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To Study The Effects Of Nebulized Salbutamol Plus Magnesium Sulphate When Compared To Nebulized Salbutamol Plus Normal Saline In Acute Exacerbations Of Asthma In Children

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Abstract

BACKGROUND : Asthma is one of the most common causes of morbidity and school absenteeism in children. Magnesium sulphate is one amongst the numerous therapeutic options available for asthmatic exacerbations. While the efficacy of intravenous magnesium sulphate in acute exacerbations of asthma has been described in multiple studies, very little is known about the role of nebulized magnesium sulphate. **AIM OF THE STUDY**: To study the effects of nebulized salbutamol plus magnesium sulphate when compared to nebulized salbutamol plus normal saline in acute exacerbations of asthma in children. **METHODS** :This is a cross-sectional Observational study was conduced in the year 2020-2021 at Dhanalakshmi Srinivasan Medical College and Hospital. preambular, Trichy, Tamil Nadu, India. 117 children of the age range 5-12 years who were managed in the Pediatric in-patient department for acute exacerbation of asthma and fulfilled the inclusion criteria. Children who were admitted during the odd numbered weeks were included in the salbutamol plus normal saline group and children who were admitted in the even numbered weeks were included in the salbutamol with magnesium sulphate group. The salbutamol + normal saline group had 58 children whereas the salbutamol + magnesium sulphate group had 59 children.

Management of asthma exacerbation was done as per standard protocol. The first group received nebulization using salbutamol 1 ml (5 mg) with 3 ml normal saline along with oxygen. The other group was nebulized with salbutamol 1ml (5mg) plus 3 ml of isotonic magnesium sulphate 10% and oxygen. Parent or the relative and the child were explained about the therapy. Nebulization was given using electricity driven nebulizer with face mask along with oxygen. **RESULTS** : Out of the 117 children 58 (49.57 %) were included in the salbutamol with normal saline group and 59(50.42%) children were allotted to the salbutamol with magnesium sulphate group. Overall The mean age of the study population was 7.215 . the mean age of the salbutamol with normal saline group was 7.127 and the mean age of the salbutamol with magnesium sulphate group was 7.34. After nebulization, there was a decline in the mean heart rate in both the groups. Both groups demonstrated a decline in the mean respiratory rate after nebulization. After nebulization both the groups showed significant improvement in mean SpO2 .Though the magnesium group had a slightly higher mean SpO2 (96.21)when compared to the salbutamol group (95.74), this difference was not statistically significant p=0.057. There was a 50.1 % improvement in the percentage predicted PEFR over baseline in the salbutamol group. There was a 66.56 % improvement from baseline percentage predicted PEFR in the magnesium group. The PAS scoring was done at 0, 30 and 60 minutes and the results analysed.the baseline score was similar in both the groups.The

magnesium group showed a better improvement with regards to the clinical scoring at 30 and 60 minutes (p=0.039). **CONCULSION**: To conclude, this study suggests that using isotonic magnesium sulphate solution as a vehicle for salbutamol 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. Further extensive large-scale studies needed on defining the role of nebulized magnesium sulphate as an adjuvant for salbutamol in children with acute severe asthma in children.

Keywords: Asthma, Magnesium sulphate, Salbutamol, PEFR

Introduction

Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyper -responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing particularly at night or in the early morning. These episodes are associated with widespread, but variable, airflow obstruction within the lung that is often reversible either spontaneously or with treatment.[1] Asthma is a complex disease which is exemplified by its clinical, physiological and pathological characteristics. The most prominent symptom is the episodic shortness of breath which is commonly nocturnal and often accompanied by cough. Episodic airway obstruction is the hallmark of asthma. The most common physical finding associated with asthma is wheeze on auscultation. [2]The pathological picture is characterized by airway inflammation which may sometimes be associated with airway remodelling. [3] Asthma is one of the most common chronic diseases that currently affects around 300 million people globally. The prevalence of asthma has risen in the developed countries over the last three decades but now appears to have stabilized, with approximately 10–12% of adults and 15% of children being affected by the disease. [4]There is a rising trend in the prevalence of asthma in developing countries due to the concomitant increase in urbanization. The factors that influence asthma may either have a causative role or may act as triggers. Asthma occurs due to environmental influences acting on a pre-existing genetic susceptibility.[5] A series of complex gene-environment interactions are involved in the cascade of mechanisms underlying asthma. Asthma is one of the most common causes of morbidity and school absenteeism in children. [6]Magnesium sulphate is one amongst the numerous therapeutic options available for asthmatic exacerbations. While the efficacy of intravenous magnesium sulphate in acute exacerbations of asthma has been described in multiple studies, very little is known about the role of nebulized magnesium sulphate. Genetic factors also influence the response to treatment. [7]Genes have been identified which modify the therapeutic response to β_2 agonists, glucocorticoids and leukotriene antagonists. Hence genetic factors are important not only as risk factors in the pathophysiologic mechanisms in asthma but also as determining factors in the response to treatment.[8] Hence this study attempts to illustrate the role of nebulized magnesium sulphate as an adjuvant to conventional therapy in paediatric patients presenting with acute exacerbations of asthma.

