Lotemax: An effective anti-inflammatory therapy

by John Sheppard, M.D.

Patients with allergies, dry eye, blepharitis, and other chronic ocular inflammation require quick and effective treatment, and controlling their condition is central to our success as cataract and refractive surgeons. Because these patients have chronic conditions, they can become lifelong patients in our practices and might recommend family members and other patients.

However, we are challenged with what to prescribe as the best maintenance therapy for patients requiring lifetime anti-inflammatory therapy, even if they require it only periodically. We must identify the best agents to treat chronic ocular inflammation in these conditions.

To assess the most effective agents for ocular inflammation, my colleagues and I conducted a lab study using a rabbit uveitis model in which all available approved prescriptive steroid preparations were compared against one another: Lotemax (loteprednol etabonate ophthalmic suspension 0.5%, Bausch & Lomb, Rochester, N.Y.), prednisolone acetate 1% (Pred Forte and generic), dexamethasone sodium phosphate 0.1%, and fluorometholone 0.1%.

We found clear advantages with Lotemax in protein exudates into the anterior chamber under identical circumstances in 60 New Zealand white rabbits. The glucocorticoid receptor
Steroid-induced lamellar keratopathy (SILK)

by Marguerite McDonald, M.D., F.A.C.S.

Recently, physicians have seen more patients with SILK, or steroid-induced lamellar keratopathy. It masks as stage III or stage IV DLK (diffuse lamellar keratitis), with interface infiltration. At the slitlamp, the cells may appear to be clumped or diffuse.

Doctors often do not measure the IOP when they see cases that resemble SILK, as they think they are dealing with DLK, and they do not want to disturb the flap. If they do take the pressure, they know automatically the patient has SILK. The pressure can be more than 30 mm Hg easily.

This misdiagnosis causes the surgeon to put the patient on even more topical steroids, and the pressure goes even higher. If perchance the surgeon stops the steroids, the IOP drops, and the cornea clears.

There are reports in the literature of SILK associated with prednisolone acetate and dexamethasone. To my knowledge, no SILK cases have been reported in association with loteprednol. This gives further, though indirect, support to loteprednol's safety profile.

Lotemax is also effective with patients who are contact lens intolerant. These patients may have dry-eye and/or allergic conjunctivitis. When we use topical loteprednol, we're treating those concomitant problems that brought them to us in the first place as contact-lens–intolerant LASIK candidates, and that now threatens to complicate their post-operative healing process.

Loteprednol in Refractive Surgery

Also treats common concomitant problems such as:

- Dry Eye
- Meibomian Gland Disease
  - Keratitis
  - Conjunctivitis
- Allergic Eye Disease

References

Surface ablation and pain control

by Marguerite McDonald, M.D., F.A.C.S.

Topical steroids also play a role in soothing pain from surface ablation. Surface ablation is becoming more popular. According to statistics from Market Scope (Manchester, Mo.), more than 200,000 surface ablations will be performed in 2007, compared to an absolute low per year of 50,000 in 2003.

The procedure is becoming popular again because wavefront-based surface ablation gives even better results than wavefront-based LASIK. The recovery is much easier and faster than it was in the past.

Modern lasers give smoother ablations, modern bandage contact lenses are much improved, and we have much better drugs to control the pain. Additionally, there are new drugs in development that cut reepithelialization time in half.

Surface ablation has been associated with increased pain. I started to conduct unfunded pain research six years ago when PRK was out of vogue.

We first gave our PRK patients only artificial tears and fluoroquinolones. The first pain scores were 10 on a scale of zero to ten—for everyone. We then started to add different agents back into our “pain control recipe”—we first added back topical acetate.

Just by adding the topical steroid, the pain scores went from an average of 10 to an average of five. After a while, we halted the study because we felt it was bordering on the unethical to proceed when the results were so clear cut. Controlling inflammation controls the pain, to a great degree.

There are many papers that prove that judicious use of topical steroids, especially in the early postoperative period, is critical for the prevention of haze and regression. In fact, patients that have had a surface ablation procedure often need to use steroids for one to two months, well as a nonsteroidal anti-inflammatory drug and an antibiotic.

Steroids are also important for LASIK. They prevent diffuse lamellar keratitis (DLK), and they are the mainstay of treatment when one encounters a case of DLK.

Treatment for DLK can go on for a month or more in severe cases. Other post-operative LASIK complications such as epithelial defects, a dislocated flap, and dry eye often require a prolonged course of steroid treatment.

In the case of a post-operative infection, once you have attacked the microbe, you have to control the cornea’s healing response and the subsequent scarring. In other words, even if you are appropriately proactive in addressing post-operative complications (i.e., if you surgically eliminate the striae, reposit the dislodged flap, and/or remove the interface debris), these patients likely will be on topical steroids for weeks, if not months.
Treating Ocular Inflammation

**Lotemax: Ideal for refractive surgery**

by Marguerite McDonald, M.D., F.A.C.S.

LASIK and surface ablation require a safe, effective topical steroid, which has to be given for one to two weeks with uncomplicated LASIK and at least one to two months with surface ablation. We know corticosteroids are incredibly effective at treating post-operative inflammation and most corneal diseases. However, their usage is limited because of side effects, even though they are the mainstay of treatment for most ocular inflammation.

