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Comparison of Efficacy of Nebulized Magnesium Sulphate with Intravenous Magnesium Sulphate in Children with Acute Asthma

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Author`s Contribution

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ABSTRACT

Background: Acute asthma is a frequent cause of pediatric emergency admissions, requiring prompt management to relieve airway obstruction and prevent respiratory failure. Magnesium sulphate, administered either intravenously or via nebulization, has been used as an adjunct to standard bronchodilator therapy due to its bronchodilatory and anti-inflammatory effects.

Objective: This study aimed to compare the efficacy and safety of nebulized magnesium sulphate with intravenous magnesium sulphate in children presenting with acute moderate-to-severe asthma.

Methodology: A total of 148 children aged 1–12 years with acute asthma were enrolled and randomly assigned into two equal groups. One group received intravenous (IV) magnesium sulphate and the other nebulized magnesium sulphate, in addition to standard asthma therapy. The Pulmonary Asthma Score (PAS) was recorded at baseline, and at 30, 60, 120, 240, and 360 minutes. The duration of Pediatric Intensive Care Unit (PICU) stay, total hospital stay, treatment efficacy, and adverse effects were compared between groups.

Results: Baseline demographic and clinical characteristics were comparable between groups ($p > 0.05$). Both treatments significantly improved PAS over time, with a faster initial reduction at 30 minutes in the nebulized group (9.53 ± 2.44 vs. 10.32 ± 2.13; $p = 0.036$). The mean PICU stay was shorter in the nebulized group (3.32 ± 4.23 vs. 5.94 ± 9.78 hours; $p = 0.036$), as was total hospital stay (28.76 ± 19.21 vs. 47.08 ± 42.71 hours; $p = 0.001$). Treatment efficacy was similar between groups ($p = 0.069$). Adverse effects occurred in 29.7% of IV-treated patients but in none of the nebulized group ($p < 0.001$).

Conclusion: Nebulized magnesium sulphate provides comparable therapeutic efficacy to intravenous administration while offering faster initial improvement, shorter recovery, and a superior safety profile. It represents a safe, effective, and practical alternative for managing acute asthma in children.

Keywords: Magnesium sulphate; Nebulization; Intravenous therapy; Acute asthma; Pediatric emergency; Bronchodilator therapy

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Introduction

Asthma is a heterogeneous disease, which is characterized by chronic airway inflammation. Asthma exacerbations are acute episodes of breathlessness, cough, wheezing, chest tightness, or a combination of these symptoms that should be documented and quantified by peak expiratory flow (PEF) or forced expiratory volume in 1 second (FEV1) measurement. It is the most common chronic lung disease in both developed and developing countries affecting more than 300 million people worldwide and causing about 255,000 deaths annually.[1,2]

Magnesium Sulphate has been shown to inhibit smooth muscle contraction, decrease histamine release from mast cells, inhibit acetylcholine release and may increase the bronchodilator effect of β2-agonist by increasing the receptor affinity.[3]

MgSO4 has been assessed in intravenous and nebulized forms. The intravenous route provides direct access to the venous system, allowing the delivery of high drug concentrations. Disadvantages include the need for intravenous access and drug administration by an infusion lasting ~20 minutes which can cause an increased level of magnesium in the blood and its side effects include headache, dizziness, hypotension, and bradycardia.[4,5] So the patient must be kept in ICU with continuous cardiac and B.P monitoring. Moreover, repeated intravenous dosing can also cause hypermagnesemia, muscle weakness, and respiratory failure.[6]

The nebulized route has the advantage of the quick onset of action and reduced incidence of side effects. Its disadvantages include a reduced dose of drug delivered compared with the intravenous form, and increased respiratory effort of the patient to increase the drug's effectiveness.[7,8]

The Global Initiative in Asthma (GINA) recommendations approve the use of inhaled MgSO4 during a crisis. Inhaled Magnesium Sulphate is easy to administer, extremely safe, and inexpensive. Several studies had confirmed the bronchodilator effects of intravenous magnesium, but its effects through inhalation are controversial.[9,10] Little work has been done regarding nebulized magnesium sulphate efficacy in acute asthma in the pediatric age group.[11] There are no local clinical trials available regarding its use in acute asthma in children so the rationale of my study is to see the efficacy of nebulized magnesium sulphate in acute severe asthma in the pediatric age group as it has fewer side effects as compared to I/V magnesium sulphate and easy to administer.

Methodology

It was a Randomized Control Trial in the setting of Department of Pediatric Medicine, King Edward Medical University, Mayo Hospital Lahore for the duration of one year (Oct 2019-Sep 2020). The sample size of 148 patients (74 patients from each group) was estimated by using a 5% level of significance and included children age 2 years to 12 years with acute moderate to severe asthma (as per operational definition) as well as children who showed poor response to standard treatment at 60 minutes. The study excluded those with a history of chronic lung disease, those with abnormal renal function tests, had contraindication for MgSO4 due to hepatic or renal disease, had previously known allergy to MgSO4 and children who have other comorbid illness. Probability simple random sampling technique was used.