Methods :This is a cross-sectional Observational study was conduced in the year 2020-2021 at Dhanalakshmi Srinivasan Medical College and Hospital. preambular, Trichy, Tamil Nadu, India. 117 children of the age range 5-12 years who were managed in the Pediatric in-patient department for acute exacerbation of asthma and fulfilled the inclusion criteria. Children who were admitted during the odd numbered weeks were included in the salbutamol plus normal saline group and children who were admitted in the even numbered weeks were included in the salbutamol with magnesium sulphate group. The salbutamol + normal saline group had 58 children whereas the salbutamol + magnesium sulphate group had 59 children. Management of asthma exacerbation was done as per standard protocol. The first group received nebulization using salbutamol 1 ml (5 mg) with 3 ml normal saline along with oxygen. The other group was nebulized with salbutamol 1ml (5mg) plus 3 ml of isotonic

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magnesium sulphate 10% and oxygen. Parent or the relative and the child were explained about the therapy. Nebulization was given using electricity driven nebulizer with face mask along with oxygen.

INCLUSION CRITERIA**:** Known asthmatic children of the age group 5-12 years who presented with acute exacerbation of asthma with **LPCH PAS[67] (Lucille-Packard Children's hospital, Stanford- Paediatric Asthma Severity Score)** of 9-10 (moderate to severe exacerbation of asthma).

Exclusion Criteria

1. Severely ill patient requiring immediate hospital care LPCH- PAS score ≥ 11
2. Altered level of consciousness
3. Hypotension
4. Any history or clinical evidence of cardiac, renal or hepatic dysfunction.
5. Use of β_2 agonists within the last 8 hours (to avoid confounding the results)
6. Use of systemic glucocorticoids within the last 7 days (to avoid confounding the results)
7. Patients who were unable to perform PEFR
8. Any evidence of chronic lung disease like BPD, cystic fibrosis and CLD
9. Fever
10. Patients in whom consent could not be obtained

Objective measure of airway obstruction was recorded with a mini peak flow meter. The procedure of using peak flow meter was demonstrated to the patient. PEFR (average of three readings) measurements were done at 0, 20 , 40 and 60 minutes. The predicted PEFR was calculated using the formula [(height in cm -100) ×5]+100. Oxygen saturation, heart rate, respiratory rate, blood pressure and DTR were monitored at 0. 30 and 60 minutes. The clinical scoring was assessed at 0, 30 & 60 minutes. Utmost care was taken to observe the child for any worsening of clinical status .No adverse events were noted during this study in both groups.

Statistical analysis: The collected data was consolidated, data decoded and analyzed. The analyses were done by SPSS 12.0 for Windows (Statistical Package for Social Sciences) software.The statistical differences between the two groups were inferred using the chi-square test. P value of < 0.05 was taken to be significant.

Results And Observations

Table :1 Group Distribution

SL.NO	GROUPS	No. OF CHILDREN n=117	PERCENTAGE 100 %
1	SALBUTAMOL+NS	58	49.57 %
2	SALBUTAMOL+MgSO4	59	50.42 %

Out of the 117 children 58 (49.57 %) were included in the salbutamol with normal saline group and 59(50.42%) children were allotted to the salbutamol with magnesium sulphate group. Children from the age group of 5 -7 years formed the majority of the study group (43.5%) followed by children between 8 to 9 years (36.7%).

Table :2 Age Distribution In Each Group

AGE GROUP	5-7 YRS	8-9 YRS	10-12 YRS
SALBUTAMOL+ NORMAL SALINE	24	23	11

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SALBUTAMOL+ MAGNESIUM SULPHATE	27	20	12

In both the groups , children were predominantly between 5 to 7 years

Table :3 Mean Heart Rate In Both Groups

	Salbutamol+NS	Salbutamol+Mgso4
0 min	**123.23**	**121.57**
30min	**97.13**	**95.97**
60min	**92.16**	**86.97**

After nebulization, there was a decline in the mean heart rate in both the groups.

Table :4 Mean Respiratory Rate In Both Groups

TIME	SALBUTAMOL+ NS	SALBUTAMOL+ MgSO4
0 min	34.97	34.03
30 min	27.73	27.23
60 min	25.4	24.13

Both groups demonstrated a decline in the mean respiratory rate after nebulization.

