

INTRAVENOUS MAGNESIUM SULFATE AS AN ADJUNCT IN THE TREATMENT OF SEVERE ASTHMATIC PATIENTS NON-RESPONDING TO CONVENTIONAL THERAPY

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Abstract - Treatment of acute asthma is based on rapid reversal of bronchospasm and arresting airway inflammation. This study was done to determine the effect of intravenous MgSO₄ for improvement of pulmonary function in patients with acute asthma non - responding to routine therapy.

This randomized, double-blind, controlled study was conducted on 48 patients, magnesium sulfate group, n=48, aged 12-85 years, 26 men, 22 women, and control (saline) group, n=33, aged 15-80 years, 17 men, 16 women, who had not responded to routine treatment. Peak expiratory flow rate (PEFR) was done before MgSO₄ (25 mg/kg) and normal saline (100 ml) as a baseline criteria and after infusion of drugs at 30 mm and 3 hr. All patients were also given bronchodilators. The main outcome was PEER. Data were analyzed by χ^2 and t-test and differences between each point, were considered significant at $p < 0.05$.

The Peak expiratory flow rate 3 hrs after baseline increased in MgSO₄ group in comparison with saline group (82.60 ± 5.8 versus 47.8 ± 8.7 $p = 0.002$). The number of breathing in MgSO₄ was also increased at 30 mm and 3 hr after baseline. Cyanosis, diaphoresis and use of respiratory accessory muscles by patients were decreased in MgSO₄ in comparison with saline group.

According to the results, it is suggested that MgSO₄ can be an adjunct agent for the treatment of patients with acute non-responding asthma.

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Key Words: Acute asthma, non-responding, magnesium sulfate (MgSO₄), peak expiratory flow rate (PEER)

biology and treatment of asthma, its morbidity and mortality are on the rise (1,2). To help avert this trend, clinicians and patients must focus their attention on the early identification and treatment of asthma exacerbation. Management of severe acute asthma attacks sometimes brings difficulty to the physician (3). The goal of management of patients with respiratory failure is to restore them to a state of quiet breathing, without complication. This goal is often achieved by pharmacology alone (4). Bronchodilator management of acute severe asthma has evolved considerably in recent years. Beta-2 agonists have emerged as the single most potent class of bronchodilators available, and the inhalational route of administration has proven to be the most effective and least toxic method of delivery except among apneic or highly uncooperative patients (5). Some current treatment strategies have focused on intravenous (IV) magnesium sulfate (MgSO₄) administration in some diseases (3). Magnesium sulfate in an IV form has been suggested as a treatment for certain emergence conditions for more than 60 years and it is currently proposed to be beneficial in treating asthma, preeclampsia, eclampsia, myocardial infarction and cardiac arrhythmia (6). Intravenous magnesium sulfate has successfully been used in the treatment of acute asthma. There is some evidence that the IV form of MgSO₄ can provide additional bronchodilation when given in conjunction with standard bronchodilating agent and corticosteroids (7). One of the important problems for clinicians is managing drug-resistant disease and non-responding patients. This study was conducted to determine whether IV MgSO₄, when used as part of a standardized treatment protocol can improve pulmonary function in non-responding patients to therapy with beta-2 agonists and corticosteroids, presenting to the our pulmonary department with exacerbation of asthma.

INTRODUCTION

Despite advancing knowledge of the pathophy-

MATERIALS AND METHODS

This was a randomized, double-blind, controlled clinical trial. Asthmatics aged 12-85 years in acute exacerbation with a peak expiratory flow rate (PEFR) less than 200 (l/min) having taken bronchodilators, corticosteroids and requiring assisted ventilation were included. All patients, who had not responded to treatment during next 6 (hr) were selected for this investigation. They were randomized to receive treatment with MgSO₄ (25 mg/kg, as MgSO₄ group) or saline (100 ml normal saline, as placebo group). Drugs were given as infusion over the 30-45 minutes. For all patients peak expiratory flow, arterial blood gas (ABG), vital signs, rate of cyanosis and diaphoresis, and use of respiratory accessory muscles were monitored before starting treatment (as baseline findings). At the start of MgSO₄ or placebo, patients were monitored continuously for 6 hr. MgSO₄ solution and normal saline were coded and dispensed in identical containers. Decoding was done at the completion of the study. All the patients received oxygen, nebulized salbutamol, IV aminophyllin and corticosteroids. PEFR was the main outcome variable. Forty-eight patients (aged 12-85 years, 26 men, 22 women) as sulfate group and thirty three patients (aged 15-80 years, 17 men, 16 women) as control group were studied. Data collected from this investigation, were analyzed using χ^2 and t-test and

difference between data was considered significant at $p < 0.05$.

