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ORIGINAL ARTICLE

EFFECTS OF CPAP ON THE PHYSICAL EXERCISE TOLERANCE OF MODERATE TO SEVERE CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Objective: The aim of this study was to evaluate the effect of continuous positive airway pressure (CPAP) on the exercise tolerance of patients with moderate to severe chronic obstructive pulmonary disease (COPD). **Methods:** ten men with COPD (69 ± 9 years), FEV_1/FVC (58.90 ± 11.86%) and FEV_1 (40.98 ± 10.97% of predict) were submitted to a symptom-limited incremental exercise test (IT) on the cyclo ergometer. Later, on another visit, they were randomized to perform a constant load exercise protocol until maximal tolerance with and without CPAP ($5cmH_2O$) in the following conditions: i) 50% of the peak workload; and ii) 75% of the peak workload. Heart rate (HR), arterial pressure (AP) and peripheral oxygen saturation were obtained at rest and during the exercise protocols. For statistical procedures, Shapiro-Wilk normality test and two-way ANOVA with Tukey *post hoc* ($p<0.05$) were performed. **Results:** There was a significant improvement in exercise time tolerance during the 75% of the peak workload protocol with CPAP when compared with spontaneous breath (SB) (438±75 vs. 344±73ms, respectively). **Conclusion:** CPAP with 5 cmH_2O seems to be useful to improve exercise tolerance in patients with COPD.

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INTRODUCTON

Patients with chronic obstructive pulmonary disease (COPD) present a reduced physical exercise tolerance that can be determined by ventilatory and/or peripheral mechanism[1,2]. Progressive increase in the expiratory airflow resistance, which limits the tidal volume gain beyond the expiratory and inspiratory reserve volumes, may be accentuated because these patients ventilate in higher pulmonary volumes at rest. Thus, they reach the maximal pulmonary capacity during physical exercise early[3]. Nowadays, peripheral muscular dysfunction has gained evidence, mainly its influence on the premature physical exercise interruption[4]. Facts such as chronic hypoxemia, oxidative stress, nutritional depletion, peripheral muscular disuse, medicament effects and vagal-sympathetic imbalance contribute to this peripheral muscular dysfuction[4]. Beyond these factors, another limiting capacity aspect of physical exercise is the blood flow redistribution to peripheral muscles despite the ventilatory muscles, especially in high intensity exercises[5].

Hence, there are known forms to decrease the ventilatory overload with repercussion on physical exercise tolerance such as oxygen supplementation[6,7], the use of bronchodilators[8], heliox[9,10,11,12,13] and non-invasive ventilation (NIV)[1,9,14,15]. NIV improves the functional residual capacity by reducing the pulmonary shunt, generating a higher ventilatory reserve[16]. Furthermore, it reduces the work of breathing and it has been explored in recent study during physical activity with COPD patients[5] and other chronic diseases[17], since there is a reduction in sympathetic response in peripheral musculature, which promotes a higher blood flow with higher tolerance on physical exercise[5,17].

Therefore, our study has the objective to evaluate acute effects of continuous positive airway pressure (CPAP) on physical exercise capacity of COPD subjects.

MATERIALS AND METHODS

Subject

Ten men with a clinical diagnosis of COPD volunteered to participate in this cross-sectional study. Subjects were recruited from a public primary health care facility and to be included in the study presented with the following characteristics: stable pulmonary function with forced expiratory volume in the first second/forced vital capacity (FEV_1/FVC) < 70%[18], ex-smokers, and presenting dyspnea and symptoms with minor or moderate efforts[19]. Exclusion criteria were: consumption of alcoholic beverages, users of addicting drugs, and regular physical activity in the past six months. All subjects were submitted to clinical evaluation and pulmonary function tests, functional capacity evaluation according to the British Modified Medical Research Council (MRC)[19], biochemical tests, electrocardiogram (ECG) and a symptom-limited physical exercise test prior to the study. All of them signed an informed consent form, and the protocol was approved by the Ethics Committee from Universidade Federal de São Carlos (UFSCar), São Carlos, SP, Brazil (protocol 238/06).

Experimental protocol

The research was conducted in an acclimatized laboratory at temperatures between

22 °C and 24 °C and relative humidity between 50% and 60%, during the same period of the day (between 8 a.m. and 12 p.m.). Prior to and on the day of the test, each subject was asked to ensure they avoided consumption of stimulating beverages and physical activity for 24 hours, and consumed light meals and slept for at least eight hours.