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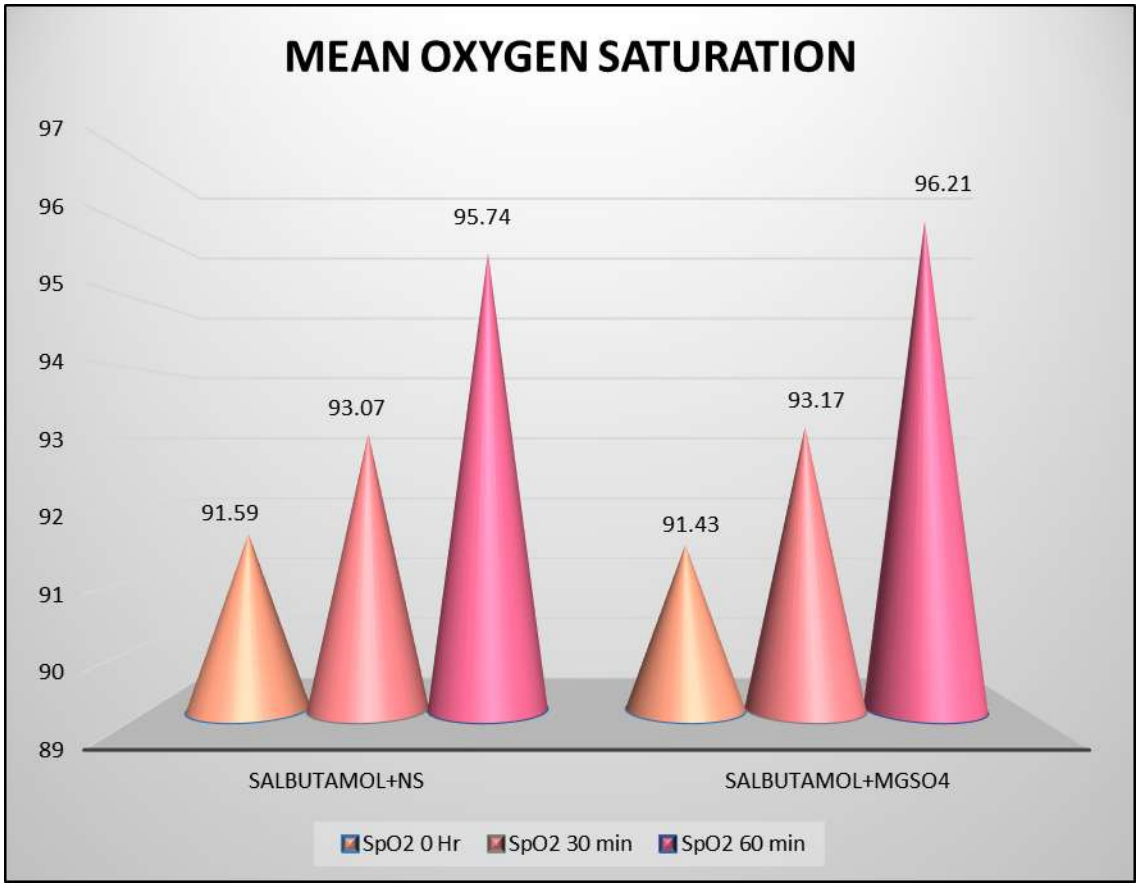
Graph :1 Mean Oxygen Saturation



After nebulization both the groups showed significant improvement in mean SpO2 .Though the magnesium group had a slightly higher mean SpO2 (96.21)when compared to the salbutamol group (95.74), this difference was not statistically significant p=0.057.

