Acute effects of different levels of continuous positive airway pressure on cardiac autonomic modulation in chronic heart failure and chronic obstructive pulmonary disease

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Abstract

Introduction: Non-invasive ventilation may improve autonomic modulation and ventilatory parameters in severely disabled patients. The aim of the present study was to evaluate the physiological influence of acute treatment with different levels of continuous positive airway pressure (CPAP) on the autonomic balance of heart and respiratory responses in patients with stable chronic obstructive pulmonary disease (COPD) and chronic heart failure (CHF).
Material and methods: A COPD group (n = 10), CHF group (n = 8) and healthy subjects (n = 10) were evaluated. The participants were randomized to receive three different levels of CPAP on the same day: sham ventilation (Sham), 5 cmH_20 (CPAP5) and 10 cmH_20 (CPAP10) for 10 min. Respiratory rate, end tidal carbon dioxide (E_TCO_2), peripheral oxygen saturation (SpO_2), heart rate (HR), blood pressure and heart rate variability in the time and frequency domains were measured during spontaneous breathing and under the sham, CPAP5 and CPAP10 conditions.
Results: All groups experienced a reduction in E_TCO_2 values during treatment with CPAP ($p < 0.05$). CPAP increased SpO_2 and HR in the COPD group ($p < 0.05$). The COPD group also had lower RMSSD values during treatment with different levels of CPAP when compared to the control group ($p < 0.05$). In the CHF group, CPAP5 and CPAP10 increased the SDNN value ($p < 0.05$). CPAP10 reduced the SDNN value in the COPD group ($p < 0.05$).
Conclusion: The findings suggest that CPAP may cause improvements in the neural control of heart rate in patients with stable COPD and CHF. For each patient, the "best CPAP level" should be defined as the best respiratory response and autonomic balance.

Key words: autonomic nervous system, cardiomyopathy, COPD, CPAP ventilation, non-invasive ventilation.

Introduction

Autonomic tone is the balance between sympathetic and parasympathetic activity and is responsible for controlling blood pressure (BP), heart rate (HR), heart contractility, ventricular filling time and vascular tone [1]. Autonomic dysfunction increases sympathetic activity and reduces parasympathetic activity, which is related to the physiopathology of some

diseases, arrhythmia and an elevated risk of mortality [2, 3].

The determination of autonomic balance through an analysis of R-R intervals offers a simple, non-invasive measure of this component of cardiovascular control. The intrinsic regulation and control of the electrical activity of the heart rate can be modulated by the sympathetic and parasympathetic nervous systems, baroreflex activity, intrinsic cardiac nervous system, cardiopulmonary reflexes and respiration [1].

Alterations in alveolar and intrathoracic pressure and the activity of lung receptors during non-invasive ventilation (NIV) could modulate the balance of autonomic heart rate control [1]. NIV has been used in the treatment of chronic obstructive pulmonary disease (COPD), obstructive sleep apnoea, chronic heart failure (CHF) and asthma [4-8]. Fietze *et al.* and Garet *et al.* employed different NIV modalities and found significant changes in intrathoracic haemodynamics, vagal efferent activity and HR in healthy individuals [9, 10].

Different modes of continuous positive airway pressure (CPAP) have been related to changes in the activity of the sympathetic nervous system, such as an increase in sympathetic nerve firing in patients with CHF and the parasympathetic activity, improved short and long-term haemodynamic function, electrical remodelling, reduced respiratory muscle work and neurohormonal modulation [7, 11-14]. Despite the many studies demonstrating the benefits of NIV, the effects of treatment with CPAP on the autonomic heart rate in patients with CHF need to be understood better.

Patients with COPD also exhibit sympathovagal imbalance of the autonomic heart rate, which has been related to an elevated risk of cardiovascular events [4, 15-17]. NIV has been used as an adjunct to COPD rehabilitation, as it increases ventilation, allows the respiratory muscles to unload during rest and physical exercise, and reduces symptoms of dyspnoea [18-23]. It has been demonstrated that bi-level positive air pressure ventilation in patients with stable COPD may reduce end tidal carbon dioxide (E_TCO_2) and HR and increase peripheral oxygen saturation (SpO_2) [4].

