Advanced glaucoma treatment: Diagnostics, pharmaceuticals, and surgical options

The role of diagnostics, pharmaceuticals, and surgical choices in the pursuit of advanced glaucoma treatment

by Reay Brown, MD

Figure 1. ASCRS members indicate their preferred therapy to add to a prostaglandin analog.

<table>
<thead>
<tr>
<th>Treatment Type</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta blocker</td>
<td>54%</td>
</tr>
<tr>
<td>Alpha agonist</td>
<td>13%</td>
</tr>
<tr>
<td>Laser Trabeculoplasty</td>
<td>11%</td>
</tr>
<tr>
<td>Topical carbonic anhydride inhibitor</td>
<td>11%</td>
</tr>
<tr>
<td>Combination aqueous suppressant</td>
<td>8%</td>
</tr>
</tbody>
</table>

Panel discusses new developments in ophthalmology diagnostics and treatments

Glaucoma is a significant problem among our patient populations. The 2015 ASCRS Clinical Survey indicated that 30% of members see 50 or more patients with glaucoma each month (average: 41 patients).

This annual survey provided additional information about members’ clinical opinions and practice patterns regarding glaucoma management, drawing responses from more than 2,000 respondents. To help

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Advanced diagnostics are improving glaucoma management, but non-compliance may alter outcomes

New diagnostic, pharmacologic, and surgical developments continue to enhance glaucoma management. To obtain optimum treatment outcomes, however, ophthalmologists need to use them well and enhance patient compliance.

Case report
A 56-year-old man referred for glaucoma with progressive field loss complained of recurrent hyperemia with his medications. His highest intraocular pressure (IOP) was 21 mm Hg. He had a long history of reference to cupping and borderline IOP. He had no history of steroid use, ocular trauma, diabetes, or hypertension. His vision was 20/20 in both eyes, his IOPs were 20 and 21 mm Hg, and his cornea was slightly thin. He had hyperemia in his conjunctiva but otherwise a normal anterior segment. He also had cupping. Images from our non-mydriatic camera showed an inferior

The non-mydriatic camera has been a huge boost to our practice, providing an image within 30 to 60 seconds.

—Richard Lewis, MD

Currently implant MIGS
24%

Plan to offer MIGS in next 12 months
29%

Do not plan to offered MIGS in next 12 months
29%

Undecided - waiting for more information
21%

Figure 2. The survey asked: “Which of the following best describes your use of/interest in MIGS?”

ophthalmologists develop more effective treatment strategies for these patients, a team of noted experts will share their insights and recommendations in this supplement.

The survey reported that 75% of members prescribe a prostaglandin analog as a first-line therapy, and 54% think brand medications are more efficacious and tolerable than generics.

Beta blockers were the preferred therapy to add to a prostaglandin analog (54%), followed by an alpha agonist, laser trabeculoplasty, topical carbonic anhydrase inhibitor, and combination aqueous suppressant (Figure 1).

Members think 31% of patients receiving 1 topical medication are not compliant and 38% of those receiving more than 1 medication are not compliant.

Twenty-four percent of respondents perform minimally invasive glaucoma surgery (MIGS), and 25% plan to offer this within 12 months (Figure 2). Therefore, nearly 50% of respondents are using MIGS or plan to within 12 months, which is an impressive adoption rate.

Respondents indicated that 8% of their cataract patients are MIGS candidates. If 3.5 million cataract surgeries are performed in the U.S. each year and 8% are MIGS candidates, this translates into 280,000 cataract plus MIGS procedures per year.

This supplement will highlight advancements in glaucoma management. Our panel of experts will discuss the impact of patient compliance on overall disease progression, as well as the safety and efficacy of new and current therapies and the use of MIGS techniques for long-term glaucoma treatment.

Dr. Brown practices with Atlanta Ophthalmology Associates in Atlanta. He can be contacted at reaymary@comcast.net.

Practice pearl: Showing patients images of their optic disc (as compared to normals) is a great motivator to enhance understanding of the disease and compliance.

