Comparison of the efficacy of candesartan and losartan: a meta-analysis of trials in the treatment of hypertension

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CRD summary
This review found that candesartan was associated with significantly greater reductions in blood pressure in patients with hypertension compared with losartan. The results of this review should be interpreted with some caution, and the reliability of the authors' conclusions is uncertain due to the absence of a formal quality assessment and possible biases in the review process.

Authors' objectives
To evaluate the comparative efficacy of candesartan and losartan in patients with hypertension.

Searching
PubMed, EMBASE (from inception) and the Cochrane Library were searched to October 2008 for relevant studies; search terms were reported. Reference lists of meta-analyses and retrieved articles were checked to identify additional studies.

Study selection
Randomised and quasi-randomised controlled trials that compared candesartan with losartan (as monotherapy or in fixed combination with hydrochlorothiazide) in patients with hypertension were eligible for inclusion. Trials had to report blood pressure measurements at baseline and end point.

The mean age of the included patients ranged from 51 to 60 years (where reported). Candesartan was given at doses ranging from 2 to 32mg; in most trials, doses of 8mg or 16mg were given. Losartan was administered at doses ranging from 25 to 100mg.

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

Assessment of study quality
The authors did not state that they assessed methodological quality.

Data extraction
Intention-to-treat data were extracted to calculate weighted mean differences (WMD) and 95% confidence intervals (CI) for changes in blood pressure. In the event of missing data, authors of the trials were contacted.

The authors did not report how many reviewers performed the data extraction.

Methods of synthesis
Pooled weighted mean differences and 95% confidence intervals were calculated using a DerSimonian and Laird random-effects model. Statistical heterogeneity was assessed using $X^2$ and $I^2$.

Sensitivity analyses were conducted to evaluate the impact of methodological differences of some trials on the results of the meta-analysis.

Results of the review
Thirteen trials (n=4,066 patients) were included in the review. Thirteen trials were randomised parallel-group trials; nine of these trials were described as double-blinded. There were two trials in which 25mg of hydrochlorothiazide were administered to patients in both the candesartan and losartan treatment arms. There were two trials in which two dosage
regimens were compared with a single dose of losartan, which meant there were 15 comparisons of candesartan with losartan.

Statistically significant greater reductions in systolic blood pressure were observed with candesartan compared with losartan across all the trials (WMD 3.22 mm Hg, 95% CI 2.16 to 4.29).

Significant reductions in systolic blood pressure were also observed when candesartan was compared with losartan in trials in which hydrochlorothiazide was not given (WMD 2.57, 95% CI 1.71 to 3.44; 11 monotherapy trials; n=3,607 patients), when low-dose candesartan (4mg and 8mg) was compared with low-dose losartan (25mg and 50mg) (WMD 2.74, 95% CI 0.83 to 4.64; four trials; n=588 patients), when high-dose candesartan (12, 16 and 32mg) was compared with high-dose losartan (100mg) (WMD 2.49, 95% CI 1.52 to 3.47; eight trials; n=2,852 patients), and when candesartan and losartan were each administered with 25mg of hydrochlorothiazide (WMD 7.03, 95% CI 4.26 to 9.80; two trials; n=459 patients).

Diastolic blood pressure was also significantly reduced with candesartan treatment compared with losartan (WMD 2.21 mm Hg, 95% CI 1.34 to 3.07) across all the trials. This pattern of reduction was observed in the monotherapy trials and for the comparisons of low-dose and high-dose treatments.

There was no statistically significant heterogeneity reported across the trials for any of the outcomes evaluated.

**Authors' conclusions**

There was compelling evidence that there were greater reductions in blood pressure achieved with the use of candesartan compared with losartan at recommended doses; these reductions were likely to confer significant protective effects against cardiovascular or cerebrovascular events.

**CRD commentary**

The review addressed a clear question. Criteria for the inclusion of studies were defined. Appropriate databases were searched, but there was no indication that unpublished material was sought. There were no reported attempts to minimise errors and bias at any part of the review process.

There was no formal assessment of trial quality. The description of included study designs did indicate that some quality standards were considered, but the overall reliability of the trials was unknown. The authors correctly acknowledged some limitations of the review.

However, the results of this review should be interpreted with caution, and the reliability of the authors' conclusions is uncertain due to the potential for publication bias, the absence of a formal quality assessment, and possible bias in the review process.

Two of the authors disclosed financial links with a number of pharmaceutical companies including Takeda (manufacturers of candesartan and funders of the review).

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

The authors did not state any implications for practice or research.

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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
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