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NON INVASIVE VENTILATION (NIV) IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) WITH HYPERCAPNIC RESPIRATORY FAILURE

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ABSTRACT
Use of noninvasive ventilation in patients with COPD has found to be effective in improving outcomes at lower costs, however there is dearth of information in patient populations unique to our context. We studied the patient characteristics that could identify and predict the successful outcome of NIV. Fifty patients of COPD were enrolled in this prospective cohort study. Successful outcomes on NIV were defined as an improvement in physiological and clinical parameters allowing cessation of NIV. 68% of patients improved on NIV on regular ward basis. Patients who improved were less acidotic (pH=7.28), less hypercapnic (PaCO2= 80.56) at presentation than those who failed to improve. Absence of Cor-pulmonale, Respiratory Rate <30 and normal serum protein at presentation were additional predictors of good outcome. NIV improves outcome at lower costs and therefore it should be is considered a standard of care to be initiated in the regular medical wards.

KEY WORDS: ventilation, COPD, NIV, Hypercapnic.

INTRODUCTION
Noninvasive ventilation (NIV) came into consideration as an alternative to invasive mechanical ventilation in acute respiratory failure caused from exacerbations of chronic obstructive pulmonary disease (COPD) in the 1980s, and its use has gradually increased since then. Effectiveness of the same has been supported by results of systematic reviews,[1] and this has led to an increase in the application of this treatment, even in complicated situations such as a do-not-intubate order in elderly patients.[2]

The use of NIV has increased significantly over time among patients hospitalized for acute exacerbation of COPD. It has been studied in randomized controlled trials showing a success rate of 80-85%[3-6].There are no available data or literature on the impact of NIV in Nepal. In country like Nepal, the burden of COPD is very high and ICU beds are limited. NIV seems to be a better option for management in patients with acute exacerbation. There is dearth of information on how well NIV is tolerated in patient populations unique to our context. Within this magnitude of the problem and background, we conducted the study to identify variables predictive of outcome in patients with acute hypercapnic respiratory failure treated with NIV.

METHODS
We conducted Prospective cohort study in the Medicine ward, Department of Internal Medicine of B. P. Koirala Institute of Health Sciences (BPKIHS, Dharan, Nepal). Patients of Chronic Obstructive Pulmonary Disease (COPD) presenting with hypercapnic Respiratory failure were enrolled in study for a period of one year from 1st February 2012. Fifty (50) consecutive Patients of Chronic Obstructive Pulmonary Disease (COPD) presenting with hypercapnic Respiratory failure were enrolled in study for a period of one year from 1st February 2012. This sample size was taken based upon published literature to conduct such studies for convenience and practicality. A verbal and informed written consent was taken. Chronic Obstructive Pulmonary Disease was diagnosed as per the American thoracic society (ATS) guidelines and from previously validated diagnostic criteria at our institute. For the purpose of the present study, hypercapnic respiratory failure was defined as PaCO2≥45mmhg on Arterial Blood Gas (ABG) analysis.

People not giving consent, people having facial deformity sufficient to affect mask fitting, severe encephalopathy unrelated to hypoxemia and/or hypercapnia, overt gastro-intestinal bleeding, acute ischemic heart disease and those who needed urgent endotracheal intubation due to cardiac or respiratory arrest, prolonged respiratory pauses and psychomotor

agitation requiring sedation were excluded from our study. A detailed socio-demographic data for every patient was collected and the information was recorded in structured proforma.

Procedure

After informed and written consent NIV (Resmed) was initiated in all patients in bilevel positive airway pressure (BiPAP) mode with inspiratory positive airway pressure (IPAP) of 8cm of H_2O and expiratory positive airway pressure (EPAP) of 4 cm of H_2O. Oxygen was supplied through separate port. IPAP and EPAP were increased every 30 minutes to a maximum 20 cm of H_2O and 16 cm of H_2O respectively.

