Magnesium sulfate for acute asthma in adults: a systematic literature review

Woo-Jung Song1,2,3 and Yoon-Seok Chang1,2,3,*

1Department of Internal Medicine, Seoul National University College of Medicine, and 2Institute of Allergy and Clinical Immunology, Seoul National University Medical Research Center, Seoul 110-799, Korea
3Division of Allergy and Clinical Immunology, Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam 463-802, Korea

Magnesium sulfate (MgSO4) has been considered as an adjunct therapy for severe and life-threatening asthma exacerbation. The literature search was performed using MEDLINE, EMBASE, Cochrane Library and Google Scholar to summarize the current state of knowledge regarding magnesium therapy in acute exacerbation of adult asthma. A total of 16 trials and 4 meta-analyses were identified. As results, intravenous MgSO4 was beneficial in severe exacerbation, but evidence for nebulized magnesium was insufficient. However, larger trials are required to draw confirmative conclusions on the efficacy. Regarding the safety concern, the risk of major toxicity appears to be very low at usual doses described in the literature. Additionally, results from 4 surveys were examined on the gaps between knowledge and practice, and on the barrier to the use of MgSO4 at emergency departments. This literature review summarized the up-to-date evidence on the issues regarding the use of MgSO4 for acute asthma. We expect more studies to be conducted for evidence making in the Asian-Pacific regions.

Key words: Asthma; Magnesium sulfate; Emergency treatment; Review

INTRODUCTION

Magnesium sulfate (MgSO4) has been considered as an adjunct therapy for severe and life-threatening asthma exacerbation. Theoretically, magnesium can induce bronchial smooth muscle relaxation in a dose-dependent manner [1] by inhibiting calcium influx into the cytosol [2], histamine release from mast cells [3], or acetylcholine release from cholinergic nerve endings [4]. It also may increase the bronchodilator effect of β2-agonist by increasing the receptor affinity [5]. Historically, in the literature, the first description on the clinical use of magnesium for asthma was reported in 1936 [6]. In 1987, Okayama et al. [7] reported rapid bronchodilating effects of intravenous (IV) MgSO4 infusion in 10 asthma patients. In 1989, its effect was also reported for...
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prevention of endotracheal intubation and mechanical ventilation in an elderly asthma patient with severe exacerbation [8].

The first randomized controlled trial (RCT) was conducted in 1989 by Skobeloff et al. [9] to investigate its efficacy. Since then, it has been examined by several RCTs and meta-analyses. At the same time, the use of nebulized MgSO₄ has also gained scientific interests. Current guidelines [10-12] suggest the use of IV MgSO₄ as an adjunct therapy to improve pulmonary functions and reduce hospital admission in certain patients with severe and life-threatening acute exacerbations unresponsive to initial treatments, whereas the evidence has been weaker for nebulized magnesium.

In this review, we aimed to summarize the current state of knowledge regarding the use of MgSO₄ in acute exacerbation of adult asthmatics.

Key question
Population: adult asthma patients with acute exacerbation
Intervention: MgSO₄ (intravenous or nebulized form)
Control: placebo
Outcome: clinical efficacy

Search strategy
The literature search was performed during the period September 2011 until December 2011. Articles were searched from MEDLINE, EMBASE, the Cochrane Library and Google Scholar. Search terms included the terms for asthma, exacerbation and magnesium. Additionally, manual searching the references for relevant articles was also performed on respiratory or emergency medicine journals. The search for unpublished data was not conducted. The search was limited to the last 25 years (1986 to 2011).

First, authors scanned titles, abstracts, and selected relevant articles for retrieval of full-text. Through a full-text review, final selection was made: RCTs were included if they were conducted on adult acute asthmatics and compared its efficacy with placebo. The quality of included RCTs was determined by the five point Jadad score [13]. Meta-analyses were included if they included the issues relevant to our key question. Suspected duplicates were excluded. Finally, 10 RCTs for IV MgSO₄, 6 RCTs for nebulized MgSO₄, and 4 meta-analyses were included. All the identified articles were originally written in English, although attempts were made to find out non-English sources including Korean and Japanese.