Neme *et al.* evaluated acute treatment with different CPAP levels in patients with stable COPD and found an improvement in ventilation and respiratory mechanics [24]. Although treatment with different modes of NIV has been used and considered effective for improvement in ventilatory mechanics, autonomic modulation and quality of life in patients with COPD, the effect of different CPAP levels on the autonomic control of heart rate in patients with stable COPD remains unclear [25].

The hypothesis of the present study was that acute treatment with CPAP would have an effect on autonomic balance and respiratory function and the effects of CPAP treatment on heart rate variability (HRV) would be closely related to the levels applied. Thus, the aim of this study was to investigate autonomic modulation in patients with COPD and CHF submitted to acute treatment with different levels of CPAP.

Material and methods

Study population

The procedures used in this study were in accordance with the recommendations of the Helsinki Declaration [26]. All subjects provided written informed consent before entering the study. The protocol received approval from the Ethics Committee of the Universidade Federal de São Carlos, São Paulo, Brazil. After all evaluations and procedures, a total of 28 male patients were divided into three groups: 10 patients with COPD, 8 patients with CHF and 10 healthy controls. All patients were submitted to the following evaluations: clinical and laboratory examinations, classification of dyspnoea, New York Heart Association (NYHA) functional classification, pulmonary function tests and electrocardiography (ECG).

The following were the inclusion criteria for the COPD group: diagnosis from a physician; forced expiratory volume in one second (FEV_1) / forced vital capacity (FVC) ratio < 0.7 and FEV_1 < 60% of predicted; clinical stability for at least three months; absence of current smoking habit; dyspnoea during low and medium physical effort; and dyspnoea during daily activities (Medical Research Council score of I-III). The following were the inclusion criteria for the CHF group: diagnosis from a physician; echocardiogram with left ventricular ejection fraction < 50%; NYHA classification score of I-III; FEV_1/FVC > 70% and FEV_1 > 70% of predicted. The control group was made up of healthy, sedentary individuals, as determined by the clinical classification of the American Heart Association [29]. Patients receiving medications are described in Table I.

Design and procedures

A double-blinded, randomized, cross-sectional study was carried out. R-R intervals (R-Ri) and physiological variables were collected for 10 min during spontaneous breathing and with three CPAP levels: sham ventilation (Sham), 5 cmH_20 (CPAP5) and 10 cmH_20 (CPAP10).

Measurements

Lung function

Spirometric tests were performed using a portable spirometer (Hand Held 2120, Vitalograph,

Table I. Anthropometric characteristics, lung function, MRC and NYHA class, echocardiography, cause of heart failure and medications in control group (CG), chronic heart failure (CHF) group and chronic obstructive pulmonary disease (COPD) group

Variable	CG (n = 10)	CHF (n = 8)	COPD (n = 10)
Anthropometric characteristics			
Age [years]	64 ±5	62 ±8	69 ±9
Height [m]	1.71 ±0.05	1.66 ±0.07	1.67 ±8.96
Weight [kg]	74 ±6	69 ±10	64 ±8*
BMI [kg/m^2]	25 ±1	24 ±3	23 ±3
Lung function			
FEV1 (% predicted)	91 ±20.0	81 ±9.1	40 ±10.9*
FEV1/CVF	101 ±7.0	82 ±4.2	58 ±11.8*
MRC / NYHA class			
I		1	1
II		4	3
III		3	6
Echocardiogram			
Left ventricular ejection fraction [%]		39 ±9	
Cause of heart failure			
Ischaemic dilated cardiomyopathy		3	
Idiopathic/non-ischaemic dilated cardiomyopathy		5	
Medications, n (%)			
Bronchodilators			10 (100)
Beta-blockers		8 (100)	
Digoxin		5 (62.5)	
Nitrates		2 (25)	
Angiotensin-converting enzyme inhibitors		7 (87.5)	
Furosemide, n (%)		3 (37.5)	
Acetylsalicylic acid, n (%)		2 (25)	

Data are presented as mean ± SD
MRC denotes classification of dyspnoea; NYHA denotes functional classification of New York Heart Association
** Significant inter-group differences between COPD group vs. CG*

Ennis, Ireland). FEV_1 and maximal voluntary ventilation were determined and compared to predicted normal values following methods described elsewhere [21, 30].

