



Role of Inhaled Isotonic Mgso₄ in Management of Acute Asthma attacks in children

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ABSTRACT

Background: Recent research has demonstrated that both Intravenous (IV) as well as inhaled magnesium sulphate (MgSO₄) could have a crucial role among severe asthmatic patients. The purpose of this work was to investigate the use of isotonic magnesium sulphate/salbutamol as compared to isotonic saline/salbutamol in the initial treatment of acute asthma exacerbation in children.

Methods: We carried out this randomized controlled clinical trial on 86 asthmatic children who were categorized into two groups: Group (A): included 43 children who were managed by intermittent inhaled normal saline (2ml)+ salbutamol alone (received 2.5 mg/dose = 0.5ml) starting at 20 minutes intervals for 3 doses, followed by 0.15 to 0.3 mg/kg/dose every 1 to 4 hours, with a maximum dose of 10 mg/dose, Group (B): included 43 children who were managed by inhaled salbutamol added with Nebulized isotonic magnesium sulphate (150mg) in 3 doses in 1st hour of treatment, Pediatric asthma severity score (PASS) was assessed before treatment and 20, 40, and 60 minutes, 2 hours after treatment with assessment of discharge data.

Results: Statistically significant difference was revealed between both groups as regard triggers of asthma attack ($p=0.014$), the most common triggering factor for asthma attack is viral upper respiratory tract infection, there was a significant decrease in PASS score in magnesium sulphate salbutamol group (decreased 26.19 %) compared to the normal saline salbutamol group (decreased 15.91%) with p value of 0.000. The number of discharged patients in magnesium sulphate salbutamol group was higher than normal saline salbutamol group (58.1% vs 51.2%).

Conclusions: nebulized isotonic magnesium sulphate is a safe drug, the use of nebulized isotonic magnesium sulphate in combination with salbutamol in acute asthma exacerbation shows superiority in efficacy to standard treatment normal saline salbutamol but without detected major difference in the rate of hospitalization.

Keywords: Inhaled Isotonic Mgso₄, Acute attacks, Asthma.

INTRODUCTION

Developed and emerging nations alike rank asthma as the leading chronic lung illness. According to large-scale, multicenter research, asthma affects as many as one in ten adults and one in three children globally, making it the most common chronic childhood condition. Asthma places a heavy financial and emotional strain on individuals and society as a whole because of the

difficulties in managing the disease and the consequences that can arise from it [1].

In asthma, breathing becomes difficult because to the chronic inflammation of the airways, which is a hallmark of this diverse lung disease. When someone has asthma, their airways become inflamed and hypersensitive, which temporarily narrows the airways that supply oxygen to their lungs. Symptoms of asthma, which can change in

severity and duration over time, include wheezing, coughing, difficulty breathing, and chest tightness. In extreme cases, asthma can cause a person to become less active and unable to speak [2].

When asthma symptoms and lung function worsen over an extended period of time, this is called an exacerbation. It is crucial to promptly assess and closely monitor patients experiencing severe exacerbations due to the life-threatening nature of these conditions [3].

There are three distinct categories of acute asthma exacerbations: mild, moderate, and severe, as well as respiratory failure [4].

Atopic and non-atopic asthma are distinguished based on phenotype. The term "atopy" refers to an individual's propensity to respond to common allergens by producing IgE antibodies. Environmental allergens, viral respiratory tract infections, exercise, hyperventilation, GERD, chronic sinusitis or rhinitis, sulfite sensitivity, obesity, environmental pollutants, cigarette smoke, certain irritants like household sprays and paint fumes, a variety of high- and low-molecular-weight compounds (insects, plants), occupational asthma, emotional factors or stress, perinatal factors (such as prematurity and increased maternal age), maternal smoking, and prenatal exposure to tobacco smoke are all potential triggers [5].

The goals of treatment include resolving the underlying inflammatory pathophysiology, preventing recurrence, and quickly relieving airflow restriction and hypoxemia. The initial line of defense against an asthma attack in the ER is a short-acting beta2-agonist (SABA) that is oxygenated. When first therapies fail, patients may be given ipratropium bromide, systemic corticosteroids (oral or intravenous), aminophylline or theophylline, intravenous magnesium, or high dosage inhaled corticosteroids [3].

There has been conflicting data to support the use of magnesium sulphate (MgSO₄) in adults and children with asthma since its original description in 1936 for acute asthma. The effectiveness of intravenous magnesium sulfate (IV MgSO₄) has been established, but the role of inhaled MgSO₄ is less well understood; hence, we shall investigate this matter further. Recent systematic reviews have indicated that both forms of magnesium sulfate may play a role in individuals

experiencing a more severe acute asthma exacerbation [3].

