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RESEARCH ARTICLE
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COMPARISON OF INTRAVENOUS VERSUS NEBULIZED MAGNESIUM SULFATE AS ADJUNCT TREATMENT IN ACUTE ASTHMA IN ADULTS IN THE EMERGENCY DEPARTMENT OF A TERTIARY CARE HOSPITAL

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ABSTRACT

Background: Magnesium sulfate ($MgSO_4$) is an established adjunct treatment for acute severe asthma, available via intravenous (IV) or nebulized routes. Limited evidence exists comparing these administration methods in adults, with most research focusing on pediatric populations.

Objective: To compare the efficacy of IV versus nebulized $MgSO_4$ as adjunct treatment in acute asthma among adults presenting to the emergency department, specifically examining dyspnea improvement and clinical outcomes.

Methods: A randomized controlled trial was conducted at Dr. Ziauddin Hospital Kemari Campus Emergency Department involving 126 adults with acute asthma exacerbations. Patients were randomized to receive either IV $MgSO_4$ (2g in 100ml normal saline over 20 minutes) or nebulized $MgSO_4$ (three 500mg doses at 20-minute intervals). All patients received standard therapy including oxygen, hydrocortisone, salbutamol, and ipratropium. The primary outcome was Visual Analogue Scale (VAS) score improvement at 120 minutes. Secondary outcomes included ICU admission rates, readmissions, mortality, and adverse events.

Results: Both groups showed significant improvement in VAS scores. The IV group demonstrated superior outcomes with 37.27% improvement in VAS scores compared to 31.01% in the nebulized group. ICU admission rates were substantially lower in the IV group (4.76%) versus nebulized group

(12.70%). Respiratory rates decreased more rapidly in the IV group (21.6% vs 19.1% reduction). No readmissions, mortality, or adverse events were reported in either group.
Conclusion: While both administration routes effectively improved acute asthma symptoms, IV $MgSO_4$ demonstrated superior outcomes in symptom relief and prevention of clinical deterioration requiring intensive care compared to nebulized administration.

Keywords: Acute asthma, magnesium sulfate, emergency medicine, nebulization, intravenous

INTRODUCTION

Asthma affects approximately 5-10% of the global population, with acute exacerbations representing a significant cause of emergency department visits and healthcare resource utilization.[1] The Global Asthma Network Phase I study indicates that asthma symptoms affect approximately 10% of children and adults globally, with severe symptoms present in 5% of school-aged children.[2] Recent data reveals significant disparities in asthma's impact worldwide, with the Global Burden of Disease Study reporting that asthma resulted in 461,069 deaths and 21.6 million disability-adjusted life years lost in 2019. Low and middle-income countries bear a disproportionate burden, accounting for 90% of the disease's impact, with some nations showing uncontrolled asthma rates as high as 90%.[2] In Pakistan, asthma affects an estimated 4.3% of the population, with approximately 15 million pediatric and 7.5 million adult cases.[3]

The Global Initiative for Asthma (GINA) defines asthma as a pathophysiologically heterogeneous respiratory condition distinguished by chronic inflammatory processes within the airways.[4] Acute exacerbations are characterized by progressive dyspnea, bronchial constriction, airway inflammation, and mucus obstruction, often requiring immediate intervention to prevent life-threatening complications.[5] Standard emergency management encompasses restoration of adequate oxygenation, amelioration of bronchial obstruction through short-acting β2-agonists (SABAs), early initiation of systemic corticosteroid therapy, and when indicated, adjunctive interventions including anticholinergic agents and intravenous magnesium sulfate.[6]

Magnesium sulfate has emerged as an important adjunctive treatment for acute severe asthma since its first introduction in the mid-1930s. The pharmacological mechanism operates through multiple cellular pathways: inhibition of transmembrane calcium flux through voltage-gated channels, suppression of calcium release from intracellular stores within the endoplasmic reticulum, stabilization of mast cells to reduce inflammatory mediator release, and inhibition of acetylcholine release at nerve terminals, ultimately resulting in bronchial smooth muscle relaxation.[7]

Two primary administration routes are available: intravenous and nebulized delivery. IV administration provides rapid systemic effects and reliable bioavailability but carries risks of systemic side effects including hypotension, arrhythmias, cutaneous vasodilation, and in cases of supratherapeutic dosing, renal toxicity.[8] Nebulized delivery offers direct pulmonary targeting with reduced systemic exposure, potentially minimizing adverse effects while allowing concurrent administration of other respiratory medications.

