

Original article:

Non invasive ventilation in hypercapnic respiratory failure in patients of COPD requiring mechanical ventilation

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Abstract:

Aims-To study the effects of NIV in hypercapnic respiratory failure in case of COPD PaCO₂>60mm, PH (7.25-7.35).

Methods: We prospectively studied cases of COPD with hypercapnic respiratory failure. All copd patients with PaCO₂>60mmHg and pH 7.25-7.35 were put on BIPAP and the result were assessed. We also studied various predictors of success with NIV like age, initial pH and PaCO₂, previous hospitalization with IMV.

Results: Out of 100 patients included in the study 82 were successfully treated with NIV. Success was higher in the lower age group than higher age. Success rate was lower in patients with previous history of mechanical ventilation, lower in patients with pH <7.30 as compared to pH>7.30. Also success rate was lower in patients with PaCO₂>80mmHg as compared to PaCO₂<60 mmHg.

INTRODUCTION- Chronic obstructive pulmonary disease is a disabling and progressive lung disorder characterized by partially reversible airflow limitation.⁽¹⁾ It is a major public health problem as it is a leading cause of mortality and morbidity worldwide.⁽²⁾ Burden of disease is expected to rise and WHO has predicted that by 2020, COPD will be the 5th most prevalent disease worldwide (currently ranked 12th) and will be among the three leading cause of death.⁽³⁾

Acute exacerbations of COPD (AECOPD) are largely responsible for the increasing mortality and morbidity associated with the disease. The frequency of hypercapnic respiratory failure in AECOPD varies from 16-35% with overall mortality of 35-43%.⁽⁴⁻⁵⁾ Acute exacerbation of COPD is treated with drugs, oxygen therapy and ventilator support. Ventilatory support is given either by Non-invasive or invasive mechanical ventilation (NIV/IMV). For ventilator support, Global initiative for chronic obstructive lung

disease(GOLD)2007 guidelines had recommended that patients with arterial $pH < 7.35$ and/or $PaCO_2 > 45$ mmHg are candidates for non-invasive ventilation whereas those with severe acidosis ($pH < 7.25$ and/or $PaCO_2 > 60$ mmHg) is recommended for invasive ventilation.

However, mechanical ventilation is many a times refused by the patients and it is not available in all hospital setting. Avoiding endotracheal intubation in patient with hypercapnic respiratory failure in COPD is the key for improving outcomes. Outcome from invasive ventilation in patients with COPD is disappointing with reported survival between 20-50%. There are studies showing that non invasive ventilation is a safe and effective tool in hypercapnic respiratory failure at $PaCO_2 > 60$ mmHg also. NIV may negate the need for intubation and complication especially ventilator associated pneumonia (VAP) which is associated with worst outcome.⁽⁸⁾ Advantages of NIV over Invasive Mechanical Ventilation include patient cooperation with physiotherapy, feeding, early mobilization, communication etc.⁽⁹⁾

New GOLD guidelines 2011 have recommended that every patient of COPD should be given a trial of non-invasive ventilation regardless of severity of acidosis. The criteria of invasive mechanical ventilation in patients with arterial $pH < 7.25$ and/or $PaCO_2 > 60$ mmHg has been removed. Mechanical ventilation is now indicated only in cases of NIV failure.

This study was designed to find out the safety of NIV in patient with $PaCO_2 > 60$ mmHg within a pH range of 7.25-7.35.

Materials and Methods:

Study was conducted at department of chest diseases and tuberculosis, SMS medical college, Jaipur on patients admitted at the hospital with diagnosis of acute exacerbation of COPD on the basis of history and the clinical examination and radiology.

On admission, patients were interviewed regarding symptoms, history of chemotherapy for pulmonary tuberculosis, past history of invasive or non-invasive mechanical ventilation, personal and family history of tuberculosis, smoking or other chronic respiratory disease and presence of co-morbidities.

A thorough clinical examination including respiratory system examination was done. Chest Xray was done to look for changes associated with COPD and to rule out other diseases like tuberculosis, bronchiectasis and pleural diseases.

After establishing diagnosis, ABG analysis was done and all patients with $PaCO_2 > 60$ mmHg and pH 7.25-7.35 were considered for study.

