

## INFLUENCE OF NON INVASIVE VENTILATION BY BiPAP® ON EXERCISE TOLERANCE AND RESPIRATORY MUSCLE STRENGTH IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS (COPD)

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*This study aimed to assess the effect of BiPAP®, by nasal mask, on exercise tolerance and respiratory muscle strength in patients with a clinical and spirometric diagnosis of moderate/severe COPD ( $FEV_1 < 60\%$  of predicted). Ten patients of  $59.4 \pm 8.9$  years old, with  $FEV_1/FVC < 70\%$  of predicted level, were treated with 30 minutes of BiPAP® (IPAP: 10 and 15  $cmH_2O$ ; EPAP: 4  $cmH_2O$ ), three days per week, during two months. Before and after the treatment, spirometry, inspiratory (MIP) and expiratory (MEP) muscle strength and the distance walked in six minutes (6MWT) were measured. We observed a significant increase (Wilcoxon,  $p < 0.05$ ) in the mean values of MIP (from  $-55 \pm 17$  to  $-77 \pm 19$ , respectively), MEP (from  $75 \pm 20$  to  $109 \pm 36$ , respectively) and walking distance (from  $349 \pm 67$  to  $448 \pm 75$ ). Based on these results, we concluded that BiPAP® improves respiratory muscle strength and exercise tolerance in these COPD patients.*

DESCRIPTORS: pulmonary disease, chronic obstructive; pulmonary ventilation; exercise tolerance

## INFLUENCIA DE LA VENTILACIÓN NO EVASIVA MEDIANTE EL BiPAP® SOBRE LA TOLERANCIA AL EJERCICIO FÍSICO Y FUERZA MUSCULAR RESPIRATORIA EN PACIENTES CON ENFERMEDAD PULMONAR OBSTRUTIVA CRÓNICA (EPOC)

*El objetivo de este estudio fue evaluar el efecto del BiPAP®, por medio de la máscara nasal, sobre la tolerancia al ejercicio físico y el desempeño muscular respiratorio en pacientes con diagnóstico clínico y espirométrico de EPOC moderada/grave ( $VEF_1 < 60\%$  del previsible). Con  $VEF_1/CVF < 70\%$  del previsible y edad promedio de  $59,4 \pm 8,9$  años, diez pacientes fueron tratados con 30 minutos de BiPAP® (IPAP=10-15 e EPAP=4  $cmH_2O$ ), en tres sesiones semanales, durante dos meses. Antes y después del tratamiento, fue medida la espirometría, la fuerza muscular inspiratoria (PI<sub>max</sub>) y expiratoria (PE<sub>max</sub>) y la distancia cubierta en seis minutos (TC6). Fueron evidenciados aumentos significativos (Wilcoxon,  $p < 0,05$ ) en el promedio de la PI<sub>max</sub> (de  $-55 \pm 17$  a  $-77 \pm 19$   $cmH_2O$ ), de la PE<sub>max</sub> (de  $75 \pm 20$  a  $109 \pm 36$   $cmH_2O$ ) y de la distancia cubierta (de  $349 \pm 67$  a  $447 \pm 75$  metros). Con base en estos resultados, se concluye que el BiPAP® mejoró el desempeño muscular respiratorio y la tolerancia al ejercicio físico en estos pacientes con EPOC.*

DESCRIPTORES: enfermedad pulmonar obstructiva crónica; ventilación pulmonar; tolerancia al ejercicio

## INFLUÊNCIA DA VENTILAÇÃO NÃO INVASIVA POR MEIO DO BiPAP® SOBRE A TOLERÂNCIA AO EXERCÍCIO FÍSICO E FORÇA MUSCULAR RESPIRATÓRIA EM PACIENTES COM DOENÇA PULMONAR OBSTRUTIVA CRÔNICA (DPOC)

*O objetivo deste estudo foi avaliar o efeito do BiPAP®, através de máscara nasal, na tolerância ao exercício físico e no desempenho muscular respiratório em pacientes com diagnóstico clínico e espirométrico de DPOC, moderado/grave ( $VEF_1 < 60\%$  do previsto). Com  $VEF_1/CVF < 70\%$  do previsto e idade média de  $59,4 \pm 8,9$  anos, dez pacientes com doença pulmonar obstructiva crônica (DPOC) foram tratados com 30 minutos de BiPAP® (IPAP=10-15 e EPAP=4  $cmH_2O$ ), em três sessões semanais, durante dois meses. Antes e após o tratamento mediu-se a espirometria, a força muscular inspiratória (PI<sub>max</sub>) e expiratória (PE<sub>max</sub>) e a distância percorrida em seis minutos (TC6). Foram constatados aumentos significativos (Wilcoxon,  $p < 0,05$ ) na média da PI<sub>max</sub> (de  $-55 \pm 17$  para  $-77 \pm 19$   $cmH_2O$ ), da PE<sub>max</sub> (de  $75 \pm 20$  para  $109 \pm 36$   $cmH_2O$ ) e da distância percorrida (de  $349 \pm 67$  para  $448 \pm 75$  metros). Com base nesses resultados conclui-se que o BiPAP® melhorou o desempenho muscular respiratório e a tolerância ao exercício físico nesses pacientes com DPOC.*