The evidence regarding optimal administration route remains conflicting. The large 3Mg trial by Goodacre et al. found no significant benefit from either form of $MgSO_4$, with hospital admission rates not differing significantly between IV $MgSO_4$ (72%), nebulized $MgSO_4$ (79%), and placebo (78%).[9] However, several meta-analyses have suggested differential effects. Recent systematic reviews have shown mixed results, with Darmawan et al. demonstrating that nebulized magnesium significantly reduced respiratory rate and improved clinical severity scores in adults, while Shan et al. found benefits for adults but limited pediatric evidence.[10],[11]

For nebulized administration, Hughes et al. found that isotonic nebulized $MgSO_4$ as an adjuvant to salbutamol resulted in clinically significant enhancement of bronchodilation in severe asthma.[12] However, other studies including Aggarwal et al. found no additional benefit from adding nebulized $MgSO_4$ to standard therapy.[13]

Notably, much of the evidence supporting nebulized $MgSO_4$ derives from pediatric studies, including Powell et al.'s MAGNETIC trial showing effectiveness in children with acute severe asthma.[14] This creates uncertainty about effectiveness in adults, as children have different airway mechanics and potentially distinct asthma endotypes compared to adults.

This knowledge gap has significant clinical implications. Emergency physicians must often choose between administration routes based on limited comparative evidence, particularly in adult populations. The decision impacts not only clinical outcomes but also resource utilization, with different routes requiring varying levels of monitoring, equipment, and nursing time. Understanding the comparative effectiveness could optimize treatment protocols and improve patient outcomes while informing resource allocation decisions.

The primary objective of this study was to compare the difference in mean VAS score for dyspnea at 120 minutes between nebulized versus IV $MgSO_4$ groups as adjuvant treatment for acute asthma in adults. Secondary objectives included comparing ICU admission rates, 7-day readmission rates, mortality, and adverse events between treatment groups. We hypothesized that nebulized $MgSO_4$ would demonstrate superior efficacy in improving dyspnea and reducing adverse outcomes compared to IV administration.

METHODS

This randomized controlled trial was conducted at the Emergency Department of Dr. Ziauddin Hospital Kemari Campus, Karachi, Pakistan, over six months following institutional ethical approval. The study protocol received approval from the institutional review board, and written informed consent was obtained from all participants prior to enrollment.

Adult patients (>18 years) presenting with acute asthma exacerbations were eligible for inclusion. Acute exacerbation was defined according to GINA guidelines as episodes of progressive dyspnea, cough, wheezing, or chest tightness with decreased lung function requiring treatment modification.[4] Exclusion criteria included fever, other respiratory diseases (bronchiectasis, tuberculosis), history of pulmonary or thoracic surgery, and inability to provide informed consent.

Sample size was calculated using data from a previous study conducted at our institution, where respiratory rate at 120 minutes in the nebulized $MgSO_4$ group was 27.40±8.23 compared to 32.16±8.33 in the control group.[15] Using an online calculator with 80% power and 5% significance level, the required sample size was 126 patients (63 per group).

Eligible patients were randomized using a lottery method into two groups. All participants initially received standard therapy including supplementary oxygen, IV hydrocortisone 100mg, salbutamol nebulization 5mg, and ipratropium nebulization 0.5mg according to British Thoracic Society guidelines.[16] Group A (IV group) received 8 mmol (2g) $MgSO_4$ in 100ml normal saline infused over 20 minutes. Group B (nebulization group) received three 5ml vials of 2 mmol (500mg) $MgSO_4$ nebulized at 20-minute intervals, totaling 1.5g over 60 minutes. Additional treatments were administered at physician discretion based on clinical need.

