



A STUDY TO EVALUATE PREDICTORS AND OUTCOME OF NON-INVASIVE VENTILATION IN TREATMENT OF ACUTE EXACERBATION OF COPD IN A TERTIARY CARE CENTRE

Pulmonary Medicine

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ABSTRACT

Background: Chronic Obstructive Pulmonary Disease (COPD) is a significant health issue globally. Acute exacerbations of COPD (AECOPD) often require hospital admission, and a subset of these patients develop acute respiratory failure (ARF) requiring ventilatory support. Non-invasive ventilation (NIV) has become a cornerstone of AECOPD-related ARF management, but predictors of its success and factors influencing outcomes remain incompletely understood. **Objective:** This prospective observational study aimed to assess the predictors and outcomes of NIV in patients admitted with AECOPD and ARF at a tertiary care centre in India. **Methods:** This study included 50 patients of AECOPD and ARF managed with NIV. Baseline characteristics, including demographics, comorbidities, smoking history, and physiological parameters like pH, PaCO₂, and HCO₃, were collected. The patient's clinical condition was assessed by ABG which was repeated at 2 hours, 6 hours, 24 hours, and discharge. If patient clinical condition worsens, and if there is no significant improvement in ABG parameters, patient were put on invasive mode of ventilation according to guidelines. **Results:** Of the 50 patients enrolled, 42 (84%) achieved success with NIV. Patients experiencing NIV failure exhibited significantly higher PaCO₂ and HCO₃ levels at admission compared to those with successful NIV. The presence of comorbidities, shorter duration of NIV were significantly associated with NIV failure. **Conclusions:** NIV is effective treatment strategy for patients with AECOPD and ARF, leading to favourable outcomes. Early detection of patients at risk of NIV failure, particularly those patients with comorbidities and severe acidosis, is crucial for optimizing patient management and resource allocation.

KEYWORDS

COPD, Acute Exacerbation, Non-Invasive Ventilation, Acute Respiratory Failure, Predictors, Outcomes

INTRODUCTION:

Chronic Obstructive Pulmonary Disease (COPD) is now one of the major three causes of death worldwide and 90% of these deaths occur in low- and middle-income countries (LMICs).^{1,2} It is currently the world's seventh biggest cause of death.³ According to the Global Burden of Diseases (GBD) study, COPD was the eighth greatest cause of Disability Adjusted Life Years (DALY) lost globally in 2005, and it rose to the fifth leading cause of DALY loss in 2013.⁴

Acute respiratory acidemia caused by sustained hypercapnia is a typical feature of severe acute COPD exacerbations (AECOPDs). Exacerbations are mainly caused by respiratory viral infections although bacterial infections and environmental factors such as ambient air pollution and excess heat may also initiate and/or amplify these events.⁵

In several randomized controlled trials (RCTs) and a recent meta-analysis, non-invasive ventilation (NIV) has been demonstrated to be an effective treatment strategy for ventilatory failure caused by acute exacerbations of chronic obstructive pulmonary disease. Several studies have indicated that non-invasive ventilation is effective in COPD patients with type II respiratory failure.⁵⁻⁶

The current study was designed to examine the predictors and outcomes related to non-invasive ventilation among patients hospitalized with chronic obstructive pulmonary disease exacerbations in order to reduce the requirement for invasive mechanical breathing.

MATERIALS AND METHODS

This prospective observational study was carried out in the Department of Respiratory Medicine at Government Medical College Kota for one-year duration. Institute Ethics Committee clearance was obtained before the commencement of the study.

Patient information sheets were explained to the patient in their language. All the queries regarding the study were answered. Written

and informed consent was obtained from patients before the study. Patients were enrolled after satisfying of the inclusion and exclusion criteria.

Complete evaluation of patients was done including clinical history, complete physical examination and all relevant investigations and was recorded in a structured proforma. All patients were given treatment according to Global Initiative for Chronic Lung Diseases (GOLD) guidelines.

