Algorithms as Management Tools in the Treatment of Dry Eye Disease

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A large, dynamic database of real world treatment outcomes—configured as a computer-based interactive algorithm—may soon become available to help eyecare providers refine management of dry eye disease.

In the years since dry eye came to light as a serious and widespread condition, research and development within the field has been fast-paced and continuous. Naturally, numerous groups have endeavored to synthesize and streamline a surplus of emerging information into practical guidance for eyecare providers who want to hone their skills in managing what is now known as dry eye disease (DED).

A decade ago now, the 2007 International Dry Eye WorkShop (DEWS) committee published the first comprehensive set of DED classification and management recommendations; a revised DEWS report—DEWS II—is expected soon.1,2 The American Optometric Association published their first clinical practice guidelines for the management of ocular surface disease in 1995 and updated them in 2010; the American Academy of Ophthalmology published a preferred practice pattern for the management of DED in 2013; and the Canadian Optometric Association published their comprehensive review of the subject in 2014.3-5

In addition, the first Dry Eye Summit convened in 2014, publishing a streamlined set of recommendations specifically intended for optometrists new to the treatment of DED.6 Clinical care guidelines for patients with Sjogren disease, a common form of aqueous deficient dry eye, have also recently been published.7 These and other guidelines are invaluable to clinicians as a compendium of the knowledge base, a marker of current understanding, and a starting point for clinical decision-making. Implementing guideline recommendations in clinical practice, however, is not always straightforward. They must be interwoven with on-the-spot clinical judgement, reconciled with one’s working understanding and practice patterns, adapted to one’s particular patient population, and sometimes questioned as new information emerges.

In other words, while clinical trials inform guidelines and guidelines inform practice, real-world practice has gray zones and nuances that even the most thoroughly considered set of precepts may not encompass or be able to predict. With information technology rapidly progressing, the key to reducing some of the uncertainty inherent in clinical practice may reside in algorithms using artificial intelligence.

Practice-derived Algorithms

A practice-derived algorithm is a...
novel means for synthesizing large quantities of clinical information, in effect adding a real-world layer of pooled information to evidence-based research and potentially enhancing the clinician’s ability to make effective treatment choices. There is a tremendous amount of in-office data generated by patient visits—a patient’s demographic information, past medical history, and ocular history; findings on screenings, examinations, and tests; and treatment regimens and outcomes—that traditionally stays in the patient chart and is applied solely to the management of that particular individual.

But if those data were aggregated along with the same parameters from a large population of similar patients and anonymously fed into a software program designed to elucidate patterns of outcomes, then a sort of living, open-ended database would be generated. The effect would be that one practitioner’s (or a group of practitioners’) lifetime experience treating a particular illness could be summarized, digitalized, and made available to others via a computer application or algorithm. With ongoing patient data entry over time, the algorithm would become increasingly reflective of widespread trends and potentially increasingly valuable to clinicians.

**DED Algorithm**

Innovation in the management of DED is particularly welcome, as its prevalence, complexity, and chronicity present unique management challenges for eye care providers. Even with a practice focused on dry eye disease, I find it challenging to assimilate all of the latest research findings into clinical practice since the field is evolving so rapidly. It behooves clinicians who see patients with DED to avail themselves to the whole body of knowledge, including new technology aimed at reducing complexity.

With over 42 years of specialty DED management experience between my colleague and I, in collaboration with information technology professionals, we are in the final stages of developing an algorithm for the management of DED using artificial intelligence.6,7 The algorithm is intended for eye care providers who wish to improve their ability to successfully manage DED and help their practice be more efficient. Upon its release—which is anticipated for end of summer 2017—it will contain data from a registry of roughly 2400 patients with...
neuropathic, neurotrophic, evaporative, and aqueous-deficient components of DED. The registry is simply a database where diagnostic information is entered electronically and the outcomes are assessed against the patient response on their return visit as to which products worked best and which did not. The data was then compared against specific diagnostic data such as osmolarity or meibomian gland expression grading.

