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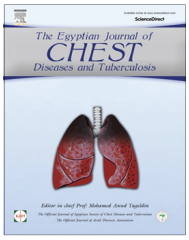

ORIGINAL ARTICLE

# Bi-level positive airway pressure ventilation for patients with stable hypercapnic chronic obstructive pulmonary disease

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**KEYWORDS**

COPD;
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**Abstract** *Background:* The role of noninvasive positive pressure ventilation (NPPV) has been well established in the treatment of acute hypercapnic respiratory failure due to chronic obstructive pulmonary disease (COPD), however, its benefits in clinically stable hypercapnic COPD patients still not well known, so this trial aimed to assess the efficacy of NPPV in patients with stable hypercapnic COPD.

*Patients and methods:* This study included 30 stable hypercapnic COPD patients hospitalized for long term stay from June 2012 to May 2014. The 30 patients who met the study criteria were randomized into the control group (15 patients: 13 males and 2 females with mean age 66 ± 6.2) maintained on standard treatment and the second group (15 patients: 12 males and 3 females with mean age 65 ± 7.3) received bi-level positive pressure ventilation added to their standard treatment after giving a written consent. The patients were evaluated and followed up after initiating this therapy.

*Results:* After 6 months of NPPV, daytime $PaCO_2$ (mmHg) during spontaneous breathing decreased from 55.2 ± 6.7 to 47.1 ± 3.1 mmHg and daytime $PaO_2$ (mmHg) on room air increased from 48 ± 6.1 to 55.1 ± 8.3 with improvement of dyspnea scale and quality of life parameters. This was achieved with mean inspiratory pressures of 19.7 ± 2.41 cm $H_2O$ and mean expiratory pressures of 6.8 ± 1.7 cm $H_2O$.

*Conclusions:* NPPV is well tolerated and can improve blood gas levels, dyspnea and quality of life parameters in patients with stable hypercapnic COPD.



## Introduction

Chronic obstructive pulmonary disease (COPD) is currently a leading cause of death and disability worldwide [1–3]. As the disease progressively aggravates, a majority of patients will develop severe COPD with chronic respiratory failure (CRF), and some have a hypercapnia condition, in which the

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partial pressure of carbon dioxide in arterial blood ($PaCO_2$) is persistently >45 mmHg. Once CRF and hypercapnia are presented, patients often develop severe dyspnea and the quality of life is worse. Meanwhile, the two-year mortality reaches 30–40% [4,5].

The clinical course of COPD is characterized by a high morbidity and mortality despite long-term oxygen therapy (LTOT) [1]. Recent alternative therapies, including lung transplantation and lung volume reduction surgery, can only be undertaken in a small number of patients, and there is no demonstration of improved long-term survival rate [2,3].

Noninvasive positive pressure ventilation (NPPV) administered via a nasal mask has proven useful in treating restrictive extra-pulmonary respiratory insufficiency and in many patients with severe COPD in acute respiratory failure [5,6]. Theoretically, NPPV could also be beneficial in patients with severe stable COPD, through several mechanisms. It could improve nocturnal ventilation, decrease the end-expiratory lung volume and hence the level of dynamic hyperinflation. In addition, NPPV could improve respiratory muscle function by resting the respiratory muscles [7] however; the efficacy of this form of therapy in patients with airflow obstruction who are in stable condition remains controversial [4]. A previous meta-analysis showed that nocturnal NIPPV for stable hypercapnic patients with COPD did not have clinically or statistically significant effects on lung function, gas exchange, or sleep efficiency [8], but on the other hand, some recent studies [9,10] using a relative high inspiratory positive airway pressure (IPAP) in NIPPV showed improvement in gas exchange. So this trial aimed to assess the efficacy of NPPV compared to conventional standard treatment in patients with stable hypercapnic COPD.

## Patients and methods

This study included 30 stable hypercapnic COPD patients hospitalized for long term stay in the period from June 2012 to May 2014, after giving written informed consent. The study protocol was approved by the ethics committee of the hospital. The diagnosis of COPD was based on clinical history, physical examination findings, and spirometric criteria according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines [1]. All patients were in stable clinical state and were free from exacerbations at least 4 weeks preceding recruitment.

An exacerbation of COPD was defined as "a sustained worsening of the patient's condition, from the stable state and beyond normal day-to-day variations, that is acute in onset and necessitates a change in regular medication" [11].

Patients were excluded if they had the following: sleep apnea syndrome, other etiologies of chronic airway obstruction (e.g. bronchiectasis) or significant co-existing medical conditions, such as left ventricular failure.

