Effective Health Care Program

Ophthalmologic Conditions
Glaucoma

Comparisons of Medical, Laser, and Incisional Surgical Treatments for Open-Angle Glaucoma in Adults

Research Focus for Clinicians

In response to a request from the public regarding treatments for open-angle glaucoma (OAG), a systematic review was undertaken to summarize the evidence regarding the comparative effectiveness and safety of medications and laser and other surgical treatments for OAG in adults. This review only included studies with clearly defined OAG participants ≥40 years of age and did not cover juvenile/congenital, traumatic, neovascular, refractory, or inflammatory glaucoma. The review included 109 clinical studies (73 randomized controlled trials, 13 observational studies, and 23 systematic reviews) that were published through October 2011. This summary is provided to assist in decisionmaking along with a patient's values and preferences. Reviews of evidence should not be construed to represent clinical recommendations or guidelines. The full report is available at www.effectivehealthcare.ahrq.gov/glaucomatreatment.cfm.

Background

Glaucoma is a leading cause of irreversible visual impairment and blindness worldwide and is a result of damage to the optic nerve. In mild glaucoma, damage to the optic nerve may be asymptomatic. As damage increases, patients begin to experience difficulty with peripheral vision, contrast sensitivity, glare, adjustments between light and dark, and clear central vision. In its most severe form, glaucoma results in total, irreversible blindness.

Treatments for OAG focus on the reduction of intraocular pressure (IOP), which secondarily prevents the worsening of visual field loss and may prevent visual impairment and blindness. When deciding among medications and laser and incisional surgeries, a clinician may perform a patient-specific risk-benefit analysis to determine which intervention is most appropriate, given the stage of disease and the risk of progression. Unless contraindicated, clinicians commonly initiate therapy with pharmacologic agents.

Conclusion

In patients with OAG, current evidence suggests that medications and laser and incisional surgeries are effective in lowering IOP. Among medications, the prostaglandin analogs are consistently superior to the other classes in terms of their IOP-lowering ability and adverse effect profile. Laser trabeculoplasty (using an argon laser, selective laser trabeculoplasty, or a diode laser) has been shown to lower IOP in patients with OAG, regardless of the type of laser used. Both topical medications and laser trabeculoplasty similarly decrease the risk of visual field loss or optic nerve damage. With regard to incisional surgeries, trabeculectomy lowers IOP more than nonpenetrating surgical procedures like viscocanalostomy and deep sclerectomy, and pressure reductions are enhanced when trabeculectomy (but not other surgical methods) is performed with mitomycin-C. Patients treated medically and/or surgically (trabeculoplasty or trabeculectomy) were less likely to experience progression of visual field loss and optic disc damage than patients who did not receive treatment.

In general, harms from medications do not threaten vision and commonly consist of conjunctival hyperemia and ocular irritation. The possible complications of surgery are more significant than medications and may include infection, bleeding, cataract formation, choroidal effusions, hyphema, and flattening of the anterior chamber. These adverse effects are more common in trabeculectomy than in nonpenetrating surgeries and may be increased in the presence of mitomycin-C.

Current evidence does not address a direct link between reductions in IOP, visual field loss, or optic nerve damage and reductions in visual impairment or vision-related quality of life. The lack of a demonstrated direct link should not be interpreted to mean that reductions in IOP, visual field loss, or optic nerve damage are not important for reducing visual impairment or maintaining vision-related quality of life, but rather that studies demonstrating this direct linkage are not available. The time required to establish relative differences in patient outcomes requires studies with lengthy followup, which are not currently available.

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Clinical Bottom Line

Lowering IOP

Medical Interventions

Overall, strong evidence from other systematic reviews (50 trials) found that:

- As single agents, prostaglandin analogs are the most effective at lowering IOP.
- Prostaglandin analogs appear to be similar in their ability to lower IOP.
- Prostaglandin analogs lower IOP more than other agents, including brimonidine (mean difference of 1.64 mmHg; 4 trials), dorzolamide (mean difference of 2.64 mmHg; 3 trials), and timolol (5% greater at 6 months; 4 trials).
- Dorzolamide and timolol in combination lower IOP the same amount as a prostaglandin analog alone.

