Evaluation the role of nebulized magnesium sulfate in the treatment of severe exacerbation of asthma in children & adolescence.

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Abstract

Asthma may arise as a result of interaction between multiple genetic and environment factors this is the case with most of called allergic asthma that occurs in patients who exhibit acute immediate hypersensitivity responses to define environmental allergen. Treatment of asthma is largely palliative and includes patient's education, avoid or control asthma triggers, immunotherapy (hyposensitization) and drug therapy. The present study aim to evaluate the role of nebulized magnesium sulfate in the treatment of severe exacerbation of asthma. A cross sectional comparative study carried out on all patients with severe exacerbation of asthma admitted to the emergency unit at Al- Sherqat general hospital at a period between March & August 2007. 80 patients with severe asthma exacerbation 44 male and 36 female their age between 5 to 19 years. All 80 patients to two major groups. Group I. 40 patients received nebulized salbutamol alone 0.15mglkg mg and after 15 min full clinical assessment of improvement done including the PEFR, respiratory rate and heart rate. Group II. 40 patients received nebulized sulbutamol 0.15mg/kg mg with nebulized magnesium sulfate o.15ml/kg. Also full clinical assessment of improvement done after 15min including the PEFR, respiratory rate and heart rate. there was more significant increase in the means of PEFR (liter/min) for all subgroups of mild intermittent, mild persistent, moderate persistent and severe persistent of the patients age (5-13) years on 15 min after receiving nebulized salbutamol with magnesium sulfate than those receiving nebulized salbutamol alone. On receiving salbutamol alone the mild intermittent, mild persistent, moderate persistent and severe persistent subgroups improved by 51.8%, 54.9%, 49.7% and 53.5% respectively. The protective effects of inhaled magnesium sulfate on exercise induced asthma in children and he found that the combination gave better protective compared to salbutamol alone. Magnesium sulfate aerosol alone did not induce bronchial dilatation it diminished both hypersensitivity and hyper reactivity of the bronchial tree to acetylcholine induced increment of histamine in the exhaled air condensate. This data allow bronchial smooth muscles and mast cell to be regarded as target for magnesium sulfate.

Introduction

Asthma is defined as a chronic inflammatory disorder of pulmonary airway passages. It characterized by reversible airflow obstruction causing cough, wheeze, chest tightness, and shortness of breath. The airflow obstruction is wide spread and variable which is often relieved either spontaneously or with treatment (1).

Asthma may arise as a result of interaction between multiple genetic and environment factors this is the case with most of called allergic asthma that occur in patients who exhibit acute immediate hypersensitivity responses to define environmental allergen, as a result of this IgE is produced which sensitize mast cells and upon encounter with specific allergy they secrets abroad bio-active mediators that lead to reversible airway obstruction (2, 3).

Treatment of asthma is largely palliative and include patients education, avoid or control asthma triggers, immunotherapy (hyposensitization) and drug therapy which is divided to quick relief medications that include short acting inhaled, β agonist, inhaled anticholinergics, short course systemic glucocorticoides and the long term control medications which include non steroidal anti inflammatory agents like

cromolyn and nedocromyl, inhaled glucocorticoides (4). Magnesium is a good alternative to suxamethonium for priming of atracurium during tracheal intubation technique since magnesium inhibit the release of acetyl choline from the motor nerve terminals. Also, magnesium tends to reduce the bronchial constriction in asthma by relaxing the muscle around the bronchial tubes (5, 6).

Serum magnesium level in asthmatic adults was significantly lower compared with general population (7), with other case control studies conducted on asthmatic adults failed to demonstrate a significant difference in serum magnesium between patients with asthma and controls (8,9).

Bronchodilating effect of magnesium sulfate was studied in ten asthmatic patients with mild attacks and concluded that intravenous infusion of MgS_{O4} produces a rapid and marked bronchial dilatation in both mild and severe asthma and may be a unique bronchial dilating agent. Also, it was found that Mg^{++} ions has been reported to have an inhibitory action on smooth muscle contraction, on histamine release from mast cells, and on acetylcholine release from cholinergic nerve terminals and to have sedative action (10).

Even those patients labeled as poor responders to conventional β- agonist therapy achieved better pulmonary function with albuterol or meta properenol with magnesium sulfate (11). These effects result in the relaxation of smooth muscle, the inhibition of cholinergic neuromuscular transmission and the stabilization of mast cells (12).

The protective effects of inhaled magnesium sulfate on exercise induced asthma in children gave better protective when compared to salbutamol alone (13).

