Evidence Table 19. Managing Exacerbations: Magnesium Sulfate

Abbreviations used in table:

AE	**adverse event**	**$MgSO_4$**	**magnesium sulfate**
ARR	**absolute risk reduction**	**P**	**placebo**
ED	**emergency department**	**PEFR**	**peak expiratory flow rate**
FEV_1	**forced expiratory volume in 1 second**	**RR**	**relative risk**
FVC	**forced vital capacity**	**SAE**	**serious adverse event**
ICS	**inhaled corticosteroid**	**SBP**	**systolic blood pressure**
ICU	**intensive care unit**	**SMD**	**standardized mean difference**
IVMg	**intravenous magnesium sulfate**	**WMD**	**weighted mean difference**

*** indicates primary outcome**

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Citation (Sponsor)	Study Design	Study Population		
		Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (if reported)
Magnesium by Nebulizer				
Blitz et al. Inhaled magnesium sulfate in the treatment of acute asthma. Cochrane Database Syst Rev 2005;(2):CD003898. (Alberta Cancer Board, Canada; Canadian Institutes of Health Research, Ottawa, Canada; Department of Emergency Medicine, University of Alberta, Edmonton, Alberta, Canada)	Meta-analysis of randomized controlled trials published between 1966 and 2003	Six trials conducted in the United States, India, New Zealand, Turkey, and Argentina with 296 patients; three included adults, one included adults and pediatric patients, two enrolled pediatric patients. Trials were published between 1995 and 2003. Methodological quality was high: five trials scored 3 on the Jadad scale. All rated a B in concealment of allocation.		Three studies enrolled severe asthmatics (FEV_1 or PEF <50% predicted). Five studies enrolled patients presenting to the emergency department (ED). Two studies excluded patients who had taken asthma medication within 12 hours. One excluded patients who had received corticosteroids in previous 7 days; one excluded patients who had received steroids, theophylline, or ipratropium bromide within 3 days of presenting to ED.
Magnesium by IV				
Boonyavorakul et al. Intravenous magnesium sulfate in acute severe asthma. Respirology 2000;5(3):221–225.	Prospective, randomized, double-blind, placebo-controlled trial (ED in Thailand)	33 (33)	**Age** ≥15 yr, mean = 39 yr **Gender** 12% male, 88% female	Acute severe asthma History of intubation, 12.1% Oral steroid use, 12.1% Inhaled steroid use, 33.3% Duration of asthma attack, median 4.5 hrs Pulse, mean = 125.5 beats/min Respiration, mean = 33.1/min Fischl index, mean = 6.02

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		Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (if reported)
Rowe et al. Magnesium sulfate for treating exacerbations of acute asthma in the emergency department. Cochrane Database Syst Rev 2000;(2):CD001490. (Canadian Association of Emergency Physicians; National Institute of Health; University of Alberta, Edmonton, Canada; Acute Care Research Group, Sudbury Regional Hospital, Sudbury, Ontario, Canada; and NHS Research and Development UK) NOTE: Review includes Silverman et al. study.	Meta-analysis of studies published between 1989 and 1997	Seven randomized controlled trials with 655 subjects; five adult and two pediatric studies		Presenting to ED for treatment of acute asthma
Porter et al. Intravenous magnesium is ineffective in adult asthma, a randomized trial. Eur J Emerg Med 2001;8(1):9–15.	Prospective, randomized, double-blind, placebo-controlled trial (urban ED in United States)	42 (42)	**Age** ≥18 yr, mean = 35 yr **Gender** 36% male, 64% female	Acute asthma exacerbation PEFR ≤100 L/min or ≤25% of predicted, mean = 89 L/min Heart rate, mean = 108 Respirations, mean = 31/min Mean arterial pressure = 100 mmHg Oxygen saturation, mean = 94% Borg dyspnoea scale, mean = 6.1
Cheuk et al. A meta-analysis on intravenous magnesium sulphate for treating acute asthma. Arch Dis Child 2005;90(1):74–77.	Meta-analysis of controlled clinical trials involving children below 18 years of age	Five trials involving 182 patients conducted in EDs and published between 1996 and 2000. Methodological quality was 4 or 5 on Jadad scale for all studies.	Children under 18 years of age	Inadequate response to first line treatment with three doses of beta$_2$-agonists