Non-invasive ventilation protocol

Mechanical ventilatory assistance was delivered using a CPAP device (Breas PV101, Sweden) and administered through a comfortably fitting face mask (Respironics, Murrysville, PA, USA). NIV was randomized and set individually for each patient in the following manner: Sham – breathing at minimal pressure to experience resistance from the equipment; CPAP5 – breathing at 5 cmH_2O of positive pressure; CPAP10 – breathing at 10 cmH_2O of positive pressure. The capnometer was attached to the orifice in the nasal mask (BCI-1050, Waukesha, USA). During NIV, the subjects were instructed to relax, breathe calmly and maintain a respiratory rate similar to spontaneous breathing during CPAP ventilation, which was visually displayed by the capnometer located in clear view directly in front of the subjects. There was an initial adaptation period (30 min) for the first randomized CPAP level. After this period, physiological and HRV parameters were recorded during 10 min. A 10-minute rest period was given between other randomized settings.

Physiological measurements

SpO_2 was continuously monitored using portable pulse oximetry (Oxifast, Takaoka, Brazil). E_TCO_2 and respiratory rate (RR) were determined using a capnometer and recorded every 10 seconds as

well as at the end of the procedures. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured using an indirect method and were analysed at baseline as well as during the last 30 s of the protocol. HRV was recorded using the Polar system (S810i). The digitally coded R-Ri length was continuously transferred to the Polar Precision Performance software, which displays an HR tachogram on the monitor. Patients were also monitored using a thoracic MC5 lead (cardiac monitor Ecafix TC500, São Paulo, SP, Brazil) to simultaneously obtain the HR in order to evaluate the signals on the monitor to exclude movement artefacts and ectopic beats prior to the HRV analysis.

HRV analysis

For the HRV analysis, the most stable sections containing 256 points within the 10 min were selected. HRV was analysed in the time (RMSSD – the square root of the sum of the squares of the differences between adjacent normal to normal intervals; and SDNN – the standard deviation of normal to normal intervals) and frequency domains [31, 32]. Absolute and normalized units and low/high frequency ratios were also calculated [3].

Statistical analysis

The data are presented as mean ± SD after testing for normal distribution (Kolmogorov-Smirnov). The sample size was calculated using the GraphPad StatMate software, version 1.01. Based on a pilot study, the target number of patients was calculated to be 10 in each group, with a 5% type I error, a 2-sided test and 90% power to detect a 5% change in E_TCO_2 between spontaneous breathing and the different CPAP levels. These calculations were based on the mean E_TCO_2 difference required for clinical significance. Inter-group differences were evaluated using one-way analysis of variance (ANOVA) with Tukey's post-hoc test. The level of significance was set at 5%. The analysis was carried out using the Statistical Package for the Social Sciences.

Results

Figure 1 shows the sample loss of each studied group. Table I displays the mean values of the demographic and anthropometric characteristics of the sample, pulmonary function, classification of dyspnoea, echocardiogram, cause of heart failure and medications used in the CHF and COPD groups.