Magnesium sulfate aerosol alone did not induce bronchial dilatation; it diminished both hypersensitivity and hyperreactivity of the bronchial tree to acetylcholine induced increment of histamine in the exhaled air condensate. These findings allow bronchial smooth muscles and mast cell to be regarded as target for magnesium sulfate (14).

The present study aim to evaluate the role of nebulized magnesium sulfate in the treatment of severe exacerbation of asthma.

Patients and Methods

A cross sectional comparative study carried out on all patients with severe exacerbation of asthma admitted to the emergency unit at Al-Sherqat general hospital at a period between March & August 2007. 80 patients with severe exacerbation asthma, a 44 male and 36 female their age between 5 to 19 years.

Careful and thorough history was taken from all patients regarding the age, sex, residence, onset of disease, nocturnal symptoms, activities, sleep interruption, school attendance, exercise number of emergency visits. After history taking, all patients under gone complete physical examination include vital signs measurements, length, chest examination to sure that patients had severe exacerbation of attack of asthma regarding the level of peak expiratory flow rate compared to the predicted average normal PEFR (liter/min). The asthma pulmonary score table (2-1)

Then, all the patients with severe exacerbation of asthma were classified according to the type of severity to mild intermittent, mild persistent, moderate persistent and severe persistent according to the level of PEFR as in table (2-2). The classification of asthma severity according to the clinical assessment before treatment.

PEFR was taken for all patients before & after treatment. The proper detection of PEFR was taken by asking the patient to take breath normally in relaxed pattern and ask to take inspiration deeply and then take off expiration as force as possible to read the PEFR (liter/min) using the peak flow meter.

Then, all 80 patients were divided into two major groups. Group I. 40 patients received nebulized salbutamol alone 0.15mglkg and after 15 min full clinical assessment of improvement done including the PEFR, respiratory rate and heart rate. Group II. 40 patients received nebulized sulbutamol 0.15mg/kg with nebulized magnesium sulfate 0.15ml/kg. Also, full clinical assessment of improvement done after 15min including the PEFR, respiratory rate and heart rate.

Data were analyzed by the ANOVA analysis using the general linear model of statistical analysis (SAS institute).

Significant differences were evaluated using Duncan's multiple rang test. All statements of significance are based on the 0.05 level of probability.

Results

Frequency distribution of the patients included in the study in table (3-1). show that most of the cases of severe exacerbation of asthma in this study are mild intermittent 30 %, while mild persistent are 26.25%, moderate persistent 23.75% and severe persistent 20%.

From the table (3-2), there was more significant increase in the means of PEFR (liter/min) for all subgroups of mild intermittent, mild persistent, moderate persistent and severe persistent of the patients age (5-13) years on 15 min after receiving nebulized salbutamol with magnesium sulfate than those receiving nebulized salbutamol alone.

On receiving salbutamol alone the mild intermittent, mild persistent, moderate persistent and severe persistent subgroups improved by 51.8%, 54.9%, 49.7% and 53.5% respectively.

While those receiving nebulized salbutamol with magnesium sulfate they improved by 67.6%, 63.6%, 63.6% and 63% respectively. The table (3-3) show more significant increase in the means of PEFR (liter/min) for all subgroups of mild intermittent, mild persistent, moderate persistent and severe persistent of the patients age (14-19) years on 15 min after receiving nebulized salbutamol with magnesium sulfate than those receiving nebulized salbutamol alone.

On receiving salbutamol alone the mild intermittent, mild persistent, moderate persistent and severe persistent subgroups improved by 49.9%, 50%, 49.9% and 52% respectively. While those receiving nebulized salbutamol with magnesium sulfate they improved by 59.5%, 60.8%, 59.4% and 62% respectively.

Table 3-4 show more significant improvement in the means of respiratory rate (cycle/min) for all subgroups of mild intermittent, mild persistent, moderate persistent and severe persistent of the patients age (5-13) years on 15 min after receiving nebulized salbutamol with magnesium sulfate than those receiving nebulized salbutamol alone.

On receiving nebulized salbutamol alone the mild intermittent, mild persistent, moderate persistent and severe persistent subgroups improved by 20.5 %, 18 %, 21 % and 17.6 % respectively. While, those receiving nebulized salbutamol with magnesium sulfate they improved by 30.6 %, 32 %, 32 % and 35 % respectively.

