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

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Magnesium sulfate ($MgSO_4$) 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 $MgSO_4$ 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 $MgSO_4$ at emergency departments. This literature review summarized the up-to-date evidence on the issues regarding the use of $MgSO_4$ 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 ($MgSO_4$) 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 β_2-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) $MgSO_4$ 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 $MgSO_4$ has also gained scientific interests. Current guidelines [10-12] suggest the use of IV $MgSO_4$ 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 $MgSO_4$ in acute exacerbation of adult asthmatics.

Key question

Population: adult asthma patients with acute exacerbation
Intervention: $MgSO_4$ (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 were 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 $MgSO_4$, 6 RCTs for nebulized $MgSO_4$, 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 $MgSO_4$ 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 $MgSO_4$ 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 $MgSO_4$.

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 $MgSO_4$

There have been 3 meta-analyses and 2 recent RCTs. The results from the Cochrane review by Rowe et al. [20] stated that IV $MgSO_4$ 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).

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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	PEFR% 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	PEFR% 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 < 200L/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	PEFR% 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 PEFR% 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	PEFR% 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.

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Table 2. Summary of randomized placebo-controlled trials for efficacy of nebulized $MgSO_4$ 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 $MgSO_4$ 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 $MgSO_4$ every 20 min (total 3 doses)	Nebulized: salbutamol Systemic: hydrocortisone	PEFR% predicted at 120 min	No benefit	5
[16]	Turkey	26 moderate to severe patients (18-60 yr)	145 mg $MgSO_4$ every 20 min (3 doses for 1st h), and 4 additional hourly doses	Nebulized: salbutamol Systemic: methylprednisolone 1 mg/kg	PEFR% predicted at 240 min, and duration of achieving target-PEFR 70% predicted	No benefit	2
[47]	New Zealand	52 severe patients, FEV1 < 50% predicted after salbutamol treatment (16-65 yr)	151 mg $MgSO_4$ every 20 min (total 3 doses)	Nebulized: salbutamol Systemic: hydrocortisone 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 $MgSO_4$ every 20 min (total 3 doses)	Nebulized: albuterol Systemic: hydrocortisone 2 mg/kg every 6 hours	FEV1% predicted at 125 min	No benefit	5
[49]	Argentina	35 patients (> 18 yr)	225 mg $MgSO_4$ (1 dose)	Nebulized: salbutamol	PEFR% predicted at 20 min	Improvement in pulmonary function	3

$MgSO_4$, magnesium sulfate; FEV1, forced expiratory volume in 1 sec; PEFR, peak expiratory flow rate.

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 $MgSO_4$ 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 $MgSO_4$ needs to be examined further in the context of current treatment guidelines. Nevertheless, the use of $MgSO_4$ should not be hesitated in patients with severe life-threatening asthma exacerbation unresponsive to standard treatments, because its toxicity was minimal.

Efficacy of nebulized $MgSO_4$

There have been 2 meta-analyses and 1 recent RCT. The Cochrane review conducted by Blitz et al. [22] showed that nebulized $MgSO_4$ 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 $MgSO_4$ 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 $MgSO_4$ 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 $MgSO_4$ therapy. Taken together, the use of nebulized $MgSO_4$ might be beneficial in treating severe exacerbation, but large trials are required for more definite conclusion.

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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	[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.
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-agoinsts in asthma exacerbations, particularly in more severe exacerbations.
IV	[20]	7 trials (total of 665 patients), including 2 pediatric trials (78 patients)	Admission to hospital Pulmonary function	Admission: OR 0.31 (0.09 to 1.02) For severe: OR 0.10 (0.04 to 0.27) 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.

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

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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 $MgSO_4$ 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. $MgSO_4$ 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 $MgSO_4$ 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 $MgSO_4$ (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 $MgSO_4$) have been reported [31]. Nebulized $MgSO_4$ 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 $MgSO_4$ therapy.

Gap and barrier to the use of $MgSO_4$

Current guidelines [10-12] suggest the use of IV $MgSO_4$ 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 $MgSO_4$ (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 $MgSO_4$. Among 9745 emergency department (ED) patients, only 2.5% received IV $MgSO_4$. In logistic regression analyses, its use was associated with older age, previous intubation history, higher respiratory rate, lower initial pulmonary functions, higher number of β_2-agonists use, and use of systemic corticosteroids. For physicians at ED, 92% had $MgSO_4$ available and 64% had recently used it. They tipped severity (96%) and poor response to initial β_2-agonists (87%) as main factors prompting the use of $MgSO_4$.

In an online survey of two national pediatric ED physicians in North America [38], 88% of physicians knew the efficacy of IV $MgSO_4$, but 37.7% of physicians did not use IV $MgSO_4$ 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 $MgSO_4$ 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 $MgSO_4$ 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 $MgSO_4$, 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.

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Table 4. Current guideline recommendations regarding the use of $MgSO_4$ 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 $MgSO_4$ in patients who have life-threatening exacerbations and in those whose exacerbations r emain 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 $MgSO_4$ 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 $MgSO_4$ IV over 20 min or 2.5 mL isotonic $MgSO_4$ (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 $MgSO_4$ (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)

$MgSO_4$, 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.

Studies from the Asia-Pacific regions

There have been four RCTs on the efficacy of $MgSO_4$ 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 $MgSO_4$ 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 $MgSO_4$ for acute asthma in this region.

CONCLUSION

IV $MgSO_4$ 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 $MgSO_4$ is less evident due to

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Table 5. Summary of surveys for practice patterns in the emergency departments regarding the use of $MgSO_4$

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 $MgSO_4$ Frequency of the use Barriers to the use	88% physicians knew its efficacy 40% physicians rarely use it in patients without impending failure 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 $MgSO_4$	93% IV $MgSO_4$ 1% nebulized $MgSO_4$
[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 $MgSO_4$; 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 $MgSO_4$ Availability Recent use	2.5% received 92% availability 64% recent use

$MgSO_4$, magnesium sulfate; ED, emergency department; IV, intravenous; CPG, current practice guideline.

insufficient evidence. The use of $MgSO_4$ 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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