ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 11, Special issue 3, 2018

Online - 2455-3891
Print - 0974-2441

Research Article

CLINICAL ASSOCIATION OF SERUM MAGNESIUM AND SERUM FIBRINOGEN LEVELS WITH ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE – A PROSPECTIVE OBSERVATIONAL STUDY

NIVENTHI A[1], PRAVEEN D[2], RANADHEER CHOWDARY P[2], VIJEY AANANDHI M[3]*

[1]Department of Pharmacy Practice, School of Pharmaceutical Sciences, Vels Institute of Science Technology and Advanced Studies, Chennai, Tamil Nadu, India. [2]Research Scholar, School of Pharmaceutical Sciences, Vels Institute of Science Technology and Advanced Studies, Chennai, India. [3]Department of Pharmaceutical Chemistry and Analysis, School of Pharmaceutical Sciences, Vels Institute of Science Technology and Advanced Studies, Chennai, India. Email: hodpchemistry@velsuniv.ac.in

Received: 10 October 2018, Revised and Accepted: 11 December 2018

ABSTRACT

Objective: Acute exacerbations (AE) are a contributing cause of worsening chronic obstructive pulmonary disease (COPD) in conditions of lung function decline, quality of liveliness, and natural selection. The most important concept of this article is the positive correlation between the serum magnesium levels at worsening of symptoms and annual number of episodes.

Methods: Blood samples from the patients who are diagnosed with AE of COPD will be collected and evaluated for serum magnesium levels and serum fibrinogen levels. Low serum magnesium is a modifiable risk factor. It is generally believed that, due to its bronchodilating effect, a decreased level of magnesium increases COPD exacerbations. The best blood biomarker for the systemic tenderness in COPD used here is plasma fibrinogen. Those with the increased fibrinogen levels had induced the higher admission rates with COPD. This clause deals with the association of both serum magnesium and serum fibrinogen levels with AE-COPD.

Results: The serum magnesium levels on discharge in stable type were found to be 2.3±0.27, and in exacerbation, it was found to be 1.56±0.37. Moreover, on discharge, serum fibrinogen levels in stable type were found to be 1.64±0.32, and in exacerbation, it was found to be 2.18±0.40.

Conclusion: Low serum magnesium levels may be a complication for AE of COPD. High serum fibrinogen levels may be a complication for AE of COPD. We hereby recommend regular screening of serum magnesium and serum fibrinogen levels for all the COPD patients to predict and prevent AE.

Keywords: Chronic obstructive pulmonary disease, Acute exacerbation, Serum magnesium, Serum fibrinogen.

 DOI: http://dx.doi.org/10.22159/ajpcr.2018.v11s3.31683

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is determined by lung disease causing breathing difficulties due to the penetration of small airways with inflammatory cells and breathlessness [1,2]. Exacerbations are worsening of the symptoms. Acute exacerbation (AE) of pulmonary disease represents a central moment in the series of COPD. The relationship between AECOPD and decrease in health status and lung function is easily accepted [3,4]. These cases take up around 50% of the direct cost for COPD [5]. AE that adjusts the quality of life, declines in respiratory functions, and increases the economic costs may occur during the course of stable COPD [6,7]. The acute worsening of respiratory symptoms that were beyond normal daily variations of symptoms is termed as COPD exacerbation.

Serum magnesium

Serum magnesium is required in such major uses as bronchodilation and contraction in respiratory tract smooth muscles, mast cell stabilization, neurohumoral mediator release, and mucociliary clearance [8]. Magnesium is thought to possess a protective effect against chronic respiratory tract diseases. It has been proposed that insufficient magnesium intake through diet may lead to the development of asthma and COPD [9,10].

It is one of the major intracellular cations. Normal value: 0.7–1 mmol/L (1.5–2 mEq/L; 1.7–2.4 mg/DL) [11,12] Critical value: <1 and >4.9 mg/DL [12].

Serum fibrinogen

Serum fibrinogen has come out as the best biomarker in this pulmonary disease and is currently being considered for alteration as a drug development tool by the USFDA and the EMA [13,14].

However, the plasma range of fibrinogen in patients with obstructive breathing disorder has been probed, and in the restrictive pulmonary disorder such as pulmonary fibrosis, the values are not yet well defined in these patients [15-18]. Normal fibrinogen ranges between 1.5 and 3.5 g/l.