From the table (3-5), it was found that more significant improvement in the means of respiratory rate (cycle/min) for all subgroups of mild intermittent, mild persistent, moderate persistent and severe persistent of the patients age (14-19) years on 15 min after receiving nebulized salbutamol with magnesium sulfate than those receiving nebulized salbutamol alone.

On receiving nebulized salbutamol alone the mild intermittent, mild persistent, moderate persistent and severe persistent subgroups improved by 18.8 %, 23 %, 18.5 % and 18.7 % respectively. While, those receiving nebulized salbutamol with magnesium sulfate they improved by 29.7 %, 32 % , 29 % and 31.6 % respectively.

From the table (3-6) show that there are no significant difference in the percent of increasing in the means of heart rate (beat/min) for all subgroups of mild intermittent, mild persistent, moderate persistent and severe persistent of the patients age (5-13) years on 15 min after receiving both types of treatments.

On receiving nebulized salbutamol alone the mild intermittent, mild persistent, moderate persistent and severe persistent subgroups improved by 17.9 %, 19.8%, 18.8 % and 21 % respectively. Also those receiving nebulized salbutamol with magnesium sulfate they improved by 18 %, 16.8 %, 15.5 % and 18 % respectively.

From the table (3-7) it was found that there are no significant difference in the percent of increasing in the means of heart rate (beat /min) for all subgroups of mild intermittent, mild persistent, moderate persistent and severe persistent of the patients age (14-19) years on 15 min after receiving both types of treatments.

On receiving nebulized salbutamol alone the mild intermittent, mild persistent, moderate persistent and severe persistent subgroups improved by 18 %, 21%, 19 %

and 23 % respectively. Also, those receiving nebulized salbutamol with magnesium sulfate they improved by 15 %, 16 %, 15.7 % and 16.8 % respectively.

Discussion

Asthma is a common problem in children and adults associated with high morbidity and mortality. It is a disease with generalized but reversible air ways obstruction, bronchial hyper-responsiveness and air ways inflammation and most of the cases of asthma are allergic in origin (1, 2,3).

Asthma is an common disorder affecting male and female equally. It's prevalence has increased in the last decades especially in the industrialized countries (2,3). It is more common in children than in adults and it was estimated that 13.9 million visits to physician offices and hospital out patients, 1.9 million emergency department visit and 484000 hospital admission were attributed to asthma in USA in 2002 (16).

The study was conducted with the aim of evaluating the therapeutic effect of nebulized magnesium sulfate clinically and through evaluation of improvement on pulmonary function of patients with severe exacerbation of asthma.

The study show that most of the cases of severe exacerbation of asthma are mild intermittent 30% while mild persistent 26.2%, moderate persistent 23.7% and severe persistent are 20%. This agree with studies done previously (8,9,10).

For the age (5-13) years on receiving nebulized salbutamol alone the sub groups of mild intermittent, mild persistent, moderate persistent, and severe persistent improved by 51.8%, 45.9%, 49.7% and 53.5% respectively. While those receiving nebulized salbutamol with magnesium sulfate they improved by 67.6%, 63.6%, 63.6% and 63% respectively and for the age (14-19) years on salbutamol alone they improved by 49.9%, 50%, 49.9% and 50% respectively. However, on receiving salbutamol with magnesium sulfate they improved by 59.5%, 60.8%, 59.4% and 62% respectively.

There was also significant improvement in the means respiratory rate (cycle/min) of the group of patients receiving nebulized salbutamol with magnesium sulfate than those receiving nebulized salbutamol alone.

For the age 5 to 13 years, on receiving nebulized salbutamol alone the subgroups of mild intermittent, mild persistent, moderate persistent and severe persistent improved by 20.5%, 18%, 21% and 17.6% respectively. While those receiving nebulized salbutamol with magnesium sulfate they improved by 30.6%, 32%, 32% and 35% respectively and for the age (14-19) years on nebulized salbutamol alone they improved by 18.8%, 23%, 18.5% and 18.7% respectively. While those received nebulized salbutamol with magnesium sulfate they improved by 29.7%, 32%, 29% and 31.6% respectively.

These results agree with the previous findings (12, 13, 17). The present study also agree with the results of the study done by Sharma et al (1994) study the effect of parantral magnesium sulfate on pulmonary function in bronchial asthma (17) & other results (18,19).

Study done by Gurkan et al (1999) found that acute asthma attacks in children not responding to β2 agonist and corticosteroids may benefit from magnesium sulfate therapy when β2 agonist are in adequate in preventing deterioration (20).

