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# A STUDY TO ASSESS THE EFFICACY OF NON-INVASIVE VENTILATION IN ACUTE EXACERBATION OF COPD WITH ACUTE RESPIRATORY FAILURE

**KEY WORDS:** COPD, ABG, Non-invasive ventilation.

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**ABSTRACT**

**OBJECTIVE:** To assess the efficacy of non-invasive ventilation in acute exacerbation of COPD with acute respiratory failure.

**MATERIALS AND METHODS:** The Present prospective study carried out at the Department of Pulmonary Medicine, Guntur Medical College, Guntur between January 2017 to June 2018. A Total of 42 patients with acute exacerbation of COPD with acute respiratory distress are included into the study.

**RESULTS:** In the present study, out of the 42 patients, 32 patients improved after NIV initiation had correction and improvement of the ABG parameters like pH, PaCO2 and hemodynamic variables like PR, BP, RR within first one hour. The patients who improved with NIV (n=32) had a decrease in duration of hospital stay than the patients requiring invasive ventilation (n=6).

**CONCLUSION:** Non-Invasive Ventilation is a promising therapeutic modality for patients with acute exacerbation of COPD with acute respiratory failure and its timely institution leads to an early and effective improvement in the pH, $PaCO_2$.

## INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) represents an important public health challenge representing the fourth leading cause of death in the world and is projected to be the third leading cause of death by 2020[1]. In India, Non-Communicable diseases account for 61.8 % of total number of deaths of which, Chronic respiratory diseases i.e. COPD, asthma and other respiratory diseases account for 10.9%, in the year 2016[2]. It is the second leading cause of death in India, running behind only to ischemic heart diseases. It is also a major cause for chronic morbidity throughout the world. In India, COPD is the second leading cause for the Disability Adjusted Life Years (DALY's), which increased from 3.1% in 1990 (8th leading cause) to 4.8% in 2016 (2nd leading cause). It is the 2nd& 5th leading cause for the DALY's in males and females respectively in the year 2016[2].More than 90% of deaths due to COPD occur in the low and middle income countries like India where besides environmental pollution and smoking, bio mass fuel exposure is also high.

Acute Exacerbation of COPD defined as *"complex events in the natural course of the disease characterized by a change in the patients baseline symptoms i.e. dyspnoea and or sputum beyond normal day to day variations, that is acute in onset and may warrant a change in regular medication"*.[1,3]These change in symptoms include worsening of dyspnoea, increased sputum purulence and volume, increased cough and wheeze. The in-hospital mortality was reported to be 12% in AECOPD and the long-term mortality in the survivors of hospitalized AECOPD patients is high being 32.4% at 1 year and 39.7% at 2 years follow up according to Indian statistics[4].

NIV (Non Invasive ventilation) refers to administration of ventilatory support without using an invasive artificial airway (endotracheal tube or tracheostomy tube). It has become an integral tool in the management of both acute & chronic respiratory failure, in both home setting and in critical care unit [6]. Positive pressure ventilation is the most commonly used method being delivered through a mask. There is improvement in the parameters like tidal volume, respiratory rate, dyspnoea; work of breathing, improvement in oxygenation could be documented by Arterial blood gas analysis (ABG). Bi-level positive airway pressure (BiPAP) with nasal or full-face mask is usually the most common mode of NIV used. NIV can also be used as a support during early extubation and is an adjunct to weaning[166].

Aim of the present study to assess the efficacy of non– invasive ventilation in acute exacerbations of chronic obstructive pulmonary disease with acute respiratory failure.

### Objectives of the study

- To assess the impact of non-invasive ventilation on the blood gas parameters in patients with AECOPD.
- To assess the need for endotracheal intubation in patients with AECOPD on non-invasive ventilation.
- To assess the impact of non-invasive ventilation on the length of hospital stay.

## MATERIALS AND METHODS

The Present prospective study carried out at the Department of Pulmonary Medicine, Guntur Medical College, Guntur between January 2017 to June 2018. A Total of 42 patients with acute exacerbation of COPD with acute respiratory distress are included into the study as per following inclusion and exclusion criteria.