Chest x-ray was done to look for changes associated with COPD and to rule out other diseases like bronchiectasis, and pleural diseases. ABG analysis was done and all patients with PaCO₂ >45 mm Hg and pH <7.35 were considered for the study. NIV-BIPAP (Bilevel Positive Airway Pressure) was used in all patients. Initially, the inspiratory positive airway pressure (IPAP) and the expiratory positive airway pressure (EPAP) were kept at levels of 8 cm of H₂O and 4 cm of H₂O respectively then gradually increased to the final IPAP and EPAP at levels of 12 cm of H₂O and 5 cm of H₂O respectively.¹⁰ After 12 hours of starting BIPAP, ABG was repeated. Every patient was advised to use BIPAP for a minimum of 16 hours a day. BIPAP was temporarily discontinued during eating, drinking, taking medicines and during nebulization. The patient's clinical condition was assessed by ABG which was repeated at 2 hours, 6 hours, 24 hours, and discharge. If the patient's clinical condition worsened, and if there was no significant improvement in ABG parameters, the patient was put on an invasive mode of ventilation according to guidelines.

RESULT

Patient Demographics

We enrolled patients during the aforementioned study period out of 50 patients 42 patients on NIV success and 8 patients were NIV failure need mechanical ventilation. The demographic and clinical details of the study population have been summarized in Table 1. In this table comorbidities, NIV duration, Mortality rates between success and failure groups show significant results with a p-value <0.005%.

Table 1. Patient Demographics

GENDER	Success (42)		Failure (8)		P-Value
	n	%	n	%	
Male	23	54.8%	2	25.0%	0.123
Female	19	45.2%	6	75.0%	
BMI					
18.5-24.9 (Normal)	30	71.4%	6	75.0%	0.902
25-29.9 (Overweight)	11	26.2%	2	25.0%	
>30 (Obese)	1	2.4%	0	0.0%	
DYSYPNEA(MMRCGRADE)					
Grade 3	23	54.8%	2	25.0%	0.123%
Grade 4	19	45.2%	6	75.0%	
COUGH AND PEDALOEDEMA					
Cough	39	92.9%	8	100.0%	0.436
Pedal oedema	15	35.7%	4	50.0%	0.445
HISTORY OF PREVIOUS EXACERBATION					
NO	32	76.20%	5	62.50%	0.418
YES	10	23.80%	3	37.50%	
COMORBIDITIES					
Yes	4	100%	9	37.50%	0.020
No	0	0%	15	62.50%	
MORTALITY RATES					
Nil	42	100.0%	4	50.0%	<0.001
Yes	0	0.0%	4	50.0%	
SMOKING INDEX	Success (42)		Failure (8)		P-Value
	n	%	n	%	
Mild	12	28.6%	2	25.0%	0.628
Moderate	8	19.0%	3	37.5%	
Severe	10	23.8%	2	25.0%	
Nil	12	28.6%	1	12.5%	
NIV DURATION					
<24 hours	0	0%	3	37.50%	<0.001
24 hours	9	21.40%	1	12.50%	
48 hours	21	50.0%	1	12.50%	
72 hours	12	28.60%	0	0%	
Nil	0	0%	3	37.50%	

Table No 2 Comparison Of PH, PaCO₂, And HCO₃ Levels Between Successful And Failed Treatment Outcomes

pH	Failure (n=8) Mean ± SD	Success (n=42) Mean ± SD	p-value
At Admission	7.12 ± 0.08	7.22 ± 0.05	<0.001**
After 2 hrs	7.36 ± 0.29	7.27 ± 0.06	0.080
After 6 hrs	7.35 ± 0.13	7.34 ± 0.06	0.850
After 24 hrs	-	7.39 ± 0.05	-
At Discharge	-	7.41 ± 0.05	-
PaCO ₂			
At Admission	119.63 ± 28.19	90.47 ± 11.65	<0.001**
After 2 hrs	66.50 ± 50.43	77.31 ± 12.55	0.280
After 6 hrs	68.00 ± 14.14	66.32 ± 9.99	0.820
After 24 hrs	-	55.48 ± 9.83	-
At Discharge	-	48.62 ± 8.45	-
HCO ₃			
At Admission	45.62 ± 6.32	37.88 ± 7.47	0.010*
After 2 hrs	39.67 ± 17.95	35.21 ± 6.04	0.300
After 6 hrs	38.50 ± 0.71	32.67 ± 5.96	0.180
After 24 hrs	-	31.32 ± 6.19	-
At Discharge	-	27.93 ± 6.33	-

