ORIGINAL ARTICLE

Randomised controlled trial of intravenous magnesium sulfate versus terbutaline for children in the management of acute exacerbation of asthma

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Abstract

Objective: To compare the effectiveness and safety of intravenous magnesium sulfate versus terbutaline in children with acute asthma exacerbations.

Method: This randomised controlled trial was conducted at the Paediatric Department of The Children's Hospital and Institute of Child Health, Multan, Pakistan, from January to August 2024, and comprised children of either gender aged 5-12 years who had a history of asthma for a minimum of six months, and presented with acute exacerbation of asthma requiring emergency treatment. The patients were randomly allocated to group A receiving intravenous magnesium sulfate and group B receiving intravenous terbutaline. After four hours of treatment, the response to treatment was measured on the basis of peak expiratory flow rate, oxygen saturation, heart rate and respiratory rate. Data was analysed using SPSS 26.

Results: Of the 120 children, 62(51.7%) were girls. The overall mean age was 8.40±2.41 years. Post-treatment peak expiratory flow rate, oxygen saturation, heart rate, tachycardia and need for hospitalisation values were significantly better in group A compared to group B ($p<0.05$).

Conclusion: Intravenous magnesium sulfate was more effective and safer than terbutaline in the management of acute asthma exacerbations in children.

Trial Registration Number: NCT06626620.

Key Words: Asthma, Heart rate, Peak expiratory flow rate, Respiratory rate, Terbutaline.

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Introduction

It is estimated that approximately 262 million children globally suffer from asthma. In the United States, around 5 million children below 18 years of age are affected by asthma.[1,2] In Pakistan, around 15 million children are suspected to be suffering from asthma.[3] Acute asthma exacerbation (AAE) is a significant cause of emergency department (ED) visits, leading up to 10% of all ED visits.[4]

Management of AAEs in children is crucial for preventing morbidity and reducing hospital admissions.[5] Standard treatment typically includes inhaled "short-acting beta-agonists" (SABAs), such as albuterol, and systemic corticosteroids to reduce airway inflammation.[6] However, in cases of severe AAEs where initial therapies fail to achieve adequate control, additional treatments are required. Intravenous (IV) magnesium sulfate (MgSO4) and terbutaline are two such adjunct therapies used in emergency settings to manage refractory asthma exacerbations.[5,7-9]

MgSO4, a smooth muscle relaxant, has been shown to have bronchodilatory effects, and is associated with improved lung function and reduced hospital admission rates in children with severe AAEs.[10] Terbutaline, a beta-2 agonist, is used IV to provide systemic bronchodilation when inhaled bronchodilators are not effective.[11] Both MgSO4, and terbutaline are recommended for treating severe AAEs that are unresponsive to initial treatments. MgSO4, typically administered as a single IV dose, has been found to improve peak expiratory flow rate (PEFR) and reduce the need for hospitalisation. It can reduce hospital admission rates by up to 68% in children with severe AAEs.[12] Terbutaline, on the other hand, is often used as a continuous IV infusion to provide rapid and sustained bronchodilation.[13] However, terbutaline has been documented with a higher risk of systemic side-effects, such as tachycardia and tremors, compared to MgSO4.[14]

Despite the established roles of both MgSO4, and terbutaline in the management of severe AAEs, there is limited comparative data on their efficacy and safety in the paediatric population. The current study was planned to fill the gap in literature by comparing the effectiveness

