European Journal of Molecular & Clinical Medicine

ISSN 2515-8260 Volume 9, Issue 3, Winter 2022

ORIGINAL RESEARCH

To Assess thelevels of Serum Magnesium in Diagnosed Cases of Chronic Obstructive Pulmonary Disease at Tertiary Care Centre

[1]Dr. RichaArora, [2]Dr. Pradeep Nirala, [3]Dr. Mazher Maqusood, [4]Dr.Abhishek Kumar

[1]Jr3, [2]Associate Professor, [3]Professor and HOD, [4]Assistant Professor, Department of Pulmonary Medicine, TMMC&RC, Moradabad, Uttar Pradesh, India

Correspondence:
Dr. PradeepNirala
Associate Professor, Department of Pulmonary Medicine, TMMC&RC, Moradabad, Uttar Pradesh, India

ABSTRACT

Aim: Hypomagnesemia has been cited as a predictor of exacerbations in bronchial asthma, but is underexplored in COPD. Hence the current research was done to define the effect of magnesium levels on the incidence of COPD exacerbations and its outcome.

Material and methods: The present prospective observational hospital-based study was conducted in the department of pulmonary medicine at TMMC and RC, Moradabad for one and half years among patients with COPD diagnosed on spirometry. On enrolment into the trial and 20 minutes after the delivery of salbutamol nebulization, spirometry was done in stable COPD patients. Samples were obtained for the estimation of serum Magnesium levels of the patients at the time of exacerbations and patients in the stable COPD group. Results of serum magnesium levels were noted in both Group A (stable COPD) and Group B (COPD with acute exacerbations) and the data was analyzed.

Results:The number of COPD patients with acute exacerbations was 36.6% while stable patients were 63.4%.Serum magnesium value among COPD patients with acute exacerbations and COPD stable patients was 1.62±0.38 and 1.92±0.41 respectively with a significant difference.Serum magnesium level showed a significant negative correlation with spirometry severity

Conclusion: In a COPD patient, there was a strong link between serum magnesium levels and the incidence of exacerbations. There was a strong negative association between serum magnesium levels, spirometry severity, and dyspnea severity. This is a controllable risk factor, and we urge that all subjects known for COPD have their serum magnesium levels checked.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is not a fully reversible condition characterized by chronic restriction of lung flow that prevents normal respiration.[1] COPD is marked by two of the most frequent illnesses, chronic bronchitis and emphysema, which overlap most of the time.[2]According to a recent study that looked at the global burden of COPD using new diagnostic criteria, the occurrence of moderate to extreme COPD is 10.1 percent.[1]It is a serious lung illness that is often wrongly diagnosed as a "smoker's cough." Due to ongoing contactwith COPD risk issues and the aging of the global people, the load of COPD is expected to rise in the future periods. COPD affects 65 million people worldwide[3], according to WHO estimates. COPD claimed the lives of almost 3 million people in 2005, accounting for 5% of all fatalities worldwide.[4]

Magnesium is an important mineral in the human body because of its involvement as a co-factor in enzyme activities. Magnesium is a vital component of life that can be found as an intracellular ion in all living cells and tissues. Magnesium's involvement in disease processes is becoming more widely understood these days.[5,6]

Serum Magnesium is needed for bronchodilation and contraction of smooth muscles in the respiratory tract, mast cell stability, neurohumoral mediator release, and mucociliary clearance, among other things. Magnesium is supposed to protect against COPD.[7]Becauseit is important in muscle tone, a reduction in Mg levels in patients is a component that is adverse to respiratory performance, as little magnesium levels cause muscular weariness. Research suggests that Mg^{2+} shortage donates to asthma exacerbations &also as a result Mg^{2+} can help individuals with bronchospasm. Although the exact mechanism of action is uncertain, Mg^{2+} has been postulated to play a function in maintaining airway patency by relaxing bronchial smooth muscle.[8-10]

