

Role of Intravenous Magnesium Sulphate in Severe Acute Asthma

Muhammad Murtaza Khair¹, Md. Zakir Hossain Sarker², Md. Ali Hossain³, Md Rashidul Hassan⁴, Mirza Mohammad Hiron⁷, Asif Mustaba Mahmud⁶, Md. Mustafizur Rahman⁷
Md. Mohiuddin Ahmed⁸, Md. Abdur Rouf⁹

Abstract

Magnesium is required after wide variety of cellular activities and biological process. It causes relaxation of bronchial smooth muscle. It is also known to reduce the amount of neurotransmitter released at motor neuron terminals diminish depolarisation action of acetylcholine at the neurotransmitter end plate and depress excitability of smooth muscle membrane. Magnesium is necessary, for steps involving the interaction of beta-agonist receptor complex, G-protein and GTP leading to activities of adenylylcyclase. It reduces superoxide production in neutrophil. Therefore magnesium has an anti inflammation for the sustain improvement in pulmonary, function test even several hours after magnesium was administered.

This is a randomised controlled clinical trial. This study enrolled 60 patients with severe acute asthma with FEV₁ less than 30% of predicted of individual and age between 18-55 Years not needing assisted ventilation. After measurement of FEV₁ and PEFR all patients received 200 mg hydrocortisone intravenous, nebulised with 2.5 mgs ulbutamol and oxygen. At the same time study group patient (n=30) received intravenous 2gm magnesium sulphate in 50 ml and the control group patient (n=30) received intravenous 50 ml of normal saline. Magnesium sulphate or normal saline was infused over 20 minutes. After 30 minutes at the end of the infusion, FEV₁ and PEFR were measured.

Initially, before infusion of MgSO₄ or saline PEFR L/min, PFER % predicted and FEV₁ L, FEV₁% predicted were similar in two groups. After 30 mins at the of infusion the PEFR L/min and PEFR % predicted were higher in study group and it was 188.5 L/min vs 171.4 L/min and 42.5% vs 38.1 % respectively and which was statistically significant (p<0.001). Similarly FEV₁ L and FEV₁ % predicted were greater in study group and it was 0.87 L vs 0.81 L and 27.7% vs 25.6% respectively which was also statistically significant (p<0.001). This prospective controlled study concluded that Intravenous magnesium sulphate has better and rapid bronchodilating effect, patients treated with intravenous magnesium sulphate get quick relief from distress and no unwanted side effect is present.

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1. Junior Consultant, NIDCH
2. Registrar, NIDCH
3. Professor of Respiratory Medicine NIDCH
4. Professor of Respiratory Medicine NIDCH
5. Asso. Professor of Respiratory Medicine NIDCH
6. Asso. Professor of Respiratory Medicine NIDCH
7. Professor of Respiratory Medicine NIDCH
8. Asso. Professor of Respiratory Medicine NIDCH
9. Registrar (Medicine), NIDCH

Introduction

Asthma is the most common respiratory crisis encountered in clinical practice. It is estimated that in the USA 1.8 million patient each year seek care for acute episode in emergency department with cost in excess of \$430 million. Yet, despite this clinical and financial burden general agreement has yet to be reached about the best way to treat the acutely presenting patient and fundamental issues such as the choice of drugs and duration of treatment have not been resolved¹.

The morbidity and mortality rates for asthma continue to increase during a period when medical interventions have produced a decline in the morbidity of many other childhood diseases². Globally it affects about 100 million people³. Asthma affects 3%-5% (approximately 14-15 million) of the US population including 6-9% (4.8 million) under 18 years of the age making it frequently encountered clinical problem both in pediatric and adult population and major cause of morbidity in the USA and around the world⁴. In our country, according to the First National Asthma Prevalence Study, 1999⁵ about 7 million people (5.2% of the total population) are suffering from asthma. At least three episodes of asthma attack in the last 12 months. More than half of these patients are innocent children that are 7.4% of the total pediatric population (I-15 years age group).

Recent epidemiological data for acute asthma suggest there are about 5,00,000 hospitalization per year in the USA of which 65% occur in patient over 18 years of age. Acute asthma represent 4% of all emergency department visit involving about 2 million people. About 15% and 25% of the emergency department visit for acute asthma result in hospitalization. About 20-30 of the patient initially managed and discharged from emergency department have relapse⁴.