The primary outcome was improvement in dyspnea measured using the Visual Analogue Scale (VAS) at 120 minutes. The VAS consisted of a 100mm horizontal line anchored by "no dyspnea at all" and "worst possible dyspnea," with patients marking their perceived breathlessness level. Secondary outcomes included: ICU admission rates after 120 minutes of observation; 7-day readmission rates; mortality; adverse events; and physiological parameters including respiratory rate and heart rate at 0, 60, and 120 minutes.

Data were collected using a standardized questionnaire including demographics, baseline asthma control level according to GINA criteria, comorbidities, and outcome measurements. VAS scores and vital signs were recorded at baseline (0 minutes), 60 minutes, and 120 minutes by research personnel. After 120 minutes, emergency department staff blinded to randomization made disposition decisions (discharge, ward admission, or ICU admission) based on clinical presentation. Patients were contacted at 7 days post-discharge to assess readmissions.

Data were analyzed using SPSS version 24. Continuous variables were expressed as mean±standard deviation and compared using independent t-tests. Categorical variables were presented as frequencies and percentages and compared using chi-square tests. A p-value <0.05 was considered statistically significant. Analysis was performed on an intention-to-treat basis.

RESULTS

A total of 126 patients were enrolled and randomized, with 63 patients in each group. No patients were lost to follow-up during the 120-minute observation period.

The mean age was 53.87±17.69 years overall, with significant age difference between groups: IV group 48.11±17.69 years versus nebulized group 59.62±15.84 years (p<0.001). The nebulized group was predominantly male (46.0% vs 33.3%), while the IV group had more females (66.7% vs 54.0%). Regarding baseline asthma control, the IV group had more patients with partly controlled symptoms (58.7% vs 41.3%), while the nebulized group had more patients with well-controlled symptoms at baseline (44.4% vs 34.9%) and more with uncontrolled symptoms (14.3% vs 6.3%). Most patients (65.9%) had no comorbidities, with hypertension being the most common comorbidity (10.3% overall).

Table 1 Gender. Comorbids, Admission, Symptom Control

Factor	IV Group N (%)	Nebulization Group N (%)
Gender (n=126)		
Male	21 (33.3)	29 (46)
Female	42 (66.7)	34 (54)
Comorbids (n=126)		
HTN	10 (15.9)	3 (4.8)
HTN, DM	3 (4.8)	14 (22.2)
None	40 (63.5)	43 (68.3)
Others	10 (15.9)	3 (4.8)
Decision after 120 minutes (n=126)		
Admitted in ICU	3 (4.8)	8 (12.7)
Discharged	60 (95.2)	55 (87.3)
Symptom Control (n=126)		
Well controlled	22 (34.9)	28 (44.4)
Partly controlled	37 (58.7)	26 (41.3)
Uncontrolled	4 (6.3)	9 (14.3)

Both groups demonstrated significant improvement in VAS scores over time. Mean VAS scores decreased from 60.48±13.37 to 37.94±11.13 in the IV group (37.27% improvement) and from 66.03±11.85 to 45.56±10.59 in the nebulized group (31.01% improvement). Despite the baseline difference in VAS scores (p=0.015), with the nebulized group starting with higher scores indicating worse dyspnea, the IV group maintained significantly lower absolute VAS scores at both 60 minutes (48.73±11.95 vs 55.40±11.19, p=0.002) and 120 minutes (37.94±11.13 vs 45.56±10.59, p=0.001). When comparing actual improvement from baseline to 120 minutes, the difference approached but did not reach statistical significance (p=0.05).

