Primary Open-Angle Glaucoma (POAG) Treatment & Management

Updated: May 18, 2017
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TREATMENT

Medical Care

Major drug classes for medical treatment of POAG include the following: alpha-agonists, beta-blockers, carbonic anhydrase inhibitors, miotic agents, and prostaglandin analogs.

Various classes of glaucoma medications, including rho kinase inhibitors, adenosine analogs, and nitric oxide–donating drops that aim at increasing trabecular outflow, are getting closer to FDA approval.

Medical marijuana is not indicated for glaucoma treatment, as marijuana lowers IOP minimally and its duration of action is very short. In the future, topical derivatives that affect cannabinoid M receptors governing aqueous dynamics may be effective, but this is still under early investigation.

The other drug classes mentioned above have much more documented duration of action and efficacy without the systemic cannabinoid adverse effects. Furthermore, other options to treat ocular pain from end-stage glaucoma have arisen (eg, trans-scleral or endoscopic cyclophotocoagulation, absolute alcohol [ethanol] or chlorpromazine retrobulbar injections), which directly and more effectively alleviate the problem than in the past when marijuana was used for eye pain from end-stage glaucoma.

Legal justification of glaucoma as an indication for systemic medical marijuana use is scientifically and medically improper, as well as unethical; education of the public and legislators is needed on this subject.

Some physicians incorrectly treat all elevated IOPs over 21 mm Hg with the above topical medications. Other physicians do not treat unless evidence of optic nerve damage exists, although nerve fiber layer loss of up to 40% may occur before visual field defects occur, so do not treat based on visual field testing alone. Most physicians select and treat those patients thought to be at greatest risk for POAG damage and/or progression (most common approach). See History for a list of risk factors for glaucomatous field loss.

In any case, the goal of treatment is reduction of the pressure before it causes progressive loss of vision. Considering the high average monthly cost of glaucoma medication, along with the possible risks of adverse effects or toxic reactions from drugs, inconvenience of use, and incidence of noncompliance, a strong reason not to treat indiscriminately exists.

Several questions should be asked when considering treatment, to include the following: Is the elevated pressure significant? Will this patient develop visual loss if left untreated? Is the treatment worth the risk of adverse effects of the medications?

One should consider treatment more strongly if the patient reliability or the consequences of missing field loss is an issue (eg, poor reliability on visual field examination, 1-eyed patient, poor availability for follow-up care, younger patient, patient whose optic nerve is difficult to visualize, history of vascular occlusion).

Treatment is highly recommended if signs of damage consistent with glaucomatous optic neuropathy (eg, disc hemorrhage; visible nerve fiber layer defects; notching or vertical ovalization of the cup; asymmetric cupping, especially if >0.7) are observed.

Progressive cupping, even in the absence of visual field loss, can be glaucoma and should be treated as such, although systemic and neurologic workup/correlation for other disorders, including possible neuroimaging studies, should be considered, particularly if there are other nonophthalmologic symptoms. Otherwise, it depends on the assessment of risk factors and benefit of therapy to the patient, as to whether therapy should be initiated.

Discussion with the patient about the pros and cons of treatment versus observation should be completed. Individualization of therapy is the key; an ideal pressure in one patient may cause glaucomatous damage in another patient. Risk factors, systemic conditions, life expectancy of the patient, quality of life issues, and the patient's desire for therapy should be weighed when considering treatment.

Due to the high risk of optic nerve damage, most ophthalmologists treat if pressures are consistently above 28-30 mm Hg. If treatment is based on a high IOP only, then it should be ensured that the risks of treatment do not exceed the risk of the disease. Other reasons to treat include such symptoms as halos, blurred vision, or pain, or recent elevation of IOP, with continuing elevation on successive visits.

Initiation of a monocular trial (see Medication) may be useful in helping to decide whether or not to treat (ie, if the medication is effective in achieving good pressure reduction without adverse effects, which may argue in favor of treatment, instead of just observation).

Considering all of the above, no consensus exists on what is the appropriate medical treatment for preventing or delaying the damage due to POAG when a patient has only elevated IOP and no other signs of POAG. To date, no one has been able to define conclusively which subgroups will develop damage if left untreated, as opposed to those who will not sustain damage even if not treated.