### Inclusion criteria:

1. Patients of AECOPD with Clinical symptoms and signs of acute respiratory distress with moderate – severe dyspnoea, using accessory muscles of respiration and respiratory rate > 30 per minute.
2. ABG showing a pH < 7.35
3. ABG showing hypoxemia: PaO2 < 60 mm Hg.
4. ABG showing hypercapnia: PaCO2 > 45 mm Hg.

### Exclusion criteria:

1. Respiratory arrest.
2. Metabolic acidosis.
3. Impaired mental status.

4. Excessive secretions.
5. Life threatening refractory hypoxemia
6. Uncooperative/agitated patients.
7. Inability to use mask because of trauma / surgery.
8. Un-drained pneumothorax
9. Dyspnoea due to other causes.
10. Severe hemodynamic instability.

The ethical committee of institution approved the study protocol. Written and informed consent was taken from all the patients or the next of kin before enrolment into the study. A total of nearly 100 patients with acute respiratory distress attending the department were screened initially. Out of these 100 patients, 42 of them were finally included into the study after attributing the acute exacerbation to COPD with thorough history taking, clinical examination, chest x-ray and laboratory investigations. All the patient's baseline clinical variables were noted and an ABG was sent at the time of admission (Table – 1). Then all the patients were started on standard medical therapy for COPD acute exacerbation. A portable non-invasive ventilator (Slepcube – BILEVEL ST DV56SE by DeVilbiss) was then connected to patients with the help of a full face – mask and it was used in the spontaneous-timed mode.

**Table 1: Baseline Demographic and Physiological characteristics of the study subjects**

| | |
|---|---|
| Number of subjects (n) | 42 |
| Age (years) | 65 ± 6.77 |
| Males | 32 |
| Females | 10 |
| Ph | 7.27 ± 0.05 |
| PaCO2 | 64.75 ± 0.05 |
| PaO2 | 66.92 ± 22.03 |
| Respiratory rate (per minute) | 34.43 ± 3.4 |
| Pulse rate (per minute) | 114.66 ± 8.15 |
| Systolic blood pressure (mm Hg) | 142.14 ± 12.79 |
| Diastolic blood pressure (mm Hg) | 85.50 ± 9.32 |
| Saturation (SPO2 - %) | 87.55 ± 5.16 |

Patients were asked to lie in supine position with the head end of the bed elevated by 45 degrees. Then the patient was started on the standard medical therapy including the oxygen, intravenous steroids, antibiotics and an inhaled bronchodilator in the nebulisation form. After suitable patient education an appropriate sized interface was placed. To make the patient feel comfortable, low pressures were given initially.

The starting parameters set were an IPAP pressure of about 10 cm of H2O and an EPAP pressure of about 5 cm of H2O. The oxygen delivery was set at a flow rate of 1-2 liters per minute. Subsequently, the adjustments in the settings were made according to the patient need and the results of the ABG. The protocol was to increase IPAP by 2-4 cm of H20 and EPAP by 1-2cm of H2O. The parameters were titrated according to the patients need. The patients were monitored closely for the level of consciousness, co-operation, mental status, physical signs, oxygen saturation, vitals and for any air leaks around the face mask if present. ABG was obtained at the end of one hour after initiation of NIV in all patients.

If there is no satisfactory response in the patient's comfort, oxygenation and ventilation non-invasive ventilation was discontinued and patient was put on invasive mechanical ventilation. The decision of intubating the patient was completely based on clinical judgment. But if there is satisfactory response then the NIV was continued for up to 6 hours from the time of initiation and an ABG was taken at the end to look for the improvement in parameters. The following criteria were taken as non-compliance with NIV:

1. Worsening dyspnoea.
2. Decreasing oxygen saturation.
3. Irritability and restlessness

The response of the patient was recorded in terms of:

- Subjective response: quantification of dyspnoea by mMRC, accessory muscle usage, mental alertness and degree of comfort.
- Objective response: respiratory rate, heart rate, blood pressure, oxygen saturation and ABG changes.

