Section: General Medicine

Research

A STUDY ON ASSOCIATION OF SERUM MAGNESIUM LEVEL WITH ACUTE EXACERBATION OF COPD AMONG PATIENTS IN GENERAL MEDICINE DEPARTMENT OF BURDWAN MEDICAL COLLEGE

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Abstract

Objective: To find out the association of serum magnesium level with acute exacerbation of COPD.

Methods: It was observational study, all patients of general medicine department, fulfilling the inclusion criteria and excluded by the exclusion criteria, admitted in OPD and outdoor of BMCH, in between 1st March 2020 to 31st September 2020. 50 patients with exacerbation of COPD and 50 patients of COPD in stable condition were selected. Serum magnesium was measured using xylidyl blue technique. Auto analyser was used for measuring serum magnesium level. This is easy, rapid and accurate method for determining magnesium levels. The integrity of the reaction was monitored using sera with known concentration (2.0mg/dl).**Results:**A vast majority of the study subjects (70%) in AECOPD group had magnesium level lower than the normal range while in stable COPD only 16% participants had low magnesium level with a statistically significant difference (p value = <0.0001). The mean magnesium level was 1.90 ±0.36 mg/dl in AECOPD and 2.03 ±0.36 mg/dl in stable COPD. Serum magnesium level was significantly lower among patients with AECOPD compared to stable COPD at the time of discharge. We found significant difference between AECOPD and stable COPS in mean serum magnesium level in mMRC grade 3 and 4 (p value = <0.05). **Conclusion:** During COPD exacerbation, serum magnesium levels decreased. This decrease was transient. We determined that serum magnesium is an independent predictor of frequent readmissions for acute exacerbations of COPD although the exact mechanism behind it remains unclear. The frequency of hypomagnesemia increased with increasing severity of COPD exacerbation. The treatment given to the patient for COPD must be given along with the regular checking of serum magnesium levels. In conclusion it is hereby recommend regular screening of serum magnesium levels for all the COPD patients to predict and prevent AE.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a preventable and treatable disease, often progressive in nature, characterized by a chronic inflammatory response of the airways and lungs to harmful gases and particles., especially tobacco and smoke.[1]

Exacerbations with reduced quality of life, accelerated decline in respiratory function, and increased economic costs can occur during stable COPD.[2,3]

A COPD exacerbation is defined as an acute worsening of respiratory symptoms (increased shortness of breath, increased cough, or change in the amount and amount of sputum) that exceeds the normal daily range of the patient symptoms.[1]

Acute COPD exacerbations (COPDAE) occur frequently with respiratory infections. It is a major cause of death and morbidity.[4]

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Few studies have investigated the factors leading to exacerbations. Advanced age, low FEV1%, advanced stage of disease, poor performance status, accompanying anxiety and/or depression, poor quality of life, history of frequent exacerbation, hypercapnia, and prolonged duration of disease have all been identified as factors causing frequent exacerbation.[5-8]

Magnesium plays an important role in neuromuscular, cardiovascular, and metabolic functions. Low magnesium levels are associated with decreased lung function and an increased incidence of COPD exacerbations.[9]

The role of Magnesium in acute exacerbation of COPD is unclear. Lower serum Magnesium levels are seen in patients with acute exacerbation as compared to patients with stable COPD.[7,8] Also, it is not clear whether serum Magnesium continues to remain low after exacerbation subsides or spontaneously corrects after stabilization of patients with improvement in acid-base balance in the stable state.

However, there is a lack of data on the impact of magnesium on the incidence of COPD-AE. An investigation into variables associated with COPD-AE and the influence of magnesium levels on the occurrence of exacerbations was conducted in this study.

METHODOLOGY

It was observational study, all patients of general medicine department, fulfilling the inclusion criteria and excluded by the exclusion criteria, admitted in OPD and outdoor of BMCH, in between 1st March 2020 to 31st September 2020. 50 patients with exacerbation of COPD and 50 patients of COPD in stable condition were selected. Serum magnesium was measured using xylidyl blue technique. Auto analyser was used for measuring serum magnesium level. This is easy, rapid and accurate method for determining magnesium levels. The integrity of the reaction was monitored using sera with known concentration (2.0mg/dl).

