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Nebulized magnesium sulphate during acute exacerbation of asthma in adults after failure of Traditional treatment

Mohamed S Elsakaya[1], Monira T Ismail[1], Mohamed N Hamed[2], Hamdy A Hendawy[3], Magdy A Omera[4]

[1]Suez Canal University, Faculty of Medicine, Department of Emergency Medicine, Ismailia, Egypt
[2]Suez Canal University, Faculty of Medicine, Department of Chest Diseases, Ismailia, Egypt
[3]Suez Canal University, Faculty of Medicine, Department of Anesthesia & Intensive, Ismailia, Egypt
[4]Portsaid University, Faculty of Medicine, Department of Anesthesia & intensive, Care, Egypt

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Abstract
The aim of this study is to evaluate the effectiveness of inhaled magnesium sulfate as a supplemental treatment in control of acute exacerbation of asthma in adults not responding to traditional treatment in the first hour. Patients who failed to respond to conventional measures randomly allocated to one of two groups: Group 1: In which patients received two doses of nebulized 300 mg MgSO4 /10 minutes apart & Group 2 (control group): in which patients received nebulized combination of (2.5 mg) salbutamol plus (250µg) ipratropium bromide up to two doses over one hour. Magnesium sulfate group showed better improvements than control group. The variables mostly predict SaO2 pre-post change. The only predictor variable was group (inhaled magnesium sulfate versus control); inhaled magnesium sulfate was associated with 1.9 greater change in SaO2 compared to control group (when all other variables were constant). Other variables were potential confounders but were not statistically significant. Inhaled MgSo4 to the traditional treatment (B2 agonist in combination with hydrocortisone) showed a better improvement in PEFR and SaO2 without recorded side effects compared to traditional treatment in control group. Magnesium sulphate (MgSO4) improves significantly the respiratory function of patients not responding to traditional treatment.

Keywords: Magnesium sulphate (MgSO4), bronchial asthma, B2 agonist in combination

Introduction

Two years ago, The Institute for Health Metrics and Evaluation (IHME) estimated as many as 334 million people have asthma and may be an additional 100 million persons by 2025 [1].

Although asthma accounts for about 1 in every 250 deaths worldwide; yet many of these are preventable e.g. suboptimal long-term medical care and delay in obtaining help during the final attack [2].

In America surveys, the number of emergency visits for asthma continues to increase. During 1999, there were approximately 2 million asthma-related emergency room visits. This represented a 26% increase since 1992 and approximately 9% of asthma patients required hospitalization, 23% needed emergency department treatment [3].

***Coresponding Author:** Monira T Ismail, Suez Canal University, Faculty of Medicine, Department of Emergency Medicine, Ismailia, Egypt
E-mail: monirataha77@yahoo.com

These increasing asthma burdens has focused attention on methods to improve treatment of the acutely ill emergency department patients and searching for additional treatments that improve the patient's condition, prevent hospitalization, or further clinical deterioration.[4].

Despite the efficacy of the inhaled beta-agonists, systemic corticosteroids, and supplemental oxygen combination, a significant proportion of patients (as many as 30%) presenting to emergency departments fail to respond to it [5].

Magnesium sulfate is a promising adjunct therapy in the acute exacerbation patients, as it is cheap, well tolerated and readily available. In their study, Blitz et al, 2005 concluded that the use of nebulized magnesium sulfate, particularly in addition to a beta-agonists, in the treatment of acute asthma exacerbation appears to produce beneficial improvement in pulmonary function and may reduce the number of hospital admissions [6].

The potential clinical benefits of inhaled magnesium sulfate have been questioned and research publications have produced

conflicting results. Although of equal or less benefit than beta – agonist in acute asthma exacerbation; there is a subset of patients with severe attack , may gain more benefit as regard pulmonary function improvement and decrease in hospital admission rate [7].

The purpose of this article was to evaluate the effectiveness of nebulized magnesium sulfate, as supplement treatment, in controlling the acute exacerbation of asthma, in a subset group of adults not responding to combination treatment of β2 agonist, intravenous steroids and O2 therapy, in the first hour.

Material and Method

This Randomized single-blind controlled trial, after being approved from the research ethics board of the Faculty of Medicine, Suez Canal University; was conducted in the Emergency department of Suez Canal University Hospital, from September 2013 to February 2014.

After informed consent signing, adult asthmatics attending the hospital, fulfilling the inclusion criteria, were recruited for the study.