DESCRIPTORES: doença pulmonar obstructiva crônica; ventilação pulmonar; tolerância ao exercício

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## INTRODUCTION

**N**oninvasive ventilation (NIV) has been used successfully for treating respiratory insufficiency due to different causes, including sleep apnea, chronic obstructive pulmonary disease (COPD) and pulmonary edema<sup>(1)</sup>. The application of bi-level positive airway pressure (BiPAP<sup>®</sup>), which associates the pressure of ventilatory support with positive final pressure, aims to increase alveolar recruitment during inspiration and prevent alveolar collapse during expiration<sup>(2)</sup>.

Some studies<sup>(3)</sup> have attempted to analyze the influence of BiPAP<sup>®</sup> on the respiratory muscles and exercise tolerance in patients with COPD. Their results showed that patients who are treated with BiPAP<sup>®</sup> two hours per day, during five consecutive days, present greater respiratory muscle rest, improved tolerance and reduced dyspnea. Similar results have been found in other studies<sup>(4)</sup>, which attributed the increase in respiratory muscle strength to the muscle rest promoted by NIV. However, other research<sup>(5)</sup> has not demonstrated any significant growth in respiratory muscle strength.

As COPD patients present ventilatory limitations that lead to progressive intolerance to efforts<sup>(6)</sup>, due to dyspnea, weakness and deconditioning of respiratory and peripheral muscles<sup>(7)</sup>, making them vulnerable to hospitalization, this study aims to assess the effects of bi-level NIV in COPD patients on exercise tolerance and respiratory muscle strength.

## MATERIALS AND METHODS

**Individuals:** We studied ten individuals, five men and five women, with a mean age of  $65.3 \pm 9.6$  years, ex-smokers, whose physicians had prescribed pulmonary rehabilitation at the Special Unit for Respiratory Physiotherapy, with a clinical and spirometric diagnosis of moderate/severe COPD ( $FEV_1 < 60\%$  of predicted), with  $FEV_1/FVC < 70\%$  of predicted, and clinically stable. These patients, who were receiving bronchodilators (berotec and/or atrovent) for cases of intense dyspnea, were submitted to a general and specific evaluation of the respiratory system and signed a consent term to participate in the proposed program, as recommended by Brazilian legislation for research involving human beings. This study was approved by the ethics

committee for research involving human beings at the institution where the study was carried out.

Inclusion criteria were the absence of associated cardiovascular diseases, orthopedic diseases, hyperresponsiveness and neuromuscular disorders that would impede the realization of experimental procedures proposed in this study.

**Experimental procedure:** Before and after treatment, patients were submitted to the following assessments:

- Spirometry: carried out by means of a Vitalograph spirometer, model 2021, according to American Thoracic Society<sup>(8)</sup> standards, to characterize the degree of obstructive pulmonary disorder.
- Respiratory Muscle Strength: obtained by using a Ger-Ar mano-vacuummeter scaled in  $cmH_2O$ . Maximum inspiratory pressure (MIP) and maximum expiratory pressure (MEP) were measured according to earlier studies<sup>(9)</sup>, with the individual in the orthostatic position and with a nose clip. MIP was measured close to the residual volume after maximum expiration. MEP was measured close to total pulmonary capacity (TPC) after maximum inspiration. Individuals were oriented to sustain pressure for more than a second and each maneuver was realized at least three times. For the sake of analysis, the highest result was taken into account;
- Six-Minute Walking Test (6MWT): to evaluate exercise tolerance, patients were submitted to a 6MWT in a flat level corridor of 30 meters length and 1.5 meters width, demarcated every 2 meters.

Patients were advised to take a light meal about two hours before the test and not to perform any intense physical exercise, nor take medication during the 24 hours before the examination, besides using comfortable clothing and shoes for taking the test.

Vital signs were measured before and at the end of the test:

- Systolic (SBP) and diastolic blood pressure (DBP), using a Diasist stethoscope and BD sphygmomanometer, through indirect auscultation;
- Cardiac frequency (CF) and peripheral oxygen saturation ( $SpO_2$ ), using a Nonin 8500A portable pulse oximeter;
- subjective feeling of dyspnea, using Borg's perceived exertion scale, ranging from "zero" for no lack of air to "ten" for a maximum feeling of lack of air.