Inputs to the algorithm to date have included a range of variables: patient characteristics, symptoms, results of screening tests (eg, OSDI, SPEED), results of ocular examination and testing (eg, surface staining, osmolarity, MMP-9), treatments (running the gamut from specific artificial tear compounds to topical ocular antiinflammatory agents), and follow-up findings from patients (eg, therapy preferences, subjective responses) and clinicians (eg, objective measures of clinical response). Once the algorithm is made available to eyecare providers, it will continue to evolve as new, real-time patient information is entered and processed with the old, assuring that next-step recommendations for diagnosis and treatment stay up to date.

The algorithm in development will also feature several novel diagnostic tools to measure partial or incomplete blinking while the subject reads from a digital device, including a patented blink evaluation test. Patients are asked to read a passage of text on an electronic tablet which records their gaze and blinks on videotape; blink number and completeness are quantified on playback and fed back into the algorithm (Figure 1).

Learnings to Date

Algorithms are supplemental to and entirely compatible for use with guidelines, and often are the clinical expression of the didactic guidelines or white papers. Certainly, since my practice habits stem from knowledge of and implementation of the previously published guidelines like DEWS and other expert opinions, it is no wonder that most of the recommendations that emerge from the algorithm are in alignment with published guidelines. For example, patients with mild DED with gland obstruction benefit from a lipid-containing tear over an osmolarity-lowering tear. Patients with mild-to-moderate DED tend to benefit from the addition of omega fatty acids and topical cyclosporine or lifitegrast. Patients with advanced rosacea with severe meibomian gland disease (MGD) often improve on oral doxycycline, short-term steroids. Removal of biofilm with microphleborexfoliation and vectored thermal pulsation in office as well as hydrating compresses and lid scrubs at home, are critical to both groups of patients with MGD-related DED.

However, the algorithm has also revealed a few surprises that have changed how I practice. In our registry of patients, for example, those with tear film osmolarity > 320 mOsmol/L—regardless of cause—report greater improvement with a hypo-osmolar artificial tear over a lipid tear; this defies the common wisdom that a lipid tear is a better choice for patients with MGD.

The most essential lesson to emerge from the algorithm is that the four components of DED—ocular surface inflammation,10 meibomian gland obstruction, tear film dysfunction, and lid biofilm—all play a role in DED; and the control of each is critical to successful management. Before coming to this awareness, our practice was to select a treatment category based largely on severity, eg, artificial tears for mild DED, topical antiinflammatory for moderate, etc; and our patient satisfaction rate using this approach hovered around 50%. Working with the algorithm—plugging in specific data regarding disease severity and characteristics, test results, patient response, and clinician response and allowing the algorithm to evolve in kind—made it clear that whenever any of these components was undertreated, patient satisfaction suffered. Only with all four components under control did we start to see the next level of success we were looking for, including patient satisfaction rates of 90%.

Implications for Clinical Practice

In summary, the example provided above of a constantly evolving, clinical algorithm carries the potential to bridge gaps in clinical care for complex, rapidly evolving ocular diseases such as DED. First, for clinicians who chose to utilize one, an algorithm could serve to confirm that guideline-recommended management practices do in fact line up with what works in real life. Second, a finely tuned algorithm could identify certain subsets of patients who stand to benefit from a measure outside of standard recommendations. Third, an algorithm can reveal unexpected patterns of treatment response that, when implemented more broadly, could lead to better outcomes for a greater proportion of patients.

Since an algorithm is basically a sophisticated synthesis of another clinician’s wealth of experience, it would likely prove useful for providers at all levels of experience. For more experienced providers, it could help challenge biases that inevitably accumulate over years of practice, bringing a fresh perspective on the dilemma of DED and the possibilities for treatment. For younger providers, an

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algorithm—while not replacing the need to develop one’s own expertise—could make them more efficient and savvy right out of the gate and could lighten the burden of inexperience. In other words, an algorithm could free the more novice practitioner from having to learn absolutely everything through trial and error, significantly shortening the trajectory to achieving consistently effective care.

**Conclusion**

Due to advances in the knowledge base for DED and cutting-edge information technology, an algorithm that can assist in diagnosis of DED and therapeutic decision-making is possible and is currently in development. It holds promise for providing greater efficiency and effectiveness in the management of dry eye and augmenting existing management resources.

