

GLAUCOMA

Surprising New Treatment for Glaucoma: Get the Drops in the Eye

BY MIRIAM KARMEL, CONTRIBUTING WRITER

Some things never change. For at least three decades researchers have been reporting that patients with glaucoma have trouble getting drops into their eyes. As early as 1980, Michael A. Kass, MD, and colleagues identified failures to take the medications correctly—sometimes referred to as “involuntary noncompliance”—as a common problem that interferes with the care of glaucoma patients.^{1,2}

At the 2008 meeting of the American Glaucoma Society, as well as the 2009 Annual Meeting of the Academy, Alan L. Robin, MD, and Amy L. Hennessy MD, MPH, reported findings from two video-documented studies: only two-thirds of patients were able to reliably get the medicated drop to the ocular surface. And when factoring in other variables, the success rate was even lower.³

The taming of the drop. After all these years, ophthalmologists still haven’t found a way to fix the problem. No matter how many solutions have been introduced—user-friendly bottles, drops tailored to the patient’s lifestyle, changes to the bottle tip, specially designed dosing aids—patients still often miss the mark. Hands may be hobbled by arthritis or Parkinson disease or stroke; eyes blink; drops land on foreheads and cheeks. Or, at the other extreme, patients marinate their eyes, pouring in half the bottle in one sitting.

Patients know how to take a pill, Dr. Robin said. “I would never say, ‘Put the

pill between your fingers, take some water, put the pill in your mouth and swallow.’ Patients know to do that. But they don’t know how to take their drops.” Dr. Robin is a clinical professor of ophthalmology at the University of Maryland in College Park.

“I think this is one of those problems that is not easy to solve,” said Dr. Kass, who is professor and chairman of ophthalmology and visual sciences at Washington University in St. Louis. “The method of administering eye-drops hasn’t changed in a very long time,” he continued. “I don’t think we have come very far.”

Dr. Robin’s videos show just how far we have not come. “Your patients have a problem,” he said.

Drops, Lies and Videotape

Adherence to medical therapies is a perennial favorite topic in ophthalmology, said Dr. Robin. But there are no controlled studies in the literature detailing how patients should administer drops. Patients, he said, may remember to take their glaucoma medications. “But where are the drops going?” Asking the patient will not necessarily reveal the answer, as Dr. Robin learned through video recordings of 204 patients—55 percent women and 74 percent Caucasian with a mean age 69.³ Seventy-six percent had severe visual field damage, and nearly all (94 percent) had used drops longer than six months.

Seventy-one percent were at least able to get a drop onto an ocular

Six Steps for One Drop



Dr. Solish would like to see studies to evaluate strategies for teaching patients to take drops. “We all have our own ways to tell patients, but we need research to know what works.” In the meantime, here’s how he advises patients to take drops:

1. **Tip** your head back or lie on a couch and look straight up at the ceiling.
2. **Hold** the bottle perpendicular to the floor and look up at the bottle tip, which should be a few inches above your eye.
3. **Pull** the lower lid down with one hand.
4. **Steady** your hands by resting the wrist of the hand holding the bottle onto the hand holding the eye lid.
5. **Apply** a drop.
6. **Keep** the bottle from touching the eye or it can become contaminated. And do not attempt to look in a mirror during instillation; this practically guarantees drops will fall to the floor.

surface. But Dr. Robin said that only about 30 percent could meet all criteria—getting the first drop, and only one drop, to reach the eye and making

sure the bottle doesn't touch the eye.

His patients used a mean of 1.4 drops over 1.2 attempts, and 40 percent touched the bottle tip to the ocular surface, potentially contaminating the applicator. Older patients struggled more with the task. And, amazingly, said Dr. Robin, there was a widespread perception among the patients that they were doing just fine.

Don't Rush to Blame the Drug

The implications of involuntary non-compliance are huge, Dr. Robin said. If a patient's condition is deteriorating, doctors assume that the medication isn't working. But his study shows that the medication has often not been given a chance if the drops aren't getting into the eye. "If you think the patient isn't doing well, watch him put his drops in."

"Drops are not like pills," said Samuel P. Solish, MD. Drops can run out before the 30-day or 90-day supply imposed by insurance companies through Medicare Part D. Patients whose drops run out early face a poor set of options: pay out-of-pocket for a new bottle, skip doses to extend the supply or wait until it's time to refill the prescription. Dr. Solish is a clinical instructor of surgery at the University of Vermont in Burlington.

