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Original Research Article

Role of CPAP by Nasal Mask and Tiotropium in Patients of COPD in Acute Exacerbation

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Abstract

Background: The patient of COPD can land into respiratory failure, which could be acute, acute on chronic or chronic. These patients need ventilatory support that could be invasive or non-invasive. CPAP is a safe modality of non-invasive ventilation. These patients may be given bronchodilators, which include methylxanthines, B2 agonists and anticholinergics. Tiotropium is a new anticholinergic, which has shown promising results in the management of COPD. Hence this study was undertaken to assess the role of CPAP by nasal mask and Tiotropium in patients of COPD in acute exacerbation.

Material and Methods: The present study was undertaken in a total of 25 patients, who were known cases of COPD diagnosed by history and clinic investigatory methods (later on confirmed by spirometry). After proper selection of patients as per our inclusion criteria, the patients were given a trial of CPAP via a nasal mask along with bronchodilators through nebulization. ABG parameters (like PaO2, PaCO2 and pH), SaO2, RR and dyspnea were compared before and after the intervention with CPAP and Tiotropium. These parameters were analyzed to assess the response of CPAP and Tiotropium in patients of acute exacerbations of COPD.

Results: Out of 25 patients, 10 (40.0%) were of the age group 51-60 years followed by 8 (32%) patients of 41-50 years age group. 20 (80%) were males, while the rest 5 were females. 13(52%) cases had moderate impairment in FeV1, while 9 (36%) had severe impairment. Mean PaCo2 of 68.15(±1.95) is seen among GOLD II cases, while 70.89(±4.11) and 76.00(±1.63) were the mean PaCo2 among grades III and IV patients.

Conclusion: Intervention with CPAP and bronchodilators are associated with improvements in various parameters like PaCO2, PaO2, pH, SPO2 and RR. Improvement was also seen with subjective parameters like breathlessness, cough and wheezing

Keywords: COPD, GOLD, CPAP, Tiotropium, Anticholinergic

Introduction

COPD is characterized by airflow obstruction, and bronchodilators are central to its management [1]. The aims of pharmacological therapy for COPD are to prevent and control symptoms, reduce the frequency and severity of exacerbations, and improve health status and exercise tolerance [1]. Improvements in FEV1 produced by bronchodilation correlate with improvements in breathlessness and health status as well as reduced exacerbation rates [2]. Exacerbations are an important component of COPD [3,4], significantly impacting on the burden of disease [5], leading to a worsening health status and increased risk of future exacerbations and death [6,7]. Exacerbations are also strong predictors of disease progression, quality of life, and prognosis [7,8]. Some patients may be more prone to exacerbations , and the prevention of exacerbations is a priority goal in COPD management [1]. In India COPD is the 2nd most common cause of lung disorder after pulmonary tuberculosis. It is equally present in rural and urban areas. In India its prevalence is 4.38/1000 in males and 3.4/1000 in females and its incidence is rising. In these patients, the labour of breathing is more. The patient of COPD lands into respiratory failure, which could be acute, acute on chronic or chronic. These patients need ventilatory support that could be invasive or non-invasive. CPAP is a safe modality of non-invasive ventilation. These patients may be given bronchodilators, which include methylxanthines, B2 agonists and anticholinergics. Tiotropium is a new anticholinergic, which has shown promising results in the management of COPD.

Hence this study was undertaken to assess the role of CPAP by nasal mask and Tiotropium in patients of COPD in acute exacerbation.

Material and Methods

A total of 25 patients were selected for study, who were known cases of COPD diagnosed by history and clinic investigatory methods (later on confirmed by spirometry. The inclusion criteria of the study were marked breathlessness, pH<7.35, $PaCO_2$>45 mm of Hg, PaO_2<60 mm of Hg, normal bulbar function, ability to clear bronchial secretions and ability to cooperate with treatment

Patients with past or present diagnosis of asthma or with history of seasonal or episodic dyspnea or wheezing, respiratory arrest, cardiovascular insufficiency, altered sensorium, obesity, copious secretions, BPH, Glaucoma, past history of hypersensitivity or abnormal response to any of these bronchodilators and associated lung conditions such as pulmonary tuberculosis, bronchiectasis, pulmonary eosinophilia, pulmonary fibrosis or Carcinoma lung were excluded from the study.

