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Efficacy of nebulized magnesium sulfate in the treatment of acute exacerbation of asthma in children

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Abstract

A double-blind randomized controlled trial was conducted to examine the efficacy of nebulized magnesium sulfate in the treatment of acute exacerbation of asthma in children. Thirty patients received nebulized salbutamol (0.15 mg/kg; minimum dose 2.5 mg) with 2.0 mL of isotonic magnesium sulfate solution and another 30 patients received same dose of salbutamol with 2.0 mL of normal saline on 3 occasions at 20 min intervals. Mean percent of predicted peak expiratory flow rate (PEFR) detected in both group at 0 min were not significantly different. But from 10 min up to 60 min, the values were significantly different among the groups. Mean respiratory rate at 0 and 10 min were similar in both groups and from 20 up to 60 min, respiratory rate improvement were significantly different. Arterial oxygen saturation (SaO_2) at presentation was not significantly different. But from 10 min up to 60 min differences were significant. With single dose of nebulization, in the magnesium sulfate with salbutamol group, by 20 min almost all (29 out of 30) patient achieved at least 60% of predicted PEFR. Within this 20 min, from control group none could achieve 60% of predicted PEFR. After 2nd dose of nebulization control group started achieving 60% PEFR value. Regarding response criteria, with 2nd dose of nebulization, at 30 and 40 min 9 (30.0%) and 17 (56.7%) patient from magnesium sulfate with salbutamol group showed good response (PEFR ≥70% predicted). But within this first 40 min time, none could show good response in control group. With 3rd dose of nebulization all from magnesium sulfate group showed good response but even at 60 min, 4 (13.3%) patient in control group failed to be included as good responder. So, it is evident that nebulization by isotonic magnesium sulfate solution with salbutamol provide early and better response as compared to conventional approach (salbutamol plus normal saline) in acute exacerbation of asthma in children.

Introduction

In patients with acute asthma exacerbation, the use of isotonic magnesium as a vehicle for nebulized salbutamol produced a significantly greater increase in peak expiratory flow compared with salbutamol in saline. The more severe the baseline obstruction, the greater the response to the combined magnesium sulfate and salbutamol, which supports the observation that magnesium is particularly effective in acute exacerbations of asthma (Nannini et al., 2000).

The anticholinergic has little role if added to the repeated dose of β_2-agonist; use of xanthine derivatives (methylxanthine) in acute asthma is controversial and steroid takes at least a few hours to act (Expert panel report-2, 1997). The use of nebulized magnesium sulfate, in addition to a β_2-agonist, in the treatment of acute

exacerbation of asthma appears to produce benefits with respect to improved pulmonary function (Blitz et al., 2005).

Bronchodilating effect of intravenous magnesium sulfate and its use and efficacy were suggested (Bloch et al., 1995; Boonyavorakul et al., 2000; Santana et al., 2001). On the contrary, data on nebulized magnesium sulfate have been scant. The effect of nebulized magnesium sulfate as a vehicle for salbutamol has been less evaluated (Kokturk et al., 2005). In pediatric population this type of study is very rare.

Quickly achieving at least 60% predicted peak expiratory flow rate (PEFR) reduces the likelihood of relapse and hospitalization rate. One of the treatment goals in acute exacerbation of asthma is to achieve as rapidly as possible a safe value for the percentage predicted peak flow of about 60% (Nannini et al., 2000).

Initial assessment of pulmonary function before treatment and repeat assessment after three dose of nebulization is necessary to categorize response (good, incomplete or poor) of individual patient (Expert panel report-2, 1997). At present, regarding assessment of response, no published study is known in pediatric population.

Most of the studies (Nannini et al., 2000; Mollick, 2003) measured 1st outcome at 10 min after completion of the nebulization. Some studies also measured 1st outcome at least 30 min after completion of nebulization. Nebulization itself may continue for 5-10 min depending upon the volume of fluid/drug and properties of the nebulizer. In practical, their 1st measurement lies at not earlier than 15-20 min from the start point. No known study done measuring outcome before 10 min after completion of nebulization. In some study, it is found that magnesium sulfate nebulization has shown better response as compared to normal saline. But no known study completed recommended schedule of 3 doses of nebulization.

