

Randomised controlled trial

The addition of nebulised magnesium to the standard asthma therapy for children with severe symptoms results in small improvements in asthma severity scores

10.1136/eb-2013-101688

Joseph J Zorc

Children's Hospital of Philadelphia, University of Pennsylvania, Philadelphia, Pennsylvania, USA

Correspondence to: Dr Joseph J Zorc, CTRB 9004, The Children's Hospital of Philadelphia, 34th and Civic Center Blvd, University of Pennsylvania, Philadelphia, PA 19104, USA; zorc@email.chop.edu

Commentary on: Powell C, 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;17:1–216.

Context

The prior research has found that magnesium sulfate given intravenously acts as a bronchodilator and improves airway obstruction in status asthmaticus.¹ The intravenous route requires substantial resources for administration and close monitoring due to concerns for adverse effects, such as hypotension. Several studies have suggested that nebulised magnesium may also have benefits.² If the efficacy was demonstrated for nebulised magnesium, it could be added to bronchodilators in the standard asthma treatment protocols, providing an important advance in the treatment of this common disorder.

Methods

This was a multicentre, placebo-controlled, randomised trial of nebulised magnesium added to the standard therapy for asthma at 30 hospitals in the UK. The authors describe it as a pragmatic trial in that it was designed around the standard asthma treatment protocols at these hospitals. They also conducted an economic evaluation of the effects of magnesium on costs to the healthcare system. Children aged 2–16 were enrolled in the accident and emergency department if they met the standard UK definitions for severe asthma including oxygen saturation <92% in room air, with the presence of breathlessness and accessory muscle use

on examination. After informed consent, participants were randomised to receive blinded doses of either 151 mg of magnesium sulfate or normal saline with each of the three nebulised treatments of albuterol and ipratropium given every 20 min. The response was determined by measuring the Asthma Severity Score (ASS) 1 h after the start of treatment. Other outcomes included additional treatment, hospital length of stay, adverse events and measures related to the economic analysis. The study was powered to detect a difference of 0.5 points in the ASS, a validated score that assesses wheezing, accessory muscle use and heart rate with a range from 0 to 9.

Findings

A total of 508 children were enrolled, and treatment groups were similar at baseline. The mean ASS was 0.25 points lower (95% CI 0.02 to 0.48) for the children who received magnesium, compared with controls, after 1 h of the treatment; the difference was sustained through 240 min. There was no difference in additional treatment, length of stay, adverse events or other secondary outcomes. A treatment-covariate analysis found a larger improvement in ASS among children with more severe exacerbations and among those with shorter symptom duration. The economic analysis found that addition of magnesium to the standard asthma therapy may be cost-effective, depending on the valuation of improvement in symptoms.

Commentary

This trial was well-planned to answer a question of pragmatic interest to paediatric care providers. The large multicentre design structured around the standard treatment protocol in the UK provides highly generalisable results. However, the main finding of a statistically significant improvement that is of questionable clinical significance will likely require further study in order to know how to translate this study to the bedside. Although nebulised magnesium appears to be safe, this study does not provide justification for routine use given the small difference between treatment groups. The subgroup analysis, which suggests that more severely affected patients may have greater benefit, fits with the findings for other asthma medications, including studies of intravenous magnesium. Subgroup analyses should always be interpreted cautiously, but further work could better define the response in higher severity patients. The economic analysis is difficult to translate to other health systems, but it is possible that clinically important benefits could be demonstrated in a defined subgroup of more severe children, or if the difference resulted in improvement in other clinically important outcomes, such as hospital admission, which was not explored here. Other factors, such as the optimal dose of magnesium, could also be explored.

Competing interests None.

References

- Rowe BH, Bretzlaff J, Bourdon C, *et al.* Magnesium sulfate for treating exacerbations of acute asthma in the emergency department. *Cochrane Database Syst Rev* 2000;(1): CD001490.
- Powell C, Dwan K, Milan SJ, *et al.* Inhaled magnesium sulfate in the treatment of acute asthma. *Cochrane Database Syst Rev* 2012;(12):CD003898.