The ABG response in the present study was defined as:

1.Corrected : increase in the pH value more than or equal to 7.35.
2.Improved : pH increase by 0.05 – 0.1.
3.Not corrected : if the increase in pH is less than 0.05, in comparison with values at 0, 1 And 6 hours.

The outcome was finally labeled as success (if the ABG was either corrected or improved) and as failure (if ABG was not corrected).

**Statistical analysis**

All the data collected was entered in MS Excel 2007. Data analysis was done using SPSS software trial version 21 for windows. Results were expressed as mean, standard deviation, frequency and percentages. ANOVA test for variance was used to assess the significant variation among different variables. For all statistical analysis $p \leq 0.05$ was considered statistically significant.

**OBSERVATIONS AND RESULTS**

In the present study most of the patients were in the 61-70 years (54.8%) age group. The next common age group was 50-60 years (28.6%) followed by 70 and above years (16.6%) age group. Most of the subjects were male sex (76.2%) group followed by the female sex (23.8%) group.

**Table 2: ABG changes of all subjects at 0, 1 and 6 hours**

| Variables | 0 Hour | 1 Hour | 6 Hour | P Value | | |
|---|---|---|---|---|---|---|
| | | | | 0 vs 1 | 1 vs 6 | 0 vs 6 |
| **pH** | **7.27 ± 0.05** | **7.30± 0.65** | **7.37± 0.03** | **P<0.05** | **P<0.001** | **P<0.001** |
| **PaCO2** | **64.75± 9.21** | **61.33± 8.26** | **55.62± 6.29** | **P = 0.05** | **P<0.005** | **P<0.001** |
| **PaO2** | **66.91± 22.03** | **70.01± 19.16** | **70.38± 7.74** | **P>0.05** | **P>0.05** | **P>0.05** |

In the present study the pH values showed an improvement within one hour after initiation of NIV which was significant ($p<0.05$) and was also significantly maintained till the end of 6 hours ($p<0.001$). Similarly, the PaCO2 values also showed a significant improvement ($p=0.05$) from the baseline values after one hour, and there is also a significant difference ($p<0.001$) in improvement even after six hours of initiation on NIV. Even though there is improvement in the PaO2 values from the baseline, it failed to show a significant difference ($p>0.05$) after one and six hours after initiation of NIV.

**Table 3: vital data characteristics of study subjects**

| Variables | 0 Hour | 1 Hour | 6 Hour | P Value | | |
|---|---|---|---|---|---|---|
| | | | | 0 vs 1 | 1 vs 6 | 0 vs 6 |
| **RR** | 34.43 ± 3.4 | 31±4.36 | 25.76± 2.87 | P<0.001 | P<0.001 | P<0.001 |
| **PR** | 97.98±13.95 | 93.75± 16.04 | 84.36± 10.11 | P > 0.05 | P<0.05 | P<0.001 |
| **SBP** | 142.1±12.79 | 138.2± 15.31 | 130.6± 9.51 | P>0.05 | P<0.05 | P<0.001 |
| **DBP** | 88.57±9.65 | 85.5±9.20 | 80.90± 6.21 | P>0.05 | P<0.05 | P<0.001 |

Among vital data characteristics of study subjects, respiratory rate is the only vital data variable which improved significantly ($p<0.001$) within the first hour of initiation of NIV and also the improvement was significantly maintained ($p<0.001$) till the end of six hours. All the other variables (PR,

SBP, DBP) did not show significant improvement (p>0.05) within one hour but showed a significant improvement (p<0.05) from one to six hour and the change was also significant (p<0.001) from the baseline till the end of six hour.

**Table 4: Duration of hospital stay of study subjects**

| Variable | Overall | NIV Patients | Patients requiring IMV |
|---|---|---|---|
| **Hospital stay** | 8.68 ± 3.89 | 7.18 ± 1.50 | 16.66 ± 2.35 |

The overall mean (SD) hospital stay in the study was 8.68 (3.89). The mean hospital stay in patients who had successful outcome with NIV is 7.18 (1.5) and those with NIV failure and requiring invasive mechanical ventilation is 16.66 (2.35). These findings show that the early use of NIV in the acute exacerbations of COPD with acute respiratory failure had shortened the length of hospital stay in successful subjects by about 2 times than the failure patients.