Inclusion criteria included the following
(1) Both sexes aged ≥ 18 years. (2) Known asthmatic in acute exacerbation [an episode characterized by a progressive increase in symptoms of shortness of breath, cough, wheeze and chest tightness and progressive decrease in pulmonary function (30% reduction in PEFR from patient best or predicted) requiring change of treatment (3) non-smoker(4) free of other chest or medical diseases (5) neither pregnant nor breast feeding(6) capable of measuring peak expiratory flow rate (PEFR) (7) Negative history of This was a descriptive, comprehensive study that included all patients presented with acute myocardial infarction with or without cardiogenic shock. allergy to magnesium sulphate or ipratropium bromide (8)No improvement on treatment in the first hour of management [failure to respond to treatment is persistent or worsening dyspnea, PEFR < 70% best or predicted , respiratory rate (RR) >30/minute, Heart rate (HR) >110/minute and Oxygen saturation (SaO2)<90% at the end of the first hour of management]
Exclusion criteria: (1) Patients showing deterioration requiring ICU or mechanical ventilation (altered conscious level, exhausted patients with respiratory fatigue, respiratory acidosis with pH < 7.2, or hypercapnia).

(2) Patients refuse to complete the study (3) patients presenting with intolerable magnesium sulphate side effects (nausea, vomiting, bradycardia or hypotension) and necessitating interruption of the second hour treatment.

Methods

On joining the study, patients gave a full detailed clinical history, underwent a thorough physical examination, and baseline data were collected using data collection sheet, including age, sex, duration of asthma, treatment and compliance, drug allergy and any history of ICU admission or hospital admission, details of the presenting attack as, symptoms, any noticed cause of attack, duration, and drug received.

Baseline records including height, weight, HR, RR, blood pressure (BP) , temperature, chest findings, complete blood count (CBC), blood glucose, serum electrolytes, chest radiography, PEFR, arterial blood gases (ABGs) and SaO2 were recorded on arrival. Dyspnea assessment, PEFR and SaO2 were repeated every 20 minutes. All studied patients were connected to portable Monitor "S/5 Light Monitor, DATEX-OHMEDA, FINLAND" for close monitoring of electrocardiogram for heart rate and rhythm, respiratory rate, noninvasive blood pressure, and Oxygen saturation (SaO2).

All patients received Oxygen therapy through facemask (FiO2 40-60%) to achieve oxygen saturation ≥ 90%, and were given an intravenous bolus injection of 200 mg hydrocortisone and nebulized salbutamol (2.5 mg) in 3 ml solution / 20 minutes by jet nebulizer for 1 hour. Patients who showed no improvement at the end of first hour were assigned sequentially to either group of study: the first group to receive 300 mg nebulized magnesium sulphate twice over the second hour (10 minutes apart), and the second group to receive nebulized combination of salbutamol (2.5 mg) plus ipratropium bromide (250µg) up to two doses, over one hour. Patients were monitored twice in the second hour, and the parameters monitored were: PEFR, SaO2 respiratory rate, heart rate, blood pressure and arterial blood gases (in deteriorating cases). Side effects of Magnesium sulphate as flushing, sweating, hypotension, depressed reflexes, flaccid paralysis, hypothermia, circulatory collapse, cardiac and central nervous system depression proceeding to respiratory paralysis, and hypocalcaemia were also monitored.

All patients were assessed at the end of second hour, and patients who did not improve, were assessed by pulmonology specialist to determine the need for ICU admission, and the following final outcome points were recorded.

1. Peak expiratory flow rate improvement (best of three trial values), 2.respiratory rate, 3. Heart rate, 4.blood pressure changes, 5. Dyspnea sensation, 6. Arterial oxygen saturation change at the end of study, 7. Fate of the patient (discharge, admission to inpatients ward, admission to ICU or mortality.

Statistical Analysis
The statistical analysis was performed using Gathered data were processed using SPSS version 15 (SPSS Inc., Chicago, IL, USA). Fisher's Exact Test comparing both groups mean and standard deviations values of age, sex, asthma severity, between groups.

Quantitative data were expressed as means ± SD while qualitative data were expressed as numbers and percentages (%).Paired t test was used to test significance of difference for quantitative variables in the same group (pre and post intervention), and Student t- test was used to test significance of difference between groups. A probability value (p-value) < 0.05 was considered statistically significant.

