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Early Effectiveness of Noninvasive Positive Pressure Ventilation on Right Ventricular Function in Chronic Obstructive Pulmonary Disease Subjects with Acute Hypercapnic Respiratory Failure

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ABSTRACT

Introduction: Noninvasive positive pressure ventilation (NIPPV) has become an integral tool in the management of acute hypercapnic respiratory failure (AHRF) in chronic obstructive pulmonary disease (COPD). This study was performed to evaluate the early effects of NIPPV on pulmonary artery pressure (PAP), serum N-terminal pro BNP (NT-proBNP), and ventilatory parameters in the COPD patients with AHRF.

Materials & Methods: This quasi-experimental study was conducted on 20 COPD patients with AHRF. The participants received the standard treatment in addition to NIPPV. There was no contraindication for NIPPV. Arterial blood gas analysis, Doppler echocardiography (for measuring PAP), and plasma NT-proBNP measurements were performed before and after NIPPV.

Results: According to the results, the mean age of the participants was 54.57±15.43 years. Furthermore, the mean pressures of carbon dioxide (PCO_2), NT-proBNP levels, and PAP were 72.33±13.96 mmHg, 4333.90±6542.20 pg/ml, and 47.5±6.38 mmHg, respectively. After one week of NIPPV, there were statistically significant differences among the mean pH, $PaCO_2$, PAP, and NT-proBNP ($P<0.001$, $P=0.003$, $P<0.001$, and $P<0.001$, respectively).

Conclusion: As the findings of the present study indicated, the application of NIPPV in the COPD patients with AHRF can not only improve arterial blood pH and carbon dioxide tension, but also instantly decrease NT-proBNP levels and PAP.

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Introduction

Acute hypercapnic respiratory failure (AHRF) is a frequent complication of chronic obstructive pulmonary disease (COPD) exacerbation. This condition is associated with major deterioration

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in pulmonary function and gas exchange (1, 2). Mechanical ventilation is necessary in most of the patients afflicted with AHRF, which can be used beside the conventional therapeutic options available for the COPD exacerbation (1). It is well-documented that the noninvasive positive pressure ventilation (NIPPV) is an effective tool for ventilatory support in the patients with AHRF due to COPD exacerbation (1, 3).

The COPD patients with mild to moderate AHRF, who have an intact airway, show airway protective reflexes, and are alert enough to follow commands, can benefit from NIPPV (4). The NIPPV can reduce the length of Intensive Care Unit or hospital stay, mortality, and need for intubation (1, 3, 5).

The B-type natriuretic peptide (BNP) and N-terminal pro BNP (NT-proBNP) have been introduced as important biomarkers with an established role in the prognosis of congestive heart failure and assessment of acute coronary syndrome risk. The benefits of these natriuretic peptides in differentiating various causes of acute dyspnea in emergency settings have also been demonstrated (6, 7). Furthermore, raised levels of BNP and NT-proBNP have been identified in not only critically ill patients, but also individuals with different non-cardiac conditions (8).

In a recent study, the serum levels of BNP was reported to correlate with the incidence of pulmonary hypertension (i.e., a major cause of death, particularly in individuals with respiratory failure) and mortality rates in the patients with chronic respiratory diseases of different etiologies (9). Long-term oxygen therapy is believed to decrease mortality rates in the patients with chronic hypoxia by lowering pulmonary artery pressure (PAP) (10) and BNP concentrations (11).

The relationship between the reduced hypercapnia and lower PAP following the application of NIPPV in the patients with chronic hypercapnic respiratory failure highlights the role of hypercapnia in the development of pulmonary hypertension (12). Regarding the reported higher levels of natriuretic peptides in the patients with hypercapnic respiratory failure (13), the NIPPV might be able to decrease PAP in these patients more rapidly than the routine medical treatment. Doppler echocardiography is generally ordered to assess PAP and the presence of pulmonary hypertension in these patients.

