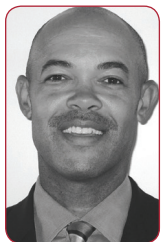


GETTING IN THE RING

Could an external drug delivery device help knock out noncompliance?

BY BRIAN FLOWERS, MD



The mainstay of glaucoma treatment is lowering IOP, which is achieved via topical ocular medication in the overwhelming majority of patients. The problems of poor adherence to and persistence with treatment for chronic asymptomatic diseases are well known. Patients' potential difficulty administering eye drops compounds the challenge; a physical inability to instill their medication may lead them to miss doses, and wastage may lead to gaps in treatment while they wait on prescription refills. The need for sustained delivery of ocular hypotensive medications is clear. Developed at ForSight Labs and acquired last year by Allergan, the bimatoprost ring (formerly called Helios) represents a novel approach to ocular drug delivery (see *Watch It Now*).

HOW IT WORKS

Available in diameters from 24 to 29 mm, the relatively large silicone ring fits in the ocular fornix. When in place, the insert is barely visible at the medial canthus (Figure). A modified ruler makes fitting the device relatively straightforward.

My practice was one of the 10 phase 2 trial sites, and I had several patients who wore the inserts for a year. The device was quite well tolerated, with the only side effect's being a slight increase in mucus production in some patients.

RESEARCH RESULTS

A phase 2 trial of the device impregnated with bimatoprost was conducted between October 2013 and

November 2014. This prospective, randomized, double-masked, active-controlled, parallel-armed study was performed at 10 sites in the United States and involved 169 patients with primary open-angle glaucoma or ocular hypertension. After signing informed consent, patients were fitted with a nonmedicated ring, which they wore for 1 month. They returned to the office and were then randomized in a 1:1 ratio to either a nonmedicated insert and timolol dosed twice daily or a bimatoprost-impregnated ring and artificial tears administered twice daily. The primary outcome measure was the mean change in diurnal IOP at weeks 2, 6, and 12. One hundred thirty patients were randomized, with 64 in the treatment group and 66 in the control group.

The bimatoprost-impregnated insert produced more than 20% IOP lowering at all time points, but it was slightly (0-1.5 mm Hg) less efficacious than twice-daily timolol at the nine time points. This result is not totally surprising, given the pharmacokinetics of prostaglandin analogues; constant dosing tends to produce a lesser effect than pulsed dosing regimens.



WATCH IT NOW

In this episode of *Glaucoma Today Journal Club*, James D. Brandt, MD, discusses the bimatoprost ring.



bit.ly/flowers0917



AT A GLANCE

- The bimatoprost ring is a relatively large silicone device that fits in the ocular fornix.
- A clear advantage of this method of sustained drug delivery is the size of the insert. Large quantities of medication and multiple drugs can be placed in a single device.
- A phase 2 trial of the ring impregnated with bimatoprost found high retention rates, favorable tolerability, and a low incidence of adverse events.

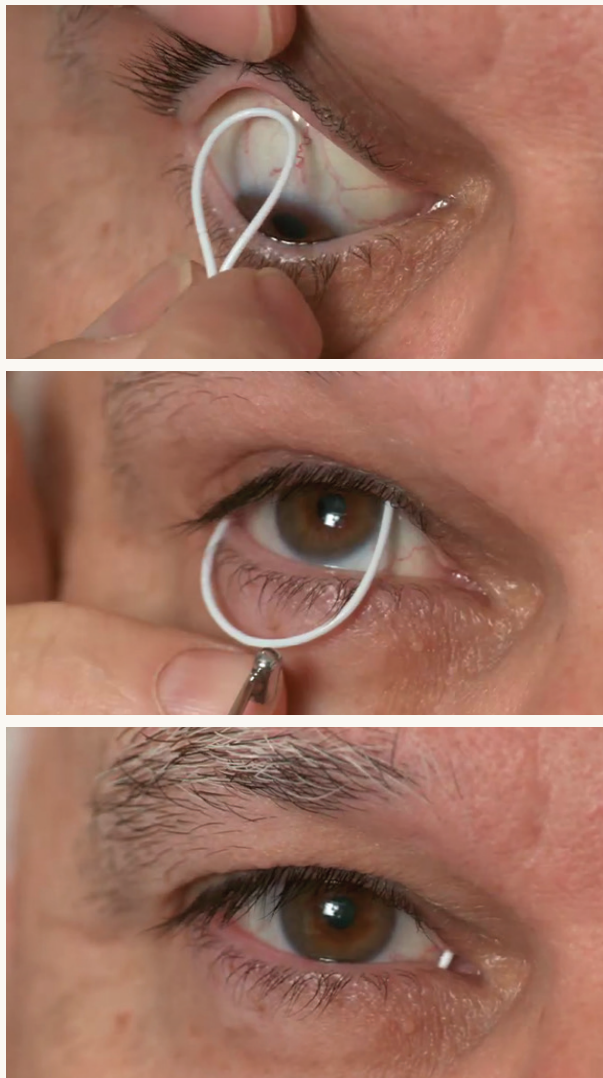


Figure. The relatively large silicone ring fits in the ocular fornix and, when in place, is barely visible at the medial canthus.

Two of the most important attributes of an externally delivered sustained-release system are that the product is retained comfortably and that patients realize if the device becomes dislodged or falls out. Retention, defined as maintenance of the insert in place without a physician's reinsertion, was very good at 93.1% at 12 weeks and 88.5% at 6 months. These results compare quite favorably to retention rates with punctal plugs, which tend to be closer to 70%. Importantly, all patients who experienced a dislodgement were aware of the event.

The incidence of adverse events was relatively low. Of the 161 patients who wore a nonmedicated insert for the first month, 151 reported no discomfort. During the active phase

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of the trial, the bimatoprost group experienced more hyperemia (9 vs 3 patients), pruritis (7 vs 2 patients), and ocular discomfort (4 vs 2 patients). All of these effects appeared to be related to the drug rather than the ring itself. The most common adverse event was an increase in mucus production, which was equally present in both groups. The change was generally mild and experienced as increased mattering around the eyes noted upon awakening. This side effect profile mirrors the experience in my clinic.

CONCLUSION

At first, I was concerned about how well the ring would be tolerated. I was therefore somewhat surprised at how little my patients noticed the device's presence in their eyes during the 30-day initial trial period. That level of tolerability changed in some patients after they received the medicated ring, but I would expect a sudden bolus of bimatoprost to affect certain patients.

The device's tolerability and patients' awareness of its dislodgement are key findings of the phase 2 trial. A clear advantage of this approach to sustained drug delivery is the size of the ring. Large quantities of medication and multiple drugs can be placed in a single device. At the moment, Allergan is investigating therapies for dry eye disease, ocular allergy, and postoperative inflammation with the ring. Additional studies are evaluating varying doses of bimatoprost with the device. I expect this delivery system to be a welcome adjunct to the treatment armamentarium for a variety of conditions. ■

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