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Improvements in OSD and DED Management

A roundtable discussion exploring turning points in standards of care.

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INTRODUCTION

James Katz, MD: Dry eye disease (DED) is a complex and multifactorial condition that affects at least 38 million individuals in the United States alone. Of these, only 18 million are diagnosed cases and 1.2 million are treated with prescription medication.[1-3] DED management therefore can be an effective practice builder, as many individuals are undertreated. Today, treatment approaches and how we diagnose and identify patients with DED and ocular surface disease (OSD) continue to evolve as our understanding of its underlying mechanisms deepens. The aim of our discussion is to review major milestones in OSD and DED management that have helped shape and define modern treatment strategies.

Marguerite B. McDonald, MD, FACS: The first treatment for DED was simply heavily preserved salt water. Over time, artificial tear formulations became much more sophisticated in composition.

Karl G. Stonecipher, MD: Ointments were another early option. Although they last longer than artificial tears, they cause blurring of vision.

Dr. McDonald: People hated them back then, and they still dislike them. Ointment remains an important part of my treatment algorithm, but only for moderate to severe cases, and I prescribe it for use at night.

Kendall E. Donaldson, MD, MS: Twenty years ago, when I did my residency and cornea fellowship, we didn't talk much about DED because of the lack of treatment options. We've come such a long way since then, and the depth of options we have is incredible. We also weren't talking about preservatives 20 years ago, and that is a big discussion I have with every patient now because it may be a component of their problem. I really want patients to understand how important the health of their ocular surface is.

Inder Paul Singh, MD: Coming out of fellowship 20 years ago, the glaucoma meetings I attended focused on IOP control. No one talked about the patient's quality of life, symptomatology, drop compliance, or DED management. Now we know the toxicity and preservatives in eye drops can wreak havoc on a patient with underlying OSD.[1] When symptoms get worse, compliance gets worse. It's amazing to see how reducing topical drops for our patients has increased their quality of life. Additionally, our ability to maintain their IOP control over time has gotten so much better by just adding DED symptomatology and management. They trust us as providers more now because we address and understand why they have their symptoms. It is a 180º shift in glaucoma management.

Dr. Katz: One of the first things I tell patients is to please stay on label and not buy generics.

Dr. McDonald: Agreed. There is less control over the excipients in generic drops and the consistency of how they are produced.

Cathleen M. McCabe, MD: And they may change over time, too. When I was in training, punctal plugs and artificial tears were the two treatment options. Artificial tears, punctal plugs, and warm compresses are all important adjunct therapies, but now I treat more of the inflammatory portion of the disease process.

A SIGNIFICANT TURNING POINT

Dr. Katz: It wasn't until the early 2000s that we finally had a prescription eye drop specifically approved for the treatment of DED, cyclosporine ophthalmic emulsion 0.05% (Restasis, AbbVie/Allergan). The drop created a space in DED treatment with immunomodulation to help reduce inflammation and improve tear production. It quickly elevated the dry eye market for eye care providers. Today, Restasis is still among the top prescribed drugs in all of eye care.

Dr. McCabe: Restasis was a revolution because suddenly we had an interest in not only identifying DED, but trying to do something about it. We started talking to patients more openly about DED. It was really a revolution in dry eye treatment.

Dr. Singh: Patients started experiencing a *wow* factor, and I think the lightbulb moment for me was seeing an improvement in goblet cell density reported in clinical studies.[2-4] The biggest change for me as a noncornea specialist was to realize I should be treating DED as early as possible to cut the inflammatory response, even in the context of glaucoma.

Dr. Donaldson: Anytime we don't have a good treatment for a condition, it's hard to have a meaningful conversation with patients. Restasis really opened the door to start asking patients if they have symptoms.

Dr. McDonald: We went from ignoring people's complaints about dry eye because we couldn't do anything about it to identifying those with clinically significant DED who don't have symptoms yet. Now, we're trying to convince those who are getting ready for LASIK or cataract surgery that we must treat an important condition for which they're asymptomatic.