As a result of the diminished muscle strength, hypomagnesemia is thought to be linked to increased airway hyperactivity and impaired pulmonary function. A drop in magnesium levels is thought to worsen COPD exacerbations as a result of these effects.Hypomagnesemia has been cited as a predictor of exacerbations in bronchial asthma but is underexplored in COPD. Hence the current research was done to define the effect of magnesium levels onthe incidence of COPD exacerbations and its outcome with the following objectives:

a. To assess the magnesium levels association with disease flare-up in stable COPD patients based on severity grading according to GOLD guidelines 2019.
b. Need to determinewhetherserum magnesium should beconsidered asaroutine investigation in COPD patients.

MATERIAL AND METHOD

The present prospective observational hospital-basedstudy was conducted in the department of pulmonary medicine at TMMC and RC, Moradabad for one and a half years after the college research committee approves patients with COPD. Patients diagnosed with COPD on spirometry and patients who gave written consent were included in the study. Patients on magnesium supplementations were excluded from the study. The sample size was calculated according to the following formula and taking the Indian prevalence of COPD to be 4.21%.[11]

$n=Z(\alpha/2)^2 \times P \times (100-P)/E^2$ Where Z =2.58

E =5%

P (prevalence) =4.21% n (sample size) = 106

However, due to the COVID pandemic, the sample size was limited to 82 for the present study.

ROUTINE INVESTIGATIONS

1. ABG (in patients presenting with exacerbations)
2. Hb, TLC
3. Chest X-ray PA view
4. Serum bilirubin, SGOT, SGPT
5. Urea, creatinine, uric acid
6. Spirometry (In stable patients)

IF NEEDED

1. USG W/A

METHODOLOGY

1. Patients attending TMU Hospital, Moradabad, fulfilling the inclusion and exclusion criteria were included in the study.
2. In group A, only the spirometrically diagnosed stable cases of COPD who presented in OPD/IPD were included. Patients in Group A were graded based on the severity as per GOLD staging.
3. In group B patients presenting in Emergency/OPD with COPD acute exacerbations and requiring hospitalization were included. At the time of enrolment detailed medical history was taken and a complete physical examination was performed. The subjects underwentthe above-mentioned investigations.
4. On enrolment into the trial and 20 minutes after the delivery of salbutamol nebulization, spirometry was done in stable COPD patients (if available) attending OPD with equipment that satisfied the American Thoracic Society performance requirements.
5. Based on the fulfillment of the inclusion criteria, the samples were obtained for the estimation of serum Magnesium levels of the patients at the time of exacerbations and patients in the stable COPD group. 5ml of venous blood sample was collected in a vacutainer andsenttothe laboratory (In Vitro Diagnostic test).
6. Serum Magnesium levels were analyzed from 1ml of supernatant hemolyzed serum by the Calorimetric endpoint method. The method was based on the reaction of Mg with xylitol blue in an alkaline solution containing EGTA.
7. We used the Hitachi Cobas C systems analyzer with the automated procedure. Magnesium values for serum obtained on a Hitachi Cobas C 501 analyzerwere compared with the corresponding reagent.
8. The integrity of the reaction was monitored by normal and abnormal control sera with known magnesium concentrations. The normal serum value ranges from 1.8-2.4mg/dl.
9. Results of serum magnesium levels were noted in both Group A stable COPD according to the grading of severity and Group B COPD with acute exacerbations and the data was analyzed.