RESULTS

MgSO₄ group showed early and significant improvement as compared to placebo group in PEFR at 30 min, and 3 hours after stopping the infusion ($p = 0.00$, 95%CI = 11.85, 27.77). The clinical asthma score also showed significant improvement in the MgSO₄ group at 30 min and 3 hrs after stopping the infusion ($p < 0.0005$). PEFR at baseline was similar in the two groups. 30 minutes after baseline (MgSO₄ and saline) the mean (\pm SEM) increase in PEFR was greater in the MgSO₄ group (62.81 ± 5.9) than in the normal saline group (46.52 ± 8.3). At 3 hr, increase in peak flow was 82.6 ± 5.8 in the MgSO₄ group compared with saline group ($p < 0.005$, 95%CI = -55.8, -13.77). There was a significant difference in PEFR from initiation of the infusion to 30 min ($p = 0.00$, 95%CI = -40.1, -22.55) and 3 hr later for the MgSO₄ group ($p = 0.00$, 95%CI = 11.85, 27.77). There was also a considerable decrease in number of breathing at baseline, 30 min and 3 hr in MgSO₄ group (Table 1). Patients in MgSO₄ group had shown significant decrease in diaphoresis, cyanosis and use of respiratory accessory muscles (Table 2.)

Table 1. Mean \pm SEM of peak expiratory flow rate and the number of breathing in MgSO₄ and saline groups

	Baseline (the time of zero)		30 min after infusion		3 hr after infusion	
	MgSO ₄	Saline	MgSO ₄	Saline	MgSO ₄	Saline
PEFR	31.46 \pm 5.6	30.00 \pm 5.9	62.81 \pm 5.9	46.52 \pm 8.3	82.60 \pm 5.8	47.8 \pm 8.7
No. of breathing	34.38	35.1	27.21	33.20	24.42	30.22

Table 2. Frequency (%) of some variables in MgSO₄ in comparison with saline group

	Baseline		30 min		3 hr		P. value χ^2
	MgSO ₄	Saline	MgSO ₄	Saline	MgSO ₄	Saline	
Diaphoresis	14 (29.2)	20 (30.3)	4 (8.3)	14 (21.2)	1 (2.10)	12(1.1)	0.02 (7.43)
Cyanosis	17 (35.4)	15 (22.7)	3 (6.3)	13 (19.7)	1 (2.10)	8 (12.1)	0.0003 (15.74)
Use of respiratory accessory muscles	48(100)	27(40.9)	34(78)	17(25.8)	11(22.9)	12(18.2)	0.06(5.38)

DISCUSSION

According to the results, it is suggested that MgSO₄ can improve the respiratory function in the non-responding patients with acute severe asthma presenting to the our pulmonary department. It could improve and increase the peak expiratory flow rate and decrease the number of breathing. The increase of PEFR was statistically significant in MgSO₄ compared

to (saline) group, thus magnesium sulfate appears to be safe and beneficial in patients who present with severe acute asthma. This finding could be supported with other studies (1,3,4,7,8). Inhaled beta-2 agonists, oxygen and systemic corticosteroids are main stays of acute care drug management, whereas other data support the use of inhaled steroids, ipratropium bromide, magnesium sulfate (9,10,11) and theophyllin (4). Assisted ventilation by face mask or intubating patients, a ventilatory strategy that prolongs exhalation time and accepts hypercapnia minimizes lung hyperinflation and

