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EFFECT OF ISOTONIC NEBULIZED MAGNESIUM SULPHATE AS ADJUVANT TO SALBUTAMOL IN TREATMENT OF ACUTE ATTACK OF WHEEZE IN CHILDREN

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Abstract

Background: *Acute wheeze in children commonly requires prompt bronchodilator therapy. Nebulized magnesium sulphate has been proposed as an adjunct to salbutamol, but its clinical benefit remains uncertain. This study evaluated the effect of isotonic nebulized magnesium sulphate added to salbutamol in children with acute wheeze.*

Methods: *A comparative interventional study was conducted in the Pediatric Department of Madina Teaching Hospital, Faisalabad, from May to October 2024. Children aged 2–12 years with acute wheeze were randomly allocated to receive either nebulized salbutamol alone or salbutamol combined with isotonic nebulized magnesium sulphate. Clinical response was assessed using the Pediatric Respiratory Assessment Measure (PRAM), along with respiratory rate, heart rate, oxygen saturation, need for additional treatment, hospital admission and adverse effects.*

Results: *A total of 108 children were included, with 54 in each group. Baseline characteristics were comparable between groups. A good treatment response was observed in 53 (98.1%) children in the magnesium sulphate group compared with 45 (83.3%) in the salbutamol-alone group (p=0.008). Fewer children receiving magnesium required additional nebulization, systemic corticosteroids, hospital admission or respiratory support, although these differences were not statistically significant. Adverse effects were mild and comparable between groups, and no serious adverse events occurred.*

Conclusion: *Adding nebulized magnesium sulphate to salbutamol improved the overall treatment response and was well tolerated in children with acute wheeze. Further larger studies are needed to establish its effect on major clinical outcomes.*

INTRODUCTION

Wheezing is a common respiratory manifestation in children and is frequently associated with acute asthma exacerbations. Acute episodes may result in significant respiratory distress and require prompt treatment to relieve bronchial obstruction and prevent further deterioration. Salbutamol, a short-acting β2-adrenergic agonist, remains the mainstay of initial bronchodilator therapy in children presenting with acute wheeze or asthma exacerbation.[1,2] However, some children have an

inadequate response to conventional treatment and require additional therapeutic interventions.[3] Magnesium sulphate has bronchodilatory properties and promotes relaxation of bronchial smooth muscle by interfering with calcium-mediated contraction. Intravenous magnesium sulphate has demonstrated benefit in selected children with severe acute asthma, but its systemic administration requires intravenous access and may produce systemic adverse effects.[4,5] Consequently, nebulized magnesium sulphate has been investigated as an adjunct to inhaled β2-agonists because it delivers the drug directly to the airways with potentially fewer systemic effects.[6]

The evidence regarding nebulized magnesium sulphate in children, however, remains inconsistent. Earlier trials reported variable effects on respiratory function and clinical severity, while systematic reviews found no consistent reduction in hospital admission or respiratory impairment.[6,7] A randomized trial of children with moderate-to-severe asthma also found no significant overall benefit from nebulized magnesium compared with placebo when added to intensive standard therapy.[8] Similarly, a randomized controlled trial from India found no significant additional improvement in pulmonary function or physiological parameters when magnesium sulphate was combined with salbutamol.[9]

More recent evidence continues to be inconclusive. A 2024 systematic review and meta-analysis involving 10 randomized controlled trials and 2,301 children found that nebulized magnesium sulphate did not significantly reduce asthma severity or hospitalization, although some improvement in peak expiratory flow was observed and adverse effects were generally minor.[10] In contrast, a randomized clinical trial from Karachi, Pakistan, reported greater improvement in Pediatric Respiratory Assessment Measure scores with higher doses of nebulized magnesium sulphate when combined with salbutamol in children with status asthmaticus.[11] Therefore, differences in patient population, disease severity and magnesium dosage may contribute to the variation in reported outcomes. Further local evidence is needed to determine its clinical usefulness in children presenting with acute wheeze. The present study was therefore conducted to assess the effect of isotonic nebulized magnesium sulphate as an adjuvant to salbutamol in children with acute wheeze at Madina Teaching Hospital, Faisalabad.

