Effects of magnesium on atrial fibrillation after cardiac surgery: a meta-analysis

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CRD summary
This review assessed the effectiveness of magnesium in preventing post-operative atrial fibrillation (AF) after cardiac surgery. The authors concluded that magnesium administration reduced post-operative AF, but did not significantly alter length of hospital stay or in-hospital mortality. Limitations in the review process, along with variation amongst the included studies, reduce the reliability of the authors' conclusions.

Authors' objectives
To assess the effectiveness of magnesium for the prevention of post-operative atrial fibrillation (AF) after cardiac surgery.

Searching
MEDLINE and the Cochrane CENTRAL Register were searched from 1966 to July 2003; the search terms were reported. The reference lists of retrieved articles were checked for additional relevant studies. Abstracts from the annual scientific meetings (2000 to 2003) of the American College of Cardiology, American Heart Association, British Cardiac Society, European Society of Cardiology, and the North American Society for Pacing and Electrophysiology were also searched. No language restrictions were applied.

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

Specific interventions included in the review
Studies that compared magnesium with placebo, immediately pre-, peri- or post-operatively, were eligible for the review. The patients in the majority of the included studies received magnesium sulphate, whilst some studies administered magnesium chloride. The route of administration was intravenous in most studies and intramuscular in one. The duration of treatment ranged from 10 to 144 hours, and the total amount of magnesium given ranged from 7 to 110 mmol.

Participants included in the review
Studies of patients who had undergone coronary artery bypass graft (CABG) or valve surgery were eligible for the review. Most of the patients in the included studies had undergone CABG surgery. Where stated, the average age of the patients ranged from 45 to 67 years, and in most studies the majority of the patients were male. Most of the included studies excluded patients with abnormal renal function, and some excluded patients with severely decreased left ventricular function and thyroid or respiratory disorders.

Outcomes assessed in the review
Studies that provided adequate data on treatment efficacy (supraventricular arrhythmia incidence) were eligible for the review. The primary outcome of interest was the incidence of post-operative AF or atrial flutter, except where total incidence of supraventricular arrhythmia was recorded. Other outcomes of interest were the incidence of stroke and length of hospital stay. Most studies used continuous electrocardiographic monitoring to detect arrhythmia, and some used Holter recordings.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection. However, they stated that two reviewers evaluated the design of each trial for inclusion.
Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Two reviewers independently extracted data from the included studies into a data extraction table designed specifically for the project. Any disagreements were resolved by consensus. The authors collected data on participant and intervention characteristics, and the incidence of the outcomes of interest (number of events and mean values). Data were extracted in an intention-to-treat format.

Methods of synthesis
How were the studies combined?
For the outcome of length of hospital stay, the weighted mean difference (WMD) between the treatment and control groups was calculated. Odds ratios (ORs) were pooled using a random-effects model.

How were differences between studies investigated?
Heterogeneity was assessed using a random-effects model. Subgroup analyses compared studies with low (less than 35 mmol), medium (35 to 50 mmol) and high (over 50 mmol) doses of magnesium; studies that gave pre-, peri- and post-operative regimens; and studies in which patients underwent CABG surgery alone, CABG and valve surgery, and valve surgery alone.

Results of the review
Twenty RCTs with a total of 2,490 patients were included in the review.

 Patients given magnesium were statistically significantly less likely to suffer AF than those given placebo (18% versus 28%; OR 0.54, 95% confidence interval, CI: 0.38, 0.75). However, there was significant heterogeneity between the trials (P<0.001).

 When comparing different dosages of magnesium, patients given low (5 RCTs) or medium (7 RCTs) doses were statistically significantly less likely to suffer AF than those given placebo: 20% versus 31% (OR 0.50, 95% CI: 0.29, 0.87) and 17% versus 32% (OR 0.36, 95% CI: 0.16, 0.82), respectively. However, those given a higher dose (6 RCTs) were not statistically significantly less likely to suffer AF than those given placebo (20% versus 23%; OR 0.87, 95% CI: 0.59, 1.29).

 When comparing different administration times of magnesium, patients given pre-operative (4 RCTs) or post-operative (10 RCTs) magnesium were statistically significantly less likely to suffer AF than those given placebo: 8% versus 25% (OR 0.19, 95% CI: 0.05, 0.76) and 22% versus 31% (OR 0.63, 95% CI: 0.41, 0.96), respectively. However, those given peri-operative magnesium (5 RCTs) were not statistically significantly less likely to suffer AF than those given placebo (25% versus 31%; OR 0.74, 95% CI: 0.53, 1.05).

 In studies in which patients underwent CABG surgery alone (14 RCTs) or valve surgery alone (1 RCT), patients given magnesium were statistically significantly less likely to suffer AF than those given placebo: 17% versus 28% (OR 0.51, 95% CI: 0.32, 0.79) and 3% versus 32% (OR 0.07, 95% CI: 0.01, 0.53), respectively. However, patients who underwent CABG and valve surgery (4 RCTs) were not statistically significantly less likely to suffer AF than those given placebo (22% versus 26%; OR 0.77, 95% CI: 0.51, 1.16).

 There was no significant difference in post-operative mortality between patients given magnesium and those given placebo (12 RCTs; OR 1.22, 95% CI: 0.39, 3.77).

 There was no significant difference in length of hospital stay between patients given magnesium and those given placebo (7 RCTs; WMD -0.07, 95% CI: -0.66, 0.53).

Authors' conclusions
Magnesium administration is effective for reducing post-operative AF. However, magnesium administration did not significantly alter length of hospital stay or in-hospital mortality. Questions remain about the optimal regimen of magnesium administration and its efficacy in combination with other drugs.

CRD commentary
The review question was clear in terms of the study design, participants, interventions and outcomes of interest. The search strategy was restricted to two electronic databases, along with handsearches of meeting abstracts and reference lists. Hence, other relevant studies, in particular unpublished studies, might have been missed, thus increasing the potential for publication bias. Language restrictions were not applied, which reduces the potential for language bias. The authors did not state how studies were assessed for relevance, other than that two reviewers evaluated the design of each trial for inclusion; the potential for error or reviewer bias cannot, therefore, be assessed. The included studies were not assessed for validity. Two reviewers independently extracted data from the included studies, thereby reducing the potential for error or reviewer bias.

Adequate details of the included studies were provided. Since there was significant heterogeneity between the studies, it might not have been appropriate to pool all of the studies together. The authors conducted appropriate subgroup analyses, but did not assess heterogeneity within these analyses. The conclusions appear to follow from the results presented. However, the potential for publication bias, the lack of a validity assessment, and the heterogeneity between studies reduce the reliability of the authors' conclusions.

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

Research: The authors stated that additional research to assess the effect of magnesium on length of hospital stay is warranted. They also stated that questions remain regarding the optimal regimen of administration of magnesium and its efficacy in combination with other drugs.

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