—Richard Lewis, MD

Dr. Brown practices with Atlanta Ophthalmology Associates in Atlanta. He can be contacted at reaymary@comcast.net.
We also can use it to explain analyzing the optic nerve and angle. OCT is useful for analyzing the nerve fiber layer with disc hemorrhages.

**Diagnostic and monitoring advances**

Diagnosis of glaucoma and identification of progression remain challenging, but they are critical to prevent damage and irreversible vision loss. Initially we need to diagnose the type of glaucoma and treat it, as well as monitor adherence.

IOP continues to drive treatment, but application tonometry measurements vary widely. Diurnal fluctuation, patient activity, caffeine intake, and other factors influence measurements and, consequently, therapy.

In March 2016, the Food and Drug Administration approved a contact lens device (Triggerfish) that monitors IOP-related changes for 24 hours, which may provide a more comprehensive view of IOP. It is based on the assumption that a 1-mm Hg IOP change causes a 3-µm change in the corneal radius of curvature. De Moraes et al. reported that the parameters measured by the device in patients with glaucoma during a 24-hour period correspond to the rate of visual field progression.1

Visual field progression analysis is another valuable tool. Included on visual field machines, it allows us to monitor treatment efficacy.

During the last decade, advances in spectral domain optical coherence tomography (OCT) have allowed us to image the disc.

I strongly recommend OCT imaging, allowing us to diagnose glaucoma, determine the area of abnormality and degree of injury, and monitor and document glaucoma progression and decide whether we need to advance treatment. OCT is useful for analyzing the optic nerve and angle. We also can use it to explain angle closure and its treatment to patients.

The non-mydriatic camera has been a huge boost to our practice, providing an image within 30 to 60 seconds. I can identify more pathology because I can see farther into the periphery than I can with my ophthalmoscope, which is a useful feature in patients with small pupils. In addition, I can show patients their optic nerves, which motivates compliance with medication regimens.

Fundus perimetry correlates the optic nerve fiber layer defect with visual field. This will allow us to pinpoint where the visual field defect is occurring on the retina.

**Compliance challenges**

Non-compliance remains a challenge, compromising treatment outcomes. Stewart et al. stated that 34% of 500 patients reported non-compliance; Patel et al. reported that 59% did not use drops as prescribed; and Konstas et al. reported that 44% missed more than 2 doses per week.2–4

In research by Kholdebarin et al., almost 29% of patients contaminated the tip of the bottle and approximately 7% of patients missed the eye when instilling drops.5

To enhance compliance, clinicians need to tailor dosing regimens to patients’ regular schedules and choose medications that require less frequent dosing.6

In addition, they need to explain to patients how therapy is expected to impact the disease and how to properly instill eye drops.

It is also important to recognize that some glaucoma medications may cause ocular surface disease, with redness and irritation.7 Furthermore, a 65.7% prevalence of glaucoma has been reported in patients with severe ocular surface disease.8

Ophthalmologists need to identify and treat ocular surface disease and determine whether glaucoma medications should be changed. Future drug-delivery options will help reduce ocular surface exposure to medications.

**Conclusion**

Advanced technology has enhanced the diagnosis of glaucoma. Patient compliance remains a critical component of effective treatment, and we need to be alert for risk factors and modify treatment accordingly.

**References**


Dr. Lewis practices with Sacramento Eye Consultants in Sacramento, California. He can be contacted at rlewisycemd@yahoo.com.
Exploring new and current glaucoma therapies: Safety, efficacy, and patient selection

by Nathan Radcliffe, MD

With the ongoing development of glaucoma medications, clinicians have an unprecedented ability to customize treatment strategies based on each patient’s needs and disease state. Moreover, the future offers even greater promise with the potential for new drugs and drug-delivery technologies.

