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Original Article

Effect of Nebulized Magnesium Sulphate in Terms of the In-Hospital Outcome of Patients Admitted with Acute Exacerbation of Chronic Obstructive Pulmonary disease

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Abstract

Objective: To evaluate the efficacy of Magnesium Sulphate (MgSO4) with the conventional treatment in acute exacerbation chronic obstructive pulmonary disease (AECOPD)

Methods: This Quasi-experimental study was conducted in Department of Internal Medicine from July 2020 to July 2022. The study involved 160 patients in total. There were two groups of patients. Group A was nebulized with 250mg of MgSO4 four times a day along with conventional treatment. Group B was given only conventional treatment. Conventional treatment included oxygen inhalation, anti-cholinergic and beta-2 agonist nebulization, intravenous steroids, and intravenous antibiotics. Both groups were followed for five days to assess the effect of nebulized magnesium.

Results: Group A required assisted ventilation for 2–3 days for 28% of the subjects (22 patients out of 80), while group B required it for 81% of the subjects (65 patients out of 80). In addition, only 9% of patients in group A and 8% of patients in group B needed assisted ventilation for four to five days. In comparison to group A, which had 33% of patients discharged on the fourth day and 20% on the fifth day or later, group B saw 53% of patients discharged on the fourth day and 20% on the fifth day or later. The results showed that PCO2 and peak expiratory flow rate (PEFR) have a significant variance between group A and group B and values have no significant variance between group A and group B on the first day and the last day.

Conclusion: Nebulized supplementation improves in-hospital outcomes in patients presenting with acute exacerbation of COPD as compared to the patients not receiving nebulized magnesium sulphate.

Keywords: Acute exacerbation, Chronic Obstructive Pulmonary Disease (COPD), Nebulized Magnesium Sulphate.

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Introduction

By 2030, chronic obstructive pulmonary disease (COPD) is anticipated to rank seventh among all diseases in terms of burden.[1] It has a prevalence rate of 2.1% in adults aged 40 or higher in Pakistan.[2] A recent report by Global Initiative for Chronic Obstructive Lung Disease, GOLD COPD 2023, defines Chronic obstructive pulmonary disease as, "an event that is marked by dyspnoea, cough, and sputum exacerbated within less than 14 days of initial infection, and/or further accompanied by tachypnea, tachycardia, or an enhanced inflammation due to pollutants, or other impurities along the airways".[3]

COPD is significantly associated with comorbidities such as cardiovascular diseases, bronchiectasis, gastro-esophageal reflux disease, mental disorders, pulmonary embolism, diabetes, skeletal muscle weaknesses, chronic kidney diseases, etc.[4] As a result, the respiratory symptoms of patients with COPD acutely worsen beyond the normal day-to-day variations, a term known as "exacerbation" to explain such a situation.[5] This acute exacerbation is accompanied by a decline in lung functions compromising the quality of life in these patients. The symptoms of an increased cough usually represent acute exacerbation of COPD. AECOPD with enhanced shortness of breath and a change in the colour of sputum[6].

The key underlying cause related to acute exacerbation of COPD is the respiratory microbiomes causing a 50% increased risk factor of correlated respiratory bacterial infection.[6] Though respiratory microbiomes, viruses, and pollution play a significant exacerbating role in AECOPD, immunity defects are another reason for its progression.[7] All these factors contributing to pulmonary decline, compromise the quality of life in COPD patients and thus increase their mortality rates across the populace under investigation. Resultantly, this also burdens heavily on a country's economy and health care system. A study indicates an estimated cost of $30 billion burdens the US economy directly by COPD per year.[8] Effective management therapies for acute exacerbations associated with COPD are therefore significantly necessary in this regard. A triple therapy, i.e, a combination of long-acting beta-agonists (LABA), long-acting muscarinic antagonists (LAMA), and Inhaled corticosteroids (ICS) has been currently in use in a treatment strategy for COPD.[8] The use of antibiotics is prevalent in inpatient settings. Respiratory oxygen therapy for the management of hypoxemia and hypercapnia is sometimes essential. Significant prevention strategies such as vaccination, pulmonary rehabilitation, and education of the populace with an action plan are also important.[9] The requirement of substantial new strategies for the treatment of symptoms related to exacerbation of COPD is still imperative for the effective management of the severity and frequency of the disease.

