Projected impact of travoprost versus both timolol and latanoprost on visual field deficit progression and costs among black glaucoma subjects

Halpern M T, Covert D W, Robin A L

Record Status

This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology

The use of travoprost 0.004% (Travatan) as an intraocular pressure (IOP)-lowering treatment for visual field deficit (VFD) progression among people with glaucoma. Individuals received one drop of travoprost in each eye daily at 8 PM.

Type of intervention

Treatment.

Economic study type

Cost-effectiveness analysis.

Study population

The study population comprised black persons with open-angle glaucoma or ocular hypertension, without severe visual field loss.

Setting

The setting was a hospital. The study was carried out in the USA.

Dates to which data relate

The effectiveness data were collected from studies published between 1987 and 2001. Most of the resource use and cost data were collected from studies published between 1996 and 1999. The price year was 2000.

Source of effectiveness data

The effectiveness data were derived from a review of published studies and some authors' assumptions.

Modelling

Modelling was used to evaluate the change in visual field over time and the probability of VFD progression for participants in each treatment group. Algorithms were used to project these outcomes (AGIS study, see Other Publications of Related Interest). The cohort of patients used to model these outcomes was obtained as a sub-sample of a randomised controlled trial (RCT) included in the review (Netland et al., see Other Publications of Related Interest). The period considered in the model was not defined clearly.

Outcomes assessed in the review

The primary outcomes assessed in the review were the changes in the visual field, the probability of VFD progression, and the mean IOP.

The change in the visual field was assessed by the increase in the VFD score (range: 0 for no defect to 20 for end-stage) at 7 years, according to the level of IOP of the patients. These changes were reported according to two alternative algorithms, a predictive algorithm and an associative algorithm.

The predictive algorithm considered three categories of patients: patients with an IOP of either less than 14 mmHg, between 14 mmHg and less than 18 mmHg, or at least 18 mmHg.

The associative algorithm considered four groups of patients: patients with IOP less than 18 mmHg in either all the medical visits, in 75% to less than 100% of the medical visits, in 50% to less than 75% of the visits, or in less than 50% of the visits.

The probability of VFD progression was assessed according to the IOP level of the patients, as reported by four different studies.

The mean IOP was assessed overall, at baseline and throughout the day, during a 1-year study period for the treatments considered at analysis (travoprost, latanoprost and timolol), as reported by one RCT included in the review.

These primary outcomes were included as parameters of the model.

Study designs and other criteria for inclusion in the review
One double-blind RCT was included in the review. The other studies appear to have been observational studies.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
At least six primary studies were included in the review of effectiveness.

Methods of combining primary studies
The authors used the results of the RCT in combination with the results of each of the other observational studies in the review, to consider different scenarios according to each one of the reviewed studies. Basically, the algorithms of the observational studies were applied to the sample of patients considered in the RCT.

Investigation of differences between primary studies
The authors reported the effectiveness results for each of the studies included in the review. However, they did not explain the differences observed between these studies. Moreover, since a meta-analysis was not undertaken, no statistical tests of heterogeneity were carried out.

Results of the review
Travoprost proved to be more effective in lowering IOP level than latanoprost and timolol, in terms of a lower mean IOP after 1 year. The mean IOP was 17.3 mmHg for travoprost (standard deviation, SD=2.5), 18.7 mmHg for

latanoprost (SD=2.4; p<0.05) and 20.5 mmHg for timolol (SD=3.4; p<0.05).

When the predictive algorithm was considered, the increase in the VFD score at 7 years was:

0.76 for patients with an IOP of less than 14 mmHg when compared to those with an IOP of between 14 and less than 18 mmHg; and

1.89 for patients with an IOP of at least 18 mmHg when compared to those with an IOP of between 14 and less than 18 mmHg.

When the associative algorithm was considered, the increase in the VFD score at 7 years for patients with an IOP of less than 18 mmHg was:

1.00 in 75% to less than 100% of the medical visits when compared to all medical visits;

2.05 in 50% to less than 75% of visits, when compared to all medical visits; and

1.93 in less than 50% of the visits, when compared to all medical visits.

