

All About the Osmolarity Number

The following advertorial is adapted from a roundtable discussion held during the 2014 ESCRS meeting in London, where participants discussed the clinical importance of assigning a number to tear osmolarity.

PARTICIPANTS



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Dr. Donnenfeld: Dry eye symptoms are the most common reason why patients come to see ophthalmologists.¹ Yet, dry eye disease is difficult to diagnose, and often misdiagnosed, because it is multifactorial. The recent introduction of point-of-service testing devices, however, has greatly improved clinicians' ability to diagnose dry eye disease. In my opinion, the most important point-of-service test is for tear osmolarity, because it has long been a benchmark for dry eye disease. Dr. Holland, can you tell us what tear osmolarity means?

Dr. Holland: The tear film is the most important refractive surface of the eye. Hyperosmolarity perpetuates the cycle that results in dry eye disease and leads to inflammation and apoptosis.

Before the advent of point-of-care diagnostics, clinicians were frustrated by the lack of reliable testing for dry eye disease. I agree that the new diagnostic tests such as the TearLab Osmolarity System (TearLab Corporation) will allow us to better treat these patients.

Dr. Donnenfeld: Dr. Harman, what does raised osmolarity do to the ocular surface?

Dr. Harman: A greater concentration of sodium within the tear film can activate inflammatory cytokines such as interleukin and metalloproteinases. This reaction creates a cycle of inflammation that causes cellular apoptosis, and then patients start feeling the symptoms of dryness and irritation. These symptoms lead to further cell degradation and more hyperosmolarity, which is why the disease needs to be measured and treated as early as possible.

Dr. Donnenfeld: Does hyperosmolarity tell you anything about the cause of the dry eye?

Dr. Harman: Hyperosmolarity does not tell us whether a patient's dry eye is evaporative or aqueous deficient, but we have shown very effectively that it is the best single overall biomarker of the function of the tear system.²

Dr. Donnenfeld: What is the predictive value of some of the other tests we perform routinely as compared to osmolarity?

Dr. Harman: In the prevalence study conducted recently within the National Health Service (Great Britain, UK),³ which examined 596 patients, osmolarity

was shown to have the highest positive predictive value of dry eye disease compared to other routine dry eye diagnostic tests. The percentage of patients who had dry eye according to hyperosmolarity was 72.3%, and there was 78.7% agreement between the incidence of hyperosmolarity and patients' DEWS scores. The correlation between the doctors' diagnosis of dry eye disease and the DEWS score was only 61%. The agreement between tear breakup time and the DEWS scores was approximately 51.2%. We did not perform Schirmer's testing.

Dr. Donnenfeld: I believe that tear osmolarity testing has now replaced Schirmer's as the single most important primary test for dry eye disease. My staff and I administer this test first, and then we perform other tests to further evaluate the disease. The tear osmolarity test is also beneficial to rule out dry eye disease. If the patient has normal osmolarity and an inter-eye difference of <8 mOsm/L, this is an indication to look for another condition with similar symptoms to dry eye.

Dr. Srinivasan, one of the original concerns that many clinicians had with tear osmolarity was its variability; one eye might have an osmolarity that was 30 milliosmoles (mOsm) different than the other eye. What does such variability between the two eyes tell you about tear osmolarity and the status of dry eye?

Dr. Srinivasan: Clinicians agree that 308 mOsm is the cutoff to indicate hyperosmolarity. Most of the studies have shown that even if there is a difference of more than 8 mOsm between eyes, if this difference remains consistent across multiple readings, then these are considered early, subclinical markers. Many patients have no corneal staining or other clinical signs and symptoms of dry eye, but still they are hyperosmolar.

Dr. Donnenfeld: So, we would expect patients who have normal tear films to have very little intra-eye variability, and dry eye patients lose that homeostatic mechanism, which explains the great variability. Over time, the osmolarity tends to increase, but the difference between the two eyes is just as important a diagnostic finding as the absolute osmolarity number.

Dr. Srinivasan: That is correct.

Dr. Holland: Hyperosmolarity is one factor, and variability is equally important in diagnosing dry eye.

Dr. Harman: We cannot expect homeostasis if we cannot keep the osmolarity within a narrow range between the eyes.

Dr. Donnenfeld: That explanation makes osmolarity a much more valuable tool. When we start seeing the osmolarity variability between eyes lessen, we know the treatment is achieving a good result. When the variability stays the same, just as when the osmolarity stays high, it tells us that we need to start searching for a better treatment plan.

THE ADVANTAGE OF ASSIGNING A NUMERICAL VALUE TO DRY EYE DISEASE

Dr. Donnenfeld: When we perform an osmolarity test on patients, what is the effect of giving them an actual number associated with their dry eye disease? How does that affect patients' acceptance of their diagnosis and their ability to be treated?

Dr. McDonald: That number has a huge effect. Patients often do not think they have dry eye, especially when they are asymptomatic. Once they are tested with the TearLab Osmolarity System, I can say to them, "this test shows that the osmolarity of your tear film is 50 points above normal, which indicates that you have dry eye." That's the end of the discussion. Then, patients become aware of this number as something they want to work to lower, just like blood pressure or cholesterol levels. Thus, having a number encourages treatment compliance.

Dr. Donnenfeld: For the first time, ophthalmologists can use lab testing to diagnose dry eye disease. I think this is going to revolutionize both the diagnosis and management of the disease.

INCORPORATING DIAGNOSTIC TESTING IN THE PRACTICE

Dr. Donnenfeld: The technicians in my practice are empowered to perform the TearLab Osmolarity Test on all patients who present with symptoms of ocular surface disease. This allows me to spend more time talking with patients about their disease rather than trying to diagnose it.

Dr. Holland: Our technicians have been trained to decide when to administer a tear osmolarity test based on answers patients give to predetermined questions. This change has improved our efficiency tremendously. By the time I see the patient, he or she has the results of the test.

Dr. McDonald: TearLab Osmolarity testing is not only the most predictive test for dry eye, but also the fastest. In my practice, it takes about 10 seconds.

Dr. Holland: If we can adopt TearLab Osmolarity as the standard test for dry eye, we may be able to prevent the disease's progression to late stages.

SURGICAL EVALUATIONS

Dr. Donnenfeld: We know that any surgery that incises the cornea damages nerves and suppresses the feedback loop that allows the brainstem to tell the lacrimal glands to produce more tears. Therefore, preoperatively diagnosing dry eye is one of the most important things we can do to improve surgical results.

Dr. McDonald, you have a busy surgical practice. How do you incorporate a dry eye workup when a patient comes in for a surgical evaluation?

Dr. McDonald: All patients receive the same psychometric questionnaire, whether they present for surgery or not. If they check off even one symptom on the questionnaire, our technician may proceed with the TearLab Osmolarity Test before the patient sees me. If the score is significantly elevated, I will examine the patient before any further testing, even dilation. Infrequently, I will notice a low tear lake or other signs of dry eye disease at the slit lamp in an asymptomatic patient, and then my staff will administer the TearLab test after I have seen the patient.

Dr. Donnenfeld: TearLab Osmolarity testing can be helpful to diagnose patients who may be symptomatic but do not have dry eye disease. Fortunately, TearLab Osmolarity testing does not interfere with our ability to test for other disease processes, whereas many other tests preclude conducting other diagnostics on the same day.

TEAR OSMOLARITY TESTING FREQUENCY

