ORIGINAL ARTICLE

Serum Magnesium Level In COPD Patients Attending A Tertiary Hospital - A Cross Sectional Study

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Abstract

The objective was to study COPD exacerbation and its relation with serum Magnesium (Mg 2+). The study included 50 patients of COPD with acute exacerbation, as defined by Anthonisens criterion. As per Anthonisens criterion, 62% of patients were in Anthonisens I, 32% in II and only 6% in III. As per GOLD criterion for staging of COPD, 34% patients were in Stage I, 50% in Stage II and 16 % in stage III. 17 patients (34%) had Hypomagnesemia 33(66%) were having normomagnesemia. 88% of patients with hypomagnesemia were in stage II and III as compared to 54.6% patients with normomagnesemia. The patients with hypomagnesemia had a longer duration of COPD (6.94±3 years) and longer duration of exacerbation of symptoms (>8 days). Three patients (17.64%) with Hypomagnesemia required Mechanical Ventilation. 64% patients with hypomagnesemia had hospital stay longer than 7 days as compared to 57.57% in patients with normomagnesemia. Hypomagnesemia is a common finding in acute exacerbation of COPD and is frequently encountered in patients who present late to the Hospital. In addition these patients usually have advanced disease stage, prolonged hospital stay and need mechanical ventilation more often.

Key Words

Serum Magnesium, COPD, Smoking , Chest Diseases

Introduction

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). 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 (4). Chronic obstructive pulmonary disease (COPD) represents an overlap of chronic bronchitis and emphysema, and patients with COPD have an element of asthmatic bronchitis (5). Bronchospasm is a contributing factor in their inability to clear secretions. This may result in reduced pulmonary gas exchange with consequences such as decreased quality of life and repeated hospitalization (6). Thus, Mg+2 may have a role in maintaining disease stability in COPD patients. That not withstanding, the relationship between serum Mg+2 levels and outcome with regard to disease flares in COPD patients has not been, hitherto, thoroughly explored. The study explores possible associations between COPD exacerbation and serum Mg+2 levels.

Material and Methods

It was a cross sectional study done in Department of Medicine Govt.Medical College, Jammu over a period of one year in which patients who presented to the OPD and Emergency with acute exacerbation of COPD based on the criterion of Anthonisens.i.e, presence of shortness of breath or severe coughing with or without increased sputum volume, were admitted and included in the study.After obtaining the detailed history, meticulous examination and baseline investigations , the patients were subjected to blood tests to determine the level of serum magnesium.Spirometery was done and patients were categorised into different stages of COPD as per GOLD staging of COPD. The patients with cerebrovascular accidents , ischemic heart disease , arterial hypertension, diabetes mellitus, arteriosclerotic disease and on medications like H2 blockers , proton pump inhibitors , thiazides , digoxin, insulin, chronic alcoholism

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and gastro-intestinal surgery were excluded.Magnesium was estimated by procedure determined by Connerty, lau and Brigg.the reference level of serum magnesium in our laboratory is 1.8-2.4mg/dl (0.74-0.99mmol/L). Hypomagnesemia was considered in patients with serum magnesium below 1.80mg/dl.