Therefore, the present study aimed to determine the early effects of NIPPV on arterial blood gases and serum levels of NT-proBNP in the COPD patients with AHRF. This study also sought to investigate the possible acute improvement in PAP following the administration of NIPPV in these patients.

Materials and Methods

This quasi-experimental study was conducted on 20 COPD patients with AHRF, referring to Ghaem Hospital affiliated to Mashhad University of Medical Sciences, Mashhad, Iran, during December 2013-February 2014. The AHRF was defined as hypercapnia ($PaCo_2$>45 mmHg) with a reduction in pH (<7.35). All NIPPV candidates within the age range of 18-75 years were recruited in this study.

The exclusion criteria were: 1) facial or cranial trauma or surgery, 2) recent upper gastrointestinal surgery or bleeding, 3) excessive respiratory secretions, 4) persistent vomiting, 5) altered mental status, 6) hemodynamic instability, 7) uncooperativeness, and 8) fixed obstruction of the upper airway. All subjects received both optimal medical therapy (for any underlying diseases) and NIPPV.

The NIPPV was initiated with a facemask (VPAP III, RESMED, USA). After explaining the technique to the participants, the correct interface and size were selected. Once the patients felt comfortable with the mask, it was secured, and the straps were tightened enough to minimize major leaks. The ventilator was initially set at an inspiratory positive airway pressure support level of 8 cm H_2O and expiratory positive airway pressure of 4 cm H_2O with bilevel positive airway pressure (BiPAP).

The BiPAP therapy continued with incremental pressure supports according to arterial blood gasometry titration for each patient. The optimal inspiratory and expiratory positive airway pressure levels were determined based on the partial pressure of CO_2 ($PaCO_2$) and O_2 (PaO_2) titrations, respectively. After the initiation of NIPPV, the subjects were monitored for comfort, respiratory rate, oxygen saturation, and dyspnea every 30 min for six hours.

In addition, the physical examination and arterial blood gas analysis were performed upon the admission and prior to the administration of NIPPV. The arterial blood gasometry was also conducted 2, 6, and 12 h after the initiation of NIPPV and repeated daily for seven days. In order to estimate the mean PAP (mPAP), Doppler echocardiographic evaluations (Vivid S5, GE Healthcare, UK) were carried out 6 h after admission and repeated on the seventh day of the treatment.

Additionally, blood samples were collected for serum NT-proBNP concentration measurements (Pro-BNP II STAT, Roche, Germany) upon admission and on the second, fourth, and seventh days after the initiation of non-invasive ventilation. The written informed consent was

obtained from all subjects. The study protocol was approved by the Ethics Committee of Mashhad University of Medical Sciences.

Statistical Analysis

The collected data were analyzed using the SPSS version 11.5 (SPSS Inc., Chicago, IL, USA). Continuous data were presented as percentage, mean, and standard deviation. Furthermore, the normality of continuous variables was checked using the one-sample Kolmogorov-Smirnov test. The demographic characteristics of the participants were also summarized through descriptive statistics. P-value less than 0.05 was considered statistically significant.

Results

A total of 20 participants were enrolled (i.e., 10 males and 10 females) in this study. According to the results, the mean age of the subjects was 54.57±15.43 years (age range: 23-78 years). The demographic characteristics of the participants are illustrated in Table 1. The mean $PaCO_2$ levels were 72.33±13.69 and 50.35±6.54 mmHg upon admission and on the seventh day of treatment, respectively. The corresponding values for the mean PaO_2 were 44.28±10.21 and 54.18±10.88 mmHg, respectively. Furthermore, the means pH were 7.27±0.05 and 7.39±0.03 at the mentioned times, respectively (Table 2).

