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Noninvasive Versus Invasive Mechanical Ventilation to Treat Patients with Hypercapnic Acute Respiratory Failure Secondary to COPD

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Abstract

Objective: Noninvasive ventilation (NIV) had been successfully used in patients with severe hypercapnic acute respiratory failure (HARF). Being lack of a large number of randomized control trials to support NIV in chronic obstructive pulmonary disease (COPD) patients with severe HARF, the effect of NIV for patients with life-threatening HARF should be further confirmed. In order to confirm the effect of NIV on selected patients with HARF due to COPD, we conducted a comparative prospective observational study of NIV *vs.* IMV (invasive mechanical ventilation) + NIV in COPD patients with HARF.

Methods: A total of 420 patients with acute respiratory failure secondary to COPD were prospective screened; 52 cases with PaCO2 ≥ 90 mmHg or PaCO2 <90 mmHg but ≥ 80 mmHg with pH value ≤ 7.20 were enrolled. Twenty-one cases received sequential IMV to NIV treatment and were designated as the IMV+NIV group; 31 cases received NIV and were designated as the NIV group. The primary outcome was hospital mortality and mortality within 30 days of discharge. The secondary outcomes included risk factors for mortality and re-hospitalization, length of hospital stay, time of mechanical ventilation and re-admission rate within 30 days of discharge.

Results: Mortality in-hospital and within 30 days of discharge had no differences between NIV group and IMV +NIV group (p=0.699). Binary logistic regression found no risk factor for mortality and re-hospitalization in two groups. The length of hospital stay (p=0.000) and time of mechanical ventilation (p=0.000) were significantly longer in the IMV+NIV group compared with the NIV group. Conclusion: Compared to IMV+NIV, NIV has similar efficacy for select patients with severe HARF secondary to acute exacerbation of COPD, and NIV can be safely used in these patients.

Keywords: Noninvasive ventilation; Chronic obstructive pulmonary disease; Acute respiratory failure; Hypercapnic; Mortality

Introduction

Noninvasive ventilation (NIV) is being used more and more in the treatment of acute respiratory failure secondary to chronic obstructive pulmonary disease (COPD) [1,2]. NIV had been successfully used in patients with severe hypercapnic acute respiratory failure (HARF) [3,4] and even in coma patients [5-7].

Being lack of a large number of randomized control trials to support NIV in COPD patients with severe HARF, invasive mechanical ventilation (IMV) is still recommended for patients with life-threatening HARF.

In our clinical work, some patients with severe HARF secondary to COPD who have declined endotracheal intubation for belief and other reasons achieved successful outcomes using NIV therapy, this was especially true for patients without facial deformity. In order to further clarify the efficacy of NIV in patients with COPD and severe HARF, we conducted the following prospective observational study to assess the efficacy of NIV versus IMV+NIV in selected COPD patients with severe HARF.

Materials and Methods

Study participants

From January 1, 2014 to June 30, 2016, all patients with HARF secondary to COPD admitted to the respiratory critical care unit (RICU) of Beijing Luhe Hospital were prospectively screened. A diagnosis of COPD according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2014 criteria was required [8]. Patients with a Glasgow Coma Score (GCS) ≥ 8, and who had PaCO2 ≥ 90 mmHg or had PaCO2 less than 90 mmHg but above 80 mmHg with a pH value ≤ 7.20 were included. Exclusion criteria were GCS8, facial deformity and trauma, hemodynamic instability, upper gastrointestinal bleeding and refusal to participate. Written informed consent was obtained from each study participant or from immediate family members. The study protocol was approved by the Ethics Committee of Luhe Hospital (Institutional Review Board approval number LH 2013-12-10), and all patients provided written informed consent.

