Guidelines for the medical treatment of glaucoma

Summary:

- This guideline should be read in conjunction with NICE guidance CG85. This document offers guidance on which pharmacological treatments should be chosen.

- The recommended treatment options in this guideline are for newly diagnosed/treated patients, there is no expectation that patients already being treated should have their treatment changed unless clinically indicated. These decisions should be made by consultant ophthalmologists.

- Diagnosis and management of ocular hypertension or chronic open angle glaucoma should be by an ophthalmologist or an optometrist trained in the diagnosis of glaucoma under supervision of a consultant ophthalmologist.

- A patient with ocular hypertension or suspected chronic open angle glaucoma with high IOP should be offered either a topical beta-blocker or topical prostaglandin analogue based on their central corneal thickness, intraocular pressure and age.

- Patients with a confirmed diagnosis of early or moderate chronic open angle glaucoma should be offered treatment with a topical prostaglandin analogue.

- The first choice beta-blocker is timolol 0.25%

- The first choice prostaglandin analogue is bimatoprost or travoprost.

- Combination therapies should only be used in cases where there is an issue with compliance with multiple drugs or as third line options where patients need further lowering of IOP than provided by monotherapy.

- Other classes of drugs should not be used except where patients have contraindications and/or side-effects from beta-blockers and prostaglandin analogues or have not achieved appropriate IOP lowering with those drugs and surgery is not appropriate.

- Tafluprost is a preservative free prostaglandin. Prescribe-able following consultant initiation as a second line preservative free formulation after beta blockers.
Glaucoma guideline

Scope
This guideline covers the medical treatment of adults who have been diagnosed with chronic open-angle glaucoma (COAG) or ocular hypertension (OHT). It does not cover surgical management or laser treatment, nor does it cover angle closure, congenital or childhood glaucoma. It is based on the NICE guidelines for COAG and OHT, which were published in April 2009 and cover diagnosis, diagnostic tests, monitoring, pharmacological, surgical, laser and complementary or alternative treatments and service models. The NICE guidance does not cover which medication to use from each pharmacological group, which is where this guidance is to be used.

Search strategy
Cochrane, TRIP, Medline, and EMBASE were searched with keywords as follows: glaucoma, ocular hypertension, intraocular pressure, carbonic anhydrase inhibitors, topical beta-blockers, prostaglandin analogues, brinzolamide, acetazolamide, dorzolamide, bimatoprost, latanoprost, travoprost, timolol, levobunolol, cost-effectiveness, QALY. The following limits were used: humans, age group 19+ (all adults), RCTs, reviews, meta-analysis, clinical trials, date range 1990-2009.

Background
In glaucoma visual field loss normally starts in the peripheral vision and is not noticed so many people with glaucoma are unaware that they have the disease. The optic nerve destruction is normally slow, progression of the optic nerve destruction can be slowed or stopped using medications, surgery or laser therapy. However, visual loss through glaucoma cannot be reversed, therefore treating glaucoma is aimed at maintaining a patient’s quality of life through preserving remaining vision.

Risk factors for glaucoma are increasing age, ethnicity (greater risk in people of black or Hispanic ethnicity), raised intraocular pressure, myopia, diabetes and a family history of glaucoma. According to Thomas et al, (2005) the NNT for patients with OHT is about 20, with a lower NNT for those patients with higher IOP, so an IOP of >26mmHg gives an NNT of 6, the NNT for early COAG is 5. The same study showed that a central corneal thickness (CCT) ≤555μm meant a three fold risk of developing glaucoma compared with a CCT >588 μm. A recent Cochrane meta-analysis confirmed that lowering IOP reduces the incidence of glaucomatous visual field defects in OPH (OR: 0.62, 95% CI 0.47-0.81) (Vass et al 2008).

Treatment options
Any treatment offered should take into account any contraindications, side effects or intolerances in each patient. At present only beta-blockers and prostaglandin analogues are licensed for both first and second line treatment of glaucoma. Patients who are on treatments not recommended in these guidelines should not routinely have their medications changed unless there are clinical grounds. There are potential risks associated with switches to alternative preparations which require monitoring. Decisions to change treatments should be made by consultant ophthalmologists.
**Beta-blockers compared to prostaglandin analogues**
The evidence assessed by NICE for the draft glaucoma guidelines showed that prostaglandin analogues are significantly more likely to achieve a greater fall in baseline IOP and to achieve a greater number of patients with acceptable IOP than beta-blockers (NICE 2008c, appendix E). This analysis also found that there was no significant difference in incidence of cardiovascular side effects or allergic reactions between PGA and BB but hyperaemia was significantly more likely to occur with PGA (NICE 2008c, appendix E).

Evidence suggests that in the UK prostaglandin analogues are in most scenarios more cost-effective than beta-blockers due to a longer time to surgery, (see Kobelt and Jonsson, 1999).

