A meta-analysis on intravenous magnesium sulphate for treating acute asthma
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CRD summary
This review determined the effectiveness of intravenous magnesium sulphate for preventing the hospitalisation of children with acute asthma. The authors stated that intravenous magnesium sulphate is likely to provide additional benefit in children with moderate to severe acute asthma who are being treated with bronchodilators and steroids. While the authors’ conclusion appears to reflect the results presented, the literature search could need updating.

Authors’ objectives
To determine the effectiveness of intravenous magnesium sulphate for preventing the hospitalisation or intensive care unit (ICU) admission of children with acute asthmatic attacks.

Searching
MEDLINE, EMBASE, the Cochrane Library, the Cochrane CENTRAL Register and China Journal Net were searched for articles in any language; no search dates were reported, although search terms were provided. The reference lists of relevant articles were also checked. Attempts to contact authors and specialists were also made.

Study selection
Study designs of evaluations included in the review
Controlled clinical trials were eligible for inclusion.

Specific interventions included in the review
Studies of intravenous magnesium sulphate, used alone or in addition to standard therapies, were eligible for inclusion. Any therapeutic dose was considered. The included trials used magnesium sulphate in combination with co-therapies, inhaled beta-2 agonists and systemic steroids, and were placebo-controlled. Further details of the intervention and cointerventions (Table 3) are available on the Archives of Disease in Childhood website (accessed 06/11/2006). See Web Address at end of abstract.

Participants included in the review
Children younger than 18 years old with acute asthma were eligible for inclusion. Paediatric patients with acute moderate to severe asthmatic attacks attending emergency departments were included in the review.

Outcomes assessed in the review
The primary outcomes measure was the rate of hospitalisation or ICU admission. The secondary outcomes included rate of persistent severe bronchoconstriction (indicated by a peak expiratory flow rate, PEFR, of less than 60%), clinical symptom scores and change in pulmonary function tests.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected articles for inclusion in the review. Any disagreements were resolved by consensus.

Assessment of study quality
The methodological quality of the primary studies was assessed using the Jadad score, which evaluates reported adequacy of randomisation, blinding and follow-up. A maximum of 5 points can be awarded; trials scoring less than 3 were considered to be of poor quality. Two reviewers independently assessed the methodological quality of the primary studies. Any disagreements were resolved by consensus.
Data extraction
Two reviewers independently extracted the data from the primary studies. Any disagreements were resolved by consensus. The baseline characteristics of the treatment and control groups (e.g. age, gender, baseline SpO2, symptom severity) and the results of pulmonary function tests were extracted.

Methods of synthesis
How were the studies combined?
The pooled odds ratio (OR), absolute risk reduction (ARR) and number-needed-to-treat (NNT) were calculated, along with their associated 95% confidence interval (CI), for rate of hospitalisation or ICU admission and PEFR less than 60%. A fixed-effect model was used if no significant statistical heterogeneity was found, and a random-effects model if significant statistical heterogeneity was shown. The mean and standard deviation were reported for the percentage change in PEFR and clinical symptom scores.

How were differences between studies investigated?
The Cochran Q test was used to assess statistical heterogeneity between the included trials (P<0.1 considered statistically significant). Sensitivity analyses, excluding studies with poor quality, were planned. The authors stated that clinical heterogeneity was explored in terms of the study design, baseline characteristics, patients recruited, intervention, co-therapies and outcomes assessed.

Results of the review
Five randomised placebo-controlled trials (RCTs; n=182) were included.

All 5 included trials were judged to be of good quality: four were awarded a score of 4, while the fifth was awarded the maximum score of 5.

Magnesium sulphate was shown to significantly reduce the incidence of hospitalisation in paediatric acute asthma compared with placebo (OR 0.29, 95% CI: 0.14, 0.59, P<0.006), based on 4 RCTs. There was no evidence of statistical heterogeneity (P=0.13). The ARR for hospitalisation was 0.26 (95% CI: 0.12, 0.39, P=0.0001) and the NNT to avoid hospitalisation was 4 (95% CI: 3, 8). None of the included trials assessed the rate of ICU admission.

A significant reduction in persistent PEFR less than 60% was shown with magnesium sulphate compared with placebo (OR 0.16, 95% CI: 0.06, 0.42, P=0.0003), based on 3 RCTs. There was no evidence of statistical heterogeneity (P=0.97).

Significant improvements in PEFR (mean difference 8.58, 95% CI: 0.94, 16.22, P=0.028; based on 3 RCTs) and clinical symptoms (mean difference 1.33, 95% CI: 0.31, 2.36, P=0.011; based on 4 RCTs) were shown for magnesium sulphate compared with placebo, although significant statistical heterogeneity was found in both analyses (P<0.0001 and P=0.0001, respectively).

No subgroup analysis was carried out for age (stratified outcome data not available), severity of asthma (lack of variation in the included population: all patients had moderate to severe asthma), or dosage (no study compared the effectiveness of different doses). A sensitivity analysis according to trial quality was not performed because the included trials were of similar quality. Possible areas of heterogeneity were highlighted in supplemental tables, available on the journal's website (accessed 06/11/2006). See Web Address at end of abstract.

The funnel plot indicated possible publication bias in favour of the intervention.

Authors' conclusions
Intravenous magnesium sulphate is likely to provide additional benefit in children with moderate to severe acute asthma who are being treated with bronchodilators and steroids.

CRD commentary
The review question was supported by clear inclusion criteria in terms of the population, intervention and outcomes. Several electronic databases were searched but no search dates were reported; the included studies were published between 1996 and 2000. Attempts were made to locate unpublished articles and publication bias was assessed. The review process was reported and efforts were made to minimise reviewer error or bias in the study selection, data extraction and quality assessment processes. The quality of the primary studies was assessed using a standardised evaluation tool and the results were reported.

A quantitative synthesis of the data might not have been appropriate given the clinical heterogeneity of the selection criteria, population, intervention and outcome measures. Statistical heterogeneity was assessed and subgroup analyses were planned, but these were not possible because of a lack of stratification or raw data. The authors acknowledged a number of these limitations including the clinical heterogeneity, small data sets and lack of subgroup analysis. The authors’ cautious conclusion appears to reflect the results presented, but the lack of reported search dates may mean that the literature search could need updating.

**Implications of the review for practice and research**

**Practice:** The authors advised caution when applying the pooled result for the primary outcome to clinical practice.

**Research:** The authors stated that further research is needed to evaluate the effectiveness of intravenous magnesium sulphate in individuals with different severity classes and in patients of different age groups. In addition, they suggested that studies should aim to further define the indications and optimal dosage of intravenous magnesium sulphate for the treatment of acute asthma.

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