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Study of serum magnesium levels in stable chronic obstructive pulmonary disease and chronic obstructive pulmonary disease exacerbations

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Abstract

Introduction: When magnesium is deficient, the action of calcium is enhanced. In contrast, an excess of magnesium blocks calcium. These interactions are important to the respiratory patient because the intracellular influx of calcium causes bronchial smooth-muscle contraction. The possibility exists that magnesium deficiency contributes to pulmonary complications. Aim of this study to check whether acute exacerbation of chronic obstructive pulmonary disease (COPD) is associated with changes in serum magnesium levels.

Methodology: 20 diagnosed with COPD- exacerbations and 20 with stable COPD were included in the study. The study was conducted for a period of 2 months to compare the serum magnesium levels in both groups. The samples were collected and the magnesium levels were evaluated by biochemical analysis.

Results: At the end of the study 45% of the participants in the exacerbations group had serum magnesium less than 1.5 mg/dl whereas none of the participants of the stable group had magnesium values less than 1.5 mg/dl. This suggests a possible association between low serum magnesium levels and exacerbations of COPD.

Conclusions: These findings indicate that pulmonary patients should be monitored routinely for magnesium deficiency.

Keywords: Acute exacerbation of chronic obstructive pulmonary disease; Magnesium; Pulmonary function test

Introduction

Chronic obstructive pulmonary disease is a disease characterized by chronic obstruction of lung airflow that interferes with normal respiration and is not fully reversible. COPD is not simply a "smoker's cough" but an under-diagnosed, life-threatening lung disease. Currently ranked as 5th leading cause of death worldwide and predicted 3rd up to 2020, it represents an important public health challenge that is both preventable and treatable. The burden of COPD is projected to increase in coming decades due to continued exposure to COPD risk factors and the aging of the world's population [1]. According to WHO estimates, 65 million people have moderate to severe (COPD). More than 3 million people died of COPD in 2005, which corresponds to 5% of all deaths globally [2]. The course of COPD is associated with acute exacerbations. An exacerbation of COPD can be defined as sustained worsening of the patient's condition from the stable state and beyond the normal day-to-day variations that is acute in onset and may warrant additional treatment in a patient with underlying COPD [3]. Frequent exacerbations are hazardous as they are associated with a significant increase in morbidity, mortality, faster decline in lung function and increased health care utilization. Etiology of acute exacerbations is varied, the most common being infections of the respiratory tract. Various studies have identified factors associated with frequent exacerbations which include previous hospitalization for COPD, FEV1%, resting dyspnea, altered blood gases, disease stage and duration, age etc. [1,4]. Predictors of acute exacerbations of COPD are not yet well-established. Identifying these predictors may be beneficial for the patients of chronic respiratory diseases. Some studies throw a light on the role of magnesium in chronic respiratory diseases. Magnesium is the second most abundant cation in the intracellular fluid. Magnesium is required for ATP generation and is a cofactor in many enzyme systems that regulate varied biochemical reactions in the body including muscle and nerve function, protein synthesis, blood glucose control and blood pressure regulation. Magnesium is involved in the active transport of calcium and potassium across the cell membrane. Magnesium is involved in important functions of the respiratory system like bronchodilation, mast cell stabilization and mucociliary clearance [5]. Hypomagnesemia is associated with increased airway hyperactivity and impaired pulmonary function. It is hypothesized that due to its bronchodilating effect, a decreased level of magnesium may increase COPD exacerbations. Rose A et al., stated that there is a possibility that magnesium deficiency may contribute to pulmonary complications in 'Role of magnesium in regulation of lung function- When magnesium is deficient, the action of calcium is enhanced. This is important as the intracellular influx of calcium causes bronchial smooth muscle contraction. Although serum levels are used to assess magnesium deficiency, cells can de deficient despite normal serum values [4]. Although the precise mechanism of this action is unknown, it has been suggested that Mg^{+2} plays a role in the maintenance of airway patency via relaxation of bronchial smooth muscle [6]. In a retrospective study, serum magnesium levels of patients with stable COPD were compared with another group of patients with

acute exacerbations by Aziz et al. Serum magnesium levels were higher in the stable period group compared to the acute exacerbation group [7]. In a prospective study conducted by Gumus et al., eighty nine patients who were hospitalized with COPD-AE were followed up at 3 monthly intervals for one year. There was significant positive correlation between number of exacerbations and serum magnesium level [5]. Serum magnesium is an independent predictor of frequent readmissions due to acute exacerbation of chronic obstructive pulmonary disease. That notwithstanding, the relationship between serum Mg^{+2} levels and outcome with regard to disease flares in COPD patients has not been, hitherto, thoroughly explored. Low serum magnesium level independently predicts readmission for AECOPD [1]. So the aim of this study is to explore possible associations between COPD acute exacerbation and serum magnesium levels.

Materials and Method

This is hospital based observational study. A total 40 cases were enrolled in the study from Tertiary Care Centre, after meeting inclusion criteria. The study was conducted for a period of two months. Institutional Ethics Committee approval has been taken and written informed consent was taken from the patients.

Inclusion criteria: In the stable group, only diagnosed cases of COPD whose respiratory function was stable for the past 4 weeks were included.

Exclusion criteria: Patients with other respiratory diseases, cancer, cirrhosis, chronic renal and heart diseases, HIV, hepatitis B and whose who were not willing to consent were excluded from the study.

Blood samples were obtained from twenty consecutive patients admitted in the ward with the diagnosis of COPD-AE and twenty patients who are known cases of COPD who have come for review. The diagnosis of COPD in these patients was based on pulmonary function tests and arterial blood gas analysis.