Emerging treatments

Prostaglandin analogs (PGAs) typically are first-line therapy, although selective laser trabeculoplasty (SLT) can be used at any point (Figure 1). PGAs generally achieve a 25–30% intraocular pressure (IOP) reduction, but each has its own safety and efficacy profile.1

Ophthalmologists often rely heavily on adjunts. In the Ocular Hypertension Treatment Study (OHTS), which sought a 20% IOP reduction, 40% of patients required 2 or more drops; however, increasing the frequency or dosage may increase non-compliance.2

Combination therapy simplifies administration, and the side effect profiles of approved fixed combinations are generally good.3–6 However, generics vary significantly from brand name drops in drop volume, viscosity, surface tension, and bottle tip.7

New PGAs are on the horizon. Latanoprostene bunod, a nitric oxide donating PGA, increases outflow through the trabecular meshwork. In the APOLLO and LUNAR studies, latanoprostene bunod administered once a day vs. timolol maleate 0.5% administered twice a day reduced mean IOP 7.5 to 9.1 mm Hg in patients with open-angle glaucoma and ocular hypertension.8,9 The effect on IOP was statistically superior (p<0.05) to timolol in both studies.

In the CONStELLATION trial, latanoprostene bunod administered once a day reduced IOP during a 24-hour period vs. timolol maleate 0.5% administered twice a day, which reduced daytime IOP only.8,10

A New Drug Application has been filed for a benzalkonium chloride-free latanoprost formulation with proprietary swollen micelle microemulsion technology, designed for solubilizing ophthalmic drugs with limited water solubility or insoluble ophthalmic drugs.11

Trabodenoson is an adenosine mimetic optimized to selectively target the A1 receptor. Phase 2 trials demonstrated dose-dependent IOP reduction in subjects with primary open-angle glaucoma or ocular hypertension that did not reach maximal efficacy.12

A new class of medication, inhibiting rho kinase (netarsudil), increases flow through the trabecular meshwork, reducing episcleral venous pressure and moderating aqueous production through norepinephrine transporter inhibition.

In Rocket 1 and Rocket 2 phase 3 studies, netarsudil achieved its primary endpoint of non-inferiority to timolol.13

Phase 3 trials are in progress for a sustained-release bimatoprost intracameral implant. Phase 1 and 2 data showed that all dose strengths had similar IOP reduction to bimatoprost 0.03% throughout week 16.14 After this time, it continued to provide statistically significant IOP reduction through 6 months of follow-up.

A flexible bimatoprost sustained-release ring is being studied, which is placed in the superior and inferior fornix.15 Mean IOP was reduced in phase 2 study patients treated with the device (mean decrease from baseline, –3.2 to –6.4 mm Hg) for 6 months compared with those receiving timolol 0.5% daily (mean decrease from baseline, –4.2 to –6.4 mm Hg). Other sustained-release options also are being studied.

Conclusion

We have many options to reduce IOP in patients with glaucoma, and many others are expected. These will allow us to tailor treatment to patients’ lifestyles, needs, disease stage, and velocity.

References

8. Valeant company website.
9. Vittitow JL, et al. Long-term efficacy and safety of latanoprostene bunod 0.024% for...
MIGS and glaucoma treatment

by Ike Ahmed, MD

Figure 1. Image shows laminar striated episcleral vein receiving aqueous from the aqueous vein.

Early intervention helps reduce disease progression

Although topical medications have been the mainstay of treating increased intraocular pressure (IOP), less than 50% of patients use their drops after 1 year. This lack of adherence is associated with vision loss. 

Looking to the future, we should consider ourselves interventionalists in treating glaucoma. With microinvasive glaucoma surgery (MIGS) and other procedures, we can intervene earlier to reduce morbidity, but safety must be established.

Early intervention

With MIGS, we take an ab-interno approach and it is minimally traumatic, providing at least modest efficacy. It has a very high safety profile and rapid recovery.

Conversely, trabeculectomy is performed for advanced progressive normotensive glaucoma (open or closed angle). It has a low IOP target (less than 12 mm Hg).

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“We have many options to reduce IOP in patients with glaucoma, and many others are expected.”

—Nathan Radcliffe, MD

Dr. Radcliffe is clinical assistant professor of ophthalmology, New York University Langone Medical Center, New York. He can be contacted at drradcliffe@gmail.com.

References:


Hg). Patients are intolerant to medications.

