ORIGINAL ARTICLE

Optimal Timing for Magnesium Sulfate Use in Pediatric Asthma Exacerbations

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Background: Intravenous magnesium sulfate ($MgSO_4$) is an effective adjunctive therapy for severe pediatric asthma exacerbations, but the optimal administration timing remains unclear.

Objective: To describe the clinical course and outcomes of children hospitalized with moderate to severe asthma exacerbations treated with intravenous $MgSO_4$, stratified by administration timing.

Materials and Methods: A retrospective descriptive case series was conducted at a single university hospital in Thailand between 2022 and 2024. Children aged 2 to 15 years receiving intravenous $MgSO_4$ were categorized into early (310 minutes or less from triage) and late (more than 310 minutes) groups. Outcomes included time to clinical improvement, oxygen therapy duration, length of hospital stay (LOS), and adverse events.

Results: Ten patients were included, with six patients in the early group and four patients in the late group. Patients in the early group showed a trend toward faster clinical improvement (range 3.5 to 6.0 versus 7.0 to 11.0 hours) and shorter duration of oxygen therapy (median 51.0 versus 94.5 hours) compared to the late group. LOS varied between groups (median 72.0 versus 107.0 hours). No mechanical ventilation or adverse events occurred.

Conclusion: Earlier administration of $MgSO_4$ appeared to be associated with faster symptom resolution and reduced oxygen requirements in the present case series. The therapy was safe and well-tolerated. However, results should be interpreted with caution due to the small sample size and retrospective design.

Keywords: Magnesium sulfate; Asthma; Child; Time-to-treatment; Treatment outcome

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Acute asthma exacerbations remain a significant cause of morbidity in children worldwide, leading to frequent emergency department (ED) visits and hospital admissions[1], consequently affecting their quality of life as well as their academic performance[2]. These acute events are characterized by a complex interplay of bronchoconstriction, airway inflammation, and increased mucus production, which collectively lead to airflow obstruction, air trapping, and ventilation-perfusion mismatch[3]. The key management for acute asthma exacerbations is the rapid reversal of bronchoconstriction and control of airway inflammation. Standard first-line therapies include repeated administration of inhaled β2-agonists and early initiation of systemic corticosteroids. While this regimen is effective for most patients[4], a subset of pediatric patients experiences severe symptoms that are refractory to initial management.

Intravenous magnesium sulfate ($MgSO_4$) is recommended as an adjunct for severe exacerbations due to its bronchodilatory and anti-inflammatory actions[5-7]. Its main therapeutic mechanism is physiological calcium antagonism. As a calcium antagonist, it inhibits calcium influx into airway smooth muscle cells, an effect that disrupts actin-myosin coupling to produce bronchodilation. Additionally, $MgSO_4$ may inhibit the release of acetylcholine from cholinergic nerve endings and histamine from mast cells.

Despite the recognized benefits of $MgSO_4$, its clinical application remains inconsistent. Many physicians are hesitant to use it due to concerns about potential side effects such as hypotension and respiratory depression[8], even though previous studies have affirmed its safety in the pediatric population

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when administered correctly[9]. This uncertainty is compounded by the fact that the optimal timing for $MgSO_4$ administration is not well established[10], and clinical practice varies considerably[11]. Some guidelines recommend its use only after failure of standard therapy, while others advocate for earlier administration in patients presenting with severe symptoms. Delays in administration may arise from logistical factors, such as the time required for intravenous access and drug preparation, institutional protocols, and human resource constraints, all of which could potentially affect patient outcomes.

The present study aimed to assess the effect of early versus late $MgSO_4$ administration on clinical outcomes in children hospitalized with asthma exacerbations. The findings would not only provide insights into the effectiveness of $MgSO_4$ administration within this time frame but also inform localized and potentially broader clinical practices for managing this common pediatric emergency.