Table 2 VAS Score, Respiratory Rate, and Heart Rate

Factor	IV Group mean±SD	Nebulization Group mean±SD
Visual analogue scale score (n=126)		
0 minutes	60.48±13.37	66.03±11.85
60 minutes	48.73±11.95	55.40±11.19

120 minutes	37.94±11.13	45.56±10.59
Respiratory rate (n=126)		
0 minutes	34.21±6.71	28.24±3.10
60 minutes	29.30±6.29	25.51±3.37
120 minutes	26.79±6.71	22.79±2.42
Heart rate (n=126)		
0 minutes	116.03±13.37	106.32±9.57
60 minutes	101.90±12.17	95.62±10.42
120 minutes	93.73±9.68	86.65±11.09

ICU admission rates differed substantially between groups, with the IV group showing significantly lower admission rates (4.76%, n=3) compared to the nebulized group (12.70%, n=8, p=0.047). The remaining 95.2% of IV group patients and 87.3% of nebulized group patients were discharged home. Respiratory rates improved more rapidly in the IV group, decreasing from 34.21±6.71 to 26.79±6.71 breaths per minute (21.6% reduction) compared to the nebulized group's decrease from 28.24±3.10 to 22.79±2.42 breaths per minute (19.1% reduction). Heart rates showed similar improvement patterns between groups, with the IV group demonstrating 19.2% improvement versus 18.5% in the nebulized group.

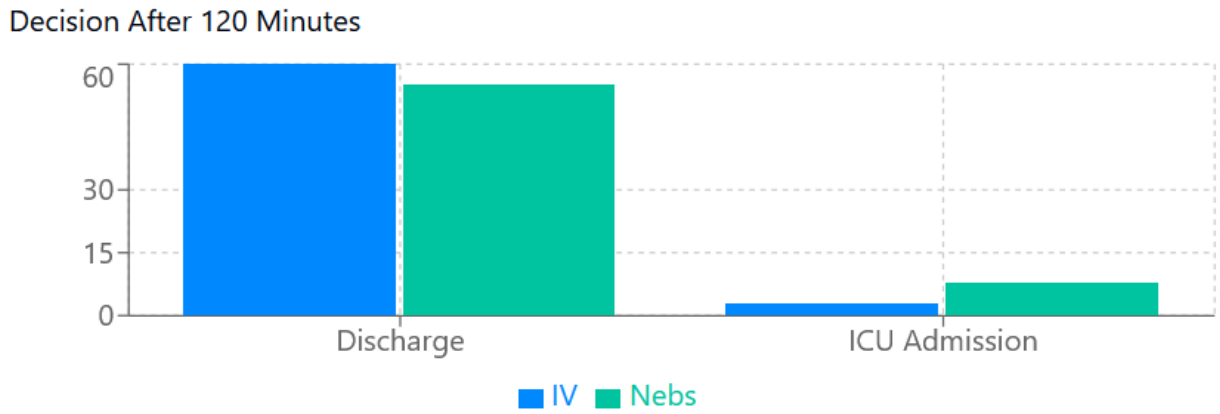

Figure 1 Discharge/Admission

No readmissions within 7 days, mortality, or adverse events were reported in either group, indicating both treatments were well-tolerated during the study period. Independent t-test analysis revealed statistically significant differences in baseline VAS scores (p=0.015), with the nebulized group having higher initial scores. The IV group maintained significantly better VAS scores at 60 minutes (p=0.002) and 120 minutes (p=0.001). ICU admission rates were significantly different between groups (p=0.047).

DISCUSSION

This randomized controlled trial provides important evidence regarding the comparative effectiveness of IV versus nebulized $MgSO_4$ in adults with acute asthma. While both administration routes demonstrated significant clinical improvements, IV $MgSO_4$ showed superior outcomes in symptom relief and prevention of clinical deterioration requiring intensive care. Our findings contrast with our initial hypothesis that nebulized $MgSO_4$ would be more effective. The IV route achieved better VAS score reduction (37.27% vs 31.01%) and substantially lower ICU admission rates (4.76% vs 12.70%). These results have important implications for emergency physicians making real-time treatment decisions and healthcare systems concerned with resource optimization.

Our results partially align with the large 3Mg trial by Goodacre et al., which found limited evidence supporting nebulized $MgSO_4$ effectiveness in adults with severe acute asthma, while showing modest benefits with IV administration.[9] However, unlike the 3Mg trial, which found minimal overall efficacy for both routes, our study demonstrated substantial improvements from baseline with both interventions, suggesting both remain viable therapeutic options despite the comparative advantage of IV administration.