The present study was carried out to see the effect of nebulized magnesium sulfate in presence of salbutamol in the treatment of acute exacerbation of asthma in children.

Materials and Methods

Duration of study

A double-blind randomized controlled trial was carried out from January to July 2006.

Study population

A total of 60 children with acute exacerbation of asthma presented to the Pediatric Pulmonology Follow-up Clinic and Asthma Centre, BSMMU were included. Children (age range 7-16 years) of either sex with acute exacerbation of asthma and capable of measuring PEFR were included. Exclusion criteria included a) severely ill patient requiring immediate hospital care, b) any evidence of respiratory tract infection or suppurative lung diseases, c) any history or evidence of cardiac, renal or hepatic dysfunction, d) use of short acting bronchodilator within 8 hours or long acting bronchodilator within 24 hours, and e) use of steroid within 7 days. They were distributed randomly as 30 patients in nebulized isotonic magnesium sulfate with salbutamol group and the rest 30 in nebulized salbutamol with normal saline i.e., control group.

Ethical issue

The protocol of the study was approved by the Ethical Committee, Bangabandhu Sheikh Mujib Medical University. Before enrolment, the aims and objectives of the study along with its procedure and benefits or draw-backs were explained to the guardian and patient (where applicable) in details in an understandable way. In case of any query, they were answered. When the guardian became satisfied, informed consent was obtained from the guardian and the patient was included in the study. They also had freedom to withdraw from the study at any time they would like.

Materials/instruments used

a) salbutamol respirator solution containing 5 mg of salbutamol per mL (Ventolin respirator solution, Glaxo Welcome Bangladesh Ltd.); b) normal saline (0.9% NaCl, Institute of Public Health, Bangladesh); c) isotonic magnesium sulfate solution (7.5 g/100 mL, 286 mOsm; d) 60 sets of identical eppendorf tube (each set containing 3 eppendorfs); e) nebulizer with face mask (medel AERO-FAMILY®); f) Pulse oxymeter (BIONICS® BPM-200); and g) Peak flow meter (Mini-Wright™, Clement Clarke International Ltd, UK).

Preparation for double-blind study

Sixty sets of identical eppendorf tube (each set containing 3 eppendorf tube) were taken and labeled serially from 1 to 60. In any set all the 3 eppendorf tube had the same label number. By following random table, prepared a coding sheet to distribute the eppendorf randomly within the two groups each containing 30 sets. According to the grouping based on label number, each set of eppendorf tube was filled with appropriate solution i.e.; isotonic magnesium sulfate solution in magnesium sulfate group and normal saline in control group. In any set, each eppendorf tube contained 2.0 mL of same fluid (either isotonic magnesium sulfate or normal saline solution). Coding sheet was returned back to and preserved by the guide till the time to analyze the data.

Clinical procedure

Clinical examinations of the patients were done with regards to the vital signs of acute attack as well as the chest findings as per requirements of the study. Questionnaire-cum-data sheet filled in. Objective measurement of airway obstruction was recorded with a peak flow meter. The procedure of using the peak flow meter was demonstrated to the patient. The use of peak flow meter was repeated at 10, 20, 30, 40, 50 and 60 min from the start point. Starting from 0 min, every patient was under continuous monitoring with pulse oxymeter and readings regarding SaO_2. Pulse and respiratory rates were recorded every 10 min starting from 0 min up to 60 min. In this step, at 0 min, each patient was given salbutamol (0.15 mg/kg; minimum dose 2.5 mg) along with the content solution of an eppendorf tube (containing 2.0 mL of either isotonic magnesium sulfate or normal saline solution), from a set based on serial, by air driven nebulizer with face mask.

Emptiness of the nebulizer was guided by lack of any further mist. When the nebulizer was sputtered it was gently shaken and then driven again until there was no more mist. First dose of nebulization done at 0 min. Immediately after recording the information/data on data sheet, this step was repeated with 2nd dose of nebulization at 20 min and 3rd dose of nebulization at 40 min from start point using the eppendorf of same set.