Globally an increase in the asthma mortality has been noticed over the past 15 years⁶. From 1984 to 1994 the national hospitalization in USA rate for asthmatic children increased by 17%. The national death rate for asthma in children and adult are more than doubled from 1975 to 1995⁷. In UK, death from asthma rose steadily during 1980s, peaked in 1988 and have been falling during 1990s. However admission to hospital for acute severe

asthma has not decreases and studies of asthma deaths, near fatal asthma and asthma admission reveal potentially preventable or avoidable factor in more than 75% of patient⁸.

Despite their effectiveness some percentage of the patient with acute asthma fail to respond to beta-2 agonist and as many as 30% of the patient presenting emergency department fails to responds adequately to beta-2 agonist and require hospitalization⁹. Currently the cornerstone of the therapy for acute asthma is the rapid reversal of the patients airways obstruction. The main stay therapy for acute exacerbation is nebulised beta-2 agonist therapy repeatedly every 20 minute for one hour (serial 3 nebulisation) as initial therapy.

Early in the course of treatment systemic corticosteroid should be administered to patient with moderate to severe exacerbation or to patient who fail to respond promptly and completely to inhaled beta agonist¹⁰. Regarding steroid it required hours to demonstrate significant benefit. Incase of hydrocortisone which is given intravenous, the peak effect on airway mechanics may be achieved more rapidly the time between administration and onset of benefit in asthma being thought to be about 5 hours compared with about 8 hour for prednisolone.

Addition of high dose of inhaled ipratropium bromide 0.5 mg in adult to an aerosolized solution of selective beta agonist has shown additional benefit in severe asthma exacerbation than either drug alone but again such improvement are usually small so that some workers reports no benefit whereas other repot trends that fail reach statistical significance¹¹.

Given the slowness of the onset of action anticholinergic and 60-90 minutes lag time before achieving a peak effect and their relatively limited bronchodilator activity, anticholinergic agent such as ipratropium bromide are not 1st line therapy for acute asthma. They do not add any therapeutic benefit to the effect of albuterol given in divided doses over I hour nor do they facilitate recovery in patient whose immediate response to sympathomimetics is impaired¹².

In the emergency department theophylline is not recommended because it appear to provide no additional benefit to optimum inhaled beta agonist

therapy and steroid and increase the adverse effect¹³. It has narrow therapeutic index and frequently associated with adverse effect even in therapeutic dose. Patient vary in dose requirement to keep plasma level therapeutic¹¹. Intravenous theophyllin is less effective than nebulised beta agonist and should therefore be reserved for the few patients who fail to respond to beta agonist

Patient like severe acute asthma is hypoxaemic and struggling to breath as a result of severe bronchoconstriction. After administration of intravenous aminophylline an adverse effect like a grand mal seizure may deliver the coup de grace and should be avoided especially rapid administration¹¹. Urgent level should be requested if suspicion about the patient taken theophyllin orally. Despite the refinement in therapeutic strategy for acute asthma emergency department visit and hospitalization continue to account for predominant proportion of health care costs for asthma.

These facts stress the need for the innovative emergency department based intervention. An efficient asthma adjunct is needed to help bridge the time to onset of corticosteroid therapy effects in subpopulation of patient with acute asthma who are resistant to standard bronchodilator treatment. This ideal drug should be fast acting safe and effective.

This study was carried out to search for adjunct to standard therapy in patient with severe acute asthma rapid recovery from severe acute asthma, to determine that there is better response when intravenous magnesium sulphate is used in the treatment of severe acute asthma and to elucidate any adverse effect of magnesium sulphate.

Materials and Methods

It was a prospective randomized case control study carried out at Asthma Out Patient Department, National Institute of Disease of the Chest & Hospital (NIDCH), Mohakhali. Dhaka from January 2003 to December 2001. Population of the study was known case of asthma patient or newly diagnosed asthma patient who presented to the emergency department with an acute asthma exacerbation. Inclusion Criteria was known cases or newly diagnosed bronchial asthma patient of either sex, age 18-55 years. FEV1 below 30% of

predicted and non-smoker. Febrile, any evidence of lower respiratory tract infection i.e. productive sputum, any history or evidence of cardiac, renal or hepatic dysfunction smoker (former or current smoker), pregnant women, breast-feeding mother, poor level of patients co-operation cyanosed patients were excluded.