RESULTS

During the study period of one year, we enrolled 50 patients in our study. The baseline characteristics of the study population are displayed in Table 1.

Table 1: Socio demographic and clinical characteristics of COPD patient enrolled.

Characteristics	Categories	Percentage (n=50)	Mean±SD
Age(in years)	50-59	18.0	69.66±8.87
	60-69	24.0	
	70-79	44.0	
	80+	14.0	
Sex	Male	44.0	
	Female	56.0	
Occupation	Exposure to indoor pollution	70.0	
	Farmer	30.0	
BMI (Kg/m^2)	<18.5	10.0	23.27±4.39
	18.5-24.99	58.0	
	>25	32.0	
Smoking Status (pack yrs)	0	2.0	
	<20	30.0	
	20-40	48.0	
	>40	20.0	
Respiratory rate (Number/minute)	<30	28.0	34.56±6.37
	>30	72.0	
Hematocrit	<45	80.0	43.09±5.78
	>45	20.0	
Total Leukocyte count (no/mm^3)	<11,000	62.0	10692±3786
	>11,000	38.0	
Total Protein(mg/dl)	<6.4	40.0	6.68±0.89
	>6.4	60.0	
Serum Albumin(mg/dl)	<3.5	54.0	3.44±0.59
	>3.5	46.0	
Ph	<7.25	38.0	7.27±0.89
	>7.25	62.0	
$PaCO_2$(mm of Hg)	60-80	42.0	85.69±15.69
	>80	58.0	
PaO_2(mm of Hg)	<60	4.0	95.55±25.76
	>60	96.0	
HCO_3	<30	50.0	30.75±7.53
	>30	50.0	

NIV was continued along with standard therapy in those who improved. It was continued for minimum of 9hours to maximum of 22 hours with mean of 13.3±0.7 hours. Treatment success was defined as an initial improvement in physiological and clinical parameters allowing cessation of NIV, while failure was defined as clinical and or physiological deterioration resulting in transfer to intensive care. The causes of failure were classified in two groups, failure due to clinical cause (clinical worsening supported by ABG and lab parameters) and failure due to mechanical cause (i.e., inability to tolerate the interface). 34(68%) of our study population improved on NIV and remaining 16(32%) patients failed to improve.

Overall outcome of NIV was successful in 34(68%) of our population showing significant improvement in clinical and blood gas values with the use of NIV. 50% of those who had cor-pulmonale didn't improve on NIV, P=0.02, RR=2.8 (CI=1.14-6.87). Total protein and serum albumin levels were both lower in the groups who didn't improve. Mean serum albumin levels of those who didn't improve was 3.11±0.59, and it was 3.61±0.53 in those who improved, P=0.05, RR=2.55(CI=0.95-6.84). On

blood gas analysis, we found that patient who didn't improve on NIV were more acidemic than those who improved, Mean pH 7.26±0.08 versus 7.28±0.09. Similarly, those with $PaCO_2$ more than 80 mmHg has 1.62 times lesser chance of improving then those with $PaCO_2$ less than 80 mmHg.

Table 2. Clinical characteristics, laboratory parameters and blood gas analysis by outcome of COPD patients enrolled.