When weighing glaucoma procedures, an important consideration is whether we will be able to decrease or eliminate medications. Even if the IOP remains the same, cessation of medications is a very important outcome measure and addresses adherence challenges.

**Bleb vs. bleb-less**

There are 3 MIGS outflow tracks: Schlemm’s canal (conventional outflow), suprachoroidal space, and subconjunctival space (non-conventional outflow).

One of the most important questions is whether we will drain externally (bleb forming) or internally (bleb-less), which depends on whether cataract surgery is performed. Phacoemulsification reduces IOP, and combining phacoemulsification with bleb surgery increases the risk of bleb failure. However, phacoemulsification and internal MIGS work synergistically.

Using a 2-stage approach, performing phacoemulsification plus internal MIGS, protects against early IOP spikes, with no impact on future bleb success. We can perform a bleb procedure later, if needed.

However, when performing a standalone procedure without cataract surgery, efficacy is particularly important. As internal stenting may not be enough to reach target IOP, we are more likely to proceed with a solo bleb procedure. We are moving toward micro-stenting approaches.

Internal MIGS procedures have shown high safety, and there are differences in the canal and suprachoroidal space. Schlemm’s canal is safe, but the procedure is slightly more difficult and efficacy is modest. Suprachoroidal devices have a significant potential space, but variability depends on healing and efficacy has been modest.

The Schlemm’s canal micro-stent (iStent) is the only MIGS device available in the United States. Early results were modest; Samuelson et al. reported that 22% more patients who received this device with cataract surgery achieved the study primary endpoint (normal IOP) vs. those who had cataract phacoemulsification alone.5,6

To increase IOP reduction, we need to place the micro-stent in the vicinity of 1 of the major aqueous outflow channels rather than placing it where there are no collectors or a high-resistance plexus system, which will be less likely to reduce IOP (Figure 1).

Blood reflex and pigmentation can provide an indication of where to target MIGS devices (Figure 2).

With multiple trabecular micro-bypass stents, we can achieve pressures in the low teens and reduce medication. Using 2 or 3 micro-bypass stents along with cataract surgery in 53 eyes, Belovay et al. reported that the overall mean IOP was 14.3 mm Hg 1 year after surgery, and topical medication was reduced in 83% of eyes 1 year after surgery.6

When Fernández-Barrientos et al. compared phacoemulsification with 2 stents (17 eyes) vs. phacoemulsification alone (16 eyes), the combination reduced medications and IOP and increased outflow significantly over phaco alone.7

New Schlemm’s canal procedures are emerging to enhance outflow, which we can compare with current procedures. Suprachoroidal devices are intriguing because they rely on space in the suprachoroidal outflow track.

**Conclusion**

Ophthalmologists have an array of options to reduce IOP, and new procedures will become available. When choosing procedures, it is important to compare risk vs. benefit vs. effort in patient selection.

**References**


Dr. Ahmed is professor of ophthalmology, University of Utah, assistant professor of ophthalmology, University of Toronto, and head of ophthalmology, Trillium Health Partners, Mississauga, Ontario, Canada. He can be contacted at ike.ahmed@utoronto.ca.
**Panel discussion**

“**As I have practiced longer, I am much less aggressive with trabs and tubes, but we need aggression in innovation because we need to try things and find out what works. MIGS is so exciting because it is safe, and new longer-acting medications are also exciting.**”

—Reay Brown, MD

**Reay Brown, MD:** Dr. Ahmed, in an average cataract case, when a patient is using 2 drops for glaucoma but the intraocular pressure (IOP) is not very high, what is your typical microinvasive glaucoma surgery (MIGS) combination?

**Ike Ahmed, MD:** When we combine glaucoma surgery with cataract surgery, safety is paramount because refractive outcomes and recovery are critical to patient satisfaction and outcomes. I think the canal space is the ideal place for safety and for a modest IOP reduction.

**Dr. Brown:** Dr. Radcliffe, what types of combinations do you use?

**Nathan Radcliffe, MD:** I combine endocyclophotocoagulation with a variety of outflow procedures, such as the micro-stent (iStent) or a goniotomy.