Statistical analysis

Coding sheet was collected from the guide, data decoded and analyzed. Results were expressed as mean ± SD. Most of the analyses were done by SPSS 12.0 for Windows (Statistical package for social sciences) software. Unpaired Student's t-tests were used to compare means between two groups. Chi-square analysis was done to compare distribution of age, sex, family history of asthma, history of smoking, medication and presenting symptoms and signs. Confidence interval was set at 95% level. Results were considered to be statistically significant at p value <0.05.

Results

Table I shows the baseline characteristics of patients of two groups. Age of the patients in magnesium sulfate group was 11.8 ± 2.4 years whereas in control group it was 10.8 ± 2.8 years. In the isotonic magnesium sulfate with salbutamol group, 12 patients were male and 18 female. On the other hand in the control group, 13 were male and 17 female. In magnesium sulfate group and control group height was 57.2 ± 5.4 inches and 54.9 ± 6.2 inches respectively. Weights of the patient in magnesium sulfate group and control group were 35.8 ± 8.9 kg and 33.9 ± 10.1 kg respectively. The duration of asthma was 1.6 ± 1.0 years in the magnesium sulfate group and 1.3 ± 0.5 years in the control group. In all cases the differences between the groups were not statistically significant.

Table II shows that there was history of taking oral short acting β_2-agonist in 26 cases in the magnesium sulfate group and 24 cases in the control group. Short acting inhaled β_2-agonist was taken by 2 and 4 patients in the magnesium sulfate group and control group respectively. The differences were not statistically significant.

All the children were conscious and not cyanosed at presentation. Table III shows that only 1 patient from magnesium sulfate group and 2 from control group were exhausted during presentation. Twenty eight patients talked in phrases and 2 in words in the magnesium sulfate group whereas 26 patients talked in phrases and 4 in words in the control group. In the magnesium sulfate group, loud and very loud wheeze was present in 25 and 5 patients respectively while in the control group they were found in 27 and 3 patients. The differences were not statistically significant in all the parameters in both the group. In all cases pulse rate

Table I

Baseline characteristics of patients

Parameters	Magnesium sulfate with salbutamol (n = 30)	Salbutamol (n = 30)	p value
Age (years)	11.8 ± 2.4	10.8 ± 2.8	>0.10^{ns}
Sex			
Male	12	13	
Female	18	17	
Height (inch)	57.2 ± 5.4	54.9 ± 6.2	>0.10^{ns}
Weight (kg)	35.8 ± 8.9	33.9 ± 10.1	>0.10^{ns}
Duration of asthma (years)	1.6 ± 1.0	1.3 ± 0.5	>0.10^{ns}
Family history of asthma	26	25	ns

Data are mean ± SD ; ns = not significant

Table II

Beta-2 agonist taken within seven days of presentation

β_2-agonist	Magnesium sulfate with salbutamol group (n = 30)		Salbutamol (control) group (n = 30)	
	No.	(%)	No.	(%)
Oral short acting	26	(86.7)	24	(80.0)
Oral long acting	2	(6.7)	2	(6.7)
Inhaler short acting	2	(6.7)	4	(13.3)
Inhaler long acting	0	(0.0)	0	(0.0)

Table III

Presenting symptoms and signs

Parameters	Magnesium sulfate with salbutamol (n = 30)		Salbutamol (n = 30)	
	No.	(%)	No.	(%)
Symptoms				
Breathlessness during				
Talking	28	(93.3)	26	(86.7)
Resting	2	(6.7)	4	(13.3)
Physical exhaustion				
Yes	1	(3.3)	2	(6.7)
No	29	(96.7)	28	(93.3)
Talks in				
Phrases	28	(93.3)	26	(86.7)
Words	2	(6.7)	4	(13.3)
Signs				
Wheeze				
Loud	25	(83.3)	27	(90.0)
Very loud	5	(16.7)	3	(10.0)
Use of accessory muscle				
No	2	(6.7)	2	(6.7)
Yes	28	(93.3)	27	(90.0)
Prominent	0	(0.0)	1	(3.3)
Pulse (per min)				
100-160	30	(100.0)	30	(100.0)
PEFR (%)				
40-60	30	(100.0)	30	(100.0)
SaO_2				
94% - 90%	29	(96.7)	28	(93.3)
<90%	1	(3.3)	2	(6.7)

was within 100-160 per min and PEFR was 40-60 percent of predicted value. In magnesium sulfate group and control group 28 and 26 patients respectively were breathless during talking while 2 and 4 patients were breathless during resting.

