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Early use of non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary diseaseon general respiratory wards: A prospective study

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***Abstract*---**Background- Chronic Obstructive Pulmonary disease (COPD) as defined by Global Initiative for Obstructive Lung Disease (GOLD) is a common preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Objectives-To evaluate outcome of NIV in terms ofTime for reversion of pH to normal, Duration of NIV, Hospital stay, Failure of NIV, Mortality and to compare the effect of noninvasive mechanical ventilation (NIV) in severelyacidotic (pH < 7.25) with mildly acidotic (pH 7.25–7.35) patients with acute hypercapnic chronic obstructive lung disease (COPD) Methods-This is a prospective observational study of COPD patients with acute Type 2 respiratory failure initiated on NIV conducted in Christian Medical College, Vellore, Tamil Nadu. The study was conducted in the Department of Pulmonary Medicine, Christian Medical College, Vellore.Assuming the mean as 12h (SD=6h), the sample size is Hence it is decided to sample 25 mild

acidosis and 25 severe acidosis cases for this study. In the present study, 53 patients were recruited from April 2017 to June 2018. 8 patients out of 53 patients were excluded as 4 patients had OSA and 4 patients were intubated in the Emergency Department. Out of 53 patients, 45 patients qualified for the study and were included in the study. SPSS (Version 22.0) was used for analysis. Results- The mean age of the study population is 66.51 ± 9.638. Majority of them were in the age group of 61-70 yrs and 71- 80 yrs each constituting 33.3%.Out of the 45 patients included in the study 31 (68.9 %) were males and 14 (31.1%) were females. In the present study, 44 (97.7%) were treated successfully with NIV and 1 patient (2.2%) died due to failure of NIV.Average time (in hours)for reversion of pH was 19.00±14.036. With minimum of 2 hrs and maximum of 84hrs. NIV was used for an average of 61.31± 22.701 with minimum of 12hrs and maximum of 120hrs. Conclusion-This study provides strong data that the provision of NIV is similarly effective in severe and mild acidotic hypercapnic COPD patients. Second, this can be achieved in a non ICU respiratory ward with educated staff. Whether this is related to the experience of the unit providing care is as yet unknown. However further studies are required to establish this and to evaluate potential predictors of success for better outcomes with NIV.

***Keywords*---**arterial blood gas, acute exacerabation, chronic obstructive pulmonary disease, arterial oxygen content, endotracheal intubation, non-invasive ventilation.

Introduction

Chronic Obstructive Pulmonary disease (COPD) as defined by Global Initiative for Obstructive Lung Disease (GOLD) is a common preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients.When the capacity of ventilation is overwhelmed, it leads to development of Respiratory failure. NIV(Non Invasive ventilation) is used to offset this excess load on the ventilator system and augments the work of breathing[1] .One of the major advances in the management of hypercapneic respiratory failure has been the ability to avoid endotracheal intubation by using of non-invasive modes. NIV works by increasing the ventilator capacity by decreasing the work of breathing and by augmenting the tidal volume.[2] The use of NIV has become a global practice, being incorporated in various guideline, however its use in Chronic Hypercapneic respiratory failure is mired in controversies.[3,4,5]In acute exacerbations , the equilibrium of load-capacity and drive relationship is disturbed by the increased load exerted on the system than it can bear.[6] This disturbance can be mediated by alteration in the resistance of the airways, chest wall elastance and development of intrinsic PEEP.[7] This manifests as increased work of breathing with trans-diaphragmatic pressures being significantly increased during acute exacerbations of COPD.[8,9]This study was contemplated as NIV has become the standard of care in

our institution, particularly in the department of pulmonary medicine and used in a substantial number of patients. The existing guidelines about the use of NIV are based on studies with small number of subjects and coming from western hemisphere with advanced and adequate medical infrastructure available with a lower threshold for intubation. So rationale behind the study is to find the predictors of success in management of acute exacerbation of COPD in patients on NIV.

Materials and Methods

This is a prospective observational study of COPD patients with acute Type 2 respiratory failure initiated on NIV conducted in Christian Medical College, Vellore, Tamil Nadu.The study was conducted in the Department of Pulmonary Medicine, Christian Medical College, Vellore. Patients admitted with Type 2 respiratory failure secondary to acute exacerbation of COPD were enrolled in the study. Taking ABGs are a routine standard of care for those patients who are on NIV and the same will be utilised. Relevant clinical data and lab values will be recorded in clinical research form.The study was conducted between April 2017 to June 2018.During the study period, patients admitted in Pulmonary medicine as in patients with acute type 2 respiratory failure secondary to exacerbation of COPD were enrolled in the study.

