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ORIGINAL ARTICLE

Nebulized Magnesium Sulphate vs Normal Saline as an Adjunct in Acute Exacerbation of Chronic Obstructive Pulmonary Disease

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ABSTRACT

Magnesium revealed to have properties of bronchodilation in chronic obstructive pulmonary disease (COPD) and asthma. A clinical benefit of nebulization with magnesium has been observed in asthma. The aim of the analysis was the therapeutic benefits comparison of using magnesium sulphate in nebulized form as an adjuvant of the normal saline solution among patients with exacerbations of COPD.

Study Design: A randomized single blind interventional study.

Place and Duration: In the Department of Medicine, Islam Medical College and Teaching Hospital Sialkot for six months duration from March 2021 to September 2021

Methods: This study involved 132 cases of acute COPD exacerbations with PEFR <300 L / min, evaluated twenty mints after initial therapy. Patients were administered salbutamol 5mg mixed with 3 ml of saline or 3 ml of isotonic magnesium sulphate three times at thirty-minute intervals using a nebulizer. At 90 minutes: Primary outcome of PEFR were measured and admission to hospital, invasive or non-invasive ventilation along with mortality were measured as 2^{ndry} outcomes.

Results: After nebulization with magnesium sulphate, the mean PEFR was 86.3 ± 11.9 l / min, 97.6 ± 19.1 l / min and 99.6 ± 15.2 l / min and 79.17 ± 14.11 l / min, 90.17 ± 18.27 l / min, and 93.17. ± 20.63 L. Statistically significant differences were found in the normal saline group at thirty, sixty and ninety minutes, correspondingly. In the magnesium group, 91.9% were admitted to the ward, 8.1% to the intensive care unit, 81.7% to the ward, and 18.3% to the salt group to the intensive care unit. The differences in ventilation and mortality were negligible.

Conclusions: In the context of AECOPD, nebulized magnesium sulphate in combination with salbutamol has a therapeutic advantage over PEFR, but has no effect on hospitalization, the need for mortality and non-invasive or invasive ventilation.

Keywords: Peak expiratory flow, magnesium sulphate and chronic obstructive pulmonary disease.

INTRODUCTION

Chronic obstructive pulmonary disease is an ailment categorized by the destruction and narrowing of the elastic recoil of the lung parenchyma, manifested by limitation of airflow and subsequent hyperinflation due to the small airway's infiltration by provocative cells[1-2]. Acute exacerbation of chronic obstructive pulmonary disease is the common disease in practice faced by an emergency doctor. Globally, it is estimated that 10% to 20% of the population suffers from COPD, causing > 30 lac demises each year[3-4]. Over ninety percent of expiries from COPD occur in middle and low revenue states[5]. It is estimated that in the Pakistani context, prevalence of COPD is 2.1% and 33% of them need hospitalizations and 27% need emergency admissions[6-7]. Treatment of COPD primarily focuses on reversing potential triggers and arresting pathogenesis, particularly infections with antibiotics, steroids, anticholinergics, and beta-2 agonists[8]. Steroids and antibiotics have played an important part in managing inflammation and infection, thus relaxing the airways and preventing exacerbations[9]. In combination with anticholinergic drugs, beta-2 agonist facilitates bronchodilation and thus relieves shortness of breath and improves respiratory parameters. Magnesium sulphate is believed to work by preventing contraction of smooth muscles by facilitation of the calcium uptake in the sarcoplasmic reticulum[10]. It prevents the sluggish calcium influx and causes instant release of calcium. It is additionally supposed to limit the acetylcholine release from the cholinergic nerve terminals and histamine release from mast cells[11]. Magnesium sulphate has been shown to stay helpful in acute exacerbation of asthma when directed intravenously and by nebulization. Due to the similarities in the Patho-physiology of AECOPD and acute asthma (e.g., bronchial hypersensitivity), the usage of magnesium sulphate in nebulized from is valuable therapeutic selection as it is easy, inexpensive and effective but although it is unproven[12]. The aim of the analysis was the therapeutic benefits comparison of using magnesium sulphate in nebulized form as an adjuvant of the normal saline solution among patients with exacerbations of COPD. The second goal was the comparison of the both groups outcomes in rapports of hospitalization, mortality and need for non-invasive or invasive ventilation.