Data extraction
The following data were extracted: study design, study population (patients, or number of pooled trials), interventions, control, co-treatments, and outcomes of interest.

Additional search
Articles were searched again from the same electronic databases to retrieve information on the practice status at emergency departments regarding the use of MgSO₄ in acute asthma patients. This search was not limited to adult population, because studies were scarce. Finally, 4 original articles were selected.

Included studies
Included RCTs were summarized in Tables 1 and 2. Overall quality of RCTs was high, having a Jadad score of 4 or 5 in 11/16 trials. The majority (13/16) of the studies were double-blinded, while two trials [14, 15] for IV and one trial [16] for nebulized MgSO₄ were single-blinded. However, heterogeneity was identified for the included trials. For RCTs on IV form, there were variations in the severity of attack, definition of severity, treatment dose (2 g bolus in 6/10 trials), co-treatments (IV theophylline/aminophylline in 5/10 trials, and nebulized ipratropium in 2/10 trials), and timing to measure outcomes. As for nebulized form, there was notable heterogeneity in the treatment dose of nebulized MgSO₄.

The included meta-analyses were described in Table 3. A meta-analysis by Mohammed et al. [17] was the most up-to-date and comprehensive one including most of published RCTs and also unpublished data such as conference abstracts. Three recently published RCTs [15, 18, 19], not included in the meta-analyses, had distinct points from previous trials in that the recent trials used nebulized ipratropium as one of the routine treatments.

Efficacy of intravenous MgSO₄
There have been 3 meta-analyses and 2 recent RCTs. The results from the Cochrane review by Rowe et al. [20] stated that IV MgSO₄ as adjunct to standard treatment was beneficial in severe acute asthma patients, both in terms of pulmonary functions and hospital admission rate. The results by Rodrigo et al. [21] were not concordant, but the number of pooled studies and patients were smaller than the Cochrane review. The recent reviews by Mohammed et al. [17] found that the efficacy was only marginal on pulmonary function (standardized mean difference (SMD) 0.25, 95% confidence interval (CI) −0.01 to 0.51), and not significant on hospital admission (relative risk (RR) 0.87, 95% CI 0.70 to 1.08).
# Table 1. Summary of randomized placebo-controlled trials for efficacy of intravenous MgSO$_4$ in acute exacerbation of adult asthmatics

| Reference | Country | Study population (age range) | Intervention | Routine co-treatment | Measures of outcome | Results | Jadad score |
|-----------|---------|------------------------------|--------------|----------------------|---------------------|---------|-------------|
| [15]      | India   | 60 severe patients (18-60 yr) | 2 g MgSO$_4$ | Nebulized: salbutamol, ipratropium Systemic: hydrocortisone 100 mg | FEV1% predicted, and discharge rate at 120 min | Improvement in pulmonary function and decrease in hospital admission | 3 |
| [19]      | UK      | 129 moderate to severe patients (≥ 16 yr) | 1.2 g MgSO$_4$ | Nebulized: salbutamol, ipratropium Systemic: hydrocortisone 200 mg | PEF% predicted, and admission rate at 60 min | No benefit even in severe patients | 5 |
| [42]      | USA     | 248 severe patients (18-60 yr) | 2 g MgSO$_4$ | Nebulized: albuterol Systemic: methylprednisolone 125 mg | FEV1% predicted, and admission rate at 240 min | Improvement in pulmonary function (in very severe patients with FEV1 < 20% predicted), but no benefit in admission rate | 5 |
| [43]      | Iran    | 81 patients with PEFR < 200 L/min, non-responding to routine therapy (12-85 yr) | 25 mg/kg MgSO$_4$ | Nebulized: salbutamol Systemic: corticosteroids, aminophylline | PEF% predicted at 180 min | Improvement in pulmonary function | 3 |
| [44]      | USA     | 42 moderate to severe patients (18-55 yr) | 2 g MgSO$_4$ | Nebulized: albuterol Systemic: methylprednisolone 125 mg | PEF% predicted, Borg dyspnea scale, and admission rate | No benefit | 5 |
| [45]      | Thailand | 33 patients with Fischl’s severity score > 4 (15-65 yr) | 2 g MgSO$_4$ | Nebulized: salbutamol Systemic: dexamethasone 5 mg | Admission rate, and severity score at 240 min | No benefit | 5 |
| [46]      | USA     | 135 patients with FEV1 < 75% predicted (18-65 yr) | 2 g MgSO$_4$ | Nebulized: albuterol Systemic: methylprednisolone 125 mg, theophylline | FEV1% predicted, and admission rate at 120 min | Improvement in pulmonary function, and decrease in admission rate, but only among severe patients with FEV1 < 25% predicted | 5 |
| [26]      | USA     | 48 patients with PEFR < 200 L/min, unresponsive to two albuterol treatments (18-60 yr) | 2 g MgSO$_4$ bolus, followed by infusion of 2 g/h over 4 h | Nebulized: albuterol Systemic: methylprednisolone 125 mg, aminophylline | PEF% predicted, FEV1% predicted at 260 min | No benefit | 4 |
| [14]      | USA     | 120 patients unresponsive to a single albuterol treatment (18-65 yr) | 2 g MgSO$_4$ | Nebulized: albuterol Systemic: methylprednisolone 125 mg, theophylline, injectable β-agonist, epinephrine | Admission rate, ED treatment time, and PEF% predicted | No benefit | 1 |
| [9]       | USA     | 38 moderate to severe patients unresponsive to beta-agonist treatment (18-70 yr) | 1.2 g MgSO$_4$ | Nebulized: metaproterenol or albuterol Systemic: methylprednisolone 125 mg, and theophylline | PEF% predicted at 45 min, and admission rate | Improvement in pulmonary function, and decrease in admission rate | 5 |