CRITERIA FOR EXACERBATIONS[1]

a) BASED ON WORSENING OF BASELINE SYMPTOMS

1. Increased dyspnea
2. Increased sputum production
3. Increased sputum purulence

b) BASED ON INVESTIGATIONS

1. Respiratory rate>25
2. Pulse rate>110bpmin
3. Type1/Type2 respiratory failure (ABG)
4. Abnormal chest radiograph
5. MMRC dyspnea grading >2

A SCALE FOR EXACERBATION ACCORDING TO ARTERIAL BLOOD GAS ANALYSIS[12]

1. Type I respiratory failure with hypoxemia but no CO2 retention and acidosis,PaO2<60mmhg, and PaCo2-<45mmhg.
2. Type 2 respiratory failure, compensated with hypoxia, carbon dioxide retention or acidosis,PaO2<60mmHg,PaCo2>45mmhg, and H+ conc<44nM PH>7.35.
3. Type 2 respiratory Failure, decompensated with acidosis and carbon dioxide retention; PaCo2>45mmhg and H+ conc>44nM (Ph<7.35).

Data was collected and subjected to statistical analysis.

STATISTICAL ANALYSIS

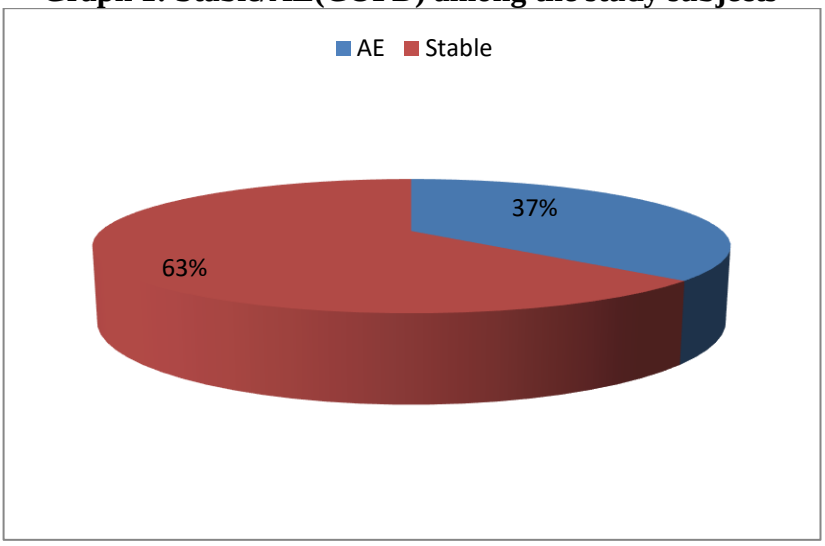
Data so collected were tabulated in an excel sheet, under the guidance of a statistician.The means and standard deviations of the measurements per group were used for statistical analysis (SPSS 22.00 for windows; SPSS inc, Chicago, USA).For each assessment point, data were statistically analyzed using one-way ANOVA. The difference between the two groups was determined using a student t-test and the level of significance was set at $p < 0.05$.

RESULTS

In the present trial out of 82 patients who were diagnosed with COPD who were found eligible for enrollment in our study,the maximum patients were male (n=70, 85.4%) the and rest were females (n=12, 14.6%). The male to female ratio in the present study was 5.83:1.In the present trial, in the stable group, only the spirometrically diagnosed stable cases of COPD who presented in OPD/IPD were included. Patients in the stable group were graded based on the severity as per GOLD staging. In the acute exacerbations group, patients presenting in Emergency/OPD with COPD acute exacerbations and requiring hospitalization were included. In the present trialamong 82 subjects aged between 23 and 79 years, the mean age was 57.85±12.11.

In the present study, the severity of dyspnea is scored by the MMRC dyspnea scale as grades 1 to 4. The maximum number of patients were in Grade II dyspnea (n=28, 34.1%), followed by Grade IV dyspnea (n=25, 30.5%). Grade III dyspnea had 24 patients (29.3%). At least were in Grade I dyspnea i.e., only 5 patients (6.1%). In the present trial, thenumber of COPD patients with acute exacerbation was 30 (36.6%) while stable patients were 52 (63.4%) as depicted in Graph 1.

