ISSN: 0975-833X

Available online at http://www.journalcra.com

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

International Journal of Current Research
Vol. 14, Issue, 04, pp.21216-21220, April, 2022

DOI: https://doi.org/10.24941/ijcr.43362.04.2022

RESEARCH ARTICLE

A STUDY OF ROLE OF INTRAVENOUS MAGNESIUM SULFATE IN ACUTE EXACERBATION OF COPD IN A TERTIARY CENTER

[1*]Dr. Aishwarya A.P., [2]Dr. Amit Kumar Sharma, [3]Dr. Atal Bihari Meena, [4]Dr. Gunjan Sharma, [5]Dr. Dipanshu Jain, [6]Dr. Varsha Raj Meena, [7]Dr. Ashish Ranjan and [8]Dr. Anil Saxena

[1]MD Respiratory Medicine (Post Graduation Resident), Government Medical College, Kota, (Rajasthan University of Health Science)
[2]MD Respiratory Medicine, Assistant Professor, Government Medical College, Kota, (Rajasthan University of Health Science
[3]MD Respiratory Medicine, Senior Resident, Government Medical College, Kota, (Rajasthan University of Health Science)
[4,5,6,7]MD Respiratory Medicine (Post graduation Resident), Government Medical College, Kota, (Rajasthan University of Health Science)
[8] MD Respiratory Medicine (Senior Professor), Government Medical College, Kota, (Rajasthan University of Health Science)

ARTICLE INFO

Article History:
Received 19th January, 2022
Received in revised form
16th February, 2022
Accepted 10th March, 2022
Published online 28th April, 2022

Keywords:
COPD, Bronchodilators, Magnesium Sulfate, Peak Expiratory Flow Rate (PEFR).

**Corresponding author:*
Dr Gunjan Sharma

ABSTRACT

Background: Acute Exacerbations of Chronic Obstructive Pulmonary Disease (AECOPD) is a common reason for hospitalization and a major cause of death and disability worldwide. Intravenous MgSO4 has shown benefits in acute severe asthma by producing bronchodilation. However, the use of intravenous MgSO4 in acute exacerbations of COPD alone or as an adjuvant to bronchodilators is lacking and more studies are needed to establish its usefulness. **Aim/Objectives**: To study the role of serum magnesium in acute exacerbation of COPD. To study the role of intravenous magnesium sulfate in acute exacerbation of COPD. **Methods:** A non-randomized, open-label, parallel-group, placebo-controlled, comparative prospective interventional study, where 100 subjects were allotted into 2 groups (group M and group P) of 50 each to receive either 2g of intravenous MgSO4 or a similar amount of normal saline as placebo along with nebulized salbutamol. The efficacy of MgSO4 was evaluated by measuring PEFR a primary outcome parameter at 0,15,30 and 45 mins. Irrespective of the group serum magnesium of all 100 patients are monitored at the time of admission **Statistical Analysis:** The statistical software SPSS V.16.0 was used for all analysis of the data &MS Word & Excel have been used to generate graphs, tables, etc. All the results are presented as mean ± SD & the range values for the continuous data. The categorical data are presented as numbers & percentages. A p-value of ≤0.05 was considered statistically significant. **Result:** The mean difference in the MgSO4 group at every observation was higher than the placebo. The mean change in PEFR (193.04± 43.47) in the MgSO4 group at 45mins observation was Significantly (p=0.0170) higher than in placebo (172.4± 41.47). The serum magnesium level was also monitored but our study was not able to prove a significant correlation between hypomagnesemia and acute exacerbation of COPD. **Conclusions:** The benefits of intravenous MgSO4 as an adjuvant to bronchodilators in AECOPD resulted in improvement of clinical condition and PEFR. The improvement in PEFR was significantly higher with MgSO4 than with placebo MgSO4 enhances the early bronchodilator response of other drugs and has significant efficacy.