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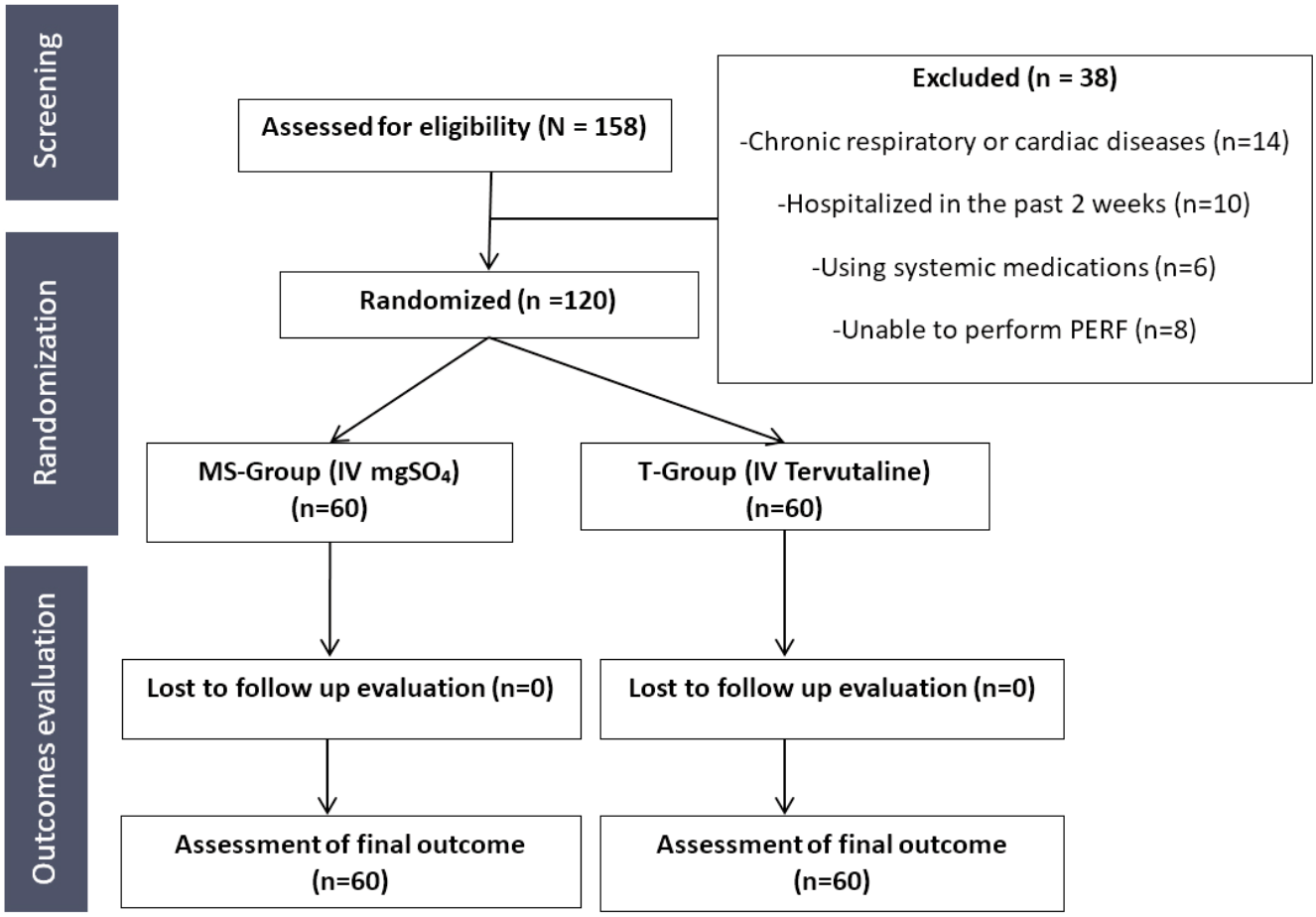

Figure-1: Consolidated Standards of Reporting Trials (CONSORT) flow diagram.

of IV MgSO4 versus terbutaline in children with AAEs.

Patients and Methods

The randomized controlled trial (RCT) was conducted at the Paediatric Department of The Children's Hospital and Institute of Child Health, Multan", Pakistan, from January to August 2024. After approval from the institutional ethics review committee, the sample size was calculated using OpenEpi calculator,[15] considering the treatment success of MgSO4 and terbutaline in AAEs in children as 97% and 70%, respectively,[16] with 99% confidence level and 90% power of study. Written informed consent was obtained from all children aged 7-17 years in addition to written informed consent from their parents or legal guardians. The assent process was conducted in an age-appropriate manner to ensure understanding and voluntary participation.