There was agreement also with a study done in Tikrit teaching hospital in 2006 by using intravenous magnesium sulfate in the treatment of asthma (21).

Regarding the heart rate there was increase in the heart rate for both types of treatments but there are no significant difference in the percent of increasing in the means of heart rate for all sub groups of mild intermittent, mild persistent, moderate persistent and severe persistent in both types of treatments which mean that this increase in the heart rate is related to salbutamol which is cardiac stimulant and not to magnesium sulfate and the use of combined magnesium sulfate and salbutamol by nebulization enable us to decrease the dose of salbutamol and to overcome its side effect of cardiac stimulation (15,16).

Finally there was no registered side effect of nebulized magnesium sulfate in this study so, it is regarded as a safe drug especially by nebulization. The present study conclude that;-

Nebulized magnesium sulfate show remarkable improvement in the PEFR (liter/min) for the patients with severe asthmatic attack. Also, there was also improvement in the respiratory rate (cycle/min) for patients with severe asthmatic attack who received nebulized magnesium sulfate.

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Table (2-1) Asthma pulmonary score [15]

Score	RR (cycle/min) <6 year	RR (cycle/min)≥6years	Wheeze	Accessory muscles
0	<30 cycle/min	<20cycle/min	None	None
1	31-45 cycle/min	21-35cycle/min	Terminal expiration	Questionable
2	46-60 cycle/min	36-50cycle/min	Entire expiration	Apparent
3	>60cycle/min	>50cycle/min	Inspiration and expiration(None) No stethoscope	Maximal activity

Asthma pulmonary score (PS)

Mild exacerbation	PEFR > 70 %	PS < 3
Moderate exacerbation	PEFR 40 - 70%	PS 4-6
Severe exacerbation	PEFR 40 %	PS > 6

Table (2-2) Classification of asthma severity according to clinical assessment before treatment [15]

Severity	Days with symptoms	Night with symptoms	PEF or FEV_1	PEF variability
Step 4 Severe persistent	Continuous	Frequent	<60%	>30%
Step 3 Moderate persistent	Daily	>1night/week	>60%-<80%	>30%
Step 2 Mild persistent	> 2 week but< 1/ day	>2 night/month	>80%	20-30%
Step 1 Mild intermittent	< 2 week	< 2 night/month	>80%	<20%

Table (3-1) Frequency distribution of the patients according to the age and type of severity of asthma.

Age (years) / Severity	Mild intermittent	Mild persistent	Moderate persistent	Severe persistent	Total
(5-13) years	11 13.75%	9 11.25 %	8 10 %	6 7.5%	34 42.5%
(14-19) years	13 16.25%	12 15 %	11 13.75%	10 12.5%	46 57.5%
Total	24 30%	21 26.25%	19 23.75%	16 20%	80 100%

Table (3-2) Effect of types of treatments on the means of PEFR (Liter/ min) for patients age (5-13) years according to type of severity of asthma.

Treatment / Severity	gp I nebulized salbutamol alone				gp II nebulized salbutamol with magnesium sulfate			
	mild intermittent liter/min	mild persistent liter/ min	moderate persistent liter/ min	severe persistent liter/ min	mild intermittent liter/min	Mild persistent liter/ min	moderate persistent liter/ min	severe persistent liter/min
on admission No treatment	148.5 ±13.8	139.5 ±11.9	156.3 ±16.2	144.3 ±15.5	148.8 ±6.1	150.8 ±8.3	152.8 ±7	158.6 ±9.8
After treatment	225.5 ±19.4	216.2 ±16.2	234 ±24.6	221.6 ±21.7	249.6 ±8.5	246.8 ±12.4	250 ±10.4	258.6 ±14.8
Percentage of difference	51.8%	54.9%	49.7%	53.5%	67.7%	63.6%	63.6%	63%

Significant difference ($p \leq 0.05$).

Table (3.3) Effects of types of treatments on the means of PEFR (liter/min) for patients age (14-19) years according to type of severity of asthma.

Treatment / Severity	gp I nebulized salbutamol alone				gp II nebulized salbutamol with magnesium sulfate			
	mild intermittent liter/min	mild persistent liter/ min	moderate persistent liter/ min	severe persistent liter/ min	mild intermittent liter/min	mild persistent liter/ min	moderate persistent liter/ min	severe persistent liter/min
on admission No treatment	212.8 ±4.3	221 ±2.3	210.8 ±4.5	220.3 ±2.6	214 ±4.3	201.2 ±5.6	214.4 ±5.2	197 ±5.9
After treatment	319.1 ±6.4	331.5 ±3.6	316.1 ±6.8	330.6 ±4.2	341.5 ±6.5	323.6 ±8.3	341.8 ±8	319.5 ±9.3
Percentage of difference	49.9%	50%	49.9%	50%	59.5%	60.8%	59.4%	62%

Significant difference ($p \leq 0.05$)

Table (3-4) Effects of types of treatments on the means of respiratory rate (cycle /min) for patients age (5-13) years according to type of severity of asthma.

