

Noninvasive Positive-Pressure Ventilation: A Cross Sectional Descriptive Study of Our First Experience in Iran

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Abstract

Background: Noninvasive positive-pressure ventilation (NIPPV) has been safely used in selected patient populations. The purpose of this study was to determine the safety and efficacy of NIPPV outside the intensive care unit (ICU) in a tertiary hospital. This descriptive, cross sectional study was performed at Masih Daneshvari Hospital, Tehran, Iran during 2011 - 2015.

Methods: Between March 2011 and June 2015, patients requiring NIPPV were enrolled in the study. The study population included all eligible patients. Census sampling was applied in this study. The patients' medical history (including comorbidities), age, sex, and hospital ward in which NIPPV was delivered were assessed retrospectively. Moreover, venous pH, partial pressure of carbon dioxide (PCO₂), and bicarbonate (HCO₃⁻) were analyzed before and after the intervention (NIPPV application).

Results: A total of 946 patients, including 598 (63.2%) men and 348 (36.8%) women, received NIPPV for inpatient hospital care. The mean age of the patients was 61.92 ± 15.5 years (range, 3 - 102 years). Indications for NIPPV included exacerbation of chronic obstructive pulmonary disease (COPD; 55.4%), obstructive sleep apnea (OSA; 6%), bronchiectasis (7.8%), concurrence of COPD and OSA (4.8%), neuromuscular disorders (1.7%), congestive heart failure (4%), postthoracotomy pain (0.6%), thoracic malignancy (2.1%), pulmonary thromboembolism (1.1%), pneumonia (7.3%), asthma (1.5%), interstitial lung disease (2.5%), tuberculosis (4%), and cystic fibrosis (1.3%). We found significant improvements in venous pH and PCO₂ with no significant changes in HCO₃⁻ (P > 0.05).

Conclusions: NIPPV could be safely used under the supervision of trained pulmonologists in non-ICU settings. This method was effective in treating acute abnormalities in venous blood gas, including pH and PCO₂.

Keywords: Noninvasive Positive-Pressure Ventilation, Safety, Efficacy, COPD, OSA, CHF, Venous Blood Gas

1. Background

Respiratory failure as a life-threatening condition is classified into 2 main categories: hypoxemic respiratory failure and hypercapnic respiratory failure (1). Regardless of the underlying etiology, patients with respiratory failure require admission to the intensive care unit (ICU) and may require invasive mechanical ventilation (IMV) (2). Noninvasive positive-pressure ventilation (NIPPV) is an increasingly accepted approach to control selected cases of acute respiratory failure (3).

In order to determine the efficiency of NIPPV in different subsets of patients, many studies and meta-analyses have been carried out (4). Integration of NIPPV in standard care results in a notable reduction in intubation rate, length of hospital stay, complications, and even mortality (5). Only a restricted number of studies consider NIPPV as an alternative to intubation in patients with acute respiratory failure (6). Nonetheless, NIPPV application is associated with lower readmission rates and fewer complications, without any major effects on mortality (5).

NIPPV was first used in 1870 by Chaussier, who used a bag with a facemask to resuscitate neonates (7). In 1936,

Poulton and Oxon designed the pulmonary plus pressure machine for patients with acute exacerbation of heart failure and pulmonary edema (8). In 1940's, Motley et al. used intermittent positive-pressure ventilation devices in high-altitude aviation to treat acute respiratory failure due to pneumonia, pulmonary edema, and acute or severe asthma exacerbation (9, 10). Nonetheless, in the subsequent decades, in spite of successful application of NIPPV in the treatment of acute respiratory failure, IMV was preferred due to technical advances in mechanical ventilators (11).

Continuous positive airway pressure (CPAP) was developed in the 1980's to treat patients with obstructive sleep apnea (OSA) or respiratory failure due to neuromuscular diseases (12, 13). Bilevel positive airway pressure (BiPAP) devices, which could provide different levels of positive pressure during inspiration and expiration, soon followed CPAP; these devices have been utilized to treat patients with OSA and neuromuscular diseases ever since (14-16).

