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Pre morbid Severity of Chronic Obstructive Pulmonary Disease as Risk Factor for Carbon dioxide Retention during Acute Exacerbation of Chronic Obstructive Pulmonary Disease.

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ABSTRACT

This was a case control study done in patients admitted with acute exacerbation of chronic obstructive pulmonary disease (COPD). Patients were grouped into categories, depending upon the arterial blood gas analysis. 30patients with carbon dioxide retention $Paco_2$ level >46mmHg which was not a compensation for metabolic alkalosis were classified as cases. 30 patients without carbon dioxide retention$Paco_2$ level <46mmHg were classified as controls. Pre morbid severity of COPD as per GOLD 2010 was compared between the two groups as risk factor for carbon dioxide retention. The data was entered into the Microsoft Office Excel 2007 and odds ratio was calculated. Patients with severe and very severe COPD showed a risk of having carbon dioxide retention 116 times that of patient with mild and moderate COPD. 50% of cases were in 61-70 years age group. Patients with severe and very severe COPD have a greater risk of carbon dioxide retention during acute exacerbation than patients with mild and moderate COPD. Patients with severe and very severe COPD develop skeletal muscle wasting and skeletal muscle dysfunction, malnutrition, hyperinflation of lungs with poor diaphragm contractility. All these lead to hypoventilation and carbon dioxide retention during acute exacerbation of COPD when ventialtory demand increases.

Keywords: Acute exacerbation of COPD, Carbon dioxide retention, Severity of COPD, Hyperinflation

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INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) isa preventable and treatable disease, 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. Acute exacerbation is the commonest cause for hospitalization, morbidity and mortality in COPD patients. Hypercapnea which occurs in acute exacerbation of COPD is a major reason foradmission to intensive care unit, invasive mechanical ventilation. In-hospital mortality of patients admitted with acute exacerbation of COPD with hypercapnic respiratory failure is very high [1]. Hypercapnea is defined as an arterial Paco2 above 46 mm Hg that is not a compensation for a metabolic alkalosis [2]. In COPD, chronic hypercapnea is adaptive response whichoccurs secondary to alveolar hypoventilation to preventrespiratory muscle fatigue by reducing the work of breathing [3].Reduced ventilation may also be due to reduced ventilatory drive. This may lead to carbon dioxide retention when it iscombined with reduced ventilation.This pattern of breathing is more common in patients with severe disease [4]. In COPD as the severity of the disease increases skeletal muscle dysfunction, weight loss, hyperinflation also increases. Hence patients with more severe COPD and who come with severe hypoxia during exacerbation may have more chances of carbon dioxide retention. Early diagnosis and prompt proper management of hypercapnea during acute exacerbation of COPD will prevent morbidity and mortality in these patients.

MATERIALS AND METHODS

This was a hospital based case control study including 30 patients in each group. The subjects were patients admitted with acute exacerbation of COPD under the department of pulmonary medicine of A.J. Institute of Medical Sciences; Mangalore over a period of one year.Ethical clearance was obtained from institutional ethical committee of A.J institute of medical sciences. Patients already diagnosed as COPD as per GOLD 2010 guidelines and on routine follow-up in outpatient department were included in the study. Only malepatients were included in the study, aged 40-80.Matching was done for Age. History regarding patient particulars, severity of COPD, smoking history was noted in the questionnaire. The information regarding the variables was collected by using a pretested questionnaire. Arterial Blood Gas analysis (ABG) was done at admission. Patients were grouped under two categories, cases and controls depending upon the ABG. All patients with $Paco_2$ level >46mmHg which was not a compensation for metabolic alkalosis were classified as cases [2]. All patients with $Paco_2$ level <46mmHg were classified as controls. Chest X-ray, blood routine investigations, ECG, echocardiography, serum electrolytes, serum total protein, albumin, and globulin were done in all patients. ABG was repeated before discharge in all patients. Patients in whom carbon dioxide levels did not return to normal on discharge were excluded from the study. Severity of COPD was compared between these two groups as a risk factor for carbon dioxide retention.

Severity of COPD was classified according to the GOLD 2010 guidelines(as this study was started in 2010) as mild, moderate, severe and very severe as per patients FEV1 before admission in OPD follow-up (Table 1).

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Table 1: Classification of severity of airflow limitation in COPD GOLD 2010

Classification of severity of airflow limitation in COPD (Based on post-bronchodilator FEV_1)		
In patients with FEV_1/FVC <70%		
GOLD 1	MILD	$FEV_1 \geq 80\%$ predicted
GOLD 2	MODERATE	$50\% \leq FEV_1 < 80\%$ predicted
GOLD 3	SEVERE	$30\% \leq FEV_1 < 50\%$ predicted
GOLD 4	VERY SEVERE	$FEV_1 < 30\%$ predicted or $FEV_1 < 50\%$ predicted plus chronic respiratory failure

Statistical Analysis

The data was entered into the Microsoft Office Excel 2007 and odds ratio was calculated .

