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SAFETY AND EFFICACY OF RAPID ADMINISTRATION OF INTRAVENOUS MAGNESIUM SULFATE IN ACUTE SEVERE ASTHMA IN CHILDREN

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ABSTRACT **Objective:** To evaluate the role and safety profile of magnesium sulfate in the management of acute severe asthma.
Study Design: A prospective experimental study.
Setting: S.N. Medical College, Agra.
Patients: Fifty-one cases of acute severe asthma aged 6-12 years. Every alternate patient was taken as a study group (n1=25) and rest were considered in the control group (n2= 26).
Intervention: Intravenous (IV) magnesium sulfate as a dose of (25 mg/kg) was given slowly within 10 minutes under vital monitoring. Serum magnesium was estimated before and after 30 minutes of magnesium sulfate infusion.
Main Outcome Measures: Asthma scoring, recurrence of symptoms and signs of asthma, and Emergency Dept. duration between these two groups.
Results: Mean serum magnesium levels before 30 minutes and after 30 minutes of therapy were 3.09 + 2.273 mg% and 3.20 + 2.265 mg%. These values were not significantly different ($p > 0.05$, t value = 0.168). There were significant improvements in asthma scoring in the case group ($P < 0.05$) as compared to the control group. There was a significant reduction in the duration of their E.D. stay ($P < 0.01$, t value = 8.8) in cases as compared to the control group. Sixteen Children in the control group and 5 children in the case group showed recurrence of symptoms and signs of asthma. This difference was significant ($P < 0.05$, t value = 4.22). Incidences of side effects of Magnesium sulfate were not significant.
Conclusion: Intravenous magnesium sulfate is a useful adjuvant to the standard treatment of acute severe asthma; this therapy not only decreased the total time duration of an asthma attack but also decreased the recurrence of acute severe asthma without any significant side effect.

KEYWORDS : Acute severe asthma, Magnesium sulfate, safety, and efficacy.

INTRODUCTION:

Asthma is a chronic inflammatory disorder of the airways in which many cells play a role, in particular mast cells, eosinophils, and T lymphocytes. In susceptible individuals this inflammation causes recurrent episodes of wheezing, breathlessness, chest tightness, and cough, particularly at night and/or in the early morning. These symptoms are usually associated with widespread but variable airflow limitation that is at least partly reversible either spontaneously or with treatment. The inflammation also causes an associated increase in airway responsiveness to a variety of stimuli.

Bronchodilators and steroids are well established effective treatments for all severities of asthma. However, there are still children with moderate to severe acute asthmatic attacks that may have insufficient improvement, leading to hospitalization or Emergency Department (E.D.) admission, and in the worst cases, severe morbidity and even mortality. There is an ongoing need to study new effective bronchodilator agents as additional therapies for relieving moderate to severe asthmatic attacks.

Magnesium sulfate is one of the agents being intensively studied as an adjunct to standard therapy for acute asthma. Magnesium is the second most abundant intracellular cation and is involved in numerous physiological functions, including protein folding, intracellular signaling, and enzyme catalysis. It has been shown that magnesium deficiency exacerbates pulmonary airways hyperreactivity. Several studies suggest that magnesium level has no effect on asthma but others had shown a contributory effect. In this study we aim to evaluate the role and safety profile of intravenous magnesium sulfate in the management of acute severe asthma.

MATERIALS AND METHODS:

Fifty-one children of age group 6 – 12 years admitted in Emergency Dept, S.N. Medical College, Agra with signs & symptoms of acute severe asthma from June 2005 to September 2006 were evaluated by history and complete clinical examination and excluded if other systems involved or other diagnosis suspected for their wheezing disorder. The severity of asthma was assessed with IAP Res. Chapter Update Guideline for Acute severe asthma (2003) as described in table 1.

Informed consent from the patients/relatives were taken in the event of including MgSo4 in the standard treatment. Group **I** – who was treated with standard therapy (management guideline by British Thoracic society, 2004) and considered as control group (26 cases). Group **II** – who was treated with standard therapy and intravenous magnesium sulfate and considered as study group (25 cases). Before and after 30 minutes of therapy both groups were compared by asthma scoring, Emergency Dept stays duration, recurrence of asthmatic attack, and statistical analysis with student t-test paired & unpaired and x^2 test. Randomization was done to avoid selection bias; therefore, cases were allotted to study and control group on an alternate basis.

Magnesium sulfate (dose of 25 mg/kg) dissolved in 5% dextrose was infused over ten minutes. Magnesium sulfate used for study purposes contained 50% magnesium sulfate (4 mEq/ml). Continuous monitoring was done during the infusion and 30 minutes after termination of infusion. Special attention was paid to vitals and deep tendon reflex.