Initially, the subjects were familiarized with the experimental equipment and environment and the researchers involved in the study. Prior to the tests, they were evaluated and examined to ensure that the directions given had been strictly followed. In addition, systolic and diastolic blood pressure, lung auscultation and peripheral saturation of Oxigen (SpO_2) were assessed.

Pulmonary function

Spirometry was performed using a Vitalograph® spirometer (Hand-Held 2021 instrument. Ennis, Ireland). The FVC test was conducted to determine the FEV_1 and FEV_1/FVC ratio. Technical procedures, criteria for acceptability and reproducibility, were performed according to the guidelines recommended by the American Thoracic Society[20]. The reference values used were those suggested by Knudson *et al.* [21].

Incremental physical exercise protocol

The assessment was performed by a cardiologist to determine the maximum load the patients were able to achieve. In addition, this step was considered important to

assess clinical and functional conditions of the cardiovascular and peripheral muscular systems of the subjects and to identify evidence of cardiorespiratory comorbidities elicited by physical exercise. Initially, the patients were evaluated using an ECG with the standard 12-lead ECG, followed by the evaluation of the electrocardiographic signal from the derivations MC5, DII modified and V2 in the following conditions: supine, sitting, apnea (15 s) and hyperventilated (15 s). The exercise test was performed on a cycloergometer with electromagnetic brakes (Quinton 400 Corival Ergometer, Groningen, Netherlands) and power increments externally controlled by a microprocessor model Workload Program (Quinton, Groningen, Netherlands). The subjects remained seated with the knees flexed at 5-10°. Initially, a 2-minute warm up period was performed with no load, corresponding to 4 watts (W). Following the warm up, the subjects performed increments of 5W every 3 minutes at 60 rpm, until physical exhaustion or it was impossible for them to maintain the pedaling speed. The test was stopped on the first indications of signs and/or symptoms such as dizziness, nausea, cyanosis, complex arrhythmias, excessive sweating, angina and peripheral oxygen desaturation. During the test, they were monitored from the MC5 derivation, DII modified and V2. Measurements of heart rate (HR), blood pressure (auscultation method) and electrocardiographic recordings were performed in the 30 final seconds of each power level and at the 1st, 3rd, 6th and 9th minutes of recovery. At the end of the recovery period, with the subject in the supine position, the standard 12-lead ECG was performed. In addition to the aforementioned variables, using formulae recommended by the American Heart Association (which considers peak load and body mass), peak oxygen consumption (VO_2 peak) achieved by the subjects was obtained. Throughout the test, peripheral oxygen saturation (SpO_2) was measured using pulse oximetry (Oxyfast, Takaoka, Brazil).

Protocol of constant load in spontaneous breath and during CPAP application

All tests were performed in four or two days (two tests per day) with an interval of 48 hours between the days. For the implementation of this protocol, initially, the subjects were kept at rest in the sitting position for about 10 minutes, aiming to achieve basal values for HR. At the same time, instantaneous HR was obtained at rest in the sitting position for 15 minutes. Subsequently, subjects were randomized by drawing to perform submaximal exercise at a constant load until maximum tolerance, with and without application of continuous positive airway pressure (CPAP – 5 cm H_2O, Breas PV101, Sweden) using a Confortgel nasal mask (Respironics, Murrysville, PA) under the following conditions: i) 50% of the peak load of the incremental test and ii) 75% of the peak load of the incremental test. Subjects were positioned in the horizontal electronically braked cyclo ergometer (Quinton 400 Corival Ergometer, Groningen, Netherlands) with knees flexed between 5° and 10°. Initially, they remained seated on the cycle ergometer at rest for 1 minute and then were instructed to pedal at a cadence of 60 rpm until maximum tolerance, that was defined when the subject could not keep the cadence. SpO_2 (Oxyfast, Takaoka, Brazil) and ECG (Ecafix 500, São Paulo, Brazil), in leads MC5, DII modified and V2, were continuously monitored throughout the experimental protocol. Blood pressure and the modified BORG scale (CR – 10) were carefully verified every two minutes to avoid interference in the collection of the variables. Constant workload tests were performed on a single day and at the same time to avoid circadian influences with an interval of 30 minutes or until cardiovascular variables returned to baseline values. A team of trained researchers conducted the tests and carefully monitored the signs and/or symptoms of exercise intolerance and who could determine when to immediately stop the test. *Data analysis*