After proper selection of patients as per our inclusion criteria, the patients were given a trial of CPAP via a nasal mask along with bronchodilators through nebulization. X ray chest PA view was used to rule out other conditions mimicking COPD exacerbation. ABG analysis was done at the time of initiating NIV to establish the presence the presence of respiratory failure in these patients. Administration of CPAP was started at a level of 5 cm of water and increased by increments of 2.5 cm of water to a maximal of 10 cm depending on the clinical response and patients' tolerability. CPAP was given for about 6-8 hours on the first day and was repeated on the second day if the clinical situation so warranted. Tiotropium was given by MDI 2 puffs, 18mcg) at the time of starting NIV and after 24 hrs. Spacer device was used to eliminate the Freon effect. The patients were constantly encouraged and motivated throughout the study in order to ensure co-operation and ally apprehension; this being a new form of modality of treatment of COPD in this region. The patients were allowed to talk to their attenders and to have food. Arrangements were available all the time to

take the patients on invasive mechanical ventilation, if that was to be needed. ABG analysis was done 24- 48 hours after the initiation of CPAP, depending on the time after which the patient felt comfortable and had reduced subjective sensation of dyspnea. Spirometry was performed one month after the intervention, when the patients had recovered from acute exacerbation.

ABG parameters (like PaO2, PaCO2 and pH), SaO2, RR and dyspnea were compared before and after the intervention with CPAP and Tiotropium. These parameters were analyzed to assess the response of CPAP and Tiotropium in patients of acute exacerbations of COPD.

All the relevant data was then entered in MS Excel. All the data analysis was performed using appropriate statistical software. Frequency distribution and cross tabulation was used to prepare the tables. Quantitative variables were expressed as the mean and standard deviation. Categorical data was expressed as percentage. Microsoft office was used to prepare the graphs. Student t- test was used to compare the means. Chi Square test was used to compare the categorical data. P value of < 0.05 was considered as significant.

Results

Out of 25 patients, 10 (40.0%) were of the age group 51-60 years followed by 8 (32%) patients of 41-50 years age group. 20 (80%) were males, while the rest 5 were females.

13 (52%) patients were belonging to grade II of COPD, while 9 (36%) were of grade III and rest 3 were from grade IV

Out of 20 males, 18 (90%) were smokers, while only one among the 5 females had history of smoking.

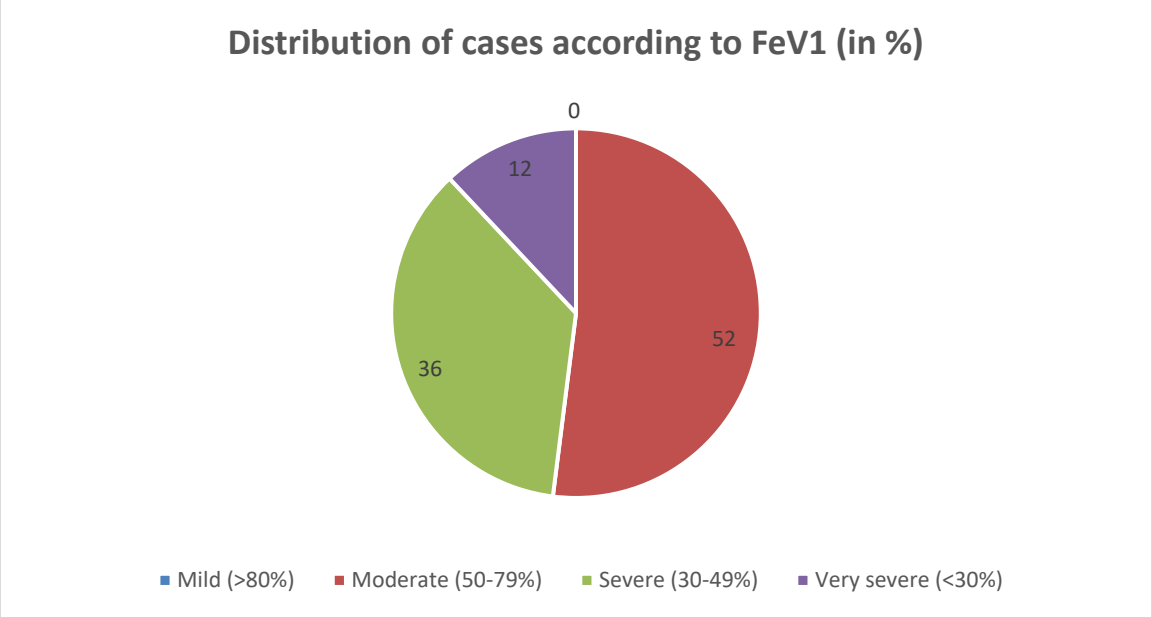

Figure 1: Distribution of cases according to FeV1

In the present study, 13(52%) cases had moderate impairment in FeV1, while 9 (36%) had severe impairment

Mean PaCo2 of 68.15(±1.95) is seen among GOLD II cases, while 70.89(±4.11) and 76.00(±1.63) were the mean PaCo2 among grades III and IV patients.

