Article Date: 8/1/2016

Three Beneficial Diagnostic Options

Tear osmolarity, MMP-9 testing, and meibography deliver the big picture

Dr. Donaldson: In the last 5 years or so, our profession has paid a great deal more attention to the ocular surface. When I think back to my years in residency, it wasn't something we talked about. In fact, we virtually ignored dry eye. We didn't consider dry eye to be part of a patient's diagnosis, and we usually moved on to address the patient's other complaints.

Now, with a better understanding of the role of the ocular surface and new diagnostic technologies and treatment strategies at our disposal, we're looking much more closely at the ocular surface.

Tear Osmolarity

Dr. Donaldson: One tool at our disposal is osmolarity testing. What is your experience with this modality?

Dr. McDonald: Hyperosmolarity is the central pathophysiological pathway by which dry eye damages the ocular surface and leads to apoptosis, or programmed cell death, and the downward spiral we know so well. This concept and tear osmolarity testing are key to understanding dry eye — to diagnosing it and to monitoring response to treatment.

Dr. Matossian: I agree. We look not only at the tear osmolarity number for each eye, but also at the interocular difference. Patients like tracking their numbers. We write their results on a business card-size form and give it to them. This way, they're able to follow the trend in their numbers over time and come to understand whether their treatment is working.

Dr. McDonald: I explain to patients, "If you're normal, you have plenty of reserves. Your score is low and you have the same tear osmolarity score almost every day, whether you had a quiet day or took a Claritin or had a glass of wine or sat on the front of a speedboat on the Fourth of July. But if you have dry eye, your score is higher, and you have no reserve, so there's huge variability from one moment to the next as you encounter these physiological challenges."

People used to say, "Ten minutes ago it was 327. Now, it's 296. It's a crummy test." No, it's a crummy disease. That's really how much the osmolarity is fluctuating. This test has won all sorts of awards for precision and repeatability in test solutions, so we can be sure that this variability is, in fact, exactly

what's going on. And that's why, from moment to moment, dry eye patients can have vision problems. They're driving along, reading a sign, and suddenly they can't read it. This is a real phenomenon.

Dr. Donaldson: That's a great point. Tear osmolarity has great variability, and we see that variability in the test. When it first came out, I think some practitioners didn't know how to interpret the results. They saw the variability and thought the test wasn't working. But variability is a characteristic of the disease. We can't interpret the test results in a bubble — we need to take the whole picture into account.

Dr. McDonald: It's a sensitive test, too. If eyes are more than 8 milliosmoles different from each other, even if they are in the normal range, it is a sign of tear film instability, and the patient has dry eye.

MMP-9 Testing

Dr. Donaldson: Is anyone using MMP-9 as part of their diagnostic testing?

Dr. Matossian: We test for MMP-9, which stands for matrix metalloproteinase 9, a biomarker for inflammation. It's a very simple test to perform. In fact, my technicians handle it. The key is that they have to perform the test before or 2 hours after any drops have been instilled in the eye.

The test looks a bit like a pregnancy test. Technicians dab the tip on the conjunctiva, then stop and ask the patient to blink. This process is continued along the entire length of the lower eyelid. Once activated, it takes approximately 10 minutes for the result. If a red line appears, then the test is positive for MMP-9, which means there is inflammation. Even a faint red line is considered a positive test. I turn up the lights in the exam room and hold a muscle light toward the display window so the patient can see the red or reddish line. I have them hold the test so they feel more engaged in their own test results. Everyone understands a positive test, and when patients see it, they feel prepared for a more aggressive treatment program.

The other way I use this test is to check if patients are compliant with their use of cyclosporine (Restasis, Allergan). If they're using cyclosporine BID, this test should be negative. So, if patients assure you that they're using Restasis, but their osmolarity numbers don't look great and their symptoms aren't improving, you can use this test to check compliance.

When I find that it's positive, we have another discussion. "Are you really using the cyclosporine twice a day as you're supposed to?" That's when the truth comes out. If they answer, "Oh, well, I've forgotten it," or, "I use it occasionally," then we take the opportunity to re-educate them about cyclosporine. We stress that cyclosporine cannot be used on an as-needed basis. They have to adhere to the prescribed dosing instructions.