Recently, the activity of magnesium sulphate along with the bronchodilators (beta2-agonists) as an adjuvant is found substantially promising for its functioning on respiratory muscles when given intravenously.[10] Additionally, due to its anti-inflammatory effects, magnesium sulphate has been extensively used as a treatment therapy, either in nebulized form or intravenously, for the treatment of asthma.[11] Magnesium is thought to have a significant role in vasodilatation and bronchodilatation because it blocks the entry of calcium ions into vascular and bronchial smooth muscle cells via voltage-dependent calcium channels.[12]

The anti-inflammatory properties of magnesium sulphate are evident due to the release of histamine inhibition from mast cells. Also, its inhibitory effect on acetylcholine makes it a potentially promising bronchodilator, (acetylcholine being a bronchoconstrictor due to its anti-muscarinic effect).[13] Various clinical trial studies, including randomized single-blinded studies of magnesium with salbutamol, have shown an increased broncho-dilating impact of therapy when given in combination. Other parallel single and double-blind studies in Randomized control trials, RCTs, also indicate reduced dyspnoea, lesser hospital stays, and fewer admissions to hospital when magnesium sulphate is given intravenously.[13] However, the results of several other studies revealed that when nebulized magnesium was administered as a bronchodilator therapeutic adjunct when a patient presented to the hospital with an AECOPD, they were unable to show any clinical benefit.[14] Though the literature reports a significantly enhanced reduction in the hospital stays by the use of magnesium infusions, nebulized magnesium may have very little or no impact in reducing hospital admissions. The requirement of non-invasive ventilation is still required.[13] The conclusive evidence for the enhanced therapeutic activity of magnesium sulphate is still unknown but the fact that it can be easily administered as an inhaler or IV and economically feasible with no or little side effects makes it a promising agent requiring potential further clinical investigations.[12]

Methods

This Quasi-experimental Study was conducted from July 2020 to July 2022 for the collection of data. In this study, 160 patients with acute exacerbation of COPD were assigned to two equal groups of 80 patients each. This sample size was calculated by using a 95% confidence level, and 10% absolute precision with the expected percentage of magnesium sulphate as 17.11% and another group as 7.06%[8]. The study protocol was approved and informed consent was obtained from patients. The non-probability convenient sampling technique was used for the selection of patients. Patients of both gender between 30 to 70 years of age admitted with acute exacerbation of COPD less than 10 years were included in this study. Acute exacerbation of COPD requiring hospital admission and any two out of four criteria: Increase in the purulence or quantity of sputum, Dyspnoea grade 3, 4, or 5 according to the MRC scale, PEFR <200 L/min and Respiratory acidosis on arterial blood gas analysis.

Patients who had any other pulmonary parenchymal disease, congenital cardiac disease, bronchogenic carcinoma, a chest radiograph showing the presence of pneumonia, pulmonary oedema, a personal or family history of atopy were excluded from the study. Seriously ill patients and patients with known Magnesium Sulphate hypersensitivity were also excluded.

A total of 160 patients with acute exacerbation of COPD were selected. The data was recorded and analysed according to a predefined methodology and criteria. Various demographics of patients and disease-related variables were discussed and noted.

Patients were divided into two groups (Group A and Group B) by Lottery Method. All the enrolled patients, regardless of the group, were given conventional treatment which include oxygen inhalation, anti-cholinergic nebulization (ipratropium bromide; 250 µg 8 hourly),

short-acting beta-2 agonist nebulization (Salbutamol), intravenous steroids (Beclomethasone 200 µg 12 hourly) and intravenous antibiotics. Group A in addition to the conventional treatment received 250mg of MgSO4/ dose given through nebulizer four times a day while group B did not. 1 vial of injection MgSO4 was taken which contains 1gm of MgSO4 (each vial contains 10ml). It was divided into 4 equal parts, each contained 250mg MgSO4 i.e., 2.5 ml solution, which were used for nebulization 4 times a day.