Surgical Interventions

- Laser trabeculoplasty effectively lowers IOP regardless of the type of laser used. ●●○
- Trabeculectomy more effectively reduces IOP than nonpenetrating surgeries such as viscocanalostomy and deep sclerectomy. ●●○
- Intraoperative mitomycin-C enhances IOP reduction when used with trabeculectomy but not when used with other surgical methods. ●●○
- These surgical comparisons demonstrated similar IOP-lowering effects (●●○):
  - Trabeculectomy performed at nasal, superior, or temporal ocular sites
  - Trabeculectomy with a fornix versus limbus conjunctival incision
  - Laser suture lysis versus adjustable sutures after fornix-based trabeculectomy
  - Fornix-based trabeculectomy plus either mitomycin-C or an Ologen™ implant
  - Limbus-based trabeculectomy with or without an intraoperative amniotic membrane graft
  - Trabeculectomy plus mitomycin-C with or without an Ex-PRESS™ minishunt
- Two-site versus one-site phacotrabeculectomy may be associated with greater reductions in IOP. ●●○
- The IOP-lowering effect of phacotrabeculectomy is not affected by the location of the conjunctival incision or the presence or absence of a peripheral iridectomy. ●●○
- Evidence was too limited to determine the comparative effectiveness of aqueous drainage devices in OAG. ○○○

Medical Versus Surgical Interventions

- Incisional surgery lowers IOP more than laser surgery or medications. ●○○
- Initial treatment with lasers tends to reduce the need for medications to achieve the same IOP. ●○○

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Circadian IOP

Medical Interventions

In keeping with investigations exploring the blunting of circadian fluctuations of IOP in an effort to reduce optic nerve damage, the following evidence was reviewed.

- Prostaglandin analogs (latanoprost, bimatoprost, and travoprost), a beta-adrenergic blocker (timolol), an alpha-adrenergic agonist (brimonidine), and a carbonic anhydrase inhibitor (dorzolamide) all lowered circadian IOP throughout a 24-hour cycle. ●○○
- Over a 24-hour cycle, prostaglandin analogs (latanoprost, bimatoprost, and travoprost) appear to lower circadian IOP more than a beta-blocker (timolol), a topical carbonic anhydrase inhibitor (dorzolamide), and an alpha-adrenergic agonist (brimonidine). ●○○
- Results for comparisons among prostaglandins were inconsistent; however, the reported difference among prostaglandins in the magnitude of IOP lowering was about 1 mmHg. ●○○

Preventing or Slowing Progression of Optic Nerve Damage and/or Visual Field Loss

Medical Interventions

- Overall, strong evidence from a Cochrane review (N = 4,979 patients; 26 trials) that included the Early Manifest Glaucoma Trial (n = 255 patients) and the Ocular Hypertension Treatment Study (n = 1,636 patients) found that medical treatment decreased the rate of visual field loss and progressive optic nerve damage.
- Evidence from 19 primary studies suggests treatment of ocular hypertension with medicines preserves visual fields better than no treatment. ●○○
- The Low-Pressure Glaucoma Treatment Study found that fewer patients treated with brimonidine (9.1%) had progression of visual field loss than those treated with timolol (39.2%; $p = 0.001$) ●○○

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Strength of Evidence Scale

(Applies Only to Analysis of Primary Research Studies)

High:	●●●	High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect.
Moderate:	●●○	Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.
Low:	●○○	Low confidence that the evidence reflects the true effect. Further research is likely to change our confidence in the estimate of effect and is likely to change the estimate.
Insufficient:	○○○	Evidence is either unavailable or does not permit a conclusion.

Clinical Bottom Line *(Continued)*

Preventing or Slowing Progression of Optic Nerve Damage and/or Visual Field Loss *(Continued)*

***Medical Interventions** (Continued)*

- All other primary studies were of insufficient size or duration to provide additional evidence about the effects of medical treatments on visual field loss and the progression of optic nerve damage. ○○○

Surgical Interventions

- Studies comparing surgical interventions did not report outcomes related to optic nerve damage or visual field loss. ○○○

Medical Versus Surgical Interventions

- Overall, strong evidence was provided from three systematic reviews (10 trials) that indicates:
  - Patients treated medically and/or surgically (trabeculoplasty or trabeculectomy) were less likely to experience progression of visual field loss and optic nerve damage than patients who did not receive treatment.
  - The two systematic reviews comparing medical versus surgical interventions did not include contemporary medications (e.g., prostaglandin analogs). In four out of five trials, patients treated with older medications had greater progression of visual field loss when compared with those randomized to laser trabeculoplasty or trabeculectomy. These results should be interpreted cautiously in light of the increased effectiveness of prostaglandin analogs.
- Evidence from included primary studies was insufficient to distinguish a difference in visual field loss between surgical techniques and medications. ○○○
- For advanced glaucoma, evidence from included primary studies was insufficient to guide clinical decisionmaking regarding initial trabeculectomy or medication. ○○○

