Dry eye disease (DED) is not at the front of most glaucoma specialists’ minds, but it is a major factor in ocular health that can be worsened by standard medical glaucoma treatment. New technologies allow eye care providers across specialties to get a clearer picture of the condition and work together to treat it.

NEW IMAGING
Meibomian gland architecture has long been something of a mystery. Until recently, available imaging techniques provided only a limited view of the glands. That changed in September 2015 with the introduction of Lipiview II (TearScience). (For more information on Lipiview II, visit bit.ly/beyeA146.) Eye care providers can now view the exquisite detail of gland architecture like never before, and what is visible is alarming: meibomian gland dropout is occurring at a startlingly young age. One of my patients is 22 years old and has lost 70% of his meibomian glands in the lower lids. By the time patients get to the glaucoma doctor, they are already behind the eight ball. Furthermore, topical glaucoma drops with preservatives can worsen ocular surface disease. That makes it important for glaucoma specialists to be aware of existing DED—even before a patient develops symptoms.

NEW CAUSES
What is causing this increase in gland dropout? One culprit is contact lenses. Their use is increasing among young patients, and contact lens wearers do not blink fully. This may be because the cornea is covered, so patients do not feel it drying out. The small amount of fluid under the contact lens may further diminish the instinct to blink fully. The second factor in the rising prevalence of DED is the growing use of electronic devices. Staring at smartphones, tablets, and the like tends to trigger partial blinking. Incomplete closure of the eyelids fails to express the meibomian glands, so the orifices where the oil exits begin to dry out, leading to a cascade of problems that cause DED. Dietary patterns also play a role. Most people no longer ingest a sufficient amount of omega-3 fatty acids, which are vital to adequate oil production. Omega-3 supplementation has been shown to ease DED. A multicenter trial found that PRN brand omega-3 fatty acid supplements lowered the Ocular Surface Disease Index Score, decreased corneal staining, lowered the tear osmolarity, and reduced inflammation.

MANAGING DED
Here is an overview of what we do in my practice to treat DED. We begin with the Standard Patient Evaluation of Eye Dryness (SPEED) questionnaire to gauge patients’ symptoms. I recommend this step to other eye care providers, including my colleagues in glaucoma.
In the chatter about new technologies for diagnosing and treating ocular surface disease, two therapies seem to be underdiscussed: punctal occlusion and nutritional supplementation.

**KEEPING TEARS ON THE EYE**

The popularity of punctal occlusion has seemingly declined. Some eye care providers have voiced concern about maintaining inflamed tears on the ocular surface, but we have not seen published or clinical support of this worry. A recent report by the American Academy of Ophthalmology found that plugs were an effective way to reduce the effects of dry eye disease (DED) and that serious complications were infrequent. Averaging the results of 15 studies that reported metrics on improvement, the investigators found that placing punctal plugs resulted in an improvement of 50% or more in symptoms, ocular surface health, and contact lens comfort, with a similar reduction in artificial tear use.

In our own practices, we have obtained excellent results from inserting medium-term dissolvable plugs such as the Comfortear Lacrisolve 180 (Paragon BioTeck). These plugs can be inserted directly into the canaliculi, they have been well tolerated by our patients, and the plugs can provide sustained relief from DED symptoms for months at a time. Although it does not resolve inflammation flagged with a positive matrix metalloproteinase-9 test result (InflammaDry; RPS), punctal occlusion dilutes the tear film, including the concentration of inflammatory components. The inflammatory cells are not trapped on the surface of the eye, because there is still outflow through the unobstructed canaliculus.

**OCULAR NUTRITION**

It remains unknown if ocular dryness is the cause or the result of inflammation, but DED seems invariably to be associated with chronic inflammation of the ocular surface. One option validated by impression cytology to reduce inflammation and improve goblet cell function is the nutritional supplement HydroEye (ScienceBased Health). It contains gamma linolenic acid (GLA) as well as omega-3 fatty acids (eicosapentaenoic and docosahexaenoic acids). A double-blind randomized trial found that this supplement decreased the production of disease-relevant inflammatory mediators. Evaluated over 6 months of use in 38 patients randomized to HydroEye supplementation or placebo, treatment significantly improved patients’ Ocular Surface Disease Index score and corneal surface asymmetry, and it reduced levels of the ocular surface inflammation markers HLA-DR and CD11c.

GLA, an omega-6 from black currant seed oil, is a precursor to stimulate tear production. In multiple clinical trials, GLA has improved DED signs and symptoms for a variety of dry eye types.

**CLINICAL APPLICATION**

Over-the-counter topical eye drops are simple and inexpensive, and in most cases, their use is a necessary precursor to insurance coverage of other DED treatment. Thus, we usually instruct our patients to start with drops after explaining that DED treatment is a process with multiple steps. When drops are not sufficient, we insert punctal plugs, a cost-efficient modality that works around the clock. We treat any inflammation that is present. Occasionally, it is so acute as to merit a topical steroid. In routine cases, however, we use HydroEye, cyclosporine ophthalmic emulsion 0.05% (Restasis; Allergan), or both; deciding which of these anti-inflammatory products to use first depends on patients’ individual circumstances and preferences.

