

Non-invasive ventilation during walking in patients with severe COPD:

A randomized cross-over trial

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Short title

NPPV during walking for severe COPD

Abstract

It was hypothesized that non-invasive positive pressure ventilation (NPPV) applied during walking avoids exercise induced hypoxemia and improves exercise performance in severe COPD patients already receiving long-term NPPV.

Twenty COPD patients (65.1±8.7 years [mean±SD], FEV₁ 27±8 %predicted, TLC 116±27 %predicted) reporting dyspnea even during mild exertion underwent two six minute walking tests with a rollator and supplemental oxygen (2.1±0.9 L/min) in a randomized cross-over design: with and without pressure-limited NPPV as used at home (inspiratory/expiratory pressure 29±4/4±1 mbar, respiratory rate 20±2 /min).

PaO₂ after walking increased by 10.5±10.8 mmHg (95%CI 5.4/15.6 mmHg; P<0.001) with NPPV, but decreased by 10.8±8.0 mmHg (95%CI -14.5/-7.1 mmHg; P<0.001) without NPPV. Dyspnea as assessed by the Borg Dyspnea Scale decreased from 6 (interquartile range 4.5/10) to 4 (interquartile range 1.5/4.5) (P<0.001) and walking distance increased from 209 (interquartile range 178/279) to 252 (interquartile range 203/314) m (P=0.027) when walking was NPPV-aided.

In chronic hypercapnic COPD high intensity NPPV can also be administered during walking with unchanged ventilator settings compared to settings used at rest, thus resulting in improved oxygenation, decreased dyspnea and increased walking distance. Therefore, NPPV during walking could prevent hypoxia induced complications and could play a future role in palliative care.

Keywords: dyspnea, exercise, non-invasive positive pressure ventilation, oxygenation, respiratory failure, six minute walking test

Introduction

The most troublesome burden of patients with chronic respiratory failure (CRF) due to chronic obstructive pulmonary disease (COPD) is dyspnea and exercise limitation. In these patients daily activities such as walking are associated with transient oxygen desaturations [1]. In addition, the cardiovascular co-morbidity responsible for death is high in patients with COPD and CRF, and these patients are at high risk to die from cardiovascular complications following exercise induced hypoxia [2, 3, 4].

Non-invasive positive pressure ventilation (NPPV) has been used as an aid to exercise training in COPD patients [5, 6]. Here, NPPV is most often used in pulmonary rehabilitation. In this setting, NPPV has been shown to increase minute ventilation despite reduced inspiratory effort [7], to unload inspiratory muscles [8, 9], and to prolong exercise induced lactataemia [10], thus reducing dyspnea on exertion and improving exercise tolerance [7, 11, 12, 13, 14, 15, 16, 17].

None of these studies, however, has primarily focused on patients with CRF already receiving NPPV for home mechanical ventilation (HMV), although these patients have the most severe limitations of physical activity and the highest risk to die from hypoxia induced cardiovascular complications [2, 3, 4]. Therefore, the present study was aimed at testing the feasibility of NPPV application during walking in patients with severe COPD who were already on HMV. In addition, in patients already receiving NPPV for treatment of pulmonary tuberculosis sequelae oxygenation has been shown to be significantly improved when NPPV was also used during exercise compared to unaided exercise [18]. Therefore, it was hypothesized that the application of NPPV results in avoidance of exercise induced hypoxemia and in improvement of exercise performance when added to supplemental oxygen compared to oxygen alone in patients with severe COPD already receiving NPPV for

long-term treatment. If so, NPPV might be a useful adjunct in daily living for patients with end-stage COPD.

Methods

The study protocol was approved by the institutional review board for human studies of the Albert-Ludwig University, Freiburg, Germany, and was performed in accordance with the ethical standards laid down 2000 in the Declaration of Helsinki. Informed written consent was obtained from all patients.

Patients

COPD patients with hypercapnic CRF (Stage IV according to GOLD-criteria [19]) reporting dyspnea even during mild exertion despite optimal treatment with anti-obstructive and anti-inflammatory medication, long-term oxygen therapy, and HMV were consecutively enrolled. Only stable patients were recruited. Patients who presented with an acute exacerbation (breathing frequency >30 per minute, pH <7.35, or clinical signs of infection), those who were planned for weaning from invasive ventilation, and those who had been intubated or tracheostomized during the last three months were excluded. Further exclusion criteria were: bronchiectasis, post tuberculosis sequelae, rib cage deformities, neuromuscular disorders and bronchial carcinoma.

Non-invasive ventilation

NPPV was applied in a pressure-limited assist/control mode. All patients had been carefully established on NPPV due to hypercapnic CRF prior to the study in hospital.

Thereby, ventilator settings had been chosen in order to maximally decrease elevated PaCO₂ levels as has been described in more detail previously by our group [20, 21, 22]. Briefly, patients were on controlled NPPV at rest for most of the time, but the assist/control mode allowed the patients to receive additional assisted breaths delivered by the machine if needed. Therefore, the most sensitive trigger threshold as individually tolerated with regard to the prevention of auto-triggering was chosen for all patients.