NIPPV has certain advantages over IMV, especially lack of need for general sedation (17, 18). NIPPV is also associated with a lower rate of complications, such as ventilator-

associated pneumonia, sinusitis, and stress ulcers (18-20), and the costs are lower than IMV (21-23). Overall, the costs of IMV include use of trained staff (nurses and respiratory therapists), ICU admission, and management of the aforementioned complications (24, 25). Unlike IMV, NIPPV does not require ICU admission, and patients can be managed in pulmonary wards, high-dependency units, postanesthesia care units, emergency rooms, and even at home. Moreover, NIPPV can prevent further patient deterioration and reduce endotracheal intubation (2).

While NIPPV has been shown to reduce intubation and mortality in patients with acute chronic obstructive pulmonary disease (COPD) and congestive heart failure (CHF) exacerbation, inappropriate use of NIPPV can delay intubation and lead to increased mortality (26). Therefore, it is imperative to choose patients appropriately in order to optimize the results. Currently, there are 4 approved indications for NIPPV: COPD exacerbation, compromised immune system with respiratory failure, cardiogenic pulmonary edema, and postintubation weaning in COPD exacerbation (23, 26-29).

NIPPV is a relatively new approach in Iran, and a great number of specialists are unfamiliar with this technique and require further training. Therefore, use of NIPPV is infrequent in most Iranian hospitals. In 2011, we established a specialized ward with trained staff at Masih Daneshvari Hospital to deliver NIPPV and pulmonary rehabilitation. Accordingly, the aim of this study was to investigate the safety and efficacy of NIPPV outside the ICU in a referral hospital for respiratory diseases. To the best of our knowledge, this is the first survey of the long-term use of NIPPV in Iran.

2. Materials and Methods

2.1. Patients

This retrospective, cross sectional study was performed at the National Research Institute of Tuberculosis and Lung Diseases (NRITLD) of Masih Daneshvari Hospital, which is a tertiary referral center for respiratory and thoracic diseases. This specialized hospital for respiratory diseases is a governmental referral center with 17 units and 446 beds. All the patients were admitted with respiratory failure according to the American Thoracic Society (ATS) / European Respiratory Society (ERS) criteria.

The inclusion criteria were use of accessory muscles, blood pH < 7.35, and paradoxical breathing. All patients in a stable clinical condition were included in our study. On the other hand, intubated patients were excluded from the study. The other exclusion criteria were patient death and reluctance to continue NIPPV. Considering the exclusion

criteria, 15% of the patients (n, 142) were excluded from the study.

The present study was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences (code, Sbm1.REC.1393.65; date, July 2, 2014). Written informed consents were obtained from all the participants.

2.2. Study Design

2.2.1. NIPPV

NIPPV was initiated with an inspiratory positive airway pressure (IPAP) of 10 cm H₂O and an expiratory positive pressure (EPAP) of 4 cm H₂O. Necessary changes were made based on the clinical criteria and venous blood gas (VBG), as required. Supplementary oxygen (3-15 lit/min) was delivered to achieve peripheral oxygen saturation above 90%, while the mask was fixed on the patient's face to minimize any air leakage. Cardiac monitoring including electrocardiography (ECG), blood pressure measurements, and continuous pulse oximetry were performed while the patients received NIPPV; the IPAP and EPAP values were recorded.

The patients' demographic and laboratory data, including age, sex, comorbidities (diabetes, cardiac diseases, and renal diseases), discharge plan, VBG, spirometric indices, ECG findings (pulmonary arterial pressure and ejection fraction [EF]), and smoking history (cigarette smoking, opium use, and exposure to smoke from traditional ovens), were recorded. VBG values were also documented before discharge or after initiation of NIPPV. The data were analyzed in SPSS version 13, using descriptive and analytical tests, including paired t test, independent t-test, and Chi square test.

2.3. Sample Size

This descriptive, cross sectional study was performed at Masih Daneshvari Hospital, Tehran, Iran during 2011-2015. The study population included all eligible patients. Census sampling was applied in this study. No sample size formula was applicable, as all patients, who were eligible to receive NIPPV at Masih Daneshvari Hospital between March 2011 and June 2015, were enrolled in the study.