Those included were children of either gender aged 5-12 years having asthma history of minimum six months who presented with AAEs requiring emergency treatment. Children having chronic respiratory diseases, like cystic fibrosis and bronchopulmonary dysplasia, or cardiac diseases, children who had been hospitalised in the preceding two weeks due to any reasons, children using oral or IV corticosteroids or other systemic medications that could affect the outcomes, and patients who were unable to undergo PEFR measurements due to any reasons were also excluded. AAE was defined as a sudden worsening of asthma symptoms, and PEFR<60% of normal. Participants were recruited using a non-probability consecutive sampling technique.

After recording baseline demographic information, medical history and clinical parameters, the patients were randomly allocated in a 1:1 ratio to group A receiving IV MgSO4 and group B receiving IV terbutaline. Randomization was performed using a computer-generated random number sequence, and allocation concealment was ensured through sequentially numbered opaque sealed envelopes prepared by an independent investigator who was not involved in

patient recruitment or outcome assessment. Children in group A received IV MgSO4 50mg/kg up to a maximum dose of 2g administered over 20 minutes, while those in group B received IV terbutaline 10mcg/kg bolus, followed by a continuous infusion of 0.4mcg/kg/min for up to four hours. Both the groups received standard asthma management, including inhaled bronchodilators and systemic corticosteroids, as per institutional protocols.

After four hours of treatment, the children's response to treatment was measured on the basis of PEFR, oxygen saturation, heart rate (HR) and respiratory rate. Any unintended or harmful reactions observed following the administration of MgSO4 or terbutaline, including but not limited to hypotension, bradycardia, tachycardia and tremors, were noted by a trained postgraduate resident. The need for hospital admission was also recorded as an outcome measure. A Consolidated Standards of Reporting Trials (CONSORT) format was followed (figure 1).[17]

Data was analyzed using SPSS 26. Continuous variables were presented as mean ± standard deviation (SD), and compared using independent t-test. Categorical variables were presented as frequencies and percentages, and were analyzed using chi-square or Fisher's exact test. P≤0.05 was considered statistically significant.

Results

Of the 158 patients assessed, 120(75.9%) were enrolled; 62(51.7%) girls and 58(48.3%) boys. The overall mean age was 8.40±2.41 years. The mean duration of asthma in group A was 3.37±1.22 years compared to 3.08±0.94 years in group B. At the baseline, the difference between the two groups was not significant for any parameter (Table 1).

Post-treatment PEFR, oxygen saturation, heart rate, tachycardia and need for hospitalization values were significantly better in group A compared to group B (Table 2).

Table-1: Intergroup comparison of baseline characteristics (n=120).

Baseline characteristics	MS-group (n=60)	T-group (n=60)	P-value
Gender			0.715
Male	30 (50.0%)	28 (46.77%)	
Female	30 (580.0%)	32 (53.3%)	
Age (years)	8.39±2.37	8.41±2.48	0.970
Duration of asthma (years)	3.37±1.22	3.08±0.94	0.142
PEFR (L/min)	123.64±21.76	120.73±21.45	0.463
Respiratory rate (breaths/min)	30.83±3.64	29.89±3.60	0.157
Heart rate (beats/min)	112.01±6.59	113.10±7.88	0.414
Oxygen saturation (%)	93.24±3.02	92.62±3.08	0.265

PFER: Peak expiratory flow rate.

Table-2: Intergroup comparison of post-treatment outcomes.

Outcome variables	MS-group (n=60)	T-group (n=60)	P-value
Post-treatment PEFR (L/min)	175.91±23.66	166.48±25.20	0.037
Post-treatment Oxygen saturation (%)	99.47±3.43	97.82±3.69	0.013
Post-treatment heart rate (beats/min)	104.17±7.25	115.46±8.08	<0.001
Post-treatment respiratory rate (resp/min)	25.59±3.48	26.30±3.83	0.290
Frequency of adverse events			
Hypotension	1 (1.7%)	-	0.315
Bradycardia	3 (5.0%)	-	0.079
Tachycardia	-	5 (8.3%)	0.022
Tremors	-	3 (5.0%)	0.079
Hospital admission	12 (20.0%)	22 (36.7%)	0.043
Duration of hospitalization	3.47±1.32	3.18±1.39	0.566

PFER: Peak expiratory flow rate.