METHODS

The survey was placed out in General Medicine Department of ESI Hospital, Ayanavaram, with the sample size random sampling of a population of 200 persons with a confidence interval of 95% and the sample size was found to be 132 patients. The duration of the study was September 2017-April 2018. The study design was a prospective observational study. The study procedure followed was ask the patient to make the arm relaxed and point the vein. The needle should form a 15 to 30° angle with the arm surface. 5 ml of blood sample is picked up. Blood samples from the patients who are diagnosed with AE of COPD will be collected and evaluated for serum magnesium levels and serum fibrinogen levels.

Study instruments

Conventional auto analyzer equipment and class assay were used.

PATIENT SELECTION

Inclusion criteria

The following criteria were included in the study:

1. Patients above 18 years of age
2. Patients identified with AE of COPD.

Exclusion criteria

The following criteria were excluded from the study:

1. Pregnant and nursing women.
2. Patient with lung carcinoma.
3. Palliative patients.
4. Patients with coagulation disorders.

RESULTS

Table 1 shows that, among 140 enrolled participants, 90 (64.2) were male and 50 (35.7) were female.

Table 2 shows that 7 (5%) of the participants belonged to the age group of 18–35 years, 27 (19.2%) of the participants belonged to the age group 36–50 years, 56 (40%) of the participants belonged to the age group 51–65 years, and 50 (35.7%) of the participants belonged to the age group 66–80 years, respectively

Table 3 discusses about the comorbidity condition among the patients.

Hypertension is seen among 32.8% of the total patients, diabetes mellitus is seen among 58.5% of patients, bronchial asthma is seen among 4.2% of patients, cardiovascular disease is seen among 14.2% of patients, and rheumatoid arthritis is seen among 5% of patients.

No patients were recorded positive test for HIV among patients.

Table 4 shows that the total number of patients' stable was found to be 22 (15.7%) and exacerbation was found to be 118 (84.2%).

Table 1: Gender distribution

S. No.	Gender	Number of patients n=140 (%)	(%)
1.	Male	90 (64.2)	64.2
2.	Female	50 (35.7)	35.7

Table 2: Age distribution

S. No.	Age group (years)	Number of patients n=140 (%)
1.	18–35	07 (5)
2.	36–50	27 (19.2)
3.	51–65	56 (40)
4.	66–80	50 (35.7)

Table 3: Comorbidities

S. No.	Comorbidity	Number of patients n=140 (%)
1.	HTN	46 (32.8)
2.	DM	82 (58.5)
3.	BA	06 (04.2)
4.	CVD	20 (14.2)
5.	HIV	00 (0)
6.	RA	07 (05)

CVD: Cardiovascular disease, HTN: Hypertension

Table 4: Types of COPD

S. No.	Type	Number of patients n=140 (%)
1.	Stable	22 (15.7)
2.	Exacerbation	118 (84.2)

COPD: Chronic obstructive pulmonary disease

Table 5 shows that stable smoking status among smoker was found to be 17, ex-smoker was 03, and non-smoker was 02.

The exacerbation smoking status among smoker was found to be 69, ex-smoker was 31, and non-smoker was 18.

*p value in exacerbation was found to be significant with 95% level of significance.

Table 6 shows about the number of admission per year in hospital with COPD.

Table 7 discusses about the Modified Medical Research Council (MMRC) grade scale; with scores of 1, number of patients were 04 (2.8%); with score of 2, numberof patients were 26 (18.5%); with score of 3, number of patients were 50 (35.7%); and with score of 4, total number of patients were 60 (42.8).

Table 8 shows that serum magnesium levels on admission in stable type were found to be 2.2±0.37, and in exacerbation, it was found to be 1.0±0.27, *p<0.05 which is statistically significant.

Table 9 shows that serum magnesium levels on discharge in stable type were found to be 2.3±0.27, and in exacerbation, it was found to be 1.56±0.37, *p<0.05 which is statistically significant.