Materials and Methods

Study design and population

The author identified patients aged 2 to 15 years who were hospitalized with a primary diagnosis of acute asthma exacerbation between 2022 and 2024. The hospital's electronic medical record (EMR) database was screened for relevant ICD-10 codes, and those results were cross-referenced with pharmacy records to confirm each patient received at least one dose of intravenous $MgSO_4$. Patients were excluded if they had chronic respiratory comorbidities (such as cystic fibrosis or bronchopulmonary dysplasia) or if their medical records were incomplete.

Patients were divided into two groups based on the timing of $MgSO_4$ administration relative to triage, using the cohort median of 310 minutes: early administration (310 minutes or less) and late administration (more than 310 minutes). This median split approach was chosen as a pragmatic method to create comparable groups based on the actual distribution of treatment times observed in the present study clinical setting. The time of triage was defined as the time the patient was first registered and assessed by a healthcare professional in the ED. The time of $MgSO_4$ administration was defined as the start of the intravenous infusion. All patients received standard care as per institutional guidelines, which included inhaled β2-agonists, systemic corticosteroids, and supplemental oxygen as needed. Oxygen therapy was weaned according to the ward protocol, which required maintaining oxygen saturation (SpO_2) greater than 95% in room air with no signs of respiratory distress for at least two hours. The decision to administer $MgSO_4$, as well as its dose and frequency, was at the discretion of the treating physician.

The present study was approved by the Human Research Ethics Committee of Suranaree University of Technology (EC-68-08). Permission to access patient medical records for data collection was obtained from the hospital director. The requirement for informed patient consent was formally waived by the Institutional Review Board (IRB), as this was a retrospective descriptive case series that had no effect on patient treatment or clinical outcomes and posed minimal risk to patients.

Data collection and variables

Data from eligible patients were collected via a structured review of their EMRs by a single investigator (PS) using a standardized data abstraction form. Collected variables included demographic characteristics (age and sex), timing, and dose of $MgSO_4$ administration, asthma severity assessed by the Siriraj Clinical Asthma Score (SCAS), and the use of adjunctive therapies such as subcutaneous terbutaline and nebulized budesonide. The SCAS, a validated scoring system, was recorded at presentation and assessed hourly by trained nursing staff using a standardized clinical monitoring form.

Study outcomes

The primary outcome was the length of hospital stay (LOS), calculated in hours from the time of admission to the time of the discharge order. Secondary outcomes included 1) time to clinical improvement, defined as the time in hours from $MgSO_4$ administration to the first documented sustained reduction in the SCAS by 3 points or more, 2) total duration of oxygen therapy in hours, 3) the need for mechanical ventilation, and 4) the occurrence of adverse events potentially related to $MgSO_4$, such as hypotension, flushing, or respiratory depression, as documented in the medical record.

Definition of asthma and severity assessment

Asthma and acute asthma exacerbation were defined according to the Global Initiative for Asthma (GINA) guidelines[4]. The severity of the exacerbation at presentation and during hospitalization was classified using the SCAS score[12]. The SCAS is a five-component score including respiratory rate, use of accessory muscles (retraction), degree of

Table 1. Clinical characteristics and outcomes of the 10 pediatric patients treated with intravenous $MgSO_4$ for acute asthma exacerbation

Case	Age (years)/ sex	SCAS	Time to $MgSO_4$ (minutes)	$MgSO_4$ dose (mg/kg)	Adjunctive therapy	Controller	Time to improve* (hours)	Oxygen duration (hours)	LOS (hours)
Early administration (≤310 minutes)									
1	9/M	6	310	50	-	-	3.5	54	72
2	5/M	8	300	25	-	-	4	46	50
3	6/M	5	235	50	-	-	4	48	74
4	9/F	6	300	50	-	-	5	67	70
5	4/M	4	300	50	Terbutaline (SC)	ICS	5	48	72
6	2/F	7	253	50	Terbutaline (SC)	ICS	6	92	121
Late administration (>310 minutes)									
7	6/M	6	380	50	-	ICS	7	96	120
8	6/M	8	350	25	-	ICS/LABA	11	93	94
9	3/M	8	480	25	-		10	56	61
10	10/M	8	555	25	-		7	96	127

SCAS=Siriraj Clinical Asthma Score; $MgSO_4$=magnesium sulfate; LOS=length of hospital stay; SC=subcutaneous; ICS=inhaled corticosteroids; LABA=long-acting beta-agonists

* Time to clinical improvement was defined as the time from $MgSO_4$ administration to a sustained reduction in SCAS of ≥3 points, assessed hourly by nursing staff.

wheezing, dyspnea, and SpO_2, with each component scored from 0 to 2 for a total range of 0 to 10. Mild exacerbation was defined as a score of less than 4, moderate as 4 to 7, and severe as greater than 7.