The groups were followed for five days to see the results in terms of in-hospital outcome, whether the patient is discharged after fulfilling the set criteria or needing assisted ventilation.

The data was processed by Statistical Package for the Social Sciences (SPSS) version 26 for analysis of data. For quantitative variables including age, PEFR (peak expiratory flow rate), and duration of COPD (chronic obstructive pulmonary disease) Mean ± SD was calculated. Frequency distribution and cumulative percentages were calculated for qualitative variables including gender and efficacy in both groups. A comparison of two groups with nebulized magnesium sulphate and without nebulized magnesium sulphate was done by applying a t-test keeping a p-value ≤0.05.

Results

Out of 160 subjects, equals were placed in both groups, (n=80 in each group). The mean age of group A was 56.55 years whereas the mean age of group B was 57.12 years.

Of 160 patients, 80 (100%) in group A were males. Similarly, 78 (98%) in group B were males and only 2 (3%) were females.

The second parameter of the study, the number of days of stay at the hospital in terms of statistical data was shown to be reduced 53% of the patients in group B were discharged on the fourth day and 20% were discharged on the fifth day or later compared to 33% discharged on the fourth day in group A and 20% discharged on the fifth day or later. (Table-1)

Table 2 is depicting comparison of both groups in outcome in terms of discharge days. Table 3 is showing the comparison of both groups in terms of MRC scale value, PEFR and PCO2 and finally table IV is showing results of independent sample t-test amongst two groups in

Table 1: *Comparison of groups in outcome 1 (Need for assisted ventilation in days)*

Need for assisted ventilation (days)	Group A (N=80)	Group B (N=80)
0 to 1	51	9
	64%	11%
2 to 3	22	65
	28%	81%
4 to 5	7	6
	9%	8%
Total	80	80

Table 2: *Comparison of groups in outcome 2 (Discharge in days)*

Discharge (days)	Group A (N=80)	Group B (N=80)
3	38	22
	48%	28%
4	26	42
	33%	53%
5 or more	16	16
	20%	20%
Total	80	80

Table 3: *Comparison of groups MRC scale value, PEFR and PCO2*

			N	Mean	Std. Deviation	Min	Max
Dyspnea grade according to MRC Scale	1st Day	Group A	80	4.35	0.51	3	5
		Group B	80	4.49	0.53	3	5
	Last Day	Group A	80	2.03	0.27	1	3
		Group B	80	1.96	0.30	1	3
PEFR	1st Day	Group A	80	192.25	10.74	150	200
		Group B	80	179.53	16.15	140	200
	Last Day	Group A	80	499.41	75.76	200	680
		Group B	80	461	48.07	380	560
Respiratory acidosis on ABGs (PCO_2)	1st Day	Group A	80	66.46	9.35	52	90
		Group B	80	79.63	7.62	56	95
	Last Day	Group A	80	47.66	4.16	38	60
		Group B	80	50.33	3.17	42	58

MRC= Medical Research Council, PEFR=Peak expiratory flow rate , PCO2=Partial pressure of carbon dioxide

Table 4: *Results of independent sample t-test*

Parameters	Day	F	P-Value
Partial pressure of carbon dioxide (PCO_2)	1st day	7.11	0.00
	last day	6.06	0.01
Medical Research Council (MRC) Scale	1st day	3.15	0.07
	last day	0.30	0.58
Peak expiratory flow rate (PEFR)	1st day	13.42	0.00
	last day	3.78	0.05

terms of MRC scale value, PEFR and PCO2.

Discussion

This study was conducted to evaluate the activity of nebulized magnesium sulphate given in combination with the standard therapy for the treatment of acute exacerbations of chronic obstructive pulmonary disease in terms of in-hospital outcomes, and the results were compared with the conventional therapy for processing. Our study suggested a substantial beneficial impact of nebulized magnesium sulphate regarding reduced ventilation support requirement on following days and an early discharge from the hospital when it is given in combination compared to standard therapy given alone. The primary outcomes of the clinical trial under investigation were significant improvements in dyspnoea severity score (DSS), peak expiratory flow rate, (PEFR), and PCO2 showing a validated enhancement of the treatment protocol. A substantial difference had been demonstrated between the Experimental (Group A) and the Standard (Group B) groups under investigation. Keeping the clinical and pathophysiological concerns related to exacerbations of COPD in mind, magnesium sulphate is supported to be used as an alternative therapy in the condition on the basis of this study.