Dr. Katz: It took us several years to educate the population on the importance of DED diagnosis and treatment. Eventually, other immunomodulators (lifitegrast ophthalmic solution 5% [Xiidra, Novartis] and cyclosporine ophthalmic solution 0.09% [Cequa, Sun Ophthalmics]) came along and added to our opportunity to prescribe treatment to DED patients. But it was the class of immunomodulators that started to change the way we treat dry eye as an inflammatory condition.

INTERVENING EARLY

Dr. Katz: There have been other advances in DED therapy. In 2011, we started applying heat and pressure to the eyelids to address the evaporative component and the meibomian glands, which are responsible for maintaining tear film stability. This was a significant advance in OSD therapy.

Dr. Stonecipher: I've been doing intense pulsed light and low level light treatments for more than 2 decades. There's been a lot of evolution in terms of devices, but we must still think about the basics: How do we keep tears from evaporating too quickly, and how do we help patients make better quality tears? There are so many co-conspirators, including rosacea, floppy eyelid disease, lid wiper epitheliopathy, and even the environment.

Dr. McCabe: We have learned how important it is to intervene early for meibomian gland dysfunction to preserve the glands before they atrophy. Honestly, dry eye permeates our entire clinic day. Every patient has a little aspect of it. Now, we have our technicians elicit patients' DED symptoms before we as surgeons even touch the eye.

TFOS LIFESTYLE REPORT

By Christopher E. Starr, MD

The TFOS Lifestyle Report provides a comprehensive review of how lifestyle and societal factors impact ocular health. A global panel of 158 experts from 38 countries produced eight reports, summarized below, and additional subcommittees focused on evidence quality, industry liaising, and public awareness. The findings and recommendations of the TFOS Lifestyle Report aim to enhance the understanding and management of ocular surface disease (OSD) in clinical practice.

Contact lens wear. Factors like sleeping in contact lenses, nonadherence to maintenance protocols, and poor hygiene practices increase the risk of contact lens–related adverse events. Additionally, wearing contact lenses when unwell or after eye surgery can lead to ocular complications. Daily disposable lenses are preferred.

Cosmetics. Cosmetics migrating into the eye can cause or exacerbate dry eye disease (DED) symptoms. Many cosmetic products contain ingredients toxic to the ocular surface, including parabens, phenoxyethanol, chlorphenesin, formaldehyde, and benzalkonium chloride. Product contamination is also a concern.

Digital screen use. Digital eye strain must be properly diagnosed and distinguished from other conditions. Symptoms of digital eye strain include burning, headache, and eye redness. The treatment options like oral omega-3 supplementation, artificial tears, and the use of specific device settings (eg, dark mode, adjusting screen brightness, increasing display size/resolution) to decrease digital strain are suggested.

Elective medications and procedures. Prolonged use of preserved artificial tears and glaucoma drops can lead to medication-induced DED. The preservatives in eye drops, especially BAK, can be toxic to the ocular surface and cause a breakdown of the tear film and damage to the corneal epithelial cells, corneal nerves, and meibomian glands. Preservative-free drops or drops with milder preservatives such as Polyquad, Purite, SofZia, and sodium perborate therefore are recommended. Several medications and procedures were linked to ocular surface complications. Other effective treatments include punctal plugs, low-level light therapy, and manuka honey eye drops. Corneal refractive surgery can contribute to dry eye. SMILE can cause more vision disturbances in the first month compared to LASIK but fewer dry eye symptoms in the long term.

Climate. Environmental factors (eg, temperature, humidity, wind speed, altitude, allergens, and air pollution) contribute to DED. High or low temperatures can exacerbate symptoms, while humidity, especially in bedrooms, can alleviate them. Wind speed and altitude can lead to conditions like corneal frostbite and photokeratitis.

Nutrition. A poor diet is the second-highest risk factor for DED. Omega-3 fatty acids, certain micronutrients (vitamins A, B12, C, and D), dietary supplements (eg, curcumin), and honey have positive effects on the ocular surface. Water intake was not found to be protective against DED.

