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Comparison of Nebulized Magnesium Sulfate Plus Salbutamol vs Saline Plus Salbutamol in the Treatment of Acute Asthma

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Abstract **Original Research Article**

Intravenous magnesium sulfate ($MgSO_4$) has successfully been used in the treatment of acute asthma and it can be safely administered via inhalation to the patient with stable asthma. Few studies have been published on the use of nebulized magnesium sulfate in the treatment of acute asthma. The present study investigated the efficacy of nebulized salbutamol plus magnesium sulfate in acute asthma as compared to nebulized salbutamol plus normal saline. This was a randomized controlled clinical trial. We enrolled 80 patients with acute asthma with peak flow <50% of predicted and age between 18-55 years; not required assisted ventilation. After measurement of peak expiratory flow, patient received 2.5mg salbutamol plus either 3 ml isotonic normal saline solution (n=40) or isotonic magnesium sulfate (n=40) through a jet nebulizer. All patients were given 100mg hydrocortisone i/v. Peak flow were reassessed 10 and 20 minutes after single nebulized treatment. Peak flow at baseline was similar in two groups. Then at 10 minutes after nebulization, the mean (±SD) percentage increase in peak flow was greater in magnesium sulfate group (57%±21%) than in the normal saline salbutamol group (43%±18%); difference 14%; (p=0.002). At 20 minutes the percentage increase in peak flow was 31% greater in the magnesium sulfate-salbutamol group_than saline-salbutamol group (91.7%±28.1% vs 60.7%±27.7 %,(p=0.000) and $MgSO_4$-salbutamol group reached PEF of more than 60% while saline salbutamol group not. In patient with acute asthma, isotonic magnesium sulfate when nebulized with salbutamol increased greater peak flow response to treatment in comparison with salbutamol plus normal saline.

Keywords: Nebulized Magnesium Sulfate, Salbutamol, Saline, Acute Asthma, Treatment.

INTRODUCTION

Bronchial asthma is a worldwide problem. Globally it affects over 330 million people (Global asthma report 2018). It affects more than 26 million US population including 6.1 million less than 18 years of age making it frequently encountered clinical problem both in pediatric and adult population and major cause of morbidity in the United States and around the world. In our country, according to the First National Asthma Prevalence Study, 1999 [1] about 7 million people (5.2% of the total population are suffering from current asthma defined as at least three episodes of asthma attack in last 12 months. More than half of these patients are innocent children that are 7.4% of the total pediatric population (1-15 years age group).Most of the death from asthma occurs due to sever acute exacerbation. It is the most common respiratory crisis encountered in clinical practice. There is no epidemiological data regarding acute asthma in our country. Recent epidemiological data for acute asthma suggest there are about 500,000 hospitalizations per year in the United States 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 patients initially managed and discharged from emergency department have a relapse [2]. Globaly an increase in the asthma mortality has been noticed over the past 15 years [3]. 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 1995 [2]. General agreement has yet to be reached about the best way to treat acutely presenting patient and fundamental issue such as choice of drugs and duration of treatment have not been resolved. Currently the corner stone of the therapy for acute asthma is the rapid reversal of the patient's airway obstruction. The main stay of therapy

for acute exacerbation is β_2-agonist therapy repeatedly every 20 minute for one hour (serial 3 nebulization) as initial therapy [4].Despite their effectiveness some percentage of the patient with acute asthma fail to respond to β_2-agonist and as many as 30% of the patient presenting emergency department fails to respond adequately to β_2-agonist and require hospitalization [5]. 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 β_2-agonist [6]. Regarding steroid, it requires hours to demonstrate significant benefit. In case of hydrocortisone, which is usually given 1/v, 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 5h, compared with about 8h for prednesolone [7].Addition of high dose of inhaled ipratropium bromide 0.5mg in adult to an aerosolized solution of selective β_2-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 report 'trends' that fail to reach statistical significance [7]. Given the slowness of the onset of action of anticholinergic and 60-90 minutes lag time before achieving a peak effect and their relatively limited bronchodilator activity, anticholinergic agents such as ipratropium bromide are not 1st line therapy for acute asthma. In the emergency department theophylline is not recommended because it appears to provide no additional benefit to optimum inhaled β_2-agonist therapy and steroid and increases the adverse effect [4]. It has narrow therapeutic index and frequently associated with adverse effect even in therapeutic dose. Patient vary widely in dose requirement to keep plasma level therapeutic [7].Intravenous theophylline is less effective than nebulized β_2-agonist and should therefore be reserved for the few patients who fail to respond to β_2-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 administration [7]. 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, which are resistant to standard bronchodilator treatment. This ideal drug should be fast acting, safe and effective.

