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Inhaled Magnesium Sulfate in the Treatment of Acute Asthma

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Abstract

Background: Asthma exacerbations can be frequent and range in severity from mild to life-threatening. The use of magnesium sulfate ($MgSO_4$) is one of numerous treatment options available during acute exacerbations. While the efficacy of intravenous $MgSO_4$ has been demonstrated, the role of inhaled $MgSO_4$ is less clear.

Objectives: To determine the efficacy and safety of inhaled $MgSO_4$ administered in acute asthma.

Specific aims: to quantify the effects of inhaled $MgSO_4$ I) in addition to combination treatment with inhaled β_2-agonist and ipratropium bromide; ii) in addition to inhaled β_2-agonist; and iii) in comparison to inhaled β_2-agonist.

Search methods: We identified randomised controlled trials (RCTs) from the Cochrane Airways Group register of trials and online trials registries in September 2017. We supplemented these with searches of the reference lists of published studies and by contact with trialists.

Selection criteria: RCTs including adults or children with acute asthma were eligible for inclusion in the review. We included studies if patients were treated with nebulised $MgSO_4$ alone or in combination with β_2-agonist or ipratropium bromide or both, and were compared with the same co-intervention alone or inactive control.

Data collection and analysis: Two review authors independently assessed trial selection, data extraction and risk of bias. We made efforts to collect missing data from authors. We present results, with their 95% confidence intervals (CIs), as mean differences (MDs) or standardised mean differences (SMDs) for pulmonary function, clinical severity scores and vital signs; and risk ratios (RRs) for hospital admission. We used risk differences (RDs) to analyse adverse events because events were rare.

Main results: Twenty-five trials (43 references) of varying methodological quality were eligible; they included 2907 randomised patients (2777 patients completed). Nine of the 25 included studies involved adults; four included adult and paediatric patients; eight studies enrolled paediatric patients; and in the remaining four studies the age of participants was not stated. The design, definitions, intervention and outcomes were different in all 25 studies; this heterogeneity made direct comparisons difficult. The quality of the evidence presented ranged from high to very low, with most outcomes graded as low or very low. This was largely due to concerns about the methodological quality of the included studies and imprecision in the pooled effect estimates. Inhaled magnesium sulfate in addition to inhaled β_2-agonist and ipratropiumWe included seven studies in this comparison. Although some individual studies reported improvement in lung function indices favouring the intervention group, results were inconsistent overall and the largest study reporting this outcome found no between-group difference at 60 minutes (MD -0.3 % predicted peak expiratory flow rate (PEFR), 95% CI -2.71% to 2.11%). Admissions to hospital at initial presentation may be reduced by the addition of inhaled magnesium sulfate (RR 0.95, 95% CI 0.91 to 1.00; participants = 1308; studies = 4; I^2 = 52%) but no difference was detected for re-admissions or escalation of care to ITU/HDU. Serious adverse events during admission were rare. There was no difference between groups for all adverse events during admission (RD 0.01, 95% CI -0.03 to 0.05; participants = 1197; studies = 2). Inhaled magnesium sulfate in addition to inhaled β_2-agonistWe included 13 studies in this comparison. Although some individual studies reported improvement in lung function indices favouring the intervention group, none of the pooled results showed a conclusive benefit as measured by FEV1 or PEFR. Pooled results for hospital admission showed a point estimate that favoured the combination of $MgSO_4$ and β_2-agonist, but the confidence interval includes the possibility of admissions increasing in the intervention group (RR 0.78, 95% CI 0.52 to 1.15; participants = 375; studies = 6; I^2 = 0%). There were no serious adverse events reported by any of the included studies and no between-group difference for all adverse events (RD -0.01, 95% CI -0.05 to 0.03; participants = 694; studies = 5). Inhaled magnesium sulfate versus inhaled β_2-agonistWe included four studies in this comparison. The evidence for the efficacy of β_2-agonists in acute asthma is well-established and therefore this could be considered a historical comparison. Two studies reported a benefit of β_2-agonist over $MgSO_4$ alone for PEFR and two studies reported no difference; we did not pool these results. Admissions to hospital were only reported by one small study and events were rare, leading to an uncertain result. No serious adverse events were reported in any of the studies in this comparison; one small study reported mild to moderate adverse events but the result is imprecise.

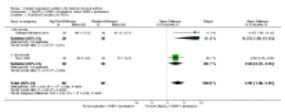
Authors' conclusions: Treatment with nebulised $MgSO_4$ may result in modest additional benefits for lung function and hospital admission when added to inhaled β_2-agonists and ipratropium bromide, but our confidence in the evidence is low and there remains substantial uncertainty. The recent large, well-designed trials have generally not demonstrated clinically important benefits. Nebulised $MgSO_4$ does not appear to be associated with an increase in serious adverse events. Individual studies suggest that those with more severe attacks and attacks of shorter duration may experience a greater benefit but further research into subgroups is warranted.Despite including 24 trials in this review update we were unable to pool data for all outcomes of interest and this has limited the strength of the conclusions reached. A core outcomes set for studies in acute asthma is needed. This is particularly important in paediatric studies where measuring lung function at the time of an exacerbation may not be possible. Placebo-controlled trials in patients not responding to standard maximal treatment, including inhaled β_2-agonists and ipratropium bromide and systemic steroids, may help establish if nebulised $MgSO_4$ has a role in acute asthma. However, the accumulating evidence suggests that a substantial benefit may be unlikely.

Figures

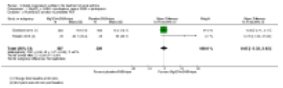
Figure 1 5 Study flow diagram: review update

Figure 2 5 'Risk of bias' summary: review...

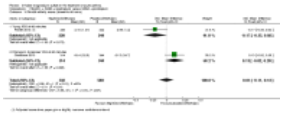
Figure 3 5 In the control group 82...



Analysis 1.1 5 Comparison 1 $MgSO_4$ + ...



Analysis 1.2 5 Comparison 1 $MgSO_4$ + ...



Analysis 1.3 5 Comparison 1 $MgSO_4$ + ...

All figures (37)

Update of

Inhaled magnesium sulfate in the treatment of acute asthma.

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