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Effect of Addition of Nebulized Magnesium Sulphate to Standard Therapy in Children with Severe Asthma

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Author`s Contribution

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ABSTRACT

Objective: To compare the outcome of addition of nebulized magnesium sulphate to the standard treatment in children with acute severe asthma.

Methodology: The trial was undertaken at the emergency of Paediatrics Department, Federal Government Polyclinic (Post Graduate Medical Institute), Islamabad from 1st April to 30th September 2019. Children between 1 to 12 years of age with acute severe asthma were initially nebulized with salbutamol thrice and ipratropium once. All the patients were also given intravenous steroid. Those not responding to this treatment and still classified as acute severe asthma were randomly divided into two groups each having 38 patients. Each patient in Group A received 2.5 ml (150 mg) of isotonic magnesium sulphate via nebulizer, thrice 20 minutes apart, while group B received 2.5 ml of isotonic saline via nebulizer, thrice 20 minutes apart. Each nebulization also contained salbutamol. Yung Asthma Severity Score (ASS) was determined at the start of treatment, at 30 minutes and at 60 minutes of treatment.

Results: After 60 minutes, the mean Asthma Severity Score of children in group A was 6.95 ± 1.29 and 7.63 ± 1.03 in group B ($p < 0.05$). In group A, 18 (47.4%) children were discharged and 20 (52.6%) were admitted in the hospital. In group B, 7 (18.4%) children were discharged while 31 (81.6%) were admitted in the hospital ($p < 0.05$).

Conclusion: It is concluded that nebulized magnesium sulphate along with salbutamol can give a better outcome than salbutamol alone in children with acute severe asthma.

Keywords: Acute severe asthma, Nebulization, Magnesium sulphate, Salbutamol, Saline.

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Introduction

Asthma is characterized by reversible obstruction of airways due to bronchospasm and increase mucous production.[1] Children who continue to experience symptoms even after treatment with bronchodilators are termed as severe asthma.[2]

Severe asthma accounts for a large number of hospital admissions. It has a high prevalence (1 out of 3 children) in the world.[3] The standard treatment of acute severe asthma includes oxygen inhalation, nebulization with salbutamol and ipratropium along with intravenous steroids.[4] Additional therapies include subcutaneous or inhaled epinephrine/adrenaline, intravenous (IV) or inhaled magnesium sulfate (MgSO4) and IV aminophylline.[5]

According to GINA (Global Initiative for Asthma) / BTS (British Thoracic Society) guidelines, usage of intravenous and nebulized magnesium sulphate can also be useful in the management of asthma[6]. Intravenous magnesium sulphate has been well established as a treatment option in acute asthma, but the efficacy of nebulized magnesium sulphate has not been established.[7]

MgSO4 inhibits the contraction of bronchial smooth muscles as it blocks the calcium ions influx to the smooth muscles. It also stops the calcium myosin interaction that results in smooth muscle relaxation. It is helpful in reduction of inflammatory mediators as it stabilizes mast

cells and T-cells. It also increases prostacyclin and nitric oxide synthesis, which can help in reducing asthma severity.[8]

Although the intravenous route of magnesium sulphate is effective in severe intractable asthma, it cannot be used regularly in routine as it requires monitoring and has side effects.[9] Contrary to that, inhaled route of magnesium sulphate is a non-invasive way that permits rapid action of drug. It also has better safety window because of less toxicity and side effects.[10] Inhaled magnesium sulphate is used for acute asthma, but its efficacy is still debatable.[11] Studies have shown that magnesium sulphate can reduce the admission rate of severe asthma.[12,13]

This study established the efficacy of nebulized magnesium sulphate for acute asthma as it has not been studied in our community. It would help us get local evidence, and we can implement the results in our local set-up and improve the outcome for children with asthma.

Methodology

A Randomized Controlled trial was conducted in the Paediatrics department, Federal Government Polyclinic (PGMI), Islamabad from 1st April 2019 to 30th September 2019. The total sample size calculated was 76 having 38 in each group. It was calculated by using Level of significance = 5%, Power of the test = 80%, Test value of the population mean (mean of asthma severity score) = 0.72[12] and anticipated population mean (mean of asthma severity score) = 0.44.[12] Non-probability consecutive sampling technique was used.