Inclusion Criteria

- COPD patients with and without exacerbation, Exacerbation is defined as an event in the natural course of the disease characterized by a change in the patient's baseline dyspnea, cough, and/or sputum that is beyond normal day-to-day variations, is acute in onset, and may warrant a change in regular medication in a patient with underlying COPD[3,113]
- Age > 18 years

Exclusion Criteria

- Renal failure
- Congestive heart failure
- Ca lung
- COPD patients admitted for other reasons
- DM, Hypertension, CAD, CVA.
- Drugs – H2 blockers, Antacids, PPIs, Diuretics, Digoxin
- Previous GI surgery

Study Variables: Serum magnesium level

Study Tools:

- History
- Clinical examination
- Serum magnesium level

Selection of Cases: Patients attending the OPD and admitted in ward were selected randomly for study. All inclusion and exclusion criteria were fulfilled.

Statistical Analysis

All recorded data was analyzed with suitable diagrams, figures, tables and findings were discussed in details to draw appropriate conclusions using standard statistical analysis. Data were analyzed using Statistical Package for the Social Sciences (SPSS) Inc, Chicago, USA; Version 21.0. Continuous variables were expressed in mean and standard deviations (SD). Categorical variables were expressed as number and percentages. Fisher's exact test, Chi-square test and Unpaired't' test was used for categorical data as appropriate. A p value < 0.05 was considered statistically significant.

RESULTS

Table 1: Age Distribution

Age Group (years)	AECOPD (n= 50)		Stable COPD (n= 50)	
	Frequency	Percentage	Frequency	Percentage
18-35 years	1	2.0	2	4.0
36-50 years	18	36.0	19	38.0
51-65 years	31	62.0	29	58.0
Total	50	100.0	50	100.0
Mean Age	54.92±9.49		53.32±9.36	
Statistical Interference	p value:0.832			

Table 1 presents the age distribution of the study participants of both AECOPD and stable COPD. In both the groups the most common age group was 51-65 years (62% in AECOPD and 58% in stable COPD). The mean age was 54.92 ±9.49 years and 53.32 ±9.36 years respectively in AECOPD and stable COPD with no significant difference (p value = 0.832).

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Table 2: Sex Distribution

Sex	AECOPD (n= 50)		Stable COPD (n= 50)	
	Frequency	Percentage	Frequency	Percentage
Male	39	78.0	37	74.0
Female	11	22.0	13	26.0
Total	50	100.0	50	100.0
Statistical Interference	Chi square:0.219 p value: 0.639			

Majority of the study participants in both AECOPD and stable COPD were males (78% in AECOPD vs. 74% in stable COPD). This observation suggests that males are more prone to develop COPD. Sex distribution showed no significant difference between groups (p value = 0.639). Data is depicted in **Table 2**.

Table 3: Residence

Residence	AECOPD (n= 50)		Stable COPD (n= 50)	
	Frequency	Percentage	Frequency	Percentage
Urban	33	66.0	30	60.0
Rural	17	34.0	20	40.0
Total	50	100.0	50	100.0
Statistical Interference	Chi square: 0.386 p value: 0.534			

Majority if the study subjects in both groups are from urban area (66% in AECOPD vs. 60% in stable COPD). Data is presented in **Table 3**. Both the groups were comparable in terms of residential status (p value = 0.534).

Table 4: Smoking Status

Smoking Status	AECOPD (n= 50)		Stable COPD (n= 50)	
	Frequency	Percentage	Frequency	Percentage
Smoker	34	68.0	30	60.0
Ex-smoker	5	10.0	7	14.0
Non-smoker	11	22.0	13	26.0
Total	50	100.0	50	100.0
Statistical Analysis	Chi square: 0.75 p value: 0.687			

Smoking status of the study participants in both AECOPD and COPD group is shown in **Table 4**. Majority of the studyparticipants in both groups were either current smoker (68% in AECOPD vs. 60% in stable COPD) or ex-smoker (10% in AECOPD vs. 14% in stable COPD). Mainly female patients were non-smokers in the study. There was no significant difference regarding smoking status between groups (p value = 0.687).