The purpose of this work was to investigate the use of isotonic magnesium sulphate in the initial treatment of acute asthma exacerbation in children, as compared with isotonic saline, in nebulized salbutamol.

METHODS

This randomized controlled clinical trial was conducted between September 2023 and February 2023 in emergency room of Zagazig pediatric university Hospital, Zaytoun specialized hospital, and Al-Galaa Military child hospital on 86 Known asthmatic children who attend the Emergency Department with acute exacerbations (mild, Moderate and severe attacks).

The sample calculated using open epi as prevalence of accessory muscle use among group using saline – salbutamol alone was 70.1 versus 40.1 among other group using magnesium sulphate plus salbutamol, found to be 43 patients in each group, total 86 power of study 80 % with CI 95%.

This study followed the guidelines [the World Medical Association's Code of Ethics (Declaration of Helsinki) for human studies]. All participants' parents provided informed and written consent. The Institutional Review Board has approved this research (IRB#5361/22-4-2019).

We included males and females who were known asthmatic at age group (5 – 15) presented to E.R. with mild, Moderate and severe attacks.

We excluded all cases who had any associated chronic diseases like bronchiectasis, cystic fibrosis, or cardiac diseases. or other chronic diseases, and those who were above 15 years or below 5 years.

All the included children were subjected to entire history taking including personal, complaint, present, past, family history, severity of asthma exacerbations and drugs taken. Clinical examination and laboratory testing were performed.

Patients were diagnosed with asthma based on clinical presentation, according to Global Initiative for Asthma (GINA 2020) [6].

Scoring of patients asthma was assessed by pediatric asthma severity score (PASS). PASS ≤ 7; mild respiratory compromise, PASS 8-11; moderate respiratory compromise, and PASS ≥ 12; severe respiratory compromise [7].

Patients were managed using the following:

Salbutamol solution:

Intermittent Nebulization: dosing intervals of 20 minutes, with a minimum dose of 2.5 mg/dose (0.5 ml), and then intervals of 1 to 4 hours, with a dose ranging from 0.15 to 0.3 mg/kg/dose (not to exceed 10 mg/dose) [8].

MgSo4 7.5 %:

For children aged 2 and up, administer three doses of 150 mg of nebulized isotonic magnesium sulfate within the first hour of treatment. Isotonic Mgso4 was 7.5 % so, 7.5 gm was dissolved in 100 ml = 75 ml Mgso4 (10 %) / 100 ml. distilled water = 7.5 Mgso4 (10 %) / 10ml. That means Mgso4 7.5 % was prepared as follow: 7.5 ml Mgso4 10 % + 2.5 ml. distilled water. So, the required dose 150mg equals to 2ml of prepared solution [9].

Patient with acute attack was subdivided into 2 groups (43 cases in each group): the 1st group (A) was managed by isotonic saline with salbutamol while the 2nd group (B) was managed by salbutamol plus isotonic Magnesium sulphate. The selected patients were subjected to the following steps: Controlled O2 if needed (to maintain O2 saturation 94-98 %), Oral prednisolone 1-2 mg/kg/ds. (max. 40mg) or IV if severe dyspnea (for moderate and severe attacks). SABA nebulizer ± isotonic magnesium sulphate. Repeat every 20 min for 1 hour, then re-assessment after 1 & 2 hours. The 1st hour was treatment hour while the second hour was observational hour. If continuing deterioration treat as severe. If improving consider for discharge plan.

Discharging criteria: Discharge was decided if SpO2>94% in room air, patient was stable after 2 hours and symptoms improved with no need for inhaled SABA. Adequate respiratory and Heart rate as normal for age, (for patients ≤5 yr: <34 breaths/min <140 beats/min, 6–12 yr: <26 breaths/min <125 beats/min, ≥12 yr: <23

breaths/min <110 beats/min. Patients were monitored for any side effects [10].

STATISTICAL ANALYSIS

For data tabulation and analysis, we relied on SPSS version 24 (SPSS Inc, Chicago, IL, USA). To show the categorical data, percentages and numbers were utilized. I used a chi-square test (χ^2) to examine the categorical variables. Presentation of quantitative data made use of standard deviation (SD), median, and range. Students used the "t" test to compare normally distributed variables between the two sets of data. To determine if there was a statistically significant difference in a non-parametric variable between the two groups of participants, the Mann-Whitney U test was utilized.

RESULTS

There was a significant decrease in PASS score in magnesium sulphate salbutamol group (decreased 26.19 %) compared to the normal saline salbutamol group (decreased 15.91%) with p value of 0.000 (Table 4, Figure 1).

