Improving the cataract patient experience by managing pain and inflammation

By Eric Donnenfeld, MD

We are at the precipice of an exciting era in ophthalmology. Two new drugs have been approved—a dexamethasone intraocular suspension and a dexamethasone intracameral insert. Additional promising options are in the pipeline.

In the 2018 ASCRS Clinical Survey, almost 90% of participants agreed that low to moderate intraocular inflammation after cataract surgery can significantly affect visual quality, vision recovery time, and patient comfort and satisfaction. Nearly 50% of respondents dose NSAIDs 4 weeks after surgery for most patients, whereas 18% do not prescribe them at all. Figure 1 shows NSAID practices for high-risk patients vs. standard patients.

More than 70% prescribe steroids for most standard patients for 4 weeks after surgery, and 14% dose them for 2 weeks or less. More than half continue or increase steroid use postop in high-risk patients, but 16% do not use steroids differently in high-risk patients.

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Inflammation/Infection
Do you use NSAIDs differently in high-risk patients vs. standard patients? (Select all that apply)

- Yes, I begin/increase the use of NSAIDs prior to surgery in high-risk patients
- Yes, I continue/increase the use of NSAIDs postoperatively
- No difference
- I don't perform cataract surgery on high-risk patients

Figure 1. Responses from the 2018 ASCRS Clinical Survey showing NSAID practices for high-risk patients vs. standard patients.
Pain is the most common adverse event associated with cataract surgeries. A clinical study of 306 patients measuring pain and satisfaction immediately after cataract surgery showed that 37% had mild to moderate pain and 34% required oral medications to manage it. Postop pain was the most significant predictor of patient dissatisfaction and was associated with low surgical experience quality ratings.

The most common cause of decreased visual acuity after cataract surgery is cystoid macular edema (CME). Patients with postop inflammation have a higher risk of corneal edema. Risk factors for CME include diabetes or other autoimmune disorders, inflammatory conditions, glaucoma, intraoperative floppy iris syndrome, and retinal vascular disease. Complex cases with longer ultrasound and irrigation times and surgical complications are associated with an increased risk of inflammation.

Unmet need
Traditionally, we have managed pain and inflammation with postop eye drops, increasing the dose in patients at risk for inflammation. Topical steroids were convenient and historically inexpensive. Steroids also are direct, noninvasive, and less likely to cause systemic effects. In addition, they provide good coverage, if patients use them.

However, clinical studies have shown that patients do not use 40–50% of prescribed drops. Patients may believe they do not need them, find the drops uncomfortable, or have physical limitations that prevent proper instillation.

In a study evaluating eye drop administration by cataract patients who did not have experience with eye drops, 31% had trouble instilling them and 92% instilled them incorrectly.

New frontier
Novel ideas and innovative solutions are emerging that will offer us new ways to prevent and manage postoperative pain and inflammation.

Approximately 2 decades ago, we had to prescribe 3 drops 4 times a day for 1 month. We have made significant strides in eliminating that regimen. Better drops are being developed with less frequent dosing, as well as combined drops, intraoperative drops and injections, and sustained-release technologies.

Sustained-release drug delivery options need to be easy to place in the eye and remove, tolerable, consistent, and cosmetically invisible but easy to identify. This will be especially important not only for cataract patients, but for patients with chronic eye disease, such as dry eye and glaucoma.

References

Dr. Holland is director of the Cornea Service at the Cincinnati Eye Institute and professor of ophthalmology at the University of Cincinnati. He can be contacted at eholland@holprovision.com.

Less than 30% instill anti-inflammatory agents intraoperatively as an injection or by adding it to the irrigating solution (9% always use; 18% sometimes use), and more than a third reported that they will never use these options.

Eighty-six percent are confident or very confident that combining corticosteroids and NSAIDs can reliably treat postoperative inflammation and control pain after routine cataract surgery.

We gathered insights from a panel of experts, who discussed ways to manage pain and inflammation associated with cataract surgery. They shared their experiences with intracameral dexamethasone, a dexamethasone intracanalicular insert, nanotechnology loteprednol, and other treatment options.

Reference

Dr. Donnenfeld practices with Ophthalmic Consultants of Long Island and Connecticut and is a clinical professor of ophthalmology at New York University and a trustee at Dartmouth Medical School. He can be contacted at ericdonnenfeld@gmail.com.
Intracameral dexamethasone helps overcome adherence obstacles

By Eric Donnenfeld, MD

Patient adherence issues to drop regimens after cataract surgery decrease postop medication efficacy and can adversely impact patients' surgical outcomes.

A newly approved product—a novel, bioabsorbable, intracameral dexamethasone drug delivery suspension—can clear this stumbling block.

Delivery system

I gained experience with this new treatment option through FDA clinical trials.

In the trials and in practice, we found that when you enter at 180 degrees and pull back slowly, the dexamethasone suspension often ends up in the anterior chamber. This is common and not a problem, but it is preferable to place it behind the iris.

Another successful technique is to place the cannula under the iris as close to the iris root as possible. Then, pull back quickly, leaving the dexamethasone behind.