2.4. Statistical Analysis

Continuous variables are presented as mean values. The treatment effects (and P-values) were assessed using a linear mixed effect model. A full dataset intention-to-treat analysis was performed on the available information of patients before and after the initiation of NIPPV. P-value < 0.05 was considered statistically significant. The data were analyzed in SPSS version 13, using descriptive and analytical tests, including paired t test, independent t test, and Chi square test.

3. Results

During 2011-2015, 946 patients, including 598 (63.2%) men and 348 (36.8%) women, received NIPPV in our inpatient care center. The mean age of the participants was 61.92 ± 15.5 years (range, 3 - 102 years). Overall, 502 patients were active cigarette smokers (53%), 38 (4%) were passive smokers, 304 (32.2%) smoked opium, and 116 (12.3%) patients, who were all women, were exposed to smoke from traditional ovens. Based on the findings, 374 (39.5%) patients had ischemic heart disease or heart failure, 159 (16.8%) had diabetes mellitus, 383 (40.4%) had hypertension, and 26 (2.7%) had renal diseases as the primary reason for admission (or comorbidity). The demographic data of the patients are presented in [Table 1](#).

Table 1. Demographic Variables and Confounding Factors in Patients Included in the Study

Variables	Values
Subjects (n)	946
Gender	
Male	598
Female	348
Age, year	61.92 ± 15.5^a
Smoking, n^b	
Active cigarette smoker	502 (53)
Passive smoker	38 (4)
Opium smoker	304 (32.2)
Exposure to smoke from traditional ovens	116 (12.3)
Comorbidity, n^b	
Heart failure	374 (39.5)
Diabetes mellitus	159 (16.8)
Hypertension	383 (40.4)
Renal disease	26 (2.7)

^aData are presented as mean \pm SD

^bData are presented as No(%)

The patients' primary diagnoses included COPD (55.4%), OSA (6%), bronchiectasis (7.8%), concurrence of COPD and OSA (4.8%), neuromuscular disorders (1.7%), CHF (4%), postthoracotomy pain (0.6%), thoracic malignancy (2.1%), pulmonary thromboembolism (1.1%), pneumonia (7.3%), asthma (1.5%), interstitial lung disease (2.5%), tuberculosis (4%), and cystic fibrosis (1.3%). The data are presented in [Table 2](#) and [Figure 1](#) with respect to the ward where the patients were admitted.

Spirometry was performed to evaluate the patients' baseline pulmonary function. However, spirometric data

were not available in 446 (47.2%) patients. Among patients with spirometric data in their medical records (n, 500), the average forced expiratory volume in 1 second (FEV1) predicted value was 32.87% (9 - 83%; CI, 61.63 - 67.19), FEV1/forced vital capacity (FVC) was 64.41% (11 - 100%; SD, 18.47), and the mean forced expiratory flow at 25 -75% of FVC (FEF25-75%) was 52% (6-130%; SD, 22.69). There was a significant relationship between smoking and FEV1% ($P = 0.00$). Moreover, the difference in FEV1% between smokers and nonsmokers, as well as active and passive smokers, was significant. In contrast, the difference in FEV1% between nonsmokers and passive smokers was not significant ($P = 0.672$) ([Figure 2](#)).

All the patients underwent ECG analyses in this study. The average left ventricular EF was 52% (20 - 80%; SD, 9.51), and the mean pulmonary artery pressure (PAP) was 53.39 mmHg (10 - 115 mmHg; SD, 17.14). According to the ECG data, 475 (50.3%) patients had PAP above 25 at rest, while 406 (43%) had PAP above 40 at rest, which signifies the diagnosis of pulmonary hypertension.

The mean venous pH before and after NIPPV was 7.31 ± 0.2 and 7.35 ± 0.12 , respectively ($P = 0.00$); the 95% CI for pH ranged from -0.05 to -0.02. The differences in change indicate the NIPPV effects in change (95% CI), with adjustments for the baseline values. The average venous PCO₂ before and after NIPPV initiation was 71.19 ± 37.72 and 62.74 ± 14.95 , respectively ($P = 0.00$); the 95% CI for PCO₂ was 6.11-11.30. Moreover, the average HCO₃⁻ before and after NIPPV initiation was 35.08 ± 8.88 and 34.66 ± 8.9 , respectively ($P = 0.184$); the 95% CI for HCO₃⁻ was -0.28 to 1.45.