MATERIAL AND METHODS

The patients with the provisional AECOPD diagnosis, probable patients were subjected to clinical evaluation and standard pre-treatment (i.e. 250 mcg ipratropium bromide, 200 mg nebulized hydrocortisone and 5 mg salbutamol),

oxygen (2 L / min intranasally by cannulas) if the oxygen saturation <90% in room air. Only subjects over 40 years of age with PEFR of <300 L / min evaluated twenty minutes after the initiation of the first ipratropium/ salbutamol nebulization were selected in the study. Patients given bronchodilator six hours and steroids twelve hours before the examination, and if the use of magnesium sulphate is contraindicated (diabetic coma, hypersensitivity, heart block hypercalcemia, hypomagnesaemia), patients not fit for spirometry and Subjects with systolic BP below 100 mmHg, patients with pneumothorax symptoms, CKD, pregnant women, and people with disease of motor neurons were omitted from the analysis. Informed consent was obtained for this 20-minute evaluation and a short questionnaire was used to obtain information on symptoms like severity, duration, smoking and medication use. Laboratory investigation including potassium, sodium, ABG complete blood count and creatinine were ordered. Patients were randomized to one of two lines of treatment. In A group (salbutamol and magnesium sulphate combination) or in B group (saline and salbutamol) were given. Therefore, the volunteers were not aware of the treatment type they were administered. Side effects observed by patients or doctors have been reported. Patients were administered salbutamol 5mg mixed with 3 ml of saline or 3 ml of isotonic magnesium sulphate three times at thirty-minute intervals using a nebulizer. At 90 minutes: Primary outcome of PEFR were measured and admission to hospital, invasive or non-invasive ventilation along with mortality were measured as 2^{ndry} outcomes. Vital signs were monitored as indicated clinically or part of clinical assessment. Afterward the concluding recruitment, the clinical team made the decision of hospital admission. After the patient was transferred to the intensive care unit, respiratory support and mortality were monitored for a week. SPSS version 20 was applied for entry of data and analysis. For each quantitative variable: standard deviation and mean were recorded. The Z test was applied to determine the significance level amid the variables, vital parameters comparison and mean variation of PEFR, and for the remaining variables: the chi-square test was used. <0.05 P-value was measured significant statistically.

RESULTS

132 total patients were randomized recruited nebulized with appropriate medications, assessed for clinical imprudent, and surveyed until discharged from hospital or death if present. Conferring to the criteria of inclusion, only subjects over forty years of age were encompassed for this study. 71.20 ± 11.25 years was the mean age was in the magnesium group and in the normal saline group; it was 69.01 ± 15.21 years. Fifteen (11.4%) patients were of 41-50 years of age, 24 (18.2%) aged 51-60, 41 (31.1%) aged 61-70, 28 (21.2%) aged 71-80, 19 (14.4%) 81-90 and a total of 4 (3.1%) patients over 90 years of age.

The most communal pervasiveness was observed in the 61-70 years age group. At start: 58 L / min was the mean PEFR in both groups. After nebulization with magnesium sulphate and salbutamol; 85.1±12.1 l / min was the mean PEFR after thirty mints, 96.8±18.7 l / min after one-hour and 98.5±14.9 l / min after 90 min.

