# THE VALUE OF OBJECTIVE DATA IN EVALUATING DED

Tear osmolarity and other tests can help diagnose and stage the disease.

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It is important to diagnose dry eye disease (DED) and initiate treatment early in its course, but several factors may impede those efforts. There is often poor correlation between the signs and symptoms of DED.[1,2] In as many as half of patients with signs of DED, no symptoms are elicited.[3] In addition, some symptoms common to DED are also associated with other ocular conditions such as blepharitis and allergy, so symptoms alone may be insufficient to make a specific etiologic diagnosis or to determine the stage or severity of the condition.

Furthermore, late stages of the disease may induce hypoesthesia of the ocular surface, and therefore, the patient's capacity to sense DED–related symptoms may be compromised. Finally, not all patients report the same dry eye symptomatology; some complain of a gritty foreign body sensation, burning, or itching, while others may describe pain and discomfort.

Clinical signs are important for the diagnosis of DED. For example, lissamine green and fluorescein staining may reveal dry, devitalized, or dead cells and areas devoid of mucin on the cornea and conjunctiva. Relevant features of DED may be picked up on examination, but more often than not, a preceding report by the patient (ie, of symptoms) is what prompts further investigation. Maintaining a high index of suspicion may help in identifying cases needing further evaluation.

Still, specific clinical signs can be discordant and therefore confusing. This variability is why objective dry eye testing is valuable: tests such as tear osmolarity can provide global metrics for diagnosing, staging, and monitoring treatment in patients with DED.

## TEAR OSMOLARITY: A GLOBAL MARKER

Elevated tear osmolarity is a feature common to both aqueous-deficient and evaporative DED.[3] Although it does not pinpoint the underlying etiology of condition, the TearLab Osmolarity Test (TearLab) can form the rationale for further investigation. This test has been described as the best single metric for diagnosis of DED, supplying data that are directly related to disease severity in a positive correlative fashion.[3] Thus, this test can also help stage the disease.

Studies demonstrate that a reduction in tear osmolarity may precede the abatement of symptoms in patients successfully treated for DED, whereas no change or elevation in osmolarity on repeat testing can indicate ineffective treatment or poor compliance.[4]

Elevated osmolarity signifies an imbalance of solute to water content in the tears. At a fundamental level, the pathogenesis of DED may be primarily evaporative or aqueous deficient or a combination of the two. Meibomian gland disease or incomplete blinking can lead to evaporative DED. Insufficient aqueous layer production from the lacrimal gland can lead to aqueous-deficient DED.

The exact effect of abnormal osmolarity on the tear film is not completely understood, but it is known that it can lead to loss of glycocalyx and microvilli on cells of the ocular surface, along with a loss of goblet cells. Tear hyperosmolarity and instability lead to dessication and desquamation of ocular surface cells. They can also trigger apoptosis of these cells and/or the release of inflammatory cytokines, such as interleukin-1 and other proinflammatory mediators. Abnormal osmolarity may also be the inciting event for compensatory mechanisms that attempt to stabilize the drop in osmolarity. For example, local mediators may trigger an increase in lipid production in an attempt to regulate and decrease tear hyperosmolarity. When that fails, osmolarity levels can increase even more, with further tear instability resulting. These failed attempts by the body to restore tear homeostasis may explain the variability in patients' signs and symptoms as well as why DED can be a progressive disease.

A tear osmolarity score of 308 mOsm/L or higher on the TearLab Osmolarity Test is indicative of DED, and higher scores are related to more severe forms. High intereye variability in tear osmolarity scores is also consistent with tear film instability secondary to DED. In healthy eyes, osmolarity is tightly regulated and similar between the two eyes; a disparity greater than 8 mOsm/L between the two eyes is an important clue to the presence of DED.