The maximum time for completion of the physical exercise during the protocol of constant workload was identified by tolerance time. The HR, subjective sensation of effort for dyspnea, and discomfort of the lower limb variables were assessed at baseline and at the peak of the protocol. *Statistical analysis*

Data were subjected to a normality test (Shapiro-Wilk) and homogeneity test (Levene test). Since a normal distribution was observed, parametric statistical tests were used. Next, a two-way ANOVA test with Tuckey *post hoc* was applied for comparisons in the two exercise load conditions, spontaneous breath and with CPAP. Analyses were performed with GraphPad Instat 3 (San Diego, CA, USA), with a significance level of $p<0.05$. All data were presented as means and standard deviation.

RESULTS

We had 24 COPD patients, from which 12 were excluded and two abandoned the current study, resulting in 10 analyzed patients, as shown in Figure 1.

In Table 1 we can observe age, anthropometric data, clinical characteristics and incremental cardiopulmonary data of the subjects. All individuals of the study were mild to moderate in Global initiative for chronic obstructive lung disease (GOLD)[18] classification, functional class of MRC between I and III and were with optimized drug therapy. Additionally, the incremental cardiopulmonary test showed that COPD patients present low functional capacity (VO_2 <15 ml/kg/min).

Table 2 exposes the cardiorespiratory data at rest and constant work load physical exercises with and without CPAP on the intensities of 50 and 75% of the incremental test. We noted a higher improve in the physical exercise time tolerance when the patients were with CPAP in the intensity of 75% of the incremental test compared with the condition without CPAP.

Figure 2 shows the time of tolerance to physical exercise of patients in the intensity of 75% of the incremental test without CPAP (SB) and with CPAP, in which we can see significantly higher values with the use of CPAP compared with the spontaneous breath condition. ($p<0.05$).

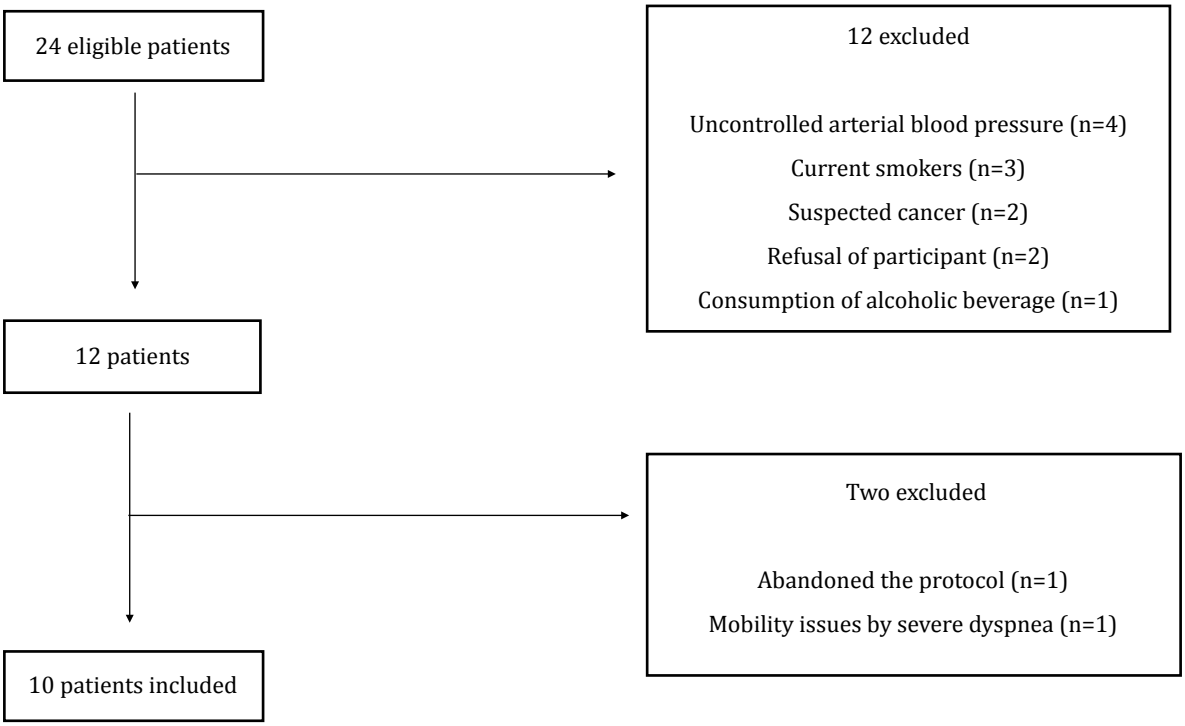

Figure 1. Flowchart of the study.