The question of medical therapy versus observation in patients with solely elevated IOP is being addressed in the OHTS, an ongoing multicenter randomized clinical trial. The OHTS is a multicenter, prospective, randomized, controlled, clinical trial studying over 1600 subjects to evaluate the safety and efficacy of medical treatment in preventing or delaying onset of visual field loss and/or optic nerve damage in patients with OHT who are at moderate risk for developing POAG. Their medical therapy goal for the treated group is stepped therapy to reduce IOP by at least 20% from the average baseline IOP with its treated absolute value of 24 mm Hg or less. So far, their results show a 10% risk over 5 years of developing glaucoma in those patients with baseline IOP of 24-31 mm Hg. This risk was reduced to 5% with medical therapy. The OHTS has also revealed the importance of pachymetry as a diagnostic tool as well as in the workup.

Several sources agree on this initial goal of 20-25% reduction, while some specialists feel that more absolute numbers of less than 15 should be the goal of treatment. See History for a list of risk factors for glaucomatous field loss.

In any case, the target IOP should be reevaluated periodically, and regular review of IOP trends should be performed to determine whether the patient is consistently maintaining that goal.

According to Preferred Practice Patterns published by the American Academy of Ophthalmology, the interval between follow-up visits should be determined based on whether the target IOP has been achieved and whether glaucoma is progressing. If there is progression, treatment should be adjusted and the patient should be monitored.
bleb with resultant transient IOP elevation, loss of 1 or more lines of visual acuity, and increased risk of cataract formation.

Risks and complications of filtering surgery include the following: hypotony, blebitis/endophthalmitis, hyphema, suprachoroidal hemorrhage or effusions, encapsulation of the antimitabolites (eg, 5-fluorouracil, mitomycin C) may be applied during or after surgery to decrease fibroblast proliferation and scar formation.

Either releasable sutures or laser suture-lysis may be used to control aqueous drainage and corresponding IOP postoperative. Alternatively, to maximize surgical success, this alternate outflow pathway is created to increase passage of aqueous from the anterior chamber to the subconjunctival space, creating a filtering bleb and, thereby,

A superficial flap of sclera is dissected anteriorly to the trabecular meshwork, and a section of trabecular meshwork is removed underneath the flap.

Trabeculectomy surgery usually is performed after MTMT and ALT have failed to control IOP adequately. If IOP is so high that ALT and SLT are likely to be ineffective in reducing fluid outflow and thereby lowering IOP.

The specific mechanism of this improved outflow is unknown, but one hypothesis is up-regulation of trabecular endothelial cells. IOP reduction obtained is usually in the 7-10 mm Hg range, and it may last up to 3-5 years following ALT.

A study by Heijl et al studied patients with low IOP levels before ALT. The study found that IOP before ALT significantly influenced the IOP reduction produced by ALT, in that a much larger decrease was observed in eyes with higher IOP before ALT.[19]

Unfortunately, the decrease in IOP is not usually permanent. Approximately 10% of treated patients will return to pretreatment IOP for each year following treatment.

Complications include a brief, but potentially significant, increase in IOP after the procedure (therefore, alpha-agonists often are used either preoperatively or postoperatively for prophylaxis of this occurrence); transient iritis or corneal opacities; peripheral anterior synechiae; and hyphema.

ALT usually is pursued after MTMT has been reached, but it may be performed sooner in the treatment algorithm if pseudoexfoliation or pigmentary glaucoma is present, or if the patient is of black ethnicity, because laser therapy may be most effective in these individuals.

Selective laser trabeculoplasty

Selective laser trabeculoplasty (SLT) uses a Q-switched 532 Nd:YAG laser to selectively target pigmented cells of the trabecular meshwork in a nonthermal manner, increasing fluid outflow and thereby lowering IOP.

The 3-nanosecond high-energy specific wavelength of light used induces the same cell replacement mechanism as traditional ALT but without the destructive burning and obliteration of structural support tissue in the meshwork. The short pulse of the laser does not allow time for heat to spread to other cells. SLT delivers just enough energy to heat melanin to the point that it releases cytokines that trigger macrophage recruitment as well as other changes leading to IOP reduction.

The laser beam bypasses surrounding tissue leaving it undamaged by light. Unlike ALT, SLT can be repeated several times. Whereas patients treated with ALT can receive only 2 treatments in their lifetime, patients treated with SLT can receive more than 2 lifetime treatments.

