Relative efficacy and safety of preservative-free Latanoprost (T2345) for the treatment of open-angle glaucoma and ocular hypertension: an adjusted indirect comparison meta-analysis of randomized clinical trials

Cucherat M, Stalmans I, Rouland JF

CRD summary

The authors concluded that preservative-free latanoprost (T2345) was better tolerated and no less effective than all other prostaglandin analogues assessed. All comparisons except one were indirect so there was insufficient data from direct comparisons to assess the validity of the indirect comparisons and the authors' conclusions should be interpreted with caution.

Authors' objectives

To assess the efficacy and tolerability of preservative-free latanoprost (T2345) for the treatment of open-angle glaucoma and ocular hypertension.

Searching

MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched up to December 2011; search terms were reported. There were no language and publication restrictions.

Study selection

Randomised controlled trials (RCTs) that had a trial duration of two months and compared preservative-free latanoprost with other prostaglandin analogues were included. Eligible patients had to have open-angle glaucoma or ocular hypertension (excluding secondary glaucoma) with a baseline intraocular hypertension of >20 mmHg and a wash-out period before randomisation if they had been treated previously. Studies that included patients who underwent intraocular laser treatment or surgery within the previous three months or who received concomitant systemic or ocular treatments during the study were excluded. Outcomes of interest were intraocular pressure (IOP) at three months and incidence of hyperaemia.

Most patients in the included trials had open-angle glaucoma and ocular hypertension. Where reported, mean ages ranged from 24 to 88 years and 39% to 75% of the participants were female. The included studies were published between 2001 and 2012. Nine trials were conducted in North America, two in Europe and 10 in various countries.

The authors did not report how many reviewers selected the trials.

Assessment of study quality

Risk of bias was assessed using criteria of randomisation, allocation concealment, blinding, withdrawals and drop-outs.

The authors did not report how may reviewers assessed study quality.

Data extraction

Data were extracted to calculate mean IOP achieved at three months and at the end of the study. The mean absolute mmHg and relative percentage change in IOP between baseline and three months were calculated as was the percentage of patients with conjunctival hyperaemia and/or ocular redness at three months. Where three months' data were not available, data were recorded at two to six months taking the longest period in the case of multiple time points.

One reviewer extracted data and a second reviewer checked for accuracy.

Methods of synthesis

Pooled odds ratios, weighted mean differences and 95% confidence intervals were calculated using a random-effects model. Statistical heterogeneity was assessed using I^2 statistics. Adjusted indirect comparisons were performed according to the methods outlined by Bucher et al. and Song et al. Placebo or active treatment was used as the common comparator. An exploratory non-inferior analysis was performed using a 1.5 mmHg non-inferiority margin (a standard

acceptance margin used in glaucoma studies).

Results of the review

Twenty-one RCTs (26 pairwise comparisons, range 26 to 690 patients) were included in the meta-analysis. Seven trials were double-blinded, 11 were single blinded, one was an open trial and information on blinding was not available for two trials. Reported follow-up ranged from three months to 24 months.

There was no statistically significant difference in mean IOP at three months between T2345 and polyquaternium-1-travoprost, BAK-bimatoprost 0.03%, BAK-bimatoprost 0.01%, BAK-travoprost, or BAK-latanoprost. There was a statistically significant difference in favour of T2345 when compared with BAK-tafluprost (WMD -0.9 mmHg, 95% CI -1.52 to -0.28).

Risk of hyperaemia was statistically significantly lower with T2345 than with polyquaternium-1-travoprost (OR 0.24, 95% CI 0.11 to 0.55), sofzia-travoprost (OR 0.37, 95% CI 0.16 to 0.84) BAK-bimatoprost 0.03% (OR 0.18, 95% CI 0.10 to 0.33), BAK-bimatoprost 0.01% (OR 0.27, 95% CI 0.13 to 0.56), BAK-tafluprost (OR 0.18, 95% CI 0.05 to 0.65), BAK-travoprost (OR 0.25, 95% CI 0.14 to 0.46) and BAK-latanoprost (OR 0.52, 95% CI 0.31 to 0.86).

The exploratory non-inferiority analysis results suggested that T2345 was also noninferior to all other prostaglandin analogues except polyquaternium-1-travoprost. In the indirect comparison of T2345 against polyquaternium-1-travoprost, the upper limit was 1.51 mmHg (which was above the widely used limit of noninferiority of 1.5 mmHg).

Publication bias was not assessed due to small number of the included trials for each comparison.

Authors' conclusions

Data suggested that preservative-free latanoprost (T2345) was no less effective than all the other prostaglandins assessed and was better tolerated.

CRD commentary

The review question and inclusion criteria were clear. Relevant sources were searched without language or publication status limitations. Appropriate methods to reduce reviewer error and bias were used for data extraction; it was unclear whether similar methods were used for study selection process and quality assessment. Appropriate criteria were used to assess the study quality but the full results were not reported and this made it difficult to determine the reliability and validity of the included studies.

The authors used appropriate methods for pooling data but did not report on heterogeneity. The comparisons were indirect except for one direct comparison between T2345 and BAK-latanoprost. There was insufficient data from direct comparisons to assess the validity of the indirect comparisons so the authors' conclusions should be interpreted with caution.

Implications of the review for practice and research

The authors did not report any implications for practice and research.

Funding

Laboratoires Thea, France.

Bibliographic details

Cucherat M, Stalmans I, Rouland JF. Relative efficacy and safety of preservative-free Latanoprost (T2345) for the treatment of open-angle glaucoma and ocular hypertension: an adjusted indirect comparison meta-analysis of randomized clinical trials. Journal of Glaucoma 2014; 23(1): e69-e75

PubMedID

23881267

DOI

10.1097/IJG.0b013e3182a075e6

Original Paper URL
http://journals.lww.com/glaucomajournal/Abstract/2014/01000/Relative_ Efficacy_ and_ Safety_ of_ Preservative_ free.24.aspx

Indexing Status
Subject indexing assigned by NLM

MeSH
Aged; Antihypertensive Agents /adverse effects /therapeutic use; Benzalkonium Compounds /adverse effects /therapeutic use; Female; Glaucoma, Open-Angle /drug therapy /physiopathology; Humans; Intraocular Pressure /drug effects; Male; Middle Aged; Ocular Hypertension /drug therapy /physiopathology; Ophthalmic Solutions; Polymers /adverse effects /therapeutic use; Preservatives, Pharmaceutical /adverse effects /therapeutic use; Prostaglandins F, Synthetic /adverse effects /therapeutic use; Randomized Controlled Trials as Topic; Tonometry, Ocular; Treatment Outcome

AccessionNumber
12013041916

Date bibliographic record published
28/08/2013

Date abstract record published
27/02/2014

Record Status
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 the reliability of the review and the conclusions drawn.