Travoprost compared with other prostaglandin analogues or timolol in patients with open-angle glaucoma or ocular hypertension: meta-analysis of randomized controlled trials

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CRD summary
This review compared travoprost versus other prostaglandin analogues or timolol as treatments for open-angle glaucoma (OAG) or ocular hypertension (OH). Overall, travoprost 0.004% was more effective than timolol 0.5% for reducing intraocular pressure in patients with OAG or OH, and appears to be equivalent to other prostaglandin analogues. This was a well-conducted review and the authors' conclusions are likely to be reliable.

Authors' objectives
To review travoprost versus other prostaglandin analogues or timolol as treatments for open-angle glaucoma (OAG) or ocular hypertension (OH).

Searching
PubMed, EMBASE, Chinese Biomedical Database and the Cochrane Controlled Trials Register were searched from inception to August 2005 for ‘travoprost’ or ‘travatan’. References were handsearched.

Study selection
The only eligible study design for this review was the randomised clinical trial; all included studies were randomised controlled trials. Populations diagnosed with primary or secondary OAG or OH were eligible; the included studies comprised a mixture of these populations. The specified intervention was travoprost compared with another analogue prostaglandin or timolol. The included studies compared travoprost, timolol, latanaprost, bimatoprost and unoprostone. Relevant outcome measures were defined as the mean intraocular pressure (IOP) during treatment and incidence of side-effects, and were reported as such in the included papers.

Two reviewers carried out the screening independently and then combined their results.

Assessment of study quality
Study validity was assessed using criteria adopted from the Cochrane Eyes and Vision Group: allocation concealment, randomisation, masking, withdrawals and drop-outs, and intention-to-treat analysis.

Two reviewers performed the validity assessment independently, and any differences were resolved by discussion and consensus.

Data extraction
The incidence of reported side-effects and the mean IOP over treatment time were extracted from each study where possible. If mean values were not presented then the IOP measured at the last visit was used. Dichotomous outcomes such as side-effects were calculated as odds ratios, while weighted mean differences (WMDs) were used for continuous outcomes such as IOP.

Methods of synthesis
A quantitative meta-analysis was carried out using fixed-effect and random-effects models to calculate pooled odds ratios and WMDs, as appropriate. Heterogeneity was assessed using $\chi^2$; where the p-value was less than 0.1 a fixed-effect model was used, otherwise a random-effect model was adopted. Publication bias was intended to be assessed using a funnel plot.

Results of the review
This review included 12 studies (n=3,048): 8 double-blind trials (n=2,517) and 4 single-blind trials (n=531).
Of the 12 trials, seven clearly reported their allocation concealment and all detailed withdrawals and drop-outs. Eight reported using intention-to-treat analysis but only five appeared to have used a sample size calculation. Publication bias was to have been assessed using a funnel plot; however, this was not carried out because of the small number of included studies.

The meta-analysis found that travoprost (0.004%) was significantly more effective at lowering IOP than timolol (0.5%); the WMD was -0.81 (95% confidence interval, CI: -1.16, 0.45, p≤0.01). Travoprost (0.004%) was also more effective than unoprostone (0.12%) in lowering IOP. There was no evidence of a significant benefit of travoprost when compared with bimatoprost (0.03%) or latanoprost (0.005%). Comparing two dosages, 0.004% travoprost was significantly better at reducing IOP than 0.0015% travoprost (WMD -0.32, 95% CI: -0.62, -0.02, p=0.04).

Data on side-effects were presented in full. To summarise, the overall incidence of side-effects was lower with timolol than with travoprost. Travoprost 0.004% caused a higher percentage of ocular hyperaemia, iris pigmentation and eyelash changes. Travoprost also caused higher rates of hyperaemia in comparison with latanoprost.

**Authors’ conclusions**
Overall, travoprost 0.004% was more effective than timolol 0.5% for reducing IOP in patients with OAG or OH, and appears to be equivalent to other prostaglandin analogues. The authors therefore advise that side-effects, compliance and cost are taken into consideration when deciding on the appropriate therapy for OAG and OH.

**CRD commentary**
This review addressed a clearly defined research question with appropriate searches, inclusion criteria, and clear quality assessment and data extraction procedures which are likely to have reduced bias. Language restrictions (only Chinese and English papers were considered) may have introduced some bias and excluded potentially relevant studies. Publication bias could have been assessed using a funnel plot, as the authors initially suggested, and this would have added to a strong review. A quantitative meta-analysis was carried out and incorporated heterogeneity where it was found. Only one analysis remained significantly heterogeneous, but this was not further explored. Overall, 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 since travoprost can cause changes in the eyelashes and iris pigmentation, patients receiving treatment for OAG or OH in only one eye should be informed of these risks. Further, since there are no clear differences in benefit among the prostaglandin analogues, side-effects, compliance and cost should be taken into consideration when deciding on the appropriate therapy.

Research: The authors stated that more research is required to explore the IOP effects of travoprost in different races, as studies to date have been predominantly carried out in Caucasian populations.

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