Antihypertensive effects and safety of eprosartan: a meta-analysis of randomized controlled trials
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CRD summary
This review found eprosartan was as effective as many first-line anti-hypertensive medications for essential hypertension, particularly for systolic hypertension alone. The review was generally well conducted and the authors’ conclusions are likely to be reliable.

Authors’ objectives
To assess the efficacy and tolerability of eprosartan compared with other blood pressure-lowering medications.

Searching
PubMed, EMBASE, and The Cochrane Library were searched to July 2010 for relevant studies; search terms were reported. The reference lists of retrieved articles, reviews and previous meta-analyses were checked to identify additional studies. There were no publication and language restrictions.

Study selection
Randomised controlled trials (RCTs) of patients with essential hypertension were eligible for inclusion if they compared eprosartan versus placebo or other blood pressure-lowering agents used as monotherapy. The primary outcome was the change from baseline to the end of treatment in systolic and diastolic blood pressure. Secondary outcomes included the therapeutic response rates and tolerability, assessed by withdrawal rates for adverse events or the numbers of adverse events reported. Trials of patients with myocardial infarction, congestive heart failure, coronary artery disease, acute or chronic hepatic disease, pregnancy or risk of pregnancy were excluded from the review.

The patients in most of the included trials presented with hypertension; other diagnoses included type 2 diabetes mellitus, isolated systolic hypertension, and cerebral events. One trial stated that the patients were overweight. The mean age of patients ranged from 27 to 70 years and the percentage of male patients ranged from 45 to 100. The length of the trials ranged from one week to 2.5 years. The comparators were placebo, losartan, telmisartan, valsartan, enalapril, nitrendipine and atenolol.

Two reviewers independently performed the study selection; a third reviewer checked the selection.

Assessment of study quality
Two independent reviewers assessed methodological quality, using a modified Jadad seven point scale for randomisation, allocation concealment, blinding, and reporting of withdrawals and losses to follow-up.

Data extraction
Two independent reviewers extracted data to calculate risk ratios for dichotomous outcomes, mean differences for continuous outcomes, and 95% confidence intervals for all estimates. Trial authors were contacted for missing information. Any disagreements between the reviewers were resolved by discussion.

Methods of synthesis
Pooled relative risks, weighted mean differences, and 95% confidence intervals for the summary estimates were calculated using a random-effects model. Statistical heterogeneity was evaluated using $X^2$ and $I^2$. Sensitivity analyses were undertaken to examine the effect of inconsistencies in reporting or differences in the measurement or definition of outcomes. The reviewers assessed the potential for publication bias using visual appraisals of funnel plots and the Egger test.

Results of the review
Twenty-two RCTs, with 6,460 participants, were included in the review. Sample sizes ranged from 20 to 1,460 patients. For methodological quality, one trial scored six points, 11 trials scored five points, five trials scored four points, two
trials scored three points, and three trials scored two points.

**Systolic blood pressure**: Statistically significant reductions in systolic blood pressure were observed with eprosartan compared with placebo (WMD 6.55, 95% CI 4.86 to 8.25; I²=91%; seven trials; n=839 patients), or losartan (WMD 2.24, 95% CI 0.08 to 4.40; I²=74%; four trials; n=969). A sensitivity analysis was conducted to examine the impact of removing the trial published as an abstract, but the result remained significant. There were no significant differences in systolic blood pressure when eprosartan was compared with telmisartan (two trials; n=179), valsartan (one trial; n=36) and enalapril (five trials; n=989), and where applicable, no statistically significant heterogeneity was observed across these trials. In one trial, atenolol was associated with greater decreases in systolic blood pressure than eprosartan (WMD -1.00, 95% CI -2.21 to 0.21; n=42).

**Diastolic blood pressure**: Treatment with eprosartan was associated with statistically significant reductions in diastolic blood pressure compared with placebo (WMD 3.95, 95% CI 2.77 to 5.13; I²=92%; seven trials; n=662). There were no significant differences in diastolic blood pressure between patients treated with eprosartan and losartan (I²=89%; four trials; n=969), valsartan (one trial; n=36) and enalapril (I²=90%; six trials; n=1,063). There was a marginal result indicating some benefit with telmisartan (WMD -2.70, 95% CI -5.43 to 0.04; I²=74%; two trials; n=179). Significant reductions in diastolic blood pressure were observed with atenolol compared with eprosartan (WMD -2.00, 95% CI -3.21 to -0.79; one trial; n=42).

Visual appraisals of funnel plots and the Egger tests showed no evidence of publication bias for any outcome in the review.

**Authors’ conclusions**
Eprosartan monotherapy was as effective as many first-line anti-hypertensive medications for essential hypertension, particularly for systolic hypertension alone.

**CRD commentary**
The review addressed a clear question and the criteria for inclusion in the review were defined and reproducible. Appropriate databases were searched for relevant trials and there were no language or publication restrictions. The authors evaluated the potential for publication bias using validated methods. Steps were taken at each stage of the review process to minimise reviewer errors and biases.

Methodological quality was assessed and the quality of the included trials ranged from medium to high. The authors decision to combine the results in a meta-analysis appears to have been justified, but there were high levels of statistical heterogeneity, which were not explored in sensitivity analyses. There was a discrepancy between the text and the figures for the number of trials, and the medication doses were unclear. The trials were generally short in duration and follow-up.

The review was generally well conducted and the authors' conclusions on the evidence presented are likely to be reliable.

**Implications of the review for practice and research**
**Practice**: The authors stated that the efficacy and tolerability of eprosartan meant that it could be considered for patients with essential hypertension.

**Research**: The authors stated that pragmatic, well-designed, long-term RCTs were required to assess the effects of eprosartan alone or in combination with other blood-pressure lowering agents. These trials should also collect data on ambulatory blood pressure changes, cerebral cardiovascular events, mortality, and other adverse events.

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**Bibliographic details**
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.