Table 5: Smoking status

S.No.	Type	Smoker	Ex-smoker	Non-smoker	p value
1.	Stable	17	03	02	0.71
2.	Exacerbation	69	31	18	0.04*

Table 6: Number of admission per year

S.No.	Number of admissions	Number of patients (%)
1.	0	06 (4.2)
2.	1	34 (24.2)
3.	2–3	90 (64.2)
4.	>3	10 (7.1)

Table 7: MMRC dyspnea grade scale

S. No.	MMRC grade	Number of patients (%)	Percentage (%)
1.	0	00 (00)	00
2.	1	04 (02.8)	02.8
3.	2	26 (18.5)	18.5
4.	3	50 (35.7)	35.7
5.	4	60 (42.8)	42.8

MMRC: Modified Medical Research Council

Table 8: Serum magnesium levels (admission)

S.No.	Type	Serum magnesium levels (mEq/L)	p value
1.	Stable (22)	2.2±0.37	0.0041*
2.	Exacerbation (118)	1.0±0.27	

All values are mean±SEM

Table 9: Serum magnesium levels (discharge)

S. No.	Type	Serum magnesium levels (mEq/L)	p value
1.	Stable (22)	2.3±0.27	0.0271*
2.	Exacerbation (118)	1.56±0.37	

All values are mean±SEM

Table 10: Serum fibrinogen levels

S.No.	Type	Admission serum fibrinogen levels	Discharge serum fibrinogen levels	p value
1.	Stable (22)	1.76±0.32	1.64±0.32	0.621
2.	Exacerbation (118)	3.16±0.39	2.18±0.40	0.0217
	p value	0.0047*	0.0216*	

All values are mean±SEM

Table 10 shows that serum fibrinogen levels on admission in stable type were found to be 1.76±0.32, and in exacerbation, it was found to be 3.16±0.39.

Moreover, on discharge, serum fibrinogen levels in stable type was found to be 1.64±0.32, and in exacerbation, it was found to be 2.18±0.40, *p<0.05 which is statistically significant.

DISCUSSION

COPD is due to the worsening of symptoms that is commonly defined as an exacerbation. Major prominence in the treatment of patients with COPD must be on the continuation of stability. There is an increasing awareness on the role of magnesium in pulmonary disease. Many patients with elevated Serum Magnesium were subjected for frequent hospitalizations in COPD [19].

The most significant finding of this work is the positive correlation between serum magnesium levels during AE and annual number of COPD-AE. The number of attacks increased in association with serum Mg levels. This is a potentially important finding.

Serum magnesium levels were assessed in the AE period for admission to hospital. Magnesium levels in the stable period were not tested. Magnesium levels could not, consequently, be compared between the stable and COPD-AE patients.

Therefore, the serum ionic magnesium level was found significantly lower in COPD cases, either in the exacerbation or in static state in comparison to healthy subjects; however, the diminution of serum ionic magnesium in subjects of AE of COPD was significantly lower than stable COPD subjects. It was also likely noted that the dyspnea was more prominent on the MMRC scale in subjects admitted with AE of COPD.

Hypomagnesemia was found as an important indicator in precipitation of AE of COPD by enhancing the episode of bronchoconstriction, and hence, evaluation of serum ionized magnesium must be retained in the routine panel of investigation to detect its disturbance in the early stage of worsening of symptoms to head off the morbidity as well as mortality in acutely ill COPD patients. Moreover, it can also be utilized as a prognostic indicator during ICU admission [21-23].

Fibrinogen is the best blood biomarker and also higher in individuals with metabolic syndrome. This indicates that fibrinogen may be a major contributor in the development of COPD comorbidities [20].

CONCLUSION

Our study revealed that there is a definite relationship between serum fibrinogen and serum magnesium levels with the AE-COPD.

- Low serum magnesium levels may be a complication for AE of COPD.
- High serum fibrinogen levels may be a complication for AE of COPD.

The treatment given to the patient for COPD must be given along with the regular checking of serum magnesium and serum fibrinogen levels. The importance of those serum levels must be educated to them for better treatment.

We hereby recommend regular screening of serum magnesium and serum fibrinogen levels for all the COPD patients to predict and prevent AE.

ACKNOWLEGMENT

The authors are very thankful to Vels Institute of Science Technology and Advanced Studies and its management for providing research facilities and encouragement.