**REFERENCES**


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Contact Lens Wear and the Ocular Surface

Anna F. Ablamowicz, OD, FAAO

Contact lenses penetrate and disrupt the tear film and have consequences for many wearers. A conscientious approach to eyecare for contact lens-wearing patients can keep them comfortable and help prevent dry eye disease.

Contact lenses have long been a safe, effective, and popular means for correcting vision. Recent estimates suggest that more than 40 million American adults—16% or 1 in 6 adults—and an increasing proportion of children and teens elect to wear contact lenses for vision correction. A perception of improved appearance and feeling unencumbered during sports and physical activity are key reasons many patients prefer contact lenses to glasses.

It is important to recognize, however, that a contact lens is a medical device that, by its presence, alters the biophysical and biochemical properties of the precorneal tear film (TF), which may predispose patients to dry eye. Among contact lens-wearing patients seen in primary care or contact lens clinics at UAB Eye Care at the University of Alabama at Birmingham, about 35% complains of dryness or discomfort due to their lenses at some point in their care. This is consistent with other reports of dry eye complaints among 30% to 50% of contact lens wearers. Contact lens-related discomfort and dryness is a leading reason for discontinuation of wear, with dropout rates estimated to be between 16% to 30%. Thus it is incumbent on eyecare providers to be knowledgeable about the TF and work closely with contact lens-wearing patients to ensure a safe, satisfying, and sustainable experience.

Normal Tear Film

Advances in research and imaging technology have vastly improved our understanding of the component structures and functions of the lacrimal functional unit (comprised of the eyelids, the corneal and conjunctival epithelium, the lacrimal glands, and the TF) and provided insights into clinically important interactions between the TF and contact lenses. The TF is a complex aqueous fluid that contains lipids, mucins, proteins, enzymes, immunoglobulins, salts, and metabolites. As the interface between the eye and the outside world, it is the most highly dynamic ocular structure, shifting continually in response to environmental conditions in order to maintain homeostasis and perform its vital functions: lubricating and nourishing the ocular surface; protecting corneal and conjunctival epithelial cells from microbes, toxins and debris; and creating a smooth liquid surface for optimal refraction of light and retinal image clarity. The TF is composed of two layers—an outer lipid layer and an inner mucous/aqueous layer. (It was recently discovered that TF mucins—while concentrated more highly toward the epithelial surface—are, in fact, incorporated into the aqueous, which shifted the working model of the tear film from three layers to the current two.) Let’s look more closely at TF architecture before considering the impact of contact lenses.

A thin outermost layer is composed mainly of polar and nonpolar lipids expressed from meibomian glands in the lids and, to a lesser extent, intercalated proteins. A chief function of the tear film lipid layer (TFLL) is to impede evaporation of tears from the ocular surface; thus a healthy TFLL is necessary to stabilize the TF and prevent evaporative dry eye disease (DED).

The aqueous layer, the watery component that comprises the bulk of the TF, is produced primarily by lacrimal glands with some electrolytes and additional fluids derived from surface epithelial cells. The aqueous supplies a nutrient- and oxygen-rich environment to the avascular cornea and cleanses the surface of particulate matter. Proteins in the aqueous help stabilize the TF and defend against damage from environmental threats. Large, secreted, gel-forming mucins are produced by conjunctival goblet cells and reside in the aqueous to primarily move pathogens and debris into the nasolacrimal duct. Membrane mucins, secreted by the corneal and conjunctival epithelial cells, anchor the TF to the ocular surface by creating a hydrophilic barrier known as the glycocalyx which aids in the smoothing and protective functions of the TF.

Contacts and the TF

A contact lens placed on the eye rests in the middle of the TF, essentially splitting it in two: a pre-lens TF (on the outside surface of the contact lens) that includes the outer TFLL and the...
outermost part of the mucous/aqueous layer, and a post-lens TF (“beneath” the lens, ie, between lens and cornea) that includes the innermost portion of the mucous/aqueous layer.4

This introduces new lens-adjacent interfaces within the TF and changes its biophysical properties.9-11 One consequence of the contact lens is destabilizing and thinning an already thin TFLL, likely related to a rearranging of different lipid types according to their affinity to the contact lens surface.9 A degraded TFLL is less able to perform its key function of retarding aqueous evaporation; the result is increased evaporative water loss and reduced overall tear volume, which is thought to initiate a vicious cycle of hyperosmolarity, dryness and inflammation associated with DED.