Citation: Dr. Aishwarya, A.P., Dr. Amit Sharma, Dr. Atal Meena, Dr. Gunjan Sharma, Dr. Dipanshu Jain, Dr. Varsha Raj Meena et al. *"*A study of role of intravenous magnesium sulfate in acute exacerbation of COPD in a tertiary center", *2022. International Journal of Current Research, 14, (03), 21216-21220.*

INTRODUCTION

The Global initiative for Obstructive lung disease describes (GOLD) Chronic Obstructive Pulmonary Airway Disease is a Preventable & Treatable Disease that is characterised by persistent airflow limitation that is usually caused by significant exposure to noxious particles or gases. (1) Episodes of acute worsening of respiratory symptoms in COPD are called exacerbations. Acute exacerbations of COPD are

characterized by respiratory distress due to irreversible bronchial obstruction, excessive mucous, and cough associated with a greater decline in lung functions, lower health-related quality of life, and an increased risk of death. Exacerbations usually occur following infection, irritation of the airways, and temperature changes. Airway inflammation, edema, mucus hypersecretion, and bronchoconstriction are the hallmark features of a severe exacerbation. 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 (4,5,6,7). 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 (8). Intravenous magnesium sulphate has been known for its broncho-dilating effect (8,9,10). The possible mechanism(s) of action of Magnesium sulphate in offering benefit in COPD exacerbations may be calcium antagonism via calcium channel and counteraction of calcium-mediated smooth muscle contraction (11,12). In addition, early administration of intravenous magnesium sulphate in the emergency department may reduce the hospital admission rate (12). However, studies investigating the use of this agent in COPD exacerbations are scarce and inconclusive (12,13,14).

Aim and objective

- To study role of serum magnesium in acute exacerbation of COPD.
- To study role of intravenous magnesium sulphate in acute exacerbation of COPD.

METHODOLOGY

The present prospective, interventional, placebo-controlled comparative study to study the role of iv MgSO4 and serum magnesium in COPD acute exacerbation.

Study subjects: The study was conducted in the Respiratory medicine department in Government medical college Kota. This study included 100 subjects diagnosed with COPD and who presented with an episode of acute exacerbation and were categorized based on Anthonisen classification. Along with routine blood investigation, serum magnesium was also sent. All eligible subjects were assigned into two groups IV magnesium sulfate and placebo in a 1:1 ratio.

Sampling: Purposive sampling

Study period: Study period – February 2020 to August 2021 (19 months)

Study design: A non-randomized, open-label, parallel-group, placebo-controlled, comparative prospective interventional study of IV magnesium and placebo as an adjuvant to nebulized salbutamol in acute exacerbations of COPD.

Inclusion Criteria

- Subjects diagnosed as COPD (GOLD criteria) presenting with acute exacerbation.
- Willingness to give informed consent.

Exclusion Criteria: 1. Subjects with severe COPD exacerbations requiring invasive ventilation, respiratory failure and in altered sensorium with bronchial asthma, residual parenchymal disease, present or past history of Tuberculosis and Bronchiectasis, past history of Cerebrovascular accidents, cardiac, hepatic, or renal dysfunction, uncontrolled diabetes mellitus, and patients maintained on dialysis.

- Known or suspected hypersensitivity to magnesium
- Pregnant and lactating women and those planning to conceive
- Unwilling to give the informed consent

Study Procedure: 100 subjects who met the inclusion and exclusion criteria were included in the study. At the time of admission along with routine blood investigation serum magnesium of all patients was sent. The subjects were assigned into 2 groups (n = 50 in each) by purposive sampling to receive either a single dose of intravenous magnesium sulphate infusion of 2g in 100 ml of normal saline slowly over a period of 20-30 minutes or a similar amount of normal saline was given as placebo along with nebulized salbutamol 5mg/ 2.5 ml administered through a face mask. The study subjects also received other supportive medications like ipratropium bromide 500mcg by inhalation, antimicrobial agents, intravenous methylprednisolone 100mg, oxygen therapy to maintain the oxygen saturation above 90%, parenteral fluids, and intensive care, if required. Following initiation of therapy serial peak expiratory flow rate was measured at 0,15,30 and 45 minutes.

Statistical methods involved: Chi-square/ Fisher Exact test was used to find the significance of study parameters on a categorical scale between two or more groups, the non-parametric setting for Qualitative data analysis.

RESULTS

Hypomagnesemia was present in 38 % of patients in group M and 36% of patients in group P. Serum magnesium levels were sent in patients before giving Iv magnesium sulfate. But all patients were given magnesium in Group M irrespective of their magnesium status. Among the study group 37% of the patients had hypomagnesemia (n= 18 in group M and n= 19 in group P) but the observation was not statistically significant (p = 0.41). This is inconsistent with many studies which showed that hypomagnesemia is a risk factor for COPD. There was a significant decrease in rhonchi after giving intravenous magnesium sulfate in Group M. 68% of patients in group M showed a decrease in rhonchi and this observation was statistically significant.

