Update on Ocular Surface Disease and Its Treatment

A variety of diagnostic and therapeutic modalities can assist in the differential diagnosis and treatment of dry eye disease.

BY MARGUERITE B. McDONALD, MD

The health of the ocular surface is critical to the pre- and postoperative management of patients undergoing both refractive and cataract surgery. The clinical presentation of ocular surface disease (OSD), however, can often be complex. Because the etiologies of OSD are multifactorial in nature, physicians often fall back on the diagnosis of dry eye disease (DED) for unspecific ocular surface pain. Treating unspecific pain such as DED may not improve patients' outcomes, and it commonly leads to frustration on the part of both patients and physicians.

There is a poor concordance between the signs and symptoms of DED.[1-5] Clinically, hyperalgesia (abnormally high pain) is often observed in cases of early or mild DED, whereas symptoms decrease in severe cases, as the downregulation of sensory receptors compromises nerve function. The disconnect between the signs and symptoms of DED makes the symptoms alone a relatively poor indicator of the severity of the disease and a confounding variable for the managing clinician.

DIAGNOSTIC TESTS FOR DED

Tear osmolarity has been reported to be the single best marker for DED.[6,7] An increase in tear osmolarity is a hallmark of DED and is regarded to be the central mechanism in the pathogenesis of damage to the ocular surface.[8] Likewise, determining if the patient has stable low (normal) tear osmolarity can indicate whether the physician should look elsewhere for the cause of the pain. Tear film hyperosmolarity has long been associated with an increase in DED's severity, because this measure provides an objective and quantitative assessment of the ocular surface.[9-12] Hyperosmolarity is known to induce apoptosis, serve as a proinflammatory stressor, and reduce the ability of mucin-like molecules to lubricate the ocular surface.[8,13,14] An elevated concentration of the tear fluid has also been implicated as the central pathogenic mechanism that is common to all forms of DED and is thus a global indicator.[6,15] Tear hyperosmolarity has been proposed as a gold standard in the diagnosis and management of the disease.[6,7,16,17] The availability of an in-office device for improved clinical testing of tear osmolarity (TearLab Osmolarity System; TearLab Corporation) has increased its use as a diagnostic tool.[18-20]

Other common objective diagnostic tests for DED include tear film breakup time, Schirmer tests, corneal and conjunctival staining, and grading of the meibomian gland. These tests are poor at differentiating normal patients from those with early/mild DED.[21] The overwhelming majority of DED sufferers are thought to fall into the early/mild category, although the accuracy of these tests improves as the severity of the disease increases. What is not evident, however, is the number of patients with earlier mild/moderate and/or episodic disease who are not diagnosed. Given the prevalence of DED and the low diagnostic rate reported, many people must be afflicted without recognition and proper treatment.[22]

NEW TREATMENT OPTIONS

In addition to the TearLab Osmolarity System, other new technologies that can facilitate the differential diagnosis and treatment of DED hold promise. For example, InflammaDry (Rapid Pathogen Screening, Inc.) is an in-office diagnostic test currently under review by the FDA that received CE Mark approval in Europe in 2011. The brainchild of Robert Sambursky, MD, InflammaDry is a single-use, self-contained handheld device that detects an excess of an unspecific inflammatory marker, matrix metalloproteinase-9, in tears in 10 minutes. A nurse or technician can perform the test. InflammaDry is low in cost, does not require additional equipment, and has a high degree of sensitivity and specificity.

The Keratograph 5 (Oculus Optikgeräte GmbH) is a diagnostic device that analyzes the tear film. The desktop unit performs six functions: automated and noninvasive tear breakup time, meibography, the measurement of objective bulbar redness, color photography, and video imaging. Keratometry, topography, and simulated fluorescein patterns (to aid the fitting of contact lenses in challenging cases) are also standard functions.

MEIBOMIAN GLAND DYSFUNCTION AND DED

Given that 86% of dry eye patients also have meibomian gland dysfunction (MGD),[23] there is growing enthusiasm among ophthalmologists for the LipiView Ocular Surface Interferometer and the LipiFlow System by TearScience. LipiView uses white light interferometry to evaluate the thickness of the lipid layer of the tears. LipiFlow delivers a computer-guided pulsating thermal treatment in 12 minutes to the four eyelids, allowing the altered meibum to become liquefied and extruded. The US clinical trial that led to the FDA's approval of these technologies documented their safety and efficacy. Most patients reported feeling better immediately, with improvements each day until a maximum benefit was reached 3 to 6 months after treatment. On average, the benefit lasts for 9 to 12 months for my patients, although the range is 6 to 36 months. It is my experience that, during this time, most patients can reduce their therapeutic regimens for DED and MGD by 50% to 70%. When the symptoms return, patients receive another treatment.