OBJECTIVES

General objectives

- To compare the bronchodilating effect of isotonic magnesium sulfate with salbutamol to normal saline with salbutamol when nebulized in acute asthma patient in the emergency room.

Specific Objectives

- To establish that magnesium sulfate nebulized with salbutamol is effective in the treatment of acute asthma patient;
- To determine that there is better response when isotonic magnesium sulfate is used instead of normal saline as a vehicle for nebulized sulbutamol in the treatment of acute asthma.
- To elucidate any adverse effect when salbutamol is nebulized with magnesium sulfate in acute asthma patient.

METHODS

We carried out a prospective control study in the Asthma Outpatient Department, National Institute of Diseases of the Chest & Hospital (NIDCH), Mohakhali, Dhaka during the period from January 2001 to December 2002 with known case of asthma patients or newly diagnosed asthma patient who presented to the emergency department with an acute asthma exacerbation. 120 patients were screened for the study. 80 patients met the criteria and included in the study. 40 were in saline salbutamol group (taken as control) denoted Group A and 40 patients were in the magnesium salbutamol group denoted Group B. Patients were allocated into two groups randomly. In each case, patient's consent was taken for the control and test groups for enrollment in the 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. After baseline PEFR reading patient of group B received single nebulization with salbutamol 0.5ml (2.5mg) diluted with 3ml isotonic magnesium sulfate solution (7.5% especially prepared by Beximco Pharmaceuticals Ltd, Bangladesh) or group A received sabutamol0.5ml (2.5mg) diluted with 3ml normal saline (Glaxo Wellcome, Bangladesh) . Both group received 100mg IV hydrocortisone. Vital signs and any adverse effects monitored for half an hour, PEFR measurement (by mini wright Peak flow meter (Clement Clark. International Ltd. London, UK) was taken again at 10 minute and at 20 minute after nebulization. We performed SPSS (Statistical Package for Social Science) software for analyzing data. Unpaired't' tests were used to compare means between two groups. Chi-square analysis was done to compare sex distribution. Initially baseline data between the two groups were compared. Then the improvement in the peak flow response were compared at different time at 10 minute and 20 minutes by unpaired student't' test. Results were

considered to be statistically significant at the p value of <0.05.

Inclusion Criteria

Known cases or newly diagnosed bronchial asthma patient of either sex, Age 18-55 years, who gave informed consent, Capable of measuring PEF, PEFR below 50% of predicted, Nonsmoker.

Exclusion Criteria

Febrile, Any evidence of lower respiratory tract infection, i.e. purulent sputum, pneumonia., Had any history or evidence of cardiac, renal or hepatic dysfunction, Pregnant women; breast feeding mother, Very tired, Poor level of patient cooperation, Smoker >5 pack-year (former or current smoker), Cyanosis or obtunded consciousness, Use of aerosol of salbutamol in the previous four hours, Use of steroid (oral/parenteral) in the preceding week