60 patients were included in this study. Group-1 (n=30) patients were treated with 2gm MgSO₄+steroid+sulbutamol. Group-11 (n=30) patients were treated with normal saline + steroid+sulbutamol. Both groups treated with oxygen through out the study period. Patients were allocated into two groups randomly. Every alternate patient attended in the emergency room who met the criteria included sequentially in each group.

In each case, patient's consent was taken for the control and study groups for enrollment in this study. A standard proforma and questionnaire was designed and filled to identify patient with acute asthma. The patients were identified as acute asthma patient according to predominant criteria following history, clinical examination and objective measurement of the airway obstruction.

As the patient presented to the emergency department of asthma center with acute respiratory distress, they were clinically assessed with brief history of attack duration medication used etc. with a view to establish the diagnosis of asthma as well as severity assessment with the help of severity assessment chart. Physical examination of the patients were done with regards to the vital signs of acute attack as well as the chest findings. The exclusion criteria were ruled out. Questionnaire were filled. Objective measurement of airway obstruction were recorded with spirometer & peak flow meter. The procedure of using the spirometer & peak flow meter were demonstrated to the patient.

Each patient received one unit of 0.5 ml salbutamol (2.5mg) diluted in 3ml normal saline via wet nebuliser, iv hydrocortisone 200 mg, and either iv magnesium sulphate 2gm in 50 ml or iv 50ml normal saline over 15-20min. After end of infusion again the patient were nebulised with 0.5ml of salbutamol. Spirometry was performed at 30 min interval (after completion of infusion). Peak flow rates were measured at the same time.

Oxygen was given to the patient by nasal cannula at the rate of 6 liter/min through out the procedure.

Statistical Analysis

Statistical analysis was done by using the statistical package for the social science (SPSS) program in computer. Chi square test and unpaired “t” test are used to compare between two groups.

A ‘P’ value less than 0.05 is consider as significant.

Results and Observations

This prospective study conducted in National Institute of Chest Disease and Hospital, Dhaka for a period of one year starting from January 2003 to December 2003. The main objective of the study was to examine the therapeutic response of magnesium sulphate in severe bronchial asthma. A total of 60 patients were evaluated. The mean age of the patients were 27.2±5.7 years ranging from 18 to 40 years. Among the studied patients, 21(35.0%) were male and the rest were female 39(65.0%). The mean age of the male patients was 26.1±4.8 years and the female patients was 27.7±6.2 years. Highest percentage of studied patients 21(35.0%) were in the age group 30 years and above, followed by 20(33.3%) in the age range below 25 years and 19(31.7%) in the age group of 25-29 years. Analysis revealed that no statistically significant mean age difference was found between male and female patients (p>0.05), although the mean age was higher among female patients compared to male patients. (Table 1)

Table-I

Age and sex distribution of the study subjects

Age in years	Sex		Total
	Male	Female	
<25	8(38.1)	12(30.8)	20(33.3)
25-29	9(42.9)	10(25.6)	19(31.7)
>30	4(19.0)	17(43.6)	21(35.0)
Total	21(35.0)	39(65.0)	60(100.0)
Mean±SD	26.1±4.8	27.7±6.2 NS	27.2±4.7

N.B

Figure in parenthesis indicate percentage
P value reached from unpaired student’s t test (p>0.05)

In this study, to compare the therapeutic efficacy of magnesium sulphate, the studied patients were

divided into two groups. Thirty patients were treated by magnesium sulphate with steroid and salbutamol and designated as group I patients and the rest were treated with normal saline with steroid and salbutamol and designated as group II patients. The mean age of the group I patients was 28.4±6.1 years ranging from 18 to 40 years and the mean age of the group II patients was 25.9±5.2 years ranging from 18-35 years. Analysis revealed that no statistically significant mean age difference was found between two groups of patients (p>0.05). (Table II)