MgSO$_4$, magnesium sulfate; FEV1, forced expiratory volume in 1 sec; PEFR, peak expiratory flow rate; ED, emergency department.
However, their analyses were not confined to severe exacerbations. Notably, two recent RCTs used nebulized ipratropium bromide as their standard treatments. The trials by Bradshaw et al. [19] did not show additional benefit of 1.2 g IV MgSO4 even in subgroups of life-threatening exacerbation. However, the trials by Singh et al. [15] showed its positive effect on forced expiratory volume in 1 second (FEV1) % predicted (vs. placebo; mean difference 6.07, 95% CI 1.87 to 10.62), but had limitations in smaller number of participants and single-blinded design.

Nebulized ipratropium is currently recommended as an additional bronchodilator for moderate exacerbation by guidelines, and is being widely used in practice. Therefore, the efficacy of IV MgSO4 needs to be examined further in the context of current treatment guidelines. Nevertheless, the use of MgSO4 should not be hesitated in patients with severe life-threatening asthma exacerbation unresponsive to standard treatments, because its toxicity was minimal.

**Efficacy of nebulized MgSO4**

There have been 2 meta-analyses and 1 recent RCT. The Cochrane review conducted by Blitz et al. [22] showed that nebulized MgSO4 improved pulmonary functions (SMD 0.55, 95% CI 0.12 to 0.98) in severe subgroups (FEV1 or peak expiratory flow <50% predicted). However, the results were based on only 87 adult asthmatics from 2 trials. The recent reviews by Mohammed et al. [17] examined more trials and found that nebulized MgSO4 had marginal benefits on pulmonary functions (SMD 0.17, 95% CI −0.02 to 0.36) and on hospital admission rate (RR 0.68, 95% CI 0.46 to 1.02). Considering the heterogeneity in treatment doses, severity of patients and small numbers of pooled studies, they concluded that evidence is insufficient to draw conclusions.

In a recent trial (n = 60) by Gallegos-Solórzano et al. [18], when added to standard treatments of nebulized albuterol and ipratropium, nebulized MgSO4 therapy improved post-bronchodilator lung functions and oxygen saturation, and reduced admission rates at 90 min. However, the largest trial (n = 100) by Aggarwal et al. [23] failed to show any benefit of additional MgSO4 therapy. Taken together, the use of nebulized MgSO4 might be beneficial in treating severe exacerbation, but large trials are required for more definite conclusion.