The ideal topical anti-inflammatory would be effective, nontoxic, inexpensive, and it would be free of complications. Yet as ophthalmologists, we are afraid to give a full course of topical anti-inflammatory treatment because of the possible side effects from misuse or overuse.

Still, we all must manage the balancing act of corneal scarring, pain, interface scarring, and intraocular inflammation versus steroid dependence and cataract. Lotemax (Bausch & Lomb, Rochester, N.Y.) is uniquely suited for refractive surgery because it’s effective and has a low complication rate.

Lotemax is a re-engineered analog prednisolone and lacks the ketone group and number 20 carbon. It was designed intelligently, removing the ketone and replacing the number 20 carbon with chloro-methyl ester, which is responsible for its potency with a very low complication rate. There are few side effects because of that key architectural change, and it does not remain in the eye long after it is not needed.

Patients on Lotemax do not usually experience the IOP rise that accompanies steroid use. We all know that dexamethasone is the “B-52 bomber” of steroids. Dexamethasone use leads to an average IOP increase of 63%. Because of its safety profile, loteprednol is an ideal steroid to prescribe for two to three months after surface ablation procedures such as PRK.

In one study in which patients used dexamethasone four times a day for four to six weeks, 30% to 33% of patients experienced an intraocular pressure (IOP) rise, with a pressure between 20 mm Hg and 30 mm Hg; 4% to 6% had an IOP that was more than 30 mm Hg. In another clinical study of patients treated 28 days or longer, an IOP elevation of >= 10 mm Hg was reported in 6.7% of patients taking prednisolone acetate. Lotemax was the safest steroid, with only 1.7% of patients experiencing an IOP rise.

**Loteprednol: Derived From Prednisolone**

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How to administer steroids

by Uday Devgan, M.D., F.A.C.S.

There are several ways that eye surgeons can administer steroids to their patients; each approach has its pros and cons. The number one reason for prescribing steroids in most practices is to control post-operative inflammation.

Topical steroid use four times a day is typical, but we also can prescribe it more frequently in forgetful patients. For example, you can tell these patients to take the medication eight times a day, hoping they will take it four times a day.

Topical steroid use can lead to problems in certain patients: those who undergo a particularly difficult surgery such as dense rock of a cataract, the use of a capsule dye, or a history of uveitis; those with a broken capsule or iris trauma; noncompliant patients; and patients who have used Flomax. These patients may need more than just topical steroids.

We also can give subconjunctival and sub-Tenon’s injections. In certain cases, I like to inject patients with dexamethasone and Kenalog (triamcinolone) while still using topical steroids. If they still have a lot of inflammation or I suspect they will be noncompliant, I may prescribe my routine topical steroid and still inject the patient on the operating room (OR) table at the end of the case.

This is best to perform in those patients who you know will never use the drops post-operatively. If there are complications, injections at the end of the case may be better than the topical route.

We also can use intravitreal injections and a preservative-free drug within the anterior chamber. However, with rapid turnover in the anterior chamber, I think any solution will be gone relatively quickly. Some suspensions may stay a little longer but not much.

Surgeons also can inject steroids in the pars plana, but that is more risky, more painful, and you may get a little bleeding. If you are using topical anesthesia, these patients still may feel it, and the risk for an IOP rise later increases.

James Gills (M.D., Tarpon Springs, Fla.) also described going through the zonules and injecting in the vitreous cavity before IOL placement. This also works but has the same issues of high pressure later, and patients may have haze or floaters.

We also can give steroids through the intravenous (IV) line or orally. I like to do this in the postoperative state when injecting subconjunctival steroids and when topical drops alone will not solve a problem such as patients with a history of particularly aggressive uveitis.

References
The reported rate of IOP spikes with prednisolone acetate use is about one out of every 14 patients; with [Lotemax], it’s far less—one out of every 50 patients.

Uday Devgan, M.D.

Lotemax: Steroid use after cataract surgery

by Uday Devgan, M.D., F.A.C.S.

Topical steroid use can have certain unwanted side effects. The main risks are a rise in intraocular pressure (IOP), posterior subcapsular cataracts, and increased infection. Increased pressure is a serious problem, as it could inadvertently give patients glaucoma.

The reported rate of IOP spikes with prednisolone acetate use is about one out of every 14 patients. This can lead to increased emergency visits, increased costs, and decreased patient satisfaction. With loteprednol etabonate ophthalmic suspension 0.5% (Lotemax, Bausch & Lomb, Rochester, N.Y.), it’s far less—one out of every 50 patients—and the rate of IOP with Lotemax is comparable to placebo.1

There are two ways to avoid the risk of IOP spikes. One way is to not treat the patient with steroids at all and instead administer a non-steroidal anti-inflammatory drug (NSAID). However, this approach is not the typical standard of care, and it might not control all the inflammation. The second approach is to offer a smarter steroid in which IOP spikes are rare or blunted.

Steroids are divided into two classes: esters and ketones. The ketone class consists of dexamethasone, prednisolone, rimexolone, fluorometholone, and the other “-ones,” while the ester class consists of loteprednol etabonate only.