Statistical analysis

Given the small sample size and the descriptive case series design, formal hypothesis testing was not performed to avoid type II errors. Data was analyzed using descriptive statistics. Continuous variables were summarized as median with interquartile range (IQR) or range, or as mean ± standard deviation (SD) where appropriate. Categorical variables were presented as frequencies and percentages. To evaluate clinical impact, the magnitude of differences between the early and late administration groups was assessed descriptively using absolute differences in medians as descriptive effect sizes. For temporal changes in SCAS, data were presented as means with 95% confidence intervals (CI). All analyses were performed using Stata Statistical Software, version 15.1 (StataCorp LLC, College Station, TX, USA).

Results

Ten pediatric patients aged 2 to 10 years (median age 6 years), and 80% were male, were included in the present case series. One-fifth had a history of prior asthma hospitalization. All patients presented with moderate to severe asthma exacerbations (median initial SCAS 6.5, range 4 to 8), with 60% classified as moderate. Comorbid pneumonia was identified in 60% of cases, all of which were clinically diagnosed with no specific pathogen identified.

Regarding standard treatment, all patients (100%) received high-flow nasal cannula oxygen therapy, and 80% received nebulized budesonide. Systemic corticosteroids were administered to all patients (100%), consisting of intravenous hydrocortisone (50%) and methylprednisolone (50%). Maintenance-controlled therapy was used in 40% of patients (4 patients), consisting of inhaled corticosteroids (ICS) alone in three patients and an ICS/long-acting beta-agonist (ICS/LABA) combination in one patient. Subcutaneous terbutaline was used as an adjunctive therapy in 20% of cases. Following the failure of initial therapy, patients received a median $MgSO_4$ dose of 50 mg/kg (range 25 to 50). The administration protocols varied as 50% received a single bolus, 40% received multiple doses, and one patient (10%) received a continuous infusion.

Clinical course and response to treatment

Individual clinical characteristics and outcomes for each patient are detailed in Table 1. The median time to $MgSO_4$ administration was 310 minutes (IQR 300 to 380), defined as early (310 minutes or less from triage) and late (more than 310 minutes from triage) groups. Six patients received $MgSO_4$ within the early timeframe. In this group (Cases 1 to 6), the time for clinical improvement was notably short, ranging from 3.5 to 6.0 hours. For instance, Case 1 and 2, who received treatment at 310 and 300 minutes, respectively, showed rapid improvement within four hours. In contrast, the four patients in the late

