Magnesium prophylaxis for arrhythmias after cardiac surgery: a meta-analysis of randomized controlled trials
Shiga T, Wajima Z I, Inoue T, Ogawa R

CRD summary
The authors of this review found that prophylactic magnesium given around the time of cardiac surgery reduced the incidence of cardiac arrhythmias, but had no effect on length of hospital stay or mortality. Given the potential for publication and selection bias, and the pooling of diverse results, the conclusions should be treated with caution.

Authors' objectives
To investigate the effects of prophylactic magnesium given to prevent arrhythmias after cardiac surgery.

Searching
MEDLINE (1966 to June 2003), EMBASE (1980 to June 2003) and the Cochrane CENTRAL Register (Issue 3 2003) were searched; the search terms were reported. No language restrictions were applied. The reference lists of identified reports and reviews were checked.

Study selection
Study designs of evaluations included in the review
Prospective, single- or double-blind, randomised controlled trials (RCTs) were eligible for inclusion. In the included studies, the duration of follow-up ranged from 1 to 30 days.

Specific interventions included in the review
Studies evaluating a single dose of prophylactic magnesium given around the time of cardiac surgery were eligible for inclusion. The route of administration could be intravenous, central or intracoronary. In the included studies magnesium was given prior to, during or after surgery. Some studies gave magnesium, in repeated doses or as an intravenous infusion, for up to 5 days post-operatively. Details of the magnesium dosing regimens in the individual studies were given in the paper.

Participants included in the review
Studies of people undergoing cardiac surgery were eligible. The surgical procedures undertaken in the included studies were coronary artery bypass graft (CABG), valve replacement, combined CABG and valve replacement, or repair of septal defect. Cardiopulmonary bypass was used in most cases. The majority of the participants were men and the mean ages ranged from 4.5 to 67 years.

Outcomes assessed in the review
The studies had to provide sufficient data, either in the publication or via contact with the authors, to calculate dichotomous outcomes to be included. The outcomes reported were the incidence of supraventricular arrhythmias (atrial fibrillation, atrial flutter, atrial tachycardia or supraventricular tachycardia) and ventricular arrhythmias (sustained or paroxysmal ventricular tachycardia, or ventricular fibrillation). Atrial and ventricular extrasystole, bigeminy and couplets were excluded from these definitions. The observation period for arrhythmias was from declamping of the aorta to the end of the study follow-up period. The secondary outcomes included adverse effects, mortality, incidence of myocardial infarction (MI), length of hospital stay, and serum magnesium concentrations at 1 day post-operatively.

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.
Assessment of study quality
Quality was assessed using the Jadad scale. Points were awarded on the basis of method of randomisation, double blinding, withdrawals and drop-outs. The maximum possible score was 5. Two authors independently assessed studies for quality. Any disagreements were resolved by consensus.

Data extraction
Two authors independently extracted the data. Any disagreements were resolved by consensus. The relative risk (RR) or mean difference was calculated, along with 95% confidence intervals (CIs).

Methods of synthesis
How were the studies combined?
The pooled RR for dichotomous data and weighted mean difference (WMD) for continuous data were calculated, along with the 95% CI, using a random-effects meta-analysis. Where there were zero values, 0.5 was added to tables to facilitate pooling. Funnel plots were used to investigate possible publication bias.

How were differences between studies investigated?
Heterogeneity was assessed using the Cochran Q statistic. Sensitivity analyses, based on the quality scores of studies, were performed to investigate heterogeneity.

Results of the review
Seventeen RCTs (2,074 participants) were included.

The median Jadad score was 4 (range: 1 to 5).

Prophylactic magnesium resulted in a statistically significant increase in serum magnesium concentrations at 24 hours (11 RCTs; WMD 0.45 mmol/L, 95% CI: 0.30, 0.59, P<0.001).

Magnesium resulted in a statistically significant decrease in the risk of supraventricular arrhythmias (16 RCTs; RR 0.77, 95% CI: 0.63, 0.93, P=0.002), ventricular arrhythmias (10 trials; RR 0.52, 95% CI: 0.31, 0.87, P<0.0001) and atrial fibrillation (12 RCTs; RR 0.71, 95% CI: 0.55, 0.93, P=0.003). There was statistically significant heterogeneity in all analyses. In the sensitivity analyses, treatment effects did not appear to have been affected by the quality scores of trials.

Length of hospital stay, incidence of MI or mortality did not appear to have been affected by the use of magnesium.

No cases of severe bradycardia or hypotension were reported, but one study reported a cardiac arrest in the magnesium group (5 RCTs).

Tests for publication bias suggested missing studies for the outcome of supraventricular arrhythmias, but not for ventricular arrhythmias.

Authors' conclusions
Prophylactic magnesium reduced the risk of supraventricular arrhythmias by 23% (atrial fibrillation by 29%) and ventricular arrhythmias by 48% after cardiac surgery, but had no effect on length of hospital stay, peri-operative MI or mortality.

CRD commentary
The review question was broad, but the inclusion criteria were clear in terms of the intervention, population, outcomes and study design. The inclusion criteria stated that studies were eligible if they assessed a single dose of magnesium, however, several included studies evaluated repeated doses or continuous infusions. Three relevant databases were searched, but tests for publication bias suggest that studies might have been missed. The data extraction and quality
assessment were carried out in duplicate, although it was unclear whether the same methods to reduce error and bias were used during the study selection process. The quality of the included studies was assessed and used as the basis of a sensitivity analysis.

There was little information on the included participants and this could affect the generalisability of the results. The authors acknowledged that their results are limited because of heterogeneity between the studies, and suggested that it might not have been appropriate to have pooled the results. It would have been interesting to see further investigations into the sources of this heterogeneity. In view of these comments, the authors’ conclusions should be treated with caution.

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

Research: The authors stated that a large RCT is needed to examine the effects of magnesium on secondary outcomes following cardiac surgery.

Bibliographic details

PubMedID
15336582

DOI
10.1016/j.amjmed.2004.03.030

Other publications of related interest
This additional published commentary may also be of interest. Maiocco G. Review: magnesium prophylaxis after cardiac surgery reduces the risk of arrhythmia and atrial fibrillation. Evid Based Nurs 2005;8:55.

Indexing Status
Subject indexing assigned by NLM

MeSH
Arrhythmias, Cardiac /blood /epidemiology /etiology /prevention & control; Bias (Epidemiology); Cardiac Surgical Procedures /adverse effects; Double-Blind Method; Effect Modifier, Epidemiologic; Hospital Mortality; Humans; Incidence; Length of Stay /statistics & numerical data; Magnesium /blood /pharmacokinetics /therapeutic use; Morbidity; Myocardial Infarction /epidemiology /etiology; Postoperative Care /methods /standards; Primary Prevention /methods /standards; Prospective Studies; Randomized Controlled Trials as Topic; Research Design /standards; Risk Factors; Sensitivity and Specificity; Treatment Outcome

AccessionNumber
12004001645

Date bibliographic record published
30/06/2006

Date abstract record published
30/06/2006

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.