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Study of serum magnesium levels in acute exacerbation of COPD

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ABSTRACT

Chronic obstructive pulmonary disease (COPD) is one of most common diseases that effect many people around the world. Serum magnesium is an independent predictor of frequent readmission due to acute exacerbations of COPD. The objective of this study is to look for correlation of serum magnesium levels during acute exacerbation of COPD and stable cases of COPD.50 male patients of COPD were selected for measuring serum magnesium levels presented with acute exacerbation at the time admission and discharge and results were compared. Serum magnesium levels at the time of admission were 1.55(mean) and at the time discharge was 2.32(mean). In our study the Z value is 12.6 with reference to Z table, the probability of occurrence (p-value) is less than 0.05 which is statistically significant. Hence prevalence of low magnesium levels in acute exacerbation of COPD is high which may predict an exacerbation

Keywords: COPD, Serum Magnesium, Acute exacerbation, Urine, Serum, Pulmonary diseases, Hypomagnesemia, Chronic Bronchitis & Emphysema

Introduction

Chronic obstructive pulmonary disease (COPD) is one of the most common diseases that affect many people around the world. COPD is now the fourth leading cause of death and is the only disease state that is rising in morbidity and mortality amongst the top five killers. A recent study conducted to determine the global burden of COPD using recent diagnostic criteria [1] estimated that the prevalence of moderate to severe COPD is 10.1%. Acute exacerbations of COPD are common in patients with moderate to severe disease. These patients experience 2 exacerbations per year on average, with a median recovery time of 7 days. Exacerbations of COPD lead to substantial economic losses in terms of medical costs, loss of productivity at work, and can have a negative impact on patients' daily life and health-related well-being. [8]Since magnesium is involved in muscle tone, therefore a decrease in magnesium in level in COPD patients represents a factor which is detrimental to respiratory function as low magnesium level induces muscle fatigue. A growing body of evidence suggests that Mg^{+2} deficiency contributes to exacerbations of asthma and, as a corollary, that Mg^{+2} is useful in alleviating bronchospasm in these patients [1-3] Sajjad Rajab *et al* studied – relationship between serum magnesium levels and acute exacerbation of COPD. They concluded that there is increased prevalence of hypomagnesaemia in acute exacerbation of COPD and is associated with prolonged hospital stay [5] Corradi M *et al* studied – metallic elements in exhaled breath condensate and serum of patients with acute exacerbation of COPD. Exhaled magnesium and manganese levels were influenced by exacerbation of COPD, an increase in their concentration respectively by 50% & 20% being observed at exacerbation in comparison with values obtained at recovery[6] Nagomi-Obradovic L *et al* studied – Evaluation of magnesium in serum and urine in patients with pulmonary diseases. In patients with acute exacerbation of COPD there was a proportional ratio between hypomagnesaemia and increased concentration of magnesium in 24hr urine probably due to renal loss. They concluded that the serious complications of magnesium metabolism derangements & the presence

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of altered cell magnesium content should be taken into account in pulmonary ICU patients [7].Even though the relationship between serum Mg^{+2} levels and outcome with regard to disease flares in COPD patients has been earlier explored, our study is intended to evaluate the possible correlation between serum Mg^{+2} levels in COPD patients at the time of exacerbation and after its control.

Aim of the study

To study the correlation between the levels of serum magnesium in acute exacerbation of COPD and stable cases of COPD.

Materials and methods

This cross sectional study was conducted on 50 male patients who were known cases of COPD, presenting with acute exacerbation from December 2010 to March 2012 in Government Chest Diseases and Tuberculosis Hospital, Hanamkonda, A.P, as defined by Anthonisens criteria [8-15]. COPD patients who have been diagnosed earlier clinically and by spirometry and who had presented with acute exacerbation defined as a change in a patient's baseline dyspnoea, cough and/or sputum beyond day-to-day variability, and sufficient to warrant a change in therapy are included in the study. Patients with Bronchial asthma, other co morbid conditions like Hypertension, Diabetes Mallitus, HIV, Pulmonary Tuberculosis, and other conditions causing hypomagnesaemia like alcoholism, renal causes(ATN),chronic diarrhea, vomiting, crohns disease, ulcerative colitis, whipples disease and Drugs(loop diuretics,thiazides,gentamycin ,cisplatin) were excluded from the study. On the day of study and at the time of discharge when patient's symptoms have come near to baseline, their symptoms – Cough, Sputum, Dyspnoea were analysed and scored. [16-21]Severity of dyspnea is scored by Modified MMRC scale.5ml of venous blood sample was collected in a vaccutainer and sent to the laboratory on the day of admission and discharge (i.e, when the patient symptoms returned to their baseline levels).Serum magnesium levels were analyzed from 1 ml of the fresh supernatant unhemolyzed serum of the centrifuged sample and the results were recorded.[22-29] In our study serum magnesium was analyzed by calorimetric method using metallochromic dye calmagite. This is a rapid, easy and accurate method of determination of magnesium in serum [30,31].We used VITROS 5600 analyzer with automated procedure. Instrument is calibrated using an aqueous Magnesium Standard (2.4mg/dl). The integrity of the reaction was monitored by normal and abnormal control sera with known magnesium concentrations. Our lab normal range for serum magnesium is 1.8-2.4 mg/dl.