The PASS score and severity of respiratory compromise did not differ significantly between both groups (Table 3).

No side effects were found after the use of inhaled Mgso4.

Non statistically significant differences were revealed between the both studied groups although the number of discharged patients in magnesium sulphate salbutamol group was higher than normal saline salbutamol group (58.1% vs 51.2%) (Table 5).

No statistically significant differences were revealed between both groups regarding age, sex risk factors or level of asthma. There was male predominance among studied asthmatic groups (Table 1).

Statistically significant difference was revealed between both groups as regard triggers of asthma attack (p=0.014). The most common triggering factor for asthma attack is viral URTI (Table 2).

Table (1): Demographic data, risk factors and level of asthma of the studied asthmatic children

Demographic data	Group A Salbutamol Plus Normal Saline (N=43)		Group B Magnesium Sulphate Solution with Salbutamol (N=43)		P- value
	No.	%	No.	%	
Age (years)					
Mean ± SD	7.32 ± 2.4		7.59 ± 2.8		0.632
Median (Range)	6.4 (5-13)		6 (5-14)		(NS)

Demographic data	Group A Salbutamol Plus Normal Saline (N=43)		Group B Magnesium Sulphate Solution with Salbutamol (N=43)		P- value
	No.	%	No.	%	
Sex					
Male	24	55.8	22	51.2	#0.665 (NS)
Female	19	44.2	21	48.8	
Smoking					
No	27	62.8	17	39.5	0.030* (S)
Yes	16	37.2	26	60.5	
Atopy					
Non-Atopic	21	48.9	14	32.6	0.124 (NS)
Atopic	22	51.2	29	67.4	
Family history of Bronchial Asthma					
Negative	14	32.6	11	25.6	0.476 (NS)
Positive	29	67.4	32	74.4	
Level of asthma control					
Uncontrolled	9	20.9	14	32.6	0.125 (NS)
Partial control	3	7.0	0	0.0	
Controlled	31	72.1	29	67.4	

Mann Whitney U test.

Chi-square test.

NS: Not significant.

Table (2): Triggers of asthma exacerbation among the studied children

Triggers	Group A Salbutamol Plus Normal Saline (N=43)		Group B Magnesium Sulphate Solution with Salbutamol (N=43)		P- value
	No.	%	No.	%	
URTI	14	32.6	16	37.2	0.014*
Cold weather	8	18.6	4	9.3	0.213
Passive Smoking	7	16.3	3	6.9	0.178
Oil fumes\ paints	4	9.3	0	0.0	0.040*
Seasonal variation	3	6.9	7	16.3	0.178
Perfume	2	4.7	3	6.9	0.644
Barbecue party	2	4.7	2	4.7	1.000
Exercise	2	4.7	0	0.0	0.152
Pollen	1	2.3	0	0.0	0.316
Food	0	0.0	2	4.7	0.152
Pesticide	0	0.0	2	4.7	0.152
Pollution\ Rubbish burn at street	0	0.0	4	9.3	0.040*

Chi-square test.

*p-value is significant.

URTI; upper respiratory tract infection,

Table (3): Pediatric asthma severity score (PASS)* among the studied asthmatic children

PASS	Group A Salbutamol Plus Normal Saline (N=43)		Group B Magnesium Sulphate Solution with Salbutamol (N=43)		P- value
	No.	%	No.	%	
PASS score					
Mean ± SD	8.86 ± 2.3		9.09 ± 2.2		0.634
Median (Range)	9 (5-13)		9 (5-14)		(NS)
Severity					
Mild	11	25.6	8	18.6	#0.640 (NS)
Moderate	28	65.1	29	67.4	
Severe	4	9.3	6	14.0	

Student t test

Chi-square test.

NS: Not significant.

Table (4): Follow up of Pediatric asthma severity score (PASS) among the studied asthmatic children

Item	PASS score			% of change in PASS	P-value
	After 20 min	After 40 min	After 60 min		
Group A Salbutamol Plus Normal Saline					
Mean ± SD	8.72 ± 2.3	8 ± 2.1	7.4 ± 1.7	↓15.91 %	0.000* (HS)
Median (Range)	9(5-13)	8(5-12)	7(5-12)		
Group B Magnesium Sulphate Solution with Salbutamol					
Mean ± SD	8.35 ± 2.4	6.9 ± 1.8	6.65 ± 1.8	↓↓26.19 %	0.000* (HS)
Median (Range)	8(5-14)	7(5-12)	6(5-11)		

Freidman test

P < 0.05 is significant.

HS: Highly Significant.