A systematic review of randomized controlled trials evaluated the effectiveness of nebulized magnesium sulphate for COPD.14 Inhaled magnesium sulphate did not significantly enhance lung function or symptoms in people with COPD, according to the review's findings. Nevertheless, nebulized magnesium sulphate has been demonstrated in certain studies to be useful in improving lung function and lowering hospital admissions in individuals with acute exacerbations of COPD.

Magnesium sulphate's effectiveness for treating acute exacerbations of adult chronic obstructive pulmonary disease was evaluated in a systemic review by Ni H et al.[13] Evaluation of the effects of nebulized magnesium sulphate against placebo was done in three studies (20 to 172 individuals). They came to the conclusion that magnesium inhalation might not have much of an effect on hospital admission or the requirement for ventilator assistance (NIV or mechanical ventilation). When compared to placebo, nebulized magnesium caused fewer ICU hospitalisations and less dyspnoea, but bigger studies are needed to provide a more accurate approximation of these outcomes. In addition, they found that nebulized magnesium sulphate, when combined with standard therapy, results in a significant reduction in the need for post-treatment breathing assistance and an earlier hospital discharge.

A clinical investigation was conducted by Comert S15 to gauge the effectiveness of nebulized magnesium sulphate. 161 patients with COPD exacerbations were enrolled in this randomised, double-blind, placebo-controlled study. There was no obvious difference between the two groups for the trial's primary endpoint, FEV1 assessed at 90 minutes. Moreover, there was no noticeable difference in the hospitalisation rates between the two groups. Our study's findings run counter to these findings. The use of nebulized magnesium sulphate had a positive effect on the patient's ability to leave the hospital sooner and needed ventilator assistance less frequently in the days after.

Bajracharya M. et al.[16] and Bhatti HU et al.[17] recently conducted two randomised control trials to compare the therapeutic advantages of nebulized magnesium sulphate as an adjuvant with standard treatment in patients with COPD exacerbation. In the context of acute exacerbation of COPD, they came to the conclusion that nebulized magnesium sulphate as an adjuvant to salbutamol has therapeutic advantage on peak expiratory flow rate (PEFR), but has no impact on hospital admission, the need for invasive or non-invasive ventilation, or mortality. The results of these two investigations were supported by our study as well.

Edwards L.18 and colleagues investigated the effects of recurrent nebulized magnesium in the treatment of acute exacerbations of COPD. They came to the conclusion that nebulized magnesium used as an adjuvant to conventional treatment in the context of acute exacerbations in COPD has no effect on FEV1.

Overall, there is conflicting data supporting the use of inhaled magnesium sulphate for COPD, and more research is required to determine its efficacy and safety in various COPD patient populations. This study has several restrictions. It is important to note that this is not a multicentre trial and that the sample size was somewhat constrained by the study's design and criteria. Further well planned randomized control trials (RCTs) are necessary to apply the findings in a broader context. These studies should establish the function of magnesium sulphate as an adjunctive treatment for COPD exacerbations.

Conclusion

Nebulized supplementation improves in-hospital outcomes in patients presenting with acute exacerbation

of COPD as compared to the patients not receiving nebulized magnesium sulphate. To support the findings of the current study, more interventional research is needed.