**Fixed combination therapies and adjunctive treatment**
Combination therapies are not recommended for first-line use. Where a patient has contraindications to, or fails treatment with, topical beta-blockers they should be treated with monotherapy prostaglandin analogue, except where there are contraindications. Bayer et al, (2004) and Haverkamp et al (2004) showed that treating with latanoprost was more clinically effective than treating with adjunctive treatments. Therefore monotherapy with a prostaglandin analogue is preferable as a first line treatment when compared to adjunctive therapy. See below for second line treatment options.

Clinicians should assess efficacy of drops. If the patient does not have a satisfactory pressure reduction then the drop should be swapped rather than another drop simply added in. If another drop is added when efficacy of the first is not established then patients can be left on drops for the rest of their lives with no benefit.

**Treatment with beta-blockers**

**Effectiveness of treatment with beta-blockers**
A Cochrane review suggested that treatment of OHT with carteolol showed 'significantly worse visual field outcome' than treatment with timolol (Vass et al, 2007: 13). Timolol was shown in a meta-analysis of six studies to achieve marginally better outcomes than betaxolol, though the results of those studies were highly variable (mean difference being 0.07dB favouring timolol CI =0.43 - +0.57) (Vass et al, 2007: 10).

**Choice of beta-blocker for treatment of OHT or suspected COAG**
Given the above it is suggested that the first choice of beta-blocker in treatment of OHT or suspected COAG where the patient has a central corneal thickness of 555 – 590 micrometers, an IOP of >25 to 32 and are aged under 60, as per NICE guidance (NICE 2009) should be Timolol.
Treatment with prostaglandin analogues
In line with NICE guidance patients diagnosed with early or moderate COAG should be offered treatment with a prostaglandin analogue. Where there is progression of visual field loss and/or disc damage in one or both eyes, despite treatment, then surgery should be offered. If surgery is not an option other medications can be added in or exchanged with the PGA.

Effectiveness of different prostaglandin analogues
According to a meta-analysis by van der Valk et al for trials up to the end of 2003 the mean difference from baseline IOP measured at peak and trough is similar for bimatoprost, latanoprost and travoprost. That study concluded that the differences between drug choices were small and other variables such as patient characteristics, quality of life, compliance and costs should be considered when choosing treatment. Similarly a meta-analysis by Li et al published in 2006 concluded that side effects, compliance and cost are taken into consideration when deciding on appropriate therapy because the clinical effectiveness of prostaglandin analogues was similar.

Cost-effectiveness of treatment with prostaglandin analogues
In a review of costs of glaucoma Schmier et al state that ‘existing studies suggest that bimatoprost may be more cost effective than other agents’ (2007: 288). See appendix 1 for cost comparisons

Summary of first line drug choices
For new patients being started on medical therapy the first-line beta-blocker should be timolol 0.25% and the first-line prostaglandin analogue should be bimatoprost.

Second-line treatment options
Other classes of drugs (carbonic anhydrase inhibitors and sympathomimetics) are not recommended in the NICE guidelines as first-line treatments and are only licensed for second-line treatment. Miotics have largely been superceded by newer drugs. The NICE guidelines suggest where there is progression of glaucomatous changes then surgery or laser therapy should be offered (NICE 2009). However not all patients in this situation will be appropriate candidates for surgery and there is therefore a need for second-line treatment options.

Carbonic anhydrase inhibitors (CAIs) are in regular use and have a place as second line treatment where further lowering of IOP is desirable and surgery is not considered appropriate. Sympathomimetics should similarly be used as third line treatment where further lowering of IOP is desirable and surgery is not considered appropriate. The suggested CAI is Brinzolamide, which is cheaper than the other common CAI Dorzolamide, (in addition Dorzolamide is a three times a day preparation if not used in conjunction with a beta-blocker). The only regularly used sympathomimetic is the alpha-agonist Brimonidine. Where compliance is an issue with patients taking more than one topical glaucoma medication combination drops could be considered.
## Appendix 1

<table>
<thead>
<tr>
<th>Section 11.6</th>
<th>Patent expiry</th>
<th>Cost of 28 days (Drug Tariff June 2011)</th>
</tr>
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<tbody>
<tr>
<td>Bimatoprost once daily</td>
<td>2017</td>
<td>300mcg/ml 3ml bottle £10.30</td>
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<tr>
<td>Latanoprost once daily</td>
<td>Sept 2011</td>
<td>2.5ml bottle £12.48</td>
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<td>Tafluprost once daily</td>
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<td>28x UDV$s £16.25</td>
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<tr>
<td>Travoprost once daily</td>
<td>2014</td>
<td>2.5ml £9.98</td>
</tr>
</tbody>
</table>
References
NICE 2008a, Glaucoma: diagnosis and management of chronic open angle glaucoma and ocular hypertension, draft version for consultation. NICE guideline, NICE.
NICE 2008c, Glaucoma: diagnosis and management of chronic open angle glaucoma and ocular hypertension, draft version for consultation. Appendices A-G. National Collaborating Centre for Acute Care.
NICE 2009, Glaucoma: diagnosis and management of chronic open angle glaucoma and ocular hypertension, Methods, evidence and guidance. National Collaborating Centre for Acute Care.