	Table 1. Sex distribution (n=132)		
Sex	Magnesium sulphate group	Normal saline Total group	p- value
Male	30 (45.5%)	29 (43.9%) 59	0.1
Female	36 (54.5%)	37 (50.1%) 73	
Total	66 (100.0%)	66 (100.0%) 132	

Table 2: PEFR alteration at starting point and after nebulization of 90 mints (n=132)

PEFR (in Magnesium L/min) at sulphate group		p-value Normal saline group
0 min	58	58
30 min	85.1±12.1	78.20±13.09 0.008
60 min	96.8±18.7	89.29±17.30 0.21
90 min	98.5±14.9	92.86±21.20 0.07

The mean PEFR was statistically significant and was 78.20±13.09 l / min, 89.29±17.30 l / min and 92.86±21.20 l / min in the salbutamol and normal saline group after 30, 60 and 90 minutes respectively. The change in heart rate and blood pressure between the 2 groups was not significant in statistics. The Z test was applied to determine the variance between the means. 7(10.6%) of total patients from the magnesium group were hospitalized in the intensive care unit, and 59(83.4%) in the ward. In the saline group, 11(16.7%) went to the intensive care unit, and 55(83.7%) to the ward**.**

Table 3: The patient's admission in ICU and ward (n=132)

Admission area	Magnesium sulphate group	Normal saline group	Total	P Value
ICU	7(10.6%)	11(16.7%)	18	0.10
Ward	59(83.4%)	55(83.7%)	114	0.11

Ventilation was statistically insignificant in 3.1% of patients in the group saline. 1.7% of patients died in the group of normal saline group, which was not statistically significant.

Table 4: Prerequisite of ventilator support (NIV/IV) in relative to treatment (n=132)

NIV/IV support	Magnesium sulphate group	Normal saline group	P Value
Yes	1(1.5%)	2(3.1)	0.10
No	65(98.5%)	64(96.9%)	0.11

Table 5: Treatment relative to mortality (n=132)

Mortality	Magnesium sulphate group	Normal saline group	p-value
Yes	0	1 (1.5%)	0.07
No	66 (100%)	65 (98.5%)	

DISCUSSION

This study was directed to inspect the therapeutic benefits comparison of using magnesium sulphate in nebulized form as an adjuvant of the normal saline solution among patients with exacerbations of COPD. Our study showed that nebulizing a combination of salbutamol and magnesium sulphate in patients with acute COPD exacerbations has a beneficial effect on bronchodilation compared to nebulizing

regular salbutamol. Though, among the two groups: no significant difference in terms of adverse events and hospitalization rates, mortality and ventilation were noted[13]. Various procedural aspects related to its interpretation were taken into account in the study design. The main cause for encompassing only those with an estimated PEFR <300 L / min (assessed 20 minutes after the initiation of the first administration of salbutamol and ipratropium) was to determine the effect of intravenous magnesium administration in the asthmatic's groups in more serious disease[14]. There was a virtuous association amid PEFR and FEV at 1 second in COPD, which supported the usage of PEFR at home rather than in the office or laboratory monitoring spirometry[15]. A more recent study of ipratropium plus terbutaline or terbutaline plus a single intravenous magnesium bolus trailed by multiple nebulization of nebulized magnesium and terbutaline did not show substantial variances amid the two groups in terms of the main variables (including hospitalization, intubation, and hospitalization) which is similar to our study[16-17]. In Edwards et al study; FEV1 score, measured at 90 minutes, exhibited no statistically significant alteration amid the magnesium sulphate group and the placebo group after modification for baseline FEV1[18]. The variances in the necessity for hospitalization were also slight, as in our study. Our study is equally comparable to the asthma studies, as it justifies the stated effectiveness of magnesium in COPD and acute asthma exacerbations. In asthma, magnesium was directed both by nebulization and intravenously. The most recent meta-analysis and Cochrane review of I.V magnesium administration showed improvement in only the severe subgroup that showed improvement in PEF and FEV1[19-20]. Additionally, the benefits of nebulized repeated administration of magnesium include ease of administration without the need for intravenous administration. As for magnesium dosing, it was based on asthma research. Most of our patients responded significantly to nebulization[21]. We are not continuing to nebulize more than three doses of magnesium sulphate, but additional doses of salbutamol are suggested if the patient has only a partial response to the first dose[22].

CONCLUSION

In the context of AECOPD, nebulized magnesium sulphate in combination with salbutamol has a therapeutic advantage over PEFR, but has no effect on hospitalization, the need for mortality and non-invasive or invasive ventilation.

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