A persistency and economic analysis of latanoprost, bimatoprost, or beta-blockers in patients with open-angle glaucoma or ocular hypertension


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
This study compared monotherapy with latanoprost 0.005%, bimatoprost 0.03% or topical beta-blockers for the treatment of open-angle glaucoma or ocular hypertension. The beta-blockers studied were timolol maleate 0.5%, timolol maleate gel 0.25%, timolol hemihydrate 0.5%, carteolo 1%, bexazolol 0.5%, metipranolol 0.3% and levobunolol 0.5%.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients aged 18 years or older with a clinical diagnosis of open-angle glaucoma or ocular hypertension, and who had started one of the monotherapies identified during the study period. Patients were excluded if they had undergone eye surgery in the 3 months prior to, or 6 months of the study period. Other reasons for exclusion included any abnormality that prevented reliable applanation tonometry, media opacity preventing reliable baseline optic-nerve or visual field examination, and known occludable angles by gonioscopy or the presence of any other clinically significant angle abnormalities. Patients with primary, acute or chronic angle closure were also excluded, as were those with secondary or congenital glaucoma, and those enrolled in a prospective clinical trial in the follow-up period.

Setting
The setting was secondary care. The economic study was carried out in South Carolina, Georgia and Florida, USA.

Dates to which data relate
The effectiveness and resource use data related to events between 1996 and 2002. No clear price year was stated.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The resource use data were collected from the same patient sample as that used in the effectiveness analysis.

Study sample
The patient sample was identified through a retrospective case-note review. The review included 53,963 case notes, from which 1,182 patients to be included in the patient sample were identified. Of these patients, 133 started treatment with latanoprost, 59 started treatment with bimatoprost, and 152 were initially treated with beta-blockers. Power calculations indicated that the sample had a statistical power of 80% to exclude a 14% difference.

**Study design**

This was a multi-centre, retrospective cohort study. The patients were followed up for at least 6 months. The retrospective nature of the study meant that there was no loss to follow-up.

**Analysis of effectiveness**

The analysis of the study data was conducted on an intention to treat basis. The primary health outcomes assessed were:

- the persistency of therapy (calculated using Kaplan Meier analysis),
- intraocular pressure,
- the number of treatment changes,
- the number of adverse events,
- the number of medicines prescribed at 6 months,
- whether the initial medicine was changed or additional medicine added, and
- the number and type of glaucoma-related hospital visits.

The three patient groups were shown to be comparable in terms of their age, gender, diagnosis, and whether it was the right or left eye receiving treatment. There appears to have been some difference in the racial composition of the three patient groups.

**Effectiveness results**

The risk ratio of discontinuing a beta-blocker compared with latanoprost was 1.08 (95% confidence interval, CI: 1.01 - 1.16). If latanoprost was compared with bimatoprost, the risk ratio of discontinuing was 1.15 (95% CI: 1.03 - 1.27).

At 6 months the mean number of medicines prescribed was 1.1 in all three patient groups (standard deviations, SDs, were 0.3 for latanoprost, 0.4 for bimatoprost and 0.4 for beta-blockers; the difference was not significant).

The patients in the latanoprost group had a mean of 0.27 (SD=0.6) changes to medicine in the first 6 months, while those in the bimatoprost group had a mean of 0.45 (SD=0.8) medicine changes. Those patients initially given beta-blockers had a mean of 0.47 (SD=0.8) changes to their medication in the first 6 months. The difference between the three groups was statistically significant, (p<0.0001).

The only adverse event that was statistically different between the three treatment groups was conjunctival hyperaemia. This was experienced by 4.8% of the latanoprost group, 11.0% of the bimatoprost group and 1.5% of the beta-blockers group, (p<0.0001).

At 6 months, intraocular pressure was 17.7 mmHg (SD=4.4) for patients treated with latanoprost, 18.2 mmHg (SD=3.7) for patients treated with bimatoprost and 18.7 mmHg (SD=3.8) for patients treated with beta-blockers, (p<0.0001).

Sixty-seven of the 357 patients initially treated with latanoprost had their treatment altered, compared with 49 of the 146 patients treated with bimatoprost and 113 of the 335 patients initially treated with beta-blockers. This difference was statistically significant, (p<0.0001).
The patients receiving latanoprost had a mean of 2.9 (SD=1.3) hospital visits in the first 6 months of treatment, compared with 3.1 (SD=1.4) visits for bimatoprost patients and 3.3 (SD=1.7) visits for patients on beta-blockers. This difference was statistically significant, (p<0.0001).