Graph 1: Stable/AE(COPD) among the study subjects



In the present study, Spirometry was performed for all subjects and the maximum number of patients were in the moderate stage (n=34, 41.5%), followed by 21 subjects in the mild stage (25.6%). 16 patients were in the severe stage (19.5%). And least was in a very severe stage (n=11, 13.4%). (Graph 2)

62 patients (75.6%) showed some abnormality in chest X-rays, whereas 20 patients had normal X-ray chest findings. In the present trial, the mean serum magnesium value was 1.81±0.42 mEq/dl. The minimum level was 1 mEq/dl and the maximum level was 2.80 mEq/dl. Mean serum magnesium value in grade I was 2.26±0.36, in grade II was 1.87±0.41,

in grade III was 1.79±0.45 and in grade, IV was 1.66±0.36 with a significant difference of p=0.01. (Table 1)

Table 1: Magnesium comparison according to MMRC Grading

MMRC Grading	Mean	SD	ANOVA Test	p-value
GRADE I	2.26	.36	4.91	0.01*
GRADE II	1.87	.41		
GRADE III	1.79	.45		
GRADE IV	1.66	.36		

*: statistically significant

In the present trial, when serum magnesium value was compared with COPD patients with acute exacerbations mean value was 1.62±0.38 and when compared with COPD stable patients mean value was 1.92±0.41 with a significant difference as p-value<0.01. (Table 2)

Table 2: Magnesium comparison according to stable/AE

Variables	Mean	SD	t-Test	p-value
Stable	1.92	.41	11.03	<0.01**
AE	1.62	.38		

*: statistically significant

In the present trial, when serum magnesium value was compared with spirometry severity a statistically significant relation was found with a p-value<0.01. For Mild mean value was 2.04±0.36, for Moderate it was 1.86±0.39, for Severe it was 1.70±0.33 and for Very Severe mean value was 1.38±0.41. (Table 3)

Table 3: Magnesium comparison according to spirometry severity

Spirometry Severity	Mean	SD	ANOVA Test	p-value
Mild	2.04	.36	8.12	<0.01**
Moderate	1.86	.39		
Severe	1.70	.33		
Very Severe	1.38	.41		

*: statistically significant

In the present trial, when serum magnesium value was compared with spirometry severity of stable patients a statistically significant relation was found with a p-valueof 0.031. For mild severity mean serum magnesium value was 2.04±0.21, for moderate severity it was 1.88±0.28 and for severe patients, it was 1.66±0.22. (Table 4)

Table 4: Magnesium comparison according to spirometry severity of stable patients

Spirometry Severity	Mean	SD	ANOVA Test	p-value
Mild	2.04	.21	3.59	0.031*
Moderate	1.88	.28		
Severe	1.66	.22		

*: statistically significant

DISCUSSION

Serum magnesium levels are becoming more commonly recognized as important in lung disease. Ample of the motivation for recognizing Mg as a risk factor and a possible therapeutic mediator in COPD patients comes from the moderately firm role of magnesium in the dealing of asthma[6]. Reduced Mg levels in COPD patients are an issue that is damaging to respiratory function because low magnesium levels produce muscular fatigue. Patients with COPD have asthmatic bronchitis, which is a combination of chronic bronchitis and emphysema. Bronchospasm exacerbates their incapability to eliminate oozes. This can result

in decreased pulmonary gas exchange, resulting in a worse quality of life and more frequent hospitalizations.[7,8]

This study was carried out including 82 diagnosed cases of Chronic Obstructive pulmonary disease (COPD) which may be either stable or with acute exacerbations, who were referred to the Department of Pulmonary Medicine. Routine blood investigations were performed for all patients included in the study. Spirometry was also performed and Serum Magnesium levels were also analyzed.

The demographic variable of the present study shows that out of 82 patients involved a maximum number of patients were male (85.4%), and the male to female ratio in the present study was 5.83:1. The result wasfroma study done by BhaumikS et al[13] (2019), who found that in their study 90% of involved subjects were males. But according to the study by Singh JP et al[14], (2012) included patients were twenty-nine and twenty-one males& females respectively.