Ethical consideration- All Patients give consent to participate in the study without affecting their course of treatment accordingly permission obtained from ethical committee of faculty of medicine in Suez Canal University

1) Approval of Research ethics committee.
2) Singing written informed consent from participants.
3) Confidentiality of data.

4) Explanation of our study to the participants.
5) An informed consent was taken from each patient or relatives.

Results

Eighty two adult asthmatics in acute exacerbation (46 males and 36 females), who failed to respond to the first hour treatment, were grouped into 2 matched groups (41patients each). The first group (Magnesium group) received nebulized magnesium sulfate while the second (control group) received nebulized beta agonist with ipratropium bromide combination

Table 1. Baseline characteristics in both groups.

		Control Group (n = 41)	Study Group (n = 41)	**Total (n = 82)**	***p value**
	Range	23 – 60	22 - 60	22- 60	0.877
	Mean ± SD	42.34±11.96	41.93±12.32	42.13 ± 12.06	
Age (years)	**≥20**	6 (14.6%)	8 (19.5%)	14 (17.1%)	0.917
	≥30	11 (26.8%)	11 (26.8%)	22 (26.8%)	
	≥40	10 (24.4%)	8 (19.5%)	18 (22.0%)	
	50 – 60	14 (34.1%)	14 (34.1%)	28 (68.3%)	
Sex	Male	23 (56.1%)	23 (56.1%)	46 (56.1%)	1.00
	Female	18 (43.9%)	18 (43.9%)	36 (43.9%)	
Duration of disease (years)	Male	23 (56.1%)	23 (56.1%)	46 (56.1%)	
	Female	18 (43.9%)	18 (43.9%)	36 (43.9%)	
	< 10	9 (22.0%)	8 (19.5%)	17 (20.7%)	0.252
	≥10	8 (19.5%)	15 (36.6%)	23 (28.0%)	
	≥20	24 (58.5%)	18 (43.9%)	42 (51.2%)	
Type of Asthma	**Childhood**	23 (56.1%)	25 (61.0%)	48 (58.5%)	0.805
	Adulthood	14 (34.1%)	11 (26.8%)	25 (30.5%)	
	Occupational	4 (9.8%)	5 (12.2%)	9 (11.0%)	

* Statistically significant at p <0.05

Table 2. Severity of asthma at the end of first hour

Severity Number (%)	**Control Group (n = 41)**	**Magnesium Group (n = 41)**	**Total (n = 82)**	**p - value**
Moderate (PEFR< 70 %)	28 (68.29%)	31 (75.61%)	59 (71.95%)	0.574
Severe (PEFR< 50 %)	12 (29.26%)	8 (19.51%)	20 (24.39%)	
Life-threatening (PEFR< 33 %)	1 (2.43%)	2 (4.87%)	3 (3.65%)	

Table 3. Control group: parameters before and after the second hour of treatment

parameters (Mean ± SD)	**Before**	**After**	**Difference**	**p -value**
Respiratory rate (Breath/min)	26.20 ± 3.39	25.37 ± 6.99	-0.83 ± 6.92	0.097
Heart rate (Beat/min)	109.93 ± 17.89	111.17 ± 19.77	1.24 ± 15.82	<0.001*
Systolic blood pressure (mmHg)	114.39 ± 9.76	110.24 ± 10.60	-4.15 ± 9.48	<0.001*
Diastolic blood pressure (mmHg)	72.20 ± 6.52	67.20 ± 8.52	-5.00 ± 7.25	<0.001*
SaO2 %	92.34 ± 1.82	93.00 ± 4.07	0.66 ± 3.62	0.003*
PEFR (% of predicted)	60.51 ± 11.01	64.88 ± 14.04	4.37 ± 8.21	<0.001*

* Statistically significant at p <0.05

Table 4. Study group: parameters before and after the second hour of treatment

parameters (Mean ± SD)	**Before**	**After**	**Difference**	**p -value**
Respiratory rate (Breath/min)	26.61 ± 4.25	21.76 ± 6.48	-4.85 ± 4.23	<0.001*
Heart rate (Beat/min)	106.15 ± 17.38	99.15 ± 16.56	-7.00 ± 10.39	<0.001*
Systolic blood pressure (mmHg)	114.15 ± 9.21	114.88 ± 11.65	0.73 ± 10.58	0.001*
Diastolic blood pressure (mmHg)	71.22 ± 7.14	70.24 ± 9.35	-0.98 ± 8.00	<0.001*
SaO2 %	92.51 ± 2.66	94.98 ± 3.39	2.46 ± 2.97	<0.001*
PEFR (% of predicted)	56.61 ± 14.20	74.17 ± 15.62	17.56 ± 13.66	<0.001*