Children between 1 to 12 years of age, both male and female which were diagnosed as severe acute asthma were included in the study. Severe asthma was defined according to GINA/BTS guidelines. Among children aged 1–5 years, severe asthma is diagnosed when all of the following criteria is met:

(A) Oxygen saturations < 92% without ventilator / oxygen supplement
(B) Severe dyspnea while talking,
(C) Heart rate of > 130 beats per minute,
(D) Respiratory rate > 50 breaths per minute
(E) Use of accessory muscles.

Among children aged ≥ 6 years, severe asthma is diagnosed when all of the following criteria is met:

(A) Oxygen saturations < 92% without ventilator / oxygen supplement
(B) Severe dyspnea while talking
(C) Heart rate > 120 beats per minute
(D) Respiratory rate > 30 breaths per minute
(E) Use of accessory muscles.

Co-existing diseases like pneumonia, tuberculosis, cystic fibrosis, restrictive lung diseases or any other infective etiology, renal or liver disease and patients with known adverse reaction to magnesium were excluded from the study.

The study was conducted after the approval of ethical committee. Informed written consent was taken from the parents of children. A structured proforma was used to record the patient's demographic data like patient's name, age and gender. A patient who fulfilled the inclusion criteria were given initial nebulization of salbutamol thrice plus ipratropium nebulization once. All the patients were given intravenous hydrocortisone (4mg/kg). Those not responding to this treatment and still classified as acute severe asthma were randomly divided into two groups, each having 38 patients. Each patient in Group A received 2.5 ml (150 mg) of isotonic magnesium sulphate via nebulizer, thrice 20 minutes apart, while group B received 2.5 ml of isotonic saline via nebulizer, thrice 20 minutes apart. In every nebulizer, 2.5 mg (in children 1 – 5 years old) or 5 mg (in children ≥ 6 years old) salbutamol was also added. The primary outcome was Yung Asthma severity score (table I below) which was calculated before the treatment and then at 30 & 60 minutes after nebulization. Patients who were still categorized as acute severe asthma after nebulization were admitted in the pediatric ward for further management.

Table I: Yung asthma severity score[14]

Score	Wheeze	Accessory muscle	Heart rate
0	Absent	0	< 80
1	Expiratory only	+	81 - 110
2	Inspiratory & expiratory	++	111 - 140
3	Audible without stethoscope / silent chest in severe asthma	+++	> 141

The score from 0 - 3 was given to each of three components; the sum of this score was the ASS.

Data was entered & analyzed using SPSS v. 23. Qualitative variables like gender and admission rate (percentage of children who were admitted in the ward if the initial treatment fails) were presented as frequency and percentages. Quantitative variables like age, weight and asthma severity score at presentation, after 30 and 60

minutes of treatment were presented as mean and standard deviation. Independent sample t-test was applied to compare the Asthma Severity Score in both groups. Chi-square test was applied to compare the outcome of children in both groups. P-value less than or equal to 0.05 was considered statistically significant.

Results

The mean age of the patients in group A was 3.79 ± 2.23 years while mean age of the patients in group B was 4.68 ± 3.01 years. In group A, there were 18 (47.4%) male children and 20 (52.6%) female children respectively. In group B, there were 17 (44.7%) male children and 21 (55.3%) female children. Table II.

Table II: Demographics of patients

	Study group	
	Group A: Magnesium sulphate	Group B: Saline
Age (years)	3.79 ± 2.23	4.68 ± 3.01
Gender		
Male	18 (47.4%)	17 (44.7%)
Female	20 (52.6%)	21 (55.3%)

In group A, at baseline, the mean ASS was 8.29 ± 0.80 which was decreased to 7.24 ± 1.10 after 30 minutes and further reduced to 6.95 ± 1.29 after 60 minutes. Similarly in group B, at baseline, the mean ASS was 8.50 ± 0.56 which was decreased to 7.66 ± 0.99 after 30 minutes and further reduced to 7.63 ± 1.03 after 60 minutes. The difference between both groups was insignificant after 30 minutes ($p > 0.05$), while significant after 60 minutes ($p < 0.05$). Table III