Table IV shows baseline PEFR (l/min) between the two groups both in absolute value and percent of predicted were similar. Absolute value (mean ± SD) for magnesium sulfate group was 164.2 ± 35.0 l/min and for control group was 146.7 ± 40.9 l/min. P value was reached by unpaired Student's 't' test and was >0.05 which was not significant. Mean of percent predicted value for magnesium sulfate group and control group

Table IV

PEFR (l/min) status at different times

Parameters	Magnesium sulfate with salbutamol group (n=30), PEFR (L/min) mean ± SD	Salbutamol (control) group (n=30) PEFR (l/min) mean ± SD	p value
Predicted	336.2 ± 71.5	305.1 ± 82.1	>0.10[ns]
0 min (baseline)	164.2 ± 35.0	146.7 ± 40.9	>0.05[ns]
Mean % of predicted	48.9 ± 2.4	48.0 ± 2.2	>0.10[ns]
10 min	192.3 ± 40.3	166.8 ± 44.0	<0.05[a]
Mean % change from 0 min	17.4 ± 5.5	14.2 ± 5.7	<0.05[a]
Mean % of predicted	57.3 ± 1.7	54.8 ± 2.0	<0.001[a]
20 min	209.2 ± 41.7	174.5 ± 46.6	<0.01[a]
Mean % change from 0 min	28.0 ± 7.0	19.4 ± 6.0	<0.001[a]
Mean % of predicted	62.4 ± 1.8	57.24 ± 1.53	<0.001[a]
30 min	229.2 ± 46.1	189.0 ± 49.8	<0.01[a]
Mean % change from 0 min	40.2 ± 8.2	29.4 ± 5.7	<0.001[a]
Mean % of predicted	68.4 ± 1.9	62.1 ± 1.6	<0.001[a]
40 min	235.3 ± 48.4	194.8 ± 52.7	<0.01[a]
Mean % change from 0 min	43.8 ± 7.1	33.2 ± 6.0	<0.001[a]
Mean % of predicted	70.1 ± 1.0	63.9 ± 1.5	<0.001[a]
50 min	250.3 ± 52.2	211.7 ± 56.9	<0.01[a]
Mean % change from 0 min	52.9 ± 8.4	44.8 ± 7.1	<0.001[a]
Mean % of predicted	74.5 ± 1.4	69.4 ± 1.7	<0.001[a]
60 min	257.8 ± 52.9	216.5 ± 57.5	<0.01[a]
Mean % change from 0 min	57.6 ± 9.1	48.2 ± 7.0	<0.001[a]
Mean % of predicted	76.8 ± 1.8	71.0 ± 1.5	<0.001[a]

Unpaired Student's 't' test; ns = not significant, [a] = significant

were 48.9 ± 2.4 and 48.0 ± 2.2 respectively and the differences were also non-significant (p value >0.10).

At 10 min, mean PEFR, mean percent change from 0 min and mean percent of predicted value for magnesium sulfate group and control group respectively were 192.3 ± 40.3 and 166.8 ± 44.0 (p value <0.05); 17.4 ± 5.5 and 14.2 ± 5.7 (p value <0.05); 57.3 ± 1.7 and 54.8 ± 2.0 (p value <0.001) respectively. So, at 10 min, there were significant differences between the groups regarding peak flow rate (absolute value), percent improvement from baseline and improvement in percent predicted value. Similar types of results were found up to 60 min of the study period.

