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No patient compliance needed with intraoperative drug

Use of a triamcinolone acetate/gatifloxacin combination in cataract surgery may eliminate the need for a therapeutic regimen.

Richard Mangan, OD, FAAO

Studies suggest that drop compliance remains the number one challenge for clinicians managing chronic eye diseases such as open-angle glaucoma and dry eye syndrome.

Studies confirm noncompliance

In the 1980s, Kass and colleagues conducted a glaucoma compliance study where they monitored medication bottles electronically without the patient's knowledge. The study demonstrated that patients overestimated their use or simply did not bother using the medication until the day of their visit. Of greater concern, physicians were unable to identify uncooperative patients half of the time.

Richard Mangan

While the postoperative management of cataract surgery is not a long-term, chronic situation, some of the barriers to good compliance still exist, as shown in the accompanying table.

This was confirmed by a study conducted at the Dunyagoz Clinic in Istanbul and the University of Cologne, Germany, by Hermann and colleagues, where a similar electronic device monitored antibiotic drop usage in postoperative cataract patients. In that study, 50% of patients took less than half of their recommended dosage. One patient took the combination drop for the first day only.

While surgeons and comanaging physicians sleep better at night with the recent development and efficacy of newer-generation fluoroquinolones such as gatifloxacin for preventing postoperative infectious endophthalmitis, we also know that the medication is effective only if it is used. Studies have indicated that the use of anti-inflammatory drugs such as prednisolone acetate or nonsteroidal medications such as Acular (ketorolac tromethamine 0.4%, Allergan) is effective at decreasing the incidence of postoperative cystoid macular edema (CME). However, we wonder if the patient is properly spacing the medication to obtain true therapeutic levels at the posterior pole.

In an ideal world, every medication would be safe, effective, inexpensive and easy to use. Trigat may be one answer.

Drug administered during surgery

Trigat is a unique formulation of triamcinolone acetate (Kenalog, Bristol-Myers Squibb) 15 mg/mL and intravenous gatifloxacin (Tequin, Bristol-Myers Squibb) 1 mg/mL. For years, Kenalog has been used effectively for managing resistant or secondary macular edema. However, when administered during cataract or clear lensectomy, the medication is simply delivered using one of the previously established corneal side ports instead of having to make a separate scleral injection. After the posterior chamber implant is safely in the bag, a blunt cannula is used to penetrate through the zonules and deliver the drug into the anterior inferior vitreous.

Triamcinolone has a long history of use by retinal surgeons for several indications. It is known to be well tolerated and to provide an anti-inflammatory effect for at least 2 weeks.

Gatifloxacin is a broad-spectrum antibiotic that has been used routinely for postcataract infection prophylaxis as a topical drop.

New England Compounding in Boston prepares this compounded medication. We chose this company because it was already providing the compound for other surgeons and was able to provide excellent documentation of its quality control procedures.

This combination is not U.S. Food and Drug Administration approved for this or any indication.

Case studies reported

Paul Koch, MD, of Koch Eye Associates, Warwick, R.I., was recently awarded Best Paper of 2005 ASCRS-ASOA symposium, for “Intracameral injection studied to replace post-op eye drops.” Dr. Koch reported that among the 250 cases using postoperative trigat, four cases of CME developed. However, none of these four cases were traditional post-cataract CME cases. Instead, they were complicated by pre-existing factors such as epiretinal membranes and diabetic eye disease.

After 1,100 cases in the series, Dr. Koch and his colleagues have had no cases of traditional postoperative CME and no infectious endophthalmitis.

Common forms of ocular medication noncompliance

Improper timing

- Medication doses being missed
- Inconsistent timing of medication (doses too close together or apart)
- Overuse of eye drops
- Gaps in prescription refills
- Therapeutic regimen that is too complex

Physical barriers

- Medication side effects
- Senility or memory problems
- Poor dexterity
- Poor vision
- Tremor
- Hemiplegia/paralysis
- Head positioning difficulty
- Extremity/neck pain
- Situational barriers
- Medication costs
- Poor doctor-patient communication
- Poor patient comprehension
- Denial/underestimation of importance
- Inconsistent family support

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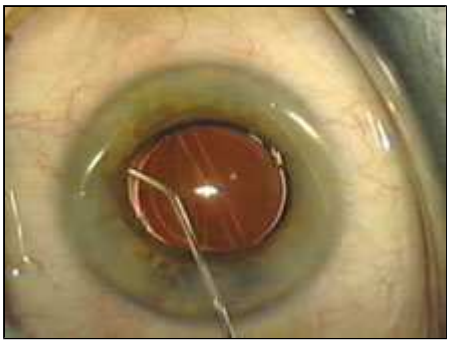
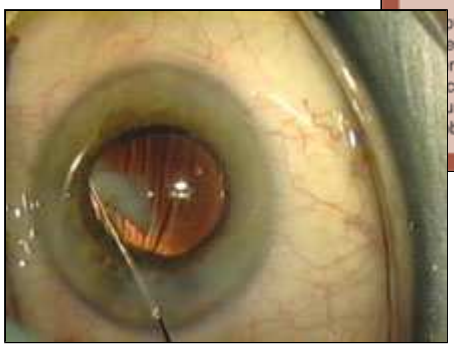
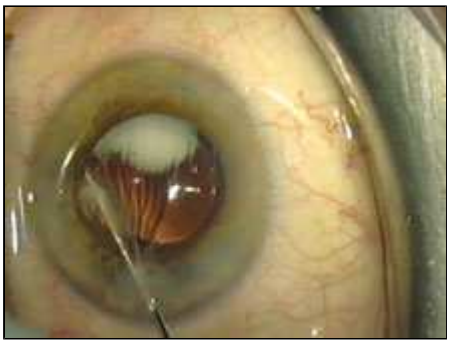


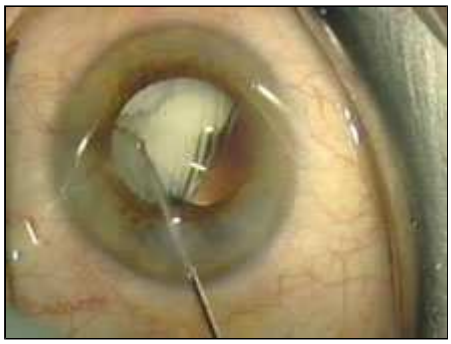
A cannula is placed between the anterior capsule and the iris, taking care to extend it past the peripheral edge of the capsule.