In group A, 18 (47.4%) children were discharged while 20 (52.6%) were admitted in the hospital. In group B, 7 (18.4%) children were discharged while 31 (81.6%) were admitted in the hospital. The difference was significant between both groups ($p < 0.05$). Table III

Table III: Change in ASS score with course of treatment. N(38)

	Study group		P – value
	Group A: Magnesium sulphate	Group B: Saline	
ASS before treatment	8.29 ± 0.80	8.50 ± 0.56	0.188 !
ASS at 30 minutes	7.24 ± 1.10	7.66 ± 0.99	0.084 !
ASS at 60 minutes	6.95 ± 1.29	7.63 ± 1.03	0.013 *

* = P – value < 0.05 (Significant) & ! = p – value > 0.05 (Insignificant)

Table VI: Comparison of outcome in both groups.

Outcome	Study Group		Total	P - value
	Group A: Magnesium sulphate	Group B: Saline		
Discharged	18 (47.4%)	7 (18.4%)	25 (32.9%)	0.007 *
Admitted	20 (52.6%)	31 (81.6%)	51 (67.1%)	
Total	38 (100%)	38 (100%)	76 (100%)	

* = P – value < 0.05 (Significant)

Discussion

Around 30% children diagnosed with acute asthma do not respond to first line therapy and 84% of this group require admission in the hospital.[15] Searching of a hazardless, non-invasive & effective approach to treat this stage can considerably decrease the rate of hospital admissions, health-care cost and psycho-social load of the disease. In our study, the mean ASS score was reduced significantly in the magnesium sulphate nebulization group as compared to standard treatment alone. Hence suggesting that magnesium sulphate nebulization can be used as an adjunct to the standard treatment. Schuh et al concluded that addition of magnesium sulphate nebulization in the treatment reduced the hospital admissions and also decreased the PRAM (Pediatric Respiratory Assessment Measure) score.[15]

In our study, we observed that with the addition of magnesium sulphate, 18 (47.4%) children got discharged from the emergency where they presented with severe asthma while 20 (52.6%) need to admit in the hospital. But with saline, 7 (18.4%) children got discharged from the emergency while 31 (81.6%) needed admission in the hospital. The difference was significant between both groups ($p<0.05$). This showed that addition of magnesium sulphate improved patient's outcome thus resulting in discharge of a greater number of patients from the emergency. This led to reduced number of admissions and decreased burden on hospital and physicians.

Mahajan P also concluded that addition of magnesium sulphate to albuterol nebulization can benefit in moderate asthma.[16] Knightly et al also studied that there is a modest role of nebulized magnesium sulphate for treating severe asthma and it also decreased the hospital admission rate

however the confidence of evidence was low.[17] Powell et al reported that usage of nebulized magnesium sulphate can improve ASS in acute severe asthma however it was not significant.[18] Nebulized magnesium sulphate with salbutamol also improved PEFR (Peak Expiratory Flow Rate) in pediatric population than salbutamol alone.[19] However, several studies have shown no benefit of nebulized magnesium sulphate.[20,21] More studies must evaluate the final result.

One of the major concerns was regarding the dose of nebulized magnesium sulphate. We used 150mg magnesium sulphate per dose, which was isotonic (7.5%w/v) and was made by hospital pharmacy. Most of the studies conducted on Pediatric population used the same dose of isotonic magnesium sulphate.[18,19,22] However, concentration of solution was different in various studies (6.3%) which may have an effect on bronchodilatory effect of magnesium sulphate.[16] Further studies must establish the effect of different concentrations of nebulized magnesium sulphate on the outcome.

Conclusion

It is concluded that magnesium sulphate along with salbutamol can give a better outcome than salbutamol alone in children with acute severe asthma. It can also result in decreased hospital admissions and lower burden on hospitals and physicians. Now in future, it is suggested to conduct more trials so we can recommend the use of magnesium sulphate along with salbutamol in local practice and in local setup.

SUGGESTION

It is suggested that further trials should be done on a large scale to get authentic and more reliable results. Furthermore, adverse effects and toxicity of magnesium sulphate must be studied if any. Financial constraints must be resolved before initiating a new trial.

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