
Meta-analysis of randomised controlled trials comparing latanoprost with brimonidine in the treatment of open-angle glaucoma, ocular hypertension or normal-tension glaucoma

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CRD summary

This review compared the effectiveness and adverse effects of latanoprost versus brimonidine for treating open-angle glaucoma, normal-tension glaucoma and ocular hypertension. The authors concluded that latanoprost is more effective in reducing intraocular pressure than brimonidine and that brimonidine causes more fatigue than latanoprost. The review was generally well-conducted and the conclusions are likely to be reliable.

Authors' objectives

To compare the effectiveness and adverse effects of latanoprost with brimonidine for treating open-angle glaucoma, normal-tension glaucoma and ocular hypertension.

Searching

MEDLINE, EMBASE and the Science Citation Index were searched through March 2006; the search terms were reported. The Cochrane CENTRAL Register (Issue 1, 2006), Current Controlled Trials, ClinicalTrials.gov, CenterWatch and the National Research Register were also searched. References of included publications were handsearched. There were no restrictions on language, date or publication status.

Study selection

Study designs of evaluations included in the review

Randomised controlled trials (RCTs) and quasi-RCTs that lasted at least 1 month were eligible for inclusion. Both parallel and crossover trials were included.

Specific interventions included in the review

Eligibility for inclusion was restricted to trials directly comparing latanoprost and brimonidine, either as sole glaucoma therapy or comparing latanoprost plus additional anti-glaucoma agent(s) with brimonidine plus the same anti-glaucoma agent(s). Additional anti-glaucoma drugs used concurrently with the interventions in the included trials were topical beta-blockers, dorzolamide and pilocarpine. Treatment durations ranged from 1 to 12 months.

Participants included in the review

Studies of patients with a diagnosis of open-angle glaucoma, normal-tension glaucoma or ocular hypertension were eligible for inclusion. There were no age or gender restrictions on the participants. The included trials had mean patient ages ranging from 52 to 77 years, and all included both male and female patients. Trials included both treatment-naive and already-treated patients, but the numbers of these patients were not clear.

Outcomes assessed in the review

Trials which assessed efficacy and/or tolerability were eligible for inclusion. Mean intraocular pressure (IOP) reduction over the course of the trial was the primary measure used to evaluate efficacy. If available, daily mean IOP values were used. Only 3 trials reported the maximum IOP reduction after drug administration. Other outcomes reported were measures of ocular haemodynamics, and adverse events including a number of eye problems (e.g. problems with eyelids and eyelashes), fatigue and headache.

How were decisions on the relevance of primary studies made?

Two reviewers independently assessed the relevance of primary studies. Any disagreements were resolved by discussion or by a third reviewer. Authors were contacted to clarify duplications and in those cases only the most complete trial was included.

Assessment of study quality

Two reviewers independently assessed study validity using the following criteria: allocation concealment, blinding, measurement bias, completeness of follow-up and use of intention-to-treat analysis. Any differences were resolved by discussion or by a third reviewer.

Data extraction

Two reviewers independently extracted data about trial characteristics, outcomes and adverse effects, using a standardised form. Any disagreements were resolved by discussion or by involving a third reviewer. Data on the weighted mean difference (WMD) of IOP from baseline to treatment end point were extracted. For trials with a crossover design, only the initial parallel phase was analysed. Relative risks (RRs) with 95% confidence intervals (CIs) were calculated for dichotomous outcomes, and WMDs with 95% CIs for continuous data.

Methods of synthesis

How were the studies combined?

The data were pooled using a random-effects meta-analysis. A funnel plot was used to explore publication bias.

How were differences between studies investigated?

Statistical heterogeneity was investigated using the chi-squared and I-squared tests. A priori subgroup analyses were conducted for trial duration, study type, glaucoma type, monotherapy versus adjunctive therapy, and other factors. Regression analyses were performed to investigate a number of predetermined factors (trial duration, trial design, trial quality, and monotherapy versus adjunctive therapy).

Results of the review

Fourteen trials involving 1,824 participants were included.

It was often unclear whether the studies met the quality criteria. Adequate allocation concealment could be determined in 7 trials, double-blinding in 4 trials, and intention-to-treat analysis in 5 trials. The withdrawal rates ranged from 0 to 19%.

For IOP reduction, there was a statistically significant effect in favour of latanoprost (post-treatment WMD 1.10, 95% CI: 0.57, 1.63). Significant heterogeneity was present (chi-squared 38.29, $p=0.001$, I-squared 66%), but only 2 trials did not show a greater IOP reduction with latanoprost than with brimonidine.

In the subgroup analyses, treatment durations of 6 months or more showed greater IOP reduction (WMD 1.64, 95% CI: 0.92, 2.36) than shorter treatment durations (WMD 0.76, 95% CI: 0.12, 1.39). There were no significant differences between patients with different diagnoses.

Superiority of latanoprost was greater (WMD 1.56, 95% CI: 0.90, 2.23) when the drugs were used as monotherapy than when they were used in combination with other glaucoma treatments (WMD 0.58, 95% CI: -0.04, 1.19).

In the 3 trials that reported measures of ocular haemodynamics, latanoprost significantly increased ocular blood flow, peak systolic velocity of the ophthalmic artery, and ocular perfusion pressure, while brimonidine had no significant effect.

A funnel plot did not show evidence of publication bias.

Risk for fatigue was statistically significantly lower with latanoprost than with brimonidine (RR 0.27, 95% CI: 0.08, 0.88). In the trials that reported fatigue, 5% of brimonidine patients and 1% of latanoprost patients experienced fatigue. Other adverse events did not show significant differences between the groups.

Authors' conclusions

Latanoprost as monotherapy is more effective in reducing IOP than brimonidine. Brimonidine causes more fatigue than

latanoprost.

CRD commentary

The review addressed a clear question in terms of the study designs, participants, interventions and outcomes. The search terms were reported in full, and publication databases and clinical trial registries were searched without language restrictions. Efforts were made to identify unpublished trials and to evaluate publication bias with a funnel plot. Two reviewers independently made decisions on relevance, extracted the data, and evaluated trial quality, thus reducing the likelihood of bias and error. Appropriate criteria were used to evaluate study validity. Appropriate statistical methods were used to combine the data and to investigate heterogeneity. This was a well-conducted review and the authors' conclusions are likely to be reliable.

Implications of the review for practice and research

Practice: The authors stated that treatment should be determined by an assessment of individual patients' risks and characteristics.

Research: The authors stated that the results of clinical trials (some currently underway) are required to demonstrate a neuroprotective effect of brimonidine.

Bibliographic details

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