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**Table 2. Summary of randomized placebo-controlled trials for efficacy of nebulized MgSO4 in acute exacerbation of adult asthmatics**

| Reference | Country | Study population (age range) | Intervention | Routine co-treatment | Measures of outcome | Results | Jadad score |
|-----------|---------|-------------------------------|--------------|---------------------|---------------------|---------|-------------|
| [18]      | Mexico  | 60 severe patients (> 18 yr) | 333 mg MgSO4 every 20 min (total 3 doses) | Nebulized: albuterol, ipratropium Systemic: methylprednisolone | FEV1% predicted, oxygen saturation, admission at 90 min | Improvement in pulmonary function and oxygen saturation, and decrease in admission rate | 4 |
| [23]      | India   | 100 severe to life-threatening patients (13-60 yr) | 500 mg MgSO4 every 20 min (total 3 doses) | Nebulized: salbutamol Systemic: hydrocortisone | PEF % predicted at 120 min | No benefit | 5 |
| [16]      | Turkey  | 26 moderate to severe patients (18-60 yr) | 145 mg MgSO4 every 20 min (3 doses for 1st h), and 4 additional hourly doses | Nebulized: salbutamol Systemic: methylprednisolone at 1 mg/kg | PEF % predicted at 240 min, and duration of achieving target-PF 70% predicted | No benefit | 2 |
| [47]      | New Zealand | 52 severe patients, FEV1 < 50% predicted after salbutamol treatment (16-65 yr) | 151 mg MgSO4 every 20 min (total 3 doses) | Nebulized: salbutamol Systemic: hydrocortisone at 100 mg | FEV1% predicted at 90 min | Improvement in pulmonary function Enhanced improvement in life-threatening asthma (baseline FEV1 <30%) | 5 |
| [48]      | USA     | 74 mild to moderate patients (18-65 yr) | 384 mg MgSO4 every 20 min (total 3 doses) | Nebulized: albuterol Systemic: hydrocortisone at 2 mg/kg every 6 hours | FEV1% predicted at 125 min | No benefit | 5 |
| [49]      | Argentina | 35 patients (> 18 yr) | 225 mg MgSO4 (1 dose) | Nebulized: salbutamol | PEF % predicted at 20 min | Improvement in pulmonary function | 3 |

MgSO4, magnesium sulfate; FEV1, forced expiratory volume in 1 sec; PEF, peak expiratory flow rate.
Formulation and optimal dose

The dose of IV magnesium was 2 g as a bolus in most trials showing its effectiveness. The Cochrane review examined the safety of 2 g magnesium to find out its minimal risk of significant adverse reaction [20]. A RCT [6] using 2 g reported no major toxicities but only minor ones in 58% of patients (sensation of flushing, mild fatigue and burning sense at IV site). In a trial using 1.2 g bolus [13], the rate of minor side effect was 8% (headache, flushing and dizziness).

For more than two decades, magnesium has been used as a tocolytic agent for preterm labor, at higher doses (such as a 6 g IV load over 20 min and followed by a continuous infusion of 2 to 4 g/h [24]). Major toxicity occurred at serum magnesium level of 9 mg/dL or higher, such as loss of reflexes, blurred vision, lethargy, muscle weakness or pulmonary edema [24]. However, magnesium is usually excreted in urine, and administration of 2 g in a bolus increases the concentration just from 2.2 to 2.8 mg/dL 30 min after the infusion [25]. Therefore, it can be concluded that the usual dose of 2 g for acute asthma has a minimal risk of major toxicity in patients with normal renal function, as suggested by

### Table 3. Summary of systematic reviews and meta-analyses: randomized placebo-controlled trials for the efficacy of MgSO\(_4\) as an adjunct therapy for acute asthma in adults