In the study group, blood samples were collected for serum magnesium estimation before starting the treatment protocol and 30 minutes after completion of therapy in a plain vial. Serum magnesium was estimated using atomic absorption spectroscopy.

This study was approved by the Ethics Committees of S N Medical College and Hospital, Dr. B R Ambedkar University, Agra, Uttar Pradesh, India

RESULTS:

A final diagnosis of bronchial asthma was made for 282 children. Out of these 282 children, 51 cases presented with acute severe asthma; thus severe asthma accounted for almost one fifth (18%) of the total childhood asthma cases. Of the 282 cases of childhood asthma, 178 were males and 104 were female. The male: female ratio in the study was 1.8:1.

Most of the cases presenting with acute severe asthma in our study belonged to the category of mild asthma. Out of 282 children, 184(65.25%) were categorized as mild asthma, 46(16.31%) were considered to be suffering from moderate asthma and the smallest

group was of children suffering from acute severe asthma, which accounted for 18% cases. Most of the cases in both groups belonged to urban areas.

There was a significant difference in respiratory rate ($p < 0.01$, $t = 17.137$), and asthma scoring ($p < 0.01$. $t = 20.13$) but there was no significant different in PEFR before ($p > 0.05$, $t = 1.11$) and after ($p > 0.05$, $t = 0.528$) therapy between control and study group. Total duration of E.D. stay of control group (10.56 hours $\pm$ 2.16 hours) in comparison study group only (5.38 $\pm$ 2.03 hours) which show significant difference between these two groups ($p < 0.01$, $t = 8.11$).

DISCUSSION

We found that intravenous magnesium sulfate therapy is a useful adjuvant to the standard therapy of acute severs asthma in children as the addition of magnesium sulfate therapy to standard protocols resulted in a remarkably superior symptomatic (subjective) and objective improvement in almost all the children. This addition not only resulted in more rapid relief of symptoms and signs of acute severe asthma but also lead to a more sustained response.

The most common age group involved was that of 10-12 years (45.10%), followed by those in the age group of 6-8 years which comprised 29.41%. Most cases belonged to an urban area (82.35%) in both groups; similar findings have been reported by paramecia et al (2002). The most common stimulus for asthma precipitation in our study was air pollution (29.41%), followed by exposure to cold (19.6%). Air Pollution was also the most common cause of acute severe asthma in other studies (Carter et al, 1996); Landau et al (1994).The three other common causes which acted as precipitating factors were exposure to cold, allergens, and recurrent early childhood infection

In our study, magnesium sulfate was used in a dose of 25 mg/kg (Ciarallo et al, 1996) given over 10 minutes. Other authors have used slightly different protocols for the administration of Magnesium sulfate. Evaluations of the impact of I V magnesium sulfate therapy revealed a remarkable improvement in symptoms and signs of asthma. The mean asthma scores of the study group patients after receiving standard therapy for bronchial asthma was 1.76; this was far superior to the post-therapy mean asthma scores of 2.38 observed in the control group. These values were found to be statistically significant ($p<.05$ and t value = 2.437).

The mean duration of stay in the ED was 10.56±2.159 hr. for the control group. On the other hand, children in the study group stayed in the ED for a mean duration of 5.38±2.03 hrs. Thus, the study group patients had a statistically significant reduction in the duration of their ED stay ($p<.01$, t value= 8.804). There was a statistically significant difference in recurrence of asthma episodes between study (5/25) and control (13/26) cases and this difference was quite significant ($p<0.05$ and t value = 4.22).

Ciarallo et al, 1996 also observed similar results, except for the duration of the hospital stay. Comparison of Peak Expiration Flow Rate values between the two groups did not show any significant difference between the two groups. Thus the control patients showed an improvement of PEFR values from a pre-therapy value of 33.8 L/min. to a post-therapy value of 88.9 L/min. Similarly, the study group patients showed an improvement of PEFR values for a pre-therapy value of 36.3 L/min to a post-therapy value of 88.0 L/min. This difference was not found to be statistically significant.

The common adverse effects observed were hotness and a burning sensation along the IV line. There was only one patient who showed hotness about 4% of patients complaining of warmth immediately after infusion and 12% there was a burning sensation along IV line. However, at the end of the study feeling of warmth was less and burning sensation along IV line came to normal. These side effects were also reported by Skobeloff et al (1989) but there was no change in blood pressure and pulse rate after the infusion in our study. These side effects are minimal when compared with the incidence of side effects of established bronchodilators like salbutamol and theophylline.

