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Non-Invasive Ventilation: First Line Therapy in the Acute Exacerbations of COPD in Emergency Department

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Abstract

Non-invasive ventilation has been a major advancement in the management of acute exacerbations of chronic obstructive pulmonary disease. It reduces the need for endotracheal intubation, thereby reducing associated complications and hospital cost. The aim of our study is to assess the efficacy of non-invasive ventilation in acute exacerbations of chronic obstructive pulmonary disease with respiratory failure. A total of 86 patients presenting with acute respiratory distress at our emergency room were initially included and evaluated. Non invasive ventilation was initiated in addition to standard medical treatment in all cases. Response to therapy in terms of improvement in patients' vitals and ABG were sequentially recorded and analyzed. Overall 72.5% (n=29) of the patients improved, whereas 27.5% (n=11) did not improve with NIV among whom 63.63% (n=7) had to be mechanically ventilated. 62.5% (n=25) showed a good ABG response with improvement in pH and decrease in $PaCO_2$ levels. Therefore, NIV should be considered to be the first line of management in acute exacerbations of COPD with respiratory failure.

Keywords: Acute Exacerbation; Chronic Obstructive Pulmonary Disease; Respiratory Failure; Non-Invasive Ventilation; Endotracheal Intubation, Arterial Blood Gas.

Introduction

Chronic obstructive pulmonary disease (COPD) is a major health problem and leading cause of morbidity and mortality worldwide. The disease burden is expected to rise in the years to come. World Health Organization has predicted that by 2020, COPD will be the 5th most prevalent disease worldwide and will be among the three leading causes of death. Acute exacerbations of COPD (AECOPD) are largely responsible for the morbidity and mortality associated with the disease. The frequency of hypercapnic respiratory failure in patients with AECOPD varies from 16-35% with overall mortality of 35-43%.

Non-invasive ventilation (NIV) is effective in the treatment of patients with acute respiratory failure (ARF) as shown by a number of controlled trials and meta-analyses. However, evidence for the use of NIV remains strongest in patients with hypercapnic ARF due to exacerbations of chronic obstructive pulmonary disease (COPD) and cardiogenic pulmonary edema. NIV is proved to reduce the need of endotracheal intubation (ETI), to prevent ETI-associated pneumonia and to decrease incidence of mortality compared to ventilated patients. The use of NIV has been continuously increasing over the last decade and has been substantiated by enough clinical evidence. The current study was planned to determine the safety and efficacy of NIV in the subgroup of patients with respiratory failure due to AECOPD presenting to the emergency room of our hospital.

Material and Methods

This was an institution based prospective study carried out in the emergency room and MICU of our

hospital over a period of twelve months. It was approved by the institutional ethics committee and an informed written consent was obtained from all patients or the next of kin before enrolment into the study. A total of 86 patients presenting with acute respiratory distress were initially evaluated. Among them, 40 patients were enrolled in the study after confirmation of the episode as acute exacerbation of COPD based on history, clinical examination, lab investigations and chest X-ray. Cases with mild to moderate respiratory acidosis (pH between 7.25-7.35) were included. Exclusion criteria included dyspnea due to other causes, metabolic acidosis, life-threatening refractory hypoxemia, impaired mental status, excessive secretions, hemodynamic instability or life-threatening arrhythmias, uncooperative or agitated patients and inability to use mask because of trauma or surgery.

The baseline clinical parameters were recorded and an ABG was obtained from all patients at the time of presentation (Table 1). All patients were started on standard medical therapy including supplemental oxygen, intra-venous steroid, antibiotics and nebulised bronchodilators (Levo-salbutamol and/or Ipratropium bromide). A portable Non-invasive ventilator with monitor (BIPAP, VIVO-30 from BREAS) was used in the spontaneous mode using full face mask. Patients were asked to lie supine with head end elevated by about 45°. After explaining the procedure and reassurance, a correct sized interface was placed. To start with, low pressures were given to acclimatize the patient. The initial trial parameters (in spontaneous mode) were set to 8 cmH_2O of IPAP and 4 cmH_2O of EPAP with oxygen flow rate of 1-2 L/ minute in patients with hypoxemia. EPAP was increased by 1-2 cms H_2O till the patient triggers the ventilator. IPAP and EPAP parameters were titrated to optimize patient's comfort. The difference between IPAP and EPAP was always maintained at not less than 4 cms H_2O.