Rolando Toyos, MD, developed the intense pulsed-light treatment for DED and MGD. A xenon flashlamp emits energy in a flash (like a camera's flash) in a band from the base of the visible spectrum (500 nm) to the border between the near and midinfrared spectrum (1,300 nm). The flashlamp is filtered to allow wavelengths of only 500 to 800 nm to reach the patient. The light is pulsed in milliseconds, depending on the setting. The area treated extends in a band across the upper cheeks and lower eyelids. According to Dr. Toyos, the immediate effect is that of an intensely warm compress, and the treatment closes off blood vessels that send inflammatory mediators to the meibomian glands and decreases *Demodex* and bacteria as well as inflammatory mediators on the skin. There may be other unexplained modes of action as well.

CONCLUSION

Several new diagnostic and therapeutic modalities are now available to aid the diagnosis and treatment of patients with OSD. These new products help ophthalmologists to treat the most common and vexing problem we face in the aging population, OSD. ■

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1. Methodologies to diagnose and monitor dry eye disease. Report of the Diagnostic Methodology Subcommittee of the International Dry Eye Workshop. *Ocul Surf*. 2007;5(2):108-123.
2. Clinch TE, Benedetto DA, Felberg NT, Laibson PR. Schirmer's test. A closer look. *Arch Ophthalmol*. 1983;101:1383-1386.
3. Goren MB, Goren SB. Diagnostic tests in patients with symptoms of keratoconjunctivitis sicca. *Am J Ophthalmol*. 1988;106:570-574.
4. Schein OD, Tielsch JM, Munoz B, et al. Relation between signs and symptoms of dry eye in the elderly. A population-based perspective. *Ophthalmology*. 1997;104:1395-1401.
5. Nichols KK, Nichols JJ, Mitchell G. The lack of association between signs and symptoms in patients with dry eye disease. *Cornea*. 2004;23:762-770.
6. 2007 Report of the International Dry Eye Workshop. *Ocul Surf*. 2007;5(2):65-204.
7. Farris RL. Tear osmolarity: a new gold standard? *Adv Exp Med Biol*. 1994;350:495-503.
8. Luo L, Li DQ, Corrales RM, et al. Hyperosmolar saline is a proinflammatory stress on the mouse ocular surface. *Eye*. Contact Lens. 2005;31:186-193.
9. Sullivan BD, Whitmer D, Nichols KK, et al. An objective approach to dry eye disease severity. *Invest Ophthalmol Vis Sci*. 2010;51:6125-6130.
10. Mastman GJ, Baldes EJ, Henderson JW. The total osmotic pressure of tears in normal and various pathologic conditions. *Arch Ophthalmol*. 1961;65:509-513.
11. Mathers WD, Lane JA, Sutphin JE, et al. Model for ocular tear film function. *Cornea*. 1996;15:110-119.
12. Liu H, Begley C, Chen M, et al. A link between tear instability and hyperosmolarity in dry eye. *Invest Ophthalmol Vis Sci*. 2009;50:3671-3679.
13. Gleghorn JP, Jones AR, Flannery CR, et al. Boundary mode frictional properties of engineered cartilaginous tissues. *Eur Cell Mater*. 2007;14:20-28.
14. Luo L, Li DQ, Pflugfelder SC. Hyperosmolarity-induced apoptosis in human corneal epithelial cells is mediated by cytochrome c and MAPK pathways. *Cornea*. 2007;26:452-460.
15. Gilbard JP, Rossi SR. Changes in tear ion concentrations in dry eye disorders. *Adv Exp Med Biol*. 1994;350:529-533.
16. Bron AJ. Diagnosis of dry eye. *Surv Ophthalmol*. 2001;45:S221-226.
17. Lemp MA, Bron AJ, Baudouin C, et al. Tear osmolarity in the diagnosis and management of dry eye disease. *Am J Ophthalmol*. 2011;151(5):792-798.
18. Versura P, Profazio V, Campos EC. Performance of tear osmolarity compared to previous diagnostic tests for dry eye diseases. *Curr Eye Res*. 2010;35:553-564.
19. Tomlinson A, McCann LC, Pearce EI. Comparison of human tear film osmolarity measured by electrical impedance and freezing point depression techniques. *Cornea*. 2010;29:1036-1041.
20. Suzuki M, Massingale ML, Ye F, et al. Tear osmolarity as a biomarker for dry eye disease severity. *Invest Ophthalmol Vis Sci*. 2010;51:4557-4561.
21. Begley CG, Chalmers RL, Abetz L, et al. The relationship between habitual patient-reported symptoms and clinical signs among patients with dry eye of varying severity. *Invest Ophthalmol Vis Sci*. 2003;44(11):4753-4761.
22. Yazdani C, McLaughlin T, Smeedley JE, Walt J. Prevalence of treated dry eye disease in a managed care population. *Clin Ther*. 2001;23(10):1672-1682.
23. Lemp MA, Crews LA, Bron AJ, Foulks GN, Sullivan BD. Distribution of aqueous deficient and evaporative dry eye in a clinic-based patient population. *Cornea*. 2012;31(5):472-478.