After approval from the Institutional Ethical Review Board (IRB) and Advanced Study and Research Board (ASRB), Ref no 14348/REG/KEMU/18 a total of 148 patients were enrolled in each group over one year. The clinical trial was also registered with Clinical Trials [NCT04497766]. Informed consent was taken from the parent or caregiver of each patient and pre-treatment evaluation with complete history including demographic data and physical examination was done. Each patient diagnosed with acute asthma as per operational definition was assessed by PAS score (as described in data collection form) at admission. All patients with acute moderate (PAS score 8-11) or Severe (PAS score12-15) asthma underwent standard treatment (that includes prop up, oxygen inhalation, inhaled short-acting beta-2 agonist, and inhaled ipratropium bromide along with systemic corticosteroids). Those showing poor response to standard treatment at 1 hour were included in the study and randomly assigned to one of the intervention groups. Group A received intravenous Magnesium Sulphate infusion (50mg/kg over 30 minutes) and Group B received Nebulized Magnesium Sulphate (100mg in 20 ml normal saline) with this dilution over 5-7 minutes in each case via ultrasonic nebulizer. Randomization to either the intravenous or nebulization group was done by the simple lottery method. Continuous BP and cardiac monitoring were done with the help of a non-invasive cardiac monitor.

For each patient pediatric asthma severity (PAS) score was recorded at admission and 30, 60, 120,240, and 360 minutes after initiating the treatment. Any adverse effects (e.g. flushing, headache, tremors, nausea, vomiting, blood pressure change, change in deep tendon reflexes) observed during the study were recorded.

Data was entered in SPSS-26. Numerical variables, PAS score, duration of the hospital and PICU stay were analyzed for normality of data by Shapiro test. The numerical variables which were normally distributed were expressed as mean ± standard deviation (SD), and those which were not normally distributed were expressed as median and interquartile range (IQR). Independent sample student's t-test was used to compare the mean reduction in PAS score in the 2 groups. The numerical variables which were normally distributed were analyzed by using Student t-test and those which were not normally distributed were analyzed using Mann Whitney U test. Qualitative variables like gender were

presented as frequency and percentage. The Chi-square was applied to compare the frequency of the efficacy and side effects in both groups. P-value ≤ 0.05 was taken as significant.

Results

A total of 148 children diagnosed with acute asthma were enrolled in the study, with 74 patients receiving intravenous magnesium sulphate (IV $MgSO_4$) and 74 receiving nebulized magnesium sulphate. The baseline characteristics of both groups were comparable, as shown in Table I. The mean age of participants was 6.25 ± 3.43 years in the IV $MgSO_4$ group and 6.29 ± 3.42 years in the nebulized group (p = 0.079). Most children were within the 1–5 year age range, accounting for 47.3% of the IV group and 48.6% of the nebulized group. The gender distribution also showed no significant difference, with males comprising 45.9% in the IV group and 58.1% in the nebulized group (p = 0.139).

Table I: Comparison of mean Age (years) in both study groups.

Characteristics	Treatment Group		P-value
	IV MgSO4	Nebulized MgSO4	
Age in years			
Mean ± SD	6.25 ± 3.43	6.29 ± 3.42	0.079
Age groups			
1-5 years	35(47.3%)	36(48.6%)	0.98
5.1-9 years	19(25.7%)	19(25.7%)	
9.1-12 years	20(27%)	19(25.7%)	
Gender of the patients			
Male	34(45.9%)	43(58.1%)	0.139
Female	40(54.1%)	31(41.9%)	
Total	74(100%)	74(100%)	

The mean Pulmonary Asthma Score (PAS) values at baseline and subsequent intervals are presented in Table II. At baseline, both groups had comparable PAS values (11.01 ± 1.53 vs. 10.68 ± 1.45; p = 0.171). A significant reduction in PAS was observed at 30 minutes in the nebulized $MgSO_4$ group compared to the IV group (p = 0.036). Thereafter, PAS continued to decline steadily in both groups at 60, 120, 240, and 360 minutes, with no statistically significant differences between the two treatment arms at these later time points. These findings suggest that both intravenous and nebulized magnesium sulphate were effective in reducing asthma severity over time, with nebulized administration producing a faster early improvement.

As shown in Table III, the mean duration of stay in the Pediatric Intensive Care Unit (PICU) was significantly shorter in the nebulized $MgSO_4$ group (3.32 ± 4.23 hours) compared to the IV group (5.94 ± 9.78 hours; p = 0.036).