SLT requires a specially designed laser, as follows:

- A short pulse to allow for thermal relaxation
- Precise wavelength to optimal melanin absorption
- Sufficient energy to heat melanin to the point that it releases cytokines
- Sufficient spot size to ensure full coverage at the trabecular meshwork

Trabeculectomy

Trabeculectomy surgery usually is performed after MTMT and ALT have failed to control IOP adequately. If IOP is so high that ALT and SLT are likely to be ineffective in reaching target IOP, then proceeding from MTMT to penetrating surgery may be indicated.

A superficial flap of sclera is dissected anteriorly to the trabecular meshwork, and a section of trabecular meshwork is removed underneath the flap.

This alternate outflow pathway is created to increase passage of aqueous from the anterior chamber to the subconjunctival space, creating a filtering bleb and, thereby, lowering IOP.

Either releasable sutures or laser suture-lysis may be used to control aqueous drainage and corresponding IOP postoperative. Alternatively, to maximize surgical success, antimetabolites (eg, 5-fluorouracil, mitomycin C) may be applied during or after surgery to decrease fibroblast proliferation and scar formation.

Risks and complications of filtering surgery include the following: hypotony, blebitis/endophthalmitis, hyphema, suprachoroidal hemorrhage or effusions, encapsulation of the bleb with resultant transient IOP elevation, loss of 1 or more lines of visual acuity, and increased risk of cataract formation.
With the risk of severe complications from trabeculectomy and the need for frequent postoperative follow-up care (ie, usually weekly for 1 month, initially), some patients with transportation, financial, or long-distance issues concerning postoperative follow-up care may be better served by tube shunt surgery instead. See the Tube versus Trabeculectomy Study below.

Vision loss may be a serious complication after trabeculectomy, with severe and ongoing unexplained loss (“snuff-out”) experienced by as many as 2% of patients. Attendant risk factors such as split fixation on visual fields prior to surgery, preoperative number of quadrants with split fixation, and postoperative choroidal effusions with eventual resolution are possible.²⁰

Drainage implant (ie, seton/tube/shunt) surgery

Generally, this procedure is performed after multiple attempts at successful trabeculectomy have failed.

A tube is placed in the anterior chamber to shunt aqueous to an equatorial reservoir, and then posteriorly to be absorbed in the subconjunctival space.

Types of implants include Molteno, Baerveldt, Ahmed, and Krupin, as follows:

- Most shunts function by allowing passive drainage of aqueous from the anterior chamber.
- The Molteno implant consists of a silicone drainage tube, which is connected to 1 or 2 acrylic plates that are sutured to the sclera.
- The Baerveldt implant is available with larger plates with increased reservoir size. The seton (tube) connected to the reservoir usually is tied off with an absorbable suture, allowing flow to initiate 4-6 weeks postoperative once some conjunctival wound remodeling has taken place, thereby reducing the risk of immediate postoperative hypotony.
- The Ahmed and Krupin implants have 1-way valves, which are designed to maintain pressure above 8 mm Hg. These implants may reduce the risk of hypotony, a complication of nonvalved shunts in the early postoperative period.

Because of less numerous postoperative visits, tube shunts may be indicated as primary surgery when patients are unable to come as frequently for follow-up care (because of transportation, financial, or long-distance issues). This can be a particular concern in rural areas that cover large distances.

A valved shunt may also be indicated as primary surgery if a patient has a strenuous job or other activities that require strenuous exertion. Severe exertion may cause a significant Valsalva maneuver, significantly increasing venous pressure postoperatively, which could result in a delayed suprachoroidal hemorrhage and possible severe loss of vision.

The Tube versus Trabeculectomy Study has been undertaken to see if glaucoma tube shunt surgery may actually be a viable first-line alternative to (or even surpass) trabeculectomy surgery.

One-year data have shown nonvalved tube shunt surgery was more likely to maintain IOP control and to avoid persistent hypotony or reoperation for glaucoma than trabeculectomy at 1 year, although both procedures produced similar IOP reduction. Failure rates during 5 years of follow-up were 29.6% in the tube group and 46.9% in the trabeculectomy group.

Less supplemental medical therapy has been needed in the trabeculectomy group at 1 year; however, at 5 years, there was no difference.