Characteristics	Categories	Improved on NIV		P-Value	Relative risk	95% Confidence Interval	
		Yes	No			Lower limit	Upper limit
Age(Years)	<70	15	10	0.23	0.6	0.25	1.39
	>70	19	6				
Sex	Male	16	6	0.52	1.31	0.56	3.04
	Female	18	10				
BMI(Kg/m^2)	<18.5	3	2	0.69	1.28	0.40	4.09
	>18.5	31	14				
Cor-Pulmonale	Present	11	11	0.02	2.8	1.14	6.87
	Absent	23	5				
Respiratory rate(no/minute)	<30	12	2	0.05	2.72	0.7	10.47
	>30	22	14				
Pneumonia	Present	27	14	0.53	1.53	0.42	5.60
	Absent	7	2				
Hematocrit	<45	29	11	0.20	1.81	0.81	4.03
	>45	5	5				
Total Protein (mg/dl)	<6.4	13	7	0.71	1.16	0.51	2.62
	>6.4	21	9				
Serum Albumin(mg/dl)	<3.5	15	12	0.04	2.55	0.95	6.84
	>3.5	19	4				
pH	<7.25	13	6	0.96	0.97	0.42	2.25
	>7.25	21	10				
$PaCO_2$(mm Hg)	<80	21	8	0.43	1.38	0.40	3.08
	>80	13	8				
PaO_2(mm Hg)	<60	2	0	0.93	1.04	0.19	5.45
	>60	32	16				
HCO_3	<30	14	11	0.07	1.42	0.18	1.11
	>30	20	5				

Table 3. Comparison of Characteristics between those who improved on NIV and those who did not.

Characteristics	Improved on NIV	Not-Improved on NIV
Mean age(Years)	68.15±8.32	72.88±9.41
BMI(kg/m^2)	23.56±4.10	22.65±5.05
Respiratory rate(Baseline)	32.29±5.33	39.38±5.83
Pneumonia	79.41%	87.5%
Hematocrit	41.99±5.79	45.45±5.18
Total leukocyte count	10482±3350	11137±4673
Total protein (mg/dl)	6.75±0.95	6.52±0.77
Serum albumin (mg/dl)	3.61±0.53	3.11±0.59
Mean pH	7.28±0.09	7.26±0.08
Mean $PaCO_2$	80.56±14.77	96.61±11.73
Mean PaO_2	100.09±25.70	85.91±23.83
Mean HCO_3	29.23±6.49	33.99±8.74

Those who improved on NIV had significant changes in pH at 1-2 hours and 4-6 hours compared to those who did not improved. pH level was normal at 6 hours in those who improved. Similarly those who improved had less hypercapnia at baseline, at 1-2 hours and even at 4-6 hours. On NIV majority of patients had significant improvement in respiratory rate within 6 hours. (Figure 1, 2, 3).

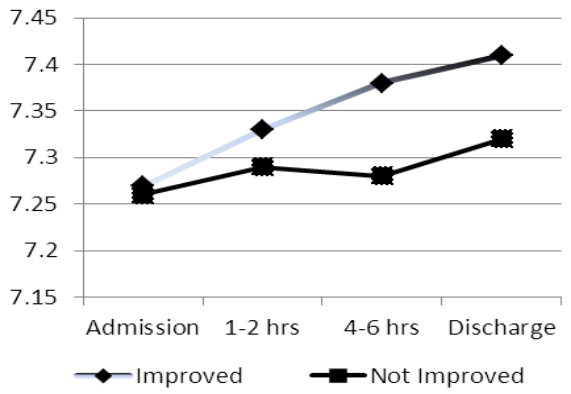

Figure 1. Change in pH with time in Patients with Hypercapnic Respiratory Failure on NIV

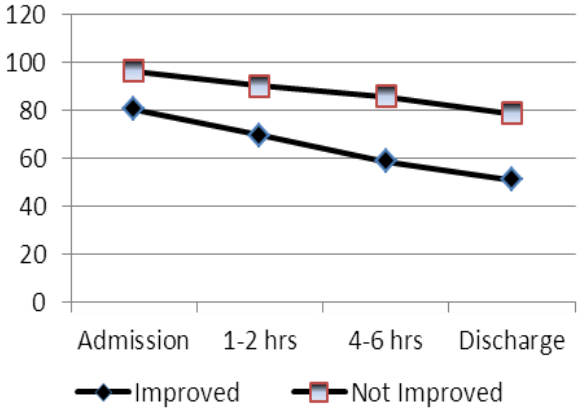

Figure 2. Change in $PaCo_2$ with time in Patients with Hypercapnic Respiratory Failure on NIV

