WHAT'S NEW IN DRY EYE MANAGEMENT?

A look at our growing list of options.

BY NICHOLAS J. BRUNS, OD, FAAO

Why are we seeing such a boom in dry eye therapies? Is it simply because dry eye disease (DED) is so common? Sure, that's a big part of it, but equally as likely, our understanding of the disease process has improved. We understand better than ever that dry eye is a multi-headed monster with secretory and evaporative components. We also understand the role the lids and inflammatory markers play in tear film stability. This article surveys some of the latest options to become available to us in the treatment of our patients with DED.

APPROVED AND IN THE ROTATION

Target: MGD

Receiving FDA approval in May, perfluorohexyloctane ophthalmic solution (Miebo, Bausch + Lomb) targets meibomian gland dysfunction (MGD) and acts as a supplement to meibum, increasing tear breakup time and improving tear film stability and thickness.[1] Think of perfluorohexyloctane as a blanket for the tear film, preventing early tear evaporation. The molecule, nonaqueous and amphiphilic, has an extremely low surface tension, yielding an almost silky feel upon instillation. The pivotal GOBI and MOJAVE studies demonstrated significant reduction in signs and symptoms of DED.[2-4] These two trials enrolled more than 1,200 patients, with the primary endpoint at week 8 being change from baseline in corneal staining and Vision Analog Scale compared with saline control; I'm seeing similar results in my practice. Many of my patients are relying much less on—or have even completely eliminated—artificial tears from their daily regimens.

Offer a Unique Route of Delivery

For patients looking for relief from the burden of eye drops, varenicline solution nasal spray 0.03% (Tyrvaya, Viatris) is a viable option. Varenicline is used twice daily in each nostril and aims to reestablish tear film stability. By binding to cholinergic receptors in the nasal mucosa, its target is the trigeminal parasympathetic pathway.[5] Patients using varenicline experience improvement in clinical signs as early as 4 weeks with maintained symptom management over 12 weeks.[6] Anecdotally, however, patients have reported symptom relief much earlier.

For those with dexterity issues, the nasal route may prove much easier to use, perhaps improving compliance. Additionally, varenicline aims to increase natural tear stability and production endogenously, working from the inside out, so to speak, leaving the natural tear film chemistry intact. This is a great option by itself, but it certainly has a place as an adjunctive therapy to traditional topical lubricants and medications.

Show the Lids Some Love

When thinking about dry eye management, we can't forget the lids! Before last year, we didn't have a true treatment for *Demodex* blepharitis. The

> MORE OFTEN THAN NOT, DRY EYE AND BLEPHARITIS ARE LINKED. IN FACT, THERE IS EVIDENCE THAT SUGGESTS BETWEEN 60% TO 70% OF PATIENTS WITH DRY EYE SYMPTOMS ALSO HAVE *DEMODEX* BLEPHARITIS.

Saturn-1 and Saturn-2 multi-center clinical trials for lotilaner ophthalmic solution 0.25% (Xdemvy, Tarsus Pharmaceuticals) showed safety and efficacy in 415 patients compared with control.[7] Lotilaner is a twice-daily drop used for 6 weeks that significantly reduces lash collarettes. Collarettes, composed of accumulated *Demodex* waste and debris, are 100% pathognomonic for *Demodex* blepharitis. The primary endpoints of both clinical trials were reduction in collarette quantity and in lid erythema and mite eradication compared with the control vehicle.

More often than not, dry eye and blepharitis are linked. In fact, there is evidence that suggests between 60% to 70% of patients with dry eye symptoms also have *Demodex* blepharitis.[8] Therapies, such as lid scrubs, tea tree oil, and meibomian gland expression, are more about managing symptoms than addressing the fundamental disease process. Lotilaner, a parasitic gamma-aminobutyric, acid-gated chloride channel antagonist, actually kills mites, thereby providing patients with symptom relief in as early as 2 weeks.

A Water-Free Cyclosporine

A familiar immunomodulator to those managing patients with dry eye, cyclosporine ophthalmic solution 0.1% (Vevye, Harrow), differs mainly in vehicle and concentration. This formulation is water-free, which is believed to increase bioavailability on the cornea. It is also preservative-free and does not contain oils or surfactants. Vevye, formerly known as CyclASol, has shown clinical safety and efficacy in early trials. It has demonstrated clinical improvements in dry eye symptoms and signs in as little as 4 weeks, while being well-tolerated.[9] Although cyclosporine is no newcomer to dry eye management, the modification and increased potency to the water-free vehicle, perflurobutylpentane, is certainly something to consider. Vevye uses perflurobutylpentane, based on semifluorinated alkanes, to spread evenly over the ocular surface with longer residual time and increased penetration of cyclosporine.[10,11]

