A systematic review and meta-analysis of telmisartan vs valsartan in the management of essential hypertension
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CRD summary
This review found no significant differences between telmisartan and valsartan in reducing diastolic or systolic blood pressure, achieving target blood pressure or adverse events in patients with abnormally high blood pressure (essential hypertension); telmisartan combined with hydrochlorothiazide was more effective in reducing blood pressure. The generally high variation within the limited evidence presented makes the reliability of these conclusions unclear.

Authors' objectives
To compare the safety and effectiveness of telmisartan versus valsartan in the management of blood pressure in patients with essential hypertension.

Searching
MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched to May 2009; search terms were reported. Bibliographies of reviews, prospective trial registers, each retrieved article and abstracts from hypertension meetings were handsearched. Only trials published as full articles were included.

Study selection
Randomised controlled trials (RCTs) and quasi-RCTs that compared telmisartan and valsartan for the management of blood pressure in patients (aged 18 years or over) with essential hypertension, and with follow-up for at least six weeks, were eligible for inclusion. To be eligible, the average seated diastolic blood pressure at trial entry had to be between 95mmHg and 110mmHg during two consecutive weeks. Average blood pressure was determined by measuring blood pressure three times at two minute intervals and calculating the mean; the differences in diastolic blood pressure had to be no more than 5mmHg. Participants also had to be confirmed with no coronary disease, stroke, congestive heart failure, secondary hypertension, poorly controlled diabetes mellitus, or chronic kidney failure. Participants should not have received any angiotensin-converting enzyme inhibitors or angiotensin receptor blockers for two weeks before randomisation. Relevant outcomes were change from baseline in seated systolic and diastolic blood pressure, response rate based on achievement of target blood pressure, and the incidence of adverse events.

The intervention dosages given were 40 to 80mg/day telmisartan and 80 to 160mg/day valsartan; two trials used forced titration for both drugs. In two trials, 2.5 and 25mg hydrochlorothiazide was also given to both intervention groups.

Two independent reviewers performed the selection, with disagreements resolved by consensus or discussion with a third reviewer.

Assessment of study quality
Methodological quality was assessed using the Cochrane quality checklist, including: allocation concealment; blinding of investigators, participants, outcome assessors, and data analysis; intention-to-treat analysis. In order to complete the checklist, data relevant to loss to follow-up and randomisation were extracted

The authors did not specifically report how many reviewers performed the quality assessment, but it appeared that it was performed by two independent reviewers.

Data extraction
Relative risks (RRs) with 95% confidence intervals (CI) were calculated for dichotomous data and mean differences (MDs) with 95% confidence intervals for continuous data.

The authors did not specifically report how many reviewers performed the extraction, but it appeared that it was
performed by two independent reviewers (since it was reported that two independent reviewers performed the analysis).

**Methods of synthesis**

Pooled relative risks and weighted mean differences (WMDs) with 95% confidence intervals were calculated using a random-effects model. To test the robustness of the analysis, results were also pooled using a fixed-effect model. Between trial heterogeneity was determined using the $\chi^2$ test.

Funnel plots were provided for some outcomes.

**Results of the review**

Six RCTs were identified (n=3,762 patients, range 70 to 1,051). Three trials had blinding of both investigators and participants; the other RCTs were open-label, two of which were endpoint blind for both assessors and participants. Four RCTs had an intention-to-treat analysis. Allocation concealment was adequate in five RCTs. Loss to follow-up ranged from 0 to 11.5%. Follow-up was for six to 12 weeks in all but one trial (where it was 52 weeks).

**Blood pressure change from baseline:** A 80mg/day dose of telmisartan was found to have a comparable effect in lowering blood pressure to 160mg/day valsartan in monotherapy (no relevant data provided). There was no difference between telmisartan and valsartan in reduction of systolic blood pressure (WMD -1.01mmHg, 95% CI -3.38 to 1.36; $I^2=95\%$) or reduction of diastolic blood pressure (WMD -0.39mmHg, 95% CI -2.24 to 1.45; $I^2=98\%$) for all six trials. Subgroup analyses found, when the drugs were combined with hydrochlorothiazide, telmisartan was significantly more effective than valsartan in reducing both systolic blood pressure (WMD -2.88mmHg, 95% CI -5.03 to -0.73; $I^2=70\%$) and diastolic blood pressure (WMD -1.73mmHg, 95% CI -2.47 to -0.98; $I^2=40\%$) for two trials. The result was still not significant for the four trials that did not additionally use hydrochlorothiazide, with a high level of heterogeneity ($I^2=96\%$ and $I^2=98\%$).

**Target blood pressure achievement:** There was no significant difference between telmisartan and valsartan in achieving the target blood pressure (four RCTs; $I^2=0\%$) or for the subgroup analysis of the trials which did not additionally use hydrochlorothiazide (two RCTs; $I^2=0\%$). However, when the drugs were combined with hydrochlorothiazide, telmisartan was significantly more effective than valsartan in achieving the target blood pressure (RR 1.09, 95% CI 1.00 to 1.19; two RCTs; $I^2=0\%$).

**Safety:** There were no significant differences in the incidence of adverse events for telmisartan compared with valsartan for headache (four RCTs; $I^2=0\%$), dizziness (three RCTs; $I^2=35\%$), infections (four RCTs; $I^2=64\%$), or pain (two RCTs; $I^2=0\%$). The incidence of reported adverse events ranged from 30 to 70%.

**Authors’ conclusions**

The blood pressure-lowering capabilities of telmisartan were comparable to valsartan in monotherapy. When combined with hydrochlorothiazide, telmisartan was more effective than valsartan. Telmisartan had the same safety in the treatment of essential hypertensive patients compared with valsartan.

**CRD commentary**

The review addressed a well-defined question for participants, interventions, study design and relevant outcomes. Relevant databases were searched, but it was not clear whether language restrictions were applied and only full article publications were included, so some studies could have been missed. Publication bias was not assessed. Efforts to reduce error and bias in study selection were clearly described and appeared to also apply to data extraction and quality assessment.

Trial quality was assessed using suitable criteria. Some relevant trial details were reported but, although baseline patient information was extracted, no relevant data were reported (e.g. age, gender, baseline blood pressure). Statistical heterogeneity was assessed; there was evidence for a high level of heterogeneity with some outcomes. The statistical method used for the meta-analysis of the RCTs seemed appropriate. Relevant subgroup analyses were performed.

The limited evidence and generally high level of heterogeneity make the reliability of the authors’ conclusions unclear.
Implications of the review for practice and research
The authors did not state any implications for practice or further research.

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