* Statistically significant at p <0.05

Table 5. Comparison of the difference of parameters before and after treatment between both groups

	Pre-post intervention Change			
parameters	**Control group (n = 41)**	**Magnesium group (n = 41)**	**Mean difference (Std. Error)**	**p -value**
Respiratory rate (Breath/min)	0.83 ± 6.92	4.85 ± 4.23	4.02 (1.27)	**0.002***
Heart rate (beat/min)	1.24 ± 15.82	7.00 ± 10.39	8.24 (2.96)	**0.007***
Systolic blood pressure (mmHg)	4.15 ± 9.48	0.73 ± 10.58	-4.88 (2.22)	**0.031***
Diastolic blood pressure (mmHg)	5.00 ± 7.25	0.98 ± 8.00	-4.02 (1.69)	**0.019***
SaO2 %	0.66 ± 3.62	2.46 ± 2.97	1.80 (.731)	**0.016***
PEFR (% of predicted)	4.37 ± 8.21	17.56 ± 13.66	13.19 (2.49)	**<0.001***

* Statistically significant at p<0.05

Table 6. Factors affecting the difference in SaO2 (n = 82)

Factors	Coefficients	Std. Error	p - value	Model Significance	(R2) ¤
(Constant)	-0.27	2.018	0.892		
Sex	0.58	0.786	0.461		
Type of treatment	1.90	0.758	0.014*		
Type of asthma	0.78	0.591	0.190	F(6,75) = 1.39 p-value = 0.230	0.10
Age (years)	-0.02	0.042	0.584		
Duration of asthma	0.02	0.045	0.647		
Severity of asthma	0.35	0.733	0.640		

Regression equation: SaO2 difference = -0.27 + 0.58(sex) + 1.90 (treatment) + 0.78(type of asthma) + (-) 0.02(age) + 0.02 (duration) + 0.35(severity of asthma)
* Statistically significant at p <0.05 ¤ Coefficient of determination

Table 7. factors affecting the difference in PEFR (n = 82)

Factors	Coefficients	Std. Error	p - value	Model Significance	(R^2) ¤
(Constant)	5.845	6.947	0.403		
Sex	-1.387	2.706	0.610		
Type of treatment	13.235	2.609	<0.001*		
Type of asthma	0.453	2.033	0.824	F(6,75) = 4.58 p-value <0.001*	0.268
Age (years)	-0.074	0.146	0.611		
Duration	0.006	0.156	0.968		
Severity of asthma (pre)	0.813	2.525	0.748		

Regression equation: PEFR difference = 5.85 + (-)1.39 (sex) + 13.24 (treatment) + 0.45(type of asthma) + (-)0.07(age) + 0.006 (duration)+ 0.81(severity of asthma) * Statistically significant at p <0.05 ¤ Coefficient of determination

Table 8. Strength of effect / association between inhaled magnesium sulfate and the disease outcome

Outcomes	Effect Measures				
	RR (95% CI)	p-value	ARR	AR%	NNT
Mortality	0.40 (0.08 – 1.94)	0.256	0.07	60%	14
ICU admission	0.37 (0.12 – 1.13)	0.081	0.07	43%	14
WARD admission	0.24 (0.08 – 0.58)	0.002*	0.32	76%	3

RR (95% CI) = Relative Risk (confidence interval) , ARR = Absolute Risk Reduction, AR% = Attributable risk percentage, NNT = Number Needed to Treat
* Statistically significant at p<0.05