Table 1. Anthropometrics and clinical characteristics of Chronic Obstructive Pulmonary Disease (COPD) Subjects.

	COPD (n=10)
Age (years)	69 ± 9
Height (cm)	167 ± 8.96
Weight (Kg)	64.44 ± 8.96
Body mass index (kg/m^2)	23.21 ± 3.33
Spirometrics	
FEV_1 (L)	0.8 ± 0.2
FEV_1 (% predict)	40.98 ± 10.97
FEV_1/FVC (%)	58.90 ± 11.86
FVC (% predict)	68 ± 13
MRC	
Class I	n=1
Class II	n=3
Class III	n=6
Clinical characteristics	
SpO_2 (%)	92 ± 3
RR (ipm)	15 ± 4
Drugs	
Short-acting bronchodilator	6
Long-acting bronchodilator	10
Incremental test	
At rest	
SAP (mmHg)	124 ± 11
DAP (mmHg)	75 ± 5
HR (bpm)	70 ± 12
Peak	
SAP (mmHg)	171 ± 17
DAP (mmHg)	80 ± 9
HR (bpm)	110 ± 20
VO_2peak (mL.kg.min)	10.15 ± 3.19
Power (watts)	27 ± 18

Values are means ± SD. FEV_1: forced expiratory volume in the first second; FEV_1/FVC: forced expiratory volume in the first second and forced vital capacity ratio; SpO_2: peripheral oxygen saturation; RR: respiratory rate; SAP: systolic arterial pressure; DAP: diastolic arterial pressure; HR: heart rate. MRC: Medical Research Council.

Table 2. Cardiopulmonary variables and Borg during exercise

Variables	50% incremental test		75% incremental test	
	SB	**CPAP**	**SB**	**CPAP**
At rest				
RF (ipm)	12± 4	13± 3	12± 4	14± 3
HR (bpm)	75± 8	78± 7	75± 8	75± 7
SAP (mmHg)	120 ±7	125± 6	120 ±7	132± 8
DAP (mmHg)	72 ±8	74± 8	72 ±8	74± 8
Submaximal exercise peak				
Tolerance time (s)	448**±**80	469**±**70	364**±**65	431±84
HR (bpm)	123±20*	124**±**19*	124**±**17*	122**±**18*
SAP (mmHg)	171±8*	168±7*	175±7*	170±7*
DAP (mmHg)	80±5	90**±**10	90**±**10	90**±**5
Dyspnea score	6±1	5±1	6±1	6±1
Leg effort score	5±0	5±1	5±1	5±1

Values are means and SD. SB: spontaneous breath; CPAP: continuous positive airway pressure; RF: respiratory frequency in incursions per minute; HR: heart rate in beat per minute; SAP: systolic arterial pressure; DAP: diastolic arterial pressure;* $p<0.05$: rest vs. exercise (t student paired test); † $p<0.05$: SB vs. CPAP in 75% of incremental test (two-way ANOVA with Tukey *post hoc*).

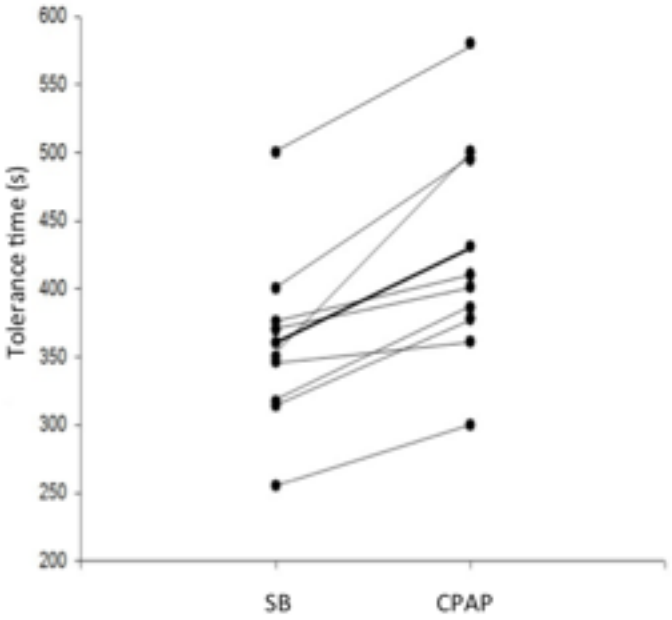

Figure 2. Tolerance time for Chronic Obstructive Pulmonary Disease Subjects during submaximal exercise at 75% of incremental test. SB: spontaneous breath. Median (bold line).

