

How Do You Approach Unexpected Results From PRK Over Prior LASIK?

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Have you ever performed a -1.00 D spherical enhancement with PRK after prior myopic LASIK only to achieve a surgical outcome of -2.50 D sphere? Alternatively, have you ever treated a patient for a -1.00 D refraction with PRK over prior myopic LASIK only to obtain a postoperative refraction of 2.25 D? Why do these unusual results occur, and how do you resolve them?

STEPHEN COLEMAN, MD

Laser technology is very precise, but it is less exact on previously operated eyes. In general, truly unexpected results following a primary procedure are relatively uncommon, whereas little surprises after enhancements are much more likely. This motivates many surgeons to strive to maintain a low enhancement rate.

Myopic LASIK commonly induces a small amount of spherical aberration (less so today compared with years past). The postoperative shape of the cornea is typically more oblate, making retreatments more challenging, particularly considering the new relationship between the peripheral and central cornea after LASIK. One pearl that I have found helpful when performing PRK over previous LASIK is to use the preoperative central keratometric values. They initially dictate the peripheral shot pattern and compensate for the cosine effect—a significant factor that

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—Stephen Coleman, MD

affects enhancement outcomes. Additionally, the role of the epithelium after LASIK is a significant variable, because it is responding to a new and different corneal shape. Optical coherence tomography technology will be very useful in furthering our understanding in this area.

STEVEN J. DELL, MD

Many corneal irregularities are minimized by the natural tendency of the epithelium to smooth over underlying problems. For example, in a keratoconic eye, the epithelium over the apex thins, which reduces the steepness in that area and may mask early forme fruste keratoconus. The epithelium is also an excellent apologist for iatrogenic insults to the cornea. An oblate cornea after myopic LASIK may have a very thick central epithelial cellular layer as a result of the epithelium's attempt to deal with the abnormal shape. After an enhancement in an eye that has undergone myopic LASIK or PRK, the epithelium may regrow with a similar, greater, or smaller number of cellular layers compared with its pre-enhancement state. This usually results in emmetropia, but occasionally, it results in under- or overcorrections. In my experience, this phenomenon is much more common after hyperopic LASIK corrections, where peripheral epithelial hypertrophy will cause hyperopic regression. Epithelial debridement is sometimes helpful in dealing with the hypertrophic epithelium.

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STERILE OPHTHALMIC SUSPENSION

Brief Summary**INDICATIONS AND USAGE:**

LOTEMAX is indicated for the treatment of steroid responsive inflammatory conditions of the palpebral and bulbar conjunctiva, cornea and anterior segment of the globe such as allergic conjunctivitis, acne rosacea, superficial punctate keratitis, herpes zoster keratitis, iritis, cyclitis, selected infective conjunctivides, when the inherent hazard of steroid use is accepted to obtain an advisable diminution in edema and inflammation.

LOTEMAX is less effective than prednisolone acetate 1% in two 28-day controlled clinical studies in acute anterior uveitis, where 72% of patients treated with LOTEMAX experienced resolution of anterior chamber cells, compared to 87% of patients treated with prednisolone acetate 1%. The incidence of patients with clinically significant increases in IOP (≥ 10 mmHg) was 1% with LOTEMAX and 6% with prednisolone acetate 1%. LOTEMAX should not be used in patients who require a more potent corticosteroid for this indication.

LOTEMAX is also indicated for the treatment of post-operative inflammation following ocular surgery.

CONTRAINDICATIONS:

LOTEMAX, as with other ophthalmic corticosteroids, is contraindicated in most viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal diseases of ocular structures. LOTEMAX is also contraindicated in individuals with known or suspected hypersensitivity to any of the ingredients of this preparation and to other corticosteroids.

WARNINGS:

Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision, and in posterior subcapsular cataract formation. Steroids should be used with caution in the presence of glaucoma.

Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical steroids. In acute purulent conditions of the eye, steroids may mask infection or enhance existing infection.

Use of ocular steroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex). Employment of a corticosteroid medication in the treatment of patients with a history of herpes simplex requires great caution.

The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation.

PRECAUTIONS:

General: For ophthalmic use only. The initial prescription and renewal of the medication order beyond 14 days should be made by a physician only after examination of the patient with the aid of magnification, such as slit lamp biomicroscopy and, where appropriate, fluorescein staining.

If signs and symptoms fail to improve after two days, the patient should be re-evaluated.

If this product is used for 10 days or longer, intraocular pressure should be monitored even though it may be difficult in children and uncooperative patients (see WARNINGS).

Fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid application. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal cultures should be taken when appropriate.

