Comparative efficacy of dronedarone and amiodarone for the maintenance of sinus rhythm in patients with atrial fibrillation

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CRD summary
This review compared the efficacy and safety of dronedarone versus amiodarone for the prevention of recurrent atrial fibrillation. It concluded that dronedarone was less effective than amiodarone, but had fewer adverse events. Limitations in the conduct and reporting of this review mean that the estimates on which these conclusions were based may not be reliable.

Authors' objectives
To compare the efficacy and safety of dronedarone versus amiodarone for the prevention of recurrent atrial fibrillation.

Searching
MEDLINE was searched from inception to 2009. Search terms were reported. In addition, ClinicalTrials.gov and bibliographies of relevant reviews were searched for further relevant published or unpublished studies available in English.

Study selection
Randomised controlled trials (RCT) that randomised adult patients with atrial fibrillation (age 18 years or over) to dronedarone, amiodarone or placebo were eligible for inclusion in the review. These RCTs also had to follow-up patients for at least six months, and report the outcomes of recurrent atrial fibrillation or all-cause mortality. Trials of patients with acute cardioversion, catheter ablation, and post-operative atrial fibrillation were excluded from the review.

Among the included trials, the mean age of patients ranged from 62 to 72 years; the proportion of males ranged from 52 to 99%. Where reported, the proportion of patients in included trials with paroxysmal atrial fibrillation ranged from 0 to 66%, persistent atrial fibrillation ranged from 0 to 100% and permanent atrial fibrillation ranged from 0 to 100%. The majority of included patients (60 to 100%) were receiving warfarin (where reported). Most trials failed to report on the concomitant use of beta-blockers and angiotensin-converting enzyme inhibitors.

The authors did not state how many reviewers selected studies for inclusion.

Assessment of study quality
Trial quality was assessed using the Delphi criteria, on which trials could score up to 9 points. Trials scoring 6 or more points were considered good quality.

The authors did not state how many reviewers performed the assessment.

Data extraction
Odds ratios (ORs) and risk differences (RDs) with 95% confidence intervals (CIs) were calculated for the outcomes of atrial fibrillation recurrence, all-cause mortality and adverse events.

The authors did not state how many reviewers performed the extraction.

Methods of synthesis
Odds ratios and risk differences were combined using a Bayesian random-effects model as described by Hedges and Olkin. In the absence of statistical heterogeneity, a fixed-effect model was used. Random-effects logistic regression with terms for each anti-arrhythmic drug and for each study was used to further explore the relationship between amiodarone and dronedarone.
Results of the review
Four RCTs that compared dronedarone against placebo (n=6,007 patients) and four RCTs that compared amiodarone against placebo (n=664 patients) were included in the review. Seven were double-blind RCTs and one RCT was single-blinded. All but one RCT were considered to be ‘good’ quality. A ninth RCT directly comparing amiodarone with dronedarone was discussed but not included in the pooled analyses.

Compared against placebo, amiodarone was associated with a significant reduction in recurrent atrial fibrillation (OR 0.12, 95% CI 0.08 to 0.19), but dronedarone was not. Neither drug was associated with a significant reduction in all-cause mortality relative to placebo, but both drugs were associated with a significant increase in adverse events requiring withdrawal (OR 1.17, 95% CI 1.36 to 2.02 for dronedarone; OR 11.04, 95% CI 1.89 to 64.5 for amiodarone).

The indirect meta-analysis suggested that amiodarone was associated with a significantly greater reduction in atrial fibrillation recurrence than dronedarone (OR 0.16, 95% CI 0.06 to 0.42), but also a significantly greater risk of adverse events leading to withdrawal (OR 6.65, 95% CI 1.13 to 39.3). These results were supported by the findings of the logistic regression analysis and the results of the direct amiodarone-dronedarone comparison trial.

Authors' conclusions
Dronedarone was less effective than amiodarone for the maintenance of sinus rhythm, but had fewer adverse events.

CRD commentary
The review question was clearly defined in terms of the participants, interventions, comparators, outcomes and study designs of interest. However, the authors did not state whether efforts were made to minimise the potential for errors and bias during the various stages of the review. Also, the inclusion of only English language trials could have potentially introduced language bias.

Few details of the synthesis methods were reported, but differences between the dronedarone and amiodarone trials, particularly in terms of type of atrial fibrillation at baseline, may have biased the indirect comparison of the drugs.

Although the authors' conclusions follow from the evidence presented, limitations in the conduct and reporting of this review mean that the estimates provided may not be reliable.

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

Research: The authors stated that more long-term data are needed to refine their estimates of efficacy and safety of dronedarone versus amiodarone, and to define the optimum balance of efficacy and toxicity for patients with atrial fibrillation.

Funding
Principal investigator supported by an American College of Cardiology Foundation/Merck Award.

Bibliographic details

PubMedID
19744618

DOI
10.1016/j.jacc.2009.04.085
Original Paper URL
http://dx.doi.org/10.1016/j.jacc.2009.04.085

Indexing Status
Subject indexing assigned by NLM

MeSH
Amiodarone /analogs & derivatives /therapeutic use; Anti-Arrhythmia Agents /therapeutic use; Atrial Fibrillation /drug therapy /physiopathology; Electrocardiography; Heart Rate /drug effects; Humans; Randomized Controlled Trials as Topic; Sinoatrial Node /drug effects /physiopathology; Treatment Outcome

AccessionNumber
12009108895

Date bibliographic record published
25/11/2009

Date abstract record published
15/09/2010

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.