| Form of MgSO\(_4\) | Reference | Number of pooled trials | Outcomes of interest | Results | Author conclusions |
|-------------------|-----------|------------------------|---------------------|---------|--------------------|
| IV                | [17]      | 9 trials (826 adult patients) | Pulmonary function Admission rate | Pulmonary function: SMD 0.25 (−0.01 to 0.51) Admission rate: RR 0.87 (0.70 to 1.08) | Evidence is weak for IV MgSO\(_4\) to improve respiratory functions and hospital admissions in adults. |
| Nebulized         | [22]      | 3 trials (161 adult patients) | Pulmonary function: 20 min, 60 min Admission to hospital | Pulmonary function: SMD 0.18 (−0.13 to 0.50) For severe (FEV1 or PEFR <50% predicted): SMD 0.55 (0.12 to 0.98) Admission: RR 0.62 (0.38 to 1.02) For severe (FEV1 or PEFR <50% predicted): the same | Nebulized MgSO\(_4\) should be considered as an adjunct therapy to beta2-agonists in asthma exacerbations, particularly in more severe exacerbations. |
| IV                | [17]      | 7 trials (430 adult patients) | Pulmonary function Admission rate | Pulmonary function: SMD 0.17 (−0.05 to 0.39) Admission rate: RR 0.68 (0.46 to 1.02) | Evidence is weak for nebulized MgSO\(_4\) to improve respiratory functions and hospital admissions. |
| IV                | [20]      | 7 trials (total of 665 patients), including 2 pediatric trials (78 patients) | Admission to hospital Pulmonary function | Pulmonary function: PEFR WMD 29.4 L/min (−3.4 to 62) For severe: FEV1% predicted WMD 9.8 (3.8 to 15.8) PEFR WMD 52.3 L/min (27.0 to 77.5) | MgSO\(_4\) appears to be beneficial in patients who present with severe acute asthma. |
| IV                | [21]      | 5 trials (374 adult patients) | Pulmonary function Admission rate | Pulmonary function: Effect size 0.02 (−0.20 to 0.24) Admission: OR 0.68 (0.41 to 1.15) | The addition of MgSO\(_4\) in patients with moderate to severe asthma exacerbations does not alter treatment outcomes. |

MgSO\(_4\), magnesium sulfate; IV, intravenous; SMD, standardized mean difference; RR, relative risk; FEV1, forced expiratory volume in 1 sec; PEFR, peak expiratory flow rate; OR, odds ratio; WMD, weighted mean difference.
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the meta-analyses [20]. The possibility exists that higher dose of IV magnesium is more effective, but still no published report has directly examined the benefit from high dose bolus therapy such as 4 g. One trial evaluated the role of continuous MgSO₄ infusion, but failed to find its additional benefit [26].

Hypermagnesemia can be managed by prompt cessation of magnesium infusion in patients with normal renal functions. However, hemodialysis and IV calcium gluconate may be required in high risk patients with renal dysfunctions, bowel obstruction [27], or in elderly patients taking magnesium-containing cathartics [28].

In cases of nebulized magnesium, optimal dosing may be more intricate. MgSO₄ is administered by a nebulizer, as a vehicle for β₂-agonist (and also as in combination). However, hypertonic or hypotonic nebulized solution can cause bronchoconstriction by itself in asthmatics [29, 30]. Therefore, larger dose of magnesium may not be feasible due to practical reasons such as nebulizer volume, or the need for specific concentration of MgSO₄ to make an isotonic solution. For example, in a trial by Aggarwal et al. [23], they made magnesium-containing solutions (10 mL, 295 mosmol/kg) as following: 1 mL of salbutamol solution, 1 mL of MgSO₄ (from IV preparation at concentration of 500 mg/mL), plus 8 mL distilled water.

At the moment, there is no available evidence to advocate the use of higher dose of nebulized magnesium for yielding a better efficacy. Moreover, no dose-response relationships (from 0 to 360 mg MgSO₄) have been reported [31]. Nebulized MgSO₄ therapy can be considered as safe, because no serious side effects were reported [22].

Monitoring serum magnesium levels

As pre-existing magnesium deficit could be associated with risk of asthma exacerbation [32-35], one might think that serum magnesium level could be measured for adequate supplementation or prediction of treatment response. However, it is predominantly an intracellular ion, and its serum level does not reflect intracellular concentrations or total body stores. Its intracellular concentration was found to be lower in acute exacerbation and returned to normal when controlled, while plasma level remained unchanged [36]. Therefore, serum level does not represent the degree of cellular deficit, and it would not be useful to monitor serum magnesium level for enhancing the efficacy of MgSO₄ therapy.