As displayed in Table 2, there were statistically significant differences in mean arterial pH and $PaCO_2$ at different time intervals (P<0.001 and P=0.003, respectively). However, the levels of PaO_2 were not significantly different at different times (P=0.133). In addition, the mPAP levels were 47.5 and 38.0 mmHg upon admission and on the seventh day of treatment, respectively. As shown in Figure 1, there was a significant difference in mPAP values after one week of treatment (P<0.001).

The mean NT-proBNP values at different times of the treatment protocol are presented in Table 3. According to Figure 2, the mean NT-proBNP values measured at various time intervals were significantly different (P<0.001).

Table 1. Demographic characteristics of the patients

Characteristic*	Value
Male/Female	10/10
Age (years)	54.75 ±15.43
History of smoking	20 (100%)
pH (mmHg)	7.27 ± 0.05
$PaCo_2$ (mmHg)	72.33 ± 13.96
PaO_2 (mmHg)	44.28 ± 10.21
PAP (mmHg)	47.5 ± 6.38
NT-ProBNP (pg/ml)	4333.90 ± 6542.20

*$PaCo_2$: Arterial carbon dioxide tension; PaO_2: Arterial oxygen tension; PAP: pulmonary artery pressure; NT-proBNP: N-terminal pro B-type natriuretic peptide

Table 2. Changes in arterial blood gases during treatment with noninvasive positive pressure ventilation (NIPPV)

	Mean pH	Mean $PaCO_2$	Mean PaO_2
Time 0	7.27 ± 0.05	72.33 ± 13.96	44.28 ± 10.21
2 hours	7.33 ± 0.07	64.27 ± 7.87	44.67 ± 10.92
6 hours	7.34 ± 0.07	60.86 ± 12.33	44.96 ± 9.53
12 hours	7.34 ± 0.05	63.95 ± 11.36	44.91 ± 10.18
24 hours	7.38 ± 0.05	58.25 ± 10.59	47.53 ± 8.45
2 days	7.39 ± 0.05	56.94 ± 9.05	50.05 ± 11.22
3 days	7.37 ± 0.08	53.53 ± 9.72	47.72 ± 12.27
4 days	7.40 ± 0.04	55.70 ± 7.15	50.18 ± 8.27
5 days	7.39 ± 0.04	50.81 ± 7.72	51.72 ± 9.48
6 days	7.39 ± 0.04	53.48 ± 8.28	50.73 ± 13.86
7 days	7.39 ± 0.03	50.35 ± 6.54	54.18 ± 10.88
P value	< 0.001	0.003	0.133

Discussion

The present study investigated the variations in arterial blood gasometry parameters, echocardiographic findings, and serum levels of NT-proBNP to clarify the early effects of NIPPV in COPD patients with AHRF. Our findings demonstrated significant reductions in mPAP and NT-proBNP following one week of treatment with NIPPV. Moreover, significant improvements in $PaCO_2$ and pH were observed immediately after the application of NIPPV.

Treatment of respiratory failure seeks to relieve clinical symptoms, enhance oxygenation and ventilation, as well as ultimately improve lifestyle and survival rates among the patients. Therefore, growing attention has been paid to the use of NIPPV in the treatment of both acute and chronic hypercapnic respiratory failure. A successful treatment of AHRF with NIPPV using continuous PAP was reported in 1976 (14). In 1981, continuous PAP was reported to be capable of reversing obstructive sleep apnea (15).

The benefits of NIPPV in the treatment of acute respiratory failure, especially COPD, was later confirmed by numerous researchers (16, 17). Due to the development of novel mask interfaces, interest in minimizing the complications caused by intubation and invasive mechanical ventilation methods, as well as the tendency to curtail the length and costs of hospitalization, NIPPV has been more commonly applied during the past 15 years. The NIPPV owes its popularity to its ease of use, noninvasiveness, and greater comfort.

