic area, significant differences were detected when Periods 1 and 5 (no load) were compared with periods in which the individuals were subjected to the use of the therapy. Sympathetic and parasympathetic areas together, a significant difference was detected regarding the sympathetic/parasympathetic ratio in the comparison between Periods 1 and 4 (p < 0.01) as well as Periods 2 and 4 (p < 0.05).

Conclusions: The findings of the present study suggest that the therapeutic use of EPAP significantly alters the parameters of heart rate variability in the frequency domain, highlighting the importance of monitoring and care during the practice of EPAP.

Key words: heart rate variability, positive expiratory pressure, healthy individuals.
avoidance of endotracheal intubation and associated complications. Other benefits include increased comfort, reducing need for sedation, preservation of speech and swallowing, preservation of upper airway functions, such as heating and humidifying inspired air, preservation of the defense functions of the mucociliary system, a lower incidence of barotraumas and a reduced need for enteral nutrition, as the patient’s swallowing capacity is unaffected. However, enteral nutrition can be maintained, if needed, with the tube set in the mask.

Noninvasive positive pressure can also be used in home care for patients with cardiovascular, respiratory, central nervous system, neuromuscular and skeletal disorders. Despite the frequent use of EPAP, the literature on this subject is scarce, especially with regard to the adverse effects [1, 2]. Respiration exerts a significant influence over autonomic cardiovascular control. During normal breathing, oscillations in ventricular volume and systemic blood pressure occur, which are detected by baroreceptors, leading to changes in RR intervals. Since these hemodynamic fluctuations during breathing (negative pressure) are predominantly due to changes in intrathoracic pressure, EPAP should be used with caution in patients with heart and lung diseases.

Current advances in bioengineering and the processing of biological signals have led to numerous opportunities for novel non-invasive therapeutic procedures as well as an increased diagnostic capacity, especially in the cardiovascular field [3, 4]. Thus, a form of cardiovascular diagnosis that merits attention is the analysis of heart rate variability (HRV) in healthy individuals submitted to different PEEP levels and no studies have evaluated HRV when different pressure levels are established using EPAP [4, 6].

Thus, the aims of the present study were to evaluate HRV in healthy individuals submitted to different positive end expiratory pressure (PEEP) levels using EPAP and investigate the application of this therapeutic resource with the hope of establishing safer therapeutic interventions.

Material and methods

Study design and patient population

The subjects were 30 healthy male volunteers between 20 and 35 years of age with no present history of smoking, body mass index (BMI) between 18 kg/m² and 30 kg/m², with no cognitive impairment that would compromise the achievement of the evaluation procedures and having signed a consent form. The study received approval from the Ethics Committee of the Universidade do Vale do Paraíba (Brazil) under process number H18/CEP2008. Individuals with a history of heart disease, coronary artery disease or any condition that would affect the results and those who failed to perform the procedures were excluded from the study.

The individuals selected underwent an evaluation that included a medical history and physical examination. The International Physical Activity Questionnaire (version 8) was used to classify the activity level of each participant. This questionnaire has been validated for the Brazilian population [7]. Based on the criteria of frequency, duration and type of physical activity, the volunteers were classified as sedentary, insufficiently active, active or very active [7].

Experimental procedure

The volunteers were first familiarized with the experimental environment and researchers involved in the study. Prior to beginning the tests, the participants were interviewed to ensure compliance with medication instructions and examined. Systolic and diastolic blood pressure, pulmonary auscultation and peripheral oxygen saturation (SpO₂) were all assessed. A single data collection session was required for each subject.

Each participant was instructed to sit in a chair with hips and knees flexed at 90°, feet flat on the floor and elbows on a table. EPAP was conducted with a PEEP valve (spring-loaded, portable, clear plastic, ranging from 5 cm H₂O and 20 cm H₂O, uni-directional flow and silicone face mask).