Table II: Mean Comparison of PAS (baseline, 30, 60, 120, 240, 360 minutes) in both study groups.

PAS	Study groups	Mean	SD	P-value
Baseline	*IV MgSO4*	11.01	1.53	0.171
	Nebulized MgSO4	10.68	1.45	
30 minutes	*IV MgSO4*	10.32	2.13	0.036*
	Nebulized MgSO4	9.53	2.44	
60 minutes	*IV MgSO4*	8.46	2.54	0.240
	Nebulized MgSO4	7.99	2.33	
120 minutes	*IV MgSO4*	7.61	2.18	0.320
	Nebulized MgSO4	7.27	1.93	
240 minutes	*IV MgSO4*	7.11	1.91	0.243
	Nebulized MgSO4	6.76	1.73	
360 minutes	*IV MgSO4*	6.77	1.85	0.633
	Nebulized MgSO4	6.64	1.57	

Table III: Mean Comparison of PICU Duration of Stay (hours) in both study groups.

Parameters	Treatment Group		P-value
	IV MgSO4	Nebulized MgSO4	
PICU duration (hours)			
Mean ± SD	5.94 ± 9.78	3.32 ± 4.23	0.036*
PICU Duration of Stay (hours)			
<1 hour	16(21.6%)	29(39.2%)	0.015*
1-12 hours	49(66.2%)	44(59.5%)	
12.1-24 hours	8(10.8%)	1(1.4%)	
24.1-36 hours	1(1.4%)	0(0%)	
Duration of hospital stay (hours)			
Mean ± SD	47.08 ± 42.71	28.76 ± 19.21	0.001**
Duration of hospital stay			
1-12 hours	13(17.6%)	16(21.6%)	0.008*
12.1-24 hours	16(21.6%)	23(31.1%)	
24.1-36 hours	11(14.9%)	19(25.7%)	
36.1-72	23(31.1%)	15(20.3%)	
>72 hours	11(14.9%)	1(1.4%)	
Total	74(100%)	74(100%)	

Moreover, 39.2% of children in the nebulized group stayed less than one hour in the PICU, compared with 21.6% in the IV group (p = 0.015). The total duration of hospital stay was also significantly reduced in the nebulized $MgSO_4$ group (28.76 ± 19.21 hours) compared to the IV $MgSO_4$ group (47.08 ± 42.71 hours; p = 0.001), indicating earlier clinical recovery and discharge among those receiving nebulized treatment.

Comparison of treatment efficacy and side effects is presented in Table IV. Clinical efficacy was achieved in 27% of patients in the IV group and 14.9% in the nebulized group; however, this difference was not statistically significant (p = 0.069). In contrast, adverse effects were significantly more frequent among those treated with IV $MgSO_4$ (29.7%) compared with none in the nebulized group (p < 0.001). Specific side effects,

detailed in Table V, revealed that nausea ($p < 0.001$), headache ($p = 0.012$), and hypotension ($p = 0.043$) occurred only in the IV $MgSO_4$ group, while flushing was rare and comparable between the groups ($p = 0.316$). No adverse effects were observed in the nebulized group, highlighting its favorable safety profile.

Table IV: Comparison of efficacy and side effects in Treatment Groups.

Parameters	Treatment Group		P-value
	IV MgSO4	Nebulized MgSO4	
Efficacy			
Yes	20(27%)	11(14.9%)	0.069
No	54(73%)	63(85.1%)	
Side effects			
Yes	22(29.7%)	0(0%)	0.000**
No	52(70.3%)	74(100%)	
Total	74(100%)	74(100%)	

***. Highly Significant at 5% level of significance*

Table V: Comparison of flushing in Treatment Groups.

Side effects	Status	Treatment Group		p-value
		IV MgSO4	Nebulized MgSO4	
Flushing	Yes	1(1.4%)	0(0%)	0.316
	No	73(98.6%)	74(100%)	
Nausea	Yes	13(17.6%)	0(0%)	<0.001**
	No	61(82.4%)	74(100%)	
Headache	Yes	6(8.1%)	0(0%)	0.012*
	No	68(91.9%)	74(100%)	
Hypotension	Yes	4(5.4%)	0(0%)	0.043*
	No	70(94.6%)	74(100%)	
Total		74(100%)	74(100%)	

Overall, both intravenous and nebulized magnesium sulphate significantly improved asthma symptoms in children. However, nebulized magnesium sulphate demonstrated comparable therapeutic efficacy with markedly fewer side effects, shorter PICU duration, and reduced hospital stay, suggesting that it may serve as a safer and more practical alternative in the management of acute asthma in pediatric patients.