Assuming the mean as 12h (SD=6h), the sample size isHence it is decided to sample 25 mild acidosis and 25 severe acidosis cases for this study.In the present study, 53 patients were recruited from April 2017 to June 2018.8 patients out of 53 patients were excluded as 4 patients had OSA and 4 patients were intubated in the Emergency Department. Out of 53 patients, 45 patients qualified for the study and were included in the study

Inclusion Criteria

Patients were regarded as having COPD based upon clinical history, radiological and lung function parameters were included if they were

1. Dyspneic/Tachypneic,
2. Hypercapnic (PaCo2>45 mmhg),
3. Acidotic (ph<7.35)
4. Breathing spontaneously on presentation in the emergency department

Exclusion Criteria

1. Cardiac instability or pulmonary oedema or myocardial infarction or congestive heart failure
2. Pneumothorax,
3. Inability to protect their airway
4. A history of asthma on prior testing
5. Facial injuries and facial fracture or facial abnormalities (due to mask leaks – ineffective)
6. Abdominal distension with risk of aspiration
7. Gastro-intestinal bleed

8. OSA-COPD overlap
9. Recent surgery to upper airway or gastro-intestinal tract
10. Tracheostomy
11. Those who do-not provide a written consent or opt out of the study or do not complete the entire duration of management or discharged against medical advice.

Statistical Analysis

All statistical analysis were performed using SPSS version 22.0 (Statistical Package for Social Sciences, Chicago, USA). All data were tested for normality of distribution using Shapiro–WilkWtests. Parametric data were expressed as mean+/- SD and nonparametric data as median (IQR) unless otherwise stated. Parametric data were compared using the unpaired Student'st-test and for nonparametric data comparisons were made for unpaired samples using the Mann–Whitney U-test. Correlations were performed using Spearman's rank correlation test. Chi square test was used to compare nominal data. P values<0.05 were accepted as statistically significant. Missing data were appropriately excluded from the analysis.The study was presented to the Institutional review board and was approved by it and by the ethics committee of Christian Medical College, Vellore (IRB Min No: 10267 IOBSERVE] dated 05.09.2016).

Results

Table 1- Demographic and baseline characteristics of the study population

CHARACTERISTICS OF THE PATIENTS	
Total no of patients (n)	45
Age(yrs)	66.51±9.63*
Sex ratio (M: F)	31:14
Height in cm	158.93±10.28*
Weight in kg	62.76±16.28*
BMI	25.340±8.22*
Respiratoryrate	25.02 ±4.30*
Heart rate	92.91±15.03*
Systolic BP	119.56±12.78*
Diastolic BP	76.84 ±7.85*
SAPS II score	43.38±8.67*
GCS	1.069±14.36*
Total Counts	12442.22 ± 6582.60*
Blood Urea	42.82 ±26.55*
PaO2/Fio2	255.44 ±132.19*
Number of patients on LTOT	5 (11.1%)
No. of patients with radiological evidence of pneumonia	15 (33.3%)
pH at presentation	7.29 ± 0.02*
PaCO2 at presentation	67.3 ± 5.61*

Never Smokers	15(33.3%)
Current Smokers	11(24.4%)
Reformed Smokers	1(2.2%)
Ex-Smokers	18(40%)
Biomass Fuel Exposure	15(33.3%)
Comorbidities	
Congestive Heart Failure	1 (2.2%)
Hypertension	19 (42.2%)
Diabetes	20 (44.4%)
Hypothyroidism Renal	1 (2.2%)
Hepatic Neoplasia	1 (2.2%)
Probable OSA History of	0
PTB	0
Pulmonary	9(20%)
Hypertension	10(22.2%)
Pulmonary Embolism	11(24.4%)
	0

As per table 1 The mean age of the study population is 66.51 ± 9.638. Majority of them were in the age group of 61-70 yrs and 71- 80 yrs each constituting 33.3%.Out of the 45 patients included in the study 31 (68.9 %) were males and 14 (31.1%) were females.Out of the 45 patients included in the study 9 patients (20 %) belonged to Group-A, 14 patients (31.1%) belonged to Group-B, 3 patients (6.7%) belonged to Group-C, 19 patients (42.2%) belonged to Group-D.The most common symptom on presentation was breathlessness seen in all the enrolled patients. Cough was present in 37 patients, i.e., 82.2%. A relatively small number of patients, 13 patients (28.9%)% and 3 patients(6.7%) respectively, also had fever and chest pain on presentation.