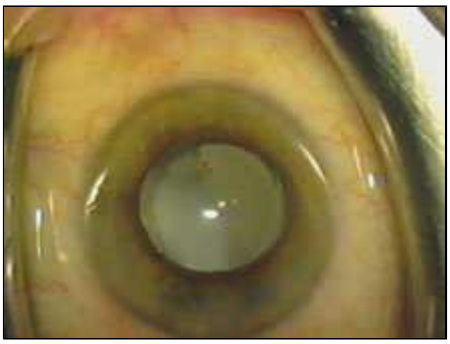
As the injection begins, a small amount of medication is refluxed into the anterior chamber. This may be visible postoperatively as “pseudo hypopyon.”



As trigat is injected into the vitreous cavity, the cornea is deformed to allow viscoelastic to exit the corneal wound and equalize the pressure in the eye.



The majority of the medication is injected into the vitreous cavity. Initially it is concentrated in the anterior vitreous space.



The characteristic white pupil is evidence of the quick diffusion throughout the eye and has become the familiar end point of an uncomplicated surgery.

Images: Mangan R

Personal study results

Kevin Scripture, MD, Judy Risch, OD, and I have found our results to be quite similar. While we have comanaged more than 2,500 patients now with trigat at the Richmond Eye Center, we performed a retrospective analysis of 500 consecutive trigat cases.

Our findings paralleled those of Dr. Koch in that we had no cases of traditional CME and no postoperative infections. Approximately 10% of these eyes required postoperative intervention with one topical medication to control a short-term spike in IOP. All pressures had normalized by 1 week.

While one could certainly manage the IOP spike by doing a paracentesis, you would then have to assume that you are releasing a clinically significant amount of this combination drug. This would then require having to start the patient on two additional drops postoperatively, as opposed to one.

Postoperative expectations

The most common short-term side effect from trigat is the transient scotomatic effect of the medication. Nearly all patients will notice a rather significant “floater” superiorly the day of surgery. It usually improves 50% the next day and typically is completely gone in 7 to 10 days. No patients who had bilateral treatments, however, wished to switch to drops for the second eye. With appropriate preoperative education, these symptoms are expected and well tolerated.

In general, initial floaters can be expected to last up to 2 or 3 weeks. Patients describe them as mossy or web like, with vision usually very good around the floaters. They will resolve as the trigat settles out of the visual axis and as the triamcinolone dissolves.

Steroid particles present in the anterior chamber can become a pseudo-hypopyon. This can be easily distinguished from infectious endophthalmitis because of the good vision that these patient routinely have and the absence of pain.

Concerns/potential risks of trigat use

General Risks

- **Antibiotic clearance:** Studies have shown that antibiotic clearance from the anterior chamber is fast, with half-life measured in hours. However, studies in rabbits by Iyer and colleagues showed that adequate vitreal concentrations of a new-generation fluoroquinolone were maintained for 12 hours in uninflamed phakic eyes.
- **Retinal/ocular toxicity:** Improper formulation could result in increased toxicity levels at the vitreoretinal level.
- **Standard of care:** Some level of medicolegal risk is always associated with any procedure that is not considered standard of care.

Intraoperative Risks

- **Zonular damage:** Mechanical or traumatic weakening of a small segment of zonules can occur.
- **Bleeding:** It is possible to nick the iris or ciliary body with the bent cannula during the blind pass under the iris.
- **Capsular rupture:** During this blind pass of the cannula under the iris, there is some risk of not extending far enough peripherally, resulting in the tip penetrating the posterior capsule.
- **Vitreous manipulation:** It can lead to a posterior vitreous detachment and, ultimately, a retinal detachment.

Postoperative Concerns

- **Floaters:** Most visual obscuration resolves in 5 to 7 days. However, it can last 2-3 weeks.
- **Pressure spikes:** Kenalog debris in the anterior chamber can lead to a temporary spike in IOP. About 8% to 10% of patients will need a short-term ocular hypotensive agent.
- **Steroid response:** A study by Jonas and colleagues has shown that intravitreal triamcinolone can cause elevated IOPs lasting 6 months or longer. We have experienced no long-term elevations in IOP and attribute this to the smaller concentration being administered in our investigation.

Source: Mangan R

Further study planned

We are in the process of a formal study to determine exact percentages of adverse results and to compare them to the more patient-dependent practice of postoperative drops.

While more formalized prospective studies are warranted, we may have come as close as one can to an ideal combination drug for the postoperative management of lenticular surgery. In our experience, trigat has been safe, effective and certainly more cost-effective now that patients have no “out-of-pocket” expense for their postoperative medication.

Development of a well-designed drug delivery system in the form of a time-released biodegradable implant may allow us to deliver trigat in a slower, more controlled manor. In theory, this would decrease clearance time of the gatifloxacin while reducing risk of ocular toxicity. Additionally, the development of a less opaque form of vitreal steroid may decrease the visual obscurations associated with triamcinolone.

For more information:

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