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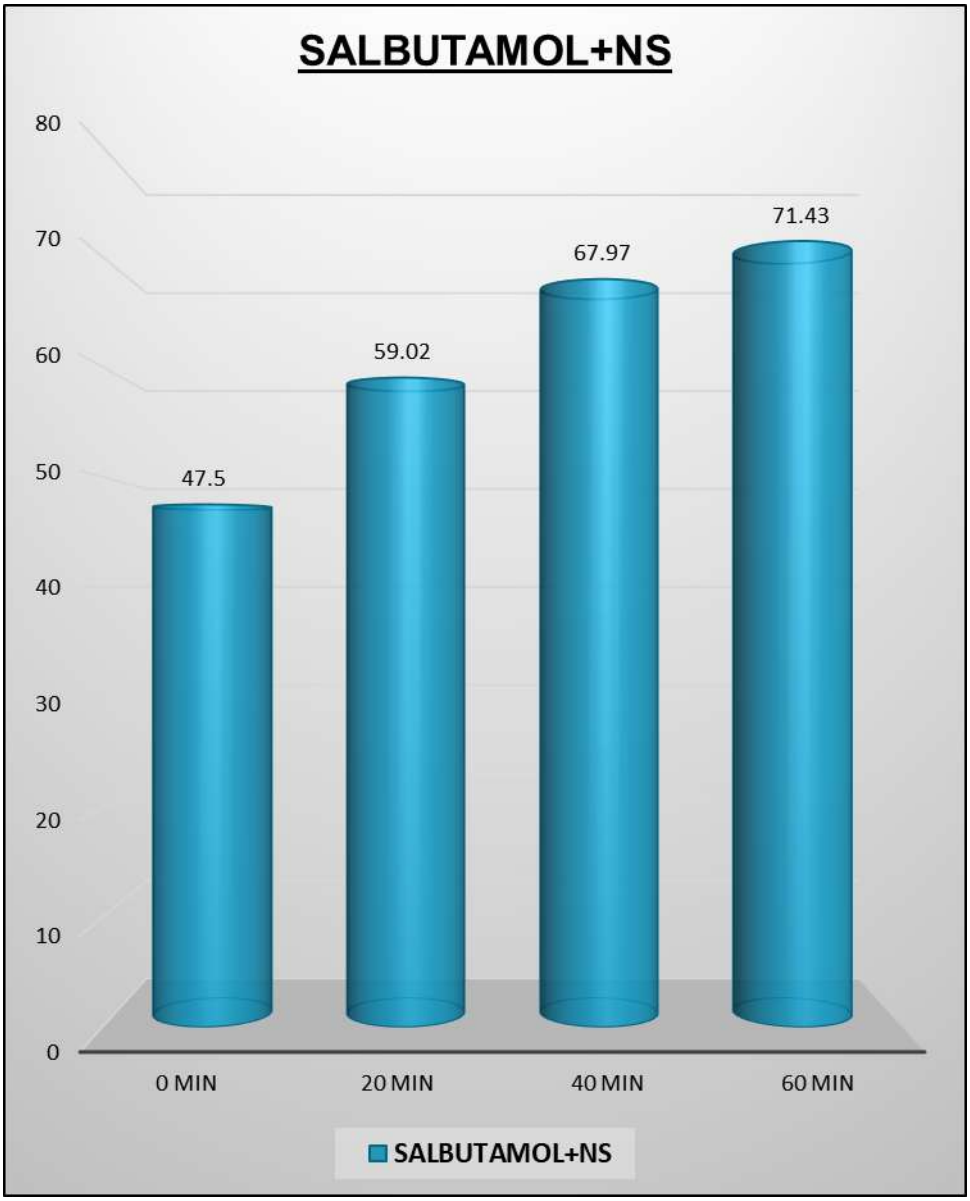
Graph :2 Mean Percentage Of Predicted Pefr Salbutamol+Ns Group



There was a 50.1 % improvement in the percentage predicted PEFR over baseline in the salbutamol group.

