Efficacy of magnesium sulfate in acute adult asthma: a meta-analysis of randomized trials

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Authors' objectives
To determine whether magnesium sulfate (MgSO4) provides an additive improvement in adults with acute asthma presenting to the emergency department (ED). The specific questions addressed were:

1. Does MgSO4 improve pulmonary function tests over the first 60 months of treatment?
2. Does MgSO4 reduce hospital admission rate when prescribed for patients with acute exacerbations of asthma?

Searching
The authors searched MEDLINE, the Science Citation Index and Current Contents from 1968 to 1998. Additional studies were located by examining bibliographic reviews of primary research, review articles and the register of Medical Editors' Trial Amnesty, and by consulting experts. The search was restricted to English language publications.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were included.

Specific interventions included in the review
Magnesium in the form of MgSO4, administered parenterally or by nebuliser.

Participants included in the review
Adult patients aged greater than 16 years, with acute asthma treated in the ED, were included. The mean age of participants was 38.3 years (plus or minus 13.4 years); 30% were men and 70% were women.

Outcomes assessed in the review
The primary assessed outcome was improvement in pulmonary function over the first 60 minutes of treatment. The secondary assessed outcome was admission rate.

How were decisions on the relevance of primary studies made?
Two authors independently reviewed the studies for inclusion. Any disagreements were resolved by consensus.

Assessment of study quality
The studies were assessed for masking, randomisation method, demographic characteristics of the sample, inclusion and exclusion criteria, asthma definition, sample size calculation and withdrawals. Each study was assessed by two authors using a 7-criteria scoring scheme, and the mean score divided by the total possible score of 14 and expressed as a value between 0 and 1.0. Two authors assessed each study for quality using a 7-criteria scoring scheme. Agreement among evaluators was assessed using the Kappa statistic.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction. Data were extracted for the following categories: study identification and year of publication; country; number of patients studied; patient demographics; exact dosage and route of all medications used; spirometric measure used; mean and standard deviation of spirometric values at baseline, and after treatment for each group; follow-up timing; statistical analysis; admission rates; and adverse effects.

The effect of treatment on the pulmonary function outcome was calculated using the effect size (ES) measure with
95% confidence intervals (CIs), as described by Glass (see Other Publications of Related Interest no.1).

**Methods of synthesis**

How were the studies combined?
For the pulmonary function outcome, the weighted mean difference and the pooled ES, along with 95% CIs, were calculated using a fixed-effect model.

For binary outcome data (admission rate), a pooled odds ratio (OR) with 95% CIs was calculated using the Mantel-Haenszel technique.

How were differences between studies investigated?
The chi-squared statistic was used to test for homogeneity for the pulmonary function outcome, whilst the Breslow and Day method (see Other Publications of Related Interest no.2) was used to test for homogeneity for the admission rate outcome.

The authors also checked the robustness of the findings in terms of methodological quality, study size and therapeutic protocol, by means of a sensitivity analysis. A mixed regression model was used to measure funnel plot asymmetry.

**Results of the review**

Five RCTs were included in the review with 374 participants. The mean sample size was 75 patients.

All studies were of good quality, scoring greater than or equal to 0.7, with a kappa value of 0.90 for inter-rater agreement.

The overall pooled ES for pulmonary function in 4 studies was statistically non significant (ES 0.02, 95% CI: -0.20, +0.24). Homogeneity was also statistically non significant (chi-squared =4.12, P>0.3).

The sensitivity analysis did not alter the results significantly in terms of methodological quality, study size and therapeutic protocol. In addition, it provided no evidence of systematic bias. Pooled results revealed that MgSO4 did not reduce admission rates significantly (OR 0.68, 95% CI: 0.41, 1.15, Z-statistic=1.35, P=0.18). The authors state that the test of homogeneity was also not statistically significant (chi-squared=6.15, P=0.1), although a P-value of 0.1 is deemed to be statistically significant by some research groups. Further analysis showed that the distribution of admission rate was skewed owing to a small number of patients with unusually high admission rates. Excluding those patients produced an OR of 0.83 (95% CI: 0.29, 1.38). There was insufficient information to pool other outcomes such as blood-pressure, heart rate or side-effects ratio.

Weak correlations were found between ES and quality (rho=-0.35, P=0.5), ES and year of publication (rho=-0.43, P=0.39), and quality and year (rho=0.30, P=0.6).

Side-effects: in one trial minor side-effects such as flushing, mild fatigue, and burning at the intravenous site, were noted in 58% of patients who received MgSO4.

**Authors’ conclusions**
The authors state that the existing evidence reveals that the administration of MgSO4 to ED patients with moderate to severe asthmatic exacerbations does not alter treatment outcomes. The authors conclude that MgSO4 does not have a role in the initial treatment of acute asthma patients. Nevertheless, the number and size of studies being pooled remains small and the current conclusions may be seriously modified by the results of large trials.

**CRD commentary**
The authors have stated the research question and inclusion and exclusion criteria. The literature search was reasonably thorough, although foreign language reports were excluded. However, it is unlikely that additional relevant studies may have been missed since the authors found no evidence of publication bias in the funnel plot analyses.
The quality of the included studies was formally assessed and the authors have reported how the articles were selected, and who performed the selection and validity assessment. The results of the validity assessment were addressed in further sensitivity analyses. The data extraction is reported in tables and discussed in the text of the review. The studies were combined in a statistical meta-analysis and heterogeneity was assessed. Further analyses were performed to assess the effects of differences between the studies. The authors’ conclusions appear to follow from the results but, as the authors state, should be viewed with caution because of limitations in the data in the included studies.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors state that further definitive controlled studies are needed to clarify efficacy in possible subsets of patients for whom MgSO4 could be beneficial. The authors state that with further evidence, such as another RCT, the use of MgSO4 could play a role in the treatment of near intubation asthmatics (forced expiratory volume in 1 s less than 25%); this has been suggested in a number of case reports.

Bibliographic details

PubMedID
10750936

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Acute Disease; Adult; Asthma /diagnosis /drug therapy /physiopathology; Emergency Treatment /methods; Female; Forced Expiratory Volume /drug effects; Humans; Magnesium Sulfate /pharmacology /therapeutic use; Male; Odds Ratio; Patient Admission /statistics & numerical data; Peak Expiratory Flow Rate /drug effects; Research Design /standards; Sensitivity and Specificity; Severity of Illness Index; Treatment Outcome

AccessionNumber
12000000726

Date bibliographic record published
31/01/2002

Date abstract record published
31/01/2002

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.