Results

The age distribution of cases was 40-76 years with mean age of 60.4±6.5 years. The maximum number of patients were in the age group of 60-69 years(48%), followed by the group 50-59(24%). 29 were males and 21 females with male to female ratio 1.38 :1.The age of female patients ranged from 45-70 years with a mean age of 58.7±4.5 years and the age of male patients ranged from 40-76 years with mean age of 62.4±7.3 years (*Table 1*).Ten patients (20%) belonged to rural areas and 40 patients (80%) to urban areas. 20 patients (40%) were non smokers , 25 were smokers (50%) and 5 were past smokers(10%) (*Table 1*). The average duration of COPD was 5.5±3.7 years and the average duration of symptoms before getting admitted to the hospital 5±3.1 days. Dyspnea (100%) was the commonest presentation at admission followed by Cough(92%) and sputum production 68% (*Table 2*). 62% of patients were Anthonisens-I , 32 were II and 6% were type III (*Table 3*).The physical examination of the 50 patients revealed cyanosis in 39 (78%) , crepts in 30 (60%), wheeze in 25 (50%) decreased air entry in 20 (40%), fever in 25(50%) and flap in 8 (16%) of patients (*Table 4*).17patients (34%) had hypomagnesemia at the time of admission and 33(66%)had normomagnesemia. The duration ofCOPD in patients with hypomagnesemia was 6.9±4.3 years as compared to6.3±4.7 years in patients with normomagnesemia (*Table 5*).According to the GOLD criterion of COPD patients , 17 (34%)pateints had Hypomagnesemia and 33(63%) had normomagnesemia. In hypomagnesemia group 2 patients were in stage -I,9 (53%) in stage -II and 6 (35%) in stage -III. On the other hand in the normomagnesemia group 15 patients(45.4%) were in stage -I, 16(48.4%)in stage -II and 2 (6.2%) in stage -III (*Table 6*).Hypomagnesemia was more common in COPD patients with longer duration of exacerbation of symptoms as compared to those patients with shorter duration of exacerbation (*Table 7*).Systemic examination revealed comparable pulse, B.P and respiratory rates in both groups. Although insignificant higher incidence of fever, hypertension and chest signs were observed in patients with hypomagnesemia as compared to patients with normal magnesium levels. (*Table 8*).The most common chest xray finding were emphsema in 19 (38%) of patients, infiltrates in10 (20%) and hyperinflated lungs and consolidation both in 8 patients(16%) each and cardiomegaly was present in 5 patients (10%) (*Table 9*).The most common ECG findings were P-pulmonale present in 20 patients (40%), followed by poor R wave progression in 14 (28%) and RBBB in 7 patients(14%) (*Table10*).Three patients (17.64%) with hypomagnesemia required non-invasive ventilation (BI-Pap) as compared to one patient (3.03) with normal magnesium levels (*Table 11*).In hypomagnesemia group 64.70% of the patients had a hospital stay of longer than 7 days as compared to 57.57% in the normomagnesemia group. The over all mortality in our study was 2% (*Table12,13*).

Discussion

There is growing awareness of serum magnesium level in pulmonary disease. Much of the impetus for recognition of Mg++ as both risk factor and potential therapeutic agent in patients with COPD comes from relatively well established role of magnesium in the treatment of acute asthma (7).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. COPD represents an overlap of chronic bronchitis and emphysema and patients of COPD have an element of asthamatic bronchitis. Bronchospasm is a contributory factor in their inability to clear secretions. This may result in reduced pulmonary gas exchange with consequences such as decreased quality of life and repeated hospitalizations. The mean age of patients was 60.4±6.5 years, with a male to female ratio of 1.38:1& predominance of urban areas (80%) in our study, which can be explained by the fact that our hospital is a tertiary care centre.The commonest symptom in our patients was dyspnea which was present in 100% of patients followed by cough in 92% and sputum purulence in 68%. This is in accordance with the study of Cerci Nato A, *et al* (8) & Rajjab S (9). Dyspnea as a main presenting symptom was also reported by others (10,11). The predominant chest signs were crepts (60%) followed by wheeze (50%) and decreased air entry (40%). This was similar to the study of Rajjab S (9) wherein crepts were present in 65%, wheeze in 48.1%, and decreased air entry in 27.3% of patients , but other studies showed the predominance of decreased breath sounds and wheezing as compared to crepts (12,13). The predominance of decreased breath sounds 50.7% during chest examination followed by wheeze has been observed by some authors during stable COPD (8).The higher incidence of crepts in our patients stems from the fact that these observations were made

Table .1 Showing the Epidemiological Profile of the Patients

	Age in Yrs					Sex			Dwelling		
	40-49	50-59	60-69	>70	Total	M	F	Total	U	R	Total
Numbers	11	12	24	3	50	29	21	50	10	40	50
Percentage	22	24	48	6	100	58	42	100	20	80	100

Smoking Status			
Current Smoker	Past Smoker	Non Smoker	Total
25	5	20	50
50	10	40	100