Each patient was closely monitored for mental status, signs of air leak around the mask and vital parameters. ABG was obtained in all patients one hour after starting of NIV. If satisfactory degree of patient comfort, ventilation and oxygenation were not achieved, BIPAP was discontinued and the patient was excluded from the study. Criteria for non-compliance included irritability and restlessness, worsening dyspnea, falling oxygen saturations and abdominal distention. However, if adequate response was achieved, NIV was continued for up to 6 hours and again an ABG was taken to assess improvement. The response of the patient was sequentially recorded.

- Subjective response: dyspnea quantified by MMRC, use of accessory muscles of respiration, degree of comfort and mental alertness.
- *Objective Response*: respiratory rate, oxygen saturation, blood pressure, heart rate and improvement in ABG.

In our study ABG response is defined as:

1. Corrected: pH increased more than or equal to 7.35.
2. Improved: increase in pH by 0.05 - 0.1
3. Not improved: increase in pH by less than 0.05, by comparing the ABG's taken at 0, 1 and 6 hrs.

The patients were divided into responders (ABG corrected or improved) and non-responders (ABG not improved). Data was entered into Microsoft Excel spreadsheet 2007 and the statistical analysis was performed by using Graphpad Prism© version 4 USA®. The data was described as mean ±SD for continuous variables and frequencies/percentages for category variables. Between group analysis was performed by using Oneway ANNOVA followed by BONFERRONI multiple comparison test. A 2 tail p-value of less than 0.05 was considered statistically significant.

Results

During the study period, a total of 86 subjects were evaluated for acute respiratory distress and out of them 40 were enrolled into the study after acute exacerbation of COPD with respiratory failure was confirmed. Those subjects who met the inclusion and exclusion criteria were started on NIV. There were 37 male and 3 female patients with a mean age of 57.5 (SD±8.2) years. 40% of the study group was in the age group of 61-70 whereas 32.5% and 27.5% were in the ages between 51-60 and 40-50 respectively. The serial clinical and arterial blood gas parameters are shown in Table 2. There was significant improvement in the clinical (respiratory rate, pulse rate and blood pressures) and ABG (pH, $PaCO_2$) parameters in patients successfully responding to NIV. However the PaO_2 values and the SPO_2 tend to decline and all of the patients required supplemental oxygen which was delivered through a port available at the facial interface.

The biochemical response and clinical outcome is shown in Tables 3 & 4 respectively. Positive biochemical response (improvement in pH and reduction in $PaCO_2$) was achieved in 27 of the patients in 1st hour of NIV. However 3 (7.5%) patients showed

a delayed improvement by the end of 6th hour. There were 2 (5%) patients whose ABG improved in the first hour but worsened by the end of 6th hour. 32 (80%) patients improved clinically within 1 hour of the initiation of NIV; however 3 of them deteriorated and did not tolerate NIV.

Overall 29 (72.5%) patients improved, whereas 11 (27.5%) did not improve with NIV and 7 (63.63%) among them had to be intubated. Among the study group 25 (62.5%) patients showed a good ABG response with improvement in pH and decrease in $PaCO_2$ levels. Even among the Non responder group, 5 (12.5%) patients showed clinical improvement. ABG response could not be assessed in the remaining 5 (12.5%) patients. All patients were followed up till discharge. There were no deaths within the study period. The patients who did not show any clinical improvement by the end of 1st hour did not improve subsequently thereby proving that the 1st hour response is important in the outcome of NIV. The most frequent complication for which the NIV had to be discontinued was the worsening dyspnea and decreasing oxygen saturation. 2 (5%) of the patients developed altered sensorium and 2 (5%) others complained of abdominal distention. Only 1 (2.5%) had dryness of mouth as shown in Table 5.

Table 1: Demographic and physiological baseline characteristics

Number of Subjects (N)	40
Age in years	57.5±8.2
Males	37 (92.5%)
Females	3 (7.5%)
RR (per min.)	33.0±4.7
PR (per min.)	95.0±14.0
SBP (mmHg)	149.0±15.0
DBP (mmHg)	93.0±11.0
pH	7.30±0.1
PaO_2 (mmHg)	53.2±6.0
$PaCO_2$(mmHg)	70.0±15.0
SPO_2 %	85.0±5.7

RR-Respiratory rate, PR-Pulse rate, SBP-Systolic blood pressure, DBP-Diastolic blood pressure