The average IPAP was about 13 mmHg (range, 6 - 22 mmHg; SD, 2.99), and the average EPAP was about 5 mmHg (range, 4 - 14 mmHg; SD, 1.44). Overall, 43 (4.5% mortality) deaths were reported in this study. Respiratory failure was the primary reason (n, 28), while the rest of the patients died secondary to massive myocardial infarction, renal failure, and severe sepsis due to aspergillosis. Home-based NIPPV was recommended to 487 (54%) patients, who were discharged alive.

5. Discussion

The purpose of this study was to provide a descriptive report of NIPPV application in a tertiary referral center for respiratory diseases in Iran. During 4 years, 946 patients received NIPPV in our inpatient care center. The number of men was higher than that of women in this study, and the age range was 3-102 years. The wide age range shows that NIPPV can be used in different patients with no age limit. We could not find any contraindications to or differences in NIPPV application at any particular age. In this regard, Schortgen et al. compared the efficacy of NIPPV between

Table 2. Absolute and Relative Description of Subjects and Wards for NIPPV Administration

	Cases ^a	General Ward	Emergency Room	CCU	ICU
COPD	524 (55.4)	337	77	73	37
Sleep apnea	57 (6)	34	6	15	2
Sleep apnea and COPD	45 (4.8)	25	6	11	3
Bronchiectasis	74 (7.8)	32	15	21	6
NMD	16 (1.7)	-	1	3	3
CHF	38 (4)	15	8	12	3
Postthoracotomy pain	6 (0.6)	3	1	1	1
Tumor	20 (2.1)	11	1	5	3
PTE	10 (1.1)	4	-	-	3
Pneumonia	69 (7.3)	45	13	6	5
Asthma	14 (1.5)	6	1	6	1
ILD	23 (2.5)	6	6	8	3
TB	38 (4)	24	8	3	3
CF	12 (1.3)	9	-	1	2

Abbreviations: COPD, chronic obstructive pulmonary disease; NMD, neuromuscular diseases; CHF, congestive heart failure; PTE, pulmonary thromboembolism; ILD, interstitial lung disease; TB, tuberculosis; CF, cystic fibrosis

^a Data are presented as No (%)

very old (> 85 years) and young patients, who were admitted to the ICU, and showed a comparable hospital survival (30).

The present results showed that FEV1% is correlated with active or passive cigarette smoking. Furthermore, more than half of our patients had PAP above 25 mmHg. Comparison of admission VBGs with those after NIPPV initiation indicated a significant improvement in pH and PCO₂, while the change in HCO₃⁻ before and after the intervention was not significant. This shows that the change in pH was mainly due to the decline in PCO₂ and that HCO₃⁻ changes required more time due to regulation by the kidney.