PEFR CHANGES

PEFR measures the degree of airflow obstruction through a hand-held peak flow meter which is said to be an economical and widely available alternative to the spirometer. Although FEV1 measurement is a better predictor of airflow obstruction PEFR can be used as a bedside alternative. Our study was conducted on subjects who presented to the emergency department, hence because of difficulties in ambulation of subjects for spirometer testing, PEFR was used as a measurement of bronchodilation.

At 0mins: The PEFR at 0 mins was taken as the baseline reading. The mean PEFR of subjects in MgSO4 was 171.2±44.03 and in Placebo was 168 ±40.33 which was not statistically significant (p=0.7055) between the groups. The total mean was 169.5 ± 42.18

significant (p<0.001), and in the placebo group, it was 1.42±0.87 which was not significant. 0 mins -30 mins. The mean difference from baseline to 30 mins in the MgSO4 group was 12.28± 1.32which was significant (<0.001) and in the placebo group, it was 3.66 ± 0.38which was also significant (p<0.001).

Table 1: Auscultatory findings showing 68% of patients in group M had rhonchi and 62 % of patients in group P

Rhonchi	Group- M		Group –P	
	No. of Patients	%	No. of Patients	%
Present	34	68	31	62
Absent	16	32	19	38
Total	50	100	50	100

Table 2. Serum Magnesium Value: Hypomagnesemia was present in 38 % of patients in group M and 36% of patients in group P

Serum Mg Value	Group- M		Group –P	
	No. of Patients	%	No. of Patients	%
<1.8	19	38	18	36
1.8-2	31	62	32	64
Total	50	100	50	100

Table 3. Rhonchi after giving IV MgSo4: a significant decrease in rhonchi after giving intravenous magnesium sulfate in Group M

Rhonchi after giving IV MgSO4	Group- M		Group –P	
	No. of Patients	%	No. of Patients	%
Same	16	32	42	84
Decreased	34	68	8	16
Total	50	100	50	100

Table 4. Comparison of PEFR between two groups after giving MgSo4 / placebo

PEFR	Group M	Group P	P-value
	Mean ±SD	Mean ±SD	
0 min	171.2±44.03	168 ±40.33	0.7055
15 min	177.32 ±42.40	169.42 ± 41.20	0.347
30 min	183.48 ±42.71	171.66 ± 40.71	0.1598
45 min	193.04±43.47	172.4±41.47	0.0170

At 15mins: The PEFR at 15 mins post-treatment showed an increase in both groups. The mean PEFR in the MgSO4 group was 177.32 ±42.40 and in the Placebo group was 169.42 ± 41.20which was not statistically significant (p=0.347). The total mean was 173.37± 41.8

At 30mins: The PEFR at 30 mins post-treatment showed an increase in both groups. The mean PEFR in the MgSO4 group was 183.48 ±42.71 and in the placebo group was 171.66 ± 40.71 and the total mean was 177.57± 41.71 (p=0.1598)

At 45mins: The PEFR at 45 mins post-treatment showed an increase in group M. The mean PEFR in the MgSO4 group was 193.04±43.47 and in the placebo group was 172.4±41.47 which was statistically significant (p=0.0170). This suggests that there is a significant difference between the group in terms of change in PEFR. By comparing with the p-value, it is evident that MgSO4 may have a significant bronchodilator response when compared with placebo at every interval of observations, however, at 45mins the MgSO4 group suggests a statistical (p=0.0170) significance.

MEAN DIFFERENCE IN PEFR FROM BASELINE

0 mins-15 mins: The mean difference from baseline at 15 mins in the MgSO4 group was 6.12± 1.63, which was

0mins -45mins: The mean difference from baseline to 45 mins in the MgSO4 group was 21.84±0.56 which was significant (p<0.001) and in the Placebo group was 4.4± 1.14 which was significant (p<0.001). The observations show a significant clinical improvement in the symptoms of COPD within the study groups but however at 15 mins in the placebo group there was no statistical and clinical significance which later demonstrated significance at 30 and 45 mins. PEFR gradually increased in both groups but it was much greater in the MgSO4 group. It also demonstrates that MgSO4 has a faster onset of action or may produce a quick symptomatic relief in comparison with placebo.