A one-way circuit with an expiratory valve was used in 18 patients, and a silent flow exhalation valve (Fa. Weinmann, Hamburg, Germany) was used in two patients. For passive humidification a heat and moisture exchanger (Hygrovent S[®], Medisize bv, Hillegom, the Netherlands) was provided if necessary.

Study design

Lung function parameters (Masterlab-Compact[®] Labor, Jaeger, Hochberg, Germany) and inspiratory mouth occlusion pressures (ZAN^{100®}, ZAN Gerätetechnik GmbH, Oberthulba, Germany) as previously described [23] were assessed at baseline. A standardized six minute walking test (6MWT) [24] was performed with the following measurements: dyspnea as assessed by the Borg Dyspnoea Scale (BDS) [25], blood gases taken from the arterialized earlobe (AVL OMNI[®], Roche Diagnostics GmbH, Graz, Austria), blood pressure, heart rate, and six minute walking distance (6MWD). Here, blood gases were taken immediately before and after the six minute walking test while breathing spontaneously with supplemental oxygen. In case of NPPV-aided walking patients were immediately switched from NPPV to supplemental oxygen alone after walking with subsequent measurements of blood gases. Patients were familiarized with the 6MWT. Resting during the six minute walking test was allowed, but was not further analyzed. Two 6MWT were performed in each patient in

a randomized cross-over design on two following days between 2 and 4 o'clock post meridiem at least six hours after cessation of nocturnal NPPV: one with supplemental oxygen alone and one with NPPV powered by internal battery in the addition to supplemental oxygen. For this purpose a rollator (model 306194-2, Fa. MEYRA, Kalletal, Germany) was used for both 6MWT on which the ventilator and the oxygen tank were placed (figure 1). The flow for supplemental oxygen and the ventilator settings used during walking were identical to the settings used at home and were not changed during the study.

Statistical analysis

Statistical analysis was performed using Sigma-Stat[®] (Version 3.1, Systat Software, Inc., Point Richmond California, USA). Data are presented as mean±standard deviation (SD) after testing for normal distribution (Kolmogorov Smirnov Test). In case of non-normally distributed data median and interquartile range was indicated. The primary outcome parameter which was the difference of the change in PaO₂ following 6MWT served as the parameter determining the minimal sample size able to ensure the desired power on intervention effect. Assuming a power (β) of 90% with an α of 0.05 to detect a change in PaO₂ of 14 mmHg (with a standard deviation of 10.5 mmHg) according to previous findings [18] and own clinical experience at least nine patients were needed for the analysis. The target sample size of twenty patients was aspired in order to increase the power of the analysis, thus more reliably allowing generalization of the findings, and also to detect changes in secondary outcome parameters which were as follows: 6MWD, change in BDS, and change in PaCO₂ following 6MWT. The paired t-test was used for the quantitative measurements, and the Wilcoxon signed rank test was used for the BDS. For

normally distributed data the 95% Confidence Interval (95%CI) was given if appropriate. Statistical significance was assumed with a P-value of <0.05.

Results

One patient refused to participate, and twenty patients completed. All patients suffered from end-stage COPD with severe impairments of lung function parameters and mouth occlusion pressures (table 1). Significant co-morbidity was evident: 14 had arterial hypertension, 7 had coronary heart disease, 1 had congestive heart failure, 6 had pulmonary hypertension, 6 had chronic atrial fibrillation, 4 had diabetes mellitus type II, and 6 were obese (BMI >30kg/m²). Nineteen patients were heavy smokers with a mean cumulative smoking dosage of 50.0±26.4 pack years with 18 of them having quit smoking. Seventeen patients were studied during a routine control visit for NPPV, and three patients receiving HMV were studied during evaluation for lung transplantation. All patients subjectively reported on severe dyspnea during mild physical exertion. Two patients additionally received long-term oral morphine therapy with a daily dosage ranging from 10 to 20 mg for treatment of dyspnea.

Mean duration of HMV used during night and also intermittently during daytime was 35.1±30.5 months, and mean flow rate of supplemental oxygen was 2.1±0.9 L/min. NPPV was applied using Legendair (Airox, Pau Cedex, France), BREAS PV403 and BREAS VIVO 40 (Breas Medical AB, Molnlycke, Sweden) in ten, eight and two patients, respectively. Mean inspiratory positive airway pressure was 28.9±4.4 mbar, mean expiratory positive airway pressure was 4.3±0.8 mbar, mean respiratory rate was 19.8±1.7 /min, and mean I:E-ratio was 1:1.8. The Profile Light mask (Respironics

Inc., Pennsylvania, USA) was acting as a nasal mask in seven patients, and an individually built nasal mask was used in four patients. The Mirage full face mask (Resmed, New South Wales, Australia) was used in eight patients, and an individually built full face mask was used in one patient. Five patients received passive humidification.