The probability of VFD progression increased with a higher level of IOP according to all the studies reviewed. It ranged from 0% for patients with an IOP of less than 16 mmHg to 100% for patients with an IOP of greater than 22 mmHg.

Methods used to derive estimates of effectiveness
The authors made some assumptions to derive the estimates of effectiveness.

Estimates of effectiveness and key assumptions
The authors assumed that there was a correlation between IOP decrease and long-term vision preservation. They also assumed that the efficacy of each drug shown in the 1-year period of the RCT was representative of the performance of the drug on a long-term basis.

Measure of benefits used in the economic analysis
Two model outcomes were obtained as summary measures of benefit:

the percentage reduction in the VFD score when travoprost was compared with either latanoprost or timolol (considering the predictive versus the associative algorithms); and

the percentage reduction in the probability of VFD progression when travoprost was compared with either latanoprost or timolol (considering the algorithms proposed for four studies in the review).

The time considered when modelling these outcomes might have been one year.

Direct costs
Most of the resource quantities were reported separately from the costs. The health services included in the economic evaluation were inpatients resources (hospitalisation and length of stay) and outpatient services (visits, dilated optic nerve examination and visual field assessment). Not all of the costs relevant to the hospital perspective adopted were considered in the economic analysis. The costs of non-physician outpatient services, other resource use such as systemic medication, and adverse reactions to medications were not included.

The direct costs and quantities of resources used were obtained from a published study, the 1996 National Health Survey, the treatment guidelines from the Preferred Practice Patterns of the American Academy of Ophthalmology, and the 2000 Medicare reimbursement rates. Therefore, the costs were mainly estimated from actual data. The price year was 2000. Discounting was not performed, but it may not have been relevant since an annual period appears to

have been considered in the estimation of costs. The costs reported were the incremental, average annual costs per patient treated with either latanoprost or timolol, compared to travoprost.

Statistical analysis of costs
The mean costs and some SDs were reported.

Indirect Costs
No indirect costs were reported.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were performed in the sense that several scenarios were considered, according to the results of different primary studies included in the review.

Estimated benefits used in the economic analysis
The incremental benefits were reported as the percentage changes in the VFD score and the probability of VFD progression when travoprost was compared with latanoprost and timolol.

There were statistically significant reductions in the percentage change in the VFD score when travoprost was compared to latanoprost (-25.4% and -29.3% with the predictive and associative algorithms, respectively; $p<0.05$) and timolol (-40.7% and -35.0% with the predictive and associative algorithms, respectively; $p<0.05$).

The probability of VFD progression was significantly lower among patients treated with travoprost than those treated with either latanoprost or timolol, ($p<0.05$). The reduction ranged from -7.8 to -18.5% for travoprost versus latanoprost, and from -7.4 to -35.1% for travoprost versus timolol, depending on the algorithm for IOP levels and medical visits considered.

The period considered for the estimation of benefits was unclear, but it may have been 1 year. Side effects were not considered, although they appear to be a relevant outcome for the type of treatment considered at analysis.

Cost results
Depending on the algorithms considered for the estimation, the incremental average annual costs per patient were $170 (SD=69; range: 70 - 263) for latanoprost compared to travoprost, and $247 (SD=112; range: 66 - 365) for timolol compared to travoprost.

Synthesis of costs and benefits
The estimated costs and health benefits were not combined since travoprost was the dominant strategy, being the most effective and least costly of the evaluated treatments.

Authors' conclusions
Compared with latanoprost and timolol, treatment with travoprost resulted in lower rates of visual field loss at a lower cost.

CRD COMMENTARY - Selection of comparators

A justification was given for one of the comparators chosen. Latanoprost was chosen because it was the prostaglandin analogue medication used in the authors' setting before the development of travoprost. However, no justification was given for the use of timolol. Moreover, the authors mentioned other types of health technologies (e.g. drugs, laser and surgical interventions) used to treat patients with glaucoma, but these were not considered in the analysis. You must decide whether these are widely used health technologies for the lowering of IOP among individuals with glaucoma in your own setting.