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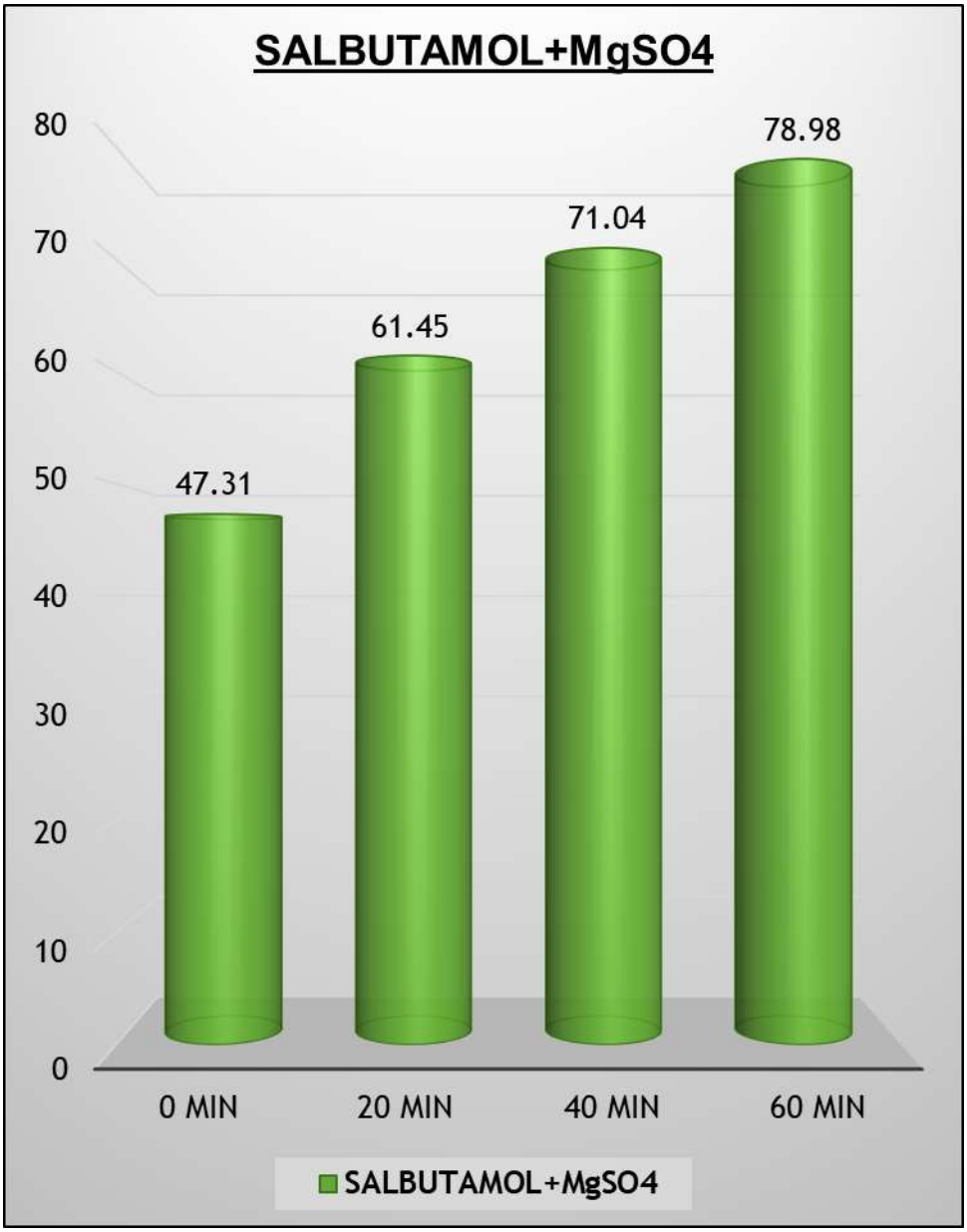
GRAPH :3 MEAN PERCENTAGE OF PREDICTED PEFR SALBUTAMOL+Mgso4 GROUP



There was a 66.56 % improvement from baseline percentage predicted PEFR in the magnesium group.

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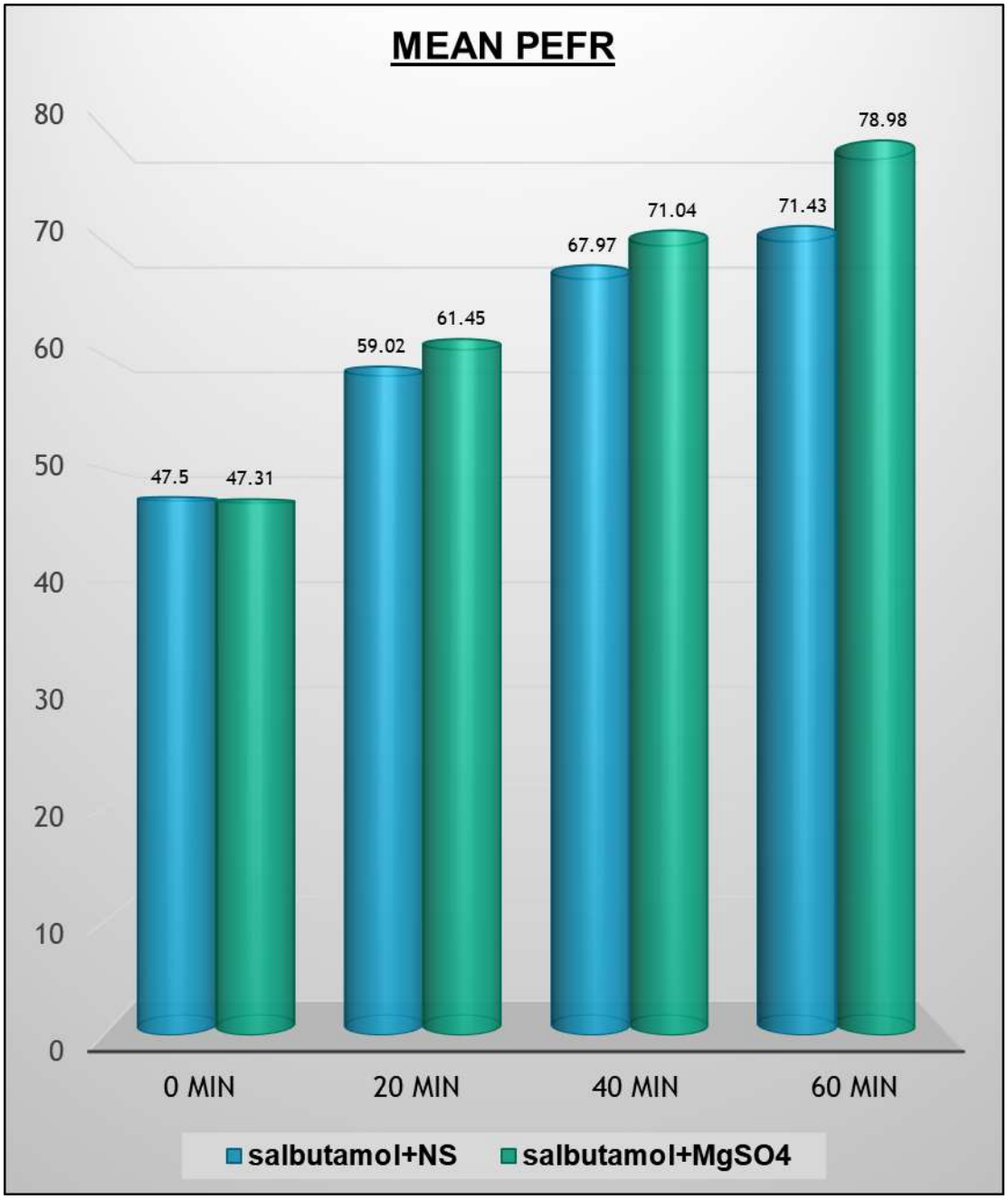
Graph :4 Mean Percentage Of Predicted Pefr – Both Groups