RESULTS

Total of 60 patients were included in the study with 30 cases and 30 controls.

Table 2: Age distribution among cases and controls

Age group(years)	Cases	Controls
41-50	2	2
51-60	9	9
61-70	15	15
71-80	4	4

The above table 2 shows the distribution of patients in different age groups. Matching was done for age between cases and controls. As shown in the above table majority (50%) were in the age group of 61-70.

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Table 3: Comparison of severity of COPD between cases and controls

Severity of COPD	CASES	CONTROLS
Mild	0	3
Moderate	1	21
Severe	9	6
Very severe	20	0

Table 3: There were 29 patients (96.66 %) in case group having severe or very severe COPD. In the control group 24 patients (80%) had mild or moderate COPD. There were no very severe COPD patients in Control group.

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Table 4: 2×2 tables for severity of COPD

Factor	Cases	Controls
Severe and Very severe COPD	29(a)	6 (b)
Mild and moderate COPD	1((c)	24(d)

Odds Ratio = ad/bc = 116

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DISCUSSION

In our study most of the patients (50% of patients) were in the age group of 61-70 years. This probably indicates the common age group of presentation in COPD patients.

In our study 96.66% of patients in the case group were having severe or very severe COPD. Only 20% patients in control group had severe or very severe COPD. In our study patients with severe or very severe COPD showed a risk of having carbon dioxide retention 116 times (odds ratio = 116) that of patients with mild or moderate COPD.

Hyperinflation is common in COPD.Hyperinflation gradually increases with the progression of COPD [5]. Hyperinflation displaces the diaphragm downwards into a flattened position there by placing it at a mechanical disadvantage. In addition, hyperinflation prevents thorax from assisting inspiration during tidal breathing because the resting volume of thorax is above the volume at which the rib cage recoils outward during inspiration [3].The insidious development of flow limitation and hyperinflation over many years allows for several adaptive mechanisms to come into play to preserve the functional strength of the overburdened inspiratory muscles, particularly the diaphragm [4].Dynamic hyperinflation results in functional inspiratory muscle weakness by maximally shortening the muscle fibres in the diaphragm [6].The presence of severe hyperinflation reduces the ability to increase ventilation when the demand arises in acute exacerbation of COPD.It reduces the ability of the lung to expand appropriately and this leads to early mechanical limitation of ventilation. In some patients, this leads to mechanical constraint on tidal volume expansion.These abnormalities in the setting of severe *ventilation perfusion* abnormalities lead to carbon dioxide retention and arterial oxygen desaturation during exacerbation of COPD [7]. During acute exacerbations of COPD, expiratory flow limitation is increased and ventilatory demand and breathing frequency may also be

increased reflecting increased ventilation/perfusion ratio abnormalities. Together, these result in increased dynamic hyperinflation [8].This is a vicious circle.

One of the important extra pulmonary manifestations of COPD isskeletal muscle dysfunction and wasting [9].With advancing disease, skeletal muscle mass decreases in COPD [10].Muscle strength and endurance are both decreased and the muscles get easily fatigued. As a part of generalized skeletal muscle dysfunction, respiratory muscle dysfunction, especially of the diaphragm is known to occur in patients with severe COPD [11, 12]. Cross-sectional area of diaphragm fibers is reduced in patients with severe COPD. This has not been found in patients with mild or moderate COPD [13, 14].

The incidence of under nutrition in patients with COPD depends on disease severity. Several studies indicate that the prevalence of nutritional abnormalities increases as disease severity increases [15, 16].Weight loss is also common with severe disease. Malnutrition is a leading cause of impaired respiratory muscle contractilityand this may promote carbon dioxide retention [17].

Ventilation-perfusion mismatch [18], abnormalities in ventilatory control [19,20], respiratory muscle weakness [21,22], abnormal pattern of breathing[23,24] and dynamic pulmonary hyperinflation[25]have been reported to contribute to chronic carbon dioxide retention in patients with COPD.A study done by Rochester DF showed that as a result of respiratory muscle dysfunction, patients with severe COPD adopt a characteristic breathing pattern during tidal breathing consisting of a rapid frequency with small tidal volume. This pattern helps to prevent respiratory muscle fatigue but predisposes the patients to develop hypercapnea [26].All these are directly proportional to severity of COPD. Hence as severity of COPD increases the chances of carbon dioxide retention during acute exacerbation also increases.

CONCLUSION

Patients with severe and very severe COPD have a greater risk of carbon dioxide retention during acute exacerbation than patients with mild and moderate COPD. In future a scoring system may have to be developed to identify COPD patients at risk to develop carbon dioxide retention during acute exacerbation. This will help to institute early aggressive appropriate treatment so that admission to intensive care unit, invasive ventilation, morbidity, mortality and duration of hospital stay can be reduced in these patients.

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