Fig 1: VITROS 5600 Analyzer

Statistical analysis and descriptive values

This cross-sectional study was conducted on 50 patients. All the patients were males and all were smokers.

Table 1: Master chart showing patients and statistical analysis

S No.	Patient ID Number	Age	Sex	Se. Mg at the time of admission mg/dl	Se. Mg at the time of discharge mg/dl
1	01	60yrs	M	1.4	2
2	02	68yrs	M	1.5	2.3
3	03	62yrs	M	1.5	2.2
4	04	60yrs	M	1.7	2,4
5	05	65yrs	M	2.3	2.4
6	06	62yrs	M	1.9	2.4
7	07	70yrs	M	1.3	2
8	08	65yrs	M	2	2.2
9	09	55yrs	M	2.2	2.3
10	10	58yrs	M	2.3	2.4
11	11	70yrs	M	2	2.2
12	12	65yrs	M	1.9	2
13	13	65yrs	M	1.4	2.2
14	14	70yrs	M	1.5	2.4
15	15	55yrs	M	1.6	2.3
16	16	65yrs	M	1.4	2.3
17	17	60yrs	M	1.3	2.2
18	18	70yrs	M	1.3	2.3
19	19	60yrs	M	1.4	2.3
20	20	65yrs	M	1.5	2.2
21	21	60yrs	M	1.4	2.1
22	22	55yrs	M	1.3	2
23	23	62yrs	M	1.6	2.3
24	24	60yrs	M	1.3	1.9
25	25	67yrs	M	1.4	1.8
26	26	70yrs	M	1.6	2.4
27	27	60yrs	M	1.7	2.3
28	28	59yrs	M	1.5	2.2
29	29	70yrs	M	1.3	2.3
30	30	55yrs	M	1.4	1.9
31	31	65yrs	M	1.5	2.3
32	32	60yrs	M	1.6	2.4
33	33	70yrs	M	1.1	2.2
34	34	60yrs	M	1.3	2.4
35	35	56yrs	M	1.3	2.4
36	36	66yrs	M	1.5	2.3
37	37	68yrs	M	1.2	1.9
38	38	70yrs	M	1.3	2
39	39	60yrs	M	1.4	2.2
40	40	65yrs	M	1.3	2.4
41	41	63yrs	M	1.5	2.4
42	42	65yrs	M	1.4	2.3
43	43	62yrs	M	1.5	2.4
44	44	70yrs	M	1.3	2.2
45	45	65yrs	M	1.4	2
46	46	55yrs	M	1.6	2.4
47	47	60yrs	M	1.4	2.3
48	48	58yrs	M	1.9	2.3
49	49	67yrs	M	2	2.2
50	50	55yrs	M	2.1	2.4
	Mean	62.96		1.55	2.232
	SD	4.89452964		0.288	0.255

Age composition

The age group of the study group ranged from 55 – 70 yrs. The mean age was 62.96 ± 4.8 yrs.

Table 2: Age group and number of patients

Age group	No of patients
55 – 60	21
61 – 70	29
Total	50

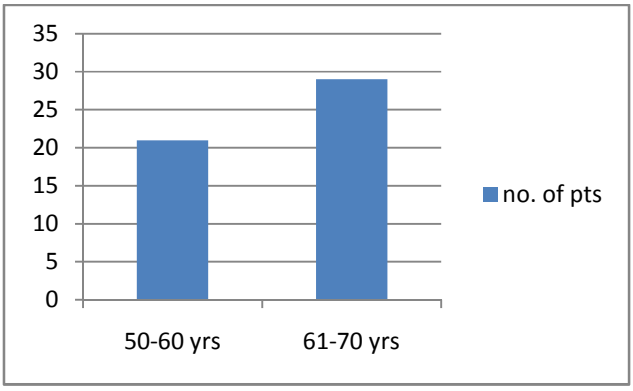

Fig 2: Age group and number of patients

Symptoms Score

On the day of study, three symptoms – cough with increased sputum volume, increased sputum purulence and dyspnoea were analysed and cumulative score was taken as 1 – 3 grades.