Table-II

Age distribution of the study subjects

Age in years	Study subjects		Total
	Group I	Group II	
<25	7(23.3)	13(43.3)	20(33.3)
25-29	11(36.7)	8(26.7)	19(31.7)
>30	12(40.0)	9(30.0)	21(35.0)
Total	30(50.0)	30(50.0)	60(100.0) ..
Mean±SD	28.4±6.1	25.9±5.2 ^{NS}	27.2±5.7

N.B

Figure in parenthesis indicate percentage
Group I = Magnesium sulphate with steroid and salbutamol
Group II = Normal saline with steroid and salbutamol
p value reached from unpaired student’s t test (p>0.05)

Table III shows the sex distribution of the studied subjects. Among group I patients, 10(33.3%) were male and 20(66.7%) were female. Similar pattern of sex distribution was found among group II patients with 11(36.7%) were male and 19(63.3%) were female. No statistically significant sex difference was found between to groups of patients (p> 0. 05).

Table-III

Sex distribution of the study subjects

Sex	Stud y subjects		Total
	Group I	Group II	
Male	10(33.3)	11 (36.7) NS	21 (35.0)
Female	20(66.7)	19(63.3) ^{NS}	39(65.0)
Total	30(50.0) ¹	30(50.0)	60(100.0)

N.B

Figure in parenthesis indicate percentage
Group I = Magnesium sulphate with steroid and salbutamol
Group II= Normal saline with steroid and salbutamol
p value reached from chi square test (p>0.05)

It was observed that cent per cent of the attended patients had presented with breathlessness, wheeze and straining in accessory muscle followed by chest tightness (90.0%), cough (85.0%), sweating (1.7%). But no patients presented with cyanosis. No statistically significant difference was found between two groups of patients ($p=0.05$) regarding

clinical presentation (Table IV). Table V shows the comparative assessment of two treatment modalities. Analysis revealed that in both the groups the significant changes of PEFR and percent predicted PEFR was found ($p<0.001$), but the percentage of improvement was statistically significant in group I patients ($p<0.001$).

Table-IV
Clinical presentation of the study subjects

Symptoms	Study subjects		
	Group I	Group II	Total
Breathlessness	30(100.0)	30(100.0)	60(100.0)
Chest tightness	27(90.0)	27(90.0)	54(90.0)
Cough	24(80.0)	27(90.0)	51(85.0)
Wheeze	30(100.0)	30(100.0)	60(100.0)
Accessory muscle use	30(100.0)	30(100.0)	60(100.0)
Sweating	1(3.3)	0(0.0)	1(1.7)
Cyanosis	0(0.0)	0(0.0)	0(0.0)

N.B

Figure in parenthesis indicate percentage

Group I = Magnesium sulphate with steroid and salbutamol

Group II = Normal saline with steroid and salbutamol

p value reached from chi-square test ($p>0.05$)

Table-V
PEFR, L/min and PEFR, % predicted before and after treatment
PEFR, % predicted

	Group I (n=30)	Group II (n=30)	Group I (n=30)	Group II (n=30)
	Mean±SD	Mean±SD	Mean±SD	Mean±SD
Before	147.1±21.8NS	148.7±22.1	32.7±4.3NS	32.8±4.5
After	188.3±22.7***	171.4±21.6	42.5±4.3***	38.1±3.2
%	28.9±9.8***	15.9±8.7	30.2±5.3***	17.1±7.6
improvement				

N.B

p value reached from unpaired student's t test

*** $p<0.001$

Table-VI
FEV₁, L and FEV₁% predicted before and after treatment

	FEV ₁ , % predicted			
	Group I	Group II	Group I	Group II
	(n=30)	(n=30)	(n=30)	(n=30)
	Mean±SD	Mean±SD	Mean±SD	Mean±SD
Before	0.71±0.12 ^{NS}	0.73±0.13	22.4±4.2 ^{NS}	23.0±4.7
After	0.87±0.11 ^{***}	0.81±0.11	27.7±3.79 ^{***}	25.6±3.8
% improvement	22.3±5.7 ^{***}	10.9±4.9	24.9±7.0 ^{***}	12.2±6.8