Table (5): Patient hospital allocation after initial Emergency Room treatment

	Group A Salbutamol Plus Normal Saline (N=43)		Group B Magnesium Sulphate Solution with Salbutamol (N=43)		P- value
	No.	%	No.	%	
Word Admission	7	16.3	2	4.7	0.078
Intermediate Care admission	9	20.9	8	18.6	0.786
Discharged	22	51.2	25	58.1	0.515
PICU admission	2	4.7	6	14.0	0.137
DAMA	3	7	2	4.7	0.413

Chi-square test.

*p-value is significant.

DAMA: discharge against medical advice.

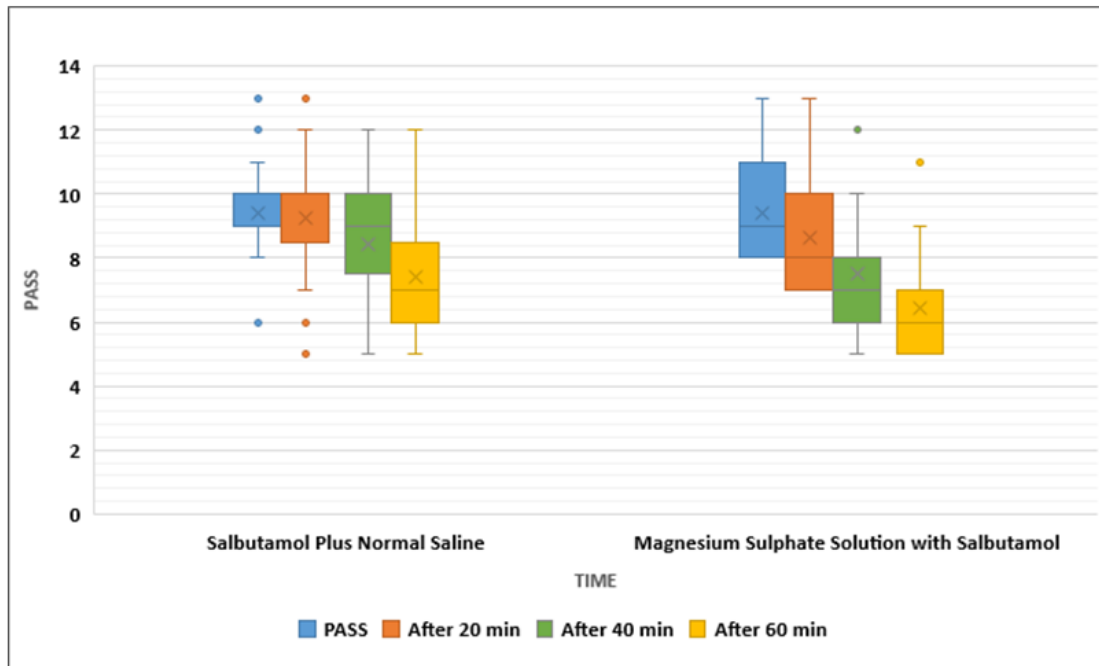


Figure (1): Box plot showing follow up of Pediatric Asthma Severity Score (PASS) among the studied asthmatic children. It shows that the magnesium sulphate effect starts early after 20 minutes and progressively improving till 60 minutes.

DISCUSSION

Factors both within and outside of the home might trigger asthma attacks. How the immune system forms and reacts to certain environmental stimuli is determined by a mix of these early life genetic and environmental variables. The lungs are the final destination of pathogens that originate in the respiratory tract, such as allergens that are breathed in or pollutants that harm the lower airways. A chronic illness developed as a result of abnormal immunological and repair reactions to damage to the airways [11].

The PASS score, a clinical measure based on several factors (respiratory rate, oxygen demand, work of breathing, retractions, and auscultation), was used to evaluate the severity of an asthma episode. The severity of an asthma exacerbation as measured during the examination is indicated by this score [7].

In this study, we aimed to compare the efficacy of traditional saline salbutamol with that of nebulized magnesium sulphate in treating acute asthma attacks. Because hyperosmolar magnesium sulfate can make airways more sensitive to histamine or bronchoconstriction [12], we opted for an isotonic solution instead [13]. By either upregulating B receptors or enhancing the affinity of B receptors to salbutamol, magnesium may enhance the bronchodilator response to salbutamol in acute

asthma. Magnesium may also have the following effects, some of which may widen the airways: Reduced calcium uptake and release by bronchial smooth muscle is one mechanism by which magnesium alleviates bronchoconstriction [14].