The 30 patients who met the study criteria were randomized into the control group (15 patients, 13 males and 2 females with mean age 66 ± 6.2) who maintained on standard treatment (bronchodilators, inhaled corticosteroids, supplemental oxygen therapy, antibiotics and systemic corticosteroids during the episodes of acute exacerbation) and the second group (15 patients, 12 males and 3 females with mean age 65 ± 7.3) received in addition to the previous medications bi-level positive airway pressure ventilation (BiPAP). The patients were connected to a ventilator (BiPAP Vision, Respironics Inc., Murrysville, Pa., USA). Initial ventilator settings were: inspiratory positive airway pressure (IPAP) was set at 10 cm $H_2O$, positive end-expiratory pressure (EPAP) at 5 cm $H_2O$ and then, IPAP and EPAP were titrated according to the patient's comfort and synchrony with the ventilator and a marked reduction in the use of accessory muscles. Arterial blood gases were measured 1 h after the initiation of ventilation and a decrease in $PaCO_2$ values >5% was considered as adequate ventilator support, this was achieved with mean inspiratory pressures of 19.7 ± 2.4 cm $H_2O$ and mean expiratory pressures of 6.8 ± 1.7 cm $H_2O$. NPPV is first used during daytime under careful supervision. Once daytime NPPV is tolerated, nocturnal NPPV is commenced. Finally, patients are instructed to use the ventilator for the entire night [12].

All patients were evaluated and followed up by:

- Spirometry, performed according to American Thoracic Guidelines as previously described [13].
- Arterial blood gas analysis.
- A 6-min walk test was performed along a flat indoor hallway using standard procedures [14].
- Dyspnea was assessed with the Medical Research Council (MRC) dyspnea scale [15].
- The evaluation of health related quality of Life (HRQoL) was made using the 12-Item Short-Form health survey version 2 (SF-12V2). The scales can be aggregated to two summary measures (PCS, physical component summary and MCS, mental component summary) [16].

### *Statistical analysis*

Results are given as means ± SD. The SPSS package (SPSS, Chicago) was used for all analyses. $P < 0.05$ was considered as statistically significant.

## Results

Table 1 shows Patients' baseline characteristics in which there were no statistically significant differences between groups according to their age, gender, body mass index, spirometric values and arterial blood gases.

Table 2 shows blood gas parameters (on room air) at the start and after 6 months of the studied patients. Significant decrease in $PaCO_2$ (mmHg) and significant improvement in $PaO_2$ (mmHg) were observed in patients who received NPPV, however there were no significant changes in the control group.

**Table 1** Characteristics of the studied patients.

| Characteristics | Control ($n$ = 15) | NIPPV ($n$ = 15) | $P$ |
|---|---|---|---|
| Age in years | 66 ± 6.2 | 65 ± 7.3 | 0.68 |
| Gender M/F | 13/2 | 12/3 | 0.62 |
| BMI (kg/m$^2$) | 24.3 ± 4.7 | 25.1 ± 3.3 | 0.59 |
| FEV1 (% pred.) | 31.1 ± 11.1 | 30.1 ± 12.2 | 0.81 |
| $PaO_2$ (mmHg) | 48.9 ± 5.8 | 48.0 ± 6.1 | 0.67 |
| $PaCO_2$ (mmHg) | 54.9 ± 7.3 | 55.2 ± 6.7 | 0.9 |

BMI = body mass index; M = male; F = female.

**Table 2** Blood gas parameters (on room air) at the start and after 6 months of the studied patients.

| Variables | Patients treated with NPPV | | | Control group | | |
|---|---|---|---|---|---|---|
| | Base-line parameters | After 6 months | *P* | Base-line parameter | After 6 months | *P* |
| pH | 7.38 ± 0.02 | 7.38 ± 0.05 | 0.99 | 7.37 ± 0.04 | 7.37 ± 0.04 | 1 |
| $PaCO_2$ (mmHg) | 55.2 ± 6.7 | 47.1 ± 3.1 | 0.008 | 54.9 ± 7.3 | 53.3 ± 6.6 | 0.52 |
| $PaO_2$ (mmHg) | 48.0 ± 6.1 | 55.1 ± 8.3 | 0.009 | 48.9 ± 5.8 | 50.0 ± 7.1 | 0.6 |
| $HCO_3^-$ (mmol/L) | 31.3 ± 5.7 | 26.9 ± 4.2 | 0.019 | 30.6 ± 5.6 | 31.4 ± 4.9 | 0.6 |

$PaCO_2$ = arterial partial pressure of carbon dioxide; $PaO_2$ = arterial partial pressure of oxygen; $HCO_3^-$ = bicarbonate.

**Table 3** Lung function parameters (during spontaneous breathing) at the start and after 6 months of the studied patients.

| Variables | Patients treated with NPPV | | | Control group | | |
|---|---|---|---|---|---|---|
| | Base-line parameters | After 6 months | *P* | Base-line parameters | After 6 months | *P* |
| FVC (% pred.) | 48.3 ± 13.3 | 49.6 ± 13.7 | 0.74 | 47.9 ± 13.3 | 46.1 ± 12.2 | 0.69 |
| FEV1 (% pred.) | 30.8 ± 10.2 | 33.4 ± 11.1 | 0.31 | 31.4 ± 10.1 | 30.1 ± 9.6 | 0.72 |
| FEV1/FVC (%) | 45.6 ± 10.1 | 46.1 ± 10.2 | 0.89 | 46.2 ± 9.7 | 45.9 ± 10.2 | 0.92 |

FVC = forced vital capacity; FEV1 = forced expiratory volume in one second.