In the present study, the average age of patients was 57.85±12.11 years, which was in harmonywith the study done by Singh JP et al[14], (2012) who found the mean age of the patients to be 60.4±6.5 years. And also, according to the study byBhaumikS et al[13] (2019), the mean age of the patients was 60 ± 6.33 years.

52 (63.4 percent) of the 82 patients in the trial had no exacerbation, meaning they were stable. The remaining 30 (36.6 percent) either had an acute exacerbation or had a history of one or more exacerbations in the past that necessitated hospitalization. The findings differed from those of BhaumikS et al[13] (2019), who showed that 16 (26.7 percent) of the 60 participants had no exacerbation, whereas the rest 73.3 percent (44/60) either experienced an exacerbation or had a history suggestive of one.

In the present study, the severity of dyspnea is scored by the MMRC dyspnea scale as grades 1 to 4. The maximum number of patients were in Grade II dyspnea (34.1%), followed by Grade IV dyspnea (30.5%). Grade III dyspnea had 24 patients (29.3%). At least were in Grade I dyspnea i.e., only 5 patients (6.1%). According to the findings of Murthy et al[31], (2016),a maximum number of patients were in Grade III (50%), followed by Grade IV (24%), 16% of patients were in Grade II and only 10% of patients were in Grade I.

In the present study, the mean FEV1of the subjects got at baseline spirometry was 60.22±22.04% of the predicted. The result of BhaumikS et al[13], (2019) found that the mean FEV1 of the study topics obtained at baseline spirometry was 60±9.7% of the predicted.

In the present study as per the GOLD criterion for the staging of COPD, 21 subjects were in the mild stage (25.6%), 34 subjects in the moderate stage (41.5%), followed by 16 patients in the severe stage (19.5%) and 11 patients in very severe stage (13.4%). The results were almost in agreement withthe findings of Singh JP et al[14], (2012)who found that34% were in stage -I, 50% in stage II, and 16% in stage III. And also, according to the findings of RajjabS[15], 50.6% of the patients were in stage II and 35.06% in stage I, and 14.28% in stage III.

In the present trial, the magnesium value in the study subjects was 1.81±0.42 mEq/dl. According to the findings of Murthy et al[16] (2016), the mean serum magnesium level was: 1.576 ± 0.336.

The average Mg^{2+} levels in subjects with stable COPD were 1.920. Exacerbation patients had significantly lower serum Mg+2 concentrations, with a mean value of 1.62038. With a p-value of 0.01, it was judged to be statistically significant. This was in line with the findings of Aziz HS et al[6] (2005), who discovered that blood Mg^{2+} levels in stable COPD patients averaged 0.91- 0.10 mmol/L (mean SD), with a 95 percent confidence interval (CI95) of 0.88 – 0.94 mmol/L. Serum Mg^{2+}values were significantly lower in patients who were experiencing an exacerbation. According to BhaumikS et al[13] (2019), the median value of

serum Magnesium in participants with current or prior exacerbations was substantially lower than in those without any exacerbation.

In the present trial, the level of magnesium is low in severe cases of dyspnea. In the present trial, when serum magnesium value was compared with spirometry severity a statistically significant relation was found with a p-value<0.01. Serum magnesium level showed a significant negative correlation with spirometry severity i.e. magnesium leveldecreased with an increase in severity. Magnesium's direct relaxing effects on bronchial smooth muscles may be due to calcium channel blocking properties, inhibition of cholinergic Neuro Muscular Junction transmission with decreased sensitivity to the depolarizing action of acetylcholine, stabilization of mast cells and T lymphocytes[3,17]and stimulation of nitric oxide and prostacycline.[8]

The limitations of the present study are first, the small sample size and the patients were from only one center with the same ethnicity, so the results cannot be generalized.