There was a significant improvement in the magnesium group(p value-0.039).

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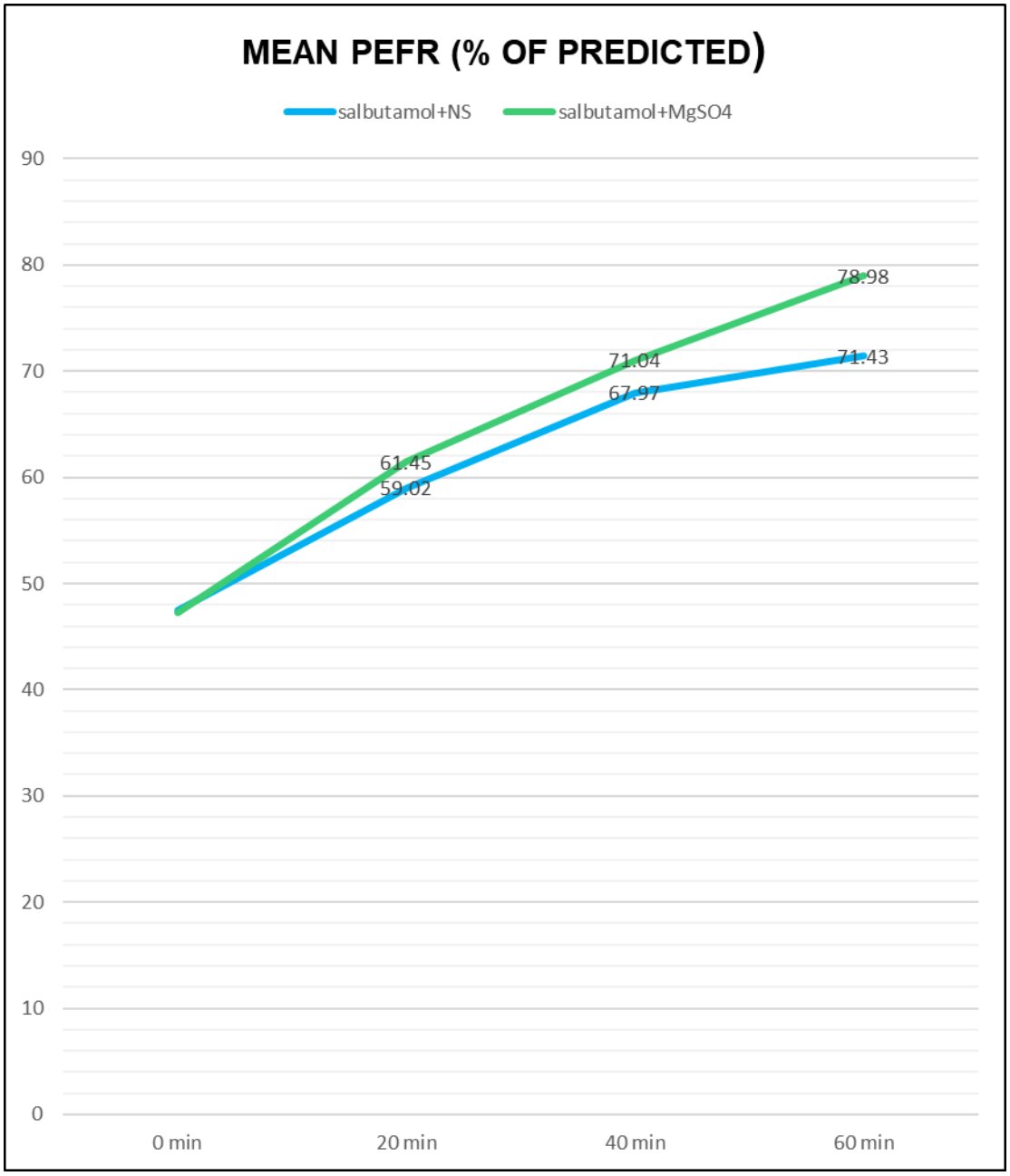
Graph :5 Mean Pefr (% Of Predicted) At 0.20.40 & 60 Minutes