DISCUSSION

The main finding of this study is the increase in the time of tolerance of physical exercise in the intensity of 75% of the incremental test with CPAP compared with the condition of spontaneous breath.

The patients were eutrophic, with level of obstruction of expiratory airflow from mild to moderate; all of them maintained the use of medications during the study protocol. During the incremental test, all subjects showed an increase in the hemodynamic variables reaching a mean of the estimated VO_2 in the peak of exercise of 10.15ml/kg/min.

Regarding the increase in the time of tolerance in the condition of 75% of incremental test with CPAP, our data corroborate literature findings. In another study that evaluated the time of tolerance of physical exercise of patients with COPD from mild to moderate with use of proportional assisted ventilation with titled flows and volumes of 5.8±0.9 cm H_2O/l and 3.5±0.8 cm H_2O/l/s, respectively, Borghi-Silva *et al.*[5] observed a higher tolerance in the conditions with the ventilatory support in higher exercise intensities. In the same way, Bianchi *et al.*[22] showed that 15 patients with COPD presented higher physical capacity with the association of proportional assist ventilation (PAV) (8.6±3.6 cm H_2O/l and 3±1.3 cm H_2O/l) and high intensity physical exercise (80% of peak workload). Dyer *et al.*[14] , who studied hospitalized patients with COPD by acute exacerbation of the disease without hypercapnia, observed a mean increase of 147 seconds in the pedal capacity with fixed load of 20 watts of patients when submitted to NIV with two pressure levels (Pressure support ventilation of 10 cm H_2O and PEEP of 5 cm H_2O). Lastly, a meta-analysis about NIV and COPD performed by Shi *et al.*[23] showed that from five selected studies[24,25,26,27], two of them had a positive association between NIV and physical exercise.

The use of NIV has been shown to be effective for patients with other chronic diseases that curse with peripheral dysfunction and consequently reduces the physical exercise tolerance. Reis *et al.*[17] observed an increase in time of tolerance of physical exercise in patients with chronic heart failure with reduced left ventricular ejection fraction when submitted to CPAP of 5 cm H_2O in the intensity of 75% of the incremental test.

The rational for these findings base on the benefits of NIV on the increase in functional residual capacity with the maintenance of expanded alveoli and consequent increase in ventilatory reserve and decrease in ventilatory workload[5,14,17]. This effect is especially important when NIV is associated with physical exercise, since these patients may early interrupt the exercise by the increase in the expiratory airflow resistance and consequent dynamic hyperinflation[28]. Additionally, we may also consider that the lower the ventilatory work demands, the lower the relative cardiac output to ventilatory muscles decreasing the sympathetic response of the peripheral muscles and consequently increasing the blood flow and oxygen supply to this area, thus increasing the time of physical tolerance[29,30].

Even though blood flow has not been directly evaluated in this study, our data allow to infer about the possibility of lower blood flow redistribution to the peripheral muscles, since the use of CPAP of 5 cm H_2O was able to significantly increase the time of tolerance in physical exercise in a constant workload protocol with high intensity (75% of the incremental test). Although the PEEP titration was recommended, the use of 5cm H_2O already was able to generate a satisfactory response on the time of tolerance of these patients.

Curiously, the results of 75% of the incremental test were not reproduced with 50%. Probably, the imposed load on the constant load protocol with 50% of the incremental test was insufficient to generate a high enough metabolic demand to increase the overload on ventilatory muscles and consequently early interrupt the physical exercise.

The limitation of the study is the absence of whole-body plethysmography to measure the static volumes as well as the echocardiography to remove the possibility of coexisting chronic heart failure and arterial blood gas analysis to separate the hypoxic and hypercapnic patients. As well as the small sample size, the recruitment of men only, and the participation of subjects only with mild to moderate severity disease.

CONCLUSION

As exposed, our study observed improve in the time tolerance of physical exercise of patients with COPD from mild to moderate with CPAP with 5 cm H_2O supply during the constant load protocol with 75% of the incremental test.

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