While males made up a larger proportion of the asthmatic population, there was no statistically significant difference in age or sex between the two groups. The mean age of the studied asthmatic children among group A is 7.32 ± 2.4 years old, with a range from 5 to 13 years old, and age of children among group B is $(7.59 \pm 2.8$ yrs. old), more than half of both groups were male.

Turker et al. [3] researched the efficacy of administering magnesium sulfate via nebulizer as an additional treatment for mild asthma attacks in children. Despite the male majority, the researchers found no significant differences in the demographic data across the groups analyzed in their study of 100 youngsters.

On the other hand, Sarhan et al. [15] reported in their study that there was a significant difference between three groups (mgso4, saline-salbutamol and mgso4-salbutamol) in age but with significant female predominance.

One risk factor for asthma in children is being male. Asthma affects almost twice as many males as girls before the age of fourteen. While the gender gap in asthma prevalence narrows somewhat as children

get older, women still have a higher incidence of the condition in adulthood. While the exact causes of this gender difference remain unknown, one possible explanation could be that males have smaller lungs and airways as infants, but larger lungs and airways in adult females [6].

As regard to the risk factors of asthma in both groups there is no statistical difference except for smoking exposure which was higher in Magnesium sulphate salbutamol group.

Similarly, Mangat et al. [16] researched the effects of nebulized magnesium sulfate vs nebulized salbutamol on adults with acute bronchial asthma, they found that the magnesium sulphate group had greater rates of smoking exposure and atopy.

There was no statistically significant difference between both groups as regard level of asthma control, where 67.4% of magnesium sulphate salbutamol group and 72.2% of normal saline salbutamol group were controlled.

According to the GINA. [6] When a patient with asthma does not have any significant risk factors, such as a history of intubation, a low forced expiratory volume in one second (FEV1), or an exacerbation within the past year, and when they report symptoms and use reliever medication less than twice weekly, without nocturnal symptoms and without activity limitation, we say that their asthma is controlled. To be considered partially controlled, symptoms must be present at least twice a week, the patient must also have nighttime symptoms and activity limitation, and if all three characteristics are present, the condition is considered uncontrolled.

The present study shows that there is statistically significant difference between both groups as regard to triggers of asthma attack. The most common triggering factor for asthma attack is viral URTI.

The leading cause of childhood asthma, by far, is viral infections of the respiratory tract. They can worsen atopic asthma and are the sole cause of coughing and wheezing for many kids. Respiratory syncytial virus causes severe respiratory symptoms in babies and human rhinoviruses cause most asthma exacerbations [17].

The second most common triggering factor for asthma exacerbation in our study is cold weather exposure. Younger children, in particular, are more susceptible to asthma attacks brought on by changes in the weather, particularly cold and high relative humidity [18]. Indirectly or directly, air temperature may affect the frequency with which asthma attacks occur. Airways may become hyper-responsive when exposed to cold air. It might indirectly cause asthma

by making people more susceptible to air pollution or viral illnesses [19].

The third common triggering factors are smoking and seasonal variations. Using Nicotine One can develop steroid resistance from smoking, whether it's actively smoking or being around someone who smokes [20]. In addition to nitric oxide and superoxide, each puff of environmental tobacco smoke comprises over 1014 oxidative molecules, a combination of gases and particles released by the burning cigarette. Tobacco smoke causes inflammation by damaging the epithelial cells lining the airways of the bronchial tubes. It boosts the amount of neutrophils in the lungs and draws them to the area as well [21].

Before the initiation of treatment there was no statistical difference between both groups as regard to PASS score and respiratory compromise. The mean PASS score of magnesium sulphate salbutamol group decreased from 8.3 ± 2.4 at 20 minute to 6.65 ± 1.8 at 60 minute. The percentage of decrease in PASS score was 26.19% in magnesium sulphate salbutamol group compared to 15.9% in normal saline salbutamol group, this difference was highly significant. More over, the magnesium sulphate effects start early after 20 minute and progressively improves till 60 minute as shown in box plot (figure 10).

Magnesium relaxes the smooth muscles of the airways by lowering their excitability and blocking the release of acetylcholine from cholinergic nerve terminals [12]. Magnesium may promote prostacyclin synthesis and nitrous oxide production while suppressing histamine release from mast cells. Multiple studies have assessed magnesium sulphate's function in the management of acute asthma attacks.

Magnesium was injected intravenously in the majority of the trials. The use of nebulized magnesium sulfate in the treatment of acute asthma has only been investigated in a small number of trials.

When it comes to treating acute bronchial asthma, a Cochrane study found that intravenous magnesium sulphate worked well [22].