**Table 5: Biochemical (ABG) response**

| Response | Subjects (n) | Percentage |
|---|---|---|
| **Corrected** | 30 | 71.4 |
| **Improved** | 2 | 4.8 |
| **Not Corrected** | 10 | 23.8 |

**Table 6: Clinical outcome**

| Outcome | Subjects (n) | Percentage |
|---|---|---|
| **Success** | 32 | 76.2 |
| **Failure** | 10 | 23.8 |
| **Total** | 42 | 100 |

The use of non-invasive ventilation in acute exacerbation of COPD with respiratory failure had a success rate of around 76.2%. All the 32 (76.2%) subjects who had shown positive response had their ABG response within one hour after putting on NIV. The patients (n=10) who did not show any clinical or biochemical (ABG) response at the end of one hour did not improve subsequently thereby proving that the first hour response is very important in the outcome of non-invasive ventilation treatment in patients with acute exacerbation of COPD. Of the 32 patients which had successful outcome 30 (71.4%) patients got the pH corrected by the end of the study, whereas 2 (4.8%) patients had only improvement in the pH and clinical symptoms, but not normalized.

There was an overall failure rate of 23.8% (n=10), in the current study with the use of NIV in patients with AECOPD. Of these 10 subjects, 60% (n=6) required invasive mechanical ventilation due to various reasons and in 30% (n=3) the patients were left against medical advice (LAMA). There was one death during the study, which could be attributable to the poor general condition of the patient and the severity of the illness. In the present study the most common cause for which NIV had to be discontinued was the worsening of breathlessness and decreasing oxygen saturation seen in six out of the nine subjects (67%), three (33%) of the patients had developed altered consciousness.

## DISCUSSION

In the present study 42 patients with symptoms and signs suggestive of acute exacerbation of COPD with respiratory failure were included. The role of NIV has been studied and was found to be more useful as an effective therapeutic modality along with standard treatment in acute exacerbations of COPD. Non-invasive ventilation is a cost effective, readily available technique and can be used readily outside the intensive care settings. The advantages of non-invasive ventilation include patient comfort, preservation of airway defenses like cough, ability to speak and eat. The complications of endotracheal intubation such as nosocomial pneumonias, injury to airways, aspiration, and post intubation laryngeal stenosis could be avoided.[6]

In the current study, the mean baseline ABG values obtained were pH of 7.27±0.05, PaCO2 of 64.75 ± 9.21 and PaO2 of 66.91 ± 22.03.The baseline characteristics of the other studies [11 12], comparable with present study show that the most of the patients with COPD acute exacerbations with acute respiratory failure, have a mean pH < 7.3 and PaCO2 > 60 mm Hg at the time of presentation, indicating the severity of obstruction.

In the present study the second sample of ABG was taken one hour after the NIV initiation and the values were pH of 7.30 ± 0.65, PaCO2 of 61.33 ± 8.26, PaO2 of 70.01 ± 19.16. In Khilnani GC et al[11] study the second sample was also taken at the end of first hour and values were pH of 7.27 ± 0.08, PaCO2 of 65.13 ± 37.63, PaO2 of 67.4 ± 20.09, which were comparable to the present study. In Agarwal et al[12] study the second sample was taken at first hour after initiation of NIV in COPD patients and the values obtained include pH of 7.33 ± 0.07, PaCO2 of 56.4 ± 16.5, PaO2 of 61.5 ± 9.7, these values were also comparable to that obtained in the present study. The findings emphasis on the fact that with the initiation of non-invasive ventilation early, the baseline ABG parameters can be improved within one hour and it is the crucial period which determines the need for endotracheal intubation.