Program implementation

We suggested that all patients who met with the inclusion criteria for this study receive IMV therapy. Patients who agreed to the sequential IMV to NIV treatment were designated as the IMV plus NIV group (IMV+NIV group). In the IMV+NIV group, the choice of

mode and parameters of IMV was determined by attending physicians according to the patient's clinical situation, but pressure support ventilation (PSV) plus positive end expiratory pressure (PEEP) was required before tracheal extubation. All patients in the IMV+NIV group were switched to NIV treatment after extubation. Patients who declined endotracheal intubation for faith or other reasons but accepted NIV treatment were considered to be in the NIV group.

NIV was implemented with a noninvasive ventilator via nasal facial mask and biphasic positive airway pressure (BiPAP) in the S/T mode. The backup respiratory rate was set at 15 breaths/min and the fraction of inspired oxygen (FiO2) was adjusted to maintaining arterial oxygen saturation between 92% and 95%. The initial inspiratory positive airway pressure (IPAP) was set at 10 cmH2O~12 cmH2O and raised by 2 to 3 cmH2O every 10 to 15 minutes according to clinical efficacy and patient's tolerance, but did not exceed 28 cmH2O. PEEP was set up at 4 cmH2O~6 cmH2O to offset intrinsic PEEP. Patients were encouraged to utilize NIV at least 10 h a day.

Other treatment methods used in the two groups were instituted by the attending physician in accordance with GOLD guidelines. For ethical reasons, patients in our study were not randomly assigned.

Extubation indications in the IMV+NIV group were as follows: Improvement of the cause of acute respiratory failure that led to the use of ventilation support, oxygenation improvement with arterial partial pressure of oxygen (PaO2) ≥ 60 mmHg, arterial partial pressure of carbon dioxide (PaCO2)70 cmH2O, fraction of inspired oxygen (FiO2) ≤ 0.4, respiratory rate ≤ 25 times/minute, PSV ≤ 12 cmH2O ~ 14 cmH2O, and PEEP ≤ 5 cmH2O.

Outcome measurements and data collection

The Glasgow Coma Score was obtained upon hospital admission. The baseline characteristics of the patients were collected on the day of hospital admission. The acute physiology and chronic health evaluation II (APACHE II) score was evaluated on the day of admission. Blood was collected for routine laboratory examination.

Arterial blood gas analysis monitoring: Arterial blood gas analysis was examined at 2 hours and 6 hours of mechanical ventilation, on the 2nd day, 3rd day, and 5th day after hospitalization, on the day of discharge.

The primary outcome was mortality in-hospital and within 30 days of discharge. The secondary outcomes included to find out any risk factors for mortality and re-hospitalization, the length of hospital stay, the time of mechanical ventilation, and the re-admission rate within 30 days of discharge.

Statistical methods

SPSS version 17.0 for Windows software (SPSS Inc., Chicago, IL, USA) was used for data management and statistical analysis. Measurement data were presented as the mean ± standard deviation, while categorical data were expressed as a number or percentage. An independent samples t-test was applied to compare the difference in measurement data between groups. For comparisons of enumeration data, the Pearson Chi-square test or continuous correction Chi-square test was used. All tests were two tailed. We used binary logistic regression analysis to identify risk factors of hospital mortality and mortality within 30 days of discharge, re-admission within 30 days of discharge, respectively. Risk factors included tracheal intubation, gender, current smoking, frequent hospitalizations in the previous year (≥ 2 times), elderly (≥ 75 years), bronchiectasis, coronary heart disease, hypertension, diabetes, chronic congestive heart failure, cerebral infarction history, home noninvasive mechanical ventilation, and antibiotic use within 3 months prior to hospitalization. A p-value of 0.05 was considered significant.

Results

A total of 420 admitted patients with respiratory failure secondary to acute exacerbation of COPD were screened. There were 73 cases with PaCO2 ≥ 90 mmHg or PaCO2<90 mmHg but ≥ 80 mmHg with pH value ≤ 7.20. Among these patients, 52 cases met our inclusion criteria and completed the study. No patients were lost during 30-day follow-up (Figure 1).