When administered intravenously alongside other medicines, magnesium sulphate improved the effectiveness of treatment for acute asthma in children, according to a recent meta-analysis. Research on patients with acute asthma using nebulized magnesium sulfate and salbutamol as separate treatments found that magnesium had a bronchodilator response that was comparable to or

less intense and shorter in duration than salbutamol. Research comparing salbutamol alone to salbutamol plus nebulized magnesium sulphate is limited [23]. The current gold standard for treating asthma exacerbation is inhaled B2 agonists [6], thus we planned our trial to examine the efficacy of adding breathed isotonic magnesium sulfate to these treatments.

Hughes et al. [24], revealed that an enhanced bronchodilator response was observed in severe asthma patients when isotonic magnesium sulfate was used as an adjuvant to salbutamol nebulizer solutions, as three doses of salbutamol alone did not produce as much bronchodilation as three doses of magnesium sulfate plus salbutamol. When compared to the same dose of salbutamol given with an isotonic saline nebulizer solution, the increase in FEV1 was about doubled when the magnesium adjuvant was added to the salbutamol nebulizer solution.

For adults with acute bronchial asthma, Abdelnabi et al. [25] compared nebulized salbutamol with nebulized magnesium sulphate. The results showed that nebulized MgSO₄ significantly dilated the airways, improved the clinical condition, increased PEF and SPO₂, and decreased HR and RR.

Though it was much less effective than salbutamol, nebulized magnesium sulfate (MgSO₄) had a clinically meaningful bronchodilator effect in patients with severe bronchial asthma [26].

Turker et al. [3] found that Adding nebulized magnesium sulfate to salbutamol in conventional treatment has little effect beyond what is already there.

So, when it comes to the function of extra magnesium sulfate nebulization in severe asthma, the findings of these few trials, which involved little patient populations, are contradictory.

Powell et al. [27] published the most comprehensive study on nebulized magnesium sulfate in children with asthma. The trial included 508 children (aged 2-16) from 30 hospitals in the UK who had severe acute asthma and had not responded to standard inhaled treatment. The trial was randomized, placebo-controlled, multi-center, and parallel. The study found that when administered with normal treatment, nebulized MgSO₄ had a statistically significant advantage over placebo in children with acute severe asthma; however, there was no clinically significant improvement in their symptoms.

One study did not find any significant effects on respiratory function when children were given

nebulized MgSO₄. Possible explanations for the observed dose-response relationship between the effects of nebulized MgSO₄ in adults and children include variations in smooth muscle responsiveness to the compound or differences in dosage.

From one study to the next, the amount of magnesium nebulized varied greatly. Methods Employed to Evaluate Nebulized Magnesium Sulfate: A single dose of 2.5 mL of isotonic MgSO₄ (6.3% solution) and 2.5 mL of saline solution was utilized by Mahajan et al. [28]. For the case of Powell et al. The following mixture was used: 2.5 milliliters of isotonic saline and 2.5 milliliters of 250 mmol/L (151 mg) of MgSO₄ [27]. The solution employed by Mohammadzadeh et al. [29] consisted of 3 mL of isotonic MgSO₄ and 3 mL of saline. An isotonic solution of magnesium sulfate (286 mOsm/l, 7.5% solution, 150 mg) and 2.5 mg of albuterol (0.5 mL) were utilized in the study by Sun et al. [30].

A 2 mL dosage (7.5% solution, 150 mg) plus 2 mL of normal saline was utilized in this study. Intravenous magnesium sulfate (MgSO₄) is associated with the following side effects: nausea, vomiting, flushing, thirst, low blood pressure, lethargy, disorientation, weak muscles, depression of the respiratory system, and cardiac arrhythmias [31].

According to Hicks et al. [32] magnesium concentration was not affected by the administration of nebulized MgSO₄ so, patients would not need routine monitoring of magnesium concentrations.

In our study, no adverse effects were reported with the use of isotonic magnesium sulphate inhalation in combination with salbutamol.

Also, the number of discharged patients in magnesium sulphate salbutamol group was higher than normal saline salbutamol group yet the difference was statistically non-significant. The discharging criteria used were SpO₂ >94 % in room air, patient is Stable after 2 hours and symptoms improved with no need for inhaled SABA and RR, HR back to normal range according to age.

The findings agree with those of earlier research as well. No difference has been detected between patients receiving and not getting nebulized Mgso₄ in reference to hospitalization, according to a recent study published by Turker et al. [3].

In a similar vein, the investigation by Alansari et al. [33] into the efficacy of nebulized magnesium in conjunction with combined nebulized bronchodilator and systemic steroid therapy for

moderate to severe asthma in children did not result in demonstrably reduced time to discharge.