The median value for magnesium levels was 2.04 mg% before therapy and 2.03 mg/dL after therapy. The most frequently observed magnesium level (Mode) was 2 mg/dL. This difference was not found to be statistically significant ($p>.05$ and t value = 0.168). The result of the present study clearly shows that the addition of magnesium sulfate therapy to standard protocols resulted in a remarkable symptomatic (subjective) and Objective improvement in almost all the patients; this response was quite superior to that obtained with standard therapy alone (Scarf one et al, 2000).

CONCLUSION:

These findings suggest that the addition of I/V Magnesium sulfate to standard therapy leads to better control and early stabilization of children with acute severe asthma. The patient in the study group received intravenous magnesium sulfate by a slow intravenous bolus over 10 minutes. Despite this relatively rapid administration of the total dose of magnesium sulfate, no major side effects of this therapy were observed in our study. Minor side effects were observed in 16% of patients in the study group cases. Thus out of a total of 25 children in the study group, only 3 children complained of a burning sensation along the intravenous line during the administration of magnesium sulfate solution. This was a transient phenomenon and it disappeared when the administration of the drug was completed. Another patient complained of feeling hot all over the body just after the injection of intravenous magnesium sulfate. This problem also settled down soon after the completion of the injection.

There were no cardiovascular complications during or after the administration of intravenous magnesium sulfate. None of the patients had any tachycardia or palpitation; hypotension was also not observed in any of the patients in the study group. Therefore we can conclude that intravenous magnesium sulfate is a useful adjuvant to the standard treatment of acute severe asthma.

HEIGHT LIGHT OF THE STUDY:

Analysis of data emerging from the current study focus towards several important POINTS:

- Intravenous magnesium sulfate therapy is a useful adjuvant to the standard therapy of acute severe asthma in children. Thus, the addition of magnesium sulfate therapy to standard protocols results in a remarkably superior symptomatic (subjective) and objective improvement in almost all the children.
- This addition not only results in more rapid relief of symptoms and signs of acute severe asthma but also leads to a more sustained response.
- Thus, there are fewer recurrences of symptoms and signs in the post-treatment phase in these patients who receive this therapy.
- This results in an early stabilization and a shorter emergency department stays of these children with acute severe asthma, thus leading to better and optimal utilization of Emergency Room services. This superiority of response to therapy can be of great value in busy emergency rooms where a rapid turnover of patients is observed.
- Reduction in recurrence rate also cuts down the anxiety level of patients as well as parents leading to a possibility of better long term control of childhood asthma.
- Despite rapid administration over 10 minutes, there were no significant side effects of intravenous magnesium sulfate therapy. Thus, this drug is a safe and effective option for rapid control of acute severe asthma.
- Thus, adjuvant therapy with intravenous magnesium sulfate emerges as an attractive option for the control of acute severe asthma because of its efficacy and safety. Still, as our study involved only a small number of patients, these findings need to be confirmed by conducting larger studies.
- Following such confirmation, the role of magnesium sulfate will be firmly established as an integrated part of therapy for acute severe asthma.

Table -1 Assessment Of Severity Of An Acute Episode Of Asthma

Score	Respiratory rate		Wheezing (+)	Accessory muscle use
	<6 yrs	>6yrs		
0	<30	<20	None	None apparent activity
1	31-45	21-35	Terminal expiration with stethoscope	Questionable increase
2	46-60	36-50	Entire expiration with a stethoscope	Increase apparent
3	>60	>50	During inspiration and expiration without a stethoscope	Maximum activity

Add score	0-3 Mild 4-6 Moderate >6 Severe	*If wheezing absent (due to minimal airflow), Score >3

IAP Respiratory Chapter Update, Treatment Acute Asthma Attacks 2003 pg. 17.

Table-2: Serum Magnesium Levels In Study Group

	Before administration of $MgSO_4$ (in mg/dL)	After administration of $MgSO_4$ (in mg/dL)
Mean	3.09	3.20
SD	2.273	2.265
Range	0.1–7.03	0.4–7.04
Median	2.04	2.03

Table-2- Serum magnesium level distribution shows there was no significant rise of serum Magnesium level before and after the therapy in the study group ($p > 0.05$, $t = 0.17$) and there was no significant side effect after fast (within 10 minutes) Magnesium sulfate infusion in these groups.

Table-3: Distribution Of Cases According To Asthma Precipitating Agents

Stimuli	No. of cases in study group	No. of cases in control group	Total No. of cases	%
Air pollution	7	8	15	29.41
Exposure to cold	6	4	10	19.6
Allergens (typically inhaled)	4	3	7	13.73
Recurrent childhood infections	3	4	7	13.73
Industrial compounds	1	2	3	5.88
Exercise	2	1	3	5.88
Emotional stress	1	-	1	1.96
Medication (aspirin & β-blocker)	-	1	1	1.96
None	1	3	4	7.84
Total	25	26	51	100

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