The EPAP obeyed the following load sequence: PEEP 5 cm H₂O, PEEP 10 cm H₂O and PEEP 15 cm H₂O. The measurements were carried out for 3 min at each load, with no breaks. Heart rate variability was collected using the Polar® 810S monitor throughout the experimental period, including 3 min before and 3 min after the completion of the sequence. The transmitter was placed on the sixth costal line of the individual at the height of the xiphoid process. Total collection time was 15 min, divided into five periods (Table I).

All collections were started at 3:00 pm at room temperature at least 2 h after a light meal. The participants were instructed not to ingest alcohol or coffee for at least 6 h prior to the test [8].

Heart rate variability analysis

Heart rate variability was analyzed in the time and frequency domains using an algorithm developed in MatLab (version 6.1, 450 Release 12.1). The section of highest stability, which included a simple line comprised of at least 256 points, was select-
ed from R-R intervals by visual inspection based on the
criteria set forth by the Task Force of the Euro-
pean Society of Cardiology and the North American
Society of Pacing and Electrophysiology [8].

Time domain analysis was calculated from the
RMSSD index [the square root of the sum of the
squares of the differences between adjacent nor-
mal-to-normal (NN) intervals] and the SDNN (stan-
dard deviation of NN intervals) [9]. Frequency
domain analysis employed the fast Fourier trans-
form of the time series. The application of this algo-
rithm permitted the identification of the power
spectral density as well as its frequency bands: very
low frequency, low frequency (LF) and high fre-
quency (HF). Two frequency bands that best repres-
ent the vagal and sympathetic activity of HR con-
trol were used in this study. Signals in the LF band
(0.04 Hz to 0.15 Hz) have been predominately attrib-
uted to high sympathetic tones and low parasym-
pathetic tones. Signals in the HF band (0.15 Hz to 0.4)
have been attributed only to parasympathetic activ-
ity [9]. Spectral components were obtained in both
absolute (ms) and normalized units (nu) [9].

Time and frequency analysis of the R-R intervals
acquired during respiratory sinus arrhythmia maneu-
ver (RSA-M) was then performed. Additionally, the
spectral analysis confirmed that all volunteers main-
tained a respiratory rate between 5 and 6 cycles/
min, which corresponds to a peak spectral density
frequency between 0.08 Hz and 0.1 Hz. Another spe-
cific routine developed in MatLab was used to cal-
culate the HR and R-R interval indices of RSA-M [10],
i.e., the expiratory/inspiratory ratio (E/I), which is
the mean of the shortest R-R interval values obtained
during the expiratory phase divided by the mean of the
shortest R-R interval values obtained during the
inspiratory phase, and the inspiratory-expiratory dif-
fERENCE (AEI), which is the difference between the
mean of the highest HR value obtained during the
inspiratory phase and the mean of the lowest HR
value obtained during the expiratory phase.

Finally, the data obtained by HRV analysis in the
time and frequency domains as well as the HR and
R-R interval values of RSA-M were transformed into
decimal logarithms for the purposes of statistical
analysis.

Statistical analysis

The Kolmogorov-Smirnov test of normality was
used to determine whether the statistical analysis
would be parametric or nonparametric. In the analy-
sis of time periods with respect to each variable in
both the time and frequency domains, the Tukey-
Kramer multiple comparison test (ANOVA with
Tukey’s contrast test) was employed, with the lev-
el of significance set at $p \leq 0.05$.

Results

All volunteers were classified as either seden-
tary or insufficiently active. Therefore, there was no
need for the differentiation of this variable in the
statistical analysis, as the possibility of major
changes in the behavior of HRV being due to dif-
ferent levels of fitness was discarded. Table II dis-
plays the descriptive statistics characterizing the
sample, such as age, weight, height, body mass
index (BMI), systolic blood pressure and diastolic
blood pressure.

