Dry Eye and Refractive Surgery

Some of the causes and options for treatment.

BY RICHARD W. YEE, MD

Success in refractive surgery depends on diagnosing dry eye disease and optimizing the ocular surface both pre- and postoperatively. You must therefore have a firm grasp of ocular anatomy and knowledge of the options for treatment.

THE CORNEAL EPITHELIUM

Produced by the corneal epithelial surface cells, glycocalyx help mucin adhere to the corneal surface, which naturally repels water. Damage to the glycocalyx and corneal epithelial cells therefore results in insufficient mucin, which, in turn, destabilizes and breaks apart the tear film before the eye can blink. Epithelial damage can also result from the increased evaporation of tears or the decreased production of the aqueous component of the tear film, both of which cause increases in osmolarity. Evaporation or the improper spreading of tears leads to the direct exposure of ocular surface cells to external insults, which may lead to their death and damage to the ocular surface.

THE BLINK

Humans blink between eight and 20 times per minute (see *Asian Eyes*), with approximately 7.5 seconds elapsing between blinks. During the blink, the muscles around the meibomian gland contract, causing it to secrete oil. Blinking spreads this mixture of oily and aqueous secretions across the ocular surface. This lubrication is highly important to wound healing and the prevention of haze after refractive surgery.

When patients present with problems related to the ocular surface or haze after refractive surgery, I often find that they have been spending long periods using a computer. The rate at which people blink decreases by more than 60% when they stare at a computer screen.[1] The resultant desiccation of the ocular surface leads to haze and the transcriptional upregulation of cytokines. This may also account for the rarer but very significant late-onset haze. When addressing postoperative problems with the ocular surface, particularly haze, therefore, take environmental factors into account. For example, 3 months after undergoing LASEK to treat -10.00 D of myopia, a patient presented with the aggressive onset of 3+ haze. I asked about his recent activities. I learned that this cycling enthusiast was riding his bike without ocular protection. I aggressively optimized his ocular surface with some of the treatments described later and instructed him to wear isolation goggles (ie, microenvironment glasses), plugged the punctum, and prescribed aggressive steroids. The haze and associated refractive regression resolved completely, and the patient maintained his 20/20 vision.

TEAR FILM BREAKUP TIME

You must carefully evaluate the tear film breakup time in candidates for refractive laser surgery. A tear film breakup time of at least 7 seconds ensures that the ocular surface is healthy enough to survive the surgery and ensures proper healing.

Figure 1. The inflammatory cascade.

ASIAN EYES

Comparative studies have shown that the ocular surface of Asian eyes differs from that of whites.[1] It seems that Asian eyelid anatomy predisposes this subset of patients to having an abnormal tear film. For example, the average tear film breakup time was 8 seconds in the Hong Kong Chinese compared with 11 to 15 seconds in whites. Asians also had lower blink rates, a higher frequency of incomplete blinking, a lower tear volume, and a greater incidence of inferior staining signifying post-LASIK dry eye.

These findings suggest that there may be other differences in treatment effects. A closer look should be taken to find other anomalies between ethnicities that might direct the type of refractive surgeries that would be optimal for the health of the ocular surface. Surgeons should approach surface ablation with special consideration of the ocular surface and environment in order to meet the needs of their diverse patients.

1. Albietz JM, Lenton LM, McLennan SG. Dry eye after LASIK: comparison of outcomes for Asian and Caucasian eyes. *Clin Exp Optom.* 2005;88(2):89-96.

One of my preferred treatments for eyes with an abnormal tear film breakup time is sodium hyaluronate and HP-Guar. These substances are similar to the glycocalyx. I find that they stay on the cornea between blinks, yet shearing force causes them to liquefy, which allows them to facilitate the spreading of the tear film. Studies have shown that, compared with methylcellulose products, sodium hyaluronate increases tear film breakup time and may even improve epithelial wound healing.[2,3]

INFLAMMATION

Regardless of the source of dry eye disease, all affected patients have an abnormal tear film or abnormal tear function. These problems lead to reduced tear clearance, increased osmolarity, irritation of the ocular surface, and the infiltration and production of pro-inflammatory cytokines. The end result is inflammation.

Once inflammation starts, damage can occur to ocular structures that will perpetuate and intensify a cycle of signs and symptoms (Figure 1).