N. B

p value reached from unpaired student's t test ***P<0.001

Table-VII
Percentage of improvement of selected parameters after two treatment modalities

Parameters	Group I	Group II	p value
PEFR, L/min	28.9±9.8	15.9±8.7	0.001
PEFR,% predicted	30.2±5.3	17.1±7.6	0.001
FEV ₁ /L L	22.3±5.7	10.9±5.0	0.001
FEV ₁ , % predicted	24.9±7.0	12.2±6.8	0.001
Pulse /min	3.3±0.3	3.3±0.6	0.710
Respiration	18.6±1.5	15.3±10.1	0.080
Systolic blood pressure (mmHg)	0.4+ 1.5	0.2±0.8	0.463
Diastolic blood pressure (mmHg)	0.0±0.0	0.1±0.7	0.321

* p value reached from unpaired student's t test

Table VI shows the comparative assessment of improvement in two treatment modalities in terms of FEV₁, L and FEV₁, % predicted. Analysis revealed that in both the groups the significant changes of FEV₁, and FEV₁% predicted was found (p<0.001), but the percentage of improvement was statistically significant in group I patients (p<0.001).

Analysis of the above table revealed that the after treatment with magnesium sulphate the percentage of improvement was significantly high in terms of PEFR L/min, PEFR predicted, FEV₁ L and FEV₁% L (p<0.001). But no statistically significant changes were observed in pulse rate, blood pressure and respiration (p>0.05) (Table VII and figure 1).

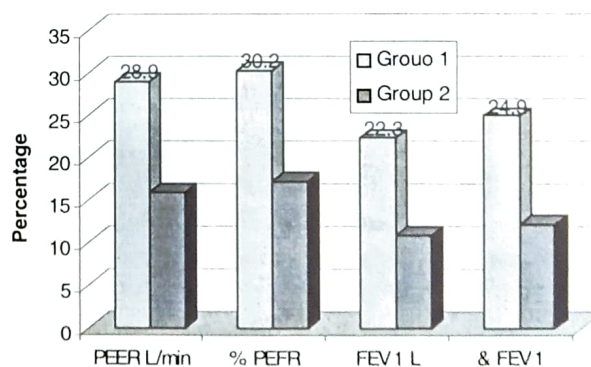


Fig-1 : *Percentage of improvement of selected parameters after two treatment modalities*

Discussion:

The published literature on adult asthmatics has yielded conflicting results though in children demonstrate magnesium to be beneficial in severe

asthma. A number of case reports indicate magnesium is beneficial for treating acute severe asthma, while results of controlled clinical trials evaluating the effect of magnesium in acutely ill ED patient widely differ¹⁴.

This prospective study conducted in National Institute of Chest Disease and Hospital, Dhaka for a period of one year starting from January 2003 to December 2003.

The studied patients were divided into two groups. Thirty patients were treated by magnesium sulphate with steroid and salbutamol and designated as group I patients and the rest were treated with normal steroid with steroid and designated as group II patients. Among the studied patients, 21 (35.0%) were male and the rest were female 39 (65.0%). The mean age of the group I patients was 28.4 ± 6.1 years ranging group 18 to 40 years and the mean age of the group II patients was 25.9 ± 5.2 years ranging from 18-35 years. Analysis revealed that no statistically significant mean age difference was found between two groups of patients ($p > 0.05$). It indicate that younger age group are suffering from severe acute asthma more than other age group. The probable causes might be they are more exposure to pollen, dust and other environmental cause.

The mean duration of suffering from asthma was 11.0 ± 4.3 years ranging from I-18 years. It indicate that majority were suffered from early childhood and also found that they had positive family history of bronchial asthma.

The mean duration of symptoms before attendance to hospital was 5.2 ± 2 days. It was 5.4 ± 2.6 days among the group I patients and 5.0 ± 1.8 days among group II patients. This duration was little bit higher compare with other study. It could be due to ignorance of patient regarding the disease. They also tried to get treatment from local doctors.

It was observed that cent percent of the attended patients had presented with breathlessness, wheeze and straining in accessory muscle followed by chest tightness (90.0%), cough (85.0%) sweating (1.7%). But no patients presented with cyanosis. .