Also, according to Powell et al. [27], only 8% of magnesium sulphate group and 4% of placebo group met the discharge criteria.

There are some limitations of this study. Firstly, there are few studies on the use of isotonic magnesium sulphate nebulization in children. Secondly, the number of studied children is small. Thirdly, we randomized the patients for the study from ER of two hospitals one of them with lower middle class, patient may receive oral medications without medical advice and did not report that on presentation to hospital. Fourthly, assessment of the improvement was clinically and there are several factors which influence the parameters of the clinical score such as salbutamol which is B2 agonist and may cause tachycardia and falsely change the score. Finally, we can not comment on the duration of action of the combination treatment.

CONCLUSIONS

nebulized isotonic magnesium sulphate is a safe drug, the use of nebulized isotonic magnesium sulphate in combination with salbutamol in acute asthma exacerbation shows superiority to standard treatment normal saline salbutamol but without detected major difference in the rate of hospitalization.

REFERENCES

1. Mummy D, Dunican E, Lampkins T, Zha W, Evans M, Schiebler M, et al. Ventilation defects in asthma on hyperpolarized gas MRI are associated with airway mucus plugs on CT. In D28. RESPIRATORY DISEASE DIAGNOSIS: PULMONARY FUNCTION TESTING AND IMAGING (pp. A6376-A6376). ATS.2018.
2. McGeachie M J, Croteau-Chonka D.C, Weiss S.T. Genomic and Precision Medicine: Primary Care: Third Edition. Elsevier; Amsterdam, the Netherlands: 2017. Asthma; pp. 231–44.
3. Turker S, Dogru M, Yildiz F, Yilmaz SB. The effect of nebulised magnesium sulphate in the management of childhood moderate asthma exacerbations as adjuvant treatment. *Allergol Immunopathol (Madr)*. 2017; 45(2):115-20.
4. Koga T, Tokuyama K, Itano A, Morita E, Ueda Y, Katsunuma T. Usefulness of modified Pulmonary Index Score (mPIS) as a quantitative tool for the evaluation of severe acute exacerbation in asthmatic children. *Allergol Int*. 2015;64(2):139-44.
5. D. T. Qosaj, S. Hasani, and H. Ymeri, "Risk factors of asthma exacerbation in children." *Arch. Dis. Child.*, 2012.
6. Ish P, Malhotra N, Gupta N. GINA 2020: what's new and why?. *J Asthma*. 2021;58(10):1273-7.
7. Maue DK, Krupp N, Rowan CM. Pediatric asthma severity score is associated with critical care interventions. *World J Clin Pediatr*. 2017;6(1):34-9.
8. Kulalert P, Phinyo P, Patumanond J, Smathakanee C, Chuenjit W, Nanthapisal S. Continuous versus intermittent short-acting β_2 -agonists nebulization as first-line therapy in hospitalized children with severe asthma exacerbation: a propensity score matching analysis. *Asthma Res Pract*. 2020; 6:6.
9. Petrou S, Boland A, Khan K, Powell C, Kolamunnage-Dona R, Lowe J, et al. Economic evaluation of nebulized magnesium sulphate in acute severe asthma in children. *Int J Technol Assess Health Care*. 2014;30(4):354-60.
10. Hasegawa K, Craig SS, Teach SJ, Camargo CA Jr. Management of Asthma Exacerbations in the Emergency Department. *J Allergy Clin Immunol Pract*. 2021;9(7):2599-610.
11. Gautam Y, Afanador Y, Ghandikota S, Mersha TB. Comprehensive functional annotation of susceptibility variants associated with asthma [published correction appears in *Hum Genet*. 2020 May 4;:]. *Hum Genet*. 2020;139(8):1037-53.
12. Nannini LJ Jr, Pendino JC, Corna RA, Mannarino S, Quispe R. Magnesium sulfate as a vehicle for nebulized salbutamol in acute asthma. *Am J Med*. 2000; 108(3):193-7.
13. Hill J, Lewis S, Britton J. Studies of the effects of inhaled magnesium on airway reactivity to histamine and adenosine monophosphate in asthmatic subjects. *Clin Exp Allergy*. 1997; 27(5):546-51.
14. Middleton E Jr. Antiasthmatic drug therapy and calcium ions: review of pathogenesis and role of calcium. *J Pharm Sci*. 1980;69(2):243-251.
15. Sarhan HA, El-Garhy OH, Ali MA, Youssef NA. The efficacy of nebulized magnesium sulfate alone and in combination with salbutamol in acute asthma. *Drug Des Devel Ther*. 2016; 10:1927-33.
16. Mangat HS, D'Souza GA, Jacob MS. Nebulized magnesium sulphate versus nebulized salbutamol in acute bronchial asthma: a clinical trial. *Eur Respir J*. 1998; 12(2):341-4.
17. Kwon JM, Shim JW, Kim DS, Jung HL, Park MS, Shim JY. Prevalence of respiratory viral infection in children hospitalized for acute lower respiratory tract diseases, and association of rhinovirus and