Patient response

New drug delivery systems are meeting a major unmet need. I estimate that 20% of patients physically cannot use drops. In the intracameral dexamethasone group, 69% of patients agreed that not having eye drops was very convenient.

I am pleased with the dexamethasone intraocular suspension because it guarantees compliance and gives the surgeon control. A surgeon may perform a perfect surgery, but postop complications can occur as a result of nonadherence with a topical regimen. Intracameral dexamethasone allows us to administer a precise dose, avoid systemic absorption and topical toxicity, and overcome obstacles to adherence.

References


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Improving the Cataract Patient Experience:
Minimizing pain and inflammation while reducing the need for topical drops

Bridging the gap: Dexamethasone punctal insert

By Alice Epitropoulos, MD

In the last several years, we have had multiple advancements in cataract surgery technology. However, until recently, we have had an unmet need for delivering medications to the eye postoperatively.

New drug delivery systems are a major step forward.

Overcoming challenges

Patient adherence to topical regimens is poor, but the new dexamethasone intracanalicular insert is an innovative route of administration and one of the surgeon-controlled solutions we can offer our patients. The insert is a corticosteroid indicated to treat postop pain and inflammation after ocular surgery, reducing patient error and nonadherence.

It delivers a tapered dose of dexamethasone over a period up to 30 days; investigators rated it as easy to insert; and it resorbs following treatment.1-3 Furthermore, it is conjugated with fluorescein to assist in visualization.

This drug delivery system is preservative-free and the punctal occlusion provided by the insert may also benefit patients with dry eye.

Three Phase 3 prospective, randomized, double-masked, vehicle-controlled trials evaluated the safety and efficacy of the dexamethasone insert in 926 patients having cataract surgery.3,4

In each Phase 3 study, more patients treated with the insert were pain-free at day 8 and had absent anterior chamber cells at day 14 vs. placebo. In one trial, the difference of absent anterior chamber cells at day 14 vs. placebo was not statistically significant.

The dexamethasone insert received FDA approval in November 2018 for the treatment of ocular pain following ophthalmic surgery. In June 2019, the FDA approved a supplemental New Drug Application with the addition of treatment of ocular inflammation to its indication.

All three trials showed the device was safe and well tolerated, with a low incidence of increased intraocular pressure.

Patients reported highly favorable outcomes in comfort, convenience, and satisfaction.5

Conclusion

Innovative drug delivery systems will improve patient compliance and reduce ocular toxicity. Manufacturers are working on additional technologies to eliminate nonadherence and treat other conditions.

References

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By Edward Holland, MD

The development of better eye drops that can be administered less frequently may help reduce therapy adherence challenges. Not only could this help our postop patients but also those with chronic ophthalmic conditions.

One strategy has been the formulation of mucus-penetrating particle nanotechnology, which was applied to loteprednol.

Twice-daily dosing
Nanotechnology loteprednol etabonate suspension 1%, which was approved by the FDA in 2018, is the first twice-daily corticosteroid for postop pain and inflammation. It was developed based on the concept that smaller particles penetrate more effectively and can potentially reduce the drug concentration.

Traditional suspension eye drops become trapped in the mucus layer, the defense system of the ocular surface, which prevents penetration of the drug. However, mucus-penetrating particles pass through the mucus layer without disrupting it, resulting in better penetration and higher drug concentrations.

In two multicenter, randomized clinical trials for FDA approval, at days 8 and 15, nanotechnology loteprednol significantly resolved pain and inflammation compared with the vehicle.

Resolution of pain to grade 0 was 43% on day 4, 56% on day 8, and 69% on day 15. Most cataract surgeons add a nonsteroidal anti-inflammatory, which is quite effective.

We also need to know whether increasing the drug penetration will worsen side effects. However, loteprednol is a very good molecule and the only available ester steroid. Ester steroids usually do not increase IOP like ketone steroids do. This clinical trial showed that there was no significant difference in side effects compared with the control.

Conclusion
I believe better formulations, muco-adhesive technology, muco-penetrating particles, smaller drug particle size, and sustained-release technology will play an important role in managing pain postop with fewer drops. This strategy also would be beneficial in treating chronic diseases such as dry eye and glaucoma.

References

Dr. Holland is director of the Cornea Service at the Cincinnati Eye Institute and professor of Ophthalmology at the University of Cincinnati. He can be contacted at eholland@holprovision.com.


Intracameral ketorolac/phenylephrine improves surgical experience

By Denise Visco, MD, MBA

Most intraoperative approaches for mydriasis and pain use off-label applications or compounded medications. I prefer not to use compounded medications because of potential risks.

Clinical evidence

Intracameral phenylephrine/ketorolac, which is added to the irrigating solution during cataract surgery, maintains iris tone during cataract surgery, prevents intraoperative floppy iris syndrome, maintains pupil dilation better than epinephrine, and decreases surgical complications. An additional indication is that it reduces pain.

Retrospective investigation

Taking a look at patients’ surgical experience, we retrospectively reviewed pain and inflammation in 2,277 eyes in our practice that had cataract surgery. A topical nonsteroidal anti-inflammatory was used 2 days before surgery and 10 weeks postop in all patients. Group 1 received intracameral phenylephrine/ketorolac, whereas Group 2 received a 4-week tapered dose of loteprednol.