The baseline characteristics of the two groups are shown in Table 1. There was no significant difference between the two groups with regard to age, sex, smoking status, frequent hospitalizations secondary to acute exacerbation of COPD in the previous year (≥ 2 times), APACHE II score, GCS, home mechanical ventilation, respiratory rate, heart rate, diastolic blood pressure, and comorbidities including diabetes, congestive heart failure, coronary heart disease, hypertension, congestive heart failure and history of cerebral infarction. Systolic blood pressure in the NIV group was significantly higher than that of the IMV+NIV group.

Characteristics	IMV +NIV group (n=21)	NIV group (n=31)	p value
Age (years)	72.7 ± 12.4	70.9 ± 10.0	0.567
Male (n, %)	14 (66.7)	14 (45.2)	0.127
Smoking (n, %)	14 (71.4)	14.3 (61.3)	0.569
Former	9 (42.9)	14 (45.2)	0.87
Current	5 (23.8)	5 (16.1)	0.49
Frequent admission in the previous year (≥ 2)	6 (28.9)	8 (25.8)	0.825
APACH II score	15.8 ± 4.7	14.3 ± 2.7	0.145

GCS	11.8 ± 1.1	12.3 ± 0.9	0.087
Home mechanical ventilation (n, %)	7 (33.3)	14 (35.5)	0.873
Respiratory rate (breath/min)	23.3 ± 7.7	22.5 ± 7.6	0.688
Heart rate (beats/min)	102.9 ± 18.2	95.1 ± 18.7	0.148
Systolic blood pressure (mmHg)	127.5 ± 26.3	146.7 ± 22.8	0.008
Diastolic blood pressure (mmHg)	77.3 ± 9.1	82.3 ± 18.7	0.259
Comorbidities (n, %)			
Diabetes	6 (28.6)	2 (6.5)	0.075
CHF	8 (38.1)	11 (35.5)	0.848
Coronary heart disease	6 (28.6)	12 (38.7)	0.451
Hypertension	10 (47.6)	22 (71.0)	0.089
History of cerebral infarction	4 (19.0)	5 (16.1)	1

IMV + NIV: Invasive Mechanical Ventilation plus Noninvasive Mechanical Ventilation; NIV: Noninvasive Mechanical Ventilation; APACHE II: Acute Physiology and Chronic Health Evaluation II; GCS: Glasgow Coma Score; CHF: Shronic Congestive Failure. Data were presented as the mean ± standard deviation, or number (%).

Table 1: Baseline Characteristics of 52 Patients Included in the IMV+NIV and NIV Groups.

Arterial blood gas analysis: Arterial blood gas analysis at baseline and on the day of discharge was similar between the two groups. The pH values and PaCO2 improved more quickly in the IMV+NIV group relative to the NIV group. The oxygenation index observed at different times yielded no differences between the two groups (Table 2).

ABG	**IMV + NIV group** (n=21)	**NIV group** (n=31)	**p value**
Baseline before MV			
pH value	7.20 ± 0.10	7.23 ± 0.06	0.109
PaCO2 (mmHg)	98.8 ± 14.7	97.2 ± 10.3	0.661
Oxygenation index	218.5 ± 55.1	238.9 ± 95.4	0.402
2 h after MV			
pH value	7.36 ± 0.10	7.30 ± 0.10	0.077
PaCO2 (mmHg)	63.6 ±12.8	79.1 ± 15.0	0.001
Oxygenation index	270.2 ± 119.4	264.2 ± 104.1	0.856
6 h after MV			
pH value	7.40 ± 0.09	7.32 ± 0.07	0.002
PaCO2 (mmHg)	51.2 ± 12.5	75.8 ± 14.5	0
Oxygenation index	230.8 ± 87.7	230.3 ± 74.2	0.982
On the second day			
pH value	7.44 ± 0.09	7.37 ± 0.09	0.004
PaCO2 (mmHg)	51.1 ± 14.3	70.2 ± 13.2	0
Oxygenation index	275.2 ± 109.4	241.6 ± 82.2	0.221