DISCUSSION

In the present comparative study, the role of magnesium sulphate and placebo were assessed in subjects with Acute Exacerbations of Chronic Obstructive Pulmonary Disease (AECOPD). It is evident that MgSO4 had some significant effects on PEFR change when compared to placebo. Not many studies have been done withMgSO4 in AECOPD and often the results are inconclusive. In contrast to various studies, our study did show some effect on PEFR change.16,17 Although, these results are supported by other similar studies where MgSO4 has shown significant effects on PEFR improvement

when used as an adjuvant to bronchodilators.14,18,19. In our study, we didn't find any significant relation between hypomagnesemia and acute exacerbation of COPD. Which was against the finding in other studies.[20,21,22.] Among the study group 37% of the patients had hypomagnesemia (n= 18 in group M and n= 19 in group P).but the observation was not statistically significant (p = 0.41). This is inconsistent with many studies which showed that hypomagnesemia is a risk factor for COPD. The study by JK singh[20] also showed patients with hypomagnesemia had a longer duration of COPD (6.94 ± 3 years) and a longer duration of exacerbation of symptoms. Bashir Ahmed shah[21] (2010) based on his study on 77 patients showed that there is a 33.8% incidence of hypomagnesemia at the time of admission. The mean serum magnesium level was significantly lower in cases than in control (1.88 ± 0.67mg/dl vs 2.3± 0.36). Sanjay tendon[22] (2021) he showed in his study that mean serum magnesium level was lower in the AECOPD group as compared to the stable group (1.60± 0.49 vs 1.99 ± 0.09). Mean serum magnesium was low in the AECOPD at the time of admission and normalized without supplementation.

Auscultatory findings: Table 1. Patients with rhonchi showed a significant decrease in rhonchi after giving magnesium sulphate IV and the values were statistically significant ($p < 0.001$). 68% (n= 34) of the patient showed a decrease in rhonchi after giving magnesium. From table 4 it is evident that MgSO4 has a significant bronchodilator effect. Not many studies have been done with MgSO4 in AECOPD and often the results are inconclusive. In contrast to various studies, our study did show some effect on PEFR change.16,17 Although, these results are supported by other similar studies where MgSO4 has shown significant effects on PEFR improvement when used as an adjuvant to bronchodilators.14,18,19.similar results were obtained in the study conducted by Gonzalez *et al* [18]and Mukerji S[19] which showed an increase in FEV1 17.11% and 27.07%**.** The study by Skorodin *et al*[14] showed that there is an increase in PEFR by about 24% in patients given IV MgSO4 than those given with placebo. MgSO4 produced a significant change in PEFR at 15,30and 45 mins post-infusion when compared to Placebo and hence demonstrates a role in improving airflow obstruction and enhancing the effects of other bronchodilators. MgSO4 produced a maximum effect at 45 mins which was significant. The doses used in COPD are comparatively lesser than doses used in eclampsia hence good safety and tolerability to intravenous MgSO4 were observed in this study. At the end of the study, MgSO4 was found to have a better outcome when compared to placebo in improving the PEFR at every interval of observation. MgSO4 was well tolerated and all the adverse events were self-limiting or responded to symptomatic management. Thus, MgSO4 has a significant role in improving the bronchodilators effects of other drugs, hence can be used as an adjuvant to other drugs in the management of AECOPD.