Validity of estimate of measure of effectiveness

The authors did not carry out a systematic review of the literature, nor did they state the criteria used to retrieve and include the studies in the review. The effectiveness estimates were combined using narrative methods. The adverse reactions associated with medications were not considered. Some of the uncertainty surrounding the effectiveness results was dealt with, in the sense that the results obtained by different studies were used to consider alternative scenarios. The authors stated that there might be other factors, apart from the IOP levels, that affect the long-term preservation of visual function in patients with glaucoma, although they cannot yet be quantified. Therefore, these other factors were not considered in the effectiveness analysis. In addition, some, but not all, of the authors' assumptions were justified with reference to the medical literature. A small sample, obtained from an RCT, was used as the cohort of patients in the model.

Validity of estimate of measure of benefit

The estimation of benefits was modelled using algorithms proposed in the medical literature. Although the authors mentioned that VFD progression might result in a decreased quality of life for glaucoma patients, this dimension was not considered as one of the measures of benefit. The disease-specific benefit measures used in the present analysis would be difficult to compare with the benefits of other health care interventions.

Validity of estimate of costs

The perspective adopted was rather narrow since only the direct hospital costs were considered in the economic analysis. As the authors stated, the indirect costs associated with the treatments were not considered, and are very important. In addition, not all of the costs relevant to the perspective adopted were included. For example, the costs associated with adverse reactions to medications, non-physician outpatient services and systemic medications were excluded from the economic analysis. Medicare reimbursement rates were considered for the estimation of costs, which may not reflect the true opportunity costs of the interventions studied. Most of the resource quantities were reported separately from the costs. Moreover, the price year was stated, which enhances the ability to conduct reflation exercises in other settings. Discounting was not performed, but was not relevant since the costs were calculated for one year.

Other issues

The authors did not make appropriate comparisons of their results with those from other studies. They also did not explicitly address the issue of the transferability of the study findings to other settings. The authors stated that the results of this study might not be generalisable to patients with different characteristics to those patients included in the study.

Implications of the study

The authors recommended further research to replicate the study. Such research should consider a larger sample population when modelling the results. They also suggested a further investigation of the true costs of the interventions analysed.

Source of funding

Supported by Alcon Research Ltd.

Bibliographic details

Halpern M T, Covert D W, Robin A L. Projected impact of travoprost versus both timolol and latanoprost on visual field deficit progression and costs among black glaucoma subjects. Transactions of the American Ophthalmological Society 2002; 100: 109-117; discussion 117-118

PubMedID

12545683

Other publications of related interest

The AGIS Investigators. The Advanced Glaucoma Intervention Study (AGIS): 7. The relationship between control of intraocular pressure and visual field deterioration. American Journal of Ophthalmology 2000;130:429-40.

Netland PA, Landry T, Sullivan EK, et al, and the Travoprost Study Group. Travoprost compared with latanoprost and timolol in patients with open-angle glaucoma or ocular hypertension. American Journal of Ophthalmology 2001;132:472-84.

Indexing Status

Subject indexing assigned by NLM

MeSH

African Continental Ancestry Group; Aged; Antihypertensive Agents /economics /therapeutic use; Cloprostenol /analogs & derivatives /economics /therapeutic use; Disease Progression; Double-Blind Method; Drug Costs; Female; Glaucoma, Open-Angle /drug therapy /economics /ethnology /physiopathology; Humans; Intraocular Pressure /drug effects; Male; Middle Aged; Ocular Hypertension /drug therapy /economics /ethnology /physiopathology; Prostaglandins F, Synthetic /economics /therapeutic use; Timolol /economics /therapeutic use; Travoprost; United States; Vision Disorders /physiopathology; Visual Fields /drug effects

AccessionNumber

22003006167

Date bibliographic record published

30/06/2004

Date abstract record published

30/06/2004