On the third day			
pH value	7.45 ± 0.13	7.41 ± 0.07	0.217
PaCO2 (mmHg)	53.3 ± 25.6	66.7 ± 14.6	0.04
Oxygenation index	267.6 ± 78.1	286.7.8 ± 97.0	0.493
On the fifth day			
pH value	7.48 ± 0.07	7.40 ± 0.06	0.003
PaCO2 (mmHg)	50.2 ± 15.1	62.8 ± 12.8	0.006
Oxygenation index	257.1 ± 76.2	256.1 ± 115.1	0.974
Day of hospital discharge			
pH value	7.45 ± 0.07	7.41 ± 0.08	0.069
PaCO2 (mmHg)	57.3 ± 21.3	64.0 ± 19.9	0.256
Oxygenation index	289.7 ± 74.2	260.9 ± 92.1	0.241
ABG: Arterial Blood Gas analysis; IMV + NIV: Invasive Mechanical Ventilation plus Noninvasive Mechanical Ventilation; NIV: Noninvasive Mechanical Ventilation; MV: Mechanical Ventilation. Data were presented as the mean ± standard deviation, or number (%).			

Table 2: Comparison of ABG Values between the Groups.

Mortality in-hospital and within 30 days of discharge in NIV group (7/31, 22.6%) was similar to that in IMV + NIV group (3/21, 14.8%), with no significant difference (p=0.699). Re-admission rate within 30 days of discharge was similar between two groups. Compared to the NIV group, the length of hospital stay and time of mechanical ventilation were significantly longer in the IMV+NIV group (Table 3). Binary logistic regression found no risk factor for mortality and re-hospitalization in both groups. Six patients died in the NIV group and two patients died in IMV+NIV group during hospitalization. One patient died during the 30-day follow-up period in each group (Figure 1).

Outcomes	**IMV + NIV group** (n=21)	**NIV group** (n=31)	**P value**
Length of hospital stay (days)	17.1 + 7.7	8.8 + 3.8	0
Time of MV (hours)	183.4 + 117.7	83.6 + 55.5	0
Death in-hospital or within 30 days of follow-up (n, %)	3 (14.8)	7 (22.6)	0.699
Re-admission within 30 days of hospital discharge (n, %)	1 (4.8)	2 (6.5)	1
IMV + NIV: Invasive Mechanical Ventilation plus Noninvasive Mechanical Ventilation; NIV: Noninvasive Mechanical Ventilation; MV: Mechanical Ventilation.			

Table 3: Clinical Outcomes between Groups.

Discussion

NIV is used worldwide to treat acute exacerbation of COPD, while the use of IMV is gradually decreasing [9-12]. In the meantime, tracheal intubation rates and mortality are also decreasing gradually [9,13]. A retrospective cohort study showed that NIV treatment for COPD patients reduced hospital mortality, the length of hospital stay and hospitalization expenses compared with IMV treatment [14]. Early studies of NIV mainly focused on mild to moderate hypercapnic respiratory failure secondary to COPD [1,2]. With oversight by a highly experienced team and close monitoring, NIV has become widely used in patients with severe HARF who had generally been considered as contradictions for NIV.

Most studies of NIV in patients with severe HARF or coma demonstrate that patients achieve successful outcomes. A prospective matched case control study found that NIV treatment for patients with moderate to severe pulmonary encephalopathy secondary to acute exacerbation of COPD decreased the time of mechanical ventilation and the incidence of nosocomial pneumonia, while in-hospital mortality, 1 year mortality rate and tracheotomy rate were similar between NIV and IMV [15]. Another study suggested that NIV has a similar effect in patients with moderate or severe pulmonary encephalopathy, and consciousness was not an absolute contradiction for NIV treatment [5]. In this study, NIV in patients with a GCS <8 achieved a similar effect as compared with IMV, but the time of mechanical ventilation and the length of hospital stay were shorter in

the NIV group. The survival rate was not significantly different between the groups.