Table V shows, at presentation, all the patient had PEFR <60% of predicted value. In the magnesium sulfate group at 10 min from the start point only 2 (6.7%) patient and at 20 min 29 (96.7%) patient achieved at least 60% of predicted PEFR. So with single dose of nebulization, almost all children (29 out of 30) achieved at least 60% predicted PEFR in magnesium sulfate group. Within this 20 min, in the control group none could achieve PEFR at least 60% of the predicted value.

Immediately after recording data as per schedule, second dose of nebulization done at 20 min (from start point). After another 10 min i.e.; at 30 min from start point 30 (100.0%) and 28 (93.3%) patient from magnesium sulfate group and control group respectively achieved at least 60 percent predicted value. From 40 min, all patient from both the group achieved PEFR at least 60 percent predicted.

Table VI shows that within 20 min, none could show the good response. Second dose of nebulization done at 20 min and after that, at 30 and 40 min only 9 (30.0%) and 17 (56.7%) patients respectively in the magnesium sulfate group showed good response.

Despite of using two doses of nebulization, within this first 40 min time, from control group none could show good response (PEFR ≥ 70.0% of predicted).

Immediately after recording data at 40 min 3rd dose of nebulization done. At 50 min, 30 (100.0%) patient from magnesium sulfate group and 9 (30.0%) patient from control group showed good response. Finally at 60 min 4

Table V

Comparison of patients achieving at least 60% of predicted value

Parameters	Magnesium sulfate with salbutamol group (n = 30)	Salbutamol (control) group (n = 30)
At 0 min PEFR		
≥60% of predicted	0	0
<60% of predicted	30	30
At 10 min PEFR		
≥60% of predicted	2	0
<60% of predicted	28	30
At 20 min PEFR		
≥60% of predicted	29	0
<60% of predicted	1	30
At 30 min PEFR		
≥60% of predicted	30	28
<60% of predicted	0	2
At 40 min PEFR		
≥60% of predicted	30	30
<60% of predicted	0	0
At 50 min PEFR		
≥60% of predicted	30	30
<60% of predicted	0	0
At 50 min PEFR		
≥60% of predicted	30	30
<60% of predicted	0	0

(13.3%) patient from the control group failed to be included as good responder.

As shown in Table VII, respiratory rate, pulse rate and SaO_2 were also recorded at 0, 10, 20, 30, 40, 50 and 60 min. At 0 min, regarding all the parameters, differences between two groups were not significant. From 10 to 60 min, differences of mean PEFR percent of predicted were always significant between the groups (p value <0.001).

Respiratory rate at 0 and 10 min were similar in both groups and from 20 up to 60 min, respiratory rate improvement were significantly different. Pulse rate differences were not statistically significant up to 40 min. At 50 and 60 min, mean pulse rate differences were significant. Only 3 patient (1 in magnesium sulfate group and 2 in control group) had SaO_2 89% (within <90% range) at presentation and within 10 min, SaO_2 was ≥90% in all cases. So, as per protocol, oxygen was not used. Mean oxygen saturation at presentation was not significantly different. But from 10 up to 60 min, improvement in mean SaO_2 was significantly different and magnesium sulfate group showed superiority.

At the end of 60 min, magnesium sulfate group showed better and significant differences in clinical improvement and all the patients from both the groups were given step care management.

Table VI

Response on percent predicted PEFR

PEFR (% predicted)	Magnesium sulfate with salbutamol group (n = 30)	Salbutamol (control) group (n = 30)
At 10 min		
Good response	0	0
Incomplete response	30	30
Poor response	0	0
At 20 min		
Good response	0	0
Incomplete response	30	30
Poor response	0	0
At 30 min		
Good response	9	0
Incomplete response	21	30
Poor response	0	0
At 40 min		
Good response	17	0
Incomplete response	13	30
Poor response	0	0
At 50 min		
Good response	30	9
Incomplete response	0	21
Poor response	0	0
At 60 min		
Good response	30	26
Incomplete response	0	4
Poor response	0	0

PEFR ≥70% of predicted value- good response; 50 to <70% of predicted value- incomplete response; <50% of predicted value- poor response. (National guidelines, 2005)