The incidence of postoperative complications at 1 year was higher in the trabeculectomy group. Serious complications resulting in reoperation and/or vision loss occurred with similar frequency in both groups at 1 year. The reoperation rate for IOP reduction was higher in the trabeculectomy group than in the tube group at 5 years.

Ciliary body ablation

Postoperative pain and inflammation are common complaints. Loss of 1 or more lines of visual acuity has been reported. Phthisis is a concern after this procedure, although it has not been reported as of yet after the diode laser method of cycloablation.

This procedure is indicated as a last resort for patients who have failed medical management and other surgeries or for those patients who have limited visual potential (often 20/200 or less).

By destroying a portion of the nonpigmented ciliary epithelium, aqueous humor production is limited.

The ciliary body epithelium can be destroyed by cyclocryotherapy, diathermy, ultrasound, transscleral Nd:YAG or diode laser (known as cyclophotocoagulation), or a newer endoscopic laser (EndoOptics, Inc.).²¹

Several of the newer surgical procedures are promising, but many ideas have been tried before and few have stood the test of time. Generally, the less complications, the less effective in lowering IOP. There is the possibility that visual loss can be better prevented, with fewer complications, and treatment can be tailored to the individual patient. If simple, safe procedures become available, surgery could be performed earlier in the disease process and adherence to medications could become less problematic.

The ideal glaucoma procedure would use the healthy portions of the outflow system and bypass the diseased portions; control IOP without infection and other risks of a thin-walled bleb; reduce the risk of hypotony during the perioperative period, with less postoperative care management and complications, as compared with trabeculectomy and setons; and provide adequate IOP control for the life of the patient.

Many innovative glaucoma surgical techniques and devices are on the horizon. Interest in this new frontier is because of the lack of an existing, ideal glaucoma procedure despite decades of research. Many devices are not yet approved by the FDA for use in the United States.

Newer techniques

Deep sclerectomy/viscocanalostomy/with or without collagen implant – This is probably not as effective as trabeculectomy and is technically more difficult, but it is associated with less complications.

360-degree suture canaloplasty (iScience) – This is a useful alternative in infants (with congenital glaucoma or juvenile glaucoma) to trabeculectomy. In adults, suture under tension left in the Schlemm canal to further open the trabecular meshwork (similar mechanism to miotics).

New devices

New devices are as follows:

- ExPress shunt (Alcon) (see below)
  - Erosion problems if used without scleral flap
  - Now mainly used underneath trabeculectomy flap to better regulate flow through sclerostomy
  - Advantage of avoiding surgical iridectomy in patients at high risk of bleeding
  - Easy to learn, appears effective, and complication rate that is similar to that of trabeculectomy
- iStent (Gluako) (see below)
• Shunt device from the anterior chamber into the Schlemm canal
  • Internal placement approach in association with cataract surgery
  • May need multiple devices placed
  • Still undergoing continuing research for long-term results

• Cypass Microstent® (Alcon) (see below)
  • Shunt device from the anterior chamber into the suprachoroidal space
  • Internal placement approach
  • Recently approved by the FDA

• Solx® gold suprachoroidal space microshunt (Solx) (see below)
  • Shunts fluid from the anterior chamber into the suprachoroidal space via gold microchannels
  • External placement approach
  • Possibly titratable effect with titanium-sapphire laser to modify microchannel size
  • US clinical trials are ongoing

• Trabectome® (NeoMedix) (see below)
  • FDA approved
  • Ablates all of the trabecular meshwork for 90 degrees to 180 degrees via electrocautery and aspiration of the internal wall of the Schlemm canal
  • Similar idea to goniotomy but prevents rescarring of the Schlemm canal edges, as all tissue is removed
  • May have a place between trabeculoplasty and anterior filtering operations
  • Safer than trabeculectomy or tube shunt but may be less effective
  • Needs more long-term data on complication rate and persistence of effect

Consultations

Neuro-ophthalmology consultation may have a role in those patients who are experiencing progressive visual loss that does not appear to follow a typical glaucomatous pattern or if there are systemic symptoms or complaints.

Activity

Some studies show that a moderate amount of exercise can decrease IOP in both POAG patients and normal individuals. Whether it results in actual long-term IOP control and prevention of visual loss has yet to be determined.

Medication