Pharmacologic strategies for prevention of atrial fibrillation after open heart surgery
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CRD summary
This review found that treatments for preventing atrial fibrillation after heart surgery were effective, but no single drug was shown to be consistently superior. The main recommendations were the use of beta-blockers, unless contraindicated, and the treatment of electrolyte deficiencies. Those at higher risk should also receive amiodarone or sotalol. There were some problems with the methodology used in the review.

Authors' objectives
To evaluate pharmacological strategies for preventing atrial fibrillation (AF) after open heart surgery.

Searching
MEDLINE was searched from 1966 to November 2003; the search terms were given. The reference lists of identified papers were checked. Only peer-reviewed articles published in English were eligible for inclusion.

Study selection
Study designs of evaluations included in the review
Only randomised controlled trials were eligible for inclusion.

Specific interventions included in the review
Studies of pharmacological treatments aimed at preventing post-operative AF were sought. The treatments in the included studies were digoxin, beta-blockers, calcium-channel blockers, magnesium, class I and III anti-arrhythmic agents, and class II anti-arrhythmic (amiodarone and sotalol). Comparisons were made with placebo or 'control' or were between-drug evaluations. Details of the drug regimens were given in the paper.

Participants included in the review
Studies of people who were undergoing heart surgery were sought. The majority of the included studies were on people undergoing a coronary artery bypass graft; others were studies on open heart surgery or valve operation. No further information on the included participants was given.

Outcomes assessed in the review
The primary outcome of interest was the rate of post-operative AF or supraventricular tachyarrhythmia (SVT).

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
The authors did not state that they assessed validity.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Details of type of surgery and drug regimen were described. The incidence of AF or SVT in each treatment group in each study were calculated, together with P-values. Notes on the outcomes in each study were made.
Methods of synthesis
How were the studies combined?
The studies were combined within tables and in a narrative, grouped by drug or class of drug used. In addition, the cumulative incidence of post-operative AF (or SVT) for each drug (or class of drug) was calculated by adding the number of people developing AF with a given strategy and dividing it by the number of people receiving that strategy.

How were differences between studies investigated?
The differences between the studies were discussed within the narrative synthesis.

Results of the review
Fifty-two trials (10,230 participants) were included.

Digoxin: the use of digoxin alone showed benefit in one study, but there was no evidence of any effect in a second. However, used in combination with beta-blockers it appeared to be effective in reducing AF (3 studies).

Beta-blockers: 2 studies showed a beneficial effect of propranolol and two showed no evidence of effect, while timolol and acebutolol showed a benefit in comparison with placebo. Comparisons between different beta-blockers showed sotalol to be superior to metoprolol, whilst both were superior to no beta-blocker. One large well-designed study showed metoprolol to be associated with a reduction in post-operative AF, but not length of hospital stay. The data suggested that beta-blockers were more effective when administered pre- as well as post-operatively.

Calcium-channel blockers: there was a lower incidence of arrhythmias with diltiazem when compared with nitroglycerin. However, evidence concerning the differences in benefit between beta-blockers and calcium-channel blockers was lacking.

Magnesium: 2 small studies showed a benefit with magnesium, whereas two others showed no benefit.

Class I anti-arrhythmic agents: 2 studies showed no benefit with quinidine or propafenone, while 2 small studies showed a non-statistically significant reduction in AF with procainamide.

Class III anti-arrhythmic agents: sotalol consistently showed a reduction in the incidence of post-operative AF (8 studies). However, other studies showed that dose-related adverse events could occur. Six studies showed a benefit of oral amiodarone, started pre-operatively, against placebo. In some of these studies the participants also received beta-blockers, and this appeared to enhance the effect. When intravenous (i.v.) amiodarone was used, 2 studies showed benefit whilst two showed no benefit. Other studies showed that a short course of i.v. amiodarone post-operatively, followed by oral therapy, was effective. This effectiveness may be improved by atrial pacing.

When events were counted across studies, the incidence of AF was 29.2% in controls, 19.3% with beta-blockers, 15.4% with sotalol, and 18% with oral or i.v. amiodarone (12.5% with both oral and i.v., 16.5% with oral alone, and 31.4% with i.v. alone). The authors also briefly discussed the use of non-steroidal anti-inflammatory agents and angiotensin antagonists.

Authors’ conclusions
Prophylactic interventions to prevent post-cardiac surgery AF were beneficial. However, no strategy was shown to be consistently superior to another. The prevention of post-operative AF should be approached using multiple interventions.

CRD commentary
This review attempted to collate a large amount of information about differing treatments of AF after cardiac surgery. The database search was restricted to MEDLINE and only peer-reviewed papers reported in English papers were sought. Thus, it is possible that studies were missed. The methods of the review (study selection, data extraction) were not described and bias might have been introduced into a review at these stages. Although inclusion criteria stated that studies had to be randomised trials, at least one included study used historical controls as the comparator. The authors
included some information about pacing and non-steroidal anti-inflammatory drugs, but the search terms used did not appear to be aimed at systematically finding studies of this type. There was no description of any quality assessment.

Information about the included studies was limited, especially regarding the participants, severity of disease, co-morbidities or concomitant therapies. These could affect the generalisability of results. Whilst a narrative review gives an overview of the outcomes of the individual treatments, the counting of incidence of AF in the different treatment groups across studies may be problematic. The benefits of using a randomised controlled design (to provide similar treatment and control groups at baseline) are lost. It would have been interesting to see a formal meta-analysis of data from individual studies assessing the same drug treatments, as this might have given a more accurate assessment of the effects of treatment. This approach was taken in another review of this topic (see Other Publications of Related Interest).

**Implications of the review for practice and research**

Practice: Beta-blockers should be used pre-operatively for open heart surgery, and continued post-operatively, unless otherwise contraindicated. Magnesium should be given if there is evidence of hypomagnesemia. People with one or more risk factors should also be given amiodarone or sotalol. The authors included a useful diagrammatic algorithm to illustrate their recommendations.

Research: The authors did not state any implications for further research.

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**Other publications of related interest**


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