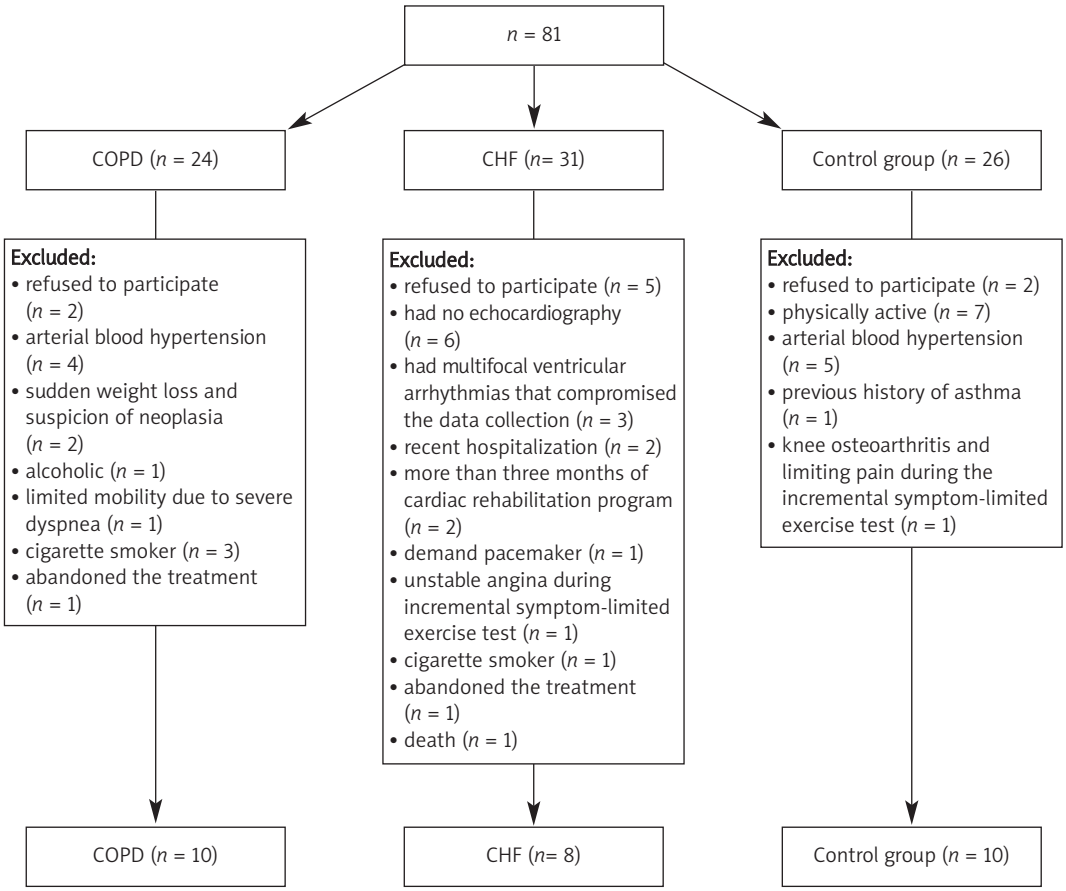

Figure 1. Flowchart – sample loss of each studied group

No significant differences were found between groups regarding age, height and body mass index (BMI). However, the COPD group had a significantly lower body mass when compared to the control group. As expected, patients with COPD had moderate-to-severe forms of the disease [28].

Effects of CPAP on physiological variables

No significant intra-group differences were found in RR between spontaneous breathing and the different CPAP levels in the control and CHF groups. However, a significant reduction in RR was found in the COPD group with all different CPAP levels when compared to spontaneous breathing ($p < 0.05$). Moreover, RR during spontaneous breathing was higher in the COPD group when compared to the control group ($p < 0.05$). A significant reduction in E_TCO_2 was found during treatment with CPAP in all groups. In the COPD group, higher CPAP levels led to a greater reduction in E_TCO_2. In the CHF group, a significant reduction only occurred in the treatment with CPAP 10 cmH_2O when compared to spontaneous breathing and sham CPAP (Table II). A significant increase in SpO_2 was found in the COPD group during treatment with the different CPAP levels when compared to spontaneous breathing. Moreover, SpO_2 in the COPD group was significantly lower than that in the control and CHF groups under all conditions (Table II). In the intra-group comparisons, a significant reduction in DBP was found during the sham CPAP and CPAP5 in the control group alone. Significantly lower SBP values in the CHF group were found during spontaneous breathing, sham CPAP and CPAP10 when compared to the control and COPD groups (Table II).