There is evidence to suggest that contact lens wear also interferes with normal meibomian gland function over time, although a statistically significant correlation between contact lens wear and meibomian gland dysfunction (MGD) has not been demonstrated in all studies.6,12,13 Meibomian gland dysfunction (MGD) is a leading cause of DED; obstructed or atrophied meibomian glands diminish the volume and quality of TF lipids, and—like contact lens wear—are associated with increased evaporative water loss. Whether or not contact lens wear is a cause of DED per se, contact lens wear can certainly exacerbate symptoms of MGD; and, reciprocally, MGD can interfere with patients’ ability to successfully wear contact lenses.

Lens-related DED Risk

Patient and environmental risk factors for DED are well described; they include age, female sex, living in a hot, low humidity climate, living at high elevation, frequent extended computer and digital device use, and taking medications that cause dryness. Among contact lens wearers, lens-related factors may also influence risk.

Patient noncompliance with lens hygiene recommendations, including lens replacement frequency and lens cleaning and storage practices, is prevalent and may contribute to ocular discomfort and dryness.14-18 According to the Centers for Disease Control, between 40% and 90% of contact lens wearers fail to follow contact lens care directions most of the time.1 It is not uncommon for patients who wear extended wear soft contact lenses to stretch out the replacement interval in order to save money; others just forget the date on which they are supposed to change to a new lens.19 While it did not examine ocular dryness specifically, a recent study revealed higher rates of contact lens-related complications among patients who did not adhere to recommended replacement frequency and most of these patients reported ocular discomfort that increased toward the end of the day.19

Although it has not been proven, it seems plausible that factors related to contact lens chemistry, such as wetting and affinity for lipid and protein deposition, may have some bearing on dry eye development. Hydrogel lenses with lower water content have been associated with lower rates of dry eye among wearers compared with higher water content lenses.5

Lipid and protein deposition patterns vary according to lens material as well as a variety of patient factors including diet.8 Silicon hydrogel lenses—now the most common category of soft contacts prescribed in the US—have higher oxygen transmissibility compared to hydrogel lenses but a greater tendency to attract deposits. The clinical significance of deposits is not clear.8,19 Protein or lipid deposits interfere with the smoothness of the lens/TF interface and likely contribute to discomfort. In addition, lipid deposits may be a marker of lipid degradation occurring in the TF which would correlate with increased dry eye risk.

Patient Care

Because contact lens wear usually worsens symptoms of dry eye, it is important to identify dry eye in all patients who seek to be fitted for contact lenses. Start by inquiring about symptoms of dry eye by administering a questionnaire such as Standard Patient Evaluation of Eye Dryness (SPEED) or Ocular Surface Disease Index (OSDI). Examine the lids and lashes for evidence of anterior blepharitis; visually inspect the tear film and assess tear break-up time as well as the tear meniscus height; and stain the conjunctival surface with lissamine green.

Perhaps the most important information in a pre-lens fitting dry eye workup comes from manually expressing the meibomian glands. Meibum that is easy to express, of high quality (clear oil rather than opaque and thick like toothpaste), and expresses from the majority of the glands in the upper and lower eyelids (indicating a lack of obstruction or atrophy) indicates healthy meibomian gland function and an absence of MGD. If dry eye disease is identified, further testing to identify the type—evaporative, aqueous deficient, or mixed—is necessary so that an appropriate treatment regimen can be recommended and carried out prior to the lens fitting.

Patients tend to appreciate the prescreening assessment when they understand why it is necessary and how it can help them succeed in contact lens wear. My practice is to show patients a diagram of the TF, explain its role in maintaining comfort and vision, and show exactly how the lens disrupts it and the implications of this disruption.