PaO₂ substantially decreased by 10.8±8.0 mmHg (95%CI -14.5 / -7.1 mmHg; P<0.001) during 6MWT when supplemental oxygen was used, but markedly increased by 10.5±10.8 mmHg (95%CI 5.4 / 15.6 mmHg; P<0.001) when NPPV was used in the addition to supplemental oxygen (table 2, figure 2). PaCO₂ increased by 3.0±2.8 mmHg (95%CI 1.6 / 4.3 mmHg; P<0.001) during 6MWT when supplemental oxygen was used, but did not significantly change when NPPV was used in the addition to supplemental oxygen (table 2). BDS increased significantly during 6MWT when receiving oxygen alone from 0 (interquartile range 0 / 0) to 6 (interquartile range 4.5 / 10) (P<0.001) as well as during NPPV-aided walking from 0 (interquartile range 0 / 0) to 4 (1.5 / 4.5) (P<0.001). BDS after walking was significantly lower when walking was NPPV-aided compared to unaided walking (P<0.001) (table 2, figure 3). Walking distance increased from 209 (interquartile range 178 / 279) to 252 (interquartile range 203 / 314) m (P=0.027) (figure 4.) in favor of NPPV-aided walking.

The differences between the values after and before walking comparing NPPV-aided and unaided walking were 21.3±12.1 mmHg (95%CI 15.6 / 27.0 mmHg; P<0.001) for PaO₂ and 3.0±2.9 (95%CI 1.6 / 4.4; P<0.001) for BDS. Accordingly, there was no significant difference for PaCO₂.

Discussion

The present study shows the impact of NPPV applied during walking on oxygenation in patients with end-stage hypercapnic COPD. PaO₂ substantially decreased during 6MWT by a mean of 11 mmHg when only supplemental oxygen was given, but markedly increased by a mean of 11 mmHg when NPPV was added to supplemental oxygen. In addition, the use of NPPV during walking resulted in significantly decreased dyspnea on exertion with a significantly prolonged walking distance.

There were numerous former studies aimed at investigating clinical effects of NPPV during exercise in patients with COPD. Most of these studies have concluded that NPPV during exercise is capable of reducing dyspnea on exertion and improving exercise tolerance [7, 11, 12, 13, 14, 15, 16, 17], although contradictory results have also been published [26]. However, the present study substantially differs from the previous ones in several aspects.

First, cycle ergometer testing [7, 12, 16, 17] or treadmill walking [11, 13] was used in the majority of previous studies. In contrast, a 6MWT was performed in the present study, since walking is suggested to more accurately reflect the exercise performance during daily activity in these patients [27]. In addition, a rollator was used which has previously been shown to improve walking distance and to increase ventilatory capacity even without ventilatory support in COPD patients [28].

Secondly, patients included in the present study had more severe COPD compared to previous studies with a mean FEV₁ of 27 %predicted and with the dependence on long-term NPPV to treat hypercapnic CRF. Further, patients were not studied during a rehabilitation program, but during hospitalisation for a routine check of NPPV. Three patients were also evaluated for lung transplantation. Therefore, the present study indicates that NPPV during exercise is also beneficial for end-stage COPD patients who are already on NPPV at home.

Thirdly, oxygenation was not addressed in many of the former investigations. Desaturations during unaided exercise have been shown in patients with severe COPD [17] and pulmonary tuberculosis sequelae [18]. However, this is the first study demonstrating a fall in PaO₂ during simple walking even if supplemental oxygen is applied in these patients, but also demonstrating a significant increase in PaO₂ even during walking when NPPV is given in the addition to supplemental oxygen. The reason for this effect of NPPV remains unclear. PaCO₂ increased during walking with oxygen alone. However, the increase of PaO₂ during NPPV aided walking is not sufficiently explained by augmentation of ventilation, since PaCO₂ remained unchanged with NPPV and oxygen. An improvement of ventilation-perfusion mismatch or pulmonary hemodynamics might have caused the beneficial effects on oxygenation, but this remains speculative. Another possibility could be the reduction of hyperinflation gained by NPPV as previously been shown [29].

Fourthly, a completely different strategy of NPPV has been applied in the present study using higher inspiratory pressures and respiratory rates than previously reported. One study measuring endurance time and dyspnea in patients with hypercapnic COPD has indicated that proportional assist ventilation is superior to pressure support ventilation and continuous positive airway pressure [12] indicating the impact of ventilatory modality on outcome parameters. In addition, recent work has demonstrated that higher pressures (10 versus 5 cmH₂O) for inspiratory pressure support resulted in larger improvements in exercise performance [16, 17]. In the most recent study PaO₂ decreased during inspiratory pressure support (10 cmH₂O) aided exercise [17]. Therefore, higher ventilator settings as chosen in the present study are suggested to provide larger benefits on oxygenation during exercise.

It might be argued that these high ventilator settings are not easily tolerated by the patient. However, previous work from our group has clearly shown that NPPV using

high inspiratory pressures and high respiratory rates is well tolerated by the majority of these patients and provides beneficial physiological and clinical effects during short- and long-term use [20, 21, 22]. In addition, an increase in expiratory positive airway pressure was not applied in the present study, but this could provide further benefits in future studies in case of dynamic hyperinflation during exercise. The same is true for an increase in expiratory time, since the expiratory time was rather short in the present study.