Citation (Sponsor)	Study Characteristics			Findings			
	Treatment	Dose	Duration of Active Treatment; Duration of Postintervention/ Off-Treatment Followup	Lung Function	Vital Signs/ Cardiovascular/ Clinical Laboratory Values	Severity/ Admissions	Safety
Magnesium by Nebulizer							
Blitz et al. Inhaled magnesium sulfate in the treatment of acute asthma. Cochrane Database Syst Rev 2005;(2):CD003898. (Alberta Cancer Board, Canada; Canadian Institutes of Health Research, Ottawa, Canada; Department of Emergency Medicine, University of Alberta, Edmonton, Alberta, Canada)	**Purpose/Objective:** To determine the efficacy of inhaled Magnesium sulfate ($MgSO_4$) administered in acute asthma on pulmonary functions and admissions Four studies compared $MgSO_4$ with $beta_2$-agonist to $beta_2$-agonist with placebo; two studies compared $MgSO_4$ to $beta_2$-agonist.			**$MgSO_4$ with $beta_2$-agonist vs.$beta_2$-agonist alone** Pulmonary functions were improve for $MgSO_4$ with $beta_2$-agonist vs. $beta_2$-agonist alone (SMD 0.23, 95% CI –0.03 to 0.50) with no difference between results from adults and those with children. There was a significant difference in results from severe asthma trials (SMD 0.55, 95% CI 0.12 to 0.98). **$MgSO_4$ vs. $beta_2$-agonist alone** There was no advantage for $MgSO_4$ alone (SMD 0.17, 95% CI –0.51 to 0.86).		**$MgSO_4$ with $beta_2$-agonist vs. $beta_2$-agonist alone** There was no clear reduction in probability of admission for $MgSO_4$ with $beta_2$-agonist (relative risk (RR) 0.69, 95%CI 0.42 to 1.12). There was no difference between adults and children or between severe and less severe asthma. **$MgSO_4$ vs. $beta_2$-agonist alone** Thre was no difference between $MgSO_4$ and $beta_2$-agonist alone based on a single trial (RR 0.50, 95% CI 0.04 to 6.12).	All studies reported no SAE in either arm.

Citation (Sponsor)	Study Characteristics			Findings			
	Treatment	Dose	Duration of Active Treatment; Duration of Postintervention/ Off-Treatment Followup	Lung Function	Vital Signs/ Cardiovascular/ Clinical Laboratory Values	Severity/ Admissions	Safety
Magnesium by IV							
Boonyavorakul et al. Intravenous magnesium sulfate in acute severe asthma. Respirology 2000;5(3):221–225.	**Purpose/Objective:** To determine whether intravenous $MgSO_4$ (IVMg) as an adjunct to a standard therapy can reduce admission rate and severity scores in patients with acute severe asthma compared with those treated by standard therapy					Admission rates were 17.65% for $MgSO_4$ and 25% for P (RR 0.71, 95% CI –0.19 to 2.67). Necessary to treat 14 patients with $MgSO_4$ to prevent one admission. Mean severity scores of two groups were same at all time points (p=0.37).	
	Arm 1 $MgSO_4$ (n=17; 17 completers)	2 g $MgSO_4$ in 50 mL of 0.9% normal saline	All patients received 5 mg intravenous dexamethasone, 2.5 mg nebulized salbutamol at 0, 20, 40, and 60 minutes. Measurements were taken at 60, 120, 180, and 240 min.				
	Arm 2 Placebo (P) (n=16; 16 completers)	2 mL of sterile water in 50 mL of 0.9% normal saline					