The six-minute walking test involved a walk during which the patient was asked to walk the longest

possible distance, during a six-month period, receiving a standardized encouragement every minute<sup>(10)</sup>. Patients were accompanied by the evaluator during the six minutes and continuously monitoring through the pulse oximeter. For the sake of analysis, CF, SpO<sub>2</sub> and subjective feeling of dyspnea were recorded before and after the test. With a view to minimizing learning effects, each patient carried out two tests before the treatment, and the longest distance was calculated.

#### Noninvasive Ventilation (NIV)

Patients were submitted to NIV by means of BiPAP<sup>®</sup>, using a nasal mask, for 30 minutes, three times per week, on alternate days, during six weeks. BiPAP<sup>®</sup> levels were adjusted according to each patient's tolerance. Patients remained comfortably seated throughout the NIV application (with IPAP set between 10 and 15 cmH<sub>2</sub>O and EPAP at 4 cmH<sub>2</sub>O), and were asked to adopt diaphragmatic breathing<sup>(11)</sup> during the application.

### STATISTICAL ANALYSIS

For the statistical analysis of physiological variables and distance walked before and after treatment with NIV, we used Wilcoxon's non-parametrical test, as data did not present a normal distribution. A p<0.05 significance level was adopted.

### RESULTS

Table 1 presents the participants' individual anthropometric and demographic characteristics related to age, gender, weight, height, body mass index (BMI), with mean values and standard deviations.

Table 1 - Individual anthropometric and demographic characteristics with mean values and standard deviations

Subjects	Age (years)	Gender	Weight (kg)	Height (m)	BMI (kg/m <sup>2</sup> )
1	72	M	78.5	1.63	29.5
2	68	M	68.5	1.66	24.9
3	66	M	89	1.76	28.7
4	78	M	66.5	1.68	23.6
5	64	M	72	1.61	27.8
6	64	F	70	1.65	25.7
7	70	F	51	1.5	22.7
8	43	F	109	1.53	46.6
9	63	F	72	1.52	31.2
10	43	F	63	1.55	26.2
<b>Mean/SD</b>	<b>65.3±9.6</b>		<b>74±15.7</b>	<b>1.61±0.1</b>	<b>28.7±6.8</b>

BMI: body mass index; SD: standard deviation.

Table 2 shows the spirometric results obtained when evaluating and reevaluating patients who received BiPAP<sup>®</sup> application. No significant changes were found between the spirometric indices obtained before and after NIV treatment.

Table 2 - Spirometric measurements in liters and percentages of predicted before and after BiPAP<sup>®</sup> treatment

	Pre-BiPAP <sup>®</sup>	Post-BiPAP <sup>®</sup>
FVC(%)	60.98±11.98	57.35±11.76 (NS)
FVC(l)	1.78±0.56	1.65±0.55 (NS)
FEV <sub>1</sub> (%)	43.25±8.92	45.09±8.18 (NS)
FEV <sub>1</sub> (l)	1.06±0.21	1.05±0.28 (NS)
FEV <sub>1</sub> /FVC (%)	58.4±17	61.8±11 (NS)
MVV (%)	42.80±8.91	44.02±6.71 (NS)
MVV (l)	37.83±8.51	39.62±10.63 (NS)
FEF <sub>25-75%</sub> (%)	17.52±10.03	19.82±9.64 (NS)
FEF <sub>25-75%</sub> (l)	0.51±0.28	0.58±0.29 (NS)

FVC: forced vital capacity; FEV<sub>1</sub>: forced expiratory volume in one second; MVV: maximum voluntary ventilation; FEF<sub>25-75%</sub>: forced expiratory flow 25-75; NS: not significant.

Table 3 presents the mean results for the following physiological answers: CF, SpO<sub>2</sub>, subjective feeling of dyspnea, MIP and MEP, as well as the distance walked during the 6MWT. We did not find statistically significant differences between the pre- and post-treatment situations for CF, SpO<sub>2</sub> and subjective feeling of dyspnea. However, differences for distance walked, MIP and MEP were statistically significant.

Table 3 - Comparison between mean values on dyspnea scale for 6MWT, MIP, MEP and distance walked, before and after treatment with BiPAP<sup>®</sup>

	Pre-BiPAP <sup>®</sup>	Post-BiPAP <sup>®</sup>	P-value
SpO <sub>2</sub> (%)	85.4±3.7	92.8±1.6	0.10
Dyspnea (0-10)	2.9±1.5	0.7±0.8	0.10
CF (bpm)	115.8±10.1	117.7±11.1	0.10
MIP (cmH <sub>2</sub> O)	-54.50±17.07	-76.66±18.87	0.007*
MEP (cmH <sub>2</sub> O)	74.70±70	109.44±35.74	0.007*
Distance walked (m)	349.1±67.4	447.6±75.29	0.005

SpO<sub>2</sub>: peripheral oxygen saturation; CF: cardiac frequency; MIP: maximum inspiratory pressure; MEP: maximum expiratory pressure.