Table 2- Outcome with NIV

Outcome with NIV	
Successn(%)	44(97.7%)
Failure n(%)	1(2.2%)
Mortality n(%)	1(2.2%)
Time for reversion of pH in hours (Mean±SD)	19.00±14.036
Total duration of NIV inhours (Mean±SD)	61.31± 22.701
Days towean (Mean±SD)	3.96± 1.551
Duration of hospital stay in days (Mean± SD)	6.672±0.620
Total Cost of Admission in rupees (Mean±SD)	55492.62±32132.84

As per table 2 In the present study, 44 (97.7%) were treated successfully with NIV and 1 patient (2.2%) died due to failure of NIV.Average time (in hours)for reversion of pH was 19.00±14.036. With minimum of 2 hrs and maximum of 84hrs. NIV was used for an average of 61.31± 22.701 with minimum of 12hrs and maximum of 120hrs. Average time (in days) to wean was 3.96± 1.551 with minimum of 1 day and maximum of 6 days. The mean duration of hospital stay was 6.672±0.620 with minimum of 3 days and maximum of 15 days.The mean cost of hospital stay in rupees was 55492.62±32132.84 with minimum of Rs.20,396 and maximum of Rs.2,07,778.

Table 3- Comparison Between Mild and Severe Acidosis Group

CHARACTERISTIC OF THE PATIENT	Mild Acidosis (N=25)	Severe Acidosis (N=20)	P Value
Age(yrs)	64.28±8.84	69.30±10.07	0.082
Gender, male,n(%)	17 (68%)	14(70%)	0.885
Height in cm	158.20±10.02	159.85±10.78	0.598
Weight in kg	66.84±18.35	57.65±11.78	0.048
BMI	27.168±9.34	23.055 ±6.01	0.096
COPD Group (A,B,C,D)	4,8,2,11	5,6,1,8	0.936
First Time Diagnosed,n%	6(24%)	5(25%)	1.000
On irregular medications,n%	14(56%)	9(45%)	0.793
On regular medications,n%	5(20%)	6(30%)	0.793
Dyspnoea,n%	25(100%)	20(100%)	-
Cough,n%	20(80%)	17(85%)	0.716
Increased sputum purulence,n%	9(36%)	6(30%)	0.671
Increased sputum volume,n%	9(36%)	6(30%)	0.671
Fever,n%	8(32%)	5(25%)	0.607
Chest Pain,n%	2(8%)	1(5%)	1.00
Hemoptysis,n%	0	0	-
Respiratoryrate	24.20±2.56	26.05±5.71	0.155
Heart rate	93.72±15.53	91.90±14.72	0.691
Systolic BP	117.60±13.31	122.00±11.96	0.256
Diastolic BP	75.92±9.00	78.00±6.15	0.364
SAPS II score (mean (SD))	41.16±7.63	46.15±9.29	0.054
GCS	14.60±0.81	14.05±1.27	0.104
Total Counts	12068.00±6575.82	12910.00±6731.22	0.675
Blood Urea	38.64±26.87	48.05±25.86	0.193
PaO2/Fio2	271.72±127.66	235.10±138.19	0.362
Number of patients on LTOT	2(8%)	3(15%)	0.642
Na	133.20±5.62	130.40±7.66	0.165
K	4.212±0.52	4.720±0.51	0.002
HCo3-	29.52±2.93	25.49±4.33	0.001
No. of patients with radiological evidence of pneumonia	7(28%)	8(40%)	0.396

pH at presentation	7.2992±0.02	7.1855±0.04	<0.0001
$PaCO_2$ at presentation	70.72±11.78	84.85±15.81	0.002
Never Smokers,n%	8(32%)	7(35%)	0.614
Current Smokers,n%	5(20%)	6(30%)	0.500
Reformed Smokers,n%	1(4%)	0	1.000
Ex-Smokers,n%	11(44%)	7(35%)	0.54
Biomass Fuel Exposure,n%	8(32%)	7(35%)	0.832

As per table 3 The two groups were similar in baseline characteristics. There was a tendency for patients with a mild acidosis to have more weight which was statistically significant (P=0.048).There was a tendency for patients with a mild acidosis to have more BMI but it was not statistically significant (P=0.096).Blood urea of severe acidotic group tended to be more but it did not reach statistical significance (Mild-38.64±26.87 ; Severe-48.05±25.86; P=0.193).Serum K+ of severe acidotic group tended to be more and was statistically significant (Mild acidosis-4.212±0.52; Severe acidosis -4.720±0.51; P=0.002). But it was clinically insignificant.Serum Hco3- of mild acidotic group tended to be more and was statistically significant (Mild acidosis -29.52±2.93; Severe acidosis -25.49±4.33; P=0.001). But it was clinically insignificant.As expected the pH was significantly lower and PaCO2 was significantly higher in the severe acidotic group (P<0.0001, P=0.002, respectively).