Table 3: Symptom score and number of patients

Symptom score	No of patients
1	11
2	19
3	20

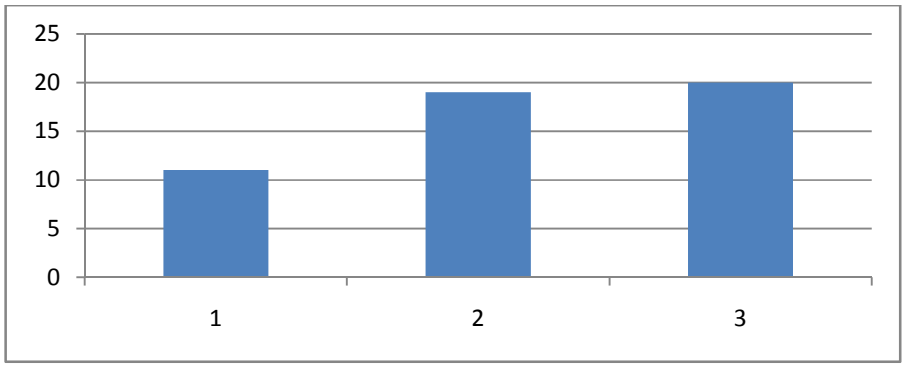

Fig 3: Symptom score and number of patients

Symptom score

At the time of admission, out of 50 patients studied 11 (22%) had symptom score 1; 19 (38%) had symptom score 2 and 20 (40%) had symptom score 3. All 50 patients had dyspnoea; 39 patients had cough with increased sputum volume and 20 patients had cough with increased sputum volume & increased sputum purulence.The mean symptom score was : 2.18,SD :± 0.89

MMRC dyspnoea scale grading

Patients were graded according to MMRC dyspnoea scale as grades 0 to 4.