RESULTS

Out of 120 patients screened over a period of 2 years only 80 patients met the study criteria and were included in the study. Most of the patients not included were those had other diagnosis such as evidence of lower respiratory tract infection, purulent sputum and premeditated in the last night or morning before their presentation. Only single visit were considered. Comparison between the baseline data of the two group shows there is no significant differences between them regarding age, gender, height, duration of asthma, days of exacerbation; vital signs also similar between the two groups (Table I).Baseline peak expiratory flow rate (litre/minute) between the two groups both in absolute value and percentage predicted were similar and statistically there were no difference between the groups. Absolute value mean ±SD for saline group was 152±43 litre/minute and for magnesium group was 152±40. P-value is reached by unpaired‘t’ test and was 0.9. Mean of percentage predicted value for saline group was 35%±11% and for magnesium group was 34%±9% (P-value 0.78) (Table IV). So, it was also similar between two groups. At 10 minute, mean of peak expiratory flow rate (absolute value) for saline group was 213±48 L/min and for magnesium group was 239±59 L/min. P-value 0.03. So, there is significant difference between the two groups. Absolute difference is about 26 litre/min. Mean of percentage predicted peak expiratory flow rate at 10 minute for group A was 49%±13% and for group B was 54%±14%, P-value were 0.09. So, there was no significant difference between the groups. (Table V). Mean of absolute increase in the peak flow rate from baseline for saline group was 60.4±20.8 and for magnesium group was 82.9±32. Absolute increase for magnesium group is about 20litre/min (average) higher than the saline group. Statistically the difference is highly significant. P value <0.001 (Table V).Percentage increase in the peak flow rate between the two group at 10 minute after nebulization shows that mean value for saline group and for magnesium group was 43%±18% and 57%±21% respectively. P-value 0.002 (<0.01) (Table V).So, at 10 minute after nebulization there is significant difference between the groups regarding peak expiratory flow rate (absolute) value, absolute improvement in PEFR and percentage improvement from baseline but no difference between the mean of percentage predicted value achieved. At 20 minute after nebulization PEFR absolute value for saline and magnesium group were 237±52 litre/minute and 290±55 litre/minute respectively. P-value <0.001 showed that is highly significant difference between the value statistically (Table VI). Mean of percentage predicted peak expiratory flow reached at 20 minute for saline group and magnesium group was 54%±12% and 65%±14% (p-value 0.001), i.e., significantly different (Table VI).Absolute increase in the peak expiratory flow rate (mean value) were 85±26 litre/min and 135±33 litre/min for Group A and Group B respectively. It also shows highly significant difference (p-value <0.001) between the groups (Table VI).Finally percentage increase in the peak expiratory flow rate from baseline value at 20 minutes were 60%±27% and 91%±28% for saline group and magnesium group respectively. P-value <0.001 (Table VI).So, at 20 minutes all the value obtained between the two group i.e., peak expiratory flow rate absolute value (mean), percentage predicted PEFR absolute PEFR increase and percentage increase in the PEFR from the baseline are significantly higher in the Group B than the Group A. There were no significant difference between the groups regarding changes in Blood pressure, Heart rate or respiratory rate either at 10 minutes or at 20 minutes (Table VII) in the both the groups. Systolic blood pressure declined about 8 mm of Hg at 20 minutes in both groups. None of the subjects could distinguish the magnesium sulphate solution and none complained of any adverse effects. Out of 40 patients in the saline group, 8 patients did not improved and their PEF percentage predicted remained below 40% after first nebulization and required addition nebulization of which 5 patients (12.5%) warranted admission. But in magnesium group, 5 patients required additional care and 2 (5%) of which warranted admission (Table VIII).

Table-I: Baseline characteristics of the patient of two groups (n=80)

	Group A (n=40)	Group B (n=40)	P-value
	Number (percent) or Mean ±SD		
Age in years	34.78±12.89	32.65±9.81	0.29^{NS}
Gender Male Female	10 (25%) 30 (75%)	11 (27.5%) 29 (62.5%)	>0.50
Years of Asthma	7.37±4.87	6.73±5.76	0.58^{NS}
Symptoms Days	4.85±3.08	5.10±3.46	0.73^{NS}
Height (inches)	59.65±2.72	61.12±3.14	0.20
Respiratory Rate (per minute)	30.05±5.90	31.0±5.97	0.47^{NS}
Pulse Rate (per minute)	118.88±11.42	120.9±11.05	0.42^{NS}
Systolic Blood Pressure (mm of Hg)	116.75±11.91	115.00±19.41	0.62^{NS}
Diastolic Blood Pressure (mm of Hg)	75.63±9.82	74.87±6.93	0.69^{NS}

