A systematic review of angiotensin receptor blockers in preventing stroke
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CRD summary
The authors concluded that angiotensin receptor blockers were beneficial in preventing stroke compared with placebo, but there was no evidence of benefit compared with angiotensin-converting enzyme inhibitors and calcium antagonists. The authors’ conclusions appeared to reflect the evidence available but, given the potential for bias in the review and the uncertainty regarding statistical heterogeneity, they should be interpreted with caution.

Authors’ objectives
To assess the effects of angiotensin receptor blockers in the prevention of stroke.

Searching
MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched for published trials; search dates and terms were not reported. In addition, journals (details not reported) were manually searched and dedicated articles were cross-referenced.

Study selection
Randomised controlled trials (RCTs) that assessed the effects of angiotensin receptor blockers in patients at high risk of cardiocerebrovascular events were eligible for inclusion in the review, if they reported the rate of stroke.

Included trials were of patients with a mean age ranging from 58.8 to 76.4 years. Disease history at entry included heart failure, type 2 diabetes, hypertension, stroke, coronary heart disease, peripheral vascular disease, cerebrovascular disease, and myocardial infarction. Angiotensin receptor blockers included candesartan, eprosartan, irbesartan, losartan, telmisartan and valsartan. Control groups received placebo, angiotensin-converting enzyme inhibitors, and calcium antagonists. Angiotensin-converting enzyme inhibitors used were captopril, enalapril, or ramipril. Calcium antagonists used were amlodipine or nitrendipine.

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

Assessment of study quality
Trial quality was assessed using the following criteria: allocation concealment, blinding, intention-to-treat (ITT) analysis, and loss to follow-up. The maximum score was 5.

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

Data extraction
Three reviewers independently extracted the data to calculate odds ratios (ORs) and 95% confidence intervals (CIs). Disagreements were resolved by discussion.

Methods of synthesis
Summary odds ratios and 95% confidence intervals were estimated using a random-effects model.

Subgroup analyses were undertaken to identify the impact of disease history at baseline and the difference in blood pressure between intervention and control groups (higher in the intervention group, or similar between groups).

Publication bias was assessed using funnel plots.

Results of the review
Twenty RCTs (n=108,286 participants) were included in the review. Eleven trials scored 5 for study quality, four trials
scored 4, four trials scored 3, and one trial scored 2. One trial was a single-blind parallel trial, one trial was open-label parallel; the remainder were double-blind parallel trials. Follow-up ranged from 0.2 to five years.

Angiotensin receptor blockers statistically significantly decreased the rate of stroke compared with placebo (OR 0.91, 95% CI 0.84 to 0.98; 11 RCTs). Subgroup analysis for trials in which blood pressure was lower in the angiotensin receptor blockers group, also showed significant reductions in the rate of stroke (five RCTs). Other subgroup analyses showed no statistically significant difference between treatment groups.

There were no statistically significant differences in the risk of stroke between angiotensin receptor blockers and angiotensin-converting enzyme inhibitors (six RCTs) or calcium antagonists (four RCTs). Subgroup analyses did not significantly alter the results.

Funnel plots showed no evidence of publication bias for trials comparing angiotensin receptor blockers with placebo or angiotensin-converting enzyme inhibitors.

**Authors' conclusions**

Angiotensin receptor blockers were beneficial in preventing stroke compared with placebo, but there was no evidence of benefit compared with angiotensin-converting enzyme inhibitors and calcium antagonists.

**CRD commentary**

The review question and inclusion criteria were clearly stated. A number of sources were searched for relevant studies, but full details, such as search dates, were not reported. Restricting the search to published trials meant that there was potential for publication bias; this was assessed in the review. There was no evidence of publication bias for trials comparing angiotensin receptor blockers with placebo or angiotensin-converting enzyme inhibitors, but it was unclear whether this was the same for trials with calcium antagonists as the control. Data extraction was undertaken in duplicate, but it was unclear whether this was true for study selection and quality assessment, so reviewer error and bias could not be ruled out.

Trial quality was assessed using appropriate criteria, with the majority of trials reported to be of high quality (only aggregate scores were reported). The authors did not state whether they formally assessed statistical heterogeneity, but heterogeneity was investigated through subgroup analysis. Details were lacking on the doses and frequency of treatment regimens, but the authors did mention the different trial durations and the need for some caution when interpreting the findings.

The authors’ conclusions appeared to reflect the evidence available but, given the potential for bias in the review and the uncertainty regarding statistical heterogeneity, they should be interpreted with caution.

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

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

**Research:** The authors stated that further RCTs are warranted to investigate the benefit of angiotensin receptor blockers in normotensive patients at high risk of cardiocerebrovascular events.

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**Bibliographic details**


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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.