Table 4: MMRC dyspnoea scale grading

MMRC dyspnea scale	No of patients
0	0
1	5
2	8
3	25
4	12

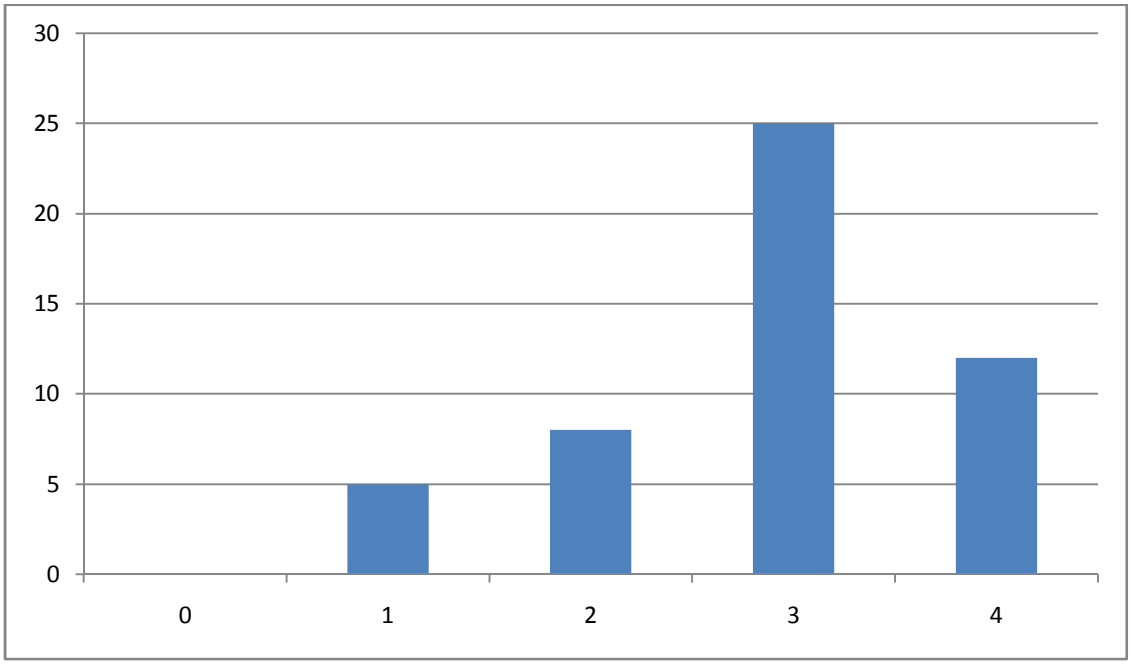

Fig 4: MMRC dyspnoea scale

MMRC dyspnoea scale

Out of 50 patients studied 5 patients had grade I dyspnoea; 8 patients had grade II dyspnoea; 25 patients had grade III dyspnoea and 12 patients had grade IV dyspnoea. The mean MMRC dyspnoea grade was: 2.88,SD: ±0.81

At the time of discharge 45 (90 %) patients had grade- I dyspnoea; 5 (10 %) patients had grade-II dyspnoea. The initial increased sputum volume and purulence in patients was reduced at the time of discharge.

Serum magnesium levels at the time of admission

Table 5: Serum magnesium level and number of patients

Serum magnesium level (mg/dl)	No of patients
1.8 – 2.4	10
1.5 – 1.7	16
1 – 1.4	24

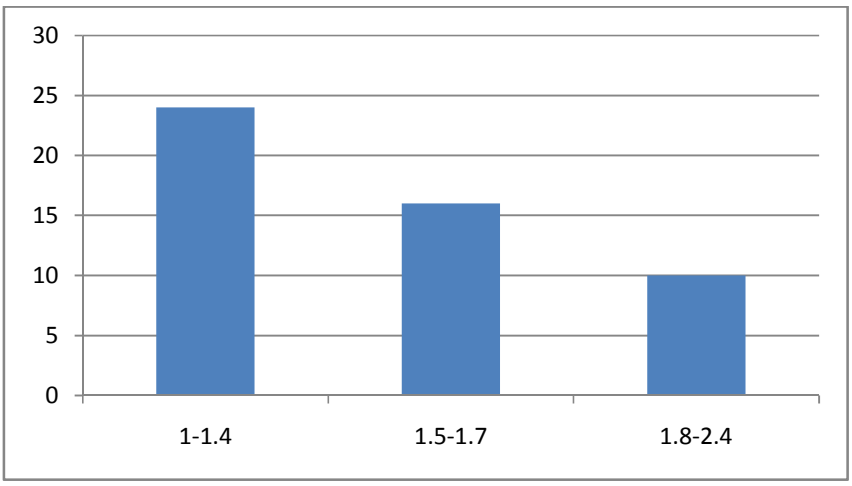

Fig 5: Serum magnesium level and number of patients

Serum magnesium levels

The mean serum magnesium level was: 1.576,SD: ± 0.336

Serum magnesium levels at the time of discharge

Table 6: Serum magnesium levels at the time of discharge

Serum magnesium level (mg/dl)	No of patients
1.8 – 2	10
2.1 – 2.4	40

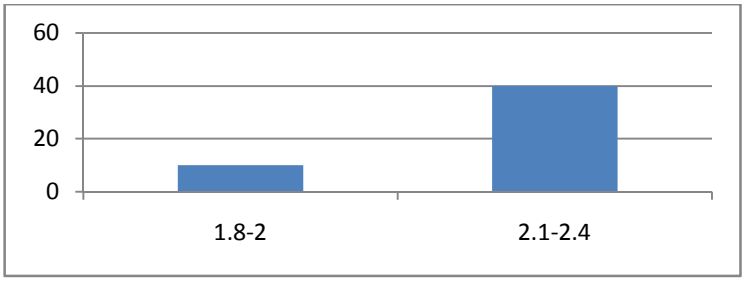

Fig 6: Serum magnesium levels at the time of discharge

Serum magnesium levels

The mean serum magnesium level was: 1.91,SD:± 0.364

Average values for the parameters studied

Table 7: Average values for the parameters studied

Parameter studied	Values
Dyspnea (MMRC)	Mean:2.88,SD: ±0.81
Symptom score	Mean: 2.18,SD: ±0.89
Serum magnesium levels at the time of admission	Mean : 1.55,SD : ±0.288
Serum magnesium levels at the time of discharge	Mean : 2.232,SD : ± 0.255