Patients in Group 1 had less pain and photophobia, half the incidence of rebound iris, and one-third the incidence of cystoid macular edema (CME) compared with Group 2. I did not expect to see such a significant difference. In fact, when we began using intracameral phenylephrine/ketorolac instead of the topical steroid with our regimen, I expected I could have more problems, not less.

In addition, by switching to intracameral phenylephrine/ketorolac, we eliminated 196 drops per eye.

Conclusion

In my practice, intracameral phenylephrine/ketorolac has resulted in a better patient experience, with less pain, and it has reduced the need for analgesics. In addition, patients have better vision on postop day 1 and we use fewer drops after surgery.

All of these benefits indicate that intracameral phenylephrine/ketorolac is good for the surgeon and good for the patient.

References


Dr. Visco is medical director and founder of Eyes of York Cataract & Laser Center in York, Pennsylvania. She can be contacted at dvisco@eyesofyork.com.
Compounded combination therapies streamline topical drop regimens

By William Wiley, MD

Prescription eye drops are a significant source of frustration for cataract surgery patients. Using multiple medications on different dosing schedules can be confusing, and they must cope with the expense and trips to the pharmacy.

To streamline the process, we began using a compounded formulation. As a result, our patients usually need to instill only 1 drop per day.

<table>
<thead>
<tr>
<th>Previous dosing schedule</th>
<th>Fewer drops</th>
<th>Fewer drops plus sub-tenons</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Steroid</strong></td>
<td>4 times a day, taper down to once a day over 30 days</td>
<td>Week 1: 4 drops per day.</td>
</tr>
<tr>
<td><strong>Antibiotic</strong></td>
<td>4 times a day for 10 days</td>
<td>Week 2: 3 drops per day.</td>
</tr>
<tr>
<td><strong>NSAID</strong></td>
<td>1 time a day for 30 days</td>
<td>Week 3: 2 drops per day.</td>
</tr>
</tbody>
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Searching for better options

When we began looking for simpler alternatives to traditional eye drop regimens, we injected a compounded formulation of triamcinolone and moxifloxacin into the vitreous. It worked well but lasted only 2 weeks and originally did not contain an NSAID. We were not sure how long the antibiotic lasted, but it did prevent endophthalmitis. Inflammation occurred postop in some patients, who needed to return to using drops. There was also a 2% risk of cystoid macular edema (CME).

To prevent postop inflammation, we placed the steroid sub-tenons, where it lasted 4 to 6 weeks. It did not cause floaters, and postop inflammation or rebound did not occur.

Bromfenac virtually eliminates CME, so we added it to our regimen, along with prednisolone and gatifloxacin to address potential abrasions, limbal relaxing incisions, or other conditions that could arise.1

We worked with a compounding pharmacy to create this formulation of prednisolone acetate 1%, gatifloxacin 0.5%, and bromfenac 0.075%. We can prescribe compounded medications from a compounding pharmacy following strict requirements under section 503B by the FDA and the Federal Food, Drug and Cosmetic Act. We bulk order the drops and provide them so patients do not need to visit the pharmacy.

It can be tapered or used with a bolus of steroid elsewhere. If we use dexamethasone intraocular suspension plus this drop, the dexamethasone ophthalmic insert in the lower punctum with this drop, or sub-tenons triamcinolone/moxifloxacin, patients need to instill only one drop of this compound per day.

The compounded drop has had a favorable safety record. We have used this technique in 4,000 eyes, virtually eliminating endophthalmitis, reducing postop inflammation, and significantly reducing CME.

Conclusion

The triple combination drop allows once-daily dosing, if used in combination with a steroid and virtually eliminates CME and endophthalmitis.

Reference


Dr. Wiley is medical director of the Cleveland Eye Clinic. He can be contacted at drwiley@clevelandeyeclinic.com.
IMPROVING THE CATARACT PATIENT EXPERIENCE:
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CME questions (circle the correct answer)

1. Which of the following are risk factors of cystoid macular edema?
   a. Diabetes
   b. Glaucoma
   c. Intraoperative floppy iris syndrome
   d. All of the above

2. What is the preferred location for dexamethasone suspension?
   a. In the anterior chamber
   b. Behind the iris
   c. In the posterior chamber
   d. In front of the iris

3. Which of the following is true of dexamethasone intracanalicular inserts?
   a. It delivers a tapered dose over 30 days.
   b. It resorbs following treatment.
   c. It is conjugated with fluorescein.
   d. All of the above

4. Which of the following is an advantage of mucus-penetrating particle (MPP) technology?
   a. The smaller particles penetrate the mucus layer more effectively.
   b. MPP technology may result in higher drug concentrations.
   c. MPP technology may help reduce patient adherence challenges.
   d. All of the above

5. Which of the following is true of intracameral phenylephrine/ketorolac?
   a. It results in a worse patient experience.
   b. It results in more pain.
   c. It reduces the need for analgesics.
   d. It results in more drops after surgery.

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