Even normal tear osmolarity can be useful information in the clinic. For instance, if osmolarity is normal in a patient with symptoms suggestive of DED, a separate disease process may be at work, such as allergy or basement membrane dystrophy. Additional evaluation for conditions such as

epithelial basement membrane dystrophy, conjunctivochalasis, and/or ocular allergy may be warranted.

## TEAR OSMOLARITY AND RESPONSE TO TREATMENT

Early recognition of DED is vital to the long-term health of the ocular surface. Early treatment in refractive or cataract surgical patients is associated with better visual outcomes.[4] Unrecognized DED in patients undergoing cataract or refractive surgery may affect the accuracy of IOL power calculations, astigmatism assessment, and other surgical planning.[5]

With effective treatment, improvement in tear osmolarity often precedes the resolution of symptoms. In one study, treatment with cyclosporine ophthalmic emulsion 0.05% (Restasis; Allergan) was associated with a drop in osmolarity scores before patients reported improvements in symptoms.[6]

Different interventions affect osmolarity in different ways. Artificial tears containing hyaluronic acid appear to be effective at reducing osmolarity, and some oral hormone replacement therapies have been shown to reduce osmolarity. Serial osmolarity testing reveals information about ongoing fluctuations that may be useful for diagnosing and staging the disease, and, once therapy is initiated, determining whether there is a response.

Serial testing may also play a role in educating patients and helping to motivate compliance. Because a reduction in osmolarity is a leading indicator of treatment response, informing patients that their abnormal osmolarity is improving, even while their symptoms persist, can help to demonstrate a benefit of their treatment and motivate compliance. Conversely, for the patient with abnormal osmolarity who is not exhibiting symptoms, an objective number may be valuable to demonstrate a benefit of sustained treatment. A lack of response on repeat osmolarity testing suggests that the intervention is not succeeding or that the patient may not be complying with the regimen.

## OSMOLARITY IN CONTEXT

The absolute score of the worse eye and the intereye difference in tear osmolarity testing are important numbers, but they provide only a piece of the dry eye equation. As noted previously, elevated osmolarity reveals instability in the tear film but not what is causing it. In our practice, we use manual expression of the meibomian glands along with meibography with the LipiView II system (TearScience) if meibomian gland dysfunction is suspected. Dynamic Meibomian Imaging with the LipiView can provide insight into the structure and function of the glands; if truncation or atrophy of the glands is noted, treatment can be directed to the underlying obstructive cause with LipiFlow thermal pulse treatment (TearScience), which may also help to lower osmolarity.

There should be a reason to perform tear testing in the first place, and it would be inappropriate to use these tests as a mass screening measure for all patients in the practice. In our clinic, we use a modified questionnaire that has some questions directed at dry eye and others at allergy to identify patients in need of additional evaluation. The value of asking questions about allergy is that it can help narrow the differential diagnosis and rule out cases with mimicking symptoms caused by another disease process. It also helps identify patients who might have concomitant ocular surface disease, such as both DED and allergy, which is often the case.

Another category of patients in need of ocular surface evaluation are those undergoing ocular surgery. DED may affect both low and high contrast vision and contrast sensitivity.[7-10] The tear-air interface is the eye's most powerful anterior refractive surface,[8] and unrecognized dry eye may yield unwanted visual effects after surgery. Preoperatively, dry eye can affect the accuracy of biometry and other measurements. Many of the tools used to evaluate and measure the eye prior to surgery depend on accurate reflection from the cornea; it stands to reason that irregularities on that surface will yield inaccurate assessments.

## CONCLUSION

Abnormal osmolarity provides an objective measure of whether the tear film is unstable, and it allows staging of DED. It is not diagnostic regarding the underlying etiology of DED on its own, however. Rather, it provides valuable objective data that builds on other indices that convey information about the health of the tear film and ocular surface and the etiologic mechanisms that produce dry eye. Tear osmolarity represents a global objective metric that provides confidence that dry eye is absent or present, how severe it is, and how well the eye is responding to treatment. ■


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