Methodology

A comparative interventional study was conducted in the Pediatric Department of Madina Teaching Hospital, Faisalabad, from May 2024 to October 2024. Children aged 2–12 years presenting with an acute attack of wheeze and fulfilling the predefined eligibility criteria were enrolled in the study after obtaining informed consent from their parents or guardians. Children with acute wheeze associated with asthma/reactive airway disease and a clinically significant respiratory distress score were included. Children requiring immediate intubation or mechanical ventilation, those with known chronic lung disease other than asthma/reactive airway disease, hypersensitivity to magnesium sulphate, significant cardiac disease, or whose parents/guardians did not provide consent were excluded. The participants were randomly allocated into two groups. The intervention group received isotonic nebulized magnesium sulphate as an adjunct to nebulized salbutamol, whereas the control group received nebulized salbutamol alone. Baseline clinical parameters were recorded before treatment, and the response to treatment was assessed at predefined intervals using the Pediatric Respiratory Assessment Measure (PRAM), along with respiratory rate, heart rate and oxygen saturation. Any adverse effects were also documented. The primary outcome was the change in clinical severity following treatment, while secondary outcomes included changes in respiratory rate, heart rate, oxygen saturation and requirement for further treatment or hospital admission.

The sample size was calculated using the proportions reported in a previous Pakistani randomized clinical trial, in which a good treatment response was observed in approximately

83.3% of children receiving salbutamol compared with approximately 99% receiving salbutamol combined with nebulized magnesium sulphate.[1] Using a 95% confidence level and 80% power, the required sample size was calculated to be 104 children, with 52 participants allocated to each group. Data were analyzed using SPSS version. Continuous variables were expressed as mean ± standard deviation, whereas categorical variables were presented as frequencies and percentages. The independent-samples t-test or Mann–Whitney U test was used for comparison of continuous variables, as appropriate, while the chi-square test or Fisher's exact test was used for categorical variables. A p-value of <0.05 was considered statistically significant. Ethical approval was obtained from the relevant institutional ethics committee before commencement of the study.

RESULTS:

The demographic characteristics of the participants were comparable between the two groups. The mean age was similar in the salbutamol-alone group (5.2 ± 2.9 years) and the salbutamol plus magnesium sulphate group (5.3 ± 2.8 years). The distribution of male and female children was also similar between the groups. The baseline PRAM score was slightly higher in the combination group (7.58 ± 1.68) than in the salbutamol-alone group (7.21 ± 2.03), but this difference was not statistically significant (p=0.448). Overall, the two groups were reasonably comparable at baseline **(Table#1)**.

Table 2: A good treatment response was observed in 53 (98.1%) children who received nebulized magnesium sulphate in addition to salbutamol, compared with 45 (83.3%) children who received salbutamol alone. This difference was statistically significant (p=0.008), suggesting a better overall treatment response with the addition of magnesium sulphate. Although fewer children in the combination group required additional nebulization (14.8% vs. 29.6%), systemic corticosteroids (13.0% vs. 24.1%), hospital admission (9.3% vs. 20.4%), or escalation of respiratory support (1.9% vs. 7.4%), none of these differences reached statistical significance (p>0.05) **(Table#2)**.

Table 3: Adverse effects were generally mild and occurred at similar frequencies in both groups. Tremor was reported in 5.6% of children in the combination group and 7.4% in the salbutamol-alone group, while tachycardia occurred in 7.4% and 9.3%, respectively. Nausea or vomiting was reported equally in both groups (3.7%). Flushing was observed in two children (3.7%) receiving magnesium sulphate and was not reported in the salbutamol-alone group; however, this difference was not statistically significant (p=0.154). Overall, adverse effects were reported in 13.0% of children in the combination group and 16.7% in the salbutamol-alone group (p=0.590). No serious adverse events were observed in either group, indicating that the addition of nebulized magnesium sulphate was generally well tolerated **(Table#3)**.

