Prophylactic amiodarone for prevention of atrial fibrillation after cardiac surgery: a meta-analysis

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CRD summary
This review evaluated the effects of amiodarone in post-operative atrial fibrillation. It concluded that amiodarone prophylaxis is associated with a significant reduction in atrial fibrillation after cardiac surgery, as well as a reduction in peri-operative ventricular tachyarrhythmias and strokes and a short but significant reduction in hospital stay. The authors' conclusions reflect the evidence presented and are likely to be reliable.

Authors' objectives
To evaluate the effect of amiodarone in post-operative atrial fibrillation (AF).

Searching
MEDLINE, EMBASE and the Cochrane Controlled Trials Register were searched to April 2006; the search terms were reported. In addition, study bibliographies and conference proceedings were searched and experts in the field were contacted. Inclusion was not restricted by language of publication.

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 amiodarone versus control were eligible for inclusion. The average amiodarone dose 24 hours after surgery was 2,300 mg (standard deviation, SD=2,000; range: 700 to 8,400). The cumulative average amiodarone was 5,300 mg (SD=3,600; range: 2,000 to 17,000). Amiodarone was started pre-operatively, intra-operatively and post-operatively.

Participants included in the review
Studies of patients undergoing cardiac surgery were eligible for inclusion. All of the studies included patients undergoing coronary artery bypass grafts with or without valvular surgery.

Outcomes assessed in the review
Studies reporting post-operative AF were eligible for inclusion. The primary outcome was post-operative AF. The secondary outcomes included: post-operative AF, heart rate at onset of AF, time to onset, duration of AF, incidence of ventricular tachyarrhythmias and neurological events, mortality and duration of hospitalisation. The outcomes were variably defined or inconsistently reported in some of the included studies.

How were decisions on the relevance of primary studies made?
Two reviewers independently screened studies for relevance, with any disagreements resolved through discussion.

Assessment of study quality
Two reviewers independently assessed validity according to the Jadad checklist, including items on: method of randomisation, allocation concealment, blinding, use of placebo, reporting of losses to follow-up, baseline differences and sample size calculations. An overall score was assigned to each included study.

Data extraction
Two reviewers independently extracted the data from the included studies. Dichotomous data on AF, ventricular
Tachyarrhythmias, strokes and mortality were converted into odds ratios (ORs) with 95% confidence intervals (CIs). Continuous data on ventricular response rate, time to onset, duration of AF and hospitalisation were converted into standardised mean differences with 95% CIs.

**Methods of synthesis**

How were the studies combined?
The ORs were pooled using a random-effects or fixed-effect model where appropriate. Continuous variables were pooled using the weighted mean difference. Publication bias was assessed using Egger's test and funnel plots.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the chi-squared and I-squared tests. Meta-regression and sensitivity analyses were carried out using key study characteristics.

**Results of the review**

Nineteen RCTs (n=3,295: 1,639 received amiodarone and 1,656 received control) were included in the review.

The included RCTs met between two and five of the Jadad validity criteria; only three met all five criteria. There was no evidence of publication bias from Egger's test or funnel plots.

There was a significant reduction in the incidence of post-operative AF associated with amiodarone, (OR 0.50, 95% CI: 0.43, 0.59, p<0.0001). There was no significant heterogeneity and the result was not significantly influenced by any study quality or clinical factors.

Statistically significant and homogeneous effects favouring amiodarone were also reported in terms of a lower ventricular response (-22 beats per minute, 95% CI: -29.6, -15.9, p<0.0001), decreased hospital length of stay (by 0.6 days, 95% CI: 0.4, 0.8, p<0.0001), reduced rate of ventricular tachyarrhythmias (0.39, 95% CI: 0.26, 0.58, p<0.0001) and reduced post-operative neurological events (0.53, 95% CI: 0.30, 0.92, p=0.02). There was no significant heterogeneity.

The results for other secondary outcomes were reported in the paper.

**Cost information**
The mean total cost from 4 studies was $18,548 (SD=2,624) for amiodarone and $21,637 (SD=4,744) for control treatments.

**Authors' conclusions**

Amiodarone prophylaxis was associated with a significant reduction in the incidence of post-operative AF after cardiac surgery, as well as a reduction in peri-operative ventricular tachyarrhythmias and strokes and a short but significant reduction in hospital stay.

**CRD commentary**
The review question was clear and was supported by appropriate inclusion criteria relating to the participants, interventions, outcomes and study designs. Attempts were made to identify all the relevant literature by searching several electronic databases and other sources without language limitations, though the range of dates searched was unclear. Validity was assessed according to published criteria, and attempts were made to minimise errors and bias at each stage of the review process. Appropriate methods were used to pool the results and investigate statistical heterogeneity. However, though some details were reported clearly, potentially important clinical information on participant characteristics and details of control treatments were not reported. Nevertheless, the authors' overall conclusions appear to reflect the evidence presented and are likely to be reliable.
**Implications of the review for practice and research**

Practice: The authors stated that there was convincing evidence to suggest that amiodarone should be considered as first-line therapy and routine prophylaxis for AF prevention after cardiac surgery. They added that the total dose of 5 to 10 g is likely to be adequate, and that the duration of therapy should be short (less than 2 weeks).

Research: The authors stated that further surveillance for the adverse effects of amiodarone is required.

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