Table 1: Comparison of Pre and Post NIV + BP PaO_2/pH/PaO2

Gold Grade	BD $PaCO_2$		BD pH		BD PaO2	
	Pre - NIV + BD $PaCO_2$	Post - NIV +BD $PaCO_2$	Pre - NIV + BD pH	Post - NIV + BD pH	Pre - NIV + BD PaO_2	Post - NIV + BD PaO_2
II	67.81(±1.72)	54.55(±4.63)	7.29(±0.03)	7.37(±0.03)	49.72(±2.90)	65.55(±3.67)
III	70.33(±3.82)	53.32(±7.11)	7.28(±0.03)	7.37(±0.02)	49.00(±12.10)	61.33(±3.93)
IV	75.00(±1.41)	55.00(±9.89)	7.26(±0.01)	7.37(±0.04)	49.00(±4.24)	62.00(±8.49)
Whole group	70.08(±3.80)	54.08(±4.66)	7.28(±0.03)	7.38(±0.02)	49.48(±3.07)	64.27(±4.45)

Comparison of Pre and Post NIV with BD PaCo2 shows there was significant reduction in values post NIV, while the pH values were found to increase. PaO2 values are found to increase in all groups after NIV.

Table 2: Comparison of Pre and Post NIV + BP SaO_2

Gold Grade	Pre - NIV + BD PaO_2	Post - NIV + BD PaO_2
II	66.38(±6.48)	88.72(±2.72)
III	71.33(±6.28)	90.33(±2.34)
IV	69.00(±9.10)	88.00(±5.66)
Whole group	66.96(±7.39)	88.96(±3.17)

Comparison of Pre and Post NIV with BD PaO2 shows there was significant increase in values post NIV in all groups irrespective COPD grading.

Table 3: Comparison of symptoms Pre and Post NIV+ BD

Situation	COPD Grade						
	Symptoms	1		2		3	
		M	F	M	F	M	F
Pre-NIV+BD	Cough with Expectoration	92%	94%	95%	92%	96%	94%
	Breathlessness	82%	88%	85%	91%	92%	94%
	Wheezing	64%	74%	69%	71%	63%	73%
	Cyanosis	11%	none	27%	15%	32%	28%
Post-NIV+BD	Cough with expectoration	63%	68%	72%	65%	76%	68%
	Dyspnoea	42%	56%	64%	74%	34%	44%
	Wheezing	23%	34%	44%	43%	42%	23%
	Cyanosis	none	none	12%	none	22%	11%

Changes in symptoms especially breathlessness, wheezing, cough with expectoration were noted following NIV support in COPD patients

Table 4: Comparison of ECG changes Pre-and Post-NIV+BD

Situation	ECG Finding	COPD Grade							
		1		2		3		4	
		M	F	M	F	M	F	M	F
Pre-NIV+BD ECG	P Pulmonale	None	none	45%	32%	52%	47%	58%	52%
	RVH	None	none	27%	26%	34%	39%	49%	43%
	T Inversion In 2,3 avf	None	none	11%	13%	17%	29%	28%	38%
Post-NIV+BD ECG	P Pulmonale	None	none	37%	22%	39%	26%	42%	37%
	RVH	None	none	22%	19%	27%	27%	38%	27%
	T Inversion In 2,3 avf	None	none	none	none	11%	13%	15%	16%

Significant reduction in adverse patterns in ECG were obtained after NIV support in COPD patients in the present study

Discussion

Present study has been carried out to assess the role of NIV (CPAP) via nasal mask and bronchodilators in patients with acute exacerbation of COPD.

The youngest patient was 45 years of age and the oldest was 71 years of age. Maximum numbers of cases were in the age- group 51-60 years. The mean age for the study population was 54.76(+-7.16) years.

Total number of males in the study was 20 (80%) and that of females was 5(20%). Total number of smokers in the study was 19(76%) and that of nonsmokers was 6(24%).