Discussion

This double-blind randomized controlled study revealed that combining nebulized isotonic magnesium sulfate with salbutamol results in early and better response in peak flow as compared with the standard approach (salbutamol plus normal saline) for nebuliza-

Table VII

Respiratory rate, pulse rate and SaO_2 % at different times

	Parameter	Respiratory rate/min	Pulse rate/min	%SaO_2
0 min	Magnesium sulfate with salbutamol group	34.0 ± 1.9	121.6 ± 6.3	90.8 ± 0.7
0 min	Salbutamol group	35.0 ± 2.0	123.2 ± 6.7	90.4 ± 0.7
0 min	p value	>0.05^{ns}	>0.10^{ns}	>0.05^{ns}
10 min	Magnesium sulfate with salbutamol group	31.2 ± 1.7	113.1 ± 8.0	92.2 ± 1.1
10 min	Salbutamol group	32.0 ± 1.6	115.7 ± 7.1	91.7 ± 0.8
10 min	p value	>0.05^{ns}	>0.10^{ns}	<0.05^{a}
20 min	Magnesium sulfate with salbutamol group	28.6 ± 1.1	101.5 ± 5.5	92.6 ± 1.0
20 min	Salbutamol group	29.2 ± 1.1	102.9 ± 5.7	92.0 ± 1.00
20 min	p value	<0.05^{a}	>0.10^{ns}	<0.05^{a}
30 min	Magnesium sulfate with salbutamol group	27.2 ± 1.0	96.0 ± 3.8	93.7 ± 0.9
30 min	Salbutamol group	27.7 ± 0.9	97.1 ± 3.6	93.2 ± 0.9
30 min	p value	<0.05^{a}	>0.10^{ns}	<0.05^{a}
40 min	Magnesium sulfate with salbutamol group	25.7 ± 0.8	91.7 ± 1.9	94.2 ± 1.0
40 min	Salbutamol group	26.3 ± 0.8	92.6 ± 2.1	93.7 ± 0.9
40 min	p value	<0.01^{a}	>0.05^{ns}	<0.05^{a}
50 min	Magnesium sulfate with salbutamol group	24.9 ± 0.9	89.1 ± 2.0	95.0 ± 0.7
50 min	Salbutamol group	25.6 ± 0.8	90.5 ± 2.3	94.6 ± 0.7
50 min	p value	<0.01^{a}	<0.05^{a}	<0.05^{a}
60 min	Magnesium sulfate with salbutamol group	24.1 ± 1.0	87.0 ± 2.3	95.5 ± 0.7
60 min	Salbutamol group	25.4 ± 0.8	88.6 ± 2.7	95.1 ± 0.6
60 min	p value	<0.001^{a}	<0.05^{a}	<0.05^{a}

Unpaired Student's 't' test; ns = not significant, ^{a} = significant

tion in the initial treatment of acute exacerbation of asthma in children. The effect was evident at 10 min and was maintained up to 60 min from the start point. This finding is consistent with that of Mollick, (2003).

PEFR expressed as percentage predicted value eliminated gender, age, weight and height bias and mean percent improvement in PEFR from baseline (0 min) eliminated the bias introduced by difference in the degree of initial airflow obstruction. Mean percent of predicted PEFR detected in both group at 0, 10, 20, 30, 40, 50 and 60 min. Results in both groups at base line were similar but from 10 up to 60 min, the values were significantly different. Mean percent improvement in PEFR from baseline was always significantly different from 10 up to 60 min and magnesium sulfate group showed superiority which is also consistent with findings of Nannini et al. (2000).