Treatment / Severity	gp I nebulized salbutamol alone				gp II nebulized salbutamol with magnesium sulfate			
	mild intermittent cycle/ min	mild persistent cycle/ min	moderate persistent cycle/ min	severe persistent cycle/ min	mild intermittent cycle/min	mild persistent cycle/ min	moderate persistent cycle/ min	severe persistent cycle/ min
on admission No treatment	52.5 ±4.5	55.5 ±2.6	52.7 ±6.3	56.6 ±3.3	60 ±0.4	61.6 ±0.9	60 ±0.7	62.6 ±1.2
After treatment	41.7 ±4.5	45.5 ±2.6	41.6 ±6.3	46.6 ±3.3	41.6 ±0.9	41.8 ±1.2	40.8 ±0.6	40.3 ±0.6
Percentage of difference	20.5%	18%	21%	17.6%	30.6%	32%	32%	35%

Significant difference ($p \leq 0.05$).

Table (3-5) Effects of types of treatments on the means of respiratory rate (cycle /min) for patients age (14-19) years according to type of severity of asthma.

Treatment / Severity	Gp I nebulized salbutamol alone				gp II nebulized salbutamol with magnesium sulfate			
	mild intermittent cycle/min	mild persistent cycle/ min	moderate persistent cycle/ min	severe persistent cycle/ min	mild intermittent cycle/min	mild persistent cycle/ min	moderate persistent cycle/ min	severe persistent cycle/ min
on admission No treatment	55.7 ±2	55.5 ±1.4	56.6 ±2.1	56.1 ±1.4	58.8 ±0.7	60.6 ±0.6	58.6 ±0.8	60.7 ±0.7
After treatment	45.2 ±1.5	42.5 ±0.8	46.1 ±1.5	43 ±0.8	41.3 ±0.8	41.2 ±0.8	41.6 ±0.9	41.5 ±0.9
Percentage of difference	18.8%	23%	18.5%	18.7%	29.7%	32%	29%	31.6%

Significant difference . ($p \leq 0.05$)

Table (3-6) Effects of types of treatments on the means of HR (beat /min) for patients age (5-13) years according to type of severity of asthma.

Treatment / Severity	gp I nebulized salbutamol alone				gp II nebulized salbutamol with magnesium sulfate			
	mild intermittent beat/min	mild persistent beat/min	moderate persistent beat/min	severe persistent beat/min	mild intermittent beat/min	mild persistent beat/min	moderate persistent beat/min	severe persistent beat/min
on admission No treatment	108.5 ±1.5	108.5 ±2	108.5 ±2	107.3 ±2.6	111.4 ±1.7	111.8 ±2.00	110.8 ±1.8	111 ±2
After treatment	130 ±4.1	130 ±0	130 ±5.7	130 ±0	131.6 ±1.6	130.6 ±0.6	112 ±2	131.3 ±0.6
Percentage of difference	17.9%	19.8%	18.8%	21%	18%	16.8%	15.5%	18%

Significant difference. ($p \leq 0.05$)

Table (3-7) Effects of types of treatments on the means of HR (beat /min) for patients age (14-19) years according to type of severity of asthma.

Treatment / Severity	gp I nebulized salbutamol alone				gp II nebulized salbutamol with magnesium sulfate			
	mild intermittent beat/min	Mild persistent beat/min	moderate persistent beat/min	severe persistent beat/min	mild intermittent beat/min	mild persistent beat/min	moderate persistent beat/min	severe persistent beat/min
on admission No treatment	94.1 ±4.3	97.5 ±3.1	96.1 ±4.6	100 ±2.1	108 ±0.5	111.8 ±2.2	108 ±0.7	112.7 ±2.5
After treatment	111.2 ±5.6	118.4 ±5.6	115 ±5	123.3 ±3.3	124.3 ±1.8	129.6 ±3	125 ±2	131.7 ±2.8
Percentage of difference	18%	21%	19%	23%	15%	16%	15.7%	16.8%

Significant difference ($p \leq 0.05$)