Table 2: Hemodynamic and biochemical variables

Variables	**0 hrs**	**1hr**	**6 hrs**	**P value**		
				0 vs.1	**1 vs.6**	**0 vs.6**
RR (per min.)	33.0±4.7	31.0±4.9	27.0±4.1	P < 0.05	P < 0.05	P < 0.001
PR (per min.)	95.0±14.0	93.0±20.0	86.0±12.0	P > 0.05	P > 0.05	P < 0.05
SBP (mmHg)	149.0±15.0	147.0±19.0	139.0±12.0	P > 0.05	P > 0.05	P < 0.05
DBP (mmHg)	93.0±11.0	89.0±12.0	84.0±6.7	P > 0.05	P > 0.05	P < 0.01
pH	7.3±0.1	7.3±0.1	7.4±0.1	P > 0.05	P < 0.01	P < 0.001
PaO_2 (mmHg)	53.2±6.0	65.1±10.4	69.0±18.0	P > 0.05	P > 0.05	P > 0.05
$PaCO_2$ (mmHg)	70.0±15.0	64.0±15.0	61.0±11.0	P > 0.05	P > 0.05	P < 0.05
SPO_2 (%)	85.0±5.7	92.0±7.1	95.0±4.7	P > 0.05	P > 0.05	P < 0.05

Respiratory rate –RR, Pulse rate –PR, Systolic blood pressure-SBP, Diastolic blood pressure-DBP

Table 3: Biochemical response

Responders	1 hr.	27 (67.5%)
	6 hrs.	25 (62.5%)
Non responders	With clinical improvement	5 (12.5%)
	With no clinical improvement	5 (12.5%)
Response could not be assessed		5 (12.5%)

Table 4: Clinical outcome

Improved	1 hr.	32 (80%)
	6 hrs.	29 (72.5%)
Not improved	MV	7 (17.5%)
	DNR	2 (5%)
	AMA	2 (5%)

MV-Mechanical Ventilation, DNR-Do not resuscitate, AMA-Against medical advice

Table 5: Complications

Complications	N	(%)
Worsening SOB & falling saturation	7	17.5%
Diminished level of consciousness	2	5%
Abdominal distension	2	5%
Dryness of mouth	1	2.5%

Table 6: Baseline characteristics in various studies

Study	pH	PaO2	PaCO2
Our study	7.30±0.1	53.2±6.0	70.0±15.0
Agarwal et al	7.27±0.07	55.6±16.1	73.1±24.3
S.P. Rai et al	7.26	61.0	75.2
R. Prasad et al	7.307±0.03	41.11±10.74	79.11±14.17

Table 7: Comparison of 2nd sample of ABG

Variables	Present Study (1 hour)	Agarwal et al (1 hour)	S P Rai et al (2 hours)	R.PRASAD et al (2 hours)
pH	7.30±0.1 (>0.05)	7.33± 0.07	7.30 (> 0.05)	7.36±0.034 (0.0002)
PaO_2	65.1±10.4	61.5±9.7	63.08 (> 0.05)	65.0±18.83
$PaCO_2$	64.0±15	56.4±16.5	68.20 (< 0.05)	74.88±17.11

Table 8: Comparison of 3rd sample of ABG

Variables	Our study (6 hours)	Agarwal et al (4 hours)	S P Rai et al (24 hours)	R.PRASAD et al (24 hours)
pH	7.40 ± 0.1 (<0.01)	7.37 ± 0.07	7.34 (<0.05)	7.48±0.07 (0.0007)
PaO_2	69.0±18.0 (>0.05)	64.2±7.9	57.17 (<0.05)	72.17±18.59
$PaCO_2$	61.0±11.0 (<0.05)	53.6±14.9	59.40 (<0.05)	61.19±10.73

Discussion

The role of NIV has been studied in various acute respiratory conditions but was found to be more useful as an effective therapeutic modality along with standard treatment in the management of acute exacerbations of COPD. NIV is a cost effective, readily available technique and can be used safely outside the ICU [1]. The advantages of NIV include patient's comfort, preservation of airway defenses like cough, ability to eat and speak. The complications of endo-tracheal intubation such as nosocomial pneumonias, injury to airways, aspiration and post-intubation laryngeal stenosis can be avoided.