Exclusion criteria:

- Patients with respiratory arrest
- Patients with haemodynamic instability
- Altered sensorium
- Uncooperative patients
- Copious secretions
- Patients with diabetes, renal failure

All patients giving consent for research in NIV were included in study. Bi-level positive airway pressure (BIPAP) was applied. Initially inspiratory positive airway pressure (IPAP) and expiratory positive airway pressure (EPAP) was kept at level of 8 cm of H₂O and 4 cm H₂O respectively and gradually increased to final IPAP and EPAP at level of 12 cm of H₂O and 5 cm of H₂O respectively. Two hours after starting BIPAP, ABG was repeated. Each patient was

advised to use BIPAP for 16 hours in a day. BIPAP was temporarily discontinued during eating, drinking, taking medicines and during nebulizations.

Assessment of favourable response was done as under:

Patient with sustained clinical improvement

Reduction in RR <24/MIN

Reduction of HR <100/MIN

Return to normal pH >7.35

PaCO₂<50mmHg

SaO₂>90%

If patient clinical condition improved, patient was continued with NIV at same pressure. ABG was repeated at 6, 24, 48 hours. A PaCO₂ <50mm was considered as a favourable outcome. however if patient condition deteriorates, shows a rise in paco₂, worsening of pH, decreasing level of consciousness, hemodynamic instability, invasive mechanical ventilation was considered.

Statistical analysis: It was a prospective, non controlled study. Sample size was calculated at 80%

power and α error of 0.05 assuming effectiveness of NIV in 70% of patient as obtained in seed article. At absolute allowable error of 10%, minimum sample size required patients considering non-cooperation and attrition. Continuous variables were expressed as mean \pm and categorical variables were recorded as percentage. Relation between two quantitative variables was assessed by using Pearson chi-square test and Fisher exact test. Mean of two variables were compared by using ANOVA test. Statistical analysis was done by using SPSS-20 software. Significance level is taken at p<0.05

OBSERVATIONS AND RESULTS

A total of 100 patients were included in the study with diagnosis of acute exacerbations of COPD. BIPAP was applied in patients having PaCO₂ more than 60mmHg and pH ranging between 7.25-7.35 in initial ABG. Outcome on NIV was assessed by improvement in type 2 respiratory failure. Various factors affecting the outcome of NIV were also assessed.

Result of the study was tabulated as follows:-

Age group(years)	Male	Female	Total
<60	35	6	41
61-80	43	11	54
>80	4	1	5
Total	82	18	100

The above table shows age and sex distribution of the study patients. Out of total 100 patient included, eighty two were males and eighteen were females. The age ranged between 45-84 years. The overall mean age was 62.43 ± 9.31 years. The mean age of male and female was 62.13 ± 8.87 years respectively. Maximum number of patients were in the age group 61-80 years (54%).

OUTCOME OF NIV

A total of 100 patients included in the study, 82 were successfully treated by NIV, thus giving a success rate of 82%.

EFFECT OF AGE OF THE STUDY PATIENTS ON NIV OUTCOME

Age (years)	Success	Failure	Total
40-60	38(92.68%)	03(7.32%)	41
61-80	13(24.07%)	13(24.07%)	54
>80	03(60%)	02(40%)	5
TOTAL	82	18	100

Two tailed $p=0.03$

As evident from above success rate was highest among 40-60 years. It was subsequently decreasing in higher age groups. The result is statistically significant.

NIV outcome with history of previous mechanical ventilation

H/O mechanical ventilation	OUTCOME SUCCESS	OUTCOME FAILURE	TOTAL
YES	8(57.14%)	6(42.86%)	14(100%)
NO	74(86.04%)	12(13.96%)	86(100%)
TOTAL	82	18	100

$X^2=6.851$

$df=1$

$p=0.009HS$

As evident above patient with past history of mechanical ventilation had shown poor outcome as compared to other group. The difference was statistically significant.

Effect of initial pH on outcome

pH range	Outcome SUCCESS	Outcome FAILURE	Total
7.25-7.30	49(75.38%)	16(24.62%)	65
7.30-7.35	33(94.29%)	2(5.71%)	35
Total	82	18	100

Two tailed p=0.027

As evident above patient with pH between 7.30 to 7.35 had shown better outcome (94.29%) as compared to pH between 7.25-7.30 which was statistically significant.

Effect of initial PaCO2 on NIV outcome

pCO2 range (mmHg)	Outcome Success	Outcome failure	Total
60-80	67(94.37%)	4(5.63%)	71
>80%	15(51.72%)	14(48.28%)	29
Total	82	18	100

X²=25.366 df=1

p<0.001

HS

As evident above patient with initial PaCO2 between 60-80 mmHg had shown better outcome as compared to patient with initial PaCO2 >80mmHg and it was statistically significant.