The findings of the present study are suggested to have important clinical implications. NPPV can be applied during daily walking in addition to its use while at rest or during night, thus alleviating dyspnea during exertion and maintaining physical activity which is highly important in severe COPD. This could be true both for palliative NPPV at home and for NPPV used for bridging to lung transplantation. Changes of ventilator settings or interface were not necessary to provide the beneficial effects of NPPV during walking. Therefore, the patient is autonomous and able to use NPPV during exertion besides its application during rehabilitation programs, once the patient has been carefully established on HMV.

Also importantly, the substantial improvement of oxygenation following NPPV aided walking could prevent death from hypoxia induced arrhythmias. Recently, it has been summarised that reduced FEV₁ is an independent and important risk factor for cardiovascular mortality in patients with COPD [4]. Thereby the risk for frequent or complex ventricular arrhythmia is substantially higher in patients with lower FEV₁/FVC ratio [4]. Furthermore, it has been suggested that hypoxemia and oxygen desaturations contribute to myocardial dysfunction, heart failure, and cardiac arrhythmia in patients with COPD [30, 31]. End-stage COPD patients receiving HMV like those in the present study have severely reduced lung function parameters and severe desaturations during daily activities even if supplemental oxygen is given.

Therefore, these patients are at high risk to die from cardiovascular complications. Although cardiac function and arrhythmias were not assessed in the present study, we would strongly suggest that improving oxygenation during exertion as achieved by NPPV can presumably reduce cardiovascular complications, thus reducing mortality in patients with severe COPD [2, 3, 4]. Certainly, this needs further investigations.

Another clinical benefit is the increase in walking distance when using NPPV as shown in the present study. Moreover, patients used NPPV during walking for the first time. Therefore, there is clearly room for further improvement of walking distance following full acclimatization to NPPV during exercise. This shows that NPPV during exertion has the potential to improve physical activity in patients with CRF due to COPD.

It might be argued that the level of supplemental oxygen was not adapted to the exercise level, since increasing the dosage of supplemental oxygen has been shown to improve exercise ability in patients with severe COPD [32]. However, this was true for non-hypercapnic COPD patients only, but was felt to be disadvantageous in the present study, since a substantial increase of PaCO₂ has previously been shown even in patients with marginal ventilatory insufficiency [32]. Nevertheless, future studies should cautiously address the impact of an increased oxygen flow rate during exercise compared to NPPV-aided exercise in patients with severe hypercapnic COPD.

The present study has some limitations which need to be addressed: Blinding for both the patient and the investigator was not possible. However, it is unlikely that this has affected oxygenation. In addition, the underlying physiological mechanisms by which NPPV improved oxygenation have not been addressed. With this regard it should be acknowledged that the inspiratory fraction of oxygen could be different

between NPPV aided and unaided walking despite similar flow rate due to changed position of oxygen source. However, changes according to these methodological inconsistencies are suggested to be minor in view of the substantial difference in oxygenation. Exercise performance during oxygen alone might also be somewhat artificially worse due to the fact that patients had to push the non-working ventilator. Finally, the study was performed in hospital only, and a 6MWT might not sufficiently address the condition at home with stairs and less space. Therefore, a conclusion for the practicability of routine NPPV during walking at home is premature. However, the current authors would suggest that the present finding will help to design future physiological and clinical studies on ventilation-aided exercise in COPD patients with severe CRF. Furthermore, future studies should also address the impact of skeletal muscle impairment and should also include subgroup analysis in order to identify patients who benefit from NPPV during walking compared to those who do not.

In conclusion, patients with severe COPD receiving HMV can also easily use NPPV during walking without changing ventilator settings or equipment. PaO₂ decreases during walking in these patients when only supplemental oxygen is given, but increases when NPPV is added to supplemental oxygen. There is also significantly less dyspnea and increased walking distance when NPPV is used. Therefore, NPPV could gain a new additional role for palliative treatment of patients with hypercapnic CRF due to COPD. In addition, NPPV during exertion might prevent death from hypoxia induced complications. Further studies are required to establish the role of NPPV as palliative treatment option during exertion in patients with severe COPD.

References

1. Soguel Schenkel N, Burdet L, de Muralt B, Fitting JW. Oxygen saturation during daily activities in chronic obstructive pulmonary disease. *Eur Respir J.* 1996; 9: 2584-9.
2. Huiart L, Ernst P, Suissa S. Cardiovascular morbidity and mortality in COPD. *Chest.* 2005; 128: 2640-6.
3. Hansell AL, Walk JA, Soriano JB. What do chronic obstructive pulmonary disease patients die from? A multiple cause coding analysis. *Eur Respir J.* 2003; 22: 809-14.
4. Sin DD, Man SFP. Chronic obstructive pulmonary disease as a risk factor for cardiovascular morbidity and mortality. *Proc Am Thorac Soc.* 2005; 2: 8-11.
5. Ambrosino N, Strambi S. New strategies to improve exercise tolerance in chronic obstructive pulmonary disease. *Eur Respir J.* 2004; 24: 313-22.
6. Ambrosino N. Assisted ventilation as an aid to exercise training: a mechanical doping? *Eur Respir J.* 2006; 27: 3-5.
7. Maltais F, Reissmann H, Gottfried SB. Pressure support reduces inspiratory effort and dyspnea during exercise in chronic airflow obstruction. *Am J Respir Crit Care Med.* 1995; 151: 1027-33.
8. Polkey MI, Kyroussis D, Mills GH, Hamnegard CH, Keilty SE, Green M, Moxham J. Inspiratory pressure support reduces slowing of inspiratory muscle relaxation rate during exhaustive treadmill walking in severe COPD. *Am J Respir Crit Care Med.* 1996; 154: 1146-50.
9. Kyroussis D, Polkey MI, Hamnegard CH, Mills GH, Green M, Moxham J. Respiratory muscle activity in patients with COPD walking to exhaustion with and without pressure support. *Eur Respir J.* 2000; 15: 649-55.
10. Polkey MI, Hawkins P, Kyroussis D, Ellum SG, Sherwood R, Moxham J.