Lifestyle. Mental health challenges, sleep quality, and chronic pain are linked to DED. Additionally, depression, anxiety disorders, stress, and poor sleep quality and sleep disturbances could also lead to DED. Chronic pain conditions like migraine and fibromyalgia increase the risk of DED. Limited data is available on the use of tobacco, cannabis, and alcohol, but caffeine has a beneficial effect on DED.

Societal challenges. Education, access to health care, and health care utilization impact OSD presentation, management, and treatment outcomes. Major influences include systemic disease, age, sex, race, employment, smoking status, COVID-19 effects, regional climate, socioeconomic effects, sanitation, violence/trauma, and cultural effects.

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Dr. Stonecipher: I agree. We're more prophylactic as opposed to reactive.

Dr. McCabe: That's where educational tools like meibography, tear osmolarity, LipiView (Johnson & Johnson Vision), and iTrace (Tracey Technologies) can help the patient understand their condition.

Dr. Donaldson: Patients relate to imagery, and it helps with compliance because a lot of the procedures and medications that we use don't make an instant difference. Getting patients to partner with us is helpful.

Dr. Katz: Another point is just how early DED starts. Teenagers and people in their 20s are developing significant gland dropout, largely due to the increased use of digital devices.

Dr. McDonald: The normal blink rate is 20 times per minute. It drops down to 3.6 times per minute when using any digital device.[5]

MYRIAD TREATMENT OPTIONS

Dr. Katz: We now also have topical steroids like loteprednol etabonate ophthalmic suspension 0.25% (Eysuvis, Kala Pharmaceuticals) and novel treatments like varenicline solution nasal spray 0.03 mg (Tyrvaya, Viatris). How have these contributed to your ability to manage patients' symptoms?

Dr. McCabe: Some patients cannot be successful with drops. Maybe they have a tremor or they have arthritis. Having a drop-free option is a wonderful alternative. As far as topical steroids, they are especially useful for patients with a lot of active dryness to be compliant with using an immunomodulator.

Dr. McDonald: The three times that I often use steroids are induction therapy for the immunomodulators, flare-ups, and for one week after combined BlephEx/LipiFlow treatment.

Dr. Singh: It gives eye care providers who maybe aren't as comfortable treating DED more confidence being able to prescribe steroids now that it's on label for that indication.

Dr. Stonecipher: Another new agent is perfluorohexyloctane ophthalmic solution (Miebo, Bausch + Lomb), which is 100% active ingredient. It's great to have so many options for both the evaporative and aqueous components of DED because now we can ensure patients have a treatment that will work and be agreeable to them. Now, we also have lotilaner ophthalmic solution 0.25% (Xdemvy, Tarsus Pharmaceuticals) to treat Demodex blepharitis. This is another treatment that's leading us down a path to where we can finally treat patients with a specific condition.

STANDARDIZING TREATMENT ALGORITHMS

Dr. Katz: Kendall, what can you tell us about

The Tear Film and Ocular Surface Society (TFOS) Dry Eye Workshop Reports (DEWS)?

Dr. Donaldson: TFOS DEWS was also a turning point. It standardized a treatment algorithm for doctors to follow. Then, ASCRS and Cedars Aspens created algorithms, but all of them overlapped to some degree. Having a more standardized approach to managing complex patients is crucial. We're so fortunate to have both procedures and medications, but knowing how to put it all together can be overwhelming.

Elizabeth Yeu, MD: Each algorithm provides something unique. Specific to the TFOS DEWS I algorithm, it provided us guidance finally on how to manage DED and OSD patients with various severity levels of disease (eg, mild, moderate, severe) for the first time by evaluating them and treating them beyond tears.

Dr. Singh: TFOS helped validate that dry eye is a disease, not just a symptom (see the accompanying sidebar for information on the TFOS Lifestyle Report).

Dr. Stonecipher: I think it's also important to enable your staff. They should know about the DED treatment algorithm and how to assess patients with a questionnaire. We use a new artificial intelligence questionnaire, *CSIdryeye.com*. It's 50 questions about a patient's medication use, lifestyle, and environment, to name a few. One of my staff members talks to patients about their results even before I see the patient.

