Antihypertensive effects of olmesartan compared with other angiotensin receptor blockers: a meta-analysis

Wang L, Zhao JW, Liu B, Shi D, Zou Z, Shi XY

CRD summary
This review found that olmesartan was associated with better antihypertensive efficacy than losartan and valsartan, for patients with hypertension. The adverse events with olmesartan were similar to those with the other angiotensin-receptor blockers. The review was generally well conducted, and the authors' conclusions are likely to be reliable.

Authors' objectives
To assess the efficacy and tolerability of olmesartan medoxomil, compared with other angiotensin-receptor blockers, in patients with hypertension.

Searching
PubMed, EMBASE, SinoMed, and Cochrane Central Register of Controlled Trials (CENTRAL) were searched to July 2010; search terms were reported. The reference lists of original studies, reviews, letters and case reports were checked to identify additional studies. There were no language restrictions.

Study selection
Randomised controlled trials (RCTs) that evaluated olmesartan monotherapy, compared with other angiotensin-receptor blockers, in patients with hypertension, with or without comorbidities, such as metabolic syndrome or chronic kidney disease, were eligible for inclusion. The primary outcomes were the changes from baseline to end-of-treatment, in diastolic and systolic blood pressure. The secondary outcome was therapeutic response, defined as a diastolic blood pressure of less than 90 millimetres of mercury (mmHg) or a reduction of at least 10mmHg, or both.

In the included trials, the patients presented with mild-to-moderate hypertension. Where reported, their mean age ranged from 48 to 73 years. The percentage of male patients, ranged from 45 to 78. Most studies lasted eight weeks; one lasted 12 months. Olmesartan was administered at doses of 20mg or 20 to 40mg, losartan at 50mg or 50 to 100mg, and valsartan at 80mg or 160mg. Candesartan was administered at a dose of 8mg and irbesartan at 150mg.

Two reviewers selected the studies; a third reviewer checked the selections.

Assessment of study quality
Two reviewers independently assessed methodological quality, using a seven-point scale based on the Jadad scale, for randomisation, allocation concealment, blinding methods, and reporting of drop-outs and losses to follow-up.

Data extraction
Two reviewers extracted data on the outcomes to calculate mean differences for continuous outcomes, relative risks for dichotomous outcomes, and 95% confidence intervals for every estimate. Any disagreements between the reviewers were resolved by discussion.

Methods of synthesis
Weighted mean differences and pooled relative risks, with 95% confidence intervals, were calculated for the summary estimates, using a fixed-effect model. The presence of statistical heterogeneity was assessed using $\chi^2$ and $I^2$. Where significant statistical heterogeneity was observed, the results were pooled using a random-effects model.

Sensitivity analyses were performed on the basis of quality assessment scores (greater or less than 4 points), and language of publication. The reviewers created L'Abbe plots to evaluate the degree of blood pressure reduction, compared with other angiotensin-receptor blockers. Meta-regression analyses were conducted to evaluate between-group differences, if heterogeneity was more than 75% and more than 10 trials were included.

Results of the review
Twenty-two trials, with 4,892 patients (range 40 to 635) were included in the review. All the trials were described as randomised, but only one reported the generation methods and none reported allocation concealment. For the quality assessment, three trials scored 5 points, twelve scored 4 points, six scored 3 points and one scored 2 points.

**Olmesartan versus losartan**: In 12 trials (2,133 patients), olmesartan was associated with a statistically significant decrease in diastolic blood pressure (WMD 1.61, 95% CI 0.59 to 2.62; $\tau^2=67\%$) and systolic blood pressure (WMD 3.19, 95% CI 0.46 to 5.92; $\tau^2=88\%$). There were no statistically significant differences in response rate (seven trials), total incidence of adverse events (10 trials), incidence of drug-related adverse events, headache, dizziness, or diarrhoea, between the groups.

Meta-regression showed that patient age, gender, study duration, sample size, year of publication, and baseline blood pressure did not contribute to the heterogeneity. The exclusion of studies not in English continued to show significant benefits for olmesartan. The exclusion of studies with less than 4 quality points, showed significant differences between groups for reduction in diastolic blood pressure (WMD 1.73, 95% CI 0.58 to 2.88), but not systolic blood pressure.

**Olmesartan versus valsartan**: In nine trials (1,595 patients), significant reductions in systolic blood pressure were observed with olmesartan, compared with valsartan (WMD 1.72, 95% CI 0.29 to 3.16; $\tau^2=24\%$). No statistically significant differences were observed between olmesartan and valsartan in diastolic blood pressure reduction, response rate (three trials), total adverse events (six trials), drug-related adverse events, headache, dizziness or diarrhoea. Statistically significant reductions in systolic and diastolic blood pressure were observed when studies with low quality scores were excluded, and for systolic blood pressure when studies not in English were excluded.

**Olmesartan versus candesartan or irbesartan**: There were no significant differences in blood pressure change observed between olmesartan and candesartan (three trials), but a significant reduction in 24-hour blood pressure was observed with olmesartan, with larger reductions for both systolic and diastolic blood pressure over the last four hours and two hours of the dosing interval. There were no differences in total adverse events between olmesartan and candesartan, and olmesartan and irbesartan (one trial).

**L'Abbe plot**: The results indicated that olmesartan provided greater reduction in blood pressure than other angiotensin-receptor blockers.

**Authors' conclusions**
Treatment with olmesartan was better than losartan and valsartan, for patients with hypertension. The adverse events with olmesartan were similar to those with the other angiotensin-receptor blockers.

**CRD commentary**
The review addressed a clear question, and the criteria for the inclusion of trials were defined. Appropriate databases were searched for relevant trials, without language restriction, and some attempts were made to identify unpublished trials. Steps were taken at each part of the review process to minimise reviewer error and bias. Methodological quality was assessed and the included trials were found to be of medium quality. The authors' decision to combine the results in a meta-analysis appears to have been justified, and the sources of heterogeneity were explored in appropriate meta-regression and sensitivity analyses.

In general, the review was well conducted, and the authors' conclusions are likely to be reliable.

**Implications of the review for practice and research**
**Practice**: The authors stated that olmesartan was a suitable choice for the control of high blood pressure.

**Research**: The authors stated that the effectiveness of olmesartan, in patients who had failed to respond to other sartans, needed to be determined. More data were required on the long-term effectiveness of olmesartan, in reducing cardiovascular morbidity and mortality, and the differences between olmesartan and angiotensin-receptor blockers other than losartan or valsartan. Pragmatic well-designed RCTs were needed with large samples, focusing on secondary endpoints, such as 24-hour blood pressure control, cardiac-cerebrovascular events, and adverse events.

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