Inspiratory pressure support prolongs exercise induced lactataemia in severe COPD. *Thorax*. 2000; 55: 547-9.

11. Keilty SE, Ponte J, Fleming TA, Moxham J. Effect of inspiratory pressure support on exercise tolerance and breathlessness in patients with severe stable chronic obstructive pulmonary disease. *Thorax*. 1994; 49: 990-4.
12. Bianchi L, Foglio K, Pagani M, Vitacca M, Rossi A, Ambrosino N. Effects of proportional assist ventilation on exercise tolerance in COPD patients with chronic hypercapnia. *Eur Respir J*. 1998; 11: 422-7.
13. Johnson JE, Gavin DJ, Adams-Dramiga S. Effects of training with heliox and noninvasive positive pressure ventilation on exercise ability in patients with severe COPD. *Chest*. 2002; 122: 464-72.
14. van 't Hul A, Kwakkel G, Gosselink R. The acute effects of noninvasive ventilatory support during exercise on exercise endurance and dyspnea in patients with chronic obstructive pulmonary disease: a systematic review. *J Cardiopulm Rehabil*. 2002; 22: 290-7.
15. Costes F, Agresti A, Court-Fortune I, Roche F, Vergnon J, Barthelemy JC. Noninvasive ventilation during exercise training improves exercise tolerance in patients with chronic obstructive pulmonary disease. *J Cardiopulm Rehabil*. 2003; 23: 307-13.
16. van 't Hul A, Gosselink R, Hollander P, Postmus P, Kwakkel G. Acute effects of inspiratory pressure support during exercise in patients with COPD. *Eur Respir J*. 2004; 23: 34-40.
17. van 't Hul A, Gosselink R, Hollander P, Postmus P, Kwakkel G. Training with inspiratory pressure support in patients with severe COPD. *Eur Respir J*. 2006; 27: 65-72.
18. Tsuboi T, Ohi M, Chin K, Hirata H, Otsuka N, Kita H, Kuno K. Ventilatory support

- during exercise in patients with pulmonary tuberculosis sequelae. *Chest*. 1997; 112: 1000-7.
19. Sutherland ER, Cherniack RM. Management of chronic obstructive pulmonary disease. *N Engl J Med*. 2004; 350: 2689-97.
 20. Windisch W, Vogel M, Sorichter S, Hennings E, Bremer H, Hamm H, Matthys H, Virchow JCJ. Normocapnia during nIPPV in chronic hypercapnic COPD reduces subsequent spontaneous PaCO₂. *Respir Med*. 2002; 96: 572-9.
 21. Windisch W, Kostic S, Dreher M, Virchow JCJ, Sorichter S. Outcome of patients with stable COPD receiving controlled noninvasive positive pressure ventilation aimed at a maximal reduction of PaCO₂. *Chest*. 2005; 128: 657-62.
 22. Windisch W, Dreher M, Storre JH, Sorichter S. Nocturnal non-invasive positive pressure ventilation: Physiological effects on spontaneous breathing. *Respir Physiol Neurobiol*. 2006; 150: 251-60.
 23. Windisch W, Hennings E, Sorichter S, Hamm H, Crie CP. Peak or plateau maximal inspiratory mouth pressure: which is best? *Eur Respir J*. 2004; 23: 708-13.
 24. Sciruba F, Criner GJ, Lee SM, Mohsenifar Z, Shade D, Slivka W, Wise RA. Six-minute walk distance in chronic obstructive pulmonary disease: reproducibility and effect of walking course layout and length. *Am J Respir Crit Care Med*. 2003; 167: 1522-7.
 25. Borg GA. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc*. 1982; 14: 377-81.
 26. Bianchi L, Foglio K, Porta R, Baiardi R, Vitacca M, Ambrosino N. Lack of additional effect of adjunct of assisted ventilation to pulmonary rehabilitation in mild COPD patients. *Respir Med*. 2002; 96: 359-67.
 27. Pitta F, Troosters T, Spruit MA, Decramer M, Gosselink R. Activity monitoring for

assessment of physical activities in daily life in patients with chronic obstructive pulmonary disease. *Arch Phys Med Rehabil.* 2005; 86: 1979-85.