Dr. Katz: How do others identify DED patients in their practices?

Dr. Donaldson: Screening tests. My staff uses the Ocular Surface Disease Index and matrix metallopeptidase 9. If they have at least two things that are indicative of OSD, then we order a topography or meibography.

Dr. Yeu: I no longer see specific dry eye evaluations, only surgical evaluations. But we must remember, every surgery evaluation must be evaluated for lid margin and dry eye disease. For me, an infrared meibography is an absolute must for every surgical evaluation because it gives a snapshot in time of their baseline meibomian gland architecture and their "reserve", if you will. Certain modern risk factors, such as overuse of digital devices or contact lenses, and even what their diet is like, well before ever coming in for the surgical evaluation, can truly destroy MG structure, creating a lack of any reserve or tolerance to potential contrast sensitivity loss of other insults to the ocular surface. I also use the placido topography to observe specifically at the quality of the mires, and I evaluate for inter-device consistency between the average K values, amount of astigmatism and the steep meridian. If there are significant differences between devices, evaporative dry eye disease can definitely lead to the etiology. I also evaluate the tear breakup time (TBUT) and the quality of the tear film. Lastly, I look at their face for rosacea, their brows for flakes, and their lid for debris, such as collarettes at the base of the upper lashes, that would be indicative of *Demodex blepharitis*. I push on the lower lids to test the quality of the meibum.

Dr. Katz: Does anyone look beyond the evaporative component and distortion in the topographical mires, like inflammatory or osmolarity testing for the aqueous component?

Dr. Singh: I use the iTrace, but also I think symptomatology is important. Listening to patients describe their symptoms is a powerful tool. And again, techs should be trained to ask those questions.

Dr. McDonald: I use almost exactly the same protocol as Kendall. Our techs use the SPEED questionnaire, and they get a tear osmolarity. If it is 317 mOsm/L or higher, then topography and meibography are ordered. For preoperative patients, if the topography or meibography are also abnormal, all testing is halted until I meet and greet the patient, explain that they have OSD, and recommend a treatment plan. Thanks to newer agents, the patient can come back in 2 to 4 weeks for the rest of their preoperative workup, and the biometry will be more accurate.

Dr. Katz: Let's talk briefly about treatment for neurotrophic keratitis (NK).

Dr. McCabe: The evolution of NK is interesting. Over the past 5 to 7 years since cenegermin-bkbj ophthalmic solution 0.002% (Oxervate, Dompé) was approved, we're seeing the condition more and more. It usually takes two visits to diagnose NK because corneal cessation must be checked before they undergo a diagnostic workup.

Dr. Katz: So when do you consider using amniotic membrane?

Dr. Yeu: We've been using it more. I always start with Oxervate, but a lot of times I end up using a self-retaining amniotic membrane as well. My mindset on artificial lubrication has changed completely, too. Artificial lubrication is no longer just palliative, it is therapeutic. All the medicines that are being approved today are based on signs and symptoms. How can we say that the ingredients that are in tears today do not improve signs and symptoms? Artificial tears, especially those that are emollient-based, improve tear breakup time.

Dr. McCabe: I love serum tears. Because this treatment is not covered by insurance, however, it's access dependent. I use scleral lenses as well for patients with graft-versus-host disease. I think the combination of scleral lenses and serum tears in patients with severe disease is extremely effective. The scleral lens represents yet another landmark improvement in dry eye management.

CONCLUSION

Dr. Katz: We've talked about so many important treatment advances in this discussion, and it's clear to see how much DED management has evolved in the past few decades. From the introduction of Restasis as the first approved treatment for DED to modern ongoing advances, DED treatment is being elevated to new heights.

Patient education and applying standardized treatment algorithms remain paramount. Today, we can offer patients personalized approaches to treating DED, and this starts with empowering your staff to assist in the diagnosis and management process. We all look forward to trialing new and exciting DED treatment modalities in the future. ■

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