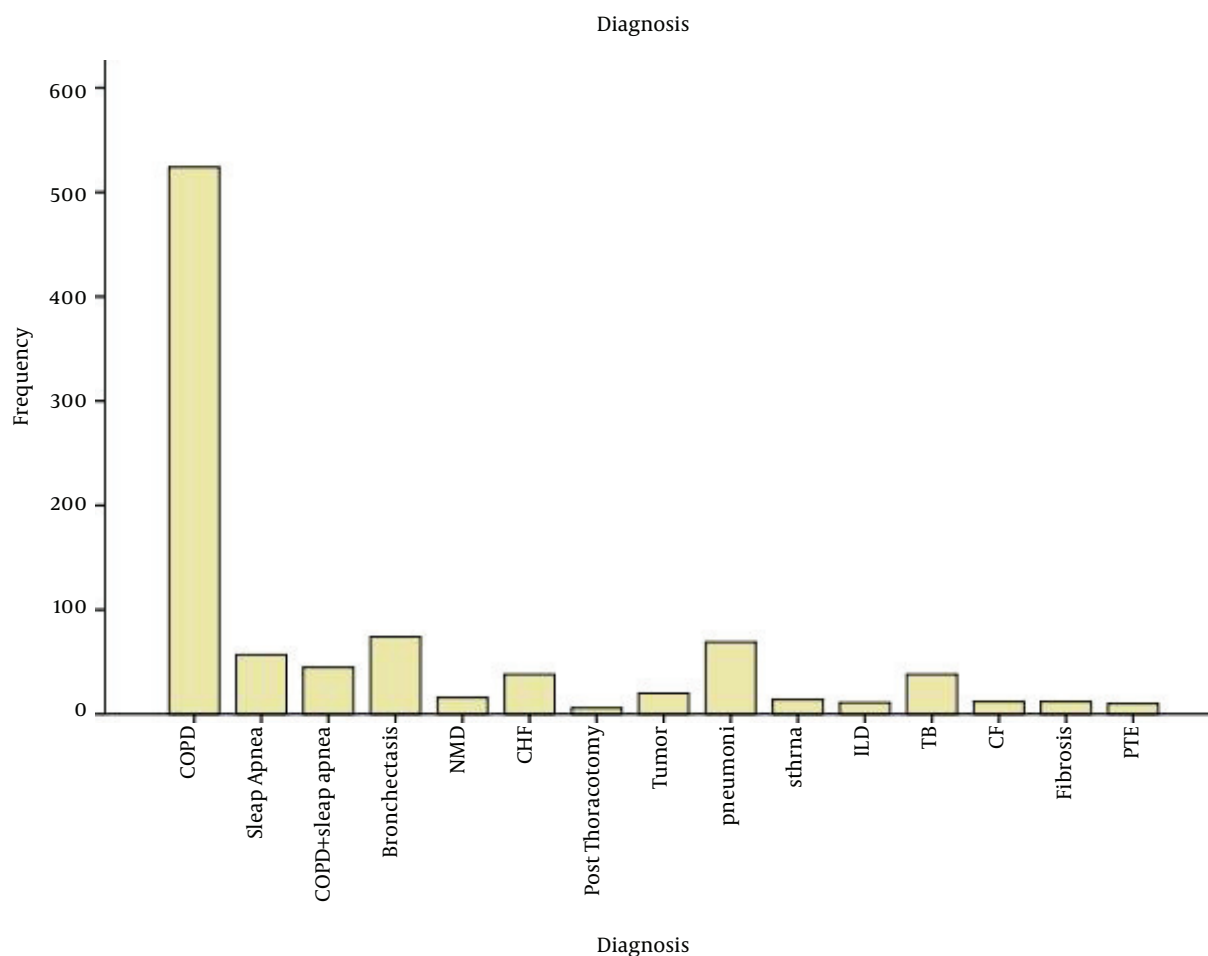
In the present study, most of the patients received NIPPV in the general respiratory ward (66%). In a study by Crimi et al., NIPPV was safely provided in the ICU, respiratory ICU, rehabilitation ward, and general respiratory ward, respectively (2). Moreover, the present results showed that NIPPV could improve gas exchange. Similarly, Diaz et al. showed that NIPPV improves PCO₂ and arterial pH even after 1 hour of utilization (31). Since the variables in our study were mostly evaluated in a large number of patients, no major interindividual differences occurred, and the data were normally distributed.

COPD and OSA were the most common indications for NIPPV in our patient population. CHF, bronchiectasis, and tumors were among other frequent indications for NIPPV

in our patients. This finding is in contrast to a study by Crimi et al., in which acute hypercapnic respiratory failure and cardiogenic pulmonary edema were the most common indications for NIPPV (2).

Multiple studies have assessed NIPPV in patients with acute COPD, CHF exacerbation, and other causes of acute and chronic respiratory failure (12, 32-38). Browning et al. found that NIPPV was routinely used in emergency rooms, especially for patients with acute cardiogenic pulmonary edema and COPD exacerbation (39). Similarly, Burnes et al. conducted a literature review, which concluded that acute COPD and CHF exacerbation were the most common indications for NIPPV. The difference in physician information about NIPPV was the most important reason for the difference in NIPPV application for COPD; the influence of NIPPV on CHF patients was the main cause of different applications in CHF (40).

