IMPLEMENTING ADVANCES IN DRUG DELIVERY

How do new treatment options fit in with existing therapeutic strategies?

BY I. PAUL SINGH, MD

The treatment of glaucoma has evolved significantly over time, and with it, so have physicians' mindsets. Quality of life and patient satisfaction are becoming increasingly important issues to glaucoma specialists, as they long have been to our cataract colleagues. In light of this mental shift and recent advances in the surgical and medical treatment of glaucoma, quality of life has joined IOP reduction, optic nerve stability, and visual field (VF) stability as a measure of success in glaucoma management.

In my practice, there has undoubtedly been a philosophical change in what is considered *controlled* versus *refractory* glaucoma. In my patient charts, I document quality of life as a reason for uncontrolled glaucoma. Even if the patient's IOP, VFs, and optic nerves are stable, if he or she is experiencing any negative side effects from treatment, then his or her glaucoma is not controlled. Fortunately, new options for drug delivery are helping physicians to modify their therapeutic strategies to better address patient quality of life and treat glaucoma at the site of action.

FLUCTUATING IOP

Glaucoma specialists are well versed in the challenges associated with eye drop use. Only about 5% of each dose penetrates the cornea and reaches the intraocular tissues.[1] Other barriers to penetration include tear volume,[1,2] tearing and blinking,[2-4] conjunctival and scleral absorption,[2-4] and corneal absorption.[1,4] These challenges necessitate the use of high concentrations of drug, which thereby increases the potential for side effects that negatively affect patient adherence. Poor adherence hinders our ability to control IOP.

The Advanced Glaucoma Intervention Study (AGIS) confirmed that long-term IOP fluctuation is associated with VF progression.[5] In a subsequent analysis of the AGIS data, Caprioli et al[6] found that, of patients with an average IOP of 20.6 mm Hg and high IOP fluctuation (>3 mm Hg), 30.3% experienced VF progression. This finding is logical—patients with high IOP and advanced glaucoma are likely to progress. However, the investigators also found that, in patients with an average IOP of 10.8 mm Hg and high IOP fluctuation, the same percentage (30.3%) experienced VF progression. A challenge with earlier disease is that we cannot see VF loss and thus may incorrectly assume that treatment can be delayed.

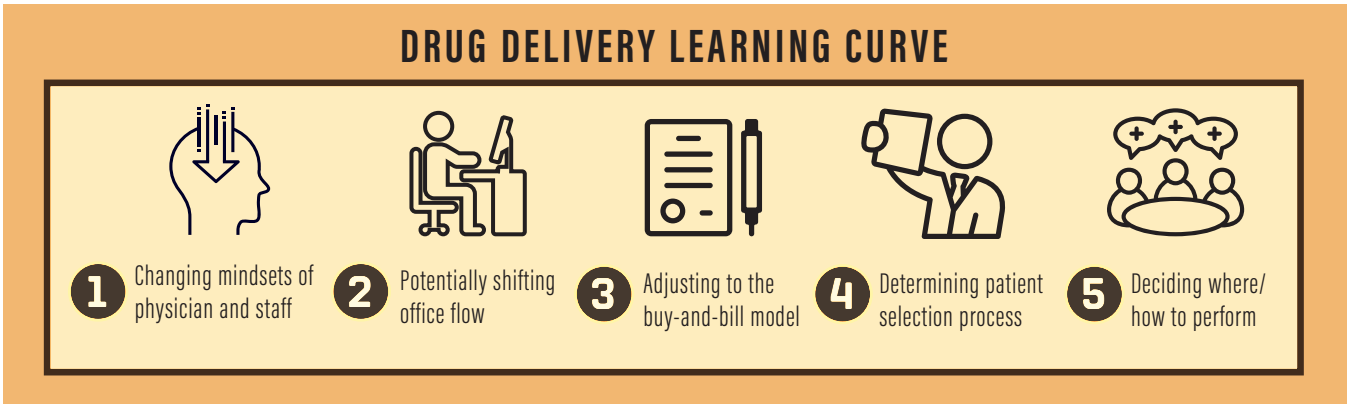
A CONTINUED NEED

Selective laser trabeculoplasty (SLT) and MIGS alone do not eliminate all medications for all patients. Data from several pivotal trials of MIGS devices indicate that a high percentage of patients can discontinue medication use after treatment, but this does not apply to every patient. We still encounter those who, despite treatment with standalone SLT or MIGS, must continue on medication. Although this outcome is always a possibility and one that is communicated to each patient, it can sometimes make us feel like we did not fully optimize the patient's quality of life through our intervention.