Table 5: mMMRC Grade

mMMRC Grade	AECOPD (n= 50)		Stable COPD (n= 50)	
	Frequency	Percentage	Frequency	Percentage
0	0	0.0	0	0.0
1	2	4.0	6	12.0
2	9	18.0	13	26.0
3	17	34.0	17	34.0
4	22	44.0	14	28.0
Total	50	100.0	50	100.0
Statistical Analysis	Chi square: 4.505 p value: 0.341			

Table 5 presents the distribution of the study subjects in both AECOPD and stable COPD according to mMRC grading. Majority of the study subjects in both AECOPD and COPD belonged to mMRC grade 3 (34% in both AECOPD and stable COPD) and grade 4 (44%in AECOPD vs. 28% in stable COPD). Above analysis both the groups were comparable in terms of mMRC grading (p value = 0.341).

Table 6: Association of Different Variables

Variables	AECOPD (n= 50)		Stable COPD (n= 50)		p value
	Mean	±SD	Mean	±SD	
Hb (gm/dl)	12.16	±0.54	13.14	±0.70	0.041
TLC	8348.00	±1690.23	8180.00	±1676.42	0.959
ESR (mm/hr)	17.10	±3.22	15.40	±3.06	0.510
Platelet	2.96	±0.34	2.97	±0.32	0.318
PCV	42.50	±3.44	43.30	±2.83	0.083
Urea (mg/dl)	32.81	±3.27	31.70	±2.18	0.095
Creatinine (mg/dl)	0.85	±0.12	0.82	±0.10	0.311

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Table 6 presents the comparison of various parameters between patients with AECOPD and stable COPD. Above analysis we found all the variables i.e. TLC, ESR, Platelet, PCV, Urea and creatinine except haemoglobin were comparable between AECOPD and stable COPD (p value = >0.05). Only haemoglobin level was significantly lower among patients with AECOPD (12.16 ±0.54 gm/dl) compared to patients with stable COPD (13.14 ±0.70) with a p value 0f 0.041.

Table 7: Distribution according to Low and normal Serum Magnesium Level at admission

Serum Magnesium Level	AECOPD (n= 50)		Stable COPD (n= 50)	
	Frequency	Percentage	Frequency	Percentage
<1.60 mg/dl	35	70.0	8	16.0
≥1.60 mg/dl	15	30.0	42	84.0
Statistical Analysis	Chi square: 29.743 p value: <0.0001			

Table 7 presents the distribution of both groups according to serum magnesium level. A vast majority of the study subjects (70%)in AECOPD group had magnesium level lower than the normal range while in stable COPD only 16% participants had low magnesium level with a statistically significant difference (p value = <0.0001).

Table 8: Comparison of Mean Serum Magnesium Level (mg/dl) at admission

Type	Mean	±SD
AECOPD	1.71	±0.44
COPD	1.90	±0.34
Statistical Inference	0.046	

Table 8 presents the comparison of mean magnesium level among patients in AECOPD and stable COPD at the time of admission. The mean magnesium level was 1.71 ±0.44 mg/dl in AECOPD and 1.90 ±0.34 mg/dl in stable COPD. Serum magnesium level was significantly lower among patients with AECOPD compared tostable COPD at the time of admission (p value = 0.046).

Table 9: Comparison of Mean Serum Magnesium Level (mg/dl) at discharge

Type	Mean	±SD
AECOPD	1.90	±0.36
COPD	2.03	±0.36
Statistical Inference	0.05	

Table 9 presents the comparison of mean magnesium level among patients in AECOPD and stable COPD at the time of discharge. The mean magnesium level was 1.90 ±0.36 mg/dl in AECOPD and 2.03 ±0.36 mg/dl in stable COPD. Serum magnesium level was significantly lower among patients with AECOPD compared to stable COPD at the time of discharge (p value = 0.046).