CMS relaxed the rules last fall when it instructed Part D insurers that while they could still impose refill restrictions, they should ensure that patients were not being denied necessary medication, said Dr. Solish. He worked with both the American Glaucoma Society and the Academy to effect that change.

Averting a waste of medicine. In order to avoid involuntary noncompliance, here are tips for physicians to help patients hit a bull's-eye.

- **Ask**, "Are you having trouble putting drops in your eyes?"
- **Make** no assumptions. Self-reporting is unreliable. Most patients will answer yes if asked whether they're taking their medications.
- **Watch** patients put in their drops, using artificial tears for practice.
- **Pick** a slow day to observe patients. "Watch them put in the drops. It will

NEEDED: New Delivery Gadgets

Errant glaucoma drops are a problem begging for a technological breakthrough. "The current technology for eyedrops is horrible because of nonadherence to therapy and execution of getting the drop in the eye," Dr. Robin said. "People need to develop alternative delivery systems. Eyedroppers are an obsolete technology."

Dr. Kass agreed. "We need to develop new techniques that would either simplify or get around the question of recurrent administration of drops," he said. "One could imagine all kinds of new approaches." Currently, a number of approaches are undergoing testing:

Position in the puncta or conjunctiva. Furthest along in the research pipeline is a punctal plug delivery system, developed by QLT, in which a core that is filled with a three-month supply of medication is inserted into a punctal plug. The QLT device, in clinical trials, has been shown to effectively deliver the drug, but researchers are working to get the device to stay in place, said Richard A. Lewis, MD, a glaucoma specialist in private practice in Sacramento, Calif., and a study investigator. "Retention of the plug in the punctum is a challenge," he said.

The device is being tested with latanoprost, but it could hold other drugs, including timolol and bimatoprost, Dr. Lewis said. For pharmacologic reasons, some drugs will be better suited for the device, he added. "They have to be stable." He noted that other researchers are testing a device that is planted under the conjunctiva.

Deliver through the posterior segment. Allergan is testing the safety and effectiveness of a brimonidine intravitreal implant in patients with glaucomatous optic neuropathy. The phase 2 trial is comparing a 200 and 400 µg brimonidine tartrate posterior segment implant vs. a sham.

In fact, various experimental devices for delivering steroids to the retina could be adapted for glaucoma treatment, Dr. Lewis said. "You could put the implant in the posterior segment and the drug would flow to the front of the eye."

be a horrifying and educational experience for you," Dr. Kass said. "The next step is to recognize the problem and to start to deal with it by training, retraining and considering alternative treatments."

- **Offer** a short eye anatomy lesson. Explain that the conjunctival sac holds 7 µl while most drop applicators release 25 to 56 µl per drop. This may help patients understand that a certain amount of medication will always flow out of the eye.
- **Train**, retrain, ask, observe, Dr. Kass said. Teach patients, or have a technician teach them, how to instill drops. Periodically observe and reinforce the lessons.
- **Ask** if the patient has trouble paying for medication.
- **Think** instillation, not medication. If the therapy isn't working, the problem may be administration of the treatment, not the treatment itself.
- **Recruit** a neighbor or family member to administer the drops.

- **Consider** alternatives. If a patient is having trouble with drops, an alternative antihypertensive strategy, such as laser or surgery, may be preferred. "If they have a problem, maybe medical therapy is the wrong thing for your patients," Dr. Robin said. "It's like saying, 'Take two pills.' But if the patient can't swallow, it's the wrong therapy."

1 Ashburn, F. S. et al. *Surv Ophthalmol* 1980;24:237-248.

2 Kass, M. S. et al. *Ann Ophthalmol* 1982; 14:775-779, 889-893.

3 Hennessy, A. L. et al. "Videotape evaluation of eyedrop instillation in glaucoma patients with visual impairment or moderate to severe visual field loss." Publication pending.

Dr. Kass reports no related interests; Dr. Lewis is a consultant to QLT and Allergan; Dr. Robin is a consultant to Alcon, Merck and Pfizer, and is on the speakers bureau for Alcon and Vistakon. Dr. Solish reports no related interests.