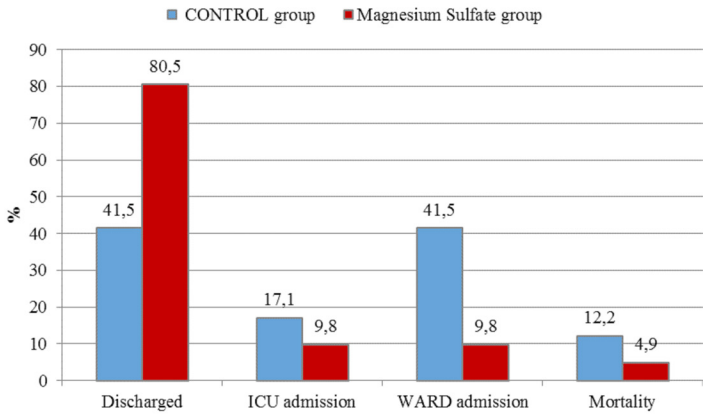

Figure 1. The different outcomes in both study and control groups

Discussion

The present study has been conducted for 6 months (from September to February) in Emergency department of Suez Canal University Hospital to evaluate the effectiveness of adding inhaled magnesium sulfate in patients with acute exacerbation of asthma who failed to respond to the traditional treatment after the first hour, which revealed that adding inhaled MgSo4 to the traditional treatment (B2 in combination with hydrocortisone) showed a better improvement in PEFR (in the study group 31 % versus 7.2% in control group) and SaO2 (in the study group 2.7% versus 0.71%in control group) without recorded side effects of inhaled MSO4 in our study with less mortality by 60%, less ICU admission by 43% and less ward admission by 76% with inhaled magnesium sulfate compared to traditional treatment.

The role of magnesium sulphate in the treatment of acute asthma has been evaluated in several studies. In most of the studies magnesium was administered intravenously.

(Mangat et al., 1998) investigated the efficacy of nebulized MgSO4 as a bronchodilator in acute asthma versus to nebulized salbutamol. This was a randomized, double-blind, controlled clinical trial. Thirty-three asthmatics aged 12-60 years in acute exacerbation, with a peak expiratory flow (PEF) <300 L /min, not having taken bronchodilators and not requiring assisted ventilation were included. The increase in PEFR was statistically significant and comparable in both groups (by 35% predicted in the MgSO4 and by 42% predicted in the salbutamol group). Two patients warranted admission in the salbutamol group and one in the MgSO4 group. Nebulized MgSO4 had a significant bronchodilator effect in acute asthma. This effect was not significantly different from that of nebulized salbutamol [8].

Similar to the present study the bronchodilator effect of MgSO4, was significant, but in contrast to the present study this effect was a significantly different from that of nebulized salbutamol, which may be due to 1) small number of their study group (n=33), while this study was done on 82 patients 2) they worked in the first hour, while the present study has been done in the second hour.

(Nannini et al., 2000) had a study on 35 patients in a randomized, double-blind, controlled trial. After measurement of peak expiratory flow, patients received 2.5 mg salbutamol plus either 3 mL normal saline solution (n = 16) or 3 mL isotonic magnesium

sulfate (n = 19) through a jet nebulizer. Peak flow was reassessed 10 and 20 minutes after treatment. There was a significant inverse correlation between baseline peak flow (percent of predicted) and the percentage increase in peak flow at 20 minutes in the magnesium sulfate group (r = -0.82, P <0.0001), but not in the saline group (r = -0.12, P = 0.67). Compared with a single dose of salbutamol; there was a greater increase in peak flow rate when a single dose of magnesium sulphate was added to nebulized salbutamol [9].

In the present study magnesium sulfate was associated with 31.2 greater change in PEFR compared to control group (r= 0.268, p= 0.001) with results paralleled with this study regarding the effect of adding inhaled MgSO4 to salbutamol.

In other study conducted on 52 patients with severe asthma, nebulization of three doses of magnesium sulphate plus salbutamol was found to produce more bronchodilation compared with three doses of salbutamol alone by Hughes et al. [10].

Which is similar with the present study, although there is a difference between the numbers of doses used in the two studies. (They used 3doses while we used 2 doses of inhaled MgSO4) and they worked in the first hour, while the present study has been done in the second hour.

Metanalysis by (Blitz et al., 2005) included four randomized controlled trials involving 296 patients were included. Two studies compared nebulized MgSO4 with β2-agonist to β2-agonist and two studies compared MgSO4 to β2-agonist alone. Three studies enrolled only adults and 2 enrolled exclusively pediatric patients [7].

Overall, there was a significant difference in PEFR between patients whose treatments included nebulized MgSO4 in addition to beta2-agonist (SMD: 0.37; 95% CI); however, hospitalizations were similar between the groups (RR: 0.64; 95% CI) (Blitz et al., 2005).