**Clinical conclusions**
The authors concluded that patients treated with latanoprost were more persistent with treatment and had a lower intraocular pressure.

**Measure of benefits used in the economic analysis**
No summary measure of health benefit was used in the economic analysis. In effect, a cost-consequences analysis was conducted.

**Direct costs**
The costs to the health care payer in the 6 months following the start of treatment were identified in this study. The resource use data were taken from the retrospective case-note review that provided the clinical effectiveness data. The cost of medicines was taken from published average wholesale prices. The costs of office visits and procedures were taken from the state health plan schedule of allowances. Some information on resource use was provided, but no breakdown of the unit costs was provided in the paper. The costs and the quantities were not reported separately. Resource use data related to events between 1996 and 2002. The price year was not reported and the paper did not report whether the costs were discounted.

**Statistical analysis of costs**
The differences between the costs of medication, cost of visits and procedures, and total costs were statistically tested. However, the test used was not reported.

**Indirect Costs**
No indirect costs were included in this study.

**Currency**
US dollars ($).

**Sensitivity analysis**
No sensitivity analysis was conducted.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section.

**Cost results**
The total cost per patient was $153.70 (SD=46.70) in the latanoprost group, $163.80 (SD=51.20) in the bimatoprost group and $119.30 (SD=78.90) in the beta-blocker group, (p<0.001).

**Synthesis of costs and benefits**
The costs and benefits were not combined.
Authors' conclusions
Patients receiving latanoprost were more persistent with therapy and had lower intraocular pressure, fewer outpatient visits and lower costs than those receiving bimatoprost or beta-blocker therapy.

CRD COMMENTARY - Selection of comparators
This study compared monotherapy with latanoprost, bimatoprost and beta-blockers for the treatment of open-angle glaucoma and ocular hypertension. No rationale for the choice of these therapies was provided. These may not be the only appropriate treatment options, and you should consider how they relate to your own setting before applying the results of this study.

Validity of estimate of measure of effectiveness
The clinical effectiveness data used in this study were taken from a retrospective cohort study. The authors reported that this provided a more representative picture of the true effect of the three treatments than would be the case with a randomised controlled trial. They argued that patients who would agree to participate in a randomised controlled trial would not be representative of the whole patient population diagnosed with open-angle glaucoma and ocular hypertension. As they did not provide any evidence to support this, it was unclear how appropriate this idea is. However, several aspects of the study design used in this paper could have introduced the potential for bias. For example, the study does not consider what confounding factors might have influenced the initial choice of treatment for the patients included in this study. In addition, the lack of blinding might have introduced bias. The authors indicated that the three patient groups were broadly comparable at baseline in terms of socio-demographic characteristics, diagnosis and whether it was their right or left eye that was receiving treatment. However, they did not report whether the groups had comparable intraocular pressures. As intraocular pressure (rather than reduction in intraocular pressure) was used as the primary outcome, this has the potential to have a substantial impact on the study results. The authors did not compare their patient sample with the patient population, so it was unclear whether it was representative of patients diagnosed with open-angle glaucoma and ocular hypertension. The clinical data were analysed on an intention to treat basis and adverse events were included, which enhances the validity of the analysis.

Validity of estimate of measure of benefit
No measure of health benefit was combined with the cost data so, in effect, a cost-consequences analysis was performed. Please see the comments in the 'Validity of estimate of measure of effectiveness' field (above).

Validity of estimate of costs
The cost perspective adopted was that of the health care insurer. The costs of medication, office visits and procedures were included in the study. The paper reported that staff time was not considered in the study, but the extent to which this was included in the costs for office visits and procedures was unclear. The difference between the resource use, medication costs, and office visit and procedure costs for each of the three patient groups was statistically tested, thus reducing the uncertainty around the results. However, the statistical test used was not reported and the difference between the total costs was not tested. Some resource use data were reported in the paper. Although this will assist the generalisability of the study, a more comprehensive breakdown of resource use and unit costs would have enhanced the generalisability of the results. The price year was not reported, which will prevent any future reflation exercises.

Other issues
The authors compared their findings with those from similar studies, but did not consider how their results could be generalised to other settings. The authors appear to have presented all appropriate data, but the difference between data relating to the initial 6 months of treatment and all data identified in the study was not always clear. The authors reported some limitations of the study. In particular, a prospective study design was not utilised and visits and timings were not standardised.

Implications of the study
The authors called for further research into the differences in therapy maintenance, intraocular pressure and costs between the three therapies considered in this study, in a prospective randomised trial.

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