Figure 1 illustrates individual results for distance walked in meters, obtained before and after treatment with NIV.

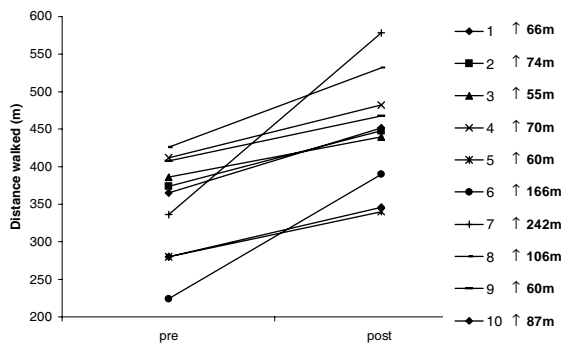


Figure 1 - Individual values for distance walked during 6MWT, obtained during evaluation and reevaluation

## DISCUSSION

Noninvasive ventilation has been used in different studies to provide greater respiratory muscle rest<sup>(4)</sup>. NIV is able to “alleviate” the inspiratory muscles’ work load, promoting a temporary rest and thus allowing for better conditions to develop respiratory muscle strength.

Our results showed that NIV through a nasal mask by means of BiPAP<sup>®</sup>, during a six-week period, significantly increased muscle strength in COPD patients, in line with literature<sup>(12)</sup>, which has demonstrated increases in MIP and MEP after the chronic application of BiPAP<sup>®</sup> in COPD patients. Increases in respiratory muscle strength through the use of pressure support have also been observed<sup>(13)</sup> when applying NIV to COPD patients during the night.

Moreover, our results indicated a probable improvement in exercise tolerance after treatment with NIV, as we found a significant increase in the distance walked during the 6MWT which, although very simple, has been frequently used in field studies<sup>(14)</sup>. Despite the physical limitations COPD patients normally present, the distance walked by all of our patients exceeded 54 meters, as shown in Figure 1. This has been mentioned<sup>(15)</sup> as a good indicator of these patients’ clinical improvement.

Similar results were found in a research<sup>(3)</sup> that assessed the effects of BiPAP<sup>®</sup> when applied for two hours during the day, for one week. This research analyzed severe but stable COPD patients, eight of whom were treated with a placebo method (without NIV) and seven with BiPAP<sup>®</sup> two hours per day for five consecutive days. These authors<sup>(3)</sup> demonstrated that BiPAP<sup>®</sup> improved tolerance and reduced patients’ dyspnea, while the placebo group did not obtain any

significant improvement. However, the study neither evidenced a clinical improvement nor an increase in these patients’ respiratory muscle strength<sup>(15)</sup>.

Noninvasive ventilation, as a resource to improve respiratory muscle strength and physical performance, may require a longer treatment time, involving orientations about diaphragmatic breathing<sup>(11)</sup>. This is characterized as Functional Respiratory Reeducation. The use of NIV for few days remains restricted to supporting a rest period for the respiratory muscles, and does not obligatory entail changes in COPD patients’ respiratory muscle strength, nor in their physical condition.

With respect to CF, SpO<sub>2</sub> and subjective feeling of dyspnea, we did not find statistically significant differences during the 6MWT, when measured after NIV treatment. These results demonstrate that, although patients walked a longer distance after the treatment, these variables remained stable. This indicates an improvement in the patients’ physical condition or tolerance, although we could not compare values for the same effort intensity, which can normally be controlled during tests carried out on ergometric equipment, such as a treadmill or bicycle. Moreover, from a clinical perspective, SpO<sub>2</sub> presented a better saturation range after NIV and perceived dyspnea, although not significant, showed a downward tendency.

Although these results are encouraging, some methodological limitations need to be highlighted, such as the lack of a control group to provide more solid support to the efficacy of this alternative and auxiliary therapeutic technique in the physical training of COPD patients. Furthermore, our findings reveal the need for new studies, involving a methodology that can explore these aspects without ignoring each COPD patient’s own physical limitations; taking into account different obstruction levels, using a larger sample and more complex evaluations, such as ergospirometry and blood lactate levels.

Finally, we can conclude that, in outpatient clinics, noninvasive ventilation is an auxiliary technique for the physical conditioning of COPD patients, especially with a view to causing a rest for their respiratory muscles, allowing for greater tolerance to burdens in respiratory muscle training. This is a relevant aspect, as these patients present limited abilities to make physical efforts, weakness and mechanical alterations in respiratory muscles.

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