Discussion

Asthma is one of the most prevalent chronic respiratory diseases in children, characterized by airway inflammation, bronchial hyper-responsiveness, and reversible airflow obstruction. Management of acute asthma focuses on rapid relief of bronchospasm through inhaled β_2-agonists such as salbutamol, supplemented by oxygen therapy and corticosteroids. Additional pharmacologic options include nebulized anticholinergic agents, subcutaneous epinephrine, aminophylline, and magnesium sulphate administered intravenously or via nebulization.[12] Magnesium sulphate acts as a smooth muscle relaxant by inhibiting calcium uptake in airway smooth muscle, stabilizing mast cell membranes, and augmenting the bronchodilatory response to β_2-agonists.[13]

The present study compared the efficacy and safety of nebulized and intravenous magnesium sulphate in children with moderate-to-severe acute asthma. The two groups were comparable in age (6.25 ± 3.43 vs. 6.29 ± 3.42 years; $p = 0.079$) and baseline severity (mean PAS = 11.01 ± 1.53 vs. 10.68 ± 1.45; $p = 0.171$), indicating well-matched cohorts. Both routes produced progressive improvement in PAS during the 6-hour observation period. The nebulized group demonstrated a significantly greater reduction in PAS at 30 minutes ($p = 0.036$), suggesting a more rapid initial bronchodilator effect. Thereafter, PAS differences at 60, 120, 240, and 360 minutes were statistically non-significant ($p > 0.05$), confirming comparable efficacy between nebulized and intravenous administration. These results are consistent with earlier studies reporting equivalent clinical improvement with either route of magnesium delivery.[14,15,22]

In this study, the mean duration of Pediatric Intensive Care Unit (PICU) stay was significantly shorter in the nebulized group (3.32 ± 4.23 hours) compared with the intravenous group (5.94 ± 9.78 hours; $p = 0.036$). Similarly, the mean total hospital stay was markedly reduced in the nebulized $MgSO_4$ group (28.76 ± 19.21 hours) relative to the intravenous group (47.08 ± 42.71 hours; $p = 0.001$). These findings indicate faster clinical recovery and earlier discharge with nebulized therapy. Sarmin et al. reported comparable results, showing shorter discharge readiness times among children receiving nebulized magnesium sulphate.[15] A Cochrane overview by Craig et al. also concluded that magnesium sulphate, particularly via nebulization, reduces hospitalization and improves airflow obstruction in pediatric asthma exacerbations.[16]

Although the proportion of patients achieving clinical efficacy did not differ significantly (27% in the intravenous group vs. 14.9% in the nebulized group; $p = 0.069$), the adverse-effect profile strongly favored nebulized therapy. Side effects occurred in 29.7% of patients receiving IV $MgSO_4$, compared with none in the nebulized group ($p < 0.001$). Nausea (17.6%), headache (8.1%), and hypotension (5.4%) were significantly more frequent with intravenous administration ($p < 0.05$ for each). These observations align with previous studies identifying dose-related flushing and rate-related

hypotension as the main adverse effects of IV magnesium.[17,21] Conversely, nebulized magnesium demonstrated an excellent safety profile, with no systemic side effects noted, corroborating earlier findings by Ciarallo et al. and Hughes et al. [18,19]

Collectively, the results of this study affirm that both intravenous and nebulized magnesium sulphate are effective in alleviating acute asthma symptoms in children. However, nebulized $MgSO_4$ achieved comparable improvement in PAS with fewer adverse events, a significantly shorter PICU stay, and reduced hospital duration. These outcomes are consistent with prior clinical and meta-analytic evidence demonstrating that nebulized magnesium is a safe, well-tolerated, and efficacious adjunct to standard bronchodilator therapy.[20–22] Hence, nebulized magnesium sulphate represents a practical and safer alternative for pediatric patients with acute asthma, especially in emergency or resource-limited settings. Further multicenter randomized controlled trials are warranted to refine dosage strategies and confirm long-term benefits.

Conclusion

This study demonstrates that both nebulized and intravenous magnesium sulphate are effective in improving respiratory function and relieving symptoms in children with acute moderate-to-severe asthma. However, nebulized magnesium sulphate offered distinct clinical advantages, including a more rapid initial response, shorter intensive care and hospital stay, and a superior safety profile. While both routes provided comparable therapeutic efficacy, adverse effects were observed only with intravenous administration, whereas nebulized treatment was well tolerated by all patients.

These findings suggest that nebulized magnesium sulphate can serve as a safe, effective, and practical alternative to intravenous therapy in the management of acute asthma in pediatric patients. Its ease of administration, absence of systemic side effects, and favorable clinical outcomes make it particularly suitable for use in both emergency and hospital settings. Further multicenter studies with larger sample sizes are recommended to validate these results and to establish standardized treatment protocols for optimal use of nebulized magnesium sulphate in acute pediatric asthma management.

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