The study compared pH levels between failure and success groups at different time points. At admission, the mean pH was significantly lower in the treatment failure group (7.12 ± 0.08) compared to the success group (7.22 ± 0.05), with a p-value of <0.001, indicating a statistically significant difference. After 2 hours, 6 hours, 24 hours, discharge pH levels were recorded between success group, and failure group does not show any significant results. (p values< 0.005) The study also analyzed PaCO₂ levels between the failure and success groups at various time points. At admission, the mean PaCO₂ was significantly higher in the failure group (119.63 ± 28.19) compared to the success group (90.47 ± 11.65), with a p-value of <0.001, indicating a statistically significant difference. After 2 hours, 6 hours, and 24 hours at discharge failure and success groups do not show any significant results. The study further examined HCO₃ levels between the failure and success groups at different time points. At admission,

the mean HCO₃ was significantly higher in the failure group (45.62 ± 6.32) compared to the success group (37.88 ± 7.47), with a p-value of 0.010, indicating a statistically significant difference. After 2 hours, 6 hours, and 24 hours, at discharge, HCO₃ Values between the failure success group did not show any significant results. (p value<0.005)

DISCUSSION

Antibiotics, systemic steroids, regulated oxygen therapy, and rapid-acting bronchodilators are the standard treatments for severe COPD exacerbations. Addition of non-invasive ventilation (NIV) to this treatment regimen has resulted in decreased rates of endotracheal intubation (ETI) thereby reducing morbidity, length of hospital stays and overall mortality [1]. There is a relative lack of data regarding the benefit of NIV in patients with severe exacerbations. Therefore, this present study was conducted to evaluate the predictors and outcomes of NIV in acute exacerbation of COPD.

Based on the defined inclusion and exclusion criteria, 50 patients of COPD presented with acute exacerbation and signs of respiratory distress, in the Department of Respiratory Medicine, Government Medical College, Kota, Rajasthan, were enrolled for the study. On the basis of success rates of NIV in these patients, they were divided into two groups: patients with successful NIV (84%) and those with failed NIV (16%). The mean age was comparable between the two groups, with no significant difference. Maximum patients were in the age group of 61-70 years in both groups. Also, the overall ratio of males was more as compared to females. A similar study was conducted by Kshatriya RM et al, 2019, wherein, they included 110 patients, of which 68 had COPD.⁽¹¹⁾ The ratio of males was higher than females. Another similar study was conducted by Selvam P et al, 2021, wherein they included 42 patients with acidosis, secondary to COPD, of which 27 were male and 15 females with a mean age of 56.83 years. The results of successful NIV in our study are similar to the study conducted by Singh VK et al⁽¹²⁾, 2006; Kshatriya RM et al, 2019⁽¹³⁾; Selvam P et al, 2021⁽¹⁴⁾.

The mean BMI was also comparable between the two groups, with maximum patients in both groups having normal BMI in the range of 18.5-24.9 and almost equal percentage of overweight patients in both groups (BMI>25). There was no significant difference between the two groups for BMI (p-value>0.05). On the contrary, Selvam P et al⁽¹⁴⁾, 2021 in their study observed that on comparing the mean BMI between success (19.62±3.22) and failure categories (26.65±5.649), it was noted that patients who were overweight (BMI >25) were predominantly present in the failure category than in success category. The length of hospital stay was more in patients with successful NIV (4.76 ± 1.23 days) as compared to patients with failure of NIV (4.25 ± 1.98 days), however, the difference was not statistically significant between the two groups (p-value- 0.356).

The measure of impairment caused due to breathlessness in patients with COPD was evaluated using the Modified Medical Research Council (MMRC) Dyspnoea Scale. We observed that there were patients with severe MMRC scoring, all patients lie in MMRC grade 3 and 4. No significant correlation could be derived based on MMRC scoring and the success rate of NIV in patients (p-value- 0.123).

Cough and pedal oedema were the common presentations in our patients. We observed that in patients with successful NIV 92.9% patients had a cough, while 35.7% had pedal oedema. While in patients with failure to NIV, 100% of patients had cough and pedal oedema was observed in 50% of patients. No significant difference was observed between the two groups (p-value>0.05).

Previous history of smoking was also evaluated in all patients and it was observed that in patients with successful NIV, maximum patients had either no history of smoking or belonged to the moderate smoking index group (57.2%), while in patients with NIV failure maximum patients belonged to moderate smoking index group (37%). No statistically significant correlation was observed between the two groups for history of smoking (p-value- 0.628). A similar study was done by Chakrabarti et al., 2009⁽¹⁵⁾, at the University Hospital at Aintree in 2006. They studied 88 patients with decompensated COPD having respiratory failure to find out predictors of the outcome of NIV support. They also found that differences in gender, smoking status, and sensorium had no impact on the outcome of NIV with P = 0.25, 0.32, and 0.18, respectively.