Effects of CPAP on HRV

A significant increase in HR occurred during treatment with sham CPAP and 5 cmH_2O compared to spontaneous breathing in the COPD group. During treatment with CPAP 5 and 10 cmH_2O, higher HR values were found in the COPD group when compared to the CHF group (Table III). In the time domain, significantly lower RMSSD values during treatment with different CPAP levels when compared to spontaneous breathing were found in the COPD group alone (Figure 2). Moreover, significantly lower RMSSD values were found during treatment with different CPAP levels in the COPD group when compared to the control group (Table III). In the CHF group, significant increases in SDNN and power spectral density were found during treatment with CPAP 5 and 10 cmH_2O when compared to spontaneous breathing (Figure 2). In the inter-group comparisons, lower SDNN values were found in the COPD group during treatment with CPAP 10 cmH_2O when compared to the control group (Table III). No significant intra-group differences in R-Ri values were found during treatment with the different CPAP levels when compared to spontaneous breathing. In the inter-group comparisons, higher R-Ri values during treatment with the different CPAP levels were found in the COPD group when compared to the control group.

Discussion

The important novel finding of the present study is that treatment with higher CPAP levels induced greater adjustment in autonomic function in patients with COPD and CHF. CPAP 5 cmH_2O led to an improvement in ventilation with no imbalance in autonomic heart rate modulation in patients with COPD. However, acute treatment with CPAP10 altered autonomic regulation, leading to an increase in sympathetic activity and a reduction in parasympathetic activity in patients with COPD. Moreover, the best responses in ventilation and autonomic balance in patients with CHF seem to be with CPAP10.

Table II. Physiological variables in control group (CG), chronic heart failure (CHF) group and chronic obstructive pulmonary disease (COPD) group during spontaneous breathing (SB) and different CPAP levels

Variable	CG (n = 10)				CHF (n = 8)				COPD (n = 10)			
	SB	Sham	CPAP5	CPAP10	SB	Sham	CPAP5	CPAP10	SB	Sham	CPAP5	CPAP10
RR [bpm]	12 ±3*	12 ±2	13 ±3	13 ±3	15 ±2	13 ±3	13 ±3	13 ±3	18 ±4	14 ±4[a]	15 ±3[a]	14 ±3[a]
ETCO2 [cmH_2O]	38 ±4	35 ±4[a]	31 ±6[a]	30 ±5[a,c]	38 ±3	35 ±5	31 ±6	31 ±6[a,c]	35 ±5	32 ±5[a]	29 ±5[a,b]	27 ±6[a,c,d]
SpO_2 [%]	97 ±1*	97±1*	97 ±1*	97 ±1*	96 ±2[†]	97 ±1[†]	97 ±1[†]	97 ±1[†]	92 ±3	94 ±2[a]	94 ±2[a]	95 ±3[a]
SBP [mmHg]	120 ±8[‡]	117 ±9*[‡]	117 ±9	118 ±7*[‡]	106 ±13[†]	106 ±9[†]	107 ±8	107 ±7[†]	120 ±7	118 ±9	116 ±9	117 ±8
DBP [mmHg]	78 ±4	74 ±7a	74 ±7a	76 ±5	71 ±10	71 ±8	70 ±9	69 ±9	72 ±8	72 ±8	73 ±8	74 ±8

*Data are presented as mean ± SD, Sham – breathing at 3 cmH_2O, CPAP5 – breathing at 5 cmH_2O positive pressure, CPAP10 – breathing at 10 cmH_2O positive pressure, RR – respiratory rate, E_TCO_2 – end tidal carbon dioxide, SpO_2 – peripheral oxygen saturation, SBP – systolic blood pressure, DBP – diastolic blood pressure, [a]significant intra-group differences compared to SB, [b]significant intra-group differences between Sham and CPAP5, [c]significant intra-group differences between Sham and CPAP10, [d]significant intra-group differences between CPAP10 and CPAP5, *significant inter-group differences between COPD group and CG, [‡]significant inter-group differences between CHF group and CG, [†]significant inter-group differences between COPD and CHF groups*