It was evident that although the cent percent of the patients were conscious, but 16(26.7%) were unable to talk and 44(73.3) were able to talks with words.

In the present study, the pulmonary functions were evaluated by measuring the PEFR L/min, PEFR %predicted, FEV₁ L and FEV₁ %predicted. Analysis revealed that the predicted PEFR increased significantly from baseline after administering the drugs in two groups of patients ($p > 0.001$). The percent of improvement was significantly higher among the patients treated by conventional drugs adjunct with magnesium sulphate ($30.2 \pm 5.3\%$) compared to group II patients treated by conventional drugs adjunct with normal saline ($17.1 \pm 7.6\%$) ($p < 0.001$).

The initial PEFR L/min was 147.1 ± 21.8 L/min in group I patients and 148.7 ± 22.1 L/min in group II patients after administration of medicine in increased to 188.3 ± 22.7 L/min in group I patients and 171.4 ± 21.6 L/min in group II patients. Analysis also revealed that mean percent improvement was significantly high in patients treated with magnesium sulphate ($28.9 \pm 9\%$) compared to patients treated with normal saline ($15.9 \pm 8.7\%$) ($p < 0.001$). It was also noted that within group, PEFR was significantly increased from baseline ($p < 0.001$).

It was evident that the FEV₁: L was increased from baseline 0.71 ± 0.12 L in group I and 0.73 ± 0.13 L in group II to 0.87 ± 0.02 L in group I and 0.81 ± 0.10 L group group II patients and the difference was statistically significant ($p < 0.001$) Analysis revealed that the mean percent of improvement was significant high among the group I patients ($22.3 \pm 5.7\%$) compared to group II patients ($10.4.9\%$) ($p < 0.001$).

It was evident that no statistically significant mean difference was found between two groups of patients in terms of percentage predicted forced expiratory volume ($p > 0.05$), although it was a bit higher in group II patients (23.0 ± 4.7) than group I patients (22.4 ± 4.2). After administration of drugs, it was increased significantly in both the groups of patients ($p < 0.001$) and the mean difference was statistically significant between two groups of patients. Analysis also found that mean percentage of improvement was significantly high among the group I patients (24.9 ± 7.0) compared to group II patients (12.2 ± 6.8) ($p < 0.001$).

Ciarallo et al. (2000) ⁷ carried out a study on - Higher dose intravenous magnesium therapy for children with moderate to severe acute asthma".

They included 30 patients between the age of 6-17.9 years and found remarkable improvement in pulmonary function. The PEFR improved in all the analyzed patients at 20 min ($p < 0.001$) 50 min ($p < 0.001$) and 110 min ($p < 0.001$). Comparing the improvement of FEV₁ from the baseline between the 2 groups yielded similar pattern. At 50 mins between the two groups the absolute change in percent predicted PEFR was 2% vs 14% and FEV₁ was 2% vs 15 respectively.

In present study both the PEFR and FEV₁ response were also significant ($p < 0.001$). Absolute change in percent predicted PEFR is 17.1% vs 30.2% and FEV₁ is 12.2% vs 24.9% respectively. Here the change is relatively higher. It may be due to different type of patient selection.

Skobeloff et al. (1989)¹⁵ conducted a study on "Intravenous magnesium sulphate for the treatment of acute asthma in the emergency department". They included 38 patients divided into two groups. They found magnesium infused group showed marked improvement than control group. "File PEFR improvement in all analyzed patients at 20, 30 and 45 mins were significantly different ($p < 0.05$), Their result compatible to this study is less significant. Reason might be due to lower dose of magnesium sulphate as well as for the selection of those patients who did not responded to three times nebulisation. Besides this they introduced magnesium sulphate after 90 mins of nebulisation.

Similar type of study carried out by Ciarallo et al. (1996)² - "Intravenous magnesium therapy for moderate to severe pediatric asthma". They included 31 patient aged 6 to 18 years and found the magnesium group had significant improvement of FEV₁ % predicted from baseline (34% vs 1.1, $p < 0.05$) at 50 mins and this improvement was sustained even greater att 10 min (75% vs 5%, $p < 0.01$). Result was similar for PEFR at 80 through 110 mins (59 vs 20% at 110 min) In present study PEFR % predicted and FEV₁ % predicted response were highly significant ($P < 0.001$). Absolute change in PEFR, % predicted was 30.2% vs 17.1% and FEV₁, % predicted was 24.9% vs 12.2%. This difference might be they took different age group of patient and introduced magnesium sulphate after three times beta-2 agonist nebulisation.