Citation (Sponsor)	Study Characteristics			Findings			
	Treatment	Dose	Duration of Active Treatment; Duration of Postintervention/ Off-Treatment Followup	Lung Function	Vital Signs/ Cardiovascular/ Clinical Laboratory Values	Severity/ Admissions	Safety
Rowe et al. Magnesium sulfate for treating exacerbations of acute asthma in the emergency department. Cochrane Database Syst Rev 2000;(2):CD001490. (Canadian Association of Emergency Physicians; National Institute of Health; University of Alberta, Edmonton, Canada; Acute Care Research Group, Sudbury Regional Hospital, Sudbury, Ontario, Canada; and NHS Research and Development UK) NOTE: Review includes Silverman et al. study.	**Purpose/Objective:** To examine the effect of additional IVMg in patients with acute asthma managed in the ED			No difference in improvement in PEFR (WMD 294, 95% CI –3.4 to 62) and % predicted FEV_1 (WMD 4.3, 95% CI –2.3 to 10.9).	Heart rate and respiratory rates did not change with IV $MgSO_4$. Slight but not clinically important change in systolic blood pressure (SBP).	*There was no significant difference in $MgSO_4$ vs. P in hospital admission (OR 0.31, 95% CI 0.09 to 1.02). In patients with severe asthma, admissions were lower with $MgSO_4$ vs. P (OR 0.10, 95% CI 0.04 to 0.27); no difference for those with mild to moderate asthma (OR 1.35, 95% CI 0.72 to 2.55).	Few adverse events (AE) were reported.
	Treatment Groups: $MgSO_4$ **Control groups:** Placebo (P)						
Porter et al. Intravenous magnesium is ineffective in adult asthma, a randomized trial. Eur J Emerg Med 2001;8(1):9–15.	**Purpose/Objective:** To test hypothesis that intravenous $MgSO_4$ would improve the outcome of severe asthmatics concurrently receiving maximal conventional therapy			*PEFR was 174 L/min in $MgSO_4$ vs. 212 L/min in P (p=0.038). Controlling for age and baseline PEFR, pulse oximetry, and heart rate, PEFR at 60 minutes in $MgSO_4$ averaged 75% that of P (95% CI 52% to 109%, p=0.132).		Groups did not differ in Borg dyspnoea scale score at 60 minutes in either univariate or multivariate analysis. There was no difference in hospital admission rate (28% of $MgSO_4$ vs. 21% of P, p=0.72).	
	Arm 1 $MgSO_4$ (n=18)	2 g in 50 mL normal saline	Patients received 2.5 mg albuterol sulfate, 125 mg methylprednisolone, and 50 ml study solution over 20 minutes at 0, 20, 40, and 60 minutes.				
	Arm 2 Placebo (P) (n=24)	50 mL normal saline					

Citation (Sponsor)	Study Characteristics			Findings			
	Treatment	Dose	Duration of Active Treatment; Duration of Postintervention/ Off-Treatment Followup	Lung Function	Vital Signs/ Cardiovascular/ Clinical Laboratory Values	Severity/ Admissions	Safety
Cheuk et al. A meta-analysis on intravenous magnesium sulphate for treating acute asthma. Arch Dis Child 2005;90(1):74–77.	**Purpose/Objective:** To evaluate the effectiveness of IVMg in preventing hospitalization or intensive care unit (ICU) admission in children with acute asthmatic attacks, either used alone on in addition to standard therapies			OR of persistent PEFR <60% predicted is 0.155 (95% CI 0.057 to 0.422, p=0.00033) Difference in % improvement of PEFR at study end, 8.58 (95% CI 0.94 to 16.22, p=0.028)		IVMg was effective in avoiding hospitalization (absolute risk reduction (ARR) 0.257, 95% CI 0.124 to 0.389, p=0.0001). Number needed to treat in avoiding hospitalization is 4 (95% CI 3 to 8). Difference in clinical symptom score at study end, 1.33 (95% CI 0.31 to 2.36, p=0.011)	
	$MgSO_4$ of any therapeutic dose either alone or in additional to standard therapies.						