Reducing Overall Visual Impairment

- Evidence was insufficient to determine the comparative effects of medical, surgical, or medical versus surgical treatments on visual impairment. ○○○
- Limited evidence suggests that the effects on the secondary outcome of visual acuity were similar for all laser and other surgical interventions studied. ●○○

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Comparative Adverse Effects

The evidence did not permit an analysis of the strength of evidence for comparative adverse effects across interventions. There were a number of issues with assessing adverse effects. For example, adverse effects were not the primary outcome for the studies, meaning that the studies were not powered to detect differences.

Below is a review of the adverse effects reported for the different interventions.

Medical Interventions

- Conjunctival hyperemia (redness) is the most commonly reported adverse effect among the observational studies of medical treatment for OAG.
- Latanoprost is less likely to cause ocular redness among the prostaglandin analogs; however, as a class, prostaglandins may produce a greater degree of ocular redness than does timolol.
- Timolol is more likely to result in systemic side effects such as shortness of breath or bradycardia.

Surgical Interventions

- Trabeculectomy produces more hypotony, hyphema, shallow anterior chambers, cataract, and choroidal detachment than the nonpenetrating procedures of deep sclerectomy or viscocanalostomy.
- The risk of epithelial toxicity was 5.85 times as great in patients who underwent primary trabeculectomy and received 5-fluorouracil postoperatively.
- There is no clear difference in adverse effects between one-site versus two-site phacotrabeculectomy.
- The adverse effects associated with glaucoma drainage devices have not been adequately compared with the adverse effects of other procedures used to treat OAG.
- Adverse effects reported from aqueous shunts include choroidal hemorrhage, choroidal complications, corneal complications, strabismus, loss of light perception, phthisis, tube exposure, retinal detachment, and infection.

Medical Versus Surgical Interventions

- Trabeculectomy is associated with cataract worsening and an increased need for cataract surgery over time when compared with medical treatments for glaucoma.
- Intraocular surgery rarely results in severe vision loss due to infection and/or bleeding. These risks are not associated with medical or laser treatments.

Patient-Related Quality of Life

Evidence from included studies did not address a direct link between treatments for OAG and relative changes in patient-reported outcomes such as vision-related quality of life due to the unavailability of studies with sufficiently long-term followup. Included studies gave the following results:

- In two studies of medical interventions, patients preferred the medication that was administered less frequently.
- According to the Collaborative Initial Glaucoma Treatment Study, the fear of blindness in newly diagnosed patients (34%) was significantly reduced 5 years after medical or surgical treatment (11%).

Gaps in Knowledge

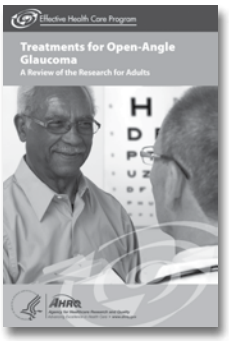
- A direct association between treatment for OAG and visual impairment and/or patient-reported outcomes needs to be established.
- Additional evidence is needed on the relative risks and benefits of current medical and surgical treatments for OAG.

What To Discuss With Your Patients and Their Caregivers

- The different types of treatment for glaucoma
- The benefits and adverse effects of medicines, laser treatments, and surgeries for OAG
- The severity of the patient's glaucoma and need for treatment
- The importance of adherence to medicine regimens
- The importance of regular and consistent followup with an ophthalmologist or glaucoma specialist to monitor disease progression over time
- Patient preferences regarding the types of treatment
- The cost of medicines and surgical treatments

Resource for Patients

Treatments for Open-Angle Glaucoma, A Review of the Research for Adults is a free companion to this clinician research summary. It can help patients talk with their health care professionals about the many options for treating OAG. It provides:



- Explanations of glaucoma and its causes
- Explanations of medical and surgical treatments
- Current evidence of the effectiveness and adverse effects of different treatments
- Questions for patients to ask their doctor

Ordering Information

For electronic copies of *Treatments for Open-Angle Glaucoma, A Review of the Research for Adults*, this clinician research summary, and the full systematic review, visit www.effectivehealthcare.ahrq.gov/glaucomatreatment.cfm. To order free print copies of this clinician research summary, call the AHRQ Publications Clearinghouse at 800-358-9295.

Source

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