Loteprednol etabonate is a derivative of prednisolone. Through retrometabolic design, the ketone group at position 20 of the prednisolone molecule was replaced with an ester group creating loteprednol etabonate. With this alteration, a new class of steroids was developed with a vastly improved safety profile. Therefore, physicians can get the efficacy they want and engineer away many of the side effects.

In long-term treatment patients, the rate of IOP spikes is significantly lower with the use of Lotemax and placebo compared with prednisolone acetate, which is about 14%.1 Even if you give Lotemax to patients who are known steroid responders, their response is noticeably blunted.

Additionally, in studies with uveitic patients, the efficacy of Lotemax and prednisolone is about the same.2 Lotemax also is effective for treating post-operative cataract inflammation. While prednisolone acetate very commonly is used off-label to treat post-operative cataract inflammation, Lotemax (loteprednol etabonate) is the only steroid that has an indication for post-operative use in its package insert.
vides an excellent combination of anti-inflammatory control and instantaneous relief.²

We looked at initial therapy for 72 dry-eye patients. Those who used Lotemax pre-treatment before they first used cyclosporine had a 75% lower stinging rate and a 68% lower Restasis discontinuation rate than those who started on Restasis alone. The Lotemax pre-treatment group showed less stinging (5.5% vs. 22.0%) and less Restasis discontinuation (2.8% vs. 8.3%) than the Restasis alone group.

The chronic blepharitis patient produces different challenges that would benefit greatly with maintenance therapy as well. Zylet (loteprednol etabonate 0.5%/tobramycin 0.3%, Bausch & Lomb) is an ideal combination therapy for patients with ocular trauma and cases that require inflammation and antimicrobial therapy control such as blepharitis, bacterial conjunctivitis, and peripheral ulcerative keratitis.

I typically use Zylet for induction four times a day over two weeks to wipe out the present Staphylococci for the patient who requires acute therapy for blepharitis. Thereafter, we will control long-term hypersensitivity with a maintenance dose of Lotemax alone, titrating to the lowest effective frequency, which is usually between twice a day (b.i.d.) and once weekly.

Red eyes occupy a great deal of time in our emergency practices. These eyes also must be well controlled prior to elective refractive or cataract surgery. The three principal causes of red eyes are: allergic conjunctivitis, blepharitis, and keratitis sicca.

Although the lion’s share of viral conjunctivitis presents to primary care providers, we also see the occasional eye with adenoviral ocular surface disease threatening a secondary bacterial infection. Again, the ideal treatment, when appropriate, is Lotemax.

Steroids control inflammation and that preparation prior to anterior segment surgery and prophylactic pre-operative down regulation of these inflammatory cascades is central to superior outcomes. In addition, concomitant therapy with non-steroids can limit the problems we see with posterior segment inflammation, with complicated posterior segment surgery,³ and with the dry-eye patient who does poorly in surgery.

References
2. Sheppard JD. Topical loteprednol pre-treatment reduces cyclosporine stinging. Presented at the ASCRS Symposium on Cataract, IOL, and Refractive Surgery, Washington DC, 2005
internalization of the Lotemax molecule was far superior compared with the other agents."

Because of these results, I know that when I prescribe Lotemax to my patients, it is not only safer, it is the most efficacious for my clinical practice. In addition, Lotemax can be dosed safely up to once an hour if necessary. Lotemax works effectively to treat uveitis, post-operative inflammation, allergies, and patients with allograft maintenance challenges.

I also have seen Lotemax help transform patients with other kinds of chronic inflammation. For example, we had one patient who regularly used preserved tears and lid scrubs and developed chronic dry eye with a neutrophic component.

The patient’s condition was not improving, and he could not wear contact lenses comfortably or see the computer. We made a simple switch to Lotemax, which treated the underlying etiology of this patient’s blepharitis and dry eye. The inflammation markedly improved, and the patient regained 20/20 vision over a two-month period.

Dry-eye and blepharitis patients

Dry eye forms the centerpiece for growth in our practice. We see many patients who are unhappy after LASIK surgery because of post-operative dry eye. A dry eye creates unpredictable refractive results and discomfort. The typical dry-eye patient is a sandwich-generation female who makes the majority of health care consumption decisions for the entire family.

Recently, there has been a paradigm shift in dry-eye disease. We now realize that dry eye is truly an inflammatory condition. A healthy tear contains a wide variety of healthy proteins, electrolytes, and cytokines, whereas the unhealthy eye contains a large number of deleterious substances and inflammatory proteins that are destructive to the ocular surface.

Control of dry eye with induction therapy using Lotemax prior to institution of topical cyclosporine pro-

"The Lotemax pre-treatment group showed a 75% less stinging rate (5.5% vs. 22%) and a 68% less Restasis discontinuation rate (2.8% vs. 8.3%) than the Restasis alone group."

John Sheppard, M.D.

Chronic Blepharitis

- Meibomian Dysfunction
- Evaporative Dry Eye
- Secondary Infection
- Selective Culture
- EyeScrub or Ocusoft
- Warm Compresses
- Doxycycline

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