Information for Patients: This product is sterile when packaged. Patients should be advised not to allow the dropper tip to touch any surface, as this may contaminate the suspension. If pain develops, redness, itching or inflammation becomes aggravated, the patient should be advised to consult a physician. As with all ophthalmic preparations containing benzalkonium chloride, patients should be advised not to wear soft contact lenses when using LOTEMAX[®].

Carcinogenesis, mutagenesis, impairment of fertility: Long-term animal studies have not been conducted to evaluate the carcinogenic potential of loteprednol etabonate. Loteprednol etabonate was not genotoxic *in vitro* in the Ames test, the mouse lymphoma tk assay, or in a chromosome aberration test in human lymphocytes, or *in vivo* in the single dose mouse micronucleus assay. Treatment of male and female rats with up to 50 mg/kg/day and 25 mg/kg/day of loteprednol etabonate, respectively, (600 and 300 times the maximum clinical dose, respectively) prior to and during mating did not impair fertility in either gender.

Pregnancy: Teratogenic effects: Pregnancy Category C. Loteprednol etabonate has been shown to be embryotoxic (delayed ossification) and teratogenic (increased incidence of meningocoele, abnormal left common carotid artery, and limb flexures) when administered orally to rabbits during organogenesis at a dose of 3 mg/kg/day (35 times the maximum daily clinical dose), a dose which caused no maternal toxicity. The no-observed-effect-level (NOEL) for these effects was 0.5 mg/kg/day (6 times the maximum daily clinical dose). Oral treatment of rats during organogenesis resulted in teratogenicity (absent innominate artery at ≥ 5 mg/kg/day doses, and cleft palate and umbilical hernia at ≥ 50 mg/kg/day) and embryotoxicity (increased post-implantation losses at 100 mg/kg/day and decreased fetal body weight and skeletal ossification with ≥ 50 mg/kg/day). Treatment of rats with 0.5 mg/kg/day (6 times the maximum clinical dose) during organogenesis did not result in any reproductive toxicity. Loteprednol etabonate was maternally toxic (significantly reduced body weight gain during treatment) when administered to pregnant rats during organogenesis at doses of ≥ 5 mg/kg/day.

Oral exposure of female rats to 50 mg/kg/day of loteprednol etabonate from the start of the fetal period through the end of lactation, a maternally toxic treatment regimen (significantly decreased body weight gain), gave rise to decreased growth and survival, and retarded development in the offspring during lactation; the NOEL for these effects was 5 mg/kg/day. Loteprednol etabonate had no effect on the duration of gestation or parturition when administered orally to pregnant rats at doses up to 50 mg/kg/day during the fetal period.

Nursing Mothers: It is not known whether topical ophthalmic administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Systemic steroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. Caution should be exercised when LOTEMAX is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS:

Reactions associated with ophthalmic steroids include elevated intraocular pressure, which may be associated with optic nerve damage, visual acuity and field defects, posterior subcapsular cataract formation, secondary ocular infection from pathogens including herpes simplex, and perforation of the globe where there is thinning of the cornea or sclera.

Ocular adverse reactions occurring in 5-15% of patients treated with loteprednol etabonate ophthalmic suspension (0.2%-0.5%) in clinical studies included abnormal vision/blurring, burning on instillation, chemosis, discharge, dry eyes, epiphora, foreign body sensation, itching, injection, and photophobia. Other ocular adverse reactions occurring in less than 5% of patients include conjunctivitis, corneal abnormalities, eyelid erythema, keratoconjunctivitis, ocular irritation/pain/discomfort, papillae, and uveitis. Some of these events were similar to the underlying ocular disease being studied.

Non-ocular adverse reactions occurred in less than 15% of patients. These include headache, rhinitis and pharyngitis.

In a summation of controlled, randomized studies of individuals treated for 28 days or longer with loteprednol etabonate, the incidence of significant elevation of intraocular pressure (≥ 10 mmHg) was 2% (15/901) among patients receiving loteprednol etabonate, 7% (11/164) among patients receiving 1% prednisolone acetate and 0.5% (3/583) among patients receiving placebo.

DOSE AND ADMINISTRATION:
SHAKE VIGOROUSLY BEFORE USING.

Steroid Responsive Disease Treatment: Apply one to two drops of LOTEMAX into the conjunctival sac of the affected eye(s) four times daily. During the initial treatment within the first week, the dosing may be increased, up to 1 drop every hour, if necessary. Care should be taken not to discontinue therapy prematurely. If signs and symptoms fail to improve after two days, the patient should be re-evaluated (See PRECAUTIONS).

Post-Operative Inflammation: Apply one to two drops of LOTEMAX into the conjunctival sac of the operated eye(s) four times daily beginning 24 hours after surgery and continuing throughout the first 2 weeks of the post-operative period.