Table-II: Age distribution of the study participants (n=80)

Age in years	Study group		Total
	Group A	Group B	
<25	11 (27.5%)	11 (27.5%)	22 (27.5%)
25-34	10 (25%)	12 (30%)	22 (27.5%)
35-44	13 (32.5%)	10 (25%)	23 (28.7%)
>45	6 (15%)	7 (17.5%)	13 (16.25%)
Total	40 (100%)	40 (100%)	80 (100%)

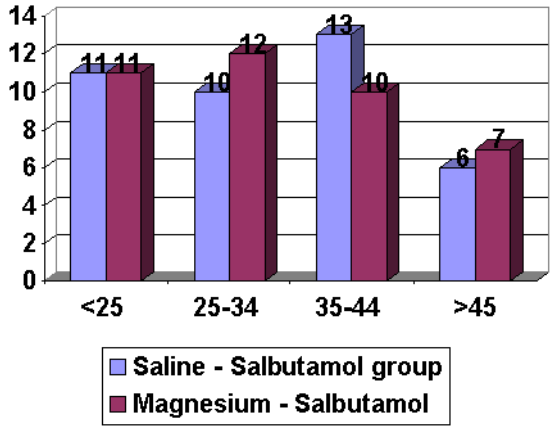

Fig-I: Bar diagram showing age distribution of the study subjects (n=80)

Table-III: Sex distribution of study subjects (n=80)

Sex	Group A	Group B	Total	P-value
Male	10	11	21	>0.5
Female	30	29	59	NS
Total	40	40	80	

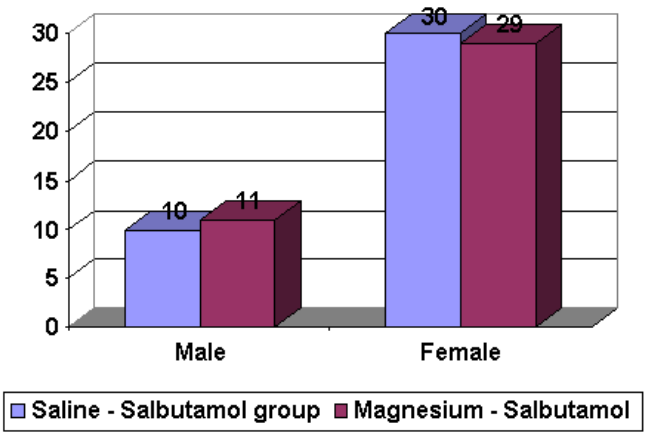

Fig-II: Bar diagram showing sex distribution of study subjects (n=80)

Table-IV: Comparison of the peak flow rates between the two groups at baseline (n=80)

At Baseline	Group A(n=40)	Group B(n=40)	P-value
	Mean ±SD		
Peak flow (L/min)	152.12±43.24	152.89±40.14	0.96 NS
Percentage predicted peak flow	35.30±11.02	34.65±9.62	0.78 NS

Table-V: Comparison of responses in PEF at 10 minutes after nebulization (n=80)

Parameter	Group A(n=40)	Group B(n=40)	P-value
	Mean ±SD		
Peak flow (L/min)	213.0±48.0	239.0±59.0	0.03
Percentage predicted peak flow	49.0±13.0	54.0±14.0	0.09
Absolute increase in PEF (L/min)	60.0±20.0	82.0±32.0	0.000
Percentage increase in PEF (%)	43.0±18.0	57.0±21.0	0.002

Table-VI: Comparison of responses in PEF at 20 minutes after nebulization (n=80)