As seen in the graph the magnesium group demonstrated a faster and higher response.

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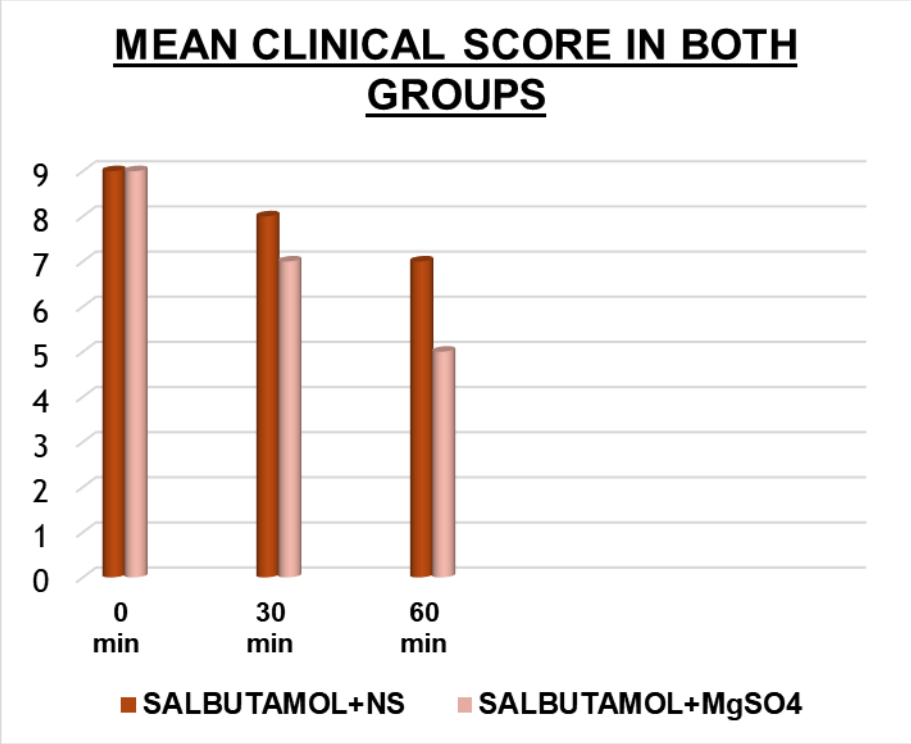
Graph :6 Mean Lpch-Pas Score In Both Groups



The PAS scoring was done at 0, 30 and 60 minutes and the results analysed.the baseline score was similar in both the groups.The magnesium group showed a better improvement with regards to the clinical scoring at 30 and 60 minutes (p=0.039).

Discussion :

Asthma is a chronic respiratory disease that is characterised by periods of relative control and episodes of deterioration referred to as exacerbations. Exacerbations range in severity from mild to status asthmaticus (acute asthma attacks that do not respond to standard bronchodilator and steroid therapy) and can result in visits to healthcare providers, emergency departments, and may at times require hospitalisations. [9]While rare, deaths from severe acute asthma do still occur. In most people, even though serious consequences are avoided, the prevention and treatment of asthma exacerbations is an important consideration of their disease. [10] Due to this impact on lifestyle, the costs to the patient and the healthcare system, and the mortality, asthma is responsible for a significant personal and social burden. cute asthma continues to be one of the main reasons for acute hospital admission in children and accounts for much morbidity, anxiety, stress, and time off school and work for the families. The use of MgSO4 for acute asthma was first described in 1936, and since then there has been increasing evidence for its use in adults and children with asthma.[11] There are a number of proposed mechanisms for its actions. In vitro studies demonstrate an inhibitory effect of MgSO4 on the contraction of bronchial smooth muscle, and the release of acetylcholine in cholinergic nerve terminals and of histamine from mast cells. There is evidence that MgSO4 may act as an anti-inflammatory agent by inhibiting the neutrophil respiratory burst in adults with asthma[12]The main effect of MgSO4 is that it blocks the calcium ion influx to the smooth muscles of the respiratory system and bronchodilation occurs. As a non-selective bronchodilator, magnesium sulphate is effective when administered intravenously in the treatment of patients with acute severe asthma not responding to conventional therapy (oxygen, nebulized salbutamol, and corticosteroids). However, the use of intravenous MgSO4 administration is not common in clinical practice, because it is prone to have adverse effects such as