CONCLUSION

The average amount ofserum magnesium in COPD patients was 1.8104mEq/dl. In a COPD patient, there was a strong link between serum magnesium levels and the incidence of exacerbations. Furthermore, there was a strong negative association between serum magnesium levels, spirometry severity, and dyspnea severity.This is a controllable risk factor, and we urge that all subjects knownforCOPDhave their serum magnesium levels checked. More research on magnesium supplementation is essential to see if it can change the sequence of the disease in a specific cohort.

REFERENCES

1. Chunk Yip. COPD: State of the art – Common Medical Diseases (II) the Eleventh Health Conference.pp36-43.
2. George RB, San Pedro GS, Stoller JK. Chronic obstructive pulmonary disease, bronchiectasis, and cystic fibrosis. In: Chest Medicine: Essentials of Pulmonary and Critical Care Medicine; 4thed (GeorgeRB, Light RW, Matthay MA, Matthay RA, Eds). Lippincott Williams and Wilkins, Philadelphia, 2000. pp.174-207.
3. Bhatt SP, Khandelwal P, Nanda S, Stoltzfus JC, Fioravanti GT. Serum magnesium is an independent predictor of frequent readmissions due to acute exacerbation of chronic obstructive pulmonary disease. Respiratory medicine. 2008; 102(7): 999-1003.
4. Pauwels RA, Buist AS, Calverley PM, Jenkins CR, Hurd SS. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Am J RespirCrit Care Med. 2001; 163(5): 1256-76.
5. Thomas L. Petty. The history of COPD. International Journal of COPD 2006: 1(1): 3-4.
6. Aziz HS, Blamoun AI, Shubair MK, Ismail MM, DeBari VA, Khan MA. Serum magnesium levels and acute exacerbation of chronic obstructive pulmonary disease: a retrospective study. Annals of Clinical & Laboratory Science. 2005; 35(4): 423-7.
7. Gourgoulianis KI, Chatziparasidis G, Chatziefthimou A, Molyvdas PA. Magnesium as a relaxing factor of airway smooth muscles. J Aerosol Med 2001; 14: 301-07.
8. Alter HJ, Koepsell TD, Hilty WM. Intravenous magnesium as an adjuvant in acute bronchospasm: a meta-analysis. Annals Emerg Med 2000: 36: 191-97
9. Hughes R, Goldkorn A, Masoli M, et al. Use of isotonic nebulized magnesium sulphate as an adjuvant to salbuterol in treatment of severe asthma: randomized, placebo-controlled trial. Lancet 2003: 361: 2114-17
10. Roy SR, Milgrom H. Managing outpatient asthma exacerbations. Curr Allergy Asthma Reports 2003; 3: 179-89.

11. Olivia Z. Roth, Nicholas P. Crocetta, Jared L. Ostroff: A Review of the 2018 GOLD Guidelines for COPD. US Pharm. 2018; 44(7): HS- 8-16.
12. Kumar GV, Keerthi CS. Study of serum magnesium levels in stable chronic obstructive pulmonary disease and chronic obstructive pulmonary disease exacerbations. Indian Journal of Immunology and Respiratory Medicine. 2017; 2(2): 33-5.
13. Bhaumik S, Choudhury A, Chakrabarti D, Dey PK. Study of serum magnesium level in COPD and its impact on exacerbation of COPD. J Evid Based Med Healthc. 2019; 6: 1235-9.
14. Singh JP, Kohli S, Devi A, Mahajan S. Serum magnesium level in COPD patients attending a tertiary hospital-a cross sectional study. JK Science. 2018; 14(4): 185.
15. Rajjab S. Serum magnesium levels and acute exacerbation of chronic obstructive pulmonary disease. SKIIMSMed J 2010.
16. Krishna Murthy MG, Kumar TP, Kumar MK. Study of serum magnesium levels in acute exacerbation of COPD. Asian Pac. J. Health Sci2016; 3(1): 56-64.
17. Landon RA, Young EA. Role of magnesium in regulation of lung function. J Am Diet Assoc 1993; 93(6): 674-677.