IN THE QUEUE

A Promising MGD Alternative

Another option for MGD, AZR-MD-001 0.5% (Azura Ophthalmics), is an ointment applied directly to the lower lid. It is a keratolytic that's aimed at reducing abnormal keratin buildup, which alters meibum quality and leads to blocked meibomian glands. It also stimulates lipogenesis, which increases overall lipid quantity in the meibum, while also killing mites and bacteria on the lash follicles. Although perfluorohexyloctane treats symptoms and preserves tear film integrity, AZR-MD-001 is the first pharmacotherapy of its kind that treats the underlying pathophysiology.

In the phase 2 trial published last summer, AZR-MD-001 met primary endpoints, showing reduction in clinical signs and symptoms of MGD with twice-weekly dosing. A total of 82 patients were included in the study and demonstrated statistically significant improvements in meibomian gland liquid secretion scores and ocular surface disease index scores.[12] Just this past December, Azura announced positive safety and efficacy in contact lens wearers specifically, reporting increased wearing time of contact lenses for patients with MGD of up to 192 minutes.[13]

More Data Requested From First-in-Class Drug for Ocular Inflammation

Facing recent setbacks leading up to FDA approval, reproxalap ophthalmic solution 0.25% (Aldeyra Therapeutics) is a potential first-in-class drug that inhibits reactive aldehyde species and reduces ocular inflammation. In studies, it has demonstrated lasting improvement of signs and symptoms for as long as 12 weeks[14]; however, the FDA has raised concerns about adequacy of clinical data. Trials are ongoing and should be completed in the next 6 months.

A Microfluidic Contact Lens

Something not technically "in the queue," but in development that we should have on our radars could be a game-changer for our patients who wear contact lenses. Researchers are working on a microfluidic contact lens to address contact lens-induced dry eye, stemming from the reduction in tear volume, tear film instability, and increased tear osmolarity, followed by inflammation and resulting in ocular discomfort and visual disturbances. In a recent study, they investigated the concept of using a contact lens with microchannels to deliver

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ADDITIONAL READING

DRY EYE DIARIES

PLATELET-RICH PLASMA EYE DROPS FOR DRY EYE DISEASE

Separating the myths from the facts.

BY MAHNIA MADAN, OD, FAAO

Platelet-rich plasma (PRP) eye drops are an option when conventional therapy fails to resolve dry eye disease (DED). The biological composition of PRP and natural tears is similar. In addition, PRP therapy supplies several essential growth factors, vitamins, and cytokines that can facilitate the recovery of damaged corneal and conjunctival epithelium, thus reducing the signs and symptoms of ocular surface disease (OSD).

Although the use of blood-based products for the treatment of OSD is increasing, many optometrists are not prescribing PRP eye drops, perhaps because they do not have all the facts about this treatment modality. This article will examine five common myths related to the use of PRP in the treatment of patients with DED.

MYTH NO. 1: THERE IS NO EVIDENCE THAT PRP IS EFFECTIVE

Despite variability in how PRP is derived or prepared, most clinical studies have confirmed that PRP eye drop therapy is effective for the treatment of moderate to severe DED, both the evaporative and aqueous-deficient forms and including neuropathic and LASIK-induced DED.[1-14] For an example of the results of PRP therapy in a patient with DED related to Sjögren syndrome see the Figure on page 62.

In addition, studies have demonstrated that PRP therapy can promote the healing of dormant corneal ulcers that have not resolved with other forms of treatment.[2] PRP therapy has also been shown to significantly reduce the mean frequency of recurrent corneal erosions in patients with epithelial basement membrane dystrophy.[3]

For more on platelet-rich plasma eye drops, read my article on five common myths related to the use of PRP in the treatment of patients with dry eye.

3-month supply. However, once patients are educated about the potential benefits of PRP therapy, they are often willing to try it. Additionally, there are foundations that help patients access their medications.

With more than 50% of patients experiencing some level of dry eye, incorporating biologics in your clinic can be a powerful tool. ■

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MAHNIA MADAN, OD, FAAO

- Optometrist, Vancouver Eye Dr, Vancouver, Canada
- President, BC Doctors of Optometry
- Member, *Modern Optometry* Editorial Advisory Board
- kmmadan@gmail.com; www.vancouvereyedr.ca; Instagram @Dr.mahnia.madan
- Financial disclosure: Co-Owner (MYE Drop); Speaker and Consultant (AbbVie, Bausch + Lomb, Labatician, Lumenis, Santen, Sun Pharma, Théa, Valeo)