These findings contrast with Hughes et al.'s study, which found isotonic nebulized $MgSO_4$ effective as an adjuvant to salbutamol in severe asthma, with significantly greater improvement in FEV_1 and lower hospital admission rates.[12] This discrepancy may reflect differences in patient populations, with Hughes focusing specifically on severe presentations (FEV_1 <50% predicted) while our study included a broader severity spectrum. The effectiveness of nebulized $MgSO_4$ in severe subgroups may become diluted when examining heterogeneous populations.

Our results align more closely with recent research by Naguib et al., who found IV $MgSO_4$ more effective than nebulized administration in adults with acute asthma exacerbations, showing greater improvement in PEFR and Fischl index measurements.[17] The consistency of these findings across different populations strengthens the evidence favoring IV administration in adults.

Recent systematic reviews have provided additional context. Darmawan et al.'s 2024 meta-analysis found that nebulized magnesium significantly reduced respiratory rate and improved clinical severity scores compared to standard therapy, though four of five studies showed improved lung function with magnesium.[10] However, their analysis included studies with varying methodologies and patient populations, which may explain the discrepancy with our findings. Similarly, a 2022 review by Bokhari et al. highlighted the conflicting evidence regarding $MgSO_4$ efficacy and emphasized the need for standardized protocols.[8]

The significantly lower ICU admission rate with IV $MgSO_4$ represents a clinically meaningful finding with substantial healthcare implications. ICU care costs 3-5 times more than regular ward care, and the reduction in ICU admissions from 12.70% to 4.76% could translate to significant cost savings and resource preservation. This difference becomes particularly important during high hospital occupancy periods when critical care resources are constrained, as evidenced during pandemic situations where critical care bed availability became a limiting factor in patient care.

From a practical standpoint, IV administration requires one-time vascular access establishment, while nebulized therapy requires repeated administrations over 60 minutes with more frequent nursing interventions. However, IV therapy requires specific monitoring for infusion-related complications including hypotension and arrhythmias. These resource considerations should be weighed alongside efficacy data when developing treatment protocols, particularly in settings with differing staffing models or resource constraints.

Our findings highlight important age-related differences in $MgSO_4$ response. Much evidence supporting nebulized $MgSO_4$ derives from pediatric research, including Powell et al.'s MAGNETIC trial showing effectiveness in children with acute severe asthma.[14] The discrepancy between pediatric and adult studies may reflect genuine physiological differences, including airway size, respiratory mechanics, and distinct asthma endotypes between age groups. Su et al.'s meta-analysis suggested that nebulized $MgSO_4$ was more effective in children with severe presentations, which may not translate to adult populations.[18]

Several factors may explain the superior performance of IV $MgSO_4$. Direct systemic delivery provides more predictable bioavailability than nebulized absorption through inflamed airways. The rapid onset of systemic effects may be particularly important in acute settings where prompt stabilization is crucial. Additionally, the bioavailability of nebulized $MgSO_4$ is influenced by factors like respiratory pattern, nebulizer performance, and deposition patterns, making drug delivery less predictable.

The conflicting evidence in the literature may be explained by several methodological factors. Studies differ significantly in patient selection criteria, with those focusing on severe, refractory asthma generally showing greater benefits than those including milder presentations. Additionally, variations in dosing protocols, with studies using widely varying regimens from 1.2g to 4g for IV administration

and different concentrations for nebulized delivery, complicate meta-analyses and clinical guideline development.

Current guidelines reflect this evidence uncertainty. The 2024 GINA guidelines suggest IV $MgSO_4$ as an adjunct treatment option for severe exacerbations, with less emphasis on the nebulized route due to limited evidence.[4] The 2024 British Thoracic Society guidelines recommend considering IV $MgSO_4$ for adults with severe acute asthma who have not responded to initial treatment, while suggesting nebulized $MgSO_4$ might be considered for children.[16] Our findings align with this age-based distinction in route selection.