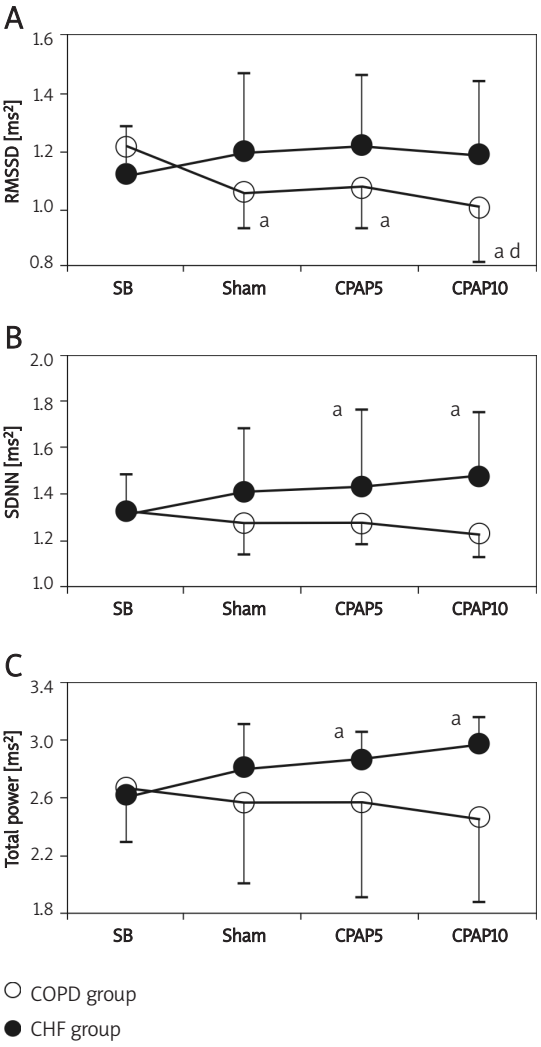

Figure 2. Heart rate variability during spontaneous breathing (SB) and different CPAP levels
[a]significant intra-group differences compared to SB, [d]significant intra-group differences between CPAP10 vs. CPAP5, Data are presented as mean ± SD, Sham – breathing at 3 cmH_2O, CPAP5 – breathing at 5 cmH_2O positive pressure, CPAP10 – breathing at 10 cmH_2O positive pressure, RMSSD (ms) index – SDNN index

These findings indicate the presence of a "best CPAP level" in the short-term administration of non-invasive CPAP acting on the modulation of autonomic tone and respiratory responses. New strategies and careful titration for finding the 'best CPAP level' for individual patients is very important, as patients with COPD and CHF have autonomic heart dysfunction related to an increased risk of cardiovascular events and mortality [7, 15].

Effects of CPAP on ventilatory parameters and autonomic balance of HR

Patients with COPD and CHF have a considerable reduction in lung function, which exacerbates the impact of the illness [33, 34]. Acute CPAP treatment in patients with stable COPD reduces symptoms of dyspnoea as well as RR and E_TCO_2 values. In COPD, the respiratory system is primarily hampered by the additional elastic load associated with dynamic hyperinflation and intrinsic positive end-expiratory pressure (PEEP). These factors predispose patients to respiratory failure by increasing the load on the respiratory muscles, while decreasing their mechanical efficiency and capacity for generating maximal pressure [35].

In the present study, CPAP likely reduced the respiratory load imposed by intrinsic PEEP. When proximal airway pressure is elevated by CPAP to a level approaching the intrinsic PEEP, the inspiratory muscles only need to lower alveolar pressure to the CPAP level to initiate inspiration.

Previous studies have demonstrated that RR and E_TCO_2 can modulate HRV [4, 36]. In the present study, a significant reduction was found in the HF band and RMSSD index, along with an increase in the LF band during acute treatment with CPAP10 in patients with COPD, indicating an imbalance in autonomic control. The HF band and RMSSD components are both generally defined as markers of vagal modulation and the LF band has been associated with sympathetic activity [3]. In this autonomic adaptation, the increase in sympathetic activity and reduction in parasympathetic activity may not be favourable, as it has been related to physiopathological diseases, arrhythmia and an increased risk of mortality [2, 3]. Interestingly, when the patients with COPD were submitted to acute treatment with CPAP5, the same responses in ventilatory parameters and autonomic balance occurred, with a reduction only in the RMSSD index. Moreover, this reduction in RMSSD was significantly lower than that during CPAP10. These results indicate that acute treatment with CPAP5 is safer than CPAP10, probably due to inducing lesser imbalance in autonomic tone in patients with stable COPD.