Table#1: Demographic Data of the Patients

Variables	Salbutamol alone (n=54)	Salbutamol + $MgSO_4$ (n=54)	p-value
Age, years, mean ± SD	5.2 ± 2.9	5.3 ± 2.8	>0.05
Female, n (%)	26 (48.0%)	29 (53.7)	>0.05
Male, n (%)	28 (52.0%)	25 (46.3)	>0.05
Baseline PRAM score, mean ± SD	7.21 ± 2.03	7.58 ± 1.68	0.448

Table#2: Treatment response and requirement for further management

Outcome	Magnesium sulphate + Salbutamol (n=54)	Salbutamol alone (n=54)	p-value
Good treatment response, n (%)	53 (98.1%)	45 (83.3%)	0.008
Required additional nebulization, n(%)	8 (14.8%)	16 (29.6%)	0.073
Required systemic corticosteroids, n (%)	7 (13.0%)	13 (24.1%)	0.143
Required hospital admission, n (%)	5 (9.3%)	11 (20.4%)	0.118
Required escalation of respiratory support, n (%)	1 (1.9%)	4 (7.4%)	0.165

Table#3: Adverse effects following treatment

Adverse effect	Magnesium sulphate + Salbutamol (n=54)	Salbutamol alone (n=54)	p-value
Tremor	3 (5.6%)	4 (7.4%)	0.695
Tachycardia	4 (7.4%)	5 (9.3%)	0.727
Nausea/vomiting	2 (3.7%)	2 (3.7%)	1.000
Flushing	2 (3.7%)	0 (0.0%)	0.154
Any adverse effect	7 (13.0%)	9 (16.7%)	0.590
Serious adverse event	0 (0.0%)	0 (0.0%)	–

Discussion:

The present study demonstrated that adding nebulized isotonic magnesium sulphate to salbutamol resulted in a significantly better treatment response compared with salbutamol alone (98.1% vs. 83.3%, p=0.008). The two groups were comparable in terms of age, sex and baseline PRAM score, suggesting that the difference in treatment response was not due to important baseline differences. Similar findings were reported by Mustafa et al. in children with acute asthma, where nebulized magnesium sulphate used as an adjunct to standard therapy was associated with better clinical improvement.[12] Mahajan et al. also reported greater improvement in lung function when nebulized magnesium sulphate was combined with albuterol compared with albuterol alone.[13]

The beneficial effect observed in the current study is further supported by Haqq et al., who found significant improvement in clinical parameters following nebulized magnesium sulphate in children with acute asthma.[14] Motamed et al. also reported improved clinical and peak-flow measurements following the addition of nebulized magnesium sulphate to conventional therapy.[15] These findings may be explained by the bronchodilatory properties of magnesium sulphate, which can reduce bronchial smooth-muscle contraction and enhance the response to β2-agonists.

However, not all studies have demonstrated a similar benefit. Türker et al. found no significant advantage of adding nebulized magnesium sulphate to standard treatment in children with moderate asthma exacerbations.[16] Likewise, Alansari et al. reported that nebulized magnesium did not significantly shorten the time to medical readiness for discharge.[17] In a large randomized trial, Schuh et al. also found no significant reduction in hospitalization among children receiving nebulized magnesium in addition to albuterol.[18] Differences in disease severity, magnesium dose and concentration, timing of

administration, concomitant therapy and outcome assessment may explain these variations. Although the present study showed fewer children requiring additional nebulization, systemic corticosteroids, hospital admission and escalation of respiratory support in the magnesium group, these differences were not statistically significant. This is in agreement with Kassab et al., who concluded that inhaled magnesium combined with β2-agonists may improve some short-term outcomes but does not consistently reduce hospital admission.[19] Similarly, a systematic review by Powell et al. found that evidence regarding nebulized magnesium in acute asthma remains heterogeneous, with benefits more apparent in selected clinical and physiological outcomes than in definitive outcomes such as admission.[20]

The safety profile in the present study was reassuring. Adverse effects were mild and comparable between the two groups, and no serious adverse events were observed. This is consistent with previous pediatric studies reporting good tolerability of nebulized magnesium sulphate.[16–20] Overall, the findings suggest that nebulized isotonic magnesium sulphate may provide additional short-term clinical benefit when used with salbutamol in children with acute wheeze. Nevertheless, the absence of a statistically significant reduction in hospital admission or escalation of treatment indicates that larger, adequately powered studies are required to establish its role in routine pediatric emergency care.

Conclusion:

The addition of isotonic nebulized magnesium sulphate to salbutamol improved the overall treatment response in children presenting with acute wheeze compared with salbutamol alone. It was well tolerated, with no serious adverse events observed. However, the effect on hospital admission and need for treatment escalation was not statistically significant. Nebulized magnesium sulphate may therefore be considered a useful adjunct to salbutamol, particularly in children with inadequate initial response, although further larger studies are needed to confirm its clinical benefit.

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