Gap and barrier to the use of MgSO₄

Current guidelines [10-12] suggest the use of IV MgSO₄ as an adjunct to standard treatment in acute severe exacerbations (Table 4). Four observational studies evaluated the implementation of treatment guidelines with regard to the use of MgSO₄ (Table 5). They were conducted in North America, UK, Australia and New Zealand.

In North America, a large-scale study [37] was conducted on patient cohorts and emergency physicians to investigate the use of IV MgSO₄. Among 9745 emergency department (ED) patients, only 2.5% received IV MgSO₄. In logistic regression analyses, its use was associated with older age, previous intubation history, higher respiratory rate, lower initial pulmonary functions, higher number of β₂-agonists use, and use of systemic corticosteroids. For physicians at ED, 92% had MgSO₄ available and 64% had recently used it. They tipped severity (96%) and poor response to initial β₂-agonists (87%) as main factors prompting the use of MgSO₄.

In an online survey of two national pediatric ED physicians in North America [38], 88% of physicians knew the efficacy of IV MgSO₄, but 37.7% of physicians did not use IV MgSO₄ in the management of severe acute asthma. Main barriers to the use were lack of needs (31%) and concerns of side effects (24%).

In a postal survey undertaken for all adult EDs within the UK [39], IV MgSO₄ was currently being used in 93% of EDs, and more than 80% of severe or life-threatening asthma patients received the therapy. The reasons for using the agent were to improve breathlessness (70%) or reduce admissions (51%). Nebulized MgSO₄ was being rarely used (1%), and the main reason was insufficient evidence (51%).

In a study conducted in Australia and New Zealand [40], they compared the gaps between clinical practice guideline (CPG) recommendations and self-reported physician management from 11 pediatric EDs. The gap between CPG and practice was particularly wide for severe to critical asthma. For IV MgSO₄, it has been utilized in the practice for 7.7% of severe asthma and 55.1% of critical asthma (in CPG: 18.2% and 45.5%, respectively). The limitation of this study was that discrepancy existed between New Zealand and Australian guidelines on the recommendation of the use of magnesium.

Taken together, overall degree of knowledge among ED physicians appears to be high among examined countries. However, the significant gaps were found between the knowledge and the practice patterns except UK.
Studies from the Asia-Pacific regions

There have been four RCTs on the efficacy of MgSO4 from the Asia-Pacific regions (two from India, and Iran and Thailand for each). Their results were conflicting, but did not have notable differences from Western studies in their study designs or outcome measures. No information was available to determine ethnic differences on the efficacy of MgSO4 therapy. However, IV aminophylline has been used at EDs more widely in Korea and Japan than Western countries due to belief that the agent is not very toxic for the Northeast Asian people such as the Korean or the Japanese. In a Japanese prospective safety survey conducted by Ohta et al. [41], IV aminophylline treatment was found to be highly safe among the Japanese adult patients (age: 15-65 years) when administered in accordance with the guidelines and instructions. Its toxicity occurred in 0.29% of 682 patients, and all of them were mild. Thus we guess that the needs for an adjunct magnesium therapy might be lower in the Northeast Asia region than Western countries.

We have no more information on the current status of knowledge and practice regarding the use of MgSO4 for acute asthma in this region.

CONCLUSION

IV MgSO4 as an adjunct to standard treatment may be beneficial in the treatment of adult patients with severe or life-threatening exacerbation. The role of nebulized MgSO4 is less evident due to

Table 4. Current guideline recommendations regarding the use of MgSO4 for acute exacerbation of adult asthma