28. Probst VS, Troosters T, Coosemans I, Spruit MA, Pitta FdO, Decramer M, Gosselink R. Mechanisms of improvement in exercise capacity using a rollator in patients with COPD. *Chest.* 2004; 126: 1102-7.
29. Diaz O, Begin P, Torrealba B, Jover E, Lisboa C. Effects of noninvasive ventilation on lung hyperinflation in stable hypercapnic COPD. *Eur Respir J.* 2002; 20: 1490-8.
30. Flick MR, Block AJ. Nocturnal vs diurnal cardiac arrhythmias in patients with chronic obstructive pulmonary disease. *Chest.* 1979; 75: 8-11.
31. Tirlapur VG, Mir MA. Nocturnal hypoxemia and associated electrocardiographic changes in patients with chronic obstructive airways disease. *N Engl J Med.* 1982; 306: 125-30.
32. Leach RM, Davidson AC, Chinn S, Twort CH, Cameron IR, Bateman NT. Portable liquid oxygen and exercise ability in severe respiratory disability. *Thorax.* 1992; 47: 781-9.

Tables

Table 1. Demographic data, lung function parameters and mouth occlusion pressures (N = 20; 8 females).

	Mean ± SD
Age (years)	65.1 ± 8.7
BMI (kg/m ²)	28.2 ± 8.6
FVC (%pred)	50.2 ± 11.1
FEV ₁ (%pred)	27.0 ± 7.5
FEV ₁ /FVC (%)	48.2 ± 12.3
TLC (%pred)	115.6 ± 27.3
RV (%pred)	244.0 ± 66.4
Plmax _{peak} (%pred)	51.7 ± 28.3
Plmax _{1.0} (%pred)	46.2 ± 22.9
P0.1 (kPa)	0.40 ± 0.20
P0.1*Ti/VT (kPa*s/L)	0.76 ± 0.29

BMI = body mass index, FEV₁ = forced expiratory volume in one second, FVC = forced vital capacity, P0.1 = mouth occlusion pressure 0.1 seconds after the onset of inspiration during normal breathing, Plmax_{peak} = peak maximal inspiratory mouth pressure, Plmax_{1.0} = plateau maximal inspiratory mouth pressure sustained for 1.0 second, RV = residual volume, SD = standard deviation, Ti = inspiratory time, TLC = total lung capacity, VT = tidal volume.

Table 2. Blood gases, heart rate, blood pressure, dyspnea, and walking distance before and after the six minute walking test.

	Supplemental oxygen[#]	NPPV + supplemental oxygen[#]	95% CI for the difference*	P-value
PaO ₂ <i>before</i> (mmHg)	72.4 ± 5.6	70.7 ± 8.1		0.16
PaO ₂ <i>after</i> (mmHg)	61.6 ± 7.9	81.2 ± 12.4	13.3 / 26.0	< 0.001
PaCO ₂ <i>before</i> (mmHg)	50.4 ± 5.7	50.1 ± 7.4		0.64
PaCO ₂ <i>after</i> (mmHg)	53.3 ± 6.5	51.5 ± 6.4	-3.5 / -0.1	0.038
SaO ₂ <i>before</i> (%)	95.1 ± 1.6	94.7 ± 2.1		0.524
SaO ₂ <i>after</i> (%)	88.8 ± 4.0	94.6 ± 3.4	3.7 / 7.9	< 0.001
pH <i>before</i>	7.40 ± 0.02	7.40 ± 0.03		0.33
pH <i>after</i>	7.37 ± 0.03	7.38 ± 0.03	NF	0.21
heart rate <i>before</i> (/min)	89.5 ± 12.2	87.6 ± 15.7		0.67
heart rate <i>after</i> (/min)	102.7 ± 14.8	101.5 ± 13.3	-10.0 / 7.7	0.79
BP _{systolic} <i>before</i> (mmHg)	119.5 ± 20.3	122.6 ± 17.2		0.49
BP _{systolic} <i>after</i> (mmHg)	133.7 ± 24.2	137.5 ± 19.0	-6.3 / 13.9	0.44
BP _{diastolic} <i>before</i> (mmHg)	69.8 ± 14.4	70.4 ± 12.6		0.85
BP _{diastolic} <i>after</i> (mmHg)	75.3 ± 15.1	80.6 ± 12.1	NF	0.034
BDS <i>before</i>	0 (0 / 0)	0 (0 / 0)		0.63
BDS <i>after</i>	6 (4.5 / 10)	4 (1.5 / 4.5)		< 0.001
6MWD (m)	222.0 ± 84.8	260.7 ± 64.9	NF	0.027

[#]mean ± standard deviation is given, except for BDS for which medians and interquartile ranges are given.

*95% confidence interval is given only for values (except BDS) after six minute walking test.

6MWD = six minute walking distance, 95% CI = 95% confidence interval, BDS = Borg Dyspnea Scale, BP = blood pressure, NF = normality test failed, NPPV = non-invasive positive pressure ventilation, PaCO₂ = arterial partial pressure of carbon dioxide, PaO₂ = arterial partial pressure of oxygen, SaO₂ = oxygen saturation.

Figure legends

Figure 1.

COPD patient during six minute walking test while on supplemental oxygen **(A)** and while on non-invasive positive pressure ventilation in addition to supplemental oxygen **(B)**.





Figure 2.