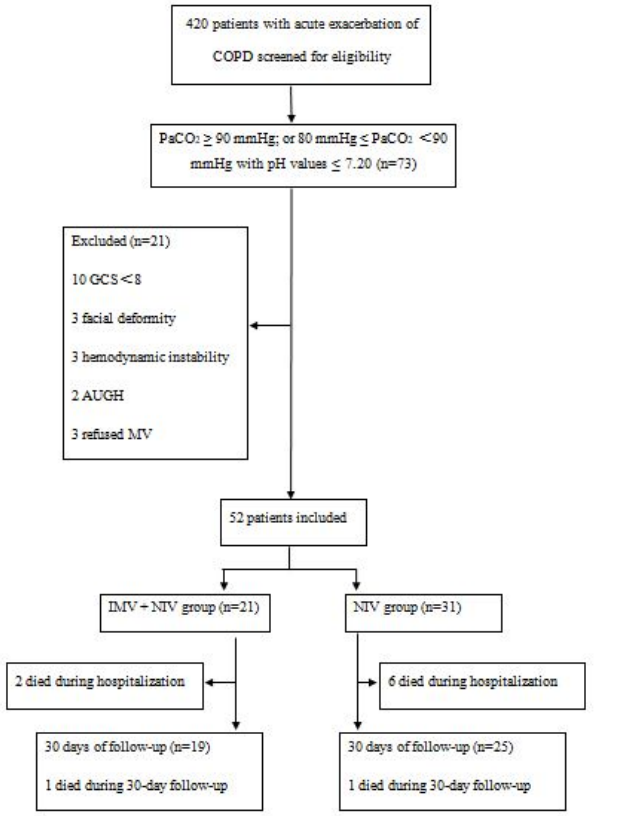

Figure 1: Acute exacerbation of chronic obstructive pulmonary disease (COPD); PaCO2, arterial partial pressure of carbon dioxide; GCS: Glasgow Coma Score; AUGH: Acute Upper Gastrointestinal Tract Hemorrhage; MV: Mechanical Ventilation; IMV: Invasive Mechanical Ventilation; NIV: Non-invasive Mechanical Ventilation.

Although the use of NIV treatment increases gradually, facial deformity, uncontrolled acute upper gastrointestinal tract hemorrhage and hemodynamic instability are generally considered contraindications of NIV. In order to compare the efficacy of IMV versus NIV for severe HARF more objectively, we excluded patients with the above situations in our study. Although some studies showed that NIV had some positive effect in COPD patients for severe HARF with a GCS<8 [6,13]. Considering patients with severe neurological dysfunction lost the airway protection capability, we also excluded these patients with a GCS<8.

In our study, mortality in-hospital and within 30 days of discharge had no differences between NIV group and IMV + NIV group, it indicates that NIV can be safely used in select patients with severe HARF secondary to acute exacerbation of COPD. No risk factor was found for mortality and re-hospitalization in two groups, it may be due to a small number of patients. Compared to the NIV group, the pH value in the IMV + NIV group improved more quickly, and the PaCO2 decreased more rapidly within 5 days in this group as well. This indicates that the arterial blood gas recovered more rapidly to a safe level in the IMV + NIV group. However, there was no significant difference in arterial blood gas results between the two groups on the day of discharge. Furthermore, the total time of mechanical ventilation and the length of hospital stay were significantly shorter in the NIV group. The results suggest that NIV has a positive treatment effect for patients with severe HARF who refuse endotracheal intubation.

Our study has two major limitations. For ethical reasons, patients were not randomly assigned upon enrollment. Secondly, the results we observed in the short-term follow up period need to be further studied and confirmed as long-term outcomes.

Conclusion

In conclusion, compared to IMV + NIV, NIV has similar efficacy for select patients with severe HARF secondary to acute exacerbation of COPD, and NIV can be safely used in these patients.

Conflict of Interest

The authors state that they have no Conflict of Interest (COI).

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