**Table 4** Quality of life of the studied patients.

| Variables | Patients treated with NPPV | | | Control group | | |
|---|---|---|---|---|---|---|
| | Baseline | After 6 months. | *P* | Baseline | After 6 months | *P* |
| MRC dyspnea scale | 4.2 ± 0.8 | 3. 1 ± 1.1 | 0.004 | 4.1 ± .6 | 4 ± .4 | 0.59 |
| SF-12 V2 | | | | | | |
| PCS | 30 ± 5 | 42 ± 5 | 0.00 | 32 ± 3 | 33 ± 4 | 0.44 |
| MCS | 30 ± 10 | 40 ± 80 | 0.004 | 31 ± 5 | 32 ± 6 | 0.43 |
| 6-min walk distance | 240 ± 30 | 270 ± 40 | 0.02 | 233 ± 31 | 235 ± 34 | 0.83 |

MRC = medical research council; SF-12 V2 = short-form health survey version 2; PCS = physical component summary; MCS = mental component summary.

Table 3 shows lung function parameters (during spontaneous breathing) at the start and after 6 months of the studied patients in which no significant changes were observed in both groups.

Table 4 shows quality of life of the studied patients: there were significant improvement of dyspnea, physical and mental components of the SF-12 and 6-min walk distance in patients who received NIPV, however there were no significant changes in these parameters the control group.

Table 5 shows no difference in the number of exacerbation and mortality in the studied patients during the study period. One patient died in each group due to COPD exacerbations.

**Table 5** Exacerbation number and mortality during the study period.

| Variables | Patients treated with NPPV | Control group | *P* |
|---|---|---|---|
| No. of exacerbation | 1.7 ± 1.6 | 1.9 ± 1.4 | 0.73 |
| Mortality number | 1 | 1 | 1 |

## Discussion

Noninvasive positive pressure ventilation (NPPV) administered via a nasal mask has proven useful in treating restrictive extra-pulmonary respiratory insufficiency and in many patients with severe COPD in acute respiratory failure [5,6]. Theoretically, NPPV could also be beneficial in patients with severe stable COPD, through several mechanisms. It could improve nocturnal ventilation, decrease the end-expiratory lung volume and hence the level of dynamic hyperinflation and improve the response of the respiratory center to $CO_2$. It could also decrease upper airway resistance and improve the quality of sleep. In addition, NPPV could improve respiratory muscle function by resting the respiratory muscles [7], However, the role of noninvasive positive pressure ventilation (NIPPV) in COPD, especially in severe stable COPD, remains controversial [4].

A previous meta-analysis showed that nocturnal NIPPV for stable hypercapnic patients with COPD did not have clinically or statistically significant effects on lung function, gas exchange, or sleep efficiency [8], but on the other hand, some recent studies [9,10] using a relative high IPAP in NIPPV showed improvement in gas exchange. Possible factor that may explain the difference between the results of these studies was the level of ventilatory pressure utilized and its consequences on effective ventilation.

In the present study there was a significant decline in $PaCO_2$ and a significant improvement in $PaO_2$ in the studied COPD patients who received NPPV, this agree with the study of Meecham Jones et al. [12] which showed significant improvements in daytime arterial $PaO_2$ and $PaCO_2$, total sleep time, sleep efficiency, overnight $PaCO_2$, and quality of life of stable hypercapnic COPD patients with NIV.

In this study there was significant improvement in 6-min walk distance after 6 months in COPD patients treated with NIV. Similar to this findings, Garrod et al. [16] demonstrated a significant improvement in the mean shuttle walk test after 8 weeks of NIV therapy.

At present, few treatments could substantially improve lung function in patients with severe stable COPD, therefore, a treatment should be considered effective if it could maintain the lung function or slow down its deterioration. Recently, Dreher et al. [10] reported that high intensity (HI) NIPPV could significantly improve $FEV_1$ and VC in a prospective randomized crossover study. The present study did not show significant change in $FEV_1$%, FVC% and FEV1/FVC in the COPD patients who received NIPPV.

As most chronic diseases could not be completely cured, many patients concerned about the quality of life much more than anything else, therefore, any treatment which could improve the quality of life should be considered effective, especially for those end stage COPD patients. In this study there was improvement in the health related quality of life assessed by SF-12 V2 and dyspnea evaluated by MRC dyspnea scale this goes with the results of some previous studies which reported significant improvements in several aspects of health related quality of life of stable hypercapnic COPD on NIPPV when comparing with the control group [17,18].

During the study period there was no difference in exacerbation number or mortality between the control group or the group which received NIPPV as one patient died in each group due to COPD exacerbation this findings are comparable with study of Vasiliki et al. [19].

The compliance of the patients using NIPPV was pretty good in the studied patients this agrees with Dreher et al. [10] who reported that treatment compliance of HI-NIPPV was even better than low intensity (LI) NIPPV.

*In conclusion* NPPV is well tolerated and can improve blood gas levels, dyspnea and Quality of Life in patients with stable hypercapnic COPD.

## Conflict of interest

No conflict of interest.

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