Conflict of Interest: *None*

Funding Source: *None*

References

1. Rehman AU, Muhammad SA, Tasleem Z, Alsaedi A, Dar M, Iqbal MO, et al. Humanistic and socioeconomic burden of COPD patients and their caregivers in Malaysia. Scientific Rep. 2021;11(1):22598.
2. Khan MA, Khan N, Walley JD, Khan MA, Hicks J, Ahmed M, et al. Effectiveness of delivering integrated COPD care at public healthcare facilities: a cluster randomised trial in Pakistan. BJGP Open. 2019; 3(1): 101634.
3. Venkatesan P. GOLD COPD report: 2023 update. Lancet Resp Med. 2023 ;11(1):18.
4. Hogea SP, Tudorache E, Fildan AP, Fira-Mladinescu O, Marc M, Oancea C. Risk factors of chronic obstructive pulmonary disease exacerbations. Clin Respir J. 2020; 14(3):183-97.
5. Erhabor GE, Adeniyi B, Arawomo AO, Akinwalere O, Adetona G, Fagbohun FT, et al. Acute Exacerbation of COPD: Clinical Perspectives and Literature Review. West Afr J Med. 2021;38(11):1129-42.
6. Moghoofei M, Azimzadeh Jamalkandi S, Moein M, Salimian J, Ahmadi A. Bacterial infections in acute exacerbation of chronic obstructive pulmonary disease: a systematic review and meta-analysis. Infection. 2020; 48(1):19-35. .
7. Ritchie AI, Wedzicha JA. Definition, causes, pathogenesis, and consequences of chronic obstructive pulmonary disease exacerbations. Clin Chest Med. 2020; 41(3):421-38.
8. Cazzola M, Calzetta L, Rogliani P, Matera MG. Triple therapy versus dual bronchodilation and inhaled corticosteroids/long-acting β-agonists in COPD: accumulating evidence from network meta-analyses. Pulm Ther. 2019;5(2):117-26..
9. Zheng JP, Zhang J, Ma LJ, Chen P, Huang M, Ou XM, et al. Clinical outcomes of using nebulized budesonide as the initial treatment for acute exacerbations of chronic obstructive pulmonary disease: A post-hoc analysis. Int J Chron Obstruct Pulm Dis. 2019;14(9):2725-31.
10. Jahanian F, Khatir IG, Ahidashti HA, Amirifard S. The Effect of Intravenous Magnesium Sulphate as an Adjuvant in the Treatment of Acute Exacerbations of COPD in the Emergency Department: A Double-Blind Randomized Clinical Trial. Ethiopian J Health Sci. 2021;31(2):267-74.
11. Jahangir A, Zia Z, Niazi MR, Sahra S, Jahangir A, Sharif MA, et al. Efficacy of magnesium sulfate in the chronic obstructive pulmonary disease population: a systematic review and meta-analysis. Adv Respir Med. 2022; 90(2): 125-33.
12. Nouira S, Bouida W, Grissa MH. Magnesium sulfate versus ipratropium bromide in chronic obstructive pulmonary disease exacerbation: a randomized trial. Am J Ther. 2014;21(3):152-8.
13. Ni H, Aye SZ, Naing C. Magnesium sulfate for acute exacerbations of chronic obstructive pulmonary disease. Cochrane Database of Syst Rev. 2022;5(5): Cd013506.
14. Shivanthan MC, Rajapakse S. Magnesium for acute exacerbation of chronic obstructive pulmonary disease: a systematic review of randomised trials. Annals of thoracic medicine. 2014;9(2):77.
15. Comert S. Role of magnesium sulphate in exacerbations of chronic obstructive pulmonary disease. J Resp Res. 2015;1(1):10-2.
16. Bajracharya M, Acharya RP, Neupane RP, Sthapit R, Tamrakar AR. Nebulized Magnesium Sulphate Versus Saline as an Adjuvant in Acute Exacerbation of Chronic Obstructive Pulmonary Disease in a Tertiary Centre of Nepal: A Randomized Control Study. J Inst Med Nepal. 2021;43(1):5-10.
17. Bhatti HU, Mushtaq Z, Arshad A, Khanum N, Joher I, Masood A. Nebulized Magnesium Sulphate vs Normal Saline as an Adjunct in Acute Exacerbation of Chronic Obstructive Pulmonary Disease. Pak J Med Health Sci. 2021;15(12):3694-6.
18. Edwards L, Shirtcliffe P, Wadsworth K. Use of nebulised magnesium sulphate as an adjuvant in the treatment of acute exacerbations of COPD in adults: a randomised double-blind placebo-controlled trial. Thorax. 2013; 68(4): 338-43.