Optimizing the Ocular Surface to Improve Outcomes With LASIK

Preoperatively confirming the presence of ocular surface disease may reduce postoperative complications.

BY TERRENCE P. O’BRIEN, MD

Ocular surface disease (OSD) is a common condition that is frequently underdiagnosed and can range in severity from asymptomatic or episodically symptomatic to a chronic debilitating state. Dysfunctional tear syndrome or dry eye disease (DED) results from the complex interrelationship between the amount of tears produced and the rate of tear evaporation that leads to hyperosmolarity and inflammation of the ocular surface. This activation of the inflammatory cascade results in an unstable, unhealthy ocular surface, leading to OSD. Optimizing the ocular surface during the preoperative management of LASIK and other keratorefractive patients may lead to faster epithelial healing and visual recovery as well as reduce the impact of DED and other complications postoperatively.

MATRIX METALLOPROTEINASE-9 ACTIVITY

Matrix metalloproteinase-9 (MMP-9) is a proteolytic enzyme that is produced by stressed epithelial cells. Elevated MMP-9 levels have been observed in the tear fluid of patients with DED and have been shown to destabilize the tear film and alter the corneal barrier function, leading to corneal epithelial irregularity and visual morbidity. Higher levels of MMP-9 are present in patients with more severe DED, and concentrations of MMP-9 in the tear film correlate with the severity of clinical examination findings.

The inconsistency and lack of correlation between the clinical symptoms and signs of DED and OSD make diagnosis and treatment challenging. Chalmers et al reported a low level of agreement between the assessment of the severity of DED between clinicians and their patients, confirming the widely suspected underdiagnosis of DED in the clinical setting. This finding is especially true in patients who do not report the symptoms of DED, because they may have reduced corneal sensitivity.

Refractive Surgery

In addition to patients who present with signs and symptoms of DED, studies have shown an important...
link between elevated levels of MMP-9 and ocular surgery. One of the most common postoperative complications of ocular surgery such as PRK and LASIK, DED affects approximately 50% of LASIK patients 1 week postoperatively, 40% 1 month postoperatively, and 20% to 40% 6 months postoperatively. Other complications such as fluctuating vision, reduced BCVA, and severe discomfort occur in approximately 10% of patients. DED is also a leading source of dissatisfaction among patients after LASIK (Figure 1).

The diagnosis of DED becomes more challenging after corneal surgery, including refractive surgery. Punctate epithelial keratopathy was detected with rose bengal or fluorescein staining in 2% to 6% of eyes that had LASIK, but symptoms of ocular dryness and irritation were found in 48% to 59% of these patients. One to 6 months after LASIK surgery, Wilson found that Schirmer tests with anesthesia detected no significant difference in tear production between eyes that developed symptoms and signs of DED versus those that did not have symptoms.

MMP-9 has also been associated with poor epithelial healing, epithelial ingrowth, and corneal ulceration after refractive surgery. Corneal wound healing after LASIK may be prolonged because of an insufficient attachment between the corneal flap and the corneal bed, and the delay is associated with elevated levels of MMP-9. MMP-9 is specifically found in the periphery of LASIK wounds, suggesting that its presence may impair flap adherence. The incidence of epithelial ingrowth is about 1% after LASIK, and in 75% of cases involving epithelial ingrowth, MMP-9 was found at the wound site. The dislocation of corneal flaps or ectasia, which consisted of a progressive deformation and thinning of the cornea after LASIK, has been shown to be related to corneal wound healing.

PREOPERATIVE SCREENING AND THERAPY
 Patients who have DED preoperatively experience more severe symptoms of tear dysfunction after LASIK, and their corneal sensitivity takes longer to recover compared to those without preoperative DED. Because preexisting OSD may be exacerbated by LASIK or PRK, its diagnosis and treatment as part of the surgical prescreening process helps to avoid complications. Successful identification and treatment of these patients in advance of surgery can also improve the ocular surface and thus allow for more accurate presurgical measurements.

Confirmation of the presence of underlying OSD such as DED will drive the initiation of appropriate therapy, especially for the perioperative management of refractive surgery. The treatment of inflammation related to OSD may involve topical cyclosporine, topical corticosteroids, oral doxycycline, topical azithromycin 1%, and systemic omega-3 essential fatty acid supplements. Anti-inflammatory therapy has been reported to improve both the signs and symptoms of OSD, and it is a targeted and effective therapeutic option for patients with underlying inflammation causing OSD. Topical anti-inflammatory therapeutics can normalize the ocular surface and improve the quality of the tear film after LASIK. Additionally, LASIK-induced neurotrophic epitheliopathy often responds to immunomodulation with topical cyclosporine, which treats the underlying inflammation and may facilitate corneal nerve regeneration and the restoration of corneal sensation. Thus, the treatment of DED before refractive surgery may reduce the risk and severity of DED postoperatively.

A NEW OPTION
 InflammaDry (Rapid Pathogen Screening, Inc.) is a new in-office diagnostic test currently under review by the FDA. This test is designed to detect abnormally elevated MMP-9 present in the late phase of the inflammatory cycle, which may be more clinically relevant than causal mechanisms or acute symptoms. Although MMP-9 activity is elevated in eyes with symptomatic DED and in a variety of other clinically easily identifiable ocular surface conditions, the test also reveals asymptomatic OSD and the hidden inflammation of DED.

Having a rapid, in-office test for elevated levels of MMP-9 available for patients that present with signs or symptoms of DED should facilitate ophthalmologists’ abilities to make an accurate diagnosis. Additionally, administering the InflammaDry test before and after corneal or refractive surgery may uncover subclinical inflammatory conditions, including the hidden inflammation of chronic DED, which could negatively affect post-surgical outcomes. This tool should give physicians an unprecedented capability of optimizing patients’ outcomes.

CONCLUSION
 DED and OSD are common conditions that may be present in patients seeking laser vision correction or other keratorefractive procedures. DED is the most common cause for dissatisfaction among patients undergoing LASIK. In-office screening with a rapid, reliable tool to detect markers for DED and OSD with high sensitivity and specificity allows surgeons the opportunity to diagnose and treat in advance of surgery to improve outcomes, reduce complications, and increase overall patients’ satisfaction.
Terrence P. O’Brien, MD, is a professor of ophthalmology and the Charlotte Breyer Rodgers distinguished chair in ophthalmology at the Bascom Palmer Eye Institute, University of Miami, Miller School of Medicine, in Palm Beach, Florida. He acknowledged no financial interest in the products or companies mentioned herein, but has served as an ad hoc nonsalaried consultant to Rapid Pathogen Screening, Inc. Dr. O’Brien may be reached at (561) 515-1544; tobrien@med.miami.edu.