A 2021 study by Farshadfar et al. investigated nebulized ketamine and IV magnesium sulfate for corticosteroid-resistant asthma, finding both effective but noting the importance of route selection in optimizing outcomes.[19] This supports our findings that administration route significantly impacts treatment effectiveness.

Recent research by Long et al. emphasized the importance of evidence-based adjunctive therapies in critically ill asthmatic patients, highlighting the need for clear protocols regarding $MgSO_4$ administration.[1] Conway and Friedman's 2020 review specifically addressing IV magnesium sulfate for acute asthma in adults provided support for its use while acknowledging the need for comparative studies with alternative routes.[7]

Several limitations warrant consideration. The single-center design may limit generalizability across different healthcare settings and patient populations. The 120-minute observation period, while practical for emergency department research, may not capture delayed effects or long-term outcomes. Baseline differences between groups, particularly in age and initial VAS scores, could have influenced comparative results despite statistical adjustments.

The inability to achieve complete double-blinding due to different administration routes represents a methodological limitation that could introduce expectation bias. Additionally, dose equivalence between routes remains uncertain, as the bioavailability of nebulized $MgSO_4$ is less predictable than IV administration.

Future studies should address these limitations through multi-center designs with stratified randomization based on asthma severity. Longer observation periods would capture delayed effects and rebound phenomena. Dose-finding studies comparing different concentrations of nebulized $MgSO_4$ could optimize effectiveness while monitoring for dose-dependent adverse effects. Research examining predictors of response could guide personalized treatment approaches.

Based on these findings, IV $MgSO_4$ appears preferable for adults with acute asthma, particularly those with severe presentations or concerning vital signs. The IV route should be prioritized when rapid stabilization is essential or when clinical deterioration is anticipated. A dose of 2g infused over 20 minutes should be considered after standard initial therapy with bronchodilators and corticosteroids has been initiated. Nebulized $MgSO_4$ remains a reasonable alternative when IV access is difficult to establish, when IV administration is contraindicated, or in healthcare settings with limited resources for IV medication administration and monitoring.

CONCLUSIONS

This randomized controlled trial demonstrates that while both IV and nebulized $MgSO_4$ provide beneficial effects as adjunctive therapy in acute asthma, IV administration offers superior clinical outcomes in adults. The IV route achieved greater improvement in dyspnea scores (37.27% vs 31.01%) and significantly lower ICU admission rates (4.76% vs 12.70%) while maintaining an excellent safety profile with no adverse events reported. These findings challenge the theoretical assumption that direct pulmonary delivery would provide superior effects and suggest that IV $MgSO_4$ should be preferred for adults with acute asthma in emergency settings. The substantial reduction in ICU admissions has important implications for healthcare resource utilization and patient outcomes, potentially resulting in significant cost savings and improved resource allocation.