Storage: Store upright between 15°-25°C (59°-77°F). DO NOT FREEZE.

KEEP OUT OF REACH OF CHILDREN.

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Bausch & Lomb Incorporated, Tampa, Florida 33637

U.S. Patent No. 4,996,335

U.S. Patent No. 5,540,930

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MARK A. KONTOS, MD

Although PRK over prior LASIK has advantages, it carries a degree of uncertainty regarding the surgical outcome. Multiple factors probably cause variable outcomes. Mitomycin C (MMC) may have a less predictable effect in this setting, and epithelial hyperplasia is also a significant factor in many of these cases. When I looked through my past cases, I noticed that the patients who had a hyperopic overcorrection tended also to have moderate-to-high myopia at the time of their primary LASIK. The patients who had little or no effect after PRK often had lower myopia at the time of their primary LASIK. I try to keep this in mind when planning treatments. Because of the unpredictable nature of this type of enhancement, a detailed discussion with the patient about all possible outcomes is critical. Sometimes, the best plan of action is to leave things as they are.

ROBERT K. MALONEY, MD

Reoperations can produce strange refractive results, and it is often hard to determine why they occur. The surgeon should be aware of the possibility of map regions from basement membrane dystrophy. These areas of thickened epithelial cells affect refraction, and their removal during PRK can produce significant refractive shifts. These thickened areas of epithelial cells are best seen with fluorescein and by looking for areas of negative staining. Another problem occurs with PRK enhancements after PRK, particularly if corneal haze is present. Accidental or intentional debridement of the haze produces a large hyperopic shift, even before laser retreatment. Subepithelial tissue from prior surgery is more likely to be inadvertently removed if a rotating brush is used to remove the epithelium for the enhancement. For this reason, I use alcohol to remove the epithelium for PRK enhancements.

“Surgeons need to carefully monitor the amount of higher-order aberrations and the depth of ablation for enhancements.”

—Louis E. Probst, MD

LOUIS E. PROBST, MD

Although the results of lifting the flap for LASIK retreatments for myopic regression are potentially more precise and definitely more convenient than PRK enhancements, it has been shown that there is an increasing risk of epithelial ingrowth associated with lifting the flap as the postoperative time increases.¹ Therefore, PRK is my preferred enhancement method, particularly in the eyes of older patients that may have looser epithelial attachments.

In my experience, a myopic outcome after an enhancement for myopic LASIK regression is rare. When this does occur, it is likely the result of epithelial hyperplasia. A reasonable additional treatment would be epithelial removal with no laser treatment and the application of MMC to prevent further epithelial hyperplasia. Surgeons should always be careful about chasing progressive myopia with additional procedures, as this may indicate other ocular pathology.

Iatrogenic hyperopia after a customized myopic enhancement for myopic LASIK regression is more common. This outcome is due to the combined effect of the treatment of the myopia and higher-order aberrations, which result in an excessive ablation depth. Surgeons need to carefully monitor the amount of higher-order aberrations and the depth of the ablation for enhancements. With customized treatments, 18 μm per spherical equivalent diopter would be the expected depth of the ablation (a -1.00 D enhancement should have an ablation depth of only 18 μm). If the treatment plan shows a proposed depth of 30 μm , this is because of the additional treatment of the higher-order aberrations, which are probably greater than 0.50 μm . The treatment sphere should be reduced with the surgeon's adjustments until the ablation depth is closer to 18 μm to avoid overcorrection. Obviously, these adjustments are critical for patients in the presbyopic age group. With these adjustments, customized myopic enhancements yield excellent results with an improvement in uncorrected vision and quality of vision.

STEPHEN A. UPDEGRAFF, MD

I think that unusual results are directly related to wound healing after surface treatments. In the case of

a myopic result, epithelial hyperplasia is the most likely culprit and typically would be associated with corneal haze but not always. I would wait a minimum of 6 months before considering the next step. If appropriate, corneal segments may be the safest and most reliable next enhancement. A hyperopic result is typically related to subclinical stromal melting from MMC, which creates a flatter-than-intended cornea. If you pan the slit beam obliquely, you may pick up an otherwise imperceptible divot. I have reduced the concentration of MMC that I use to 0.01%, and I do not exceed 30 seconds of application. I also rinse the eye with continuous irrigation (50 mL). Surface treatments are easy until you are faced with these outcomes. That is why it is best not to plan a LASIK case with surface retreatment as your sole fallback for fine-tuning. ■

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1. Caster AI, Friess DW, Schwendeman FJJ. Incidence of epithelial ingrowth in primary and retreatment laser in situ keratomileusis. *J Cataract Refract Surg.* 2010;36(1):97-101.