Discussion

A significant number of acute exacerbations of COPD are associated with hypercapnic respiratory failure. Ventilatory management in such patients include both NIV and invasive mechanical ventilation. Numerous studies have been conducted at many centers in the past and highlighted the benefits of NIV usage in acute exacerbation of COPD in terms of reduced need of endotracheal intubation and invasive mechanical ventilation, shorter length of hospital stay and decreased mortality. This present study was undertaken to understand the role of NIV in patients with acute hypercapnic respiratory failure due to acute exacerbations of COPD, to determine the predictors of success and outcome of NIV in such patients and compare the effect of NIV in severely acidotic (pH < 7.25) with mildly acidotic (pH 7.25–7.35) on time to normalise pH, to improve PaCO2, duration of NIV treatment, length of stay in hospital and survival. In this study NIV was successful in 44 patients and failed in 1 (2.2%) patient with a success rate of 97.7%. The reported success rates in the patients treated with NIV in previous controlled studies were :Plant et al[10]- 85% (100/118), Brochard et al[11] - 74%, Celikel et al[12] - 93.4 % (14/15), Avdeev et al[13] - 88%, Verma at al[14] - 90%. The results obtained in our study were comparable to the above mentioned studies.In the present study, 1 patient (2.2%) died due to failure of NIV leading to a failure rate of 2.2% and mortality rate of 2.2%. A low mortality rate in this study was nearer to the study done by Brochard et al[11] where it was 9% with the use of NIV. Use of NIV was associated with rapid improvement in gas exchange, decreased need for endotracheal intubation and decreased complications. Patient who died was a 77 year old lady who was a known COPD- Group-B patient on regular medications and regular Influenza and Pneumococcal vaccinations and had severe acidosis at presentation with pH-7.4 and PaCo-69. She was a known hypertensive and had Pulmonary hypertension. She was a non-smoker but had

significant biomass fuel exposure.In the present study, mean duration of hospital stay was low with the use of NIV i.e. 6.672±0.62 with minimum of 3 days and maximum of 15 days. The results were comparable to study done by Rizvi et al where length of hospital stay was 10.6±5.6 days (range 3 to 23 days).[15] Rapid reversal of blood gases, absence of sedation, reducednumber of complications and shorter weaning time of NIV, all probably contribute in shortening the hospital stay. The shorter hospital stay with the use of NIV may be cost effective as compared to conventional treatment alone where hospital stay is long. The mean cost of hospital stay in Rs. was 55492.62±32132.84 with minimum of Rs. 20,396 and maximum of Rs.2,07,778.There was a significant improvement in pH after 1-2 hr of NIV (Mild acidosis-7.3128±0.05; Severe acidosis-7.2665±0.07; P=0.018). In mild acidotic group pH improved from 7.2992±0.02 at baseline to 7.3128±0.05 at 1-2 hrs. In severe acidotic group pH improved from 7.1855±0.04 at baseline to 7.2665±0.07 at 1-2 hr. The improvement in pH is similar to study done by Fionnuala Crummy et al where in mild acidotic group pH improved from 7.29±70.03 to 7.32±70.04 after 1hr and in severe acidotic group pH improved from 7.15±70.1 to 7.27±70.1 after 1hr.[16] Improvement in pH was similar in two groups at 4-6 hrs,10-12hrs and 24hrs but did not reach statistical significance.

Conclusion

The primary aim of the study was not achieved as there was low failure rate i.e., only 1 patient (2.2%) failed while on NIV and ultimately died. However, the results in the present study showed that NIV is a promising therapeutic modality for management of patients with exacerbations of COPD who have respiratory acidosis even after standard medical therapy with success rate of success rate of 97.7%. Its timely institution leads to a rapid and profound improvement in blood gas variables that culminates into avoiding intubation and invasive ventilation with its associated complications. The protocol is simple to implement and monitor.

In the present study, the results showed that both mild acidotic group(pH -7.25-7.35) and the severe acidotic group(pH < 7.25) took a similar length of time for pH to normalise ,with similar duration of NIV treatment, days to wean, NIV requirements (IPAP and EPAP) and hospital length of stay. Outcome with NIV was successful in 25 patients (100%) in mild acidotic group and 19 patients(95%) in severely acidotic group.

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Conflict of Interest- None declared

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