Prevention of recurrent atrial fibrillation with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers: a systematic review and meta-analysis of randomized trials


CRD summary
This review concluded that angiotensin converting enzyme inhibitors and angiotensin II type 1 receptor blockers were associated with a significant reduction in atrial fibrillation, although the trials were not specifically designed to measure this outcome. Although the review had some methodological limitations, it was generally well conducted. Differences between the included trials should be considered when interpreting results.

Authors' objectives
To evaluate the efficacy of angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers in the prevention of recurrent atrial fibrillation.

Searching
PubMed, EMBASE, CINAHL, and The Cochrane Library (databases unspecified) were searched to December 2009 for articles published in English. Search terms were reported. Reference lists of retrieved articles were handsearched.

Study selection
Randomised controlled trials (RCTs) that compared angiotensin-receptor blockers or angiotensin-converting enzyme inhibitors versus control in patients with known atrial fibrillation were eligible for inclusion. Trials had to have a follow-up of at least six weeks and report on recurrent atrial fibrillation. Trials of new onset atrial fibrillation were excluded.

The included trials studied different angiotensin-converting enzyme inhibitors (enalapril, lisinopril, perindopril or ramipril) and angiotensin-receptor blockers (candesartan, irbesartan, losartan or valsartan) in patients with atrial fibrillation. The control treatments included placebo, amiodarone, or amiodarone-amlodipine. The mean age of included patients was 64 years.

The authors did not state how many reviewers performed study selection.

Assessment of study quality
Trial quality assessment was undertaken using the US Preventive Services Task Force criteria, which rated trials as good, fair or poor quality.

Two reviewers independently performed quality assessment. Disagreements were resolved by discussion or consultation with a third reviewer.

Data extraction
Data were extracted on recurrence of atrial fibrillation and used to calculate risk ratios (RRs) and 95% confidence intervals (CIs).

Two reviewers independently performed data extraction. Disagreements were resolved by discussion or consultation with a third reviewer.

Methods of synthesis
A fixed-effect meta-analysis was used to calculate pooled risk ratios and 95% confidence intervals for angiotensin-receptor blockers alone. A Mantel-Haenszel random-effects meta-analysis was used to calculate pooled risk ratios and 95% confidence intervals for angiotensin-receptor blockers or angiotensin-converting enzyme inhibitors, and for angiotensin-receptor blockers alone. Heterogeneity was assessed using Cochran's Q and I².

Results of the review
Eight RCTs (2,323 patients) were included in the review. The study sample size ranged from 18 to 1,442 patients. The
length of follow-up ranged from six weeks to 36 months. All of the trials were rated as good quality.

Compared with control treatments, angiotensin-receptor blockers and angiotensin-receptor blockers were associated with a statistically significantly reduced risk of atrial fibrillation recurrence (RR 0.61, 95% CI 0.44 to 0.85; I²=79.6%). When the drugs were analysed separately, the risk of atrial fibrillation was statistically significantly reduced with angiotensin-receptor blockers (RR 0.64, 95% CI 0.44 to 0.94; I²=85.3%) and angiotensin-receptor blockers (RR 0.55, 95% CI 0.38 to 0.80; I²=0%) compared with control treatments.

**Authors' conclusions**
Angiotensin-receptor blockers and angiotensin-receptor blockers were associated with a significant reduction in atrial fibrillation, although the included trials were not designed to measure this a priori.

**CRD commentary**
Inclusion criteria for the review were clearly defined. Several relevant sources were searched. There was the potential for language bias, as only articles in English were included. Publication bias was not assessed and could not be ruled out, which the authors acknowledged. Attempts were made to reduce reviewer error and bias during data extraction and quality assessment, but the authors did not state if the same methods were used for study selection.

Trial quality assessment used a standard checklist, which indicated the good quality of the included trials. However, there were baseline differences across the trials, which the authors acknowledged. Trials were combined using appropriate statistical methods; statistical heterogeneity was assessed. Some of the analyses had significant levels of statistical heterogeneity.

The review was generally well conducted, but the potential for biases within the review and heterogeneity across trials should be considered when interpreting results.

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

**Practice**: The authors did not state any implications for practice.

**Research**: The authors stated that large-scale RCTs designed a priori to measure recurrent atrial fibrillation were needed. Additional research was also required to determine the impact of one agent over another in secondary atrial fibrillation.

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