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nausea, vomiting, facial flushing, hypotension and decreased tendon reflexes. The aerosolised route offers the advantage of lower dosage, quicker onset of action direct delivery of the drug to the airway smooth muscle and lower incidence of side effects when compared to the intravenous route. [13] At present, there are only a few studies about the effects of nebulized MgSO4 in the treatment of acute asthma in children, and the conclusions are controversial.This study was done among the children who were admitted in our paediatric ward for acute exacerbations of asthma. 117 children were included in this study. In this study, the majority of the children were from the age group of 5 -7 years with a mean age of 7.21 years (range 5 years to 12 years). It was observed that 67% of the children had a positive family history of asthma. A male preponderance was observed in both the study groups (58 %). In childhood the prevalence of asthma is noted to be more in males. There was no significant difference between males and females in both groups with regards to clinical scoring, heart rate, oxygen saturation, duration of hospital stay percentage of predicted PEFR at baseline and after treatment.[14] Clinical severity score (LPCH-PAS) done at baseline and after one hour showed significant improvement in both the groups. In the salbutamol with normal saline group the mean score at admission was 9.56 and at one hour 6.67 which showed a decline of 31 %.In the magnesium group the mean score was 9.66 and 5.22 at admission and 1 hour after therapy respectively, which indicates a decline of 46 %.The magnesium group demonstrated a greater decline in the mean score when compared to the salbutamol group (p value =0.021) which is statistically significant. The mean respiratory rate at baseline was similar in both groups (salbutamol group- 34.97 and MgSo4 group 34.03) and from 30 to 60 minutes, decrease in respiratory rate was slightly more in the MgSO4 group, (salbutamol group-25.4 & MgSO4 -23.13) but this was not statistically significant (p value = 0.0630). Mean oxygen saturation at presentation was not significantly different.[15] After nebulization both the groups showed significant improvement in mean SpO2 .Though the magnesium group had a slightly higher mean SpO2 (96.21) when compared to the salbutamol group (95.74), this difference was not statistically significant (p=0.057). These results are comparable to that of the study done by Haqq et al to compare the effects of salbutamol plus magnesium sulphate with salbutamol with normal saline. Similarly, there was no statistically significant difference in the mean heart rate and blood pressure of both the groups at 0 and 60 minutes.[16] The mean respiratory rate at baseline was similar in both groups (salbutamol group- 34.97 and MgSo4 group 34.03) and from 30 to 60 minutes, decrease in respiratory rate was slightly more in the MgSO4 group, (salbutamol group-25.4 & MgSO4 -23.13) but this was not statistically significant (p value = 0.0630) PEFR was expressed as percentage predicted value in order to eliminate gender, age, weight and height bias .The percentage of predicted PEFR was measured in both group at 0, 20, 40, and 60 minutes. Results in both groups at base line were similar but from 20 minutes to 60 minutes the improvement in magnesium group was statistically significant (p value = 0.039) when compared to the salbumol + NS group. Similar results were demonstrated by the following studies.[17]The mean age of presentation was 7.21 years. Sixty seven percent of the children had a positive family history of bronchial asthma.The magnesium group demonstrated a greater decline in the mean clinical score when compared to the salbutamol group (p value =0.021) which is statistically significant .The magnesium group demonstrated a statistically significant improvement in mean percentage of predicted PEFR from 20 to 60 minutes which correlates with the improvement in clinical scoring. Thus, the addition of magnesium sulphate as a vehicle for salbutamol results in a rapid and greater bronchodilatory response when compared to normal saline. Since the inhaled route is non-invasive , it is preferable in children as against intravenous administration of magnesium sulphate.[18] Treatment of severe asthma may be challenging inspite of the use of several medications including parenteral corticosteroids. Intravenous magnesium sulphate is one ancillary drug for severe cases but its inhaled use is yet to be elaborated by further studies.[19,20]

Conclusion

To conclude, this study suggests that using isotonic magnesium sulphate solution as a vehicle for salbutamol nebulization results in early response and greater improvement in PEFR as compared with the

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standard approach (salbutamol nebulization with normal saline) in the initial treatment of acute exacerbation of asthma in children. Further extensive large-scale studies needed on defining the role of nebulized magnesium sulphate as an adjuvant for salbutamol in children with acute severe asthma in children.

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