Noppen et al. (1990)¹⁶ carried out a study on "Bronchodilating effect of intravenous magnesium sulphate in acute severe bronchial asthma". They included 6 patients aged 45-60 years. They infused magnesium sulphate 0.615 mmol/min for 20 mins. They found marked improvement at 20 min $P < 0.05$. But FEV₁, fell after 30 mins though it did not reach the baseline value. Addition of beta-agonist after 30 mins causes significant improvement of FEV₁ in all patients $p < 0.05$. Their result was less significant than recent study probably due to administration of two drugs separately at 30 mins interval. Results of their study and present study suggest that magnesium has bronchodilating effects in asthmatic patient.

Skorodin et al. (1995)¹⁷ conducted a study with "Magnesium sulphate in exacerbation of chronic obstructive pulmonary disease". They included 72 patients of aged 62-66 years and found remarkable improvement in pulmonary function. The PEFR improvement at all of the analyzed patient at 30 and 45 min were (162.3 vs 143, $p < 0.03$) and (161.3 vs 143.3, $p < 0.03$) respectively. They showed that magnesium sulphate have got not only significant bronchodilating effect, but also rapid improvement, which was similar to present study.

"Magnesium sulfate as a vehicle for nebulised salbutamol in acute asthma" This work carried out by Nannini et al. (2000)¹⁸ in Argentina. They enrolled 35 patients with acute asthma in randomized double-blind controlled trial. They found isotonic magnesium sulphate plus salbutamol increase the peak flow in comparison to salbutamol plus normal saline. This result is consistent with current study in spite of different route of administration of drug.

Devi et al. (1997)¹⁹ conducted a study - "Intravenous magnesium sulphate in acute severe asthma not responding to conventional therapy". They took 47 children of age between 1-12 years. They found significant improvement in PEFR at 30 mins and 1st, 2nd, 3rd, and 7th hours after stopping the infusion ($p < 0.05-0.01$) They could have got more significant effect, if they had taken responder group. Moreover dose of magnesium sulphate was also less than recent study.

Okayama et al. (1987)²⁰ conducted a study on "Bronchodilating effect of intravenous magnesium

sulphate in acute bronchial asthma". They included 10 patient of 45-62 years and found significant improvement of FEV₁ at 20 min. Which declined and again improved by taking beta-2 agonist similar to initial one. If they had used both drugs simultaneously they could be availed better response. They also found in all patient that dyspnea was decreased after magnesium infusion. Which was similar observation with current study.

Silverman et al. (2002) have done similar type of study on Intravenous magnesium sulphate in the treatment of acute severe asthma. They took 254 patients from different hospitals of 18 to 60 years. They found remarkable improvement in pulmonary function. The FEV₁ improved on patients treated with magnesium sulphate 48.2% vs 43.5% at 240 mins. In current study FEV₁ in among the magnesium sulphate group improved 27.7% vs 25.6% at 50 mins. So, both the studies show improvement in pulmonary function. As their study revealed gradual improvement of all the parameter, so it can be concluded that present study is consistent with their study.

Small sample size is one of the limitations of this study.

In current study blood magnesium sulphate were not estimated before and after the infusion.

Measurement of PEFRL/min, PEER % predicted, FEV1 L and FEV1 % predicted can be monitored for longer period.