Changes of arterial partial pressure of oxygen (PaO_2) before and after six minute walking test while on supplemental oxygen **(A)** and while on non-invasive positive pressure ventilation in addition to supplemental oxygen **(B)**.

Mean values are given with standard deviation.

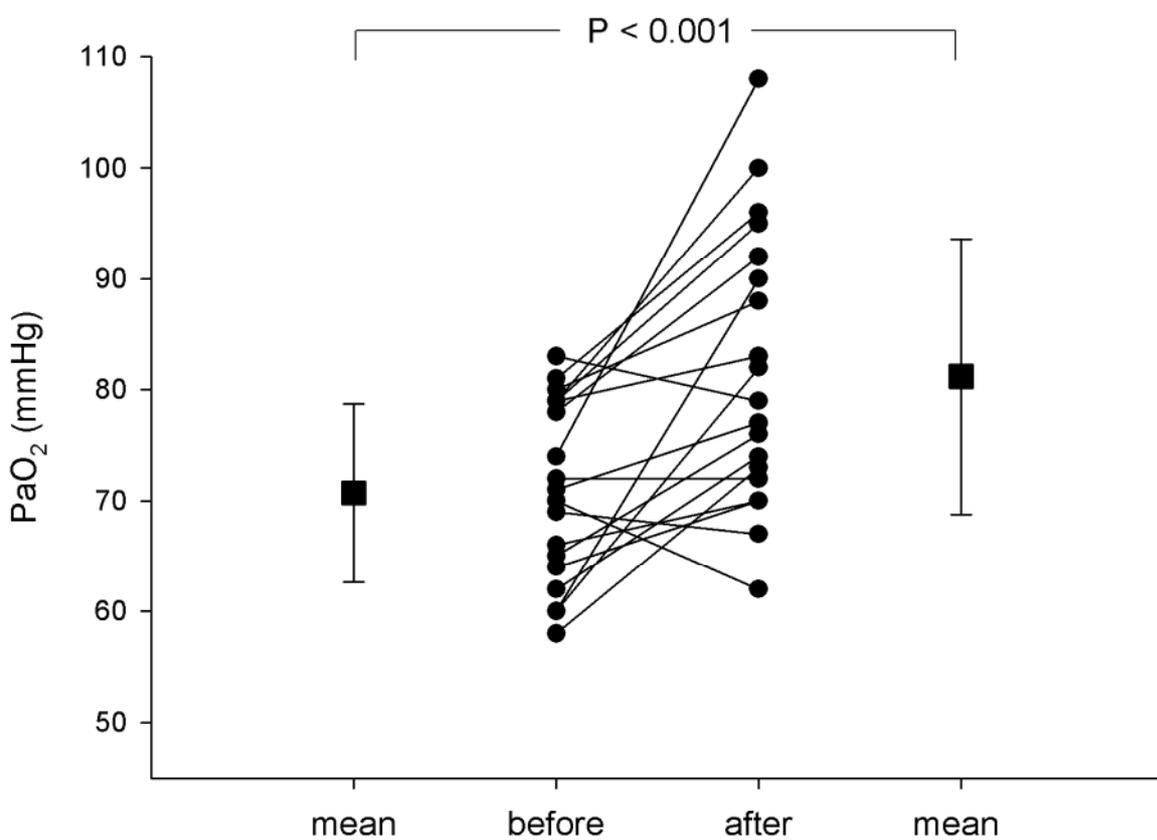
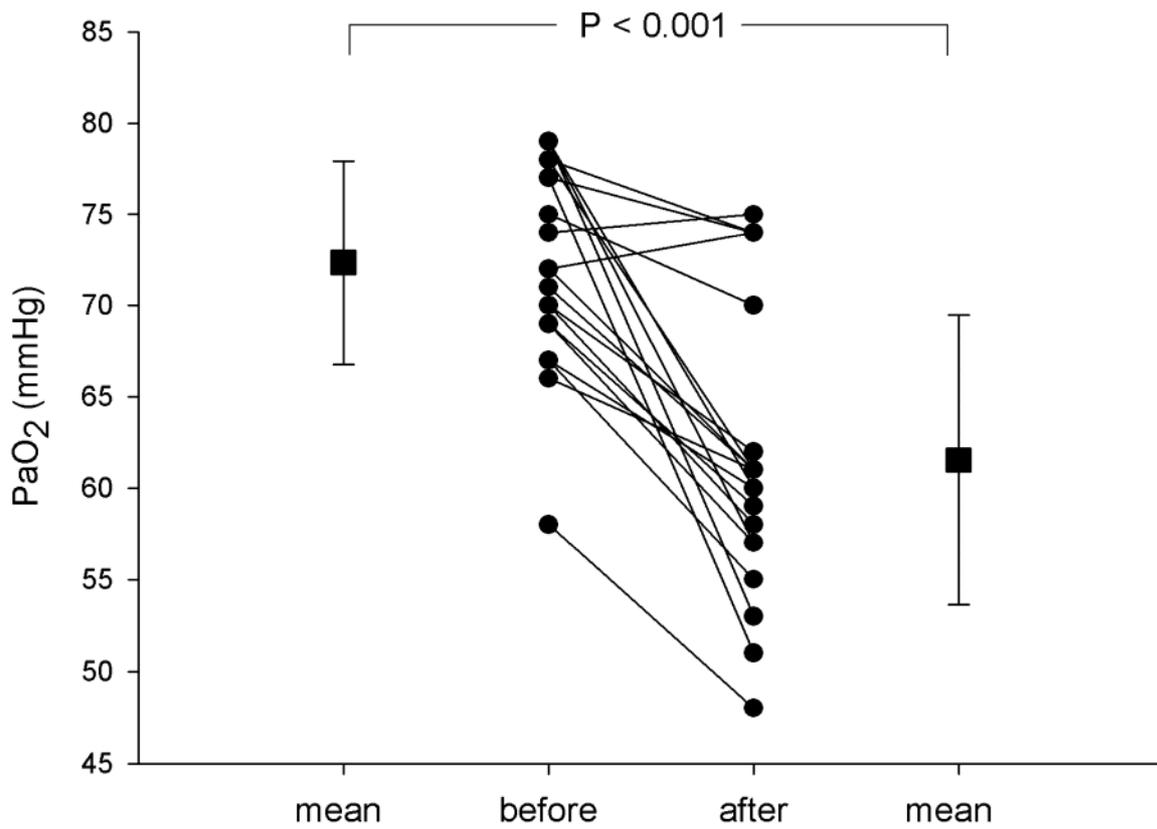


