Intravenous magnesium for prevention of atrial fibrillation after coronary artery bypass surgery: a systematic review and meta-analysis

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CRD summary
This review concluded that giving intravenous magnesium sulphate to people who are undergoing elective coronary artery bypass grafting reduces the risk of post-operative atrial fibrillation. The review was well conducted and the authors' conclusion is likely to be reliable.

Authors' objectives
The aim was to assess the effects of peri-operative intravenous magnesium sulphate in preventing atrial fibrillation (AF) after coronary artery bypass grafting (CABG).

Searching
MEDLINE, EMBASE and the Cochrane Controlled Trials Register were searched from the earliest date to December 2003; the search terms were given. The reference lists of retrieved articles were also checked. No language restrictions were applied.

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

Specific interventions included in the review
Studies of prophylactic magnesium sulphate, as a bolus or continuous infusion, given as a specified dose were eligible for inclusion. The comparison was with placebo or no intervention. The doses ranged from 7.5 to 25 g and the duration of treatment from 2 to 5 days. Some of the included studies excluded those taking amiodarone or beta-blockers, whereas in other studies between 23 and 69% of participants were taking beta-blockers concomitantly.

Participants included in the review
Studies of adults (aged 18 years or older) undergoing elective CABG, using on- or off-pump procedures, were eligible for inclusion. There was no limitation on the number of grafts or conduit types included. People with chronic or paroxysmal AF, or a history of any arrhythmias, were excluded. The mean age of the participants in the included studies ranged from 52 to 65 years. People with severe heart failure, renal failure, or re-do CABG were excluded from the included studies.

Outcomes assessed in the review
The primary outcome of interest was the incidence of AF following CABG. This was defined as totally irregular atrial rhythm measured using a continuous electrocardiogram (EEG) and confirmed by a standard lead EEG. Studies that did not specify the method of detection of AF, or the follow-up time, were excluded.

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

Assessment of study quality
Each study was assigned a quality score (1 being the lowest and 11 the highest) based on items relating to adequate randomisation, allocation concealment, blinding of the patients, caregiver or outcome assessor, similarity of baseline prognostic factors, treatments and compliance of groups, and intention-to-treat principles. A minimum score of 5 was
set to justify a trial being classed as "high quality". Two reviewers independently assessed the quality of the included studies.

Data extraction
Two reviewers independently extracted the data using pre-designed extraction forms. Any discrepancies were resolved by a third reviewer. The data were checked and cross-checked, and authors were contacted where necessary. Data on the occurrence of AF were extracted from each study and used to derive a relative risk (RR) with 95% confidence intervals (CIs). For studies that evaluated more than one comparison, data were extracted on the comparison between magnesium and placebo, if possible.

Methods of synthesis
How were the studies combined?
The results from the individual studies were pooled using a fixed-effect model (if homogeneous) or a random-effects meta-analysis. The pooled RR and 95% CIs were calculated. If heterogeneity prohibited pooling, the data were presented as a narrative overview. The number-needed-to-treat (NNT) to prevent one person developing AF was calculated. A funnel plot was used to check for publication bias.

How were differences between studies investigated?
Clinical heterogeneity was considered by examining the characteristics of the study populations, interventions, comparison group and outcomes. Statistical heterogeneity was assessed using the chi-squared (threshold for significance P<0.10). Attempts were made to identify any sources of heterogeneity that might have been caused by differences in clinical characteristics. Sensitivity analyses were conducted; these excluded low-quality studies.

Results of the review
Eight RCTs (1,033 participants) were included. Of these, seven were placebo controlled and one was a comparison against no treatment.

Two studies scored 7 for methodological quality, three scored 6, one scored 5 and two scored 4.

There was evidence of statistical heterogeneity (Q=23.67, d.f.=7, P<0.001) when pooling all 8 RCTs. When the 2 low-quality trials were removed from the analysis there was no evidence of statistical heterogeneity (Q=5.35, d.f.=5, P=0.37). Results were presented for the 6 'high-quality' RCTs only.

Magnesium sulphate was associated with a significant reduction in post-operative AF (RR 0.64, 95% CI: 0.47, 0.87, P=0.004). The NNT to prevent one person developing AF was 11.

Cost information
The authors estimated the saving in reduced length of hospital stay by preventing AF and the cost of magnesium treatment. They calculated that there could be a potential saving of about US$9,600 per 11 people given magnesium sulphate.

Authors' conclusions
Magnesium sulphate is associated with a significant reduction in the incidence of AF after CABG, compared with placebo. Comparisons with other anti-arrhythmic drugs are warranted.

CRD commentary
This was a clearly written review. The aims were stated and the inclusion criteria appeared appropriate. Several relevant databases were searched and attempts were made to minimise language bias. While the authors did not explicitly search for unpublished studies, a visual assessment of the funnel plot did not suggest the presence of publication bias. The
authors used appropriate methods to minimise reviewer bias and error in the study selection and data extraction processes. Quality was assessed using a scoring system, which may be problematic. However the authors gave clear details of the results of the quality assessment, including where points were scored.

The methods used to explore differences across the included studies were appropriate and were considered in the analysis. Adequate details of each included study were given, which suggests that the meta-analysis was appropriate, and the decision to remove 2 studies from the final analysis because of heterogeneity seems justified. In conclusion, this was a well-conducted review and the authors' conclusions are supported by the data it presented.

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

Research: The authors stated that further trials should look at comparisons with other anti-arrhythmic agents, as well as the additive effect of magnesium and other agents such as beta-blockers or amiodarone.

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