REFERENCES

1. Long B, Lentz S, Koyfman A, et al. Evaluation and management of the critically ill adult asthmatic in the emergency department setting. Am J Emerg Med. 2021;44:441-451.
2. Mortimer K, Reddel HK, Pitrez PM, et al. Asthma management in low and middle income countries: case for change. Eur Respir J. 2022;60(3):2103179.
3. Khan MA. Monthly and seasonal prevalence of asthma and chronic obstructive pulmonary disease in the District Dera Ismail Khan, Khyber Pakhtunkhwa, Pakistan. Egypt J Bronchol. 2025;16(1):63.
4. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. 2024. Available at: www.ginasthma.org
5. Reddel HK, Bacharier LB, Bateman ED, et al. Global Initiative for Asthma Strategy 2021: Executive Summary and Rationale for Key Changes. Am J Respir Crit Care Med. 2022;205(1):17-35.
6. Hasegawa K, Craig SS, Teach SJ, et al. Management of Asthma Exacerbations in the Emergency Department. J Allergy Clin Immunol Pract. 2021;9(7):2599-2610.
7. Conway J, Friedman B. Intravenous Magnesium Sulfate for Acute Asthma Exacerbation in Adults. Acad Emerg Med. 2020;27(10):1061-1063.
8. Bokhari SA, Haseeb S, Kaleem M, et al. Role of Intravenous Magnesium in the Management of Moderate to Severe Exacerbation of Asthma: A Literature Review. Cureus. 2022;14(9):e28892.
9. Goodacre S, Cohen J, Bradburn M, et al. Intravenous or nebulised magnesium sulphate versus standard therapy for severe acute asthma (3Mg trial): a double-blind, randomised controlled trial. Lancet Respir Med. 2013;1(4):293-300.
10. Darmawan D, Rengganis I, Rumende CM, et al. Effectiveness and Safety of Nebulized Magnesium as Last Line Treatment in Adults with Acute Asthma Attack: A Systematic Review and Meta-Analysis. Acta Med Indones. 2024;56(1):3-12.
11. Shan Z, Rong Y, Yang W, et al. Intravenous and nebulized magnesium sulfate for treating acute asthma in adults and children: a systematic review and meta-analysis. Respir Med. 2013;107(3):321-30.
12. Hughes R, Goldkorn A, Masoli M, et al. Use of isotonic nebulised magnesium sulphate as an adjuvant to salbutamol in treatment of severe asthma in adults: randomised placebo-controlled trial. Lancet. 2003;361(9375):2114-7.
13. Aggarwal P, Sharad S, Handa R, et al. Comparison of nebulised magnesium sulphate and salbutamol combined with salbutamol alone in the treatment of acute bronchial asthma: a randomised study. Emerg Med J. 2006;23(5):358-62.
14. Powell CV, Kolamunnage-Dona R, Lowe J, et al. MAGNEsium Trial In Children (MAGNETIC): a randomised, placebo-controlled trial and economic evaluation of nebulised magnesium sulphate in acute severe asthma in children. Health Technol Assess. 2013;17(45):v-vi, 1-216.
15. Ahuja G, Kumar A, Ghori U, et al. Effectiveness of Nebulized Magnesium Sulphate as an Adjuvant Therapy (With Salbutamol) in the Management of Acute Asthma. 2020:39.
16. NICE guideline. Asthma: diagnosis, monitoring and chronic asthma management (BTS, NICE, SIGN). 2024. Available at: www.nice.org.uk/guidance/ng245
17. Naguib M, Saad NA, Farouk M, et al. A comparative study of the efficacy and safety of nebulized versus intravenous magnesium sulfate in adults with acute asthma exacerbations: a randomized controlled study. Bull Pharm Sci Assiut Univ. 2024;47(1):289-301.
18. Su Z, Li R, Gai Z. Intravenous and Nebulized Magnesium Sulfate for Treating Acute Asthma in Children: A Systematic Review and Meta-Analysis. Pediatr Emerg Care. 2018;34(6):390-395.
19. Farshadfar K, Sohooli M, Shekouhi R, et al. The effects of nebulized ketamine and intravenous magnesium sulfate on corticosteroid resistant asthma exacerbation; a randomized clinical trial. Asthma Res Pract. 2021;7(1):15.
20. Song WJ, Chang YS. Magnesium sulfate for acute asthma in adults: a systematic literature review. Asia Pac Allergy. 2012;2(1):76-85.

21. Kew KM, Kirtchuk L, Michell CI. Intravenous magnesium sulfate for treating adults with acute asthma in the emergency department. Cochrane Database Syst Rev. 2014;(5):CD010909.
22. Javor E, Grle SP. Limitations of the results from randomized clinical trials involving intravenous and nebulised magnesium sulphate in adults with severe acute asthma. Pulm Pharmacol Ther. 2019;55:31-37.
23. Sarhan HA, El-Garhy OH, Ali MA, et al. The efficacy of nebulized magnesium sulfate alone and in combination with salbutamol in acute asthma. Drug Des Devel Ther. 2016;10:1927-33.
24. Louis R, Satia I, Ojanguren I, et al. European Respiratory Society guidelines for the diagnosis of asthma in adults. Eur Respir J. 2022;60(3):2101585.
25. Dougherty RH, Fahy JV. Acute exacerbations of asthma: epidemiology, biology and the exacerbation-prone phenotype. Clin Exp Allergy. 2009;39(2):193-202.