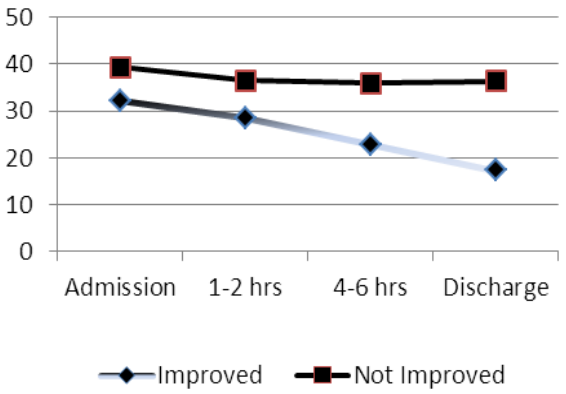

Figure 3. Change in Respiratory with time in Patients with Hypercapnic respiratory failure on NIV

DISCUSSION

Mean age of patients admitted in our study was 69.66 years which was consistent with other similar studies conducted by Plant et al (2000)[7]- mean age of 69 years, Keenan et al (2005)[8] -mean age of 69 years, McLaughlin et al (2009)[9]-mean age of 71 years.

In our study female predominance among COPD cases was observed. Male: Female differences in respiratory diseases are often divided into sex-related (biological) and gender related (environmental and socio-cultural) differences. Female smokers have been found to be more susceptible to the lung damaging effects of smoking than men, they probably experience reduced lung functions and COPD at a lower level of exposure and/or at an earlier age than men.[10] Recently, a meta-analysis demonstrated that beyond 45 years of age, female smokers had a faster annual decline in FEV1 than male smokers.[11] Our study revealed that 98% of patients were smoker which reflects increasing trends of tobacco smoking in this particular population. In Nepal 33.7% of urban population and 46.35% of rural population smokes tobacco. Another striking finding in our study was 52% of female were housewives and they had significant exposure to indoor pollution due to use of biomass fuels. In developing countries women and young girls spend more time in proximity to biomass smoke, with average of 4-6 hours of daily in kitchen, enclosed space with poor ventilation. Exposure to biomass fuel smoke was found to be associated with 2.3 fold of increased odds of COPD compared with no exposure to biomass smoke in recent meta-analysis conducted by HU et al.[12]

We found that 44% of the patients had clinical and Electrocardiographic evidence of Cor-pulmonale. The reported prevalence varies considerably from 20%–91% (Scharf et al 2002[13]; Thabut et al 2005[14]).

Our findings has shown that in selected patients with an acute exacerbation of COPD with hypercapnic respiratory failure necessitating NIV, 80% of patients were ultimately discharged from hospital, 68% of patients improved on NIV on regular ward basis, whereas 18% of them were transferred to Intensive care Unit for invasive ventilator support. Out of 14 %(N=7) of patient who didn't tolerate NIV, 6 of them improved. Failure because the patient could not tolerate NIV needs to be distinguished from patients who tolerate NIV but still deteriorate. In those who don't tolerate NIV, ventilation using alternate route may be successful.

Our literature search identified various series that describe the use of NIV for hypercapnic respiratory failure on regular ward basis. Similar study conducted elsewhere reported success rate very much comparable with our study. Farha et al (2006)[15] reported a success rate of 69% (N=76), Mclaughlin et al (2009)([9]) reports success rate of 67% (N=392), whereas in Southeast Asia Singh et al (2006)[16] reports 74% success rate (N=50). Success rate observed in our study is lower than that reported by Farha et al, it could be because patients enrolled in our study were older (69.66 years vs. 63 years), more hypercapnic (PaCo2=85.69 vs. 77 mm of Hg). Plant et al (2000) reported a failure rate of only 15 %, much lower than our study.