An online market survey (n = 203) directed at eyecare practitioners conducted in 2016 reported clinicians estimating the frequency of dry eye among contact lens wearers as 44%.20 Clinicians in this survey classified 66% as having evaporative dry eye versus 34% as aqueous deficient. While symptom assessment has remained the prevailing preferred method in making a diagnosis of dry eye in contact lens wearers, all patients, even those who have no complaints, should receive a careful assessment of the ocular surface when returning for examination and contact lens progress checks. In patients who do present with complaints of discomfort while wearing contact lenses, a careful history with detailed information about lens wear time, care system, and replacement frequency is essential in order to determine potential causes and contributory factors to the discomfort. Identifying and treating a coexisting pathology that may be responsible for dryness should be done prior to assess-
ing the relationship between the contact lens and the ocular surface and eyelids. Corneal staining, tear breakup, and meibomian gland evaluation should be used in determining the type of dry eye present before a treatment plan is crafted. While not cited as a preferred diagnostic method in the survey, the phenol red thread test should be used to establish whether the production of tears is adequate. In addition to determining the type of dry eye that may be contributing to contact lens discomfort and dryness, my practice is to perform conjunctival staining with lissamine green, which can reveal if the lens is fitting poorly as seen with a green ring of staining surrounding the limbus. Staining with lissamine green in the far temporal and nasal bulbar conjunctiva may also be indicative of disruption to the glycolcalyx and could explain symptoms of dryness and/or irritation. Evaluation of the lid wiper region of the eyelid after lissamine green instillation can provide an insight into whether increased friction is present between the eyelid and the contact lens during blinking.

For lens-wearing patients who complain of discomfort, I recommend a nightly warm compress using a commercial heating mask and a gel drop artificial tear before bedtime for those with signs of mild to moderate evaporative dry eye. I have found the placement of punctal plugs to be highly effective in many patients with persistent signs of ocular surface staining and poor tear production. Lens-related complaints may resolve with refitting in a different lens material and/or a lens with a more frequent replacement schedule since patient-lens compatibility cannot be predicted. It may take a few tries to find a lens that provides a patient with adequate, comfortable wear time but with the multitude of lenses available on the market and the assortment of diagnostic and treatment options available to practitioners today, clinicians should feel confident the “right” lens is out there for their determined patients.

Conclusion

The vast majority of patients who want to wear contact lenses can, including those with dry eye—when discovered early and treated effectively. Advances in contact lens materials and designs that counter TF interference will continue to expand options for lens wearing patients.

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1. Which expert panel was convened for the purpose of encouraging optometrists to undertake DED care?
   A. International Dry Eye Workshop
   B. Dry Eye Summit
   C. Ocular Surface Workshop
   D. Sjogren Syndrome Panel

2. Which of the following does NOT occur when a contact lens is placed on the eye?
   A. Surface tension drops
   B. Aqueous layer is divided
   C. TFLL gets thinner
   D. TF volume is reduced

3. An algorithm for DED management would fulfill which of the following purposes?
   A. Supplement current dry eye management
   B. Replace professional guidelines
   C. Reduce duration of optometry training
   D. Encourage self-diagnosis among patients

4. Which of the following is NOT characteristic of pooled data in an algorithm?
   A. Gathered prospectively
   B. Compared to a control
   C. Comes from and feeds back into a system
   D. Expands over time

5. Which of the following is characteristic of healthy meibum?
   A. Thick
   B. Pasty appearance
   C. Clear oily appearance
   D. Sea salt smell

6. Which of the following is NOT a patient parameter in the DED algorithm described in the article?
   A. Symptoms
   B. Test results
   C. Time since last visit
   D. Follow-up results

7. Which of the following is NOT a function of the TF?
   A. Nourishing surface epithelium
   B. Flushing away debris
   C. Creating a smooth light refractive surface
   D. All of the above are TF functions

8. Which of the following is NOT a component of the lacrimal functional unit?
   A. Precorneal tear film
   B. Crystalline lens
   C. Meibomian glands
   D. Corneal epithelium

9. According to the algorithm in development referenced here, which of the following ocular components must be controlled for optimal DED management?
   A. Meibomian gland obstruction
   B. Inflammation and biofilm
   C. Tear film dysfunction
   D. All of the above

10. Which of the following is true of the normal mucous/aqueous layer of the tear film (TF)?
    A. It is the outermost layer of the TF
    B. It is the thinnest layer of the TF
    C. Aqueous is produced by the lacrimal gland
    D. Mucins are produced by meibomian glands