Efficacy and tolerability of nonpenetrating filtering surgery in the treatment of open-angle glaucoma: a meta-analysis
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CRD summary
This generally well-conducted review concluded viscocanalostomy and deep sclerectomy (non-penetrating eye surgery) were significantly less effective than trabeculectomy in treating open-angle glaucoma; deep sclerectomy plus mitomycin C was also less effective than trabeculectomy plus mitomycin C. However, viscocanalostomy and deep sclerectomy had fewer complications than trabeculectomy. Given limitations with the evidence base, the reliability of these conclusions is unclear.

Authors' objectives
To evaluate the efficacy and tolerability of non-penetrating filtering surgery compared with trabeculectomy in the treatment of open-angle glaucoma.

Searching
MEDLINE, EMBASE and the Cochrane Library were searched from 1966 to March 2008; search terms were reported. Bibliographies of each retrieved article and relevant reviews were handsearched. Abstracts of annual meetings of the American Academy of Ophthalmology, the Association for Research in Vision and Ophthalmology, and the meeting programmes and abstracts of the Royal College of Ophthalmologists, were also searched.

Study selection
Randomised controlled trials (RCTs) that compared non-penetrating filtering surgery versus trabeculectomy for the treatment of primary and secondary open-angle glaucoma were eligible for inclusion. Eligible trials had to evaluate efficacy outcomes or postoperative complications. Anti-metabolites could be used intraoperatively, but trials that used other intra-ocular surgery (such as phacoemulsification - emulsification of the lens) were excluded. Randomisation had to be prospective.

The primary efficacy outcome was complete success rate, defined as the proportion of patients with normal endpoint intra-ocular pressure without any anti-glaucoma surgery or medication after at least one year of follow-up. The secondary efficacy outcome was the proportion of patients with qualified success, defined as normal endpoint intra-ocular pressure with or without anti-glaucoma medication after at least one year of follow-up. Relevant postoperative complications included hyphaema, shallow/flat anterior chamber, hyptony, choroidal detachment, inflammation and cataract.

In included trials, non-penetrating filtering surgery interventions were deep sclerectomy, deep sclerectomy with collagen implant, deep sclerectomy with hyaluronate implant, deep sclerectomy plus mitomycin C, deep sclerectomy with hyaluronate implant plus mitomycin C, and viscocanalostomy. Trabeculectomy was the intervention in the control groups, with mitomycin C or anti-metabolites in some trials. Several different criteria for normal intra-ocular pressure were used across the included trials.

Two reviewers performed the selection.

Assessment of study quality
Methodological quality was assessed by two reviewers independently based on the method developed by Jadad and Schulz, assessing randomisation, blinding and withdrawal. However, the authors did not allocate a score related to randomisation method. Blinding was categorised as double-blind, single-blind or open label; the percentage of withdrawals was calculated. A quality score out of 5 was reported.

Data extraction
The numbers of events for each outcome were extracted in order to calculate rate difference (risk difference - RD) with
95% confidence intervals (CI) and number needed to treat (NNT)/number needed to harm using intention-to-treat analyses. Two independent reviewers performed the extraction.

**Methods of synthesis**
Risk differences were pooled using a random-effects model (DerSimonian and Laird) since heterogeneity was expected. Between-trial heterogeneity was determined using the Q statistic and $I^2$ test. Overall number needed to treat/number needed to harm and their ranges were calculated.

Sensitivity analyses were performed to evaluate the effect of trial design and publication date on complete success rates.

**Results of the review**
Seventeen relevant RCTs were identified (n=906 patients, range 17 to 168; n=1,071 eyes, range 22 to 258). Trial design included six single-blind RCTs and 11 open label RCTs. Six trials scored 4 out of 5 for quality, ten trials scored 3, and one trial scored 2. Withdrawals were generally low (range 0 to 3%). Follow-up ranged from three to 84 months.