REFERENCES

1. Global initiative for chronic obstructive pulmonary disease .Global strategy for the diagnosis management and prevention of COPD. Updated 2021.
2. Global initiative for chronic obstructive lung disease .Global strategy for the diagnosis management, and prevention of COPD.2007.available from http\\www. goldcopd.org.
3. Mathers CD, Loncar D. Projections of global mortality and burden of diseases from 2002 to 2030.PLoS Med.2006;3(11).
4. Alter HJ, Koepsell TD, Hilty WM. Intravenous magnesium as an adjuvant in acute bronchospasm: a meta-analysis. Annals Emerg Med 2000:
5. Hughes R, Goldkorn A, Masoli M, Weatherall M, Burgess C, Beasely R. Use of isotonic nebulized magnesium sulphate as an adjuvant to salbuterol in treatment of severe asthma: randomized, placebo-controlled trial. Lancet2003:361:2114–2117.
6. Roy SR, Milgrom H. Managing outpatient asthma exacerbations. Curr Allergy Asthma Reports 2003;3:179–189.
7. Gourgoulianis KI, Chatziparasidis G, Chatziefthimou A, Molyvdas PA. Magnesium as a relaxing factor of airway smooth muscles. J Aerosol Med2001;14:301–307.
8. 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; 4th ed (George RB, Light RW, Matthay MA, Matthay RA, Eds) Lippincott Williams and Wilkins, Philadelphia, 2000; pp 174–207.
9. Snow V, Lascher, Mottur-Pilson C. Evidence base for management of acute exacerbations of chronic obstructive pulmonary disease. Ann Intern Med2001;134:595–599.
10. Siafakis NM, Vermeire P, Pride NB, Paoletti P, Gibson J, Howard P. Optimal assessment and management of chronic obstructive pulmonary disease (COPD). The European Respiratory Society task force. Eur Resp J1995;8:1398–1420. : a multicenter randomized controlled trial. Chest. 2002;122Fogarty A, Lewis SA, Scrivener SL, Antoniak M, Pacey S, Pringle M, Britton, J. Oral magnesium and vitamin C supplements in asthma: a parallel group, randomized, placebo-controlled trial. Clin Exp Allergy 2003;33:1355–1359.
11. . Ruljancic N, Popovic-Grle S, Rumenjak V, Sokolic B, Malic A, Mihanovic M, Cepelak I. COPD: magnesium in the plasma and polymorphonuclear cells of patients during a stable phase. Copd. 2007;4:41–47.
12. Silverman RA, Osborn H, Runge J, Gallagher EJ, Chiang W, Feldman J, Gaeta T, Freeman K, Levin B, Mancherje N, Scharf S. IV magnesium sulfate in the treatment of acute severe asthma:489–497.
13. Abreu Gonzalez J, Hernandez Garcia C, Abreu Gonzalez P, Martin Garcia C, Jimenez A. Effect of intravenous magnesium sulfate on chronic obstructive pulmonary disease exacerbations requiring hospitalization: a randomized placebo-controlled trial. Arch. Bronconeumol. 2006;42:384–387.
14. Skorodin MS, Tenholder MF, Yetter B, Owen KA, Waller RF, Khandelwahl S, Maki K, Rohail T, D'Alfonso N. Magnesium sulfate in exacerbations of chronic obstructive pulmonary disease. Arch. Intern. Med. 1995;155:496–500.
15. Do Amaral AF, Rodrigues-Junior AL, Terra Filho J, Vannucchi H, Martinez JA. Effects of acute magnesium loading on pulmonary function of stable COPD patients.Med. Sci. Monit. 2008;14:524–529.
16. Solooki M, Miri M, Mokhtari M, Valai M, Sistanizad M, Kouchek M. Magnesium Sulfate in Exacerbations of COPD in Patients Admitted to Internal Medicine Ward.Iran J Pharm Res IJPR [Internet]. 2014;13(4):1235–9.
17. Edwards L, Shirtcliffe P, Wadsworth K, Healy B, Jefferies S, Weatherall M. *et al*. Use of nebulized magnesium sulfate

as an adjuvant in the treatment of acute exacerbations of COPD in adults: a randomised double-blind placebo-controlled trial. Thorax [Internet]. 2013;68(4):338–43

18. Gonzalez JA, Garcia CH, Gonzalez PA, Garcia CM, Jimenez A. Effect of intravenous magnesium sulfate on chronic obstructive pulmonary disease exacerbations requiring hospitalization: A randomized placebo-controlled trial: ArchBronconeumol 2006; 42: 384–7. Respiratory Medicine: COPD Update. 2006 Dec 31;2(3):114
19. Mukerji S, Shahpuri B, Smith N, Armstrong P, Hardy M, Marchant G, *et al*. Intravenous magnesium sulfate as an adjuvant therapy in acute exacerbations of disease:a single center, 2015;128(1425):34–42.
20. Serum Magnesium Level In COPD Patients Attending A Tertiary Hospital – A cross Sectional Study JP.Singh, Sahil Kohli, Arti Devi, Sahil Mahajan dec 2012
21. Shah B, Naik M, Rajab S, Muddasar S, Dhobi G, Khan A, Banday K, Baba S. Serum Magnesium Levels in Exacerbation of COPD: A Single Centre Prospective study from Kashmir, India. jms [Internet]. 2010Jun.21 [cited 2022Jan.2];13(1):15-9. Available from:
22. Tandon, S., Shukla, A., & Nagdeote, S. (2021). Assessment of Serum Magnesium Level in Acute Exacerbation of COPD. International Journal of Health and Clinical Research, 4(7), 82–85. Retrieved from https://ijhcr.com/index.php/ijhcr/article/view/1311

****