Medicine by the Numbers

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Intravenous Magnesium Sulfate for Acute Asthma Exacerbation in Children and Adults

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Details for This Review

Study Population: Adults (n = 972, from 11 studies) and children (n = 115, from three studies) who were treated in the emergency department for acute asthma exacerbations

Efficacy End Points: Hospital admission

Harm End Points: Medication adverse effects (bradycardia, hypotension, fatigue, flushing, nausea, or headache)

Narrative:

Adults. The Cochrane review of adults identified 14 studies (n = 2,313) that met the initial inclusion criteria.[1] The final analysis included data from 972 adults in 11 studies. Three studies were excluded because both adults and children participated, and data pertaining only to adults were not provided. All participants presented to the emergency department with an asthma exacerbation, although definitions and inclusion criteria varied. In eight of the studies, patients received a single 2-g infusion of intravenous magnesium sulfate; in the remaining three studies, patients received a 1.2-g infusion. All participants were rated for degree of exacerbation severity, which was then verified using British Thoracic Society/Scottish Intercollegiate Guidelines Network (BTS/SIGN) criteria.[2] All of the studies included exacerbations of at least moderate severity.

The Cochrane review revealed a significant reduction in hospital admissions in all adults, regardless of asthma severity, who received intravenous magnesium sulfate compared with those who received placebo (50% vs. 57%; number needed to treat [NNT] = 21; odds ratio [OR] = 0.75; 95% CI, 0.60 to 0.92; high-quality evidence). Subgroup analysis of adults who initially presented with life-threatening asthma (based on 2012 BTS/SIGN criteria) found that 31% in the magnesium treatment group were admitted vs. 39% in the placebo group (NNT = 13). The one study that specifically evaluated the differences in admissions to the intensive care unit found no statistically significant difference between the two groups.

The most commonly cited adverse effects were flushing, fatigue, nausea, headache, and tingling and burning at the administration site. Three studies showed a statistically significant increase in adverse effects in the magnesium sulfate group compared with the placebo group, but the other eight studies did not. Only four studies reported on hypotension; two of these studies showed a statistically significant increase in the rate of hypotension in the magnesium sulfate group vs. the placebo group, whereas the other two studies found no difference.

Children. The Cochrane review of children was based on data from three studies including 115 total children who presented to the emergency department with an acute asthma exacerbation.[3] All studies were randomized, double-blind, placebo-controlled trials. The dose of intravenous magnesium sulfate ranged from 25 to 75 mg per kg. Patient age ranged from one year to 18 years.

The rate of hospital admission was 55% in the magnesium sulfate group compared with 77% in the placebo

INTRAVENOUS MAGNESIUM SULFATE FOR ACUTE ASTHMA EXACERBATION

Benefits	Harms
NNT = 5 in children (prevented hospital admission)	No adults or children had serious adverse effects
NNT = 21 in adults (prevented hospital admission)	
NNT = 13 in adults with life-threatening exacerbations (prevented hospital admission)	
22% lower admission rate in children	
7% lower admission rate in adults	
8% lower admission rate in adults with life-threatening asthma exacerbations	

NNT = number needed to treat.

The NNT Group Rating System

Green	Benefits greater than harms
Yellow	Unclear benefits
Red	No benefits
Black	Harms greater than benefits

group (NNT = 5; OR = 0.32; 95% CI, 0.14 to 0.74). There was no statistically significant difference in adverse effects between the two groups. The studies were of good methodological quality, but study heterogeneity and the small number of study participants raised questions about the quality of the data and results.

Caveats: Intravenous magnesium sulfate appears to have a greater benefit in children than in adults. However, although the studies of children were judged to be of good methodological quality, the small number of participants and the heterogeneity of trials led to low confidence in the results.

In adults, the greatest benefit of intravenous magnesium sulfate occurred in patients with life-threatening asthma exacerbations. The severity of the exacerbation was based on the patient's initial presentation and was determined retrospectively from data extracted from the various studies included in the meta-analysis. The BTS/SIGN guidelines have been updated (2019), using the previous categories plus the addition of a new level of severity labeled "near-fatal asthma exacerbation" for patients who require mechanical ventilation.

Although it appears that patients who presented in life-threatening distress benefited the most from intravenous magnesium sulfate, other factors, such as more attention from hospital staff or shorter time to receive treatment, may have played a role in the better outcomes in this subgroup.

The studies differed in the timing, dosage, and frequency of magnesium sulfate administration; types of other medications given; and the order in which medications were administered. This made it difficult to determine the exact degree of effect attributable to treatment with magnesium sulfate.

Conclusion: Our NNT color recommendation is green. Most of the benefit from this intervention appeared to be in children (NNT = 5) and in sicker adults who initially presented with life-threatening asthma exacerbations (NNT = 13). However, further randomized controlled trials of children are required to achieve the larger sample size needed to provide more definitive evidence for the effectiveness of magnesium sulfate in this population. In adults, further studies using more uniform treatment protocols will be required to minimize confounding factors and to confirm the apparent benefit of magnesium sulfate in this population.

This series is coordinated by Christopher W. Bunt, MD, *AFP* assistant medical editor, and Daniel Runde, MD, from the NNT Group.

A collection of Medicine by the Numbers published in *AFP* is available at https://www.aafp.org/afp/mbtn.

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References

1. 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.
2. British Thoracic Society. Scottish Intercollegiate Guidelines Network. British guideline on the management of asthma. July 2019. Accessed December 10, 2020. https://www.brit-thoracic.org.uk/quality-improvement/guidelines/asthma
3. Griffiths B, Kew KM. Intravenous magnesium sulfate for treating children with acute asthma in the emergency department. *Cochrane Database Syst Rev.* 2016;(4):CD011050. ■