As discussed earlier, NIPPV can successfully treat the COPD patients with hypercapnic respiratory failure. Pandey et al. introduced the mentioned condition as one of the most common indications for the application of NIPPV. They also reported the effectiveness of this technique in the patients with COPD (18). In a randomized trial, Plant et al. recruited 236 patients with acute exacerbation of COPD. They provided the subjects with standard medical therapy either alone or in combination with NIPPV. They found that the application of NIPPV could accelerate the

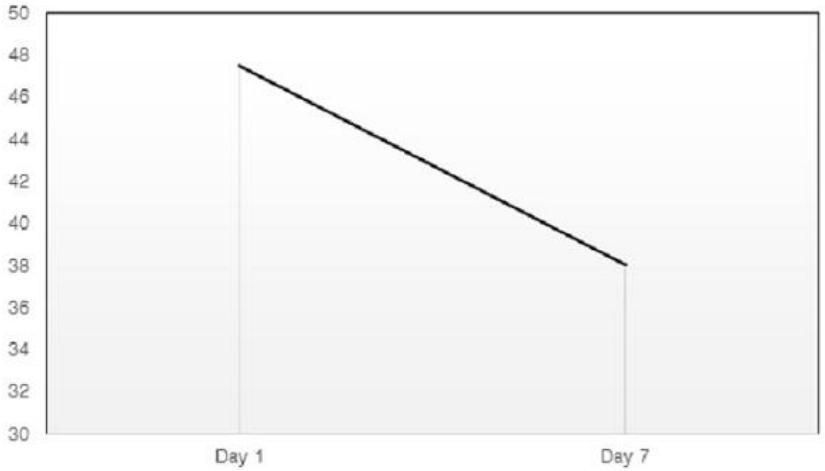

Figure 1. Changes in the mean pulmonary artery pressure at different times during the treatment with noninvasive positive pressure ventilation

Table 3. Changes in serum levels of N-terminal pro B-type natriuretic peptide (NT-proBNP) at different times

	Day 1	Day 2	Day 3	Day 7
Mean NT-proBNP	4333.90 ± 6542.20	2127.00 ± 3364.00	1304.90 ± 2357.00	1047.25 ± 200.6.00

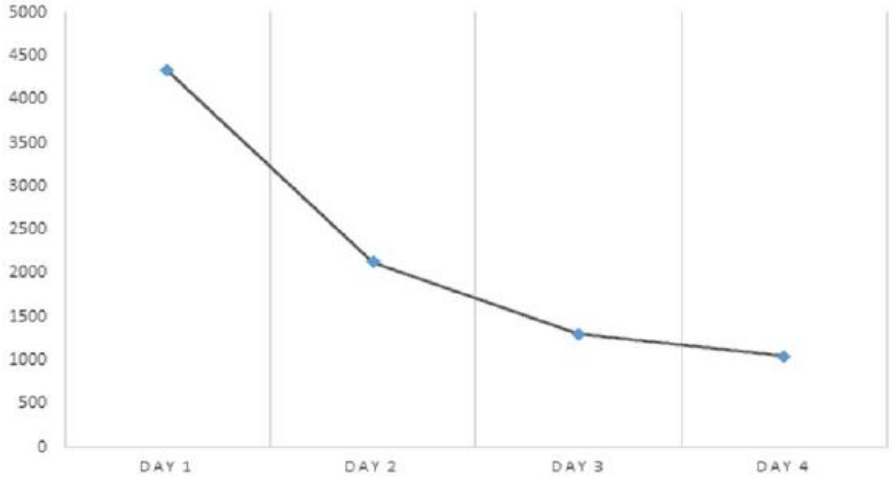

Figure 2. Changes in the serum levels of N-terminal pro B-type natriuretic peptide at different times

improvements in arterial pH, respiratory rate, and breathlessness (18).

Lower need for future mechanical ventilation and decreased mortality rates were also reported following the application of NIPPV in the patients with acute respiratory failure, particularly COPD (19). We observed significant improvements in pH and $PaCO_2$ over time. The PaO_2 levels were also enhanced; however, the difference was not significant. Likewise, Brochard et al. reported significant improvements in pH and $PaCO_2$ one hour after NIPPV initiation (20). Additionally, Plant et al. noticed similar improvements in the mentioned parameters after four hours. They reported that NIPPV accelerated the recovery process (18).

