



A REVIEW OF THE MOST IMPACTFUL GLAUCOMA STUDIES



How will you use the information in the management of your patients?

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Glaucoma is a disease characterized by a progressive optic neuropathy that can be caused by a variety of etiologies, including both primary and secondary mechanisms, with the main modifiable risk factor being high IOP. Visual field defects, along with structural (both OCT and optic nerve head) and functional changes are typically seen. We rely on an abundance of evidence to guide our management decisions; therefore, it behooves us to be familiar with the main points of the most recent and relevant literature.

This article provides a brief review of the important early glaucoma studies and gets a bit more in-depth with the latest studies.

THE EARLY STUDIES OHTS

The Ocular Hypertension Treatment Study (OHTS) found that topical ocular hypotensive medications were effective in preventing or postponing the onset of primary open-angle glaucoma (POAG) in patients with ocular hypertension. A 20% reduction in IOP led to a 4.4% probability of

developing POAG, compared to 9.5% in the group that received no treatment.¹

EMGT

The Early Manifest Glaucoma Trial (EMGT) concluded that immediate treatment to reduce IOP by 25% in patients diagnosed with open-angle glaucoma (OAG) delayed progression of the disease, as the treatment group showed 45% progression compared with 62% progression in the control group. Beneficial treatment effects were observed in older and younger patients, in those with normal-tension

glaucoma (NTG), high-tension glaucoma, and in early and later stages of the disease.²

CNTGS

The Collaborative Normal-Tension Glaucoma Study (CNTGS) found that a 30% reduction in IOP helped prevent progression of NTG. A faster rate of progression was seen in women, patients with migraine headaches, and patients with presence of disc hemorrhages.³

CIGTS

The Collaborative Initial Glaucoma Treatment Study (CIGTS) demonstrated that both topical therapy and trabeculectomy were effective in lowering IOP. The 5-year results showed that surgery lowered IOP to between 14 mm Hg and 15 mm Hg on average, compared with between 17 mm Hg and 18 mm Hg achieved with topical therapy. IOPs were lower in the surgical group at all postoperative visits.⁴

AGIS

The Advanced Glaucoma Intervention Study (AGIS) was a 10-year multi-part study that found that patients who had initial trabeculectomy showed a greater decrease in IOP compared with initial argon laser trabeculoplasty (ALT). The AGIS Report 9 concluded that Black patients had a lower risk

of progression when treated with ATT (ALT, trabeculectomy, trabeculectomy) compared with White patients, who had higher success with TAT (trabeculectomy, ALT, trabeculectomy).⁵

THE NEWER STUDIES

SALT

The Steroids After Laser Trabeculoplasty (SALT) study examined whether short-term use of topical steroid therapy and nonsteroidal antiinflammatory drugs (NSAIDs) affected the efficacy of selective laser trabeculoplasty (SLT).⁶ This double-masked, randomized, placebo-controlled clinical trial included 96 eyes. Patients with IOPs higher than 18 mm Hg were randomized into three groups. Each patient was instructed to take prednisolone 1%, ketorolac 0.5%, or saline tears four times daily for 5 days starting on the day they had SLT performed. Outcomes were measured at 1, 6, and 12 weeks.

No statistically significant difference in IOP reduction was noted at week 6 between the groups. However, significantly greater IOP reduction was measured at week 12 in patients treated with prednisolone and ketorolac. This study showed that steroid or NSAID drops after SLT may improve IOP reduction. Long-term studies would

be beneficial in determining lasting effects. These results suggest that eye care providers should consider placing patients on a corticosteroid or NSAID drop after SLT to improve the efficacy of IOP reduction.

ZAP

The Zhongshan Angle Closure Prevention (ZAP) trial assessed the efficacy of laser peripheral iridotomy (LPI) in preventing primary angle-closure glaucoma or acute angle closure in a Chinese population of primary angle closure suspects.⁷ This randomized controlled trial included 889 patients between 50 and 70 years of age. One eye was randomly selected to receive an LPI, while the fellow eye was untreated to assess the natural history of angle closure suspects. The main outcome was the incidence of primary angle-closure disease by 72 months, demonstrated with three endpoints: (1) increased IOP above 24 mm Hg, (2) development of peripheral anterior synechiae in at least 1 clock hour, or (3) an episode of acute angle closure.