generally results in a good outcome. Nonresponding asthmatic patients are important clinical problems for clinicians. Some studies suggested that administration of systemic corticosteroids and beta-adrenergic agonists were useful for those patients (5, 10). Authors suggested that $MgSO_4$ could be used as an adjunct agent in the treatment of acute asthma (10,12). $MgSO_4$ was used as an inhalation dosage form and as a vehicle for nebulized beta-2 agonists in acute asthma. It had shown therapeutic effectiveness in those cases (9,11). Many reports have shown that magnesium sulfate has certainly a role as an adjunct to traditional therapy in asthma and asthma-like conditions and has been helpful in the treatment of acute exacerbation of asthma (10). Intravenous $MgSO_4$ may be useful when conventional treatment has failed (12,13). It seems clear that IV $MgSO_4$ also is effective for the suppression of bronchial smooth muscle contractions. Children who were treated with IV $MgSO_4$ for moderate to severe asthma had significantly greater improvement in short-term pulmonary function without any considerable alteration in blood pressure (14), suggesting a role for this agent as an adjunct in the treatment of such patients. Mg^{2+} is a natural calcium antagonist and intracellular Mg^{2+} is thought to modulate smooth muscle contractions and it is known to have a direct effect on calcium uptake, resulting in smooth muscle relaxation (10). Finally our data also support previous studies (15,16) that $MgSO_4$ is helpful in decreasing asthmatic complications. It seems that administration of $MgSO_4$ in addition to improvement of pulmonary function and helpfulness in the treatment of our patients with acute non-responding asthma, can decrease admission rate in patients with acute severe asthma.

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REFERENCES

1. Levy BD, Kitch B, Fanta CH. Medical and ventilatory management of status asthmaticus. *Intensive Care Med.* 24 (2): 341-4; 1998.
2. Corbridge TC, Hall JB. The assessment and management of adults with status asthmaticus. *Am J Respir Crit Care Med* 151(5): 1296-316; 1995.
3. Curkan F, Haspolat K, Bosnak M, Dikici B, Dorman O, Ece A. Intravenous magnesium sulfate in the management of moderate to severe acute asthmatic children non-responding to conventional therapy. *Eur J Emerg Med.* 6(3): 201-5; 1999.
4. Gluckman TJ, Corbridge T. Management of respiratory failure in patients with asthma. *Cuvr Opin Pulm Med.* 6(1): 79-85; 2000.
5. Moan MJ, Fanta CH. Bronchodilator therapy in the management of acute asthma. *Compr Ther.* 21(8): 421-7; 1995.
6. Frakes MA, Richardson LE. Magnesium sulfate therapy in certain emergency conditions. *Am J Emerg Med.* 15(2): 182-7; 1997.
7. Mangat HS, D'Souza GA, Jacob MS. Nebulized magnesium sulfate versus nebulized salbutamol in acute bronchial asthma: a clinical trial. *Eur Respir J.* 12 (2): 341-46; 1998.
8. Nannini U, Pendino JC, Coma RA, Mannarino S, Quispe R. Magnesium sulfate as a vehicle for nebulized salbutamol in acute asthma. *Am J Med.* 108(3): 193-7; 2000.
9. Rodrigo C, Rodrigo C, Burschtin O. Efficacy of magnesium sulfate in acute asthma; a meta-analysis of randomized trials. *Am J Emerg Med.* 16(2): 216-21; 2000.
10. Skotniki AB, Jablonski MJ, Musial JS. The role of magnesium in the pathogenesis and therapy of bronchial asthma. *Przegl Lek.* 54(9): 630-3; 1997.
11. Meral A, Coker M, Tanac R. Inhalation therapy with magnesium sulfate and salbutamol sulfate in bronchial asthma. *Turk J Pediatr.* 38(2): 169-75; 1996.
12. Bloch H, Silverman R, Mancherje N, Grants, Jagminas L, Scharf SM. Intravenous magnesium sulfate as an adjunct in the treatment of acute asthma. *Chest.* 107(6): 1576-81; 1995.
13. Swain R, Kaplan - Machlis B. Magnesium for the next millennium. *South Med J.* 92(11): 1040-7; 1999.
14. Clarallo L, Sancer AH, Shannon MW. Intravenous magnesium therapy for moderate to severe pediatric asthma, results of a randomized placebo -controlled trial. *J Pediatr* 129(6): 809-14; 1996.
15. Skorodin MS, Tenholder MF, Yetter B, Owen KA, Wailer RF. Magnesium sulfate in exacerbations of chronic obstructive pulmonary disease. *Arch Intern Med.* 155(5): 496-500; 1995.
16. Emelianova AV, Goncharova VA, Sinitisinga TM. Magnesium Sulfate in management of bronchial asthma. *Kim Med Mosk.* 74(8): 55-8; 1996.