| Guideline [Reference] | Recommendation |
|-----------------------|----------------|
| GINA [10]             | Intravenous magnesium sulphate (usually given as a single 2 g infusion over 20 min) is not recommended for routine use in asthma exacerbations, but can help reduce hospital admission rates in certain patients, including adults with FEV1 <25-30% predicted at presentation, adults and children whose FEV1 fails to respond to initial treatment, and children whose FEV1 fails to improve above 60% predicted after 1 hour of care (Evidence A). Nebulized salbutamol administered in isotonic magnesium sulfate provides greater benefit than if it is delivered in normal saline (Evidence A). |
| NAEPP [11]            | Consider intravenous MgSO4 in patients who have life-threatening exacerbations and in those whose exacerbations remain in the severe category after 1 hour of intensive conventional therapy (Evidence B). A recent meta-analysis of six trials suggests that the use of nebulized MgSO4 in combination with SABAs may result in further improvements in pulmonary function, but further research is needed. |
| BTS/SIGN [12]         | Consider giving a single dose of IV magnesium sulphate for patients with: • acute severe asthma who have not had a good initial response to inhaled bronchodilator therapy • life threatening or near fatal asthma (Grade of recommendation B). |
| National Asthma Council Australia [50] | Magnesium sulphate (via nebuliser or IV, as available) can be added to improve airflow, although the evidence to support this is not strong. Suggested doses are 1.2-2 g of MgSO4 IV over 20 min or 2.5 mL isotonic MgSO4 (250 mmol/L) by nebuliser. |
| India [51]            | In patients with acute severe asthma who have not had a good initial response, administration of a single dose of intravenous magnesium sulfate (2 g over 20 min) improves pulmonary function when used as an adjunct to standard therapy. The treatment should however be used with great caution under proper monitoring. |
| Japanese Society of Allergology [52] | No statement |
| Korean Academy of Asthma, Allergy and Clinical Immunology [53] | Intravenous MgSO4 (as 2 g a single bolus over 20 min) is not routinely recommended for acute asthma exacerbation. However, it can be beneficial in patients with FEV1 <25-30% predicted, or FEV1 <60% predicted after 1 hour of initial emergency treatment (Evidence A). Bronchodilating effects may be further enhanced by inhalation of salbutamol and MgSO4 together (Evidence A). (translated into English by authors) |

MgSO4, magnesium sulfate; GINA, Global Initiative for Asthma; NAEPP, National Asthma Education and Prevention Program; BTS, British Thoracic Society; SIGN, Scottish Intercollegiate Guidelines Network; FEV1, forced expiratory volume in 1 sec; SABA, short-acting beta-agonist.
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insufficient evidence. The use of MgSO₄ has excellent safety profile if appropriately administered. Studies are needed to investigate its role and to identify the gaps between guidelines and practice patterns in the Asia-Pacific region.

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Table 5. Summary of surveys for practice patterns in the emergency departments regarding the use of MgSO₄

| Reference | Region | Study population (patient age) | Patient data acquisition | Practitioner survey | Measures of outcome | Results |
|-----------|--------|-----------------------------|--------------------------|---------------------|-------------------|---------|
| [38]     | North America | 199 pediatric emergency physicians | None | E-mail based survey | Knowledge of the efficacy of IV MgSO₄ | 88% physicians knew its efficacy |
|          |        |                             |                          |                     | Frequency of the use of MgSO₄ | 40% physicians rarely use it in patients without impending failure |
|          |        |                             |                          |                     | Barriers to the use | Perceived lack of need (30.8%), concern for side effects (23.2%) |
|          |        |                             |                          |                     |                   |         |
| [39]     | UK     | Emergency physicians at 180 EDs | None | Postal survey | Current usage of IV and nebulized MgSO₄ | 93% IV MgSO₄, 1% nebulized MgSO₄ |
|          |        |                             |                          |                     |                   |         |
| [40]     | Australia and New Zealand | Pediatric emergency physicians at 11 EDs | None | Standardized anonymous survey (site-coded) | Comparison of clinical practice guideline and reported physician management | IV MgSO₄: 7.7% for severe asthma (vs. 18.2% site CPG), 55.1% for critical asthma (vs. 45.5% site CPG) |
|          |        |                             |                          |                     |                   |         |
| [37]     | North America | 9,745 patients (2-54 yr) Emergency physicians at 119 EDs | Observational cohort study | E-mail based survey | % patients who received IV MgSO₄ | 2.5% received |
|          |        |                             |                          |                     | Availability Recent use | 92% availability 64% recent use |

MgSO₄, magnesium sulfate; ED, emergency department; IV, intravenous; CPG, current practice guideline.
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