The baseline physiological characteristics of our patients at the onset of NIV were comparable to earlier Indian studies by Agarwal [2] et al, Rai [3] et al & Prasad [4] et al. In our study, the 2nd sample of ABG was taken 1 hour after the institution of NIV, where as in the studies by Rai et al and Prasad et al, the 2nd sampling of ABG was done at the end of 2 hours. Successful treatment with NIV is associated with an improvement in pH, PaO_2 and $PaCO_2$ within 1 hour of treatment. If the ABG parameters do not improve, invasive ventilation should be considered. There was a concern that delay in starting mechanical ventilation in severely ill patients may be harmful. But Conti [5] et al, in their prospective randomized controlled study of NIV versus immediate MV in patients with exacerbation of COPD showed that positive response to early use of NIV in a sicker group of patients is comparable to MV. Results of other studies [6] in more severely ill patients in outpatient setting were not as good as those seen in the ICU studies, suggesting that a NIV trial may be preferable in sick patients admitted in a higher dependency setting where a patient can be immediately switched over to MV, in case NIV fails. Retrospective analyses, uncontrolled studies, and some randomized controlled trials (RCTs) indicate that NPPV can be successfully initiated in the emergency department (ED) [7,8].

In our study, NIV was found to be successful in 72.5% cases causing rapid and sustained improvement in gas exchange in patients with respiratory failure. The overall success rate was similar to that described elsewhere, both from India [2,3,4] and the European-American countries [9,10].

In a prospective randomized placebo controlled trial by Thys et al in 2002 [11], it was found that clinical outcome was better with use of NIV support than with the conventional medical treatment alone. The application of NIV led to a true physiological improvement which could not be explained by placebo effect. Many recent studies have established the role of NIV in decreasing the morbidity and mortality in patients hospitalised for acute exacerbations of COPD [12,13,14].

In general, the factors predicting success of NIV in hypercapnic respiratory failure include pH at admission, pH after one hour of NIV trial and the severity of underlying illness. Short term application of NIV was well studied but very few studies evaluating the long term effectiveness of NIV in COPD with chronic respiratory failure are available.

The improvement in pH and the partial pressures of oxygen and carbon dioxide values of our study is comparable with that of the other studies as shown in Tables 6, 7 and 8. In our study as the 3rd sample of ABG was taken 6 hours later, whereas in the study by Agarwal et al the 3rd ABG sampling was done at the end of 4 hours. In the studies by Rai et al and R.Prasad et al, the 3rd ABG sample was delayed and taken after 24 hours of institution of NIV. Our study shows that 12.5% (n=5) of the patients who did not show initial biochemical response improved clinically proving that in chronic respiratory failure, ABG may take longer time to show improvement. Hence outcome assessment is based on the clinical improvement of the patient irrespective of the biochemical response. The patients who did not show any clinical improvement by the end of 1st hour did not improve subsequently thereby indicating that the 1st hour of NIV is important in predicting the outcome in COPD patients with respiratory failure. The disadvantages of NIV include slow improvement of blood gases, the need for a conscious and cooperative patient and decreased ability to clear bronchial secretions due to application of facemask. Ventilators specifically designed for NIV with a full face mask as an interface are recommended [15].There are no absolute contraindications to NIV although a number of them have been suggested. Nebulised bronchodilator therapy should be administered through the ventilator tubing if the patient is feared to go into respiratory distress during breaks of NIV [16]. Agitation and distress are commonly seen in patients with hypercapnic respiratory failures. Few recent studies have shown the effectiveness of mild anxiolytic drugs while on NIV with a caution for respiratory depression [17]. Ventilator-patient asynchrony is commonly encountered which causes increased discomfort and work of breathing ultimately leading to NIV failure. Increasing the trigger sensitivity and pressure support under continuous monitoring and assurance to the patients are key to successful outcome [18,19]. The optimum duration of NIV have not been extensively studied and normalisation of pH and pCO2 are usually considered as a guide to weaning. Further studies are required to evaluate the effect of NIV on reducing recurrence and severity of exacerbations of COPD.

Our study had limitations both technical as well as statistic. These include lack of an objective indicator as to when NIV should be discontinued. The relatively small number of patients and lack of a control group had an impact on the statistical analysis of group differences. The patients in the study group were monitored till discharge but the good initial response, however cannot predict long term outcome.

Conclusions

1. This study provides a strong evidence for the use of NIV (BIPAP) as a first line intervention in patients of acute exacerbations of COPD with respiratory failure. Continuous and efficient monitoring of patient's clinical and ABG status after NIV administration improves the outcome.
2. First hour clinical and biochemical response is a very important factor in the overall outcome. Supplemental oxygen therapy helps in maintaining the oxygen saturation as well as the PaO_2.
3. Early ABG sampling within one hour after initiating NIV does impact the clinical decision to streamline those who are successful in therapy and can be continued with NIV. Those who do not improve should be immediately considered for invasive ventilation, so that any adverse outcome due to delay in ventilatory support can be averted.
4. NIV can be safely administered in an emergency room with monitoring facilities and trained nursing staff.

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