Blitz concluded that nebulized inhaled magnesium sulfate in addition to β2-agonist in the treatment of an acute asthma exacerbation, appears to have benefits with respect to improved pulmonary function in patients with severe asthma and there is a trend towards benefit in hospital admission [7].

(Gandia et al., 2012) conducted a placebo-controlled, double-blind clinical trial with seventy six adult patients with severe bronchial asthma. Subjects were randomized into four groups receiving: NaCl 0.9%, MgSO4 alone, β2-agonist alone, and the combination of MgSO4+ β2-agonist [11].

Repeated measures of FEV (1) were performed at 0, 5, 10, and 20 minutes after the end of the inhalations. In the MgSO4 and MgSO4 + β2-agonist groups, a blood samples were taken before and after inhalation to determine serum magnesium levels.

Inhaled MgSO4 led to a significant improvement of the FEV (1) from the 15(Th) minute after its inhalation. (2) β(2-)agonist significantly increased FEV(1) from the 5(th)minute (3) inhaled MgSO4 + β(2-)agonist led to a significantly greater FEV(1) from the 5(th)minute than inhaled MgSO4alone or inhaled β(2-) agonist alone ($p<0.05$) 4) There was a correlation between low serum magnesium level and the increase in FEV(1)after inhalation of MgSO4 + β(2-)agonist ($p<0.001$). The study Concluded that inhaled MgSO4, in combination with β2-agonist, appeared to have benefits in the treatment of severe bronchial asthma, especially when associated with hypomagnesemia.

Although the previous study differ in that we used PEFR while they used FEV1, in addition to the different study groups between the two studies, parallel to the present study, inhaled MgSO4 appeared to have an additive effect in treatment of severe asthma.

As regard in contrast, (Meral et al., 1996) applied inhalation therapy with magnesium sulfate and salbutamol sulfate to two groups, each consisting of 20 patients with acute asthma. The effects of inhaled magnesium sulfate and salbutamol sulfate were compared. The evaluation of patients was done using respiratory score, peak expiratory flow rate with a Wright peak flow meter, respiration rate, heart rate and blood pressure. Although magnesium sulfate's bronchodilating effect continued for approximately one hour, treatment of acute asthma using salbutamol sulfate inhalation was found to be more successful and its effect continued for six hours [12].

In contrast also (Bessmertny et al., 2004) conducted a study in adults with mild to moderate acute asthma showed no benefit of administering three doses of magnesium sulphate along with salbutamol as compared with placebo plus salbutamol [13].

(Aggarwal et al., 2006) studied a total of 100 patients presented to an emergency department with an acute attack of bronchial asthma were randomized to two groups: nebulization with a combination of salbutamol and magnesium sulphate (group A) and nebulization with salbutamol only (group B). Both groups received nebulization 3 times at intervals of 20 minutes. Salbutamol and magnesium sulphate were administered in doses of 0.5 mg and 500 mg, respectively, and the solutions were made isotonic to plasma osmolality [14].

Pulse rate, blood pressure, and PEFR were measured at baseline and at 15, 60, 75, and 120 minutes. Serum magnesium levels and blood gases were measured at 0 and 120 minutes in both groups.

No significant difference between the groups in rise in PEFR and the study suggests that there is no therapeutic benefit of adding magnesium sulphate to salbutamol nebulization in the treatment of patients with acute severe or life threatening asthma [14].

This contrast between Aggarwal's study and the present study may be due to 1) the different doses as Salbutamol and magnesium sulphate were administered in doses of 0.5 mg and 500 mg, but the present study used nebulized salbutamol (2.5 mg)/ 3 ml solution / 20 minutes 2) selection of patients was in the first hour, but in the present study patients who failed to response to the traditional treatment after the first hour.

(Powell et al., 2012) had seven studies involved adults exclusively. There was no statistically significant improvement in PEFR when inhaled MgSO4 and β2-agonist was compared with β 2-agonist alone (SMD 0.23). There was no clear advantage in terms of hospital admissions (RR. 0.76 and 95% CI) [15].

So Powell et al., concluded that there was no good evidence that inhaled MgSO4 can be used as a substitute for inhaled β2 agonists. When used in addition to inhaled β2 agonists (with or without inhaled ipratropium), there is no overall clear evidence of improved pulmonary function or reduced hospital admissions. However, individual study results from three trials suggest possible improved pulmonary function in those with severe asthma exacerbations (FEV1 less than 50% predicted) [15].