Dr. Donaldson: Sometimes, if a patient has a positive MMP-9 test while taking cyclosporine, I supplement it with a steroid or serum tears. I move up to the next level of topical treatment.

Dr. McDonald: I also use the MMP-9 test to differentiate dry eye from other inflammatory conditions. MMP-9 is a non-specific marker for inflammation. If a patient is positive for MMP-9 but has normal osmolarity, that person doesn't have dry eye, but some other condition is inflaming the eye. I tell myself that I must have missed something. I go back and look again to find signs of allergic conjunctivitis, epithelial basement membrane dystrophy, conjunctival chalasis, or another inflammatory problem.

Dr. Epitropoulos: The use of point-of-care testing, such as MMP-9 or tear osmolarity, underscores how important it is that we establish protocols for dry eye testing in our practices. We can't use these point-of-care tests to analyze the tears once patients have had drops or lights in their eyes, so we need to test early in the visit. That begins with a validated dry eye questionnaire as patients walk in the door. If they're symptomatic, then we empower our technicians to automatically test for tear osmolarity and MMP-9. We may be able to bill for the test — if we have that protocol in place and the patient has symptoms or signs.

Dr. Donaldson: Our protocol is similar. Patients complete the Ocular Surface Disease Index (OSDI) questionnaire, and, if they score high enough, they undergo MMP-9 testing. By the time I see the patient, I already know what the test revealed about the presence of inflammation. Having that in place saves a great deal of time.

Meibography

Dr. Donaldson: How about meibography? Are we all using that as well?

Dr. Epitropoulos: We know that 86% of our dry eye patients have meibomian gland dysfunction (MGD).[1] It's important to evaluate for this disease by examining the lids and lashes as part of every routine ophthalmic evaluation. I perform meibography on many of my patients who are symptomatic, although I know that means I'm missing some cases in patients who are asymptomatic. Meibography is an excellent tool to identify this disease, and can be performed after drops have been instilled. We can actually educate our patients, show them what their glands look like compared with healthy glands, and convey the message that this is a progressive disease. If it's not treated, it can cause glandular atrophy and loss of function.

There are two meibography units on the market: The Keratograph 5M (Oculus) and the LipiView II (TearScience). I use the LipiView II, which analyzes the lipid layer, records the number of partial or complete blinks, and also obtains high-definition images of the meibomian glands.

Dr. McDonald: Both the Keratograph 5M and the LipiView II overlap in the area of meibography. The Keratograph 5M offers additional tests to help diagnose and evaluate dry eye. But there's no way to overstate the importance of showing that meibography picture to the patient. It can shock patients into compliance. And if I'm recommending that the patient undergo a thermal pulsation treatment, such as LipiFlow (TearScience), I say, "You know, when these last few glands are gone, they're gone. They produce a critical component of the tear film. We don't think they can be resuscitated, and you've already lost 80% of them." Meibography is an incredibly effective tool.

Dr. Donaldson: Patients really like to see the disease. It induces compliance when they can picture what's going on, whether they see it in meibography images or even slit lamp photos. It's extremely effective to show them Demodex crawling on their lashes — they're instantly compliant with their treatment regimen and their follow-up appointments (hoping to see eradication of the mites that previously inhabited their lashes). The combination of diagnostic data and imaging techniques helps us learn what we need to know and it also helps patients visualize and understand what's causing their symptoms, making them more compliant with treatment.

Dr. Epitropoulos: I want to point out that in addition to the diagnostic testing we've discussed for patients with dry eye complaints, there is the issue of asymptomatic patients. A prevalence study showed that 47% of patients diagnosed with dry eye are asymptomatic.[2] We should look for this disease in all of our patients and screen every surgical patient as well.

Dr. Donaldson: I started doing that a few months ago. Just incorporating OSDI, tear osmolarity, and MMP-9 testing for all of our preoperative patients has made a huge difference for us. We're doing our best to identify at-risk patients before surgery. If we have an unhappy patient after surgery, we can re-address the measurements and treatment we initiated before surgery. Patients reflect back on the fact that we have been paying attention to this problem throughout the surgical process (beginning before their procedure). ■

References

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Ophthalmology Management, Volume: 20 , Issue: August 2016, page(s): 18-20