Correlation between serum magnesium and acute exacerbation of COPD:

$Z = \bar{X}_1 - \bar{X}_2 / \sqrt{SD_1^2/n_1 + SD_2^2/n_2}$

($\bar{X}_1$: 1.55; $\bar{X}_2$: 2.32; SD_1 : 0.28; SD_2 : 0.25; n_1 : 50; n_2 : 50)

$Z = 1.55 - 2.32 / \sqrt{0.00165 + 0.0013}$

$Z = - 0.682 / 0.054$

$Z = - 12.6$

n_1: number of patients in 1st group; SD_1: standard deviation of group 1; $\bar{X}_1$: mean ofmagnesium levels of group 1; n_2: number of patients in 2nd group; $\bar{X}_2$: mean of magnesium levels of group 2 ; SD_2 : standard deviation of group 2 ;
In our study Z value is 12.6, with reference to the'z' table,the probability of occurrence(p value) is less than 0.05.Hence the serum magnesium level is statistically significant.

Discussion

Much of the impact of COPD is due to the constellation of symptoms that is commonly termed an exacerbation. Major emphasis in the management of patients with COPD must be on the maintenance of stability. Bach *et al* [34] noted that antibiotics, bronchodilators, corticosteroids, and non-invasive positive-pressure ventilation remain the mainstay of therapy, but they pointed out the need for the identification of risk factors and the limited utility of diagnostic predictors of the course of COPD. There is a growing awareness on the role of magnesium in pulmonary disease. The significance of Mg^{+2} as both a risk factor and potential therapeutic agent in patients with COPD comes from the relatively well-established role of Mg^{+2} in the treatment of acute asthma. There are few studies which have shown the role of serum magnesium in COPD patients as a risk factor for acute exacerbation and for frequent hospitalization. Our study was a cross-sectional study , where we studied serum magnesium levels at the time of admission and at the time of discharge and both the values were compared. The relationship between serum magnesium and acute exacerbation of COPD was studied earlier by Aziz *et al*; Bhatt, S.P. *et al*; Sajjadrajab *et al*;Aziz *et al*., examined serum Mg^{+2} levels in an unselected group of COPD patients with clear symptoms of exacerbation and compared these to a group of patients reporting for routine clinic visits and in no apparent distress from the sequelae of bronchospasm, generally considered to indicate an exacerbation. Mean serum magnesium levels at the time of AECOPD was 0.77± 0.10 mmol/L. Mean serum magnesium levels in stable COPD patients was 0.91±0.10 mmol/L. Patients with acute exacerbation of COPD had significantly lower concentrations of serum magnesium and they suggest that low levels of serum magnesium may serve as a risk factor for acute exacerbation of COPD. Sajjadrajab *et al* studied serum magnesium levels in a group of 77 patients who presented with acute exacerbation of COPD. Serum magnesium levels were determined at the time of exacerbation, at discharge and one month after discharge. They reported that the mean serum

magnesium levels of patients with acute exacerbation of COPD was statistically significantly lower 1.88±0.67 mg/dl (mean±SD) than serum magnesium of stable COPD patients 2.30±0.36 (mean±SD). They observed the association of hypomagnesaemia with acute exacerbation of COPD. Bhatt S.P.*et al*., in their series of 100 patients admitted with a diagnosis of acute exacerbation of COPD was retrospectively followed from the time of index admission until next admission. The sole predictor of frequent readmissions was serum magnesium level (1.77+/-0.19 vs. 1.86+/-0.24mEq/L; adjusted odds ratio 0.003, 95% Confidence intervals <0.001-0.55; p=0.03). [32, 33] They observed that serum magnesium is an independent predictor of frequent readmissions due to acute exacerbation of COPD and is an easily modifiable risk factor.

David Holmes et al.,in their study observed that COPD patients with low serum magnesium levels are at increased risk for hospital admission for acute exacerbation compared to patients with normal serum magnesium levels.

Conclusion

The prevalence of hypomagnesaemia in acute exacerbation of COPD is high.

Low serum magnesium may predict acute exacerbation of COPD.

Low serum magnesium levels may be a risk factor for acute exacerbation of COPD for which further large scale studies are required.

Low serum magnesium is a modifiable risk factor.

Limitations: sample size was less & females were not included in the study.

Further large scale studies are required to determine the role of magnesium in the treatment of acute exacerbation of COPD.

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