Parameter	Group A (n=40)	Group B(n=40)	P-value
	Mean ±SD		
Peak flow (L/min)	237.0±52.0	290±55.0	0.000
Percentage predicted peak flow	54.0±12.0	65.0±14.0	0.001
Absolute increase in PEF (L/min)	85.0±26.0	135.0±33.0	0.000
Percentage increase in PEF (%)	60.0±12.0	91.0±28.0	0.000

Table-VII: Compare of the patients vital sign between the two groups after 20 minutes (n=80)

Signs	Group A Group	Group B	P-value
	Mean ±SD		
Respiratory rate (per minute)			
Baseline	30.05±5.90	31.0±7.97	>0.1 (NS)
At 20 minutes	22.87±5.72	22.76±4.30	>0.1 (NS)
Heart rate (per minute)			
Baseline	118.88±11.42	120.90±11.05	>0.1 (NS)
At 20 minutes	100.52±12.15	102.37±11.32	>0.1 (NS)
Blood pressure (mm of Hg)			
a) Systolic - Baseline	116.75±11.91	115.0±19.41	>0.1 (NS)
At 20 minutes	108.72±11.03	107.12±13.23	>0.1 (NS)
b) Diastolic - Baseline	75.63±9.82	74.88±6.93	>0.1 (NS)
At 20 minutes	73.56±8.72	74.26±9.62	>0.1 (NS)

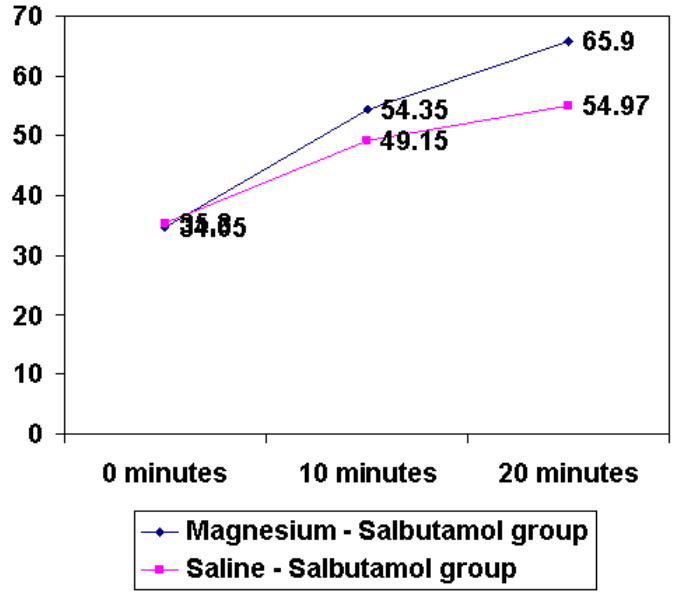

Fig-III: The figure shows more improvement in $MgSO_4$-Salbutamol group both at 10 and 20 minutes (n=80)

Table-VIII: Profile of the response and management of the patients in the two groups (n=80)

Group	Enrolled	No additional care	Additional care	Warranted admission
A	40	32	8	5 (12.5%)
B	40	35	5	2 (5%)