In the current study the third sample of ABG was taken at the end of sixth hour after initiation of ABG, the values obtained were pH of 7.37 ± 0.03, PaCO2 of 55.62 ± 6.29, PaO2 of 70.38 ± 7.74. In Khilnani GC et al[11] study the third sample was taken at sixth hour in the NIV initiated group and the values were pH of 7.32 ± 0.09, PaCO2 67.2 ± 13.5, these values were comparable to the present study, but the PaCO2 was slightly on higher side because of the baseline value of higher PaCO2 levels which touched the present study values approximately after 24 hours of NIV treatment. The PaO2 values couldn't be compared as there was no record of the values. In Agarwal et al[12] study the third sample was taken at the end of fourth hour after the initiation of NIV, and the values were pH of 7.37 ± 0.07, PaCO2 53.6 ± 14.9, PaO2 of 64.2 ± 7.9. The values obtained in this study even though were comparable to the present study, the standard deviation of pH, PaCO2, PaO2 from the mean were large enough suggesting that a third sample obtained at sixth hour could give us a better insight into the ABG parameters and their reliability. Further the study subjects is also small (n=24) in Agarwal et al [12] study. The advantage of the fourth hour sampling is patient could be assessed at an earlier time period. The studies further emphasis on the fact that with the use of non-invasive ventilation, the change in the ABG parameters can be sustained further reducing the need for invasive ventilation.

In the present study, the mean length of hospital stay in patients with acute exacerbation of COPD was 8.68 ± 3.89 which is in co-relation with the Khilnani GC et al [11] study where the mean length of hospital stay was 9.4 ± 4.3.

In our study the number of patients requiring endotracheal intubation due to worsening of symptoms was 6 out of the 42 (14.28%), who were started on non-invasive ventilation. The study is comparable with Agarwal et al[12] study in terms of the endotracheal intubation rates(12.5%). In Khilnani GC et al[11] study out of the 20 patients who received NIV 3 patients required endotracheal intubation due to various complications and worsening of symptoms. The Overall non-invasive ventilation was successful in about 76.1% in the present study which is in co-relation with the Agarwal et al[12] study which had a success rate of about 87.5% in the COPD group and Khilnani GC et al[11] study which had a success rate of about 70.0%. The statistical analysis from the above studies including the present study show the fact that the requirement of endotracheal intubation is reduced by the initiation of NIV early in the course of the exacerbations.

**Strengths of the study**

- The prospective nature of the study.

- The study sample which is relatively large when compared with some of the other Indian studies.
- Since it is a tertiary care centre study the transition from non-invasive ventilation to invasive mechanical ventilation could be done easily.
- Patients with the other causes of respiratory failure were excluded from the study there by reducing the confounding variables.

**Limitations of the study**

- The study did not have a control group.
- The patients in the study group were followed for only a brief period of six hours.
- Unmeasurable confounders at the patient and hospital level could not be excluded.
- The initiation of non-invasive ventilation and transition to invasive mechanical ventilation (when the need arise) were completely the clinicians judgment.
- The patients who required endotracheal intubation could be more sick which explains the increased morbidity in these patients.

## CONCLUSIONS AND SUMMARY

In the present study, out of the 42 patients, 32 patients improved after NIV initiation had correction and improvement of the ABG parameters like pH, PaCO2 and hemodynamic variables like pulse rate, blood pressure, respiratory rate within first one hour. The patients who improved with NIV (n=32) had a decrease in duration of hospital stay than the patients requiring invasive mechanical ventilation (n=6).

Non-Invasive Ventilation also works immediately leading to rapid improvements in the blood gas parameters. The initial response obtained through the blood gas parameters especially pH, $PaCO_2$ could be taken as predictors of success of NIV in acute exacerbation of COPD with acute respiratory failure. But the patient should be monitored carefully in the initial one hour for the need of invasive ventilation if the parameters worsen or remain unchanged.

In summary, Non-Invasive Ventilation is a promising therapeutic modality for patients with acute exacerbation of COPD with acute respiratory failure and its timely institution leads to an early and effective improvement in the pH, $PaCO_2$ besides correction in hemodynamic variables leading to a reduction in the incidence of the need for invasive ventilation and a reduction in the morbidity in these patients. There is also reduction in the duration of hospital stay in those patients with Non-Invasive Ventilation.

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