Table.2 Distribution of Cases As Per Clinical Presentation

Symptom	No.(n)	Percentage(%)	Mean±SD
Dyspnea	50	100	5.8±3.4(1-20)
Cough	46	92	5.2±4.1(1-18)
Sputum production	34	68	5.5±3.5(1-19)

Table .4 Distribution of Cases As Per Physical Examination

Physical Examination Findings	No.(n)	Percentage (%)
Cyanosis	39	78
Crepts	30	60
Wheeze	25	50
Decreased Air Entry	20	40
Fever	25	50
Flap	8	16

Table .6 COPD Stage With Serum Magnesium

COPD Stage	Hypo-magnesemia 17		Normo magnesemia 33	
	No.	%	No.	%
I	2	12	15	45.5
II	9	53	16	48.4
III	6	35	2	6.2

during acute exacerbations of COPD. In our study 62% of patients were in Anthonisens -I, 32% in Anthonisens -II and 6% in Anthonisens -III. This was similar to the study of Rajjab S (9) where 64% of patients were in Anthonisens -I, 31.2%in Anthonisens -II and 3.9% in Anthonisens -III respectively. In our study as per GOLD criterion for staging of COPD, 34%of patients were in stage -I, 50% in satge -II and 16% in stage III. Maximum number of patients were having stage I and II disease (84%), this is comparable to earlier studies (11,15). In the study of Rajjab S (9), 50.6% patients were in stage -

Table.3 Distribution of Cases As Per Anthonisens Criteria

Anthonisens Type	No.(n)	Percentage (%)
Type I	31	62
TypeII	16	32
Type III	3	6
Total	50	100

Table .5 Distribution of Cases As Per Serum Magnesium & Duration of Symptoms At The Time of Admission

	Hypomagnesemia Number(%)	Normomagnesemia Number(%)
Patients	17(34%)	33(66%)
Duration of COPD(yrs) Mean±SD	6.9±4.3	6.3±4.7

Table .7 Duration of Symptoms With Serum Magnesium

Symptom (Days)	Hypomagnesemia	Normomagnesemia
Dyspnea	7.1±4.6	5.5±3.2
Cough	7.2±3.9	4.6±2.4
Sputum Production	5.8±4.8	4.6±3.5
Duration of COPD exacerbation	8.0±5.4	5.2±3.3

Table. 8 Relation of Systemic Examination Findings With Serum Magnesium

Chest Signs	Hypomagnesemia (n=17)		Normomagnesemia (n=33)		PValue
	No.	%	No.	%	
Cynosis	14	82.35	25	75.75	0947
Crepts	11	64.79	19	57.57	0959
Wheeze	9	52.94	16	48.48	0944
Decreased Air Entry	7	41.17	13	39.39	0.01

II and 35.06% in stage I and 14.28% in stage III. i.e., maximum number of patients were in stage I and stage

Table. 9 Relation Of Chest X-Ray Findings With Serum Magnesium

X-Ray Findings	Hypomagnesemia(n=17)		Normomagnesemia(n=33)		Total(50)	
	No.	Percentage (%)	No.	Percentage (%)	No.	Percentage (%)
Emphysema	8	47.05	11	33.33	19	38
Infilterates	3	17.64	7	21.21	10	20
Hyperinflated	2	11.76	6	18.18	8	16
Consolidation	2	11.76	6	18.18	8	16
Cardiomegaly	2	11.76	3	9.09	5	10

Table . 10 Relation Of ECG Findings With Serum Magnesium

ECG	Hypomagnesemia		Normomagnesemia		Total	
	NO.	%age	No.	%age	No.	%age
P Pulmonale	6	35.29	14	42.42	20	40
RBBB	3	17.64	4	12.12	7	14
RAD	1	5.88	2	6.06	3	6
Poor R Progression	4	23.52	10	30.30	14	28
LAD	1	5.88	0	0	1	2
LAHB	2	11.76	1	3.03	3	6
Normal	0	0	2	6.06	2	4