**Dr. Brown:** Do any of you recommend cataract surgery a bit earlier to take advantage of IOP reduction?

**Richard Lewis, MD:** Cataract surgery is probably our single best glaucoma therapy. It’s valuable in angle closure. It tends to be curative and changes the dynamic. Even in open-angle glaucoma, it reduces pressure but it also presents other opportunities, such as a MIGS procedure or other options.

**Dr. Radcliffe:** I do but I also try to avoid the temptation. If it is urgent to remove the cataract because we need to reduce IOP, that does not sound like a MIGS patient to me, so I am very careful about that. If I’m counting on significant pressure reduction, I use a trabeculectomy or tube.

**Dr. Brown:** Regarding medications, if you’re adding a second eye drop, when do you consider a combination eye drop as your second choice as opposed to a single medication?

**Dr. Lewis:** The second medication once again raises the question of compliance and whether we will have enough additivity. None of the secondary medications, at least timolol and a prostaglandin, were sufficiently additive to achieve approval by the Food and Drug Administration, but 50% of ophthalmologists use timolol as their second medication. It’s inconsistent.

**Dr. Brown:** Yes, we all want to help the patient, but we don’t want to cause problems that they did not have before.

There is so much in the pipeline. What are you most excited about as we enter the golden age of glaucoma treatment?

**Dr. Ahmed:** I teach my residents and fellows that 13 is the new 21. If patients truly have glaucoma, with damage to their optic nerve, I think they need to significantly reduce IOP. The longer we follow our patients, we often wish we were more aggressive because we see visual field progression. Patients who have lower targets tend to be stable for a longer period of time, even if they have moderate disease. Therefore, the problem is how to achieve that safely. That is why I think combinations—medications, MIGS, drug delivery—allow us to get there. Therefore, I tend to be more aggressive than I may have been early in my career.

**Dr. Lewis:** As a point-counterpoint, I received a phone call from a patient in whom I performed trabeculectomy in both eyes 18 years previously because of very high IOPs. He had been in his 30s. He complained that his eye was “not feeling right.” We found that he had endophthalmitis. Therefore, as aggressively as we want to reduce pressure, we have to balance it against the long-term risk of complications from our procedures.

**Dr. Ahmed:** You’re absolutely right. That’s why I think we were not eager to get there with our OLD therapies, but I think our new therapies will allow us to get there and stay there.

**Dr. Brown:** As I have practiced longer, I am much less aggressive with trabs and tubes, but we need aggression in innovation because we need to try things and find out what works. MIGS is so exciting because it is safe, and new longer-acting medications are also exciting.
Advanced glaucoma treatment: Diagnostics, pharmaceuticals, and surgical options

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CME questions (circle the correct answer)

1. Dr. Ahmed reported that microinvasive glaucoma surgery (MIGS) _____________.
   a. Enables rapid recovery
   b. Eliminates the need for medication
   c. Is performed for advanced glaucoma
   d. Has a low IOP target (less than 12 mm Hg)

2. According to Dr. Ahmed, internal MIGS and phacoemulsification ________________.
   a. Cannot be performed together
   b. Impact future bleb success
   c. Cause IOP spikes
   d. Work synergistically

3. Dr. Lewis shared that applanation tonometry measurements are affected by _________.
   a. The use of other tests
   b. Corneal radius of the curvature
   c. Diurnal fluctuations
   d. Visual field progression

4. Dr. Lewis explained that, in managing glaucoma, fundus perimetry correlates ______ with the visual field.
   a. Applanation tonometry readings
   b. Optic nerve fiber layer defect
   c. 24-hour IOP changes
   d. Gonioscopy

5. Dr. Radcliffe shared that in the APOLLO and LUNAR studies, latanoprostene bunod reduced mean intraocular pressure _____________.
   a. 3.4 to 7.1 mm Hg
   b. 9.3 to 10.1 mm Hg
   c. 7.5 to 9.1 mm Hg
   d. 5.2 to 6.5 mm Hg

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