In the patients with CHF, acute treatment with different levels of CPAP promoted few changes in respiratory function and autonomic balance. During acute treatment with CPAP5 there were no changes in respiratory response when compared to spontaneous breathing. However, there was a significant increase in the SDNN index. A reduction in this index is an independent predictor of mortality [3, 37]. Interestingly, acute treatment with CPAP10 caused a significant reduction in E_TCO_2 and an increase in the SDNN index at the same proportion as CPAP5. Moreover, CPAP10 led to a significant increase in total power of spectral density, which reflects a mixture of both autonomic inputs [3, 12]. Based on these acute responses, treatment with CPAP10 offers greater advantages and safety in patients with CHF. There is a clear association between reduced HRV and

Table III. Heart rate variability values in time domain (TD) and frequency domain (FD) of control group (CG), chronic heart failure (CHF) group and chronic obstructive pulmonary disease (COPD) group during spontaneous breathing (SB) and different CPAP levels

HRV Index	CG (n = 10)				CHF (n = 8)				COPD (n = 10)			
	SB	Sham	CPAP5	CPAP10	SB	Sham	CPAP5	CPAP10	SB	Sham	CPAP5	CPAP10
TD												
HR [bpm]	1.83 ±0.06	1.82 ±0.05	1.83 ±0.05*	1.83 ±0.06*	1.82 ±0.06	1.82 ±0.04	1.82 ±0.04†	1.82 ±0.04†	1.86 ±0.07	1.86 ±0.07	1.89 ±0.06	1.92 ±0.06[a,c,d]
R-Ri [ms]	2.95 ±0.06	2.95 ±0.05*	2.96 ±0.05*	2.95 ±0.06*	2.94 ±0.07	2.91 ±0.04	2.91 ±0.04	2.90 ±0.03	2.92 ±0.07	2.89 ±0.07	2.89 ±0.07	2.88 ±0.06
RMSSD [ms]	1.29 ±0.14	1.36 ±0.25*	1.34 ±0.15*	1.30 ±0.21*	1.12 ±0.10	1.20 ±0.13	1.22 ±0.14	1.19 ±0.19	1.22 ±0.17	1.06 ±0.27[a]	1.08 ±0.25[a]	1.01 ±0.26[a,d]
SDNN [ms]	1.46 ±0.13	1.48 ±0.19	1.45 ±0.16	1.47 ±0.19*	1.31 ±0.06	1.41 ±0.16	1.44 ±0.09[a]	1.48 ±0.10[a]	1.33 ±0.18	1.28 ±0.28	1.28 ±0.33	1.23 ±0.28
FD												
PSD	2.93 ±0.26	2.96 ±0.38*	2.90 ±0.33*	2.94 ±0.39*	2.62 ±0.12	2.81 ±0.31	2.87 ±0.19[a]	2.97 ±0.20[a]	2.67 ±0.37	2.57 ±0.55	2.57 ±0.65	2.46 ±0.57
LF [ms^2]	2.38 ±0.32*	2.50 ±0.40	2.41 ±0.33	2.57 ±0.41*	2.06 ±0.20	2.37 ±0.46	2.29 ±0.39	2.45 ±0.40	1.84 ±0.58	1.90 ±0.69	1.89 ±0.79	1.89 ±0.63
HF [ms^2]	2.17 ±0.28	2.31 ±0.54	2.27 ±0.32	2.10 ±0.45	1.81 ±0.30	1.90 ±0.39	1.98 ±0.37	1.93 ±0.56	1.90 ±0.40	1.62 ±0.46	1.60 ±0.49	1.55 ±0.51[a]
LFnu	1.76 ±0.14*	1.74 ±0.17	1.74 ±0.10	1.86 ±0.06[a,c,d,*]	1.80 ±0.11	1.82 ±0.13	1.77 ±0.16	1.82 ±0.17	1.60 ±0.30	1.80 ±0.11	1.79 ±0.16	1.82 ±0.10[a]
HFnu	1.55 ±0.22	1.55 ±0.28	1.60 ±0.20	1.39 ±0.16	1.50 ±0.24	1.36 ±0.39	1.47 ±0.38	1.30 ±0.45	1.64 ±0.30	1.52 ±0.16	1.49 ±0.22	1.48 ±0.19
LF/HF ratio	0.21 ±0.36	0.19 ±0.44	0.14 ±0.29	0.47 ±0.22	0.26 ±0.30	0.47 ±0.52	0.30 ±0.53	0.52 ±0.61	–0.07 ±0.62	0.28 ±0.28	0.29 ±0.38	0.34 ±0.29