Figures 1–3 illustrate the variables of the fre-
cquency domain (sympathetic area, parasympathetic
area and sympathetic-parasympathetic ratio). A sig-
nificant increase ($p < 0.001$) was found in the symp-
athetic area when comparing Periods 1 and 4 and
and a significant reduction ($p < 0.001$) was found when
comparing Periods 4 and 5 (Figure 1). The mean
value of this variable was 526.89 ±55.50 ms$^2$ in the
first period, 2811.0 ±721.10 ms$^2$ in the fourth period.

Table I. Periods, times and loads during experiment

| Period | 1 | 2 | 3 | 4 | 5 |
|--------|---|---|---|---|---|
| Time   | 0–3 min | 3–6 min | 6–9 min | 9–12 min | 12–15 min |
| Load   | No load | 5 cm H$_2$O | 10 cm H$_2$O | 15 cm H$_2$O | No load |

Table II. Descriptive measures of age, weight, height, BMI and systolic and diastolic blood pressure

| Variable          | $N$ | Minimum | Maximum | Median | Mean | SD |
|-------------------|-----|---------|---------|--------|------|----|
| Age [year]        | 27  | 20      | 35      | 27     | 26.78 | 3.77 |
| Weight [kg]       | 27  | 27      | 53      | 98     | 74.5  | 10.13 |
| Height [m]        | 27  | 1.60    | 1.89    | 1.75   | 1.75  | 0.06 |
| BMI [kg/m$^2$]    | 27  | 19.06   | 29.08   | 24.2   | 24.11 | 2.58 |
| Systolic pressure [mm Hg] | 27  | 110     | 130     | 120    | 119.28 | 6.48 |
| Diastolic pressure [mm Hg] | 27  | 55      | 80      | 70     | 71.96 | 8.64 |
positive airway pressure generated by this device can be compared (with some caution) to conditions offered by devices that generate airflow and therefore increase blood pressure.

In a study involving 16 men with congestive heart failure, Butler et al. [11] found that CPAP in the airways increased HRV in both the time and frequency domains. According to the authors, different mechanisms may contribute to this increase, such as the mechanical or reflex effects of lung inflation. The authors found no significant change in RR intervals. In the present study, however, there was a significant reduction in this interval, resulting in a significant increase in heart rate when the device was initiated. This may be explained by the different techniques applied. As stated above, EPAP supplies pressure in the airways during expiration, whereas CPAP provides continuous pressure during both expiration and inspiration, which reduces the respiratory work and maintains the heart rate steady.

Garet et al. [12] evaluated healthy individuals using positive pressure and found a significant reduction in parasympathetic stimulation after the withdrawal of positive airway pressure. The results of the present study corroborate these results.

Valipour et al. [8] conducted a study involving healthy individuals in which PEEP was set up through CPAP and found results different from those reported here. In the study, ten volunteers (5 men and 5 women) were evaluated and a significant reduction in the parasympathetic area was observed. The same limiting factor can be applied to both the study cited and the present investigation, namely, the difficulty in controlling the respiratory rate, which is a factor that exerts a significant influence over HRV [13]. However, the factors that could explain the differences in results between studies are the method of providing positive pressure, the inclusion of women in the sample and the small number of volunteers studied.

The increase in the parasympathetic area, which is well supported and demonstrated in the literature, was one of the results of the present study. However, there was also an increase in sympathetic stimulation, which has been described elsewhere. We suggest that this stimulation is due to the increased respiratory work caused by the use of EPAP. Macefield [14] suggests that the increase in intrathoracic pressure during inflation of the lungs increases sympathetic activity due to the unloading of baroreceptors by reducing cardiac filling pressures. Similar results are reported by Ikeda et al. [15] and Heindl et al. [16]. In this context, the results obtained in the present study seem justified when analyzed in light of those reported in the literature.

The results of the present study underscore the importance of monitoring and care during the use

Discussion

As mentioned in the introduction of the present study, there are no scientific studies relating the use of EPAP and HRV. However, the conditions for
An Analysis of heart rate variability in individuals subjected to different positive end expiratory pressure levels using expiratory positive airway pressure (EPAP), particularly in cases of tachycardia and arrhythmia. One of the limitations of the present study was the difficulty in finding literature for a more specific grounding of the results. Thus, there is a need for further studies that can better characterize and confirm these hypotheses and extrapolate this analysis to patients with specific diseases.