**REFERENCES**


**ACKNOWLEDGMENTS**

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questionnaire can help tease out symptoms in patients who may feel something but not know that it is DED. Next, we evaluate tear osmolarity (TearLab Osmolarity System; Tearlab), followed by a test for matrix metalloproteinase-9 (InflammaDry; RPS). (For more on tear osmolarity, please see Dr. O’Dell’s article on p. 26.) If the tear osmolarity results are asymmetric or higher than 308 mOsm/L, the test result is positive, suggesting that the patient is hyperosmolar and has DED. Patients who are MMP-9 positive, they might be more responsive to anti-inflammatories, cyclosporine 0.05% (Restasis; Allergan), and lifitegrast ophthalmic solution 5%, (Xiidra; Shire). We look for signs of collagen vascular or rheumatic disease and, if indicated, perform the test for Sjögren syndrome (Sjö; Bausch + Lomb), in addition to rheumatoid arthritis and lupus.

Next, we perform imaging with the Lipiview II Ocular Surface Interferometer (TearScience) to see if the meibomian glands are formed correctly or if they have dropped out, become truncated, or dilated. We then stain the cornea with fluorescein and lissamine green, and a technician or optometrist will examine the ocular surface. We find gland expression valuable. What is the quality of the oil secreted? Is it healthy and similar in appearance to olive oil, or does it resemble something like toothpaste or creamy Italian dressing?

Once we have a clear picture of the patient’s ocular health, we can determine a treatment strategy, if warranted. For example, patients with blocked meibomian glands can benefit from LipiFlow Thermal Pulsation (TearScience). Sheri Rowen, MD, speaks with Steven Vold, MD, regarding dry eye disease and how it pertains to glaucoma.

On July 11, the FDA approved Shire’s Xiidra (lifitegrast ophthalmic solution) 5%, a prescription eye drop solution indicated for the signs and symptoms of dry eye disease (DED) in adults. Xiidra is the only prescription eye drop indicated for the treatment of both the signs and symptoms of this condition, and it is the first treatment to be approved for DED in more than a decade, Shire reports. The company expects to launch the product in the United States in the third quarter of 2016.

Xiidra is dosed twice per day, approximately 12 hours apart, in each eye. The safety and efficacy of the drug was studied in 1,181 patients (1,067 of whom received lifitegrast 5%) in four placebo-controlled, 12-week trials.

Assessment of symptoms was based on change from baseline in patient-reported eye dryness score (0-100 visual analogue scale). Assessment of signs was based on inferior corneal staining score (0-4 scale). In all four studies, a larger reduction in eye dryness score was observed with Xiidra at 6 and 12 weeks. In two of the four studies, an improvement in eye dryness score was seen with Xiidra at 2 weeks. At week 12, a larger reduction in inferior corneal staining score favoring Xiidra was observed in three of the four studies. The most common adverse reactions reported in 5% to 25% of patients were instillation site irritation, altered taste sensation (dysgeusia), and reduced visual acuity.

The inflammation associated with DED is thought to be primarily mediated by T cells and associated cytokines, reported Shire. One effect of this process may be increased expression of intracellular adhesion molecule-1 (ICAM-1), which may be overexpressed in corneal and conjunctival tissues in DED. Lifitegrast is a small-molecule integrin antagonist that binds to the integrin lymphocyte function-associated antigen-1 (LFA-1), a cell surface protein found on leukocytes, and blocks the interaction of LFA-1 with its cognate ligand ICAM-1. The interaction of LFA-1 and ICAM-1 can contribute to the formation of an immunological synapse, resulting in T-cell activation and migration to target tissues. According to Shire, in vitro studies demonstrated that lifitegrast may inhibit T-cell adhesion to ICAM-1 in a human T-cell line and may inhibit secretion of inflammatory mediators (cytokines) in human peripheral blood mononuclear cells. The drug’s exact mechanism of action in DED is not known.
(Continued from page 34)
Science) to melt the oil and express it. The goal is to release the blockages in the glands that are impeding the flow of natural oil. (For more information on LipiFlow Thermal Pulsation, visit bit.ly/beyeA173.) The device heats the meibum to a critical temperature, and then pulsation expresses the glands of their thickened blockages. The glands are therefore opened, and the meibum can freely flow again with each natural full blink thereafter.

Patients who blink incompletely and those with blepharitis often develop a level of biofilm on the lid margin. This clear, wrinkly-looking film grows over the gland’s orifices and blocks the oil from emerging. We use Blephex (Scope Ophthalmics) to gently remove the film. (For more information on Blephex, visit bit.ly/beyeA175.)

After treatment, I can see the oil start coming out again, so elements of the biofilm were actually blocking the orifices from releasing oil. We then ask patients to use Avenova (NovaBay), which contains hypochlorous acid, to get rid of bacteria, treat their blepharitis, and prevent biofilm on a daily basis thereafter. Because blepharitis is chronic in nature, they will continue to use this product.

GLAUCOMA DROPS

Benzalkonium chloride, a common preservative in topical glaucoma drops, can worsen existing DED and increase patients’ risk of developing the condition. It is therefore worthwhile for practitioners to consider preservative-free options. These include Zioptan (tafluprost ophthalmic solution; Merck) and Timoptic (timolol maleate ophthalmic solution; Valeant Pharmaceuticals), which comes in a unit-dose container. I have switched patients with significant DED to preservative-free drops and observed a real benefit. Alphagan-P (brimonidine tartrate ophthalmic solution; Allergan) contains Purite, and Travatan Z (travoprost ophthalmic solution; Alcon), has sorbit, both of which are gentler on the ocular surface than benzalkonium chloride. (For more on the role that medications play in DED, read Drs. Marshall and Noecker’s article on page 23.)

By watching for signs and symptoms of DED, glaucoma specialists can tailor treatments to these patients.


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