Results demonstrated that primary angle-closure disease occurred in 19 treated eyes compared with 36 untreated eyes, which was statistically significant. The corresponding incidence was 4.19 per 1,000 eye-years for treated eyes and 7.97 per 1,000 eye-years for control eyes. Eyes treated with LPI showed a 47% reduction in risk of progression to primary angle closure compared with untreated eyes. Nevertheless, the rate of developing angle-closure disease in primary angle-closure suspects was less than 1% per year. It was also estimated that 44 people need to be treated to prevent one case of angle closure over 6 years.

Due to the low incidence of angle closure, the ZAP study concluded that LPI, despite its effective prophylactic effect, should not be performed routinely for primary-angle closure suspects. Instead, phacoemulsification

AT A GLANCE

- ▶ The SALT study showed that steroid or NSAID drops after SLT may improve IOP reduction.
- ▶ Five-year results of the CIGTS study showed that surgery lowered IOP to between 14 mm Hg and 15 mm Hg on average, compared with between 17 mm Hg and 18 mm Hg achieved with topical therapy.
- ▶ The LiGHT study demonstrated that SLT should be offered as an initial treatment for patients with OAG and ocular hypertension over topical therapy alone.

lens extraction has shown superiority in angle-closure glaucoma over LPI, which is a beneficial alternative producing equivalent outcomes. Clinicians should weigh the risks and benefits for all treatment options in patients who are primary angle-closure suspects.

EAGLE

The Effectiveness of early lens extraction for the treatment of primary angle-closure glaucoma (EAGLE) study was a multicenter, randomized controlled trial studying the efficacy of clear lens extraction compared to LPI and topical medical therapy as first-line treatment in patients with primary angle-closure glaucoma or angle closure with elevated IOP.⁸ Inclusion criteria were patients 50 years of age or older, with no cataracts, IOP > 30 mm Hg, or primary angle-closure glaucoma. Outcomes were assessed at baseline and up to 36 months after randomization. The primary endpoints were IOP, patient-reported health status, and cost-effectiveness ratio per quality-adjusted life year gained at 36 months after treatment.

Mean health status score, measured with the European Quality of Life-5 Dimensions questionnaire, was higher in the clear lens extraction group. IOP was 1.18 mm Hg lower in the clear lens extraction group compared with the LPI group. It was also found that significantly fewer patients who received clear lens extraction needed any additional surgical or topical treatment to control IOP. Only 21% of the clear lens extraction group received additional treatment to control IOP, compared with 61% of the LPI group, who received at least one glaucoma drop.

Overall, the EAGLE study concluded that clear lens extraction should be considered first-line therapy, as it shows greater efficacy and

cost-effectiveness over LPI for patients with angle-closure glaucoma or angle closure suspects with elevated IOP.

LIGHT

The Laser in Glaucoma and ocular HyperTension (LiGHT) study compared SLT to topical glaucoma therapy as first-line treatments for OAG and ocular hypertension.⁹ This randomized controlled trial included treatment-naïve patients with OAG or ocular hypertension. The study outcomes were health-related quality of life at 3 years, cost-effectiveness, clinical effectiveness, and safety.

A total of 718 patients were randomized to receive SLT or eye drops. SLT using a gonioscopy lens was delivered to 360° of the trabecular meshwork, with 100 shots of energy between 0.3 mJ to 1.4 mJ. The eye drop group included multiple classes of topical therapies. Prostaglandin analogues were first line, beta blockers were second line, topical carbonic anhydrase inhibitors were third line, and alpha agonists were fourth line. Combination drops were also used. At 36 months, no statistically significant difference in health-related quality of life scores and clinical outcomes were found between both groups. However, 74.2% of patients who received SLT did not require drops to meet their target IOP at 36 months. Patients with SLT were also within their target IOP at more visits (93%) than patients in the eye drop group (91.3%). In the eye drop group, 5.8% of patients had disease progression compared to 3.8% in the SLT group. Glaucoma surgery was not required in any patients who received SLT compared to 11 patients in the eye drop group.

Over 36 months, SLT was shown to be more cost-effective than treatment with eye drops only. The LiGHT study demonstrated that SLT should be offered as an initial treatment

for patients with OAG and ocular hypertension over topical therapy alone. This supports a change in the usual paradigm of glaucoma treatment and clinical practice.

KEEP AN OPEN MIND

Glaucoma is a complex disease to diagnose and manage. Laser therapy, topical eye drops, drug delivery devices, and surgical intervention continue to comprise our treatment and management options. Although past studies have shaped our existing treatment paradigm, future studies will no doubt enhance our understanding of the most effective and efficient ways to treat this disease. ■

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