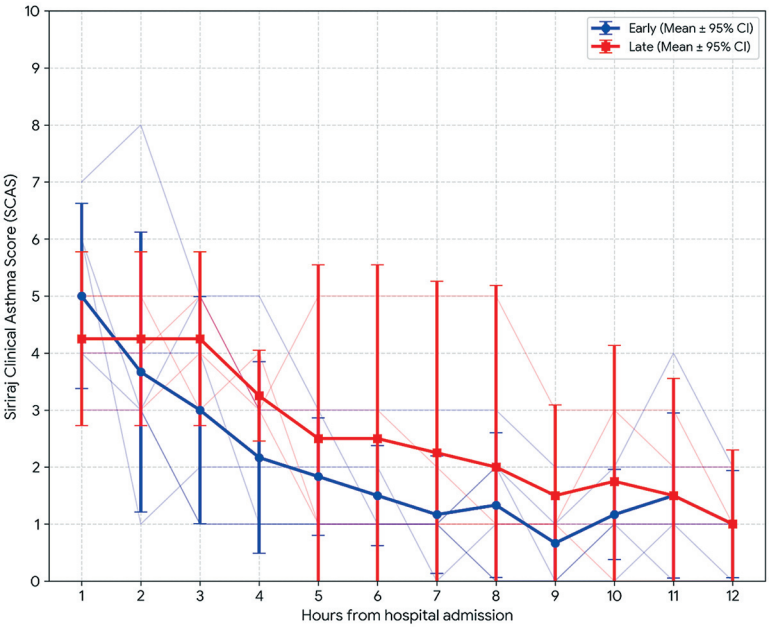

Figure 1. Temporal changes in mean Siriraj Clinical Asthma Score (SCAS) relative to hours from hospital admission.

Faint lines represent individual patient trajectories (Spaghetti plot), while solid lines represent the mean SCAS for each group. Error bars denote the 95% confidence interval (CI).

Early=early magnesium sulfate administration group; Late=late magnesium sulfate administration group

administration group experienced a longer interval before improvement (range 7.0 to 11.0 hours).

Temporal changes in SCAS

Figure 1 illustrates the individual clinical courses and the mean changes in SCAS over the first 12 hours of admission. All 10 patients remained hospitalized and were followed for the entire duration shown. Patients in the early group showed a consistent downward trend in SCAS from hour 1 to hour 4 of admission, while no significant change was observed in the late group over the same period.

Oxygen therapy and safety

The duration of oxygen therapy appeared shorter in the early administration group, with a median of 51.0 hours (range 46 to 92) compared to the late administration group with a median of 94.5 hours (range 56 to 96), with the exception of Case 9. Despite these differences in acute response, the total LOS varied widely across both groups (range 50 to 127 hours). No patients required mechanical ventilation. Regarding safety, no adverse events (e.g., hypotension or respiratory depression) were documented. Serum magnesium levels were monitored post-administration in four patients (Cases 1, 2, 9, 10), with levels ranging from 1.9 to 4.7 mg/dL, and no clinical signs of hypermagnesemia were observed.

Discussion

This retrospective descriptive case series described the clinical impact of early (310 minutes or less) versus late intravenous $MgSO_4$ administration. The author observed that patients who received treatment earlier showed a trend toward faster clinical improvement and a shorter duration of oxygen therapy, making this one of the few studies to demonstrate this benefit[13]. However, this early clinical benefit did not translate into a distinct reduction in the overall LOS. These findings are consistent with the pharmacologic properties of $MgSO_4$, which acts rapidly to relax airway smooth muscle by inhibiting calcium influx and exerts anti-inflammatory effects that can alleviate the severity of the exacerbation[5,14]. These mechanisms contribute to early reversal of bronchospasm and enhanced gas exchange[15], which explains the observed reduction in oxygen requirement and the more rapid improvement in clinical scores in the early treatment group[13,16].

Comparison with existing literature

The present study results align with and build upon the existing literature, a meta-analysis by

Cheuk et al., a Cochrane review by Griffiths et al., and a recent systematic review by Ambrożej et al. All concluded that while intravenous $MgSO_4$ improves lung function and reduces the risk of hospitalization when administered in the ED, its effect on the duration of hospitalization for already admitted patients is less clear[16-18]. The author's observation that early administration shortens the time to clinical improvement is consistent with a study by Singhi et al., which found that $MgSO_4$ was effective in producing rapid clinical improvement in children with acute severe asthma[19].

Despite clear early clinical benefits, the lack of a significant reduction in LOS suggests a disconnect between acute physiological improvement and the complex decision-making process surrounding hospital discharge. Several factors may contribute to this observation. First, the direct bronchodilatory effects of a single dose of $MgSO_4$ may wane over time[20], while the underlying airway inflammation persists, requiring continued observation and treatment with corticosteroids, which may ultimately dictate the LOS. Second, the presence of comorbidities, such as pneumonia[21], can prolong recovery and oxygen requirements independently of the asthma exacerbation itself.