One way to fill this gap may be by combining existing laser and surgical treatments with innovations in drug delivery. If, for example, a patient requires a prostaglandin analogue after standalone SLT or MIGS, he or she can be offered a sustained-release drug delivery device to help address compliance issues and further improve quality of life.

New solutions for drug delivery include biodegradable intracameral implants, nonbiodegradable intracameral implants, and external biodegradable and nonbiodegradable implants. These devices are placed near the site of action and may enable the pathophysiology of the disease to be altered with early use.

The first treatment in this space to gain FDA approval is the bimatoprost implant 10 mcg (Durysta, Allergan), a sustained-release biodegradable implant that is supplied in a single-use applicator with a 28-gauge needle. In the phase 3 ARTEMIS study, of 279 eyes given a third treatment with the bimatoprost implant, 86% were off medications at 1 year.[7] Morphologically, bimatoprost treatment has been shown to cause enlarged spaces for outflow between muscle bundles in



the anterior ciliary muscle as well as a remodeled anterior ciliary body.[8] Matrix metalloproteinase expression is dose-related with exposure to bimatoprost.[9] The theoretical benefits of a 24-hour release of bimatoprost to the target tissue could be a remodeling of the outflow system and the potential to change the natural disease course. In the phase 1/2 trials, nearly 25% of patients receiving one 10 mcg implant maintained efficacy and did not require rescue medications, even at 24 months after implantation.

Two other drug delivery devices in the pipeline are the OTX-TIC (Ocular Therapeutix), a preservative-free travoprost implant administered via an intracameral injection, and the iDose (Glaukos), a sustained-release travoprost implant. In preclinical models of the OTX-TIC, a steady state in vitro and in vivo release was achieved through 4 months, correlating to a 4-to-6-month duration of effect in humans.[10] OTX-TIC also demonstrated an IOP lowering effect of approximately 25% to 30% through 4 months. Phase 2 data of the iDose showed initial efficacy through week 12, with all patients achieving at least a 30% IOP reduction. More patients in the iDose groups did not require additional medication through week 12 compared with controls. (Editor's note: For more updates from the pipeline, see pg 37.)

THERAPEUTIC PROGRESSION

The implementation and use of novel sustained drug delivery options will likely be dependent on the device type. A punctal plug is likely to be a first-line or second-line treatment in the office, as it is reversible. An injection at the slit lamp is also likely to be a first- or second-line treatment, but the physician must decide where and when to perform the procedure. It will take time to figure out these nuances, but ultimately these new products will change glaucoma care.

Historically, my therapeutic progression went from medication, to laser, to MIGS, to trabeculectomy or tube shunt implantation, to transscleral cyclophotocoagulation (TSCPC). My new therapeutic progression goes from laser, to MIGS, to more laser, to trabeculectomy or tube shunt implantation, and then to TSCPC, with the addition of drug delivery at any stage of the paradigm. I do feel that drug delivery will also help increase my utilization of standalone MIGS, as I now have a safe, in-office method of achieving the goals of IOP redcuction and medication burden reduction in the event standalone MIGS was not enough.

In my practice, we conducted a study of patients undergoing SLT and MIGS to determine whether our technicians were saving any time as a result of our performing these procedures. We found that technicians saved 4 minutes per patient at each visit with the reduction of one medication (either single or combination) and 6 minutes per patient with the reduction of two medications after SLT or MIGS. This was due to fewer pharmacy callbacks, less time spent confirming patient compliance, and less time needed to refill prescriptions.

CONCLUSION

Advances in drug delivery are bringing glaucoma physicians one step closer to prioritizing patient satisfaction, improving compliance, and minimizing the treatment burden. As more options enter the market, the device chosen for each patient will likely be selected based on the disease stage and whether the procedure will be performed in a surgery center or in the office.

Overcoming the drug delivery learning curve may require close consideration of the following factors:

- Mindset of physician and staff;
- Office flow;
- Buy-and-bill model;
- Patient selection process; and
- Location of each procedure.

Once any necessary adjustments are made, physicians can start to better tailor treatment to each patient and continue to place quality of life and patient satisfaction at the forefront of care. ■

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I. PAUL SINGH, MD
- President, The Eye Centers of Racine and Kenosha, Wisconsin
- Member, *Glaucoma Today* Editorial Advisory Board
- ipsingh@amazingeye.com
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