In this study, in the magnesium sulfate with salbutamol group at 10 min from the start point only 2 (6.7%) patient and at 20 min almost all (29 out of 30) patients achieved at least 60% of predicted PEFR. Following 1st dose of nebulization at 0 min, within this 1st 20 min, from the

control group none could achieve PEFR at least 60% of the predicted value. Second dose of nebulization done at 20 min and after another 10 min i.e, at 30 min from start point, 30 (100.0%) and 28 (93.3%) patient from magnesium sulfate group and control group respectively achieved at least 60 percent predicted value. From 40 min, all patient from both the group achieved PEFR at least 60 percent predicted. In acute exacerbation of asthma, to reduce the likelihood of relapse and hospitalization rate, achieving as rapidly as possible a safe value for the percentage predicted peak flow of about 60% is needed which is suggested as the cut-off point between discharge from Emergency Department and admission into the hospital (Nannini, 1995). According to Gina (2005), patient with post treatment lung function (FEV_1/PEF) in the range of 40-60% of predicted value can potentially be discharged, assuming adequate follow-up is available in the community and compliance is assured. Patients with objective evidence of lung function 60 percent predicted or greater can usually be discharged (Gina, 2005).

Ten min after 2nd dose of nebulization i.e, at 30 and 40 min only 9 (30.0%) and 17 (56.7%) patients respectively in the magnesium sulfate group showed good response (PEFR ≥70% predicted). Despite of using two doses of nebulization, within this first 40 min time, from control group none could show good response. With three doses of nebulization, at 50 min, 30 (100.0%) patients from magnesium sulfate with salbutamol group and 9 (30.0%) patient in the control group showed good response. Finally at 60 min 4 (13.3%) patient in the control group failed to be included as good responder. At present no known study done before to see this type of response.

In the present study, all patient of magnesium sulfate group achieved 70% PEFR after 3 dose of nebulization. Nannini et al. (2000) conducted study with patient aged 18 years and over and found significant benefit after single dose of nebulization with isotonic magnesium sulfate. But the effect is much better in the present study. Hughes et al. (2003) undertaken a double-blind placebo controlled study and found significantly greater improvement in FEV_1 with nebulized salbutamol plus isotonic magnesium sulfate solution than salbutamol plus normal saline. In that study 3 doses of nebulization were done and observations were made at 30 min interval and the response was similar as 10 min interval in the present study. Mollick, (2003), carried out prospective controlled study in adult population and also found the similar response after 20 min of completion of treatment.

The current recommendation for initial treatment of acute asthma is 3 doses of nebulization at 20 min interval for 1 hour but most of the studies (Mangat et al., 1998; Nannini et al., 2000; Hughes et al., 2003; Mollick, 2003) did not follow. Moreover, they recorded peak flow at 10 and/or 20 and/or 30 min after completion of nebulization. But nebulization itself continues for 5-10 min depending upon the amount of fluid and properties of nebulizer. The outcome could be different if those protocols were adopted to see the effect of 3 doses of nebulization from the start point.

Though intravenous magnesium sulfate can be used as an adjunct to conventional nebulization and other therapy but if nebulization of salbutamol with isotonic magnesium sulfate can exert the same effect, use of this combination nebulization may be convenient both for the physician and for the patient (Mollick, 2003). So the nebulized magnesium sulfate is preferable to IV magnesium.

Acute exacerbation of asthma requires start of treatment even at home and in the protocol of home management of asthma, oxygen administration is not recommended (Expert panel report-2, 1997). Acute hypoxia has no effect on short acting β_2-agonist (salbutamol) induced broncho-dilatation in patients with asthma (Dagg et al., 2001). Improvements in oxygen saturation following bronchodilator administration documents the presence of relative preexisting hypoxemia which is reversed to some degree with bronchodilators (Yamamoto et al., 1992). In our study, oxygen saturation also raised to a safe value in all patients.

Following current recommendation for initial treatment of acute exacerbation of asthma, in this study, nebulization was done as one dose every 20 min for 1 hour and found that patient gets comfort earlier if salbutamol nebulization done with isotonic magnesium sulfate solution.

Conclusion

This study suggest that a) combining isotonic magnesium sulfate solution 2.0 mL with salbutamol for nebulization results in early response and greater improvement in PEFR as compared with the standard approach (salbutamol nebulization with normal saline) in the initial treatment of acute exacerbation of asthma in children and b) patient treated by nebulized isotonic magnesium sulfate solution with salbutamol quickly achieves a safe value for the percentage predicted peak flow and at the end of initial treatment shows good response.

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