BENZALKONIUM CHLORIDE

Used to prevent the microbial contamination of multidose containers and to enhance the corneal penetration of certain drugs, benzalkonium chloride (BAK) has little effect on a healthy ocular surface. With chronic, long-term exposure or in the setting of dry eye, however, BAK lessens the integrity of epithelial cells, increases the number of conjunctival inflammatory cells,[4] causes a loss of goblet cells,[4] reduces tear function,[5] and decreases the tear film breakup time.[5]

When patients present with dry eye disease, determine whether they are using any medications preserved with BAK. If so, you may wish to switch them to a BAK-free alternative, if one is available.

TOPICAL CYCLOSPORINE A

Topical treatment with the immunomodulatory agent cyclosporine A inhibits T-cell–mediated ocular inflammation in dry eye disease, and I have seen this to be a very good treatment for patients with meibomian gland dysfunction. You can systematically assess for this condition through a detailed examination of the ocular surface. Check the orifices of the meibomian gland for fine sprigs of vascularity. Invert the eyelid with a cotton-tipped applicator to express meibum to grade flow. Lastly, observe the quality of meibum, ranging from clear to toothpaste-like. If the patient presents a combination of neovascularity, obstructed flow, and cloudy meibum, proceed with treatments for meibomian gland dysfunction.

Cyclosporine was well tolerated in clinical trials. In my own evaluations, I have found that cyclosporine produced a statistically significantly greater improvement in the quality of meibomian gland secretions and a statistically significantly greater decrease in lissamine green staining compared with artificial tears. This approach helps both the aqueous and lipid components during the period of wound healing and remodeling after surface ablation.

ANTERIOR BLEPHARITIS

Posterior blepharitis is a general term for inflammation of the posterior lid segment, and this condition is often related to anterior blepharitis, inflammation of the anterior lid margin. Inflammation on the outer half of the eyelid is mostly bacterial in origin, described as seborrheic and *Staphylococcus* depending on the organisms involved. Seborrheic blepharitis is the more common of the two; it manifests as cylindrical dandruff at the base of the eyelid. The cause of this condition is *Demodex follicularum*, a mite that is part of the arachnid family. The *Demodex* is also responsible for rosacea. Thus, physicians of patients suffering from rosacea should take the time to check their eyelids for dandruff. *Staphylococcus* blepharitis flares up due to a hypersensitivity to the bacteria *Staphylococcus aureus*. Although blepharitis is not a severe disease, it should be taken seriously because of the irritating symptoms associated with the problem.

ALTERNATIVE TREATMENTS

Several effective treatment options for dry eye target local inflammatory processes. Topical corticosteroids such as Lotemax (Bausch & Lomb, Rochester, NY) and Pred

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Forte (Allergan, Inc., Irvine, CA) are effective anti-inflammatory agents. Dry eye disease is chronic, however, and the toxicity of corticosteroids limits their potential for long-term use.

Researchers are studying antibiotics such as AzaSite (Inspire Pharmaceuticals, Inc., Durham, NC) and tetracycline for the reduction of the inflammatory processes associated with microbial colonization in dry eye disease.[6] Although antibiotics may be used long term, concerns about these agents include possible phototoxic reactions and increasing bacterial resistance. Also under investigation as possible dry eye therapies are omega-3 fatty acids, flaxseed oil, tea tree oil for anterior *Demodex*-related blepharitis, and autologous serum (used postoperatively during wound healing and in cases of very severe dry eye and nonhealing epithelial defects). Lacriserts (Aton Pharma, Inc., Lawrenceville, NJ) are also helpful in situations when the patient cannot produce enough surface-protective components.

Isolation techniques are critical to the understanding and prevention of acute and late-onset haze. Goggles, wraparound sunglasses, and microenvironment glasses (MEGs; SeeFit Inc., Houston, TX) can protect the compromised ocular surface after laser surgery and reduce the cytokines stimulated by the constant desiccation from environmental factors such as wind turbulence from cycling or dry eyes related to chronic staring at a computer screen.

These additional treatment alternatives are important to consider, because it is very important to optimize all aspects of the ocular surface during the 4- to 6-week period of wound healing and surface remodeling that is critical to maximizing visual outcomes following laser refractive surgery. ■

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