Discussion

The current study shows that while both the treatment modalities led to improvements, IV $MgSO_4$ demonstrated superior efficacy in terms of post-treatment PEFR, HR, and the need for hospital admissions compared to terbutaline. Also, there was no case of tachycardia post-treatment in the MgSO4 group compared to 5(8.3%) in the terbutaline group.

Singhi et al. reported that MgSO4 significantly improved lung function and reduced AAE severity compared to terbutaline and aminophylline. The study demonstrated a 97% treatment success rate with IV $MgSO_4$ as opposed to 70% for both terbutaline and aminophylline (p=0.006).[16] Ambrożej et al. reported a significant improvement in lung function with IV $MgSO_4$, with a mean PEFR improvement of 26.8% (95% confidence interval [CI]: 18.41-54.79).[18] These findings exhibit that IV $MgSO_4$ is a potent bronchodilator capable of providing rapid improvement in respiratory parameters. The current results regarding post-treatment oxygen saturation are supported by Multafa et al.[19]

The post-treatment respiratory rate in the current study was slightly lower in the MgSO4 group than in the terbutaline group, suggesting that while both treatments were effective in stabilising respiratory function, IV $MgSO_4$ may offer a slight advantage in reducing respiratory effort, a benefit also noted by Doymaz et al.[20] Post-treatment HR was significantly lower with MgSO4 in the current study , which was in line with an earlier study.[21] The elevated HR with terbutaline can be attributed to the beta-adrenergic effects of terbutaline, which increase sympathetic tone and cardiac workload.[22] Conversely, the

role of $MgSO_4$ as a calcium antagonist contributes to its ability to lower HR by reducing myocardial contractility and vascular resistance.[23] This cardioprotective effect is crucial in contributing cardiovascular complications due to the increased systemic stress of an AAE.

The incidence of adverse events in the current further underscores the safety profile of IV $MgSO_4$. Schuh et al.[24] reported that $MgSO_4$ had fewer side-effects even when compared to placebo, with no significant increase in adverse events, such as hypotension or bradycardia. Liu et al. highlighted that IV $MgSO_4$ significantly improved respiratory function without increasing adverse events in paediatric patients with moderate to severe asthma.[25]

One of the most clinically relevant findings of the current study was the significantly lower rate of hospital admissions in IV $MgSO_4$ group compared to the terbutaline group (p=0.043). The finding mirrors the outcomes reported by Ambrożej et al.[18] Contemporary guidelines also recommend the use of IV $MgSO_4$ in children with severe asthma exacerbations not responding to conventional initial treatment.[25] The efficacy of IV $MgSO_4$ observed in the current study also supports the conclusions of a systematic review,[26] which found that IV $MgSO_4$ reduces the need for hospital admission and improved respiratory function in severe asthma.

The favourable safety profile of IV $MgSO_4$, with minimal adverse events, supports its use in emergency settings. However, the potential for bradycardia and hypotension, though rare, necessitates careful monitoring, particularly in patients with underlying cardiac conditions or those receiving concomitant medications that may affect cardiovascular function.

The current study has several limitations. It was conducted at a single tertiary care centre, which may limit the generalisability of the findings. The post-treatment evaluation period was limited to the first four hours, so long-term outcomes and relapse rates could not be assessed. Although PEFR was used as a key objective measure, its reliability may be affected in younger or less cooperative children.

Conclusion

IV MgSO4 was found to be more effective and safer than terbutaline in the management of AAEs in children. MgSO4 can be considered a preferred adjunct therapy in children with AAEs.

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AUTHORS' CONTRIBUTIONS:
AZ: Concept, drafting, final approval and agreement to be accountable for all aspects of the work.
AF & MTA: Data acquisition, analysis, drafting, final approval and agreement to be accountable for all aspects of the work.
MSZ: Concept, design, drafting, final approval and agreement to be accountable for all aspects of the work.