In another study in India, COPD exacerbation was the most common reason for NIPPV utilization (41). Chiner et al. reported that the most common indications for NIPPV were COPD exacerbation, obesity hypoventilation syndrome, neuromuscular diseases, and kyphoscoliosis, respectively. These diseases were the most common causes of NIPPV utilization at home, as well (42). As the results indicated, NIPPV could be used in various settings, such as ICU, coronary care unit, pulmonary ward, emergency room, and even at home. In addition, NIPPV is more afford-

Figure 1. The Frequency of Patient Diagnoses

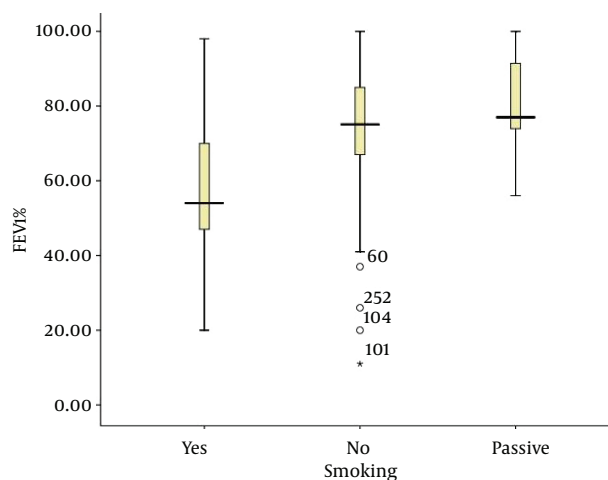
The primary diseases in patients were diagnosed as COPD (F, 524), OSA (F, 57), bronchiectasis (F, 74), concurrence of COPD and OSA (F, 45), neuromuscular disorders (F, 16), congestive heart failure (F, 38), postthoracotomy pain (F, 6), thoracic malignancy (F, 20), PTE (F, 10), pneumonia (F, 69), asthma (F, 14), ILD (F, 23), TB (F, 38), and CF (F, 12) (COPD, chronic obstructive pulmonary disease; NMD, neuromuscular diseases; CHF, congestive heart failure; PTE, pulmonary thromboembolism; ILD, interstitial lung disease; TB, tuberculosis; CF, cystic fibrosis).

able than IMV, which can be only used in the ICU.

A study performed in 71 hospitals in the USA showed that NIPPV could be safely used in any location, although ICU was the most common setting for the initiation of NIPPV (55%), followed by emergency departments (26%) and general medical wards (18%) (12). Additionally, in a study by Chiner et al., NIPPV was most frequently used in the emergency department, followed by the general medicine ward, hospital-based home care, and other wards (42). Moreover, Elliot et al. reported that NIPPV could be safely used in the emergency department when trained staff are available (43). To the best of our knowledge, the current study is the first report of NIPPV application in a general respiratory ward, as a more common location in

comparison with cardiac care unit and emergency room.

In the present study, NIPPV was used most frequently in the general medicine ward. The advantages of NIPPV application in the ward include lower nurse staffing and low costs. However, considering the retrospective design of this survey, there were some missing patient data, which made the data analysis difficult. Moreover, evaluation of NIPPV complications was not possible due to lack of patient follow-up, and complications could not be compared between NIPPV and IMV. Further studies are required to compare the efficacy and complications of NIPPV and IMV. Long-term follow-up can determine the advantages and disadvantages of NIPPV. In addition, indications for NIPPV or IMV should be specified in the patients.

Figure 2. The Relationship Between FEV1 and Smoking

There was a significant relationship between smoking and FEV1% ($P = 0.00$). Moreover, the differences in FEV1% were significant between smokers and nonsmokers, as well as active and passive smokers. In contrast, the difference in FEV1% between nonsmokers and passive smokers was not significant ($P = 0.672$) (FEV1, forced expiratory volume in 1 second).

5.1. Conclusion

NIPPV was more cost-effective than IMV, as it was routinely used outside the ICU or coronary care unit. We also showed that NIPPV could be safely utilized outside the ICU if delivered by trained nurses who are guided by pulmonologists. We recommend educating nurses, respiratory therapists, and other house staff in order to use NIPPV more frequently and reduce the healthcare costs. Moreover, encouraging pulmonologists and other house staff to use NIPPV instead of IMV can reduce the costs and complications and increase survival in selected patient populations.

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Footnote

Conflicts of Interest: All authors declare that they do not have any financial interests or conflicts, related to the materials of this study.

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