In contrast our study showed, reduction 43% in ICU admission and 76% ward admission with inhaled magnesium sulfate compared to traditional treatment (RR. 0.22 with a p-value 0.0002).

(Goodacre et al., 2013) had enrolled adults (aged ≥16 years) with severe acute asthma at emergency departments of 34 hospitals in the UK, excluded patients with life-threatening features or contraindication to study drugs. We used a central randomization system to allocate participants to intravenous MgSO4 (2 g in 20 min) or nebulized MgSO4 (three 500 mg doses in 1 h) alongside standard therapy including salbutamol, or placebo control plus standard therapy alone. Rates of hospital admission did not differ between patients treated with either form of MgSO4 compared with controls or between those treated with nebulized MgSO4 and intravenous MgSO4. Change in breathlessness did not differ between active treatments and control, but the change was greater for patients in the intravenous MgSO4 group than it was in the nebulized MgSO4 group. These finding suggested that nebulized MgSO4 has no role in the management of severe acute asthma in adults and at best suggest only a limited role for intravenous MgSO4 in this setting. [16].

Which against our results, may be due to their usage of different dose of MgSO4 plus large sample size they used. Thus the results of these few studies, were conflicting with regard to the role of additional nebulization of magnesium sulphate in acute asthma.

LIMITATIONS OF THE STUDY

1. Some of the patients had received variable doses of inhaled β agonists or oral steroids before arrival at emergency department.
2. Exclusion of patients' age from <18 or > 60 years.
3. The present study has been done only in single center rather than multiple centers
4. Some patients refused to be rolled in the study.
5. Although despite the small number of the present study patients (n=82), and the tight inclusion criteria as regard asthma exacerbation, and a possibility of a selection bias,
6. The spontaneous improvement of symptoms, as observed in natural history of asthma, makes drug trial results in asthmatics, with inherent queries, especially in small number of patients with difficulty to control for pre-hospital admission treatment, type and dose.

Conclusion

The common practice of treating severe asthma uses a combination of medications aimed at bronchodilation and anti- inflammation, antagonizing the triad of increased airway secretions, inflammation and reversible bronchoconstriction of asthma.

Intravenous magnesium sulfate (MgSO4) may be added in severe cases unresponsive to standard treatment but requires special monitoring.

Magnesium's pharmacological action is based upon its ability to inhibit the release of calcium from vesicles in the sarcoplasmic reticulum, resulting in bronchial smooth muscle relaxation.

All patients were connected to Datex Ohmeda monitor for close monitoring of electrocardiogram for heart rate and rhythm, respiratory rate, noninvasive blood pressure, pulse oximetry for Oxygen saturation (SaO2). Oxygen therapy was initiated to achieve oxygen saturation ≥ 90%. All patients were received an intravenous bolus injection of 200 mg hydrocortisone and nebulized salbutamol (2.5 mg)/ 3 ml solution / 20 minutes by jet nebulizer for 1 hour .

Patients who failed to respond to conventional measures in the first hour were enrolled in the study and randomly allocated to one of two groups: Group 1: In which patients received nebulized magnesium sulfate (Two doses of nebulized 300 mg MgSO4 /10 minutes apart). Group 2 (control group): in which patients received nebulized combination of (2.5 mg) salbutamol plus (250µg) ipratropium bromide up to two doses over one hour.

The parameters monitored were: PEFR, SaO2 respiratory rate, heart rate and noninvasive arterial blood pressure (in deteriorating cases). Those patients showed no improvements were assessed by another physician (Specialist) to determine the need for ICU admission.

The present study concluded that adding inhaled MgSo4 to the traditional treatment (B2 agonist in combination with hydrocortisone) showed a better improvement in PEFR and SaO2 without recorded side effects with less mortality, less ICU admission and less ward admission compared to traditional treatment in control group.

Recommendations

• The use of inhaled MgSO4 as a supplemental treatment in control of acute exacerbation of asthma in adults not responding to the traditional treatment (short acting β2-agonist and hydrocortisone) in the first hour.

• Further studies to Measure serum magnesium level pre and post treatment to clarify the relation between hypomagnesaemia to both severity of asthma and response to treatment.

• Further studies to compare between the effects of intravenous and inhalational MgSO4 in bronchial asthma.

Competing interests

The authors declare that they have no competing interest.

Financial Disclosure

The financial support for this study was provided by the investigators themselves.

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