Figure 3.

Borg Dyspnea Scale following six minute walking test while on supplemental oxygen and while on non-invasive positive pressure ventilation (NPPV) in addition to supplemental oxygen.

Median values with 25th (lower bar) and 75th percentile (upper bar) are given.

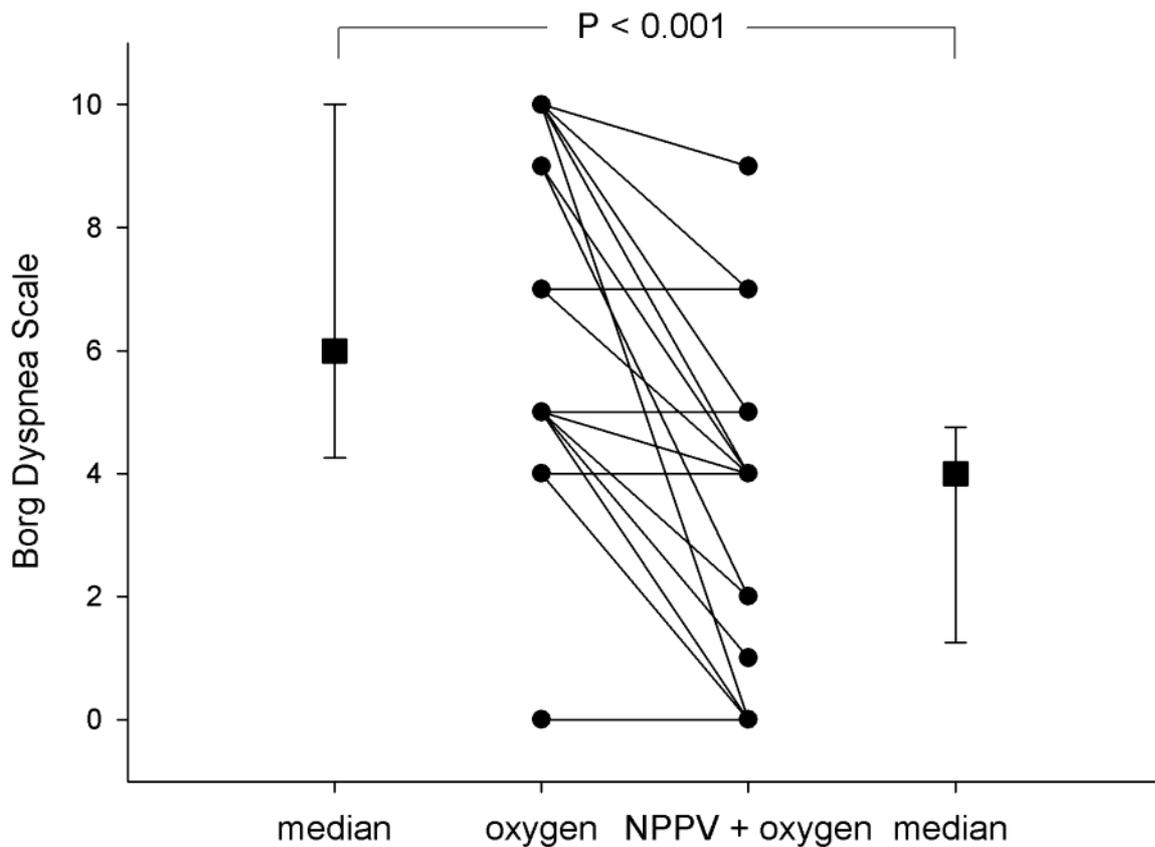


Figure 4.

Walking distance after six minute walking test while on supplemental oxygen and while on non-invasive positive pressure ventilation (NPPV) in addition to supplemental oxygen.