Brain natriuretic peptides are known as reliable biomarkers of left ventricular overload or heart failure. Comparisons between the cases of acute dyspnea and acute heart failure have revealed lower, sometimes even normal, BNP levels in the patients with pulmonary dyspnea (3, 18). Higher BNP levels can be expected in severe pulmonary diseases. The NT-proBNP has been introduced as an important prognostic indicator of pulmonary hypertension outcome (13).

In the present study, we found highly elevated NT-proBNP concentrations in the COPD patients with AHRF. Such a finding can facilitate the differential diagnosis of dyspnea in emergency departments. The NT-proBNP levels of > 900 pg/mL have been proposed as a cut-off point in the diagnosis of acute heart failure in the individuals with 50-75 years of age. Furthermore, a cut-off point of 300 pg/mL could successfully exclude acute heart failure with a negative

predictive value of 98% in all age groups (3).

The studies conducted in emergency settings do not generally include details about the pulmonary function or blood gases and the severity of pulmonary diseases. Regarding this, these studies might have underestimated the cases of severe respiratory diseases, compared to the present study. In two studies investigating the levels of natriuretic peptides in individuals with hypercapnic respiratory failure, higher levels of BNP and atrial natriuretic peptide were reported (21, 22). Therefore, these hormones can be used as appropriate biomarkers of right ventricular overload. Overall, NT-proBNP levels in severe hypercapnic respiratory failure might reach values observed in acute decompensated heart failure. The mentioned condition can serve as a differential diagnosis in the individuals with dyspnea and elevated NT-proBNP levels.

According to our findings, the application of NIPPV could significantly decrease NT-proBNP levels in the COPD patients with hypercapnic respiratory failure (P<0.001). Likewise, Budweiser et al. reported higher NT-proBNP and ProBNP levels in the patients with chronic hypercapnic failure than those in the healthy controls. They also reported that the employment of NIPPV within the treatment procedure caused significant reductions in NT-proBNP and improvements in pulmonary function and arterial blood gases.

In the mentioned study, the subjects had higher NT-proBNP concentrations, even when there was no evidence of cardiac failure (13). While our participants presented with high BNP levels upon admission (i.e., higher than the threshold for acute heart failure), significant reductions were observed in their BNP concentrations following the application of NIPPV.

In the current study, one week of NIPPV application could significantly improve mPAP (P<0.001). Such a beneficial acute effect of NIPPV on mPAP in the patients with respiratory failure can be attributed to the effects of this treatment modality on cardiac output. In the present study, the mPAP values on the first and seventh days of treatment were 47.5±6.38 and 38.0±7.14 mmHg, respectively. Similarly, Dursungulu et al. reported NIPPV to significantly reduce mPAP and systolic PAP in the subjects (43.8±16.9 and 66.7±23.3 mmHg vs. 26.6±8.4 and 41.8±14.6 mmHg, respctively; P<0.0001 for both). This treatment modality could also significantly improve all parameters of arterial blood gases (23).

Nevertheless, further studies with larger sample size and longer follow-up is required to confirm the effects of NIPPV on ventilatory parameters and serum levels of NT-pro BNP in hypercapnic respiratory failure. Future studies are also recommended to enhance the generalizability of their findings by recruiting larger sample size with other acute hypercapnic respiratory failure conditions, such as kyphoscoliosis and sleep apnea.

Conclusion

Our findings demonstrated the early effectiveness of NIPPV in treating the respiratory failure caused by COPD. The NIPPV can not only correct the ventilatory disturbances rapidly, but also enhance the right ventricle function assessed by PAP and NT-pro BNP.

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Conflict of Interest

The authors declare no conflict of interest.

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