- influenza virus with asthma exacerbations. *Korean J Pediatr.* 2014; 57(1):29-34.
18. Kadhim Yousif M, Al Muhyi AA. Impact of weather conditions on childhood admission for wheezy chest and bronchial asthma. *Med J Islam Repub Iran.* 2019; 33:89.
 19. Shoraka HR, Taheri Soodejani M, Abobakri O, Khanjani N. The Relation between Ambient Temperature and Asthma Exacerbation in Children: A Systematic Review. *J Lung Health Dis,* 2019, 3(1): 9-9
 20. Hurst SM, McGhie TK, Cooney JM, Jensen DJ, Gould EM, Llyall KA, et al. Blackcurrant proanthocyanidins augment IFN-gamma-induced suppression of IL-4 stimulated CCL26 secretion in alveolar epithelial cells. *Mol Nutr Food Res.* 2010; 54 Suppl 2:159-70.
 21. Abdeltawab A, El Askary A, Saad M. Environmental Tobacco Smoke Exposure and Relation to Asthma Exacerbations and Severity among Primary School Children. *Acta Adriatica.* 2018, 1. 20-6.
 22. Rowe BH, Bretzlaff JA, Bourdon C, Bota GW, Camargo CA Jr. Magnesium sulfate for treating exacerbations of acute asthma in the emergency department. *Cochrane Database Syst Rev.* 2000; 2000(2):CD001490.
 23. Shan Z, Rong Y, Yang W, Wang D, Yao P, Xie J, et al. Intravenous and nebulized magnesium sulfate for treating acute asthma in adults and children: a systematic review and meta-analysis. *Respir Med.* 2013;107(3):321-30.
 24. Hughes R, Goldkorn A, Masoli M, Weatherall M, Burgess C, Beasley R. Use of isotonic nebulised magnesium sulphate as an adjuvant to salbutamol in treatment of severe asthma in adults: randomised placebo-controlled trial. *Lancet.* 2003; 361(9375):2114-7.
 25. Abdelnabi E. A, Kamel M. M, Ali A. E. Nebulized magnesium sulphate versus nebulized salbutamol in acute bronchial asthma. *Egypt. J. Chest Dis. Tuberc,* 2012, 61(3): 29-34.
 26. Turker S, Dogru M, Yildiz F, Yilmaz SB. The effect of nebulised magnesium sulphate in the management of childhood moderate asthma exacerbations as adjuvant treatment. *Allergol Immunopathol (Madr).* 2017; 45(2):115-20.
 27. Powell C, Kolamunnage-Dona R, Lowe J, Boland A, Petrou S, Doull I, et al. Magnesium sulphate in acute severe asthma in children (MAGNETIC): a randomised, placebo-controlled trial [published correction appears in *Lancet Respir Med.* 2013;1(4):285]. *Lancet Respir Med.* 2013;1(4):301-8.
 28. Mahajan P, Haritos D, Rosenberg N, Thomas R. Comparison of nebulized magnesium sulfate plus albuterol to nebulized albuterol plus saline in children with acute exacerbations of mild to moderate asthma. *J Emerg Med.* 2004; 27(1):21-5.
 29. Mohammadzadeh I, Mohammadi M, Khodabakhsh E. The effect of nebulized salbutamol plus magnesium sulphate in comparison with nebulized salbutamol plus normal saline in acute asthmatic attack in children. *JBUMS,* 2014, 16(3): 7-12.
 30. Sun YX, Gong CH, Liu S, Yuan XP, Yin LJ, Yan L, et al. Effect of inhaled MgSO₄ on FEV₁ and PEF in children with asthma induced by acetylcholine: a randomized controlled clinical trial of 330 cases. *J Trop Pediatr.* 2014;60(2):141-7.
 31. Hicks M. A, Tyagi A. Magnesium sulphate. *Stat Pearls [Internet].* 2020.
 32. Hicks MA, Tyagi A. Magnesium Sulfate. In: *StatPearls. Treasure Island (FL): StatPearls; 1, 2023.*
 33. Alansari K, Ahmed W, Davidson BL, Alamri M, Zakaria I, Alrifaii M. Nebulized magnesium for moderate and severe pediatric asthma: A randomized trial. *Pediatric Pulmonol.* 2015; 50(12):1191-9.

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