Need for intubation and invasive mechanical ventilator support in our study was 18% much lower than those reported by Brochard et al, Mclaughlin et al and Singh et

al, but higher than that of Farha et al and plant et al. In our patients, the overall mortality was 10%, and 10% of patients left hospital against medical advice, although it needs to be pointed out that patients were included in our analysis irrespective of co-morbidities, age or presence of electrolyte disturbance. Plant et al reported a mortality of 20% in controls compared with 10% in those receiving NIV (P=0.05). Avdeev et al.[17] reported a reduction of mortality from 31 to 8% favoring NIV (P<0.05) while Bott et al.[18] report a significant reduction for patients receiving NIV compared with usual medical care (4 vs. 30%, respectively, P=0.0104). Patients who failed to improve were older than those who improved. (72 vs. 68 years). Presence of cor-pulmonale was associated with poor outcome in our study (P=0.02, RR=2.8, 95% CI=1.14-6.87). Cor-pulmonale in cases of COPD correlates with severity of disease and associated with poor outcome[19]. Presence of Pulmonary Hypertension doubles the mortality in COPD (Oswald-Mammosser et al 1995[20]). Studies showed an increase in PAP between 1.5–2.8 mm Hg/year (Weitzenblum et al 1985[21]). Those who develop severe PH (mPAP >40 mm Hg) suffer an extremely poor prognosis (5-year survival ~15% vs~55% in those with less severe PH (mPAP 20–40) (Chaouat et al 2005[22]).

Patients who improved on NIV were less acidotic (pH=7.28 vs. 7.26), less hypercapnic ($PaCO_2$= 80.56 vs. 96.61) than those who failed to improve. Similarly baseline respiratory rate was significantly higher in those who failed to improve (39 vs. 32, P=0.05, RR=2.72, 95% CI=0.7-10.47). Severity of acidosis and hypercapnia at baseline has been found to be strongly associated as a predictor of poor outcome in various studies. In our study too, acidosis and hypercapnia was more in those who didn't improve. Although NIV is less likely to be effective when patients are more acidotic this should not preclude a trial of NIV as the mode of ventilator support of first choice because the benefits of NIV compared with intubation and mechanical ventilation are greater.[23]

SUMMARY AND CONCLUSION

Non-Invasive ventilation (NIV) is becoming a rapidly upcoming modality in the management of respiratory failure due to COPD; however there was dearth of information on how well NIV is tolerated in patient populations unique to our context.

Findings from our study indicate that, in selected patients with an acute exacerbation of COPD with hypercapnic respiratory failure necessitating NIV, clinical improvement can be achieved in 68% of patients by using NIV on regular ward basis, whereas 18% might require transfer to Intensive care Unit for invasive ventilator support, however 80% of these patients can ultimately be discharged from hospital with acceptable clinical improvement.

Among our patients who failed to improve on NIV, the causes of failure was clinical (56.25%) followed by mechanical (43.75%) i.e., inability to tolerate the interface.

Presence of Cor-pulmonale, Respiratory Rate >30 and Hypoalbuminemia at presentation were the predictors of failure and these factors can predicts poor outcome of NIV. All these patients would require invasive ventilation in the COPD sooner or later. In clinical practice, in patients presenting with COPD and hypercapnia, failure to improve on NIV because of inability to tolerate NIV needs to be distinguished from patients who tolerate NIV but still deteriorate.

In those who don't tolerate NIV, ventilation using alternate route may be successful. By contrast, those who fail despite being able to tolerate NIV are likely to have a poor outcome regardless of further ventilator support, because of more severe lung disease prior to the exacerbation.

Our study provides convincing evidence that use of NIV, especially in the early course of disease, can revolutionize the management of patients with acute exacerbation of COPD. NIV seems to be a better option for management of patients presenting with COPD and with less severe ARF and without failure of any other organ because it significantly reduces the intubation, complication, and mortality rates.

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Conflict of interest

Conflicts of interest declared none.

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