Table 10: Comparison of serum Magnesium level on Admission according to mMRC grading

mMRC Grade	AECOPD (n= 50)	Stable COPD (n= 50)	p value
0	-	-	-
1	1.70 ±0.50	1.73 ±0.42	0.469
2	1.78 ±0.36	1.73 ±0.36	0.11
3	1.68 ±0.42	1.89 ±0.22	0.015
4	1.70 ±0.46	1.90 ±0.33	<0.0001

Table 10 demonstrates the comparison of mean magnesium level at admission according to mMRC grading. And we found significant difference between AECOPD and stable COPD in mean serum magnesium level in mMRC grade 3 and 4 (p value = <0.05).

DISCUSSION

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality and is therefore a major public health concern. Prevalence of COPD worldwide ranges from 4% to 10%.[1][14]
World health organisation (WHO) predicts that COPD will become the third leading cause of mortality by 2030, owing to decrease in cardiac diseases and stroke over the period of 1970-2002, but the rates of incidence and prevalence of COPD doubled in these years.[10]Hospitalization for acute exacerbation accounts for nearly 70% of COPD-related health expenditure.[11]
Previous studies reported there have been few predicators for exacerbation of COPD and one such independent indicator is serum magnesium. Magnesium is the second most abundant cation in the intracellular fluid. It plays an important role in muscular tone andexcitability.[12] Hypomagnesemia is associated with increased airway response and decreased muscle strength.[13]

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Serum magnesium also plays a vital role in bronchodilation, airway smooth muscle relaxation, mucociliary clearance.[14] Extracellular rise in magnesium level has shown to inhibit contractile tension of smooth muscle.[15] **Alamoudi et al** showed similar results in asthma patients.[16]

Aziz et al studied the levels of magnesium in COPD patients with acute exacerbations, and stable COPD patients. He found out serum magnesium levels was 0.77±0.10mmol/L for AECOPD patients. Stable patients of COPD had magnesium on the range of 0.91±0.10 mmol/L. He found out patients with acute exacerbation of COPD had hypomagnesemia compared to stable COPD patients.[17]

Sajjadrajab et al studied serum magnesium levels in patients presented with acute exacerbation, at the time of discharge and after one month of discharge. They reported serum magnesium levels were reduced in AECOPD patients 1.88±0.67mg/dl, to that if stable COPD patients 2.30±0.36mg/dl. They observed reduced serum magnesium levels during AECOPD.[18]

David Holmes et al, observed that the patients with low serum magnesium levels are at increased risk of exacerbation and hospital admission in compared with stable COPD patients with normal magnesium levels.[19]

TamizhSelvan.R et al in their study reported Mean serum magnesium level at the time of admission was 1.287 mg/dl (SD±0.33) and the time of discharge was 2.009 mg/dl (SD± 0.2955). The association of serum magnesium level and acute exacerbation of COPD was found to be statistically significant with p value less than 0.05.[20]

Corradi et al determined higher serummagnesiumlevels in periods of COPD-AEcompared to stable periods.Anegative correlation was shown betweenmagnesium and predicted FEV1%.However, they did not search the correlation between frequency of COPD-AE and magnesium levels.[21]

Our study and studies done by other researchers suggest that acute exacerbation of COPD is associated with significant hypomagnesemia. In our study, we measured serum Mg levels in patients with AECOPD at the time of admission as well as at discharge and showed that low serum magnesium during the acute stage reverted to normal without magnesium supplementation. We also found an association between serum Mg level and severity of COPD exacerbation.

CONCLUSION

During COPD exacerbation, serum magnesium levels decreased. This decrease was transient. We determined that serum magnesium is an independent predictor of frequent readmissions for acute exacerbations of COPD although the exact mechanism behind it remains unclear. The frequency of hypomagnesemia increased with increasing severity of COPD exacerbation. The treatment given to the patient for COPD must be given along with the regular checking of serum magnesium levels. In conclusion it is hereby recommend regular screening of serum magnesium levels for all the COPD patients to predict and prevent AE.

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