In patients with successful NIV, only 23.8% had a previous history of

exacerbation, while in patients with NIV failure, 37.5% had a previous history of exacerbation. However, no significant correlation could be derived (p-value -0.418).

We also recorded the data for comorbidities among our patient population and observed that in patients with NIV failure, all patients had some existing comorbidities present, while in patients with successful NIV, only 37.5% of patients had comorbidities. This difference was statistically significant (p-value- 0.020). Similar to our study, Selvam P et al, 2021 observed that the percentage of comorbidities was higher in the NIV failure group. Moretti M et al 2000⁽¹⁶⁾ showed that the incidence of comorbidities was more in the NIV failure category than in the success category. But Talwar D and Dogra V⁽¹⁷⁾, 2016 concluded that the incidence of comorbidities was equal both in success and failure groups.

We observed a significant correlation between mortality and NIV. In patients with successful NIV, no deaths were reported, however, in patients with failure of NIV, 50% of patients died (p-value <0.001). Similar to our study, Shaheena M et al, 2018⁽¹⁸⁾, observed that in-hospital mortality was considerably less in the NIV group (OR=5.411, 95% CI: 1.017–28.79 and P=0.047).

The duration of NIV in the first 24h, 48h and 72h was significantly higher in patients with NIV failure as compared to successful NIV (p value<0.001).

The ABG parameters were also recorded for all patients. The majority of patients had severe acidemia at the time of admission (pH <7.35), this difference was significantly different between the NIV failure and successful patient group (p-value <0.001). The pH levels were eventually maintained in both groups. Fewer studies have shown that the improvement in pH within a short period after initiation of NIV predicts the outcome. Selvam P et al⁽¹⁴⁾, 2021 observed that patients who present with initial pH >7.25 have a better outcome without any need for invasive ventilation. A study conducted by Claude KH et al., 2013, proved that improvement in pH and reduction in PaCO₂ were observed within 2 hours of initiation of NIV in COPD patients. Lightowler JV et al⁽⁹⁾, 2003, did a similar study that showed that patients with baseline pH <7.22 went for NIV failure in COPD patients. Another study done by Liu J et al⁽²⁰⁾, 2016, also concluded that severe acidosis is a significant predictor for NIV failure in COPD patients. Cavalleri M et al.,⁽²¹⁾ 2018 in their study, have shown that patients with initial pH <7.23 are more prone to NIV failure.

At the time of admission, PCO₂ levels were significantly higher in NIV failure groups as compared to the successful NIV group (p-value <0.001). The levels were back to normal in both the groups after 2hrs of NIV. Therefore, a patient who presents with initial PaCO₂ <90 at the time of admission, appears to be a good predictor of successful NIV. Our results are in line with a study by Selvam P et al, 2021⁽¹⁴⁾, wherein they observed that patients who present with PaCO₂ <70 are a good predictor of successful NIV. Liu J et al., 2016⁽²²⁾, did a similar study that showed that patients with baseline PaCO₂ >88 went for NIV failure in COPD patients. Cavalleri M et al., 2018⁽²³⁾, showed that patients with initial PaCO₂ >85 mmHg were liable for NIV failure.

Similarly, the HCO₃ levels were also significantly higher in the failure group as compared to the successful NIV patient group (p-value - 0.010). In the NIV group, the levels were significantly decreased within 24 hours and maintained till discharge.

CONCLUSION

In this study, it was observed that patients with acute respiratory failure secondary to COPD who were treated with NIV had a better outcome with reduced incidence of NIV failure. NIV was successful in 80% of patients presenting with COPD. Among the failure group, severe acidosis, hypercapnia and higher HCO₃ levels at the time of presentation predict NIV failure. And also, it was observed that mortality rates were higher in the NIV failure group. Thus, early NIV in stable COPD patients seems to have a beneficial effect on the rate and severity of exacerbations, arterial blood gases and clinical symptoms.

LIMITATIONS

In comparison to many of the studies mentioned above, we had a low number of enrolled patients which may limit its external validity.

Given our inability to record accurate pO₂/FiO₂ at admission, we were

unable to calculate any severity score (i.e., SAPS or APACHE) and thus its implications on outcomes as other studies have reported.

Conflict Of Interest - None

Funding – None

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