**Efficacy**: The complete success rate was significantly lower for viscocanalostomy than trabeculectomy (RD -0.16, 95% CI -0.30 to -0.02; $I^2=0$%; three RCTs; NNT=7, range 3 to 50) and significantly lower for viscosanalostomy than trabeculectomy plus anti-metabolites (RD -0.39, 95% CI -0.53 to -0.24; $I^2=17.5$%; three RCTs; NNT=3, range 1 to 5). The qualified success rate was not significantly different for viscosanalostomy versus trabeculectomy (two studies) but it was significantly lower for viscosanalostomy versus trabeculectomy plus anti-metabolites (RD -0.19 to -0.01; three RCTs; NNT=7, range 3 to 100).

The complete success rate was also significantly lower for deep sclerectomy than trabeculectomy (RD -0.10, 95% CI -0.19 to 0.00; $I^2=0$%; five studies) and also significantly lower for deep sclerectomy plus mitomycin C than trabeculectomy plus mitomycin C (RD -0.16, 95% CI -0.32 to -0.01; $I^2=0$%; two RCTs; NNT=3, range 1 to 5). The qualified success rate was not significantly different for deep sclerectomy versus trabeculectomy (five RCTs) or for deep sclerectomy versus trabeculectomy plus mitomycin C (one RCT). Sensitivity analyses for complete success rate to find the effect of study design and earlier publication (before 2004) versus later studies (2004 and later) did not change the overall effects, although some results were no longer significant.

**Tolerability**: For viscosanalostomy versus trabeculectomy, rates of postoperative complications were significantly lower for hyphaema (RD -0.08, 95% CI -0.16 to 0.00; seven RCTs), shallow/flat anterior chamber (RD -0.16, 95% CI -0.23 to -0.09; five RCTs; NNT=7, range 4 to 12), hypotony (RD -0.12, 95% CI -0.24 to 0.00; seven RCTs), choroidal detachment (RD -0.15, 95% CI -0.24 to -0.05; three RCTs; NNT=7, range 4 to 20), and cataract (RD -0.09, 95% CI -0.16 to -0.03; five RCTs; NNT=12, range 6 to 34). There were also significantly lower rates of postoperative complications for deep sclerectomy versus trabeculectomy for hyphaema (RD -0.11, 95% CI -0.20 to -0.02; seven RCTs; NNT=10, range 2 to 12), shallow/flat anterior chamber (RD -0.22, 95% CI -0.34 to -0.09; seven RCTs; NNT=5, range 2 to 9), hypotony (RD -0.09, 95% CI -0.16 to -0.01; six RCTs; NNT=2, range 6 to 100), choroidal detachment (RD -0.16, 95% CI -0.25 to -0.07; four RCTs; NNT=7, range 4 to 15), but there was no significant difference for cataract (four RCTs).

**Authors’ conclusions**
Viscosanalostomy and deep sclerectomy were less effective than trabeculectomy in the treatment of open-angle glaucoma; deep sclerectomy plus mitomycin C was also less effective than trabeculectomy plus mitomycin C. However, viscosanalostomy and deep sclerectomy were associated with fewer complications than trabeculectomy.

**CRD commentary**
The review addressed a well-defined question in terms of participants, interventions, study design and relevant outcomes. Relevant databases were searched and some efforts were made to identify unpublished studies, but it was not clear if any language restrictions were applied, so some studies could have been missed. Publication bias was not assessed. Efforts were made to reduce error and bias during the review process, but it was not reported how differences in opinion were resolved.

Trial quality was assessed using suitable criteria. Relevant study details were reported but few patient details were
reported (such as age or gender). Statistical heterogeneity was assessed. The statistical method used for the meta-analysis of the RCTs seemed appropriate; sensitivity analyses were performed. Most of the included trials were relatively small and two thirds were open label.

The review was generally well-performed but, due to the relatively small sizes of the included trials and uncertainty about the optimal measurement of complete success, the extent to which the authors’ conclusions are reliable is unclear.

Implications of the review for practice and research

Practice: The authors did not state any implications for practice.

Research: The authors identified a need for further research to establish the best measure of complete success. Pragmatic RCTs evaluating the favourable effect of mitomycin C as an adjunct of non-penetrating filtering surgery in treating open-angle glaucoma were also needed; multi-centre double-blind RCTs with large sample sizes (500 patients or more) and long term follow-up of at least five years.

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