The samples were obtained and estimation of magnesium was carried out by automated biochemistry analyzer (photometry) by dye binding method using commercial kit from Human, Germany. For this study a serum magnesium value less than 1.5 mg/dl is taken as hypomagnesaemia. Descriptive statistics such as mean, SD and percentage were used.

Results

In the exacerbation group there were 9 cases whose serum magnesium was less than 1.5mg/dl and 5 cases with magnesium value ranging between 1.5 and 2 mg/dl and 6 cases with value more than 2mg/dl. In the stable group there were no cases recording less than 1.5 mg/dl, 4 cases with values between 1.5 and 2 mg/dl and the rest had magnesium values more than 2mg/dl. (Fig. 1)

The mean serum magnesium value in the stable group was 2.33 mg/dl whereas in the group comprising of acute exacerbations it was 1.69 mg/dl.

There were nine cases of hypomagnesemia in the recorded 20 cases of acute exacerbations whereas none of the cases in the stable group recorded a value less than 1.5mg/dl.(Fig. 2)

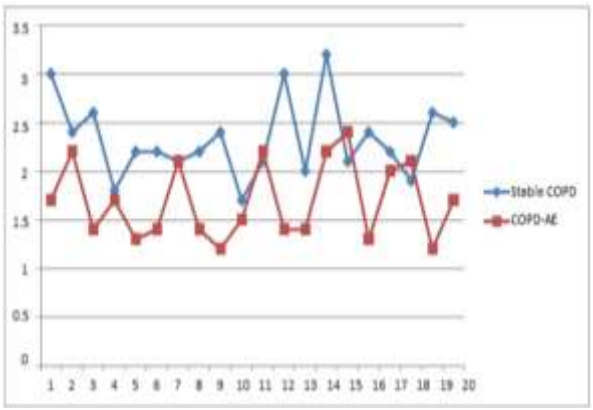

Fig. 1: The serum magnesium levels recorded in patients of stable COPD and COPD acute exacerbations are recorded in the graph above. The y-axis represents of level of magnesium in the serum in mg/dl and the x-axis represents each patient numbered consecutively in their group.

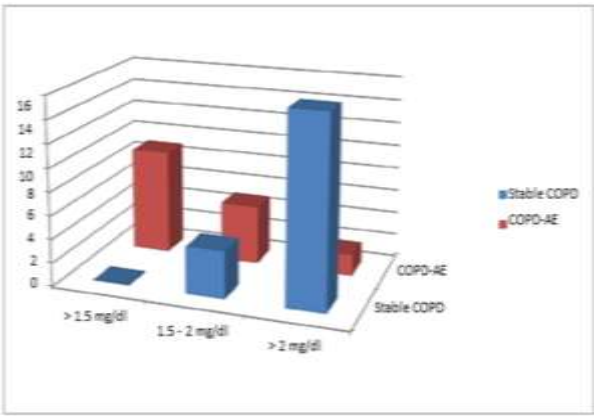

Fig. 2: X-axis shows range of serum magnesium values and the y-axis shows the number of patients

Discussion

COPD represents an overlap of chronic bronchitis and emphysema and patients of COPD have an element of hyper responsive airways. There is growing awareness of serum magnesium level in pulmonary diseases. Magnesium disturbance is a well-known abnormality seen in patients with pulmonary disease [8, 9].

In this study, 45% of the participants in the exacerbations group had serum magnesium less than 1.5 mg/dl whereas none of the participants of the stable group had magnesium values less than 1.5 mg/dl. 5 cases in this group showed magnesium value ranging between 1.5 and 2 mg/dl and 6 cases with value more

than 2mg/dl.

In this study, in stable COPD group, there were no cases recording less than 1.5 mg/dl, 4 cases with values between 1.5 and 2 mg/dl and the rest had magnesium values more than 2mg/dl.

There were nine cases of hypomagnesemia in the recorded 20 cases of acute exacerbations whereas none of the cases in the stable group recorded a value less than 1.5mg/dl.

As compared to study by Singh et al., 88% of the patients with hypomagnesemia were having stage II and stage III disease (15/17) as compared to 54.6% with normal magnesium level in stage II and III [10].

The mean serum magnesium value in the stable group was 2.33 mg/dl whereas in the group comprising of acute exacerbations it was 1.69 mg/dl. This showed significant correlation between hypomagnesaemia and COPD exacerbation. This observation was accordance with studies conducted by Aziz et al. [7] and Singh et al. [10].

The potential mechanism for the direct relaxing effects of magnesium on bronchial smooth muscles include calcium channel blocking properties, inhibition of cholinergic neuro-Muscular Junction transmission with decreased sensibility to the depolarising action of acetylcholine, stabilization of mast cells and T lymphocytes and stimulation of nitric oxide and Prostacycline [11, 12] .

In the study by Bhatt et al. [1], serum magnesium is one of the predictor of in hospital mortality and morbidity in patients with acute exacerbation of chronic obstructive pulmonary disease. In the study by Bhatt et al. [1], serum magnesium is an independent predictor of frequent readmissions due to acute exacerbation of chronic obstructive pulmonary disease.

Even though there are some studies implicating low serum levels of magnesium with exacerbations of chronic respiratory conditions, the cause of this decline is not clearly known. It would be even better if serum magnesium levels are monitored serially in the same cases over a period of time. In such a setting, variations in the serum magnesium levels can be monitored in the same person over the course of the disease and the possibility of magnesium being a possible predictor for exacerbations can be assessed. However, this kind of study was not possible because of the time constraint.

Conclusions

The mean magnesium value of the exacerbation group was lower than that of the stable group. There were nine recorded cases of hypomagnesaemia of the 20 cases in the acute exacerbations group whereas none of the stable cases recorded a value less than 1.5mg/dl.

Conflicts of interest: None declared

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