In conclusion, the results of the present study demonstrate that EPAP significantly alters heart rate variability parameters in the frequency domain.

References
1. Keenan SP, Sinuff T, Cook DJ, Hill N. Which patients with acute exacerbation of chronic obstructive pulmonary disease benefit from noninvasive positive-pressure ventilation? A systematic review of the literature. Ann Intern Med 2003; 138: 861-70.
2. Yang M, Yuping Y, Yin X, et al. Chest physiotherapy for pneumonia in adults. Cochrane Database Syst Rev 2010; 2: CD006338.
3. Malik M, Writing C. Heart rate variability. Standards of measurement, physiologic interpretation, and clinical use. Eur Heart J 1996; 17: 354-81.
4. Ribeiro MP, Brum JM, Ferrario CM. Análise espectral da frequência cardíaca – conceitos básicos e aplicação clínica. Arquivos Brasileiros de Cardiologia 1992; 59: 141-50.
5. Publio AZ, Tuzi DA, Possoni HC, Rocha SM. Estudo da pressão positiva expiratória a sua eficácia na atelectasia: uma revisão literária. Fisioterapia em Movimento 2004; 17: 43-50.
6. Oliveira Dj, Gomes MED, Aguirre LA. Análise da variabilidade da frequência cardíaca baseada no estudo de modelos identificados. In: Congresso Brasileiro De Engenharia Biomédica, 18. 2002, São José dos Campos. Anais... São José dos Campos: UNIVAP 2002; 355-9.
7. Matsudo S, Araújo T, Matsudo V, Andrade D, Andrade E, Oliveira LC. Questionário internacional de atividade física (IPAC): estudo de validade e reproduzibilidade no Brasil. Revista Brasileira de Atividade Física e Saúde 2001; 6: 5-18.
8. Vailpour A, Schneider F, Kössler W, Saliba S, Burghuber OC. Heart rate variability and spontaneous baroreflex sequences in supine healthy volunteers subjected to nasal positive airway pressure. J Appl Physiol 2005; 99: 2137-43.
9. Task Force of European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability: standards of measurement, physiologic interpretation, and clinical use. Circulation 1996; 93: 1043-65.
10. O'Brien IA, O'Hare P, Corrall RM. Heart rate variability in healthy subjects: effect of age and the derivation of normal ranges for tests of autonomic function. Br Heart J 1986; 55: 348-54.
11. Butler GC, Naughton MT, Rahman MA, Bradley TD, Floras JS. Continuous positive airway pressure increases heart rate variability in congestive heart failure. J Am Coll Cardiol 1995; 25: 672-9.
12. Garet M, Barthelemy JC, Degache F, Pichot V, Duverney D, Roche, F. Modulations of human autonomic function induced by positive pressure – assisted breathing. Clin Physiol 2006; 26: 15-20.
13. Pöyhönen M, Syväoja S, Hartikainen J, Ruokonen E. The effect of carbon dioxide, respiratory rate and tidal volume on human heart rate variability. Acta Anaesthesiol Scand 2004; 48: 93-101.
14. Macefield VG. Sustained activation of muscle sympathetic outflow during static lung inflation depends on a high intrathoracic pressure. J Autonomic Nervous System 1998; 68: 135-9.
15. Ikeda T, lwase S, Saito M, Mano T. Effects of positive and negative pressure breathing on muscle sympathetic nerve activity in humans. Aviation, Space, and Environmental Medicine 1997; 68: 494-8.
16. Heindl S, Dodt C, Krahwinkel M, Hasenfuss G, Andreas S. Short term effects of continuous positive airway pressure on muscle sympathetic nerve activity in patients with chronic heart failure. Heart 2001; 85: 185-90.