Pharmacological management of primary open-angle glaucoma: second-line options and beyond

Webers C A, Beckers H J, Nuijts R M, Schouten J S

CRD summary
This review concluded that a combination of drugs from different first-choice classes in the treatment of primary open-angle glaucoma was associated with an additional intra-ocular pressure (IOP) decrease, but the exact magnitude of this effect remained unclear. Without further details on study quality and given the other methodological concerns it is difficult to judge the reliability of the authors’ conclusions.

Authors’ objectives
To assess the efficacy of second-line intra-ocular pressure (IOP) lowering medical options in the treatment of primary open-angle glaucoma when first-line therapy was effective but additional IOP-lowering was necessary.

Searching
MEDLINE, EMBASE and Cochrane Controlled Trials Register were searched from January 1990 to June 2007 in English, French, German and Dutch. The search terms were reported.

Study selection
Randomised clinical trials that evaluated second-line IOP-lowering medical options in patients with primary open-angle glaucoma were eligible for inclusion. Studies that had a run-in phase with a monotherapy drug followed by random assignment to one of the study groups were eligible for inclusion. Studies that used a combination of drugs to start IOP-lowering therapy were excluded. The review outcomes were change in IOP at peak and/or trough, or on the diurnal curve. The measure time point was one month from baseline or the closest time point thereafter, within a maximum of three months.

Most included studies had a run-in therapy of β-adrenoceptor antagonists. The treatment arm of included studies was the combination therapy of first-choice glaucoma drugs. First-choice glaucoma drugs included the following major classes: carbonic anhydrase inhibitors; hypotensive lipids; α2-adrenoceptor agonists; and β-adrenoceptor antagonists. Most treatment arms used combinations of a β-blocker with a carbonic anhydrase inhibitor, an α2-adrenoceptor agonist or a hypotensive lipid. The mean age of patients in included studies ranged from 54 to 71 years.

The authors state neither how the papers were selected for the review nor how many reviewers performed the selection.

Assessment of study quality
The authors did not state they assessed validity.

Data extraction
Data were extracted on the percentage mean changes and standard deviations (SDs) in IOP for peak and/or trough, or on the diurnal curve. The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
The studies were combined in a narrative synthesis, supported by accompanying data tables.

Results of the review
Forty-two randomised clinical trials were included in the review. The total number of patients in the review was not reported.

Carbonic Anhydrase Inhibitors (50 treatment arms): When topical carbonic anhydrase inhibitors were added to a β-blocker regimen, the additional decrease in IOP ranged from 11.3% to 23.1% at trough and from 10.2% to 23.1% at peak; the additional decrease in IOP on the diurnal curve ranged from 14.4% to 26.9%.
Hypotensive Lipids (16 treatment arms): When prostaglandin analogues were added to a β-blocker regimen, the additional decrease in IOP ranged from 25.5% to 26.0% at trough and from 23.5% to 27.7% at peak; the additional decrease in IOP on the diurnal curve ranged from 24.0% to 29.9%.

α2-Adrenoceptor Agonists (19 treatment arms): When α2-adrenoceptor agonists were added to a β-blocker regimen, the additional decrease in IOP ranged from 7.3% to 14.9% at trough and 15.7% to 27.6% at peak; the additional decrease in IOP on the diurnal curve in one treatment arm was 12.5%.

β-Adrenoceptor Antagonists (four treatment arms): When β-adrenoceptor antagonists were added to a prostaglandin analogue, the additional decrease in IOP at peak ranged from 19.2% to 20.2%; the additional decrease in IOP on the diurnal curve ranged from 10.6% to 15.0%.

Authors’ conclusions
The combination of drugs from different first-choice classes in the treatment of primary open-angle glaucoma was associated with an additional IOP decrease, but the exact magnitude of this effect remained unclear.

CRD commentary
This review’s inclusion criteria were clear. Several relevant databases were searched. Efforts were made to find published studies with language restrictions, but there was no apparent search for unpublished studies, thereby introducing the potential for both publication and language biases. It was unclear whether the authors made sufficient attempts to minimise errors and biases in the review process. A formal validity assessment was not carried out.

The authors did not assess the level of clinical heterogeneity between the included studies and it was difficult to assess whether the decision to adopt a narrative synthesis was appropriate. The authors’ conclusions reflected the evidence presented. However, without further details on study quality and given the other methodological concerns it is difficult to judge their reliability.

Implications of the review for practice and research
Practice: The authors stated that combination therapies of glaucoma drugs may be beneficial in patients requiring a low target IOP or a large decrease in IOP.

Research: The authors did not state any implications for research.

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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.