DISCUSSION

(ii) This prospective, controlled study has shown that combining isotonic magnesium sulfate to salbutamol results in greater improvement in peak flow compared with the standard approach (salbutamol and normal saline) for nebulization in the initial treatment of acute exacerbation of bronchial asthma. The effect was evident within 10 minutes and was maintained at 20 minutes after the nebulization is complete. PEFR expressed as percentage predicted value eliminate gender, age and height bias and percentage improvement in PEFR from baseline eliminate the bias introduced by difference in the degree of initial airflow obstruction. Difference in percentage improvement of PEF detected both at 10 minutes and 20 minutes [(43%±18% vs 57%±21% at 10 minutes, p-value 0.002 and 60%±27% vs 91%±28% at 20 minutes, p-value 0.000 (<0.001)]. But the percentage predicted PEF achieved at 10 minutes not significantly different between the groups (49%±13% vs 54%±14%). Though ultimately at 20 minutes percentage predicted value were significantly different (54%±12% vs 65%±14%).One of the treatment goals in acute asthma is to achieve as rapidly as possible a safe value for the percentage predicted peak flow of about 60% [8] in order to reduce the likelihood of relapse and prevent hospitalization. At 10 minutes the mean percent of predicted peak flow in the magnesium sulfate – salbutamol group was 54%±14% which was slightly greater than in the saline salbutamol group (49%±13%) but both value were below 60% (percentage predicted peak flow).At 20 minutes the mean percentage of predicted peak flow in Group B was 65%±14% which is greater than that of expected safe value for the percentage predicted value of about 60% and the value achieved is comparable with those seen with a higher dose (5mg) of salbutamol nebulization in a study in acute asthma [9]. Hyperosmolar solution delivered by jet nebuliser might induce bronchoconstriction. So, we chose an isotonic solution of magnesium sulfate. This may explain why some studies that used hypertonic magnesium found neither bronchodilator nor protective effect despite greater doses of magnesium. Hill and co-worker [10], used 3ml of normal saline as placebo and 3ml normal saline containing 180mg magnesium sulfate for nebulization, [the osmolarity was 817 mosm/kg (saline 290 mosm/kg)] in his study to see the effect of inhaled magnesium on airway reactivity to histamine and adenosine monophosphate. They found that in histamine study, the provocative dose required to reduce FEV_1 by 20% (PD_{20} FEV_1) was significantly lower after magnesium nebulization than after placebo and concluded that magnesium did not protected the airway, moreover caused increased reactivity. This was due to hyper osmolar $MgSO_4$ solution used by them that probably caused increased reactivity. Similarly study conducted by Mitchem and Salzman [11] used 4cc of 50% of $MgSO_4$ (2 gm) plus 0.5 cc salbutamol (2.5mg) as nebulization. This study was similar to the present study but they used hyperosmolar solution of $MgSO_4$ plus albuterol & failed to show significant bronchodilator effect over that of albuterol (+ saline) alone (P-value at 0.27). Nannini *et al*. [12] conducted similar study to the present study. They used 3cc