Patients were classified into various grades based on Gold's criteria. In our study, none of the patients were in grades 0 and 1. Out of 25 patients, 13 (52%) were in grade 2, 9(36%) were in grade 3, and 3 (12%) of patients were in grade 4.

In evaluating the duration of symptoms, it was found that 8(32%) of patients had symptoms of disease for 10-15years, 11(44%) for 15-20) years and 6(24%) had symptoms for >20 years.In our study it was found that there was a positive correlation between PaCO2 and COPD grade; higher the grade, greater was the level of mean PaCO2. The most common presenting complaint in our study group was that of increased cough and sputum production; followed by breathing difficulty, whistling sound and cyanosis.

ABG parameters, RR and subjective sensation of breathlessness were compared before and after the intervention with CPAP and bronchodilators. It was found there was significant improvement in these parameters.

The bronchodilator used in our study was Tiotropium, which is a synthetic quaternary anticholinergic agent that is closely related to ipratropium. It has two important features: it is functionally selective for specific muscarinic receptors that mediate airway smooth muscle contraction, and has an extremely long duration of action, making it well suited for once daily therapy. It binds to all three muscarinic receptor subtypes but dissociates rapidly from M2 receptors (Disse and Speck [9], 1993). The potential for inhibition of airway inflammation by anticholinergic gents has been postulated (Morr H. 1979 [10]). Following inhalation of single doses of tiotropium, the FeV1 rises and reaches a peak in about 1-3 hours(Noord, Smeets, 2002 [11]). Tiotropium was given to our patients at the time of starting nasal CPAP. The dose given was 2 puffs (9 mcg each, total dose 18 mcg)

via MDI with spacer device. The spacer was used to avoid deposition of the drug in the throat, the freon effect. This dose was repeated after 24 hrs. None of our patients developed side effects of tiotropium (like dry mouth), possibly due short duration of the study.

Nasal CPAP was generally well tolerated by the patients. One of the patients developed pressure sore. Two patients found the mask highly uncomfortable and did not use it.

The respiratory rate decreased in all the patients in all grades of CODP. The mean RR before the study was 32.08 (+-3.17), which decrease to 20.50(+-1.41) after the study (p <. 001). All our patients had a decreased sensation of breathlessness after the study. There was also an improvement in ABG parameters after the study and the differences were statistically significant with p value <0.001.

Our study indicates that nasal CPAP breathing and tiotropium improves ventilatory pattern, relieves the sensation of dyspnoea, and improves gas exchange in patients of COPD with acute exacerbation. The change may be due to recovery of the inspiratory muscles due to a reduction of respiratory work. The improvements in arterial blood gases would also contribute to a decrease in the respiratory frequency.

The reduction in PaCO2 was probably due to both an increase in ventilation and a decrease in ratio of dead space over tidal volume. Previous investigations have demonstrated that in mechanically ventilated patients of COPD, the use of PEEP increases the change in volume for a given change in pressure. In addition, improvement in respiratory muscle function in itself will

Improve ventilation because a higher inspiratory pressure can be generated. The improvement in PaO_2 was also the result of better ventilation perfusion relationship.

Out of 25 patients, 19 patients completed the study. In the remaining 6 patients, 3 showed worsening of ABG parameters and were intubated, 2 patients could not tolerate the mask, and 1 patient developed pressure sore due to the mask.

To summarize, out of 25 patients, 19 patients benefited from treatment by nasal CPAP and tiotropium. The success rate of randomized controlled trials of NIV mostly in acute exacerbations of COPD published, both within and outside the ICU. Brochard *et al*, 1995 [12] showed that NIV for patients with exacerbation so COPD in the ICU reduced the intubation (11/43 vs. 31/42, p< 0.001) and mortality rates (4/43 vs. 12/42, p =0.02) compared with conventional medical therapy. NIV also improved pH, PaO2, RR, and encephalopathy score at one hour and was associated with a shorter hospital stay (23days vs. 35 days, p=0.005) and a lower complication rate (16% vs. 48%, p=0.001).

Conclusion

Various conclusions that can be drawn from the study include patients with higher grade of COPD with history of smoking have higher level of PaCO2 as compared to non-smokers.Intervention with CPAP and bronchodilators are associated with improvements in various parameters like PaCO2, PaO2, pH, SPO2 and RR and the Improvement was also seen with subjective parameters like breathlessness, cough and wheezing

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