Table. 11 Requirement of Mechanical Ventilation

Ventilation mode	Hpomagnesemia (n=17)		Normomagnesemia (n=33)	
	No.	%age	No.	%age
Non-Invasive(BiPap)	3	17.64	1	3.03
Invasive Ventilation	0	0	0	0

Table .12 Relation of Hospital Stay With Serum Magnesium

Hospital Stay	Hypomagnesemia (n=17)		Normomagnesemia (n=33)	
Days	No. Of Patients	%age	No. Of Patients	%age
=7	6	35.29	14	42.4
>7	11	64.70	19	57.57

Table. 13Patient Outcome With Serum Magnesium

	Hypomagnesemia		Normomagnesemia	
Outcome	No.	%age	No.	%age
Surviving	16	94.11	32	96.97
Dead	0	0	1	3.03

II (85.71%).In our study seventeen patients (34%) had hypomagnesemia and 33 (66%) were having normomagnesemia. About 88% of the patients with hypomagnesemia were having stage II and stage III disease (15/17) as compared to 54.6% with normal magnesium levels. This observation can be explained by the fact that stage II and III of COPD are associated with hypoxemia and subsequently chronic respiratory insufficiency superadded with hypoxemia has been described as a cause of magnesium depletion and hypomagnesemia . In the study by Rajjab S (9), 33.76% patients had hypomagnesemia and 66.23% had normomagnesemia. In hypomagnesemia group 34.6% were having stage III, 57.7% stage II and 7.7% were having stage I disease, whereas in patients with normal magnesium levels 3.9% were having stage III, 47.1% were having stage II and 49% were having stage I disease according to GOLD criterion for staging of COPD. The

mean serum magnesium of patients with hypomagnesemia was 1.7±0.86 mg/dl as compared to 2.15±mg/dl in patients with normomagnesemia. This observation was in accordance with other studies (9,10,13).In our study patients with hypomagnesemia had history of COPD for a longer duration 6.9±4.3 years as compared to patients with normomagnesemia. This observation has not been observed in earlier studies, the possible explanation for this is that frequent medication has been described as a cause for hypomagnesemia and magnesium depletion . The most common findings in the chest x ray were Emphysema in 19 patients (38%), followed by Infiltrates in 10 (20%) and hyperinflated Lung and Consolidation both in 8(16%) in each and cardiomegaly in 5 (10%).The most common ECG findings were P -pulmonale in 20(40%) patients , followed by poor R wave progression in 14(28%) and RBBB in 7 (14%). In study by Rajjab S, P pulmonale was present in 49 (63%), poor R wave progression in 37 (48%) and RBBB and RAD in 13(16.9%) each. Three patients 17.64% with hypomagnesemia required non invasive ventilation (BI-pap) as compared to one patient (3.03%) with normal magnesium levels. In the hypomagneseium group 64.70% had a hospital stay longer than 7 days as compared to 57.75% in normomagnesemia group, these factors are associated with prolonged hospital stay in addition to requirement of non-invasive ventilation and also had hypotension and gram negative septicaemia. The correlation with prolonged hospital stay with the need of mechanical ventilation has been studied by Groenewegen KH, *et al* (14) and Roberts CM, *et al* (15). 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 (5,6), stabilization of mast cells and T lymphocytes(7,8) and stimulation of nitric oxide (12) and prostacycline . The mortality rate in our study group was 2% which is comparable with the study of Rajjab S(9) 2.59%. In a study conducted by Bhatt SP ,*et al*, the mortality rate in acute exacerbation of COPD was observed to be 5% (16), the main predictor of mortality in acute exacerbation observed in the study was high serum creatinine and low serum sodium . In another study conducted in Hyderabad , India , the mortality rate was 10.4% (17).

Conclusion

Hypomagnesemia is a common finding in acute exacerbation of COPD and is frequently encountered in patients who present late to hospital after developing the acute exacerbation (>8 days). In addition these patients usually have advanced disease stage { stage II(50%) and stage III (16%)}, prolonged hospital stay (> 7 days) and need mechanical ventilation more often . The mortality rate has no correlation with serum Magnesium levels. "

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