isotonic magnesium sulfate (7.5%) plus salbutamol 0.5 cc (2.5mg) for one group and 3cc saline (0.9%) plus salbutamol 0.5cc (2.5mg) for other group. PEF improvement was found at 10 minutes and maintained at 20 minutes. They found only the percentage increase in the peak flow at 10 minutes (61%±45% vs 31%±28%, p-value 0.03) and at 20 minutes (100%±100% vs 43%±31%) were significantly different between the groups. But the absolute PEF value (at 10 minute, 284±24 vs 258±25, p-value 0.47 and at 20 minutes 332±119 vs 282±107, p-value 0.2), percentage predicted value achieved (at 10 minutes 56%±4% vs 49%±5%; at 20 minutes 65%±18% vs 54%±19%) is not significantly different between the groups. Here again the percentage predicted value reached with $MgSO_4$ group is safe value (>60%); not reached by saline group similar to the present study. But the number of patients was 16 for saline salbutamol group and 19 for magnesium-salbutamol group. Magnat, D'Souza and Jacob [18] used 3.2% $MgSO_4$ 3ml (65mg) solution and compared it directly with salbutamol-saline solution in acute asthma and found a significant bronchodilating effect of $MgSO_4$ that was similar to that of the nebulized salbutamol. Their study and result of the present study suggest that magnesium has bronchodilating effect on airway smooth muscle in acute asthmatic and that both magnesium and salbutamol may have additive effect on bronchial smooth muscle. Indeed combining terbutaline, a b_2-agonist and magnesium is unlikely to result in serious short term adverse events, if used acutely in patients with relatively normal cardiac and metabolic function. $MgSO_4$ may acts by potentiating the effects of b_2-agonist on magnesium requiring enzymes such as adenylcyclase, and sodium-potassium ATPase or perhaps by offsetting β_2-agonist tachyphylaxis [13].Several studies used intravenous $MgSO_4$ for acute asthma successfully. Intravenous $MgSO_4$ can be used as an adjunct to conventional nebulization and other therapy but if nebulization of salbutamol plus magnesium sulfate can do the same effect it will be convenient both for the therapist and for the patient. So the nebulized magnesium sulfate (+salbutamol) is preferable to intravenous magnesium.Most of the study to see the effect of magnesium sulfate on asthma were conducted in acute asthma [beginning with Rosella and Pla [14] and Haury [15] used mainly intravenous magnesium sulfate in patient refracting or not responding to conventional treatment. But very few studies were conducted till date with nebulized magnesium ± salbutamol in acute asthma. Works done on nebulized magnesium and our study showed significant bronchodilating effect of nebulized magnesium (±salbutamol) on airway in acute asthma patient and the effects are comparable to conventional bronchodilator treatment. Magnat & co-worker's used $MgSO_4$ alone and Nannini *et al*. [12] used magnesium sulfate and salbutamol combined like the present study. Both the study showed bronchodilating action of magnesium sulphate in acute asthma. Sample size is one of the limitations of this study. Most who were excluded due to associated smoking history, lower respiratory tract infection and history of taking bronchodilator or steroid? Some patients may conceal the drug history which may influence the result of the study; some other patient could not mentioned the name of the drug accurately which they had taken previously. In this study, another group could be included with nebulization with magnesium sulfate alone like Magnat and co-worker, which could explain more clearly the role of nebulise magnesium sulfate in the treatment of acute asthma and regarding its side effect. Current recommendation for initial treatment of acute asthma is that serial three nebulization at 20 minutes interval for 1 hour [16], according to response. We adopted one nebulization to see the effect even in severe acute asthma patients whose peak flow rate were average 35% of the predicted. The outcome could be more if those protocols were adopted to see the effect and outcome of the nebulizations in the study. Emergency room setting in our country is not adequate. Even in the Asthma Centre, NIDCH, the study faced unavailability of the more oxygen cylinder, due to lack of which we had to exclude some of the patient from the study. Few patients failed to get immediate administration of steroid injection as per protocol. Oxygen was used as 5 Litre/min (40% oxygen) by nasal cannula though Nannini *et al*. [12] used jet nebuliser driven by oxygen. British Thoracic Society [17] also recommended this.This study was hospital-based as dealing with emergency but not multicentred. Objective measurements were done with PEF not with FEV_1 (spirometry). Though, the correlation between PEFR and FEV_1 in asthma is good. So the recommendations from the prospective control study are: Isotonic magnesium sulfate 3 ml should be used instead of conventional normal saline with salbutamol 0.5 ml (2.5 mg) in the serial nebulization of acute asthma as initial treatment in the emergency department as well as in the admitted patient.

Limitations of the study

This was a single centre study with small sample size. So, study results might not reflect the scenarios of the whole country.

Recommendations

Patient not responding to initial nebulization with saline salbutamol must try with magnesium-salbutamol nebulization in the asthma ward. Isotonic magnesium sulfate should be available in the market for use in acute asthma treatment in 3 ml ampoule because use from 500 ml bag has the chance of contamination of the solution and risk of infection from direct inhalation. Further multicentred broad based study should also be carried out using magnesium sulfate with salbutamol in our Asthma Centre as well as other institution treating acute asthma patient before recommending it in the National Asthma Guideline for management of acute asthma patient.

CONCLUSIONS

This prospective controlled study concluded that nebulization with Isonotic Magnesium Sulfate and Salbutamol combined have better bronchodilating effect than salbutamol and normal saline in acute asthma. Patients treated with nebulized Magnesium Sulfate and Salbutamol quickly reach the safe value than saline-salbutamol. Magnesium Sulfate plus Salbutamol can be nebulized safely without any unwanted side effect.

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