Reference:

1. Weiss KB, Geson PS & Hodgson TA. A economic evaluation of asthma in United States. *N Eng J Med*. 1992; 326: 862-6.
2. Ciarallo L, Saucer AH & Shannon MW. Intravenous magnesium therapy for moderate to severe pediatric asthma: Result of a randomized trial. *J Pediatr* 1996; 129: 80
3. Hassan MR, Hossain MA, Mahmud AM, Kabir ARML, Amin MR, Bennoor KS & Rahman MM (ed) Nation asthma guidelines for medical practitioners. 2edn . Asthma Asssocation , Bangladesh, Dhaka. 2001; 66: 9-14.
4. Kavuru MS & Widemann HP. In: Diagnosis and management of asthma. 2edn. Professional Cmmunication Inc. Cleveland, Ohio, 1998; 23
5. Kabir ARML, Hassan MR, Rahman AKMF, Mahmud AM & Hossain MA. First national asthma prevalence study (NAPS) in Bangladesh : Prevalence of asthma. 1st international Conference on Asthma & Chest Disease, Asthma asssocation, Bangladesh, Mohakhali, Dhaka 1999; 6.
6. ISAAC LS. A hypothesis generator for asthma quoted in Kabra SK. 2000, 'Magnesium sulphate in asthma .' *Indian Journal of Pediatrics*, 1998; 67(2): 119-20.
7. Ciarallo I, Brousseau D & Reinert S. Higher-dose intravenous magnesium therapy 101 - children with moderate to severe acute asthma. *Arch pediatr Adolesc Med* 2000; 154: 979-83.
8. Harrison B. Acute severe asthma in adult in *Medicine International Bangladesh edn*. The Medicine Publishing Company, UK, 1999- ,99(4): 64-8.
9. Kelsen SG, Kelsen DP, Fleegler BE, Jones EC & Roman T. Emergency room assessment and treatment of patient with acute asthma :Adequency of the conventional approach. *AmJ Med*. 1979; 64: 622-8.
10. Littenberg B & Gluck EH. A controlled trial of mehyl prednisolone in emergency treatment of acute asthma.' *Th New England Journal of Medicine*, 1986; 314 .150-152. Manat HS, D'Souz GA & Jacob MS. Nebulised magnesium sulphate versus nebulised salbutamol in acute bronchial asthma: a clinical trail. *Eur.Respir.J*. 1998; 12: 341-4.
11. Seaton D. Drug in lung disease In A Seaton & D Seaton (eds) *Crofton and Douglas's Respiratory disease*. Blackwell Science 2000; Edinburg. 193-310.
12. McFadden Jr ER, Elsanadi N, Strauss L, Galan G, Dixon L, McFadden CB et al. The influence of parasympatholytics on the resolution of the acute attacks of asthma. *Am J Med*. 1997; 102: 7-13.
13. National asthma education and prevention program, 1997. Expert Panel Report-2: Guidelines for the diagnosis and management of asthma . National Institute of Health Publication, no.97-405 LBethesda MD; US

- department of health and human services.
14. Silverman RA, Osborn H, Runge J, Gallagher EJ, Chiang W, Feldman J, Gaeta T, Freman K, Levin B, Mancherje N and Scharf S. IV Magnesium Sulfate in the Treatment of acute severe asthma. *CHEST* 2000; 122: 489-97.
15. Skobeloff EM, Spivey WH, Mcnamara RM & Greenspon L. Intravenous magnesium sulphate for the treatment acute asthma in the emergency department. *JAMA*. 1989; 262: 9.1210-3
16. Noppen M, Vanmaele L, Impens N & Schandevyl W. Bronchodilating effect of intravenous magnesium sulphate in acute severe bronchial asthma. *Chest* 1990; 97: 2. 373-6.
17. Skorodin MS, Tenholder MF, Yetter B, Owen KA, Waller RA, Khandelwahl S. et al. Magnesium sulphate in exacerbation chronic obstructive pulmonary disease. *Arch Intern Med*. 1995; 155: 496-500.
18. Nannini LJ Jr, Pendino JC, Corona RA, Mannario S & Quispe R. Magnesium sulphate as vehicle for nebulised salbutamol in acute asthma. *Am J Med*. 2000; 108: 193-7.
19. Devi PR, Kumar L, Sainghi SC, Prasad R & Singh M. Intravenous magnesium sulphate in acute severe asthma not responding to conventional therapy. *Indian Pediatrics*. 1997; 34: 389-97.
20. Okayama H Aikawa T, Okayama M, Sasaki I-I, Mue S & Takishima I'. Bronchodilating effect of magnesium sulphate in bronchial asthma. *JAMA*. 1987; 257: 8. 1076-8