*Data are presented as mean ± SD, Sham – breathing at 3 cmH_2O, CPAP5 – breathing at 5 cmH_2O positive pressure, CPAP10 – breathing at 10 cmH_2O positive pressure, HR – heart rate, R-Ri – electrocardiographic R-R intervals, RMSSD – root mean square of successive differences in R-R intervals in ECG, SDNN – standard deviation of normal R-R intervals in ECG, PSD – total power spectral density, LF – low frequency, HF – high frequency, LFnu – normalized LF units, HFnu – normalized HF units, LF/HF ratio – global sympathovagal balance, [a]significant intra-group differences compared to SB, [c]significant intra-group differences between Sham and CPAP10, [d]significant intra-group differences between CPAP10 and CPAP5, *significant inter-group differences between COPD group and CG, †significant inter-group differences between COPD and CHF groups*

poor outcomes in a number of chronic and acute heart diseases [38].

The different pressure levels administered were enough to improve SpO_2 in the patients with COPD, whereas no changes occurred in the healthy subjects or patients with CHF. As expected, lower SpO_2 levels at rest were found in the patients with COPD. These conditions during walking and exercise are a critical problem during rehabilitation [20, 39]. Moreover, CPAP has been used in the treatment of a number of diseases, particularly COPD and obstructive sleep apnoea [2, 39, 40].

In the present study, acute treatment with CPAP increased SpO_2 and did not alter BP in patients with COPD. Moreover, no alterations in BP occurred in patients with CHF during acute treatment with CPAP. Ensuring SpO_2 and maintaining BP is favourable to haemodynamic responses. While CPAP is effective in treating diverse acute and chronic conditions, its benefits to BP remain unclear [40].

Treatment with different levels of CPAP did not alter HR in any of the groups, except the COPD group during treatment with 10 cmH_2O. Although automaticity is intrinsic to different cardiac tissues with pacemaker properties, the HR and contractile activity of the myocardium are largely modulated by sympathetic and vagal outflows [1]. Acute treatment with CPAP5 and 10 decreased the RMSSD index in patients with COPD, which is predominantly vagally mediated, reflected in an increase in HR [3]. The decrease in the RMSSD component was significantly lower during acute treatment with 5 cmH_2O.

Regarding the limitations of the present study, it should be taken into consideration that the patients with CHF were receiving beta-blockers and the COPD group was using bronchodilators, which could have influenced the outcome. However, we intended to evaluate these patients under real-life conditions. Additionally, more studies are necessary

to evaluate women under the same COPD and CHF conditions.

Autonomic dysfunction, an increase in sympathetic activity and a reduction in parasympathetic activity have been reported in patients with COPD and CHF. These dysfunctions are associated with physiopathological diseases, arrhythmia and an increased risk of cardiovascular events and mortality. CPAP has been extensively used as an effective component during rehabilitation in this population, as it improves ventilatory parameters, haemodynamics and autonomic balance. The findings of the present study reveal that treatment with different levels of CPAP promotes different autonomic responses. Thus, finding an individual's "best CPAP level" increases the safety and efficiency of treatment.

In conclusion, these findings suggest that CPAP may improve the neural control of heart rate in patients with stable COPD and CHF. For each patient, a "best CPAP level" should be defined in association with the greatest ventilatory response and autonomic balance. In cases in which two or more CPAP levels resulted in a better ventilatory response and sympathetic activity, the "best CPAP" was the level associated with the greatest ventilatory response and the least reduction in parasympathetic activity.

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