Clinical and system-level implications

Most importantly, non-clinical factors often play a dominant role in discharge timing. Studies on hospital discharge processes have shown that delays are frequently caused by institutional routines, discharge planning, variations in physician criteria for what constitutes "discharge readiness", and the need for patient and family education to ensure a safe transition to home care[22,23]. Even when a patient is physiologically stable, they may not be discharged until a formal consultation is completed, a home care plan is established, or a specific time of day is reached. Therefore, while an intervention like early $MgSO_4$ can accelerate recovery in the initial, critical hours, its effect on the final discharge time can be diluted by these systemic factors. Moreover, the small sample size and retrospective design of the present study may limit the generalizability of these findings, preventing definitive conclusions regarding LOS. Despite the lack of impact on LOS, the benefits of faster clinical improvement and reduced oxygen duration are highly clinically relevant. For the patient, this means a quicker reduction in respiratory distress and discomfort. For the healthcare system, especially in resource-limited settings, reducing the duration of oxygen therapy can conserve valuable resources and potentially improve patient flow in high-acuity areas like the ED or pediatric intensive care unit. The present study's finding that $MgSO_4$ was administered safely, with no adverse events recorded, reinforces its favorable safety profile and should encourage its timely use in moderately to severely ill children who are not responding to standard therapy.

Limitation

The present study has limitations that warrant consideration. First, the small sample size (10 participants) makes the study underpowered, limiting statistical analysis and increasing the risk of confounding. Second, the retrospective single-center design restricts causal inference and limits generalizability to settings with different protocols. Third, the use of a median split to define early versus late administration may be arbitrary and could obscure clinically meaningful timing thresholds specific to individual pathophysiology. Fourth, the decision to administer $MgSO_4$, including dose and frequency, was left to the physician's discretion, introducing potential treatment selection bias. Fifth, data abstraction by a single investigator may have introduced observer bias, despite the use of a standardized form. Sixth, potential confounders such as prior asthma control, medication adherence, and environmental triggers were not assessed. And finally, reliance on EMR documentation may have resulted in incomplete data, and details regarding infectious comorbidities were undefined in many cases. Larger, prospective studies are needed to validate these preliminary trends.

Conclusion

The present case series suggests that early administration of intravenous $MgSO_4$ may facilitate rapid clinical improvement and reduce the duration of oxygen therapy in pediatric asthma exacerbations. While the small sample size limits definitive causal conclusions, the observed trends support the potential benefit of optimizing administration timing. Further prospective studies with larger populations are warranted to confirm these findings.

What is already known about this topic?

Intravenous $MgSO_4$ is an established adjunctive therapy for severe pediatric asthma that improves lung function and reduces hospital admissions when administered in the ED. However, its clinical application is inconsistent, and the optimal timing

for its use and its effect on the LOS for hospitalized patients remains unclear.

What does this study add?

This descriptive case series suggests that early administration of $MgSO_4$ in hospitalized children with severe asthma exacerbations may be associated with faster clinical improvement and a reduced duration of oxygen therapy. Although a reduction in overall hospital stay was not observed, the findings support the safety of early intervention and highlight its potential value in conserving resources and improving patient flow in resource-limited settings.

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Author's contributions

PS: Conceptualization, methodology, investigation, formal analysis, writing-original draft, writing-review & editing.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics approval and consent to participate

This study was approved by the Human Research Ethics Committee of Suranaree University of Technology (Approval No. EC-68-08). Permission to access patient medical records was granted by the hospital director. The requirement for informed patient consent was formally waived by the Institutional Review Board (IRB) due to the retrospective, observational nature of the study, which posed minimal risk to patients and had no impact on their clinical care.

Clinical trial registration

Not applicable. This study is a retrospective observational case series and does not meet the definition of a clinical trial requiring registration.

Use of artificial intelligence

During the preparation of this work, the author used Google Gemini to identify and correct grammatical errors and improve the readability of the English language. After using this tool, the author reviewed and edited the content as needed and takes full responsibility for the final content of the publication.

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Conflicts of interest

The authors declare no conflict of interest.

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