Change of estimated mean PaCO₂ with time since start of NIV

Time since Start of NIV (HRS)	Estimated mean PaCO ₂ (mmHg)	SE of mean	Mean difference with initial PaCO ₂	SE of Mean difference
0	73.475	1.147	-	-
2	70.889	1.295	2.587	0.152
6	67.182	0.991	6.294	0.403
24	59.885	0.851	13.621	0.531
48	53.614	0.709	19.861	0.648
End	47.456	0.204	26.019	1.107

The above table shows change in mean PaCO₂ of study population over time after application of NIV. Mean PaCO₂ of the study population at start of NIV was 73.475mmHg, which reduced significantly over time. Difference between mean initial PaCO₂ over different time intervals was found highly significant by ANOVA test (p<0.001).

Discussion: NIV has been established as a useful therapy for management of respiratory failure in acute exacerbation of COPD. GOLD guideline 2011 recommends NIV trial to every patient with COPD exacerbation before invasive ventilation regardless of severity of respiratory failure. NIV has the potential to be a much cheaper option than the conventional mechanical ventilation by reducing complication and length of stay in hospital and in some cases by avoiding ICU admission.

The use of NIV in COPD exacerbation is recommended over pH<7.35 and/or PaCO₂>45mmHg. There are studies that have shown the success in even at higher PaCO₂.^(6,17) Present study was undertaken to assess the role of NIV in patients of COPD with higher PaCO₂ level, who were potential candidates for mechanical ventilation.

The overall success rate of NIV in this study was 82%. A similar study by Khilnani GC et al⁽¹⁷⁾ had shown success rate of 85% with mean PaCO₂ 85.4mmHg and mean pH 7.23 at the beginning of study. Another study by McLaughlin KM et al⁽⁷⁾ reported success rate of 72 % in pH >7.25. In present study the mean initial PaCO₂ was 73.475±10.06 mmHg and pH was 7.29±0.028. Higher success rate in the present study can be explained by the better initial blood gas measurements.

Various studies have shown that age is a critical factor in NIV outcome. Scarpazza P et al⁽¹⁵⁾ and Antonelli et al⁽¹⁶⁾ suggested that age > 40years is an independent factor for NIV failure.

In present study success rate was highest in the age group 40-60 years. The success rate was significantly lower in higher age groups. (p=0.03)

In the present study we found 14 patients having previous history of any form of mechanical ventilation for COPD exacerbation. In our study we found a statistically significant poor outcome in patients with previous history of mechanical ventilation (p=0.009). Studies have shown that exacerbation frequency is an important independent risk factor for treatment failure.⁽¹¹⁾

Acidosis is an indicator of the more severe form of COPD and has been shown to predict mortality in a number of studies on acute exacerbation of COPD.⁽¹³⁾

Ambrosino et al⁽¹²⁾ found that patients in whom NIV treatment had failed, were significantly more academic at baseline than those who were successfully treated (pH 7.22 ± 0.08 versus 7.28 ± 0.04 $p < 0.005$)

In the present study we took patients with initial pH range of 7.25-7.35. Patients with more severe acidosis (pH < 7.30) shown a poor outcome as compared to patients with pH > 7.30 and that was statistically significant ($p = 0.027$).

Various studies⁽¹⁴⁾ have shown PaCO₂ as an independent predictor of the need to initiate NIV in AECOPD patients. A study by Bhatt SP et al⁽¹⁸⁾ had shown that patients with stable COPD with PaCO₂ < 52 mmHg can be treated successfully with domiciliary NIV. A study by K M McLaughlin et al⁽⁹⁾ NIV shows improvement even at mean PaCO₂ = 75 mmHg.

In the present study we took patients with more severe form of COPD with PaCO₂ > 60 mmHg. This

study had shown that patients with initial PaCO₂ between 60-80 mmHg reported better outcome as compared to patients with higher PaCO₂ level (80 mmHg). The results were statistically significant ($p < 0.001$)

In previous studies the success was defined by initial improvement in blood gas parameters.^(6,7,17) In the present study we took the first ABG after 2 hours of NIV initiation. This study had shown that decline in mean PaCO₂ after 2 hours is significantly lower than initial PaCO₂. Similar results has been shown by the studies by Khilnani GC et al⁽¹⁷⁾, Ambrosino M et al.⁽¹²⁾

CONCLUSION

Present study suggests that NIV is highly effective in treating patients with hypercapnic respiratory failure in AECOPD even at high PaCO₂ (60 mmHg) with pH 7.25-7.35. This study also shows that patients with advance age, history of previous mechanical ventilation, high initial PaCO₂ and low pH have lower chance of success with NIV.

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