REFERENCES

1. Nee MW. Pathology, pathogenesis, and pathophysiology. ABC of chronic obstructive pulmonary disease. BMJ 2006;352:1202-4.
2. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2008;177:19-26.
3. Doll H, Miravitlles M. Health-related QOL in acute exacerbations of chronic bronchitis and chronic obstructive pulmonary disease: A review of the literature. Pharmacoeconomics 2005;23:345-63.
4. Donaldson GC, Seemungal TA, Bhowmik A, Wedzicha JA. Relationship between exacerbation frequency and lung function decline in chronic obstructive pulmonary disease. Thorax 2002;57:847-52.
5. Anzueto A, Leimer I, Kesten S. Impact of frequency of COPD exacerbations on pulmonary function, health status and clinical outcomes. Int J Chron Obstruct Pulmon Dis 2009;4:245-51.
6. Hurst JR, Wedzicha JA. Management and prevention of chronic obstructive pulmonary disease exacerbations: A state of the art review. BMC Med 2009;7:40.
7. Vestbo J, Hurd SS, Agustí AG, Jones PW, Vogelmeier C, Anzueto A, *et al.* Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med 2013;187:347-65.
8. Gourgoulianis KI, Chatziparasidis G, Chatziefthimiou A, Molyvdas PA. Magnesium as a relaxing factor of airway smooth muscles. J Aerosol Med 2001;14:301-7.
9. Britton J, Pavord I, Richards K, Wisniewski A, Knox A, Lewis S, *et al.* Dietary magnesium, lung function, wheezing, and airway hyperreactivity in a random adult population sample. Lancet 1994;344:357-62.
10. Snow V, Lascher S, Mottur-Pilson C; Joint Expert Panel on Chronic Obstructive Pulmonary Disease of the American College of Chest Physicians and the American College of Physicians-American Society of Internal Medicine. Evidence base for management of acute exacerbations of chronic obstructive pulmonary disease. Ann Intern Med 2001;134:595-9.
11. Bringhurst DM, Krane SM, Kronenberg HM. Bone and mineral metabolism in health and disease. In: Longo FA, Kasper DL, Hauser SL, Jameson JL, Loscalzo J, editors. Harrison's Principles of Internal Medicine. 18th ed. New York: McGraw-Hill; 2012.
12. Williamson MA, Snyder LM, Wallach JB. Wallach's Interpretation of Diagnostic Tests. 9th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins Health; 2011.
13. Pinto-Plata V, Toso J, Lee K, Park D, Bilello J, Mullerova H, *et al.* Profiling serum biomarkers in patients with COPD: Associations with clinical parameters. Thorax 2007;62:595-601.
14. Monroe DM, Hoffman M, Roberts HR. Molecular biology and biochemistry of the coagulation factors and pathways of hemostasis. In: Prchal JT, Kaushansky K, Lichtman MA, Kipps TJ, Seligsohn U, editors. In: Williams Hematology. 8th ed. New York; 2010.
15. Davalos D, Akassoglou K. Fibrinogen as a key regulator of inflammation in disease. Semin Immunopathol 2012;34:43-62.
16. Duvoix A, Dickens J, Haq I, Mannino D, Miller B, Tal-Singer R, *et al.* Blood fibrinogen as a biomarker of chronic obstructive pulmonary disease. Thorax 2013;68:670-6.
17. Fibrinogen. Lab Tests Online: Welcome! Available from: https://www.labtestsonline.org.au/learning/test-index/fibrinogen. [Last accessed on 2018 Oct 08].
18. Wedzicha JA, Seemungal TA, MacCallum PK, Paul EA, Donaldson GC, Bhowmik A, *et al.* Acute exacerbations of chronic obstructive pulmonary disease are accompanied by elevations of plasma fibrinogen

and serum IL-6 levels. Thromb Haemost 2000;84:210-5.

19. Groenewegen KH, Postma DS, Hop WC, Wielders PL, Schlösser NJ, Wouters EF, *et al*. Increased systemic inflammation is a risk factor for COPD exacerbations. Chest 2008;133:350-7.
20. Dahl M, Tybjaerg-Hansen A, Vestbo J, Lange P, Nordestgaard BG. Elevated plasma fibrinogen associated with reduced pulmonary function and increased risk of chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2001;164:1008-11.
21. Hogg JC. Pathophysiology of airflow limitation in chronic obstructive pulmonary disease. Lancet 2004;364:709-21.
22. Bumbacea D, Campbell D, Nguyen L, Carr D, Barnes PJ, Robinson D, *et al.* Parameters associated with persistent airflow obstruction in chronic severe asthma. Eur Respir J 2004;24:122-8.
23. Barnes PJ, Shapiro SD, Pauwels RA. Chronic obstructive pulmonary disease: Molecular and cellular mechanisms. Eur Respir J 2003;22:672-88.