Treatment of resistant atrial fibrillation: a meta-analysis comparing amiodarone and flecainide

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Authors' objectives
To compare the efficacies of two antiarrhythmic drug therapies, amiodarone hydrochloride and flecainide acetate, in maintaining normal sinus rhythm in patients with resistant chronic atrial fibrillation.

Searching
Current Contents: Clinical Practice was reviewed and MEDLINE was searched from January 1983 to August 1993 for English language studies. Bibliographies of identified articles were searched to locate additional articles.

Study selection
Study designs of evaluations included in the review
Prospective clinical trials were included.

Specific interventions included in the review
Amiodarone hydrochloride and flecainide acetate, of varying dosage, continued for at least 3 months.

Participants included in the review
Patients with documented chronic atrial fibrillation (defined as a persistent rhythm of longer than 2 weeks in duration) that was refractory to treatment with other antiarrhythmic agents (typically class 1A) or sotalol hydrochloride.

Outcomes assessed in the review
Conversion of chronic atrial fibrillation to normal sinus rhythm (as documented by 12-lead electrocardiogram) and/or the subsequent maintenance of normal sinus rhythm (described as an absence of recurrent episodes of atrial fibrillation as documented by Holter monitoring and/or patient reports).

How were decisions on the relevance of primary studies made?
Potential articles were photocopied and distributed to reviewers. The methods section for each study was reviewed in accordance with pre-determined inclusion criteria.

Assessment of study quality
The authors do not state that they assessed validity.

Data extraction
Results of the individual studies were not reviewed until inclusion status was determined. Data were reviewed and extracted by two Professors at the University of Arizona Heart Center.

Methods of synthesis
How were the studies combined?
Information regarding the number of patients remaining in normal sinus rhythm (NSR) was extracted from each individual study. The proportion of patients remaining in NSR for each study was compared with a reference standard proportion which represented the proportion of patients receiving quinidine who would be expected to maintain NSR at different times (based on the meta-analysis of Coplen et al; see ‘Other Publications of Related Interest’). The quinidine reference standard proportion was set at 70%, 58% and 50% for 3, 6 and 12 months after conversion to NSR, respectively.
The rate difference (the rate observed minus the rate for the quinidine standard) was calculated for each study, and the rate differences were pooled. A z score was obtained for the rate differences for both amiodarone and flecainide. Rate differences were considered to be significantly different from the quinidine standard when the two-tailed P value was less than .05.

How were differences between studies investigated?
The authors do not state how differences between the studies were investigated.

Results of the review
There were 6 amiodarone studies (315 patients) and 2 flecainide studies (163 patients).

Amiodarone.
After 3 months of therapy, the proportion of amiodarone-treated patients remaining in normal sinus rhythm (NSR) was significantly greater than that expected with the quinidine standard: 72.6% compared with 70%. The pooled rate difference was 3.5% (SD 2.7, z 9.5, p<0.0001).

After 6 months of therapy (5/6 studies, 226 patients), 71% of those treated with amiodarone remained in NSR compared to 58% on the quinidine standard. The pooled rate difference was 13.8% (SD 2.3, z 31.4, p<.0001).

After 12 months of therapy (2 studies, 107 patients), 60% of those treated with amiodarone remained in NSR compared with 50% on the quinidine standard. The pooled rate difference was 10.4% (SD 1.5, z 15.7, p<.0001).

There was a 29% incidence of adverse effects with approximately 9.5% of patients requiring discontinuation of therapy.

Flecainide.
After 3 months of therapy, 48.5% of patients treated with flecainide remained in NSR compared to 70% on the quinidine standard. The pooled rate difference was -21.4% (SD 1.9, z 40.5, p<.0001).

After 12 months of therapy, 34% of patients treated with flecainide remained in NSR compared to 50% on the quinidine standard. The pooled rate difference was -15.7% (SD 1.3, z 29.8, p<.0001).

The total incidence of adverse effects was not reported; however 8.6% of patients discontinued therapy.

Authors' conclusions
Low-dose amiodarone is more efficacious and equally well-tolerated when compared with flecainide in the treatment of patients with chronic atrial fibrillation who are refractory to type IA antiarrhythmic agents. Maximum efficacy is achieved when amiodarone therapy is coupled with direct current conversion.

Given the adverse effects on mortality observed with the class IA agents, trials evaluating the impact of amiodarone on mortality in this patient population are necessary before clinical practice is widely effected.

CRD commentary
A well-written review, with details of individual studies and of study selection criteria presented, although more details of the search strategy used would have been helpful. The study designs included were unusual; there being no randomised controlled trials in this area, the comparator values were taken from a previous meta-analysis. Although the authors acknowledge differences in patient populations between the previous and the current meta-analysis, they state that this would only underestimate the efficacy of the drugs in question in the current meta-analysis. This may be true, however, as the use of indirect comparisons in meta-analysis (although sometimes necessary as in this review) is methodologically complicated, it may be wise to interpret the results of this review with caution at the present time.
Bibliographic details

PubMedID
7677555

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Adolescent; Adult; Aged; Aged, 80 and over; Amiodarone /adverse effects /therapeutic use; Anti-Arrhythmia Agents /adverse effects /therapeutic use; Atrial Fibrillation /drug therapy; Chronic Disease; Drug Resistance; Female; Flecainide /adverse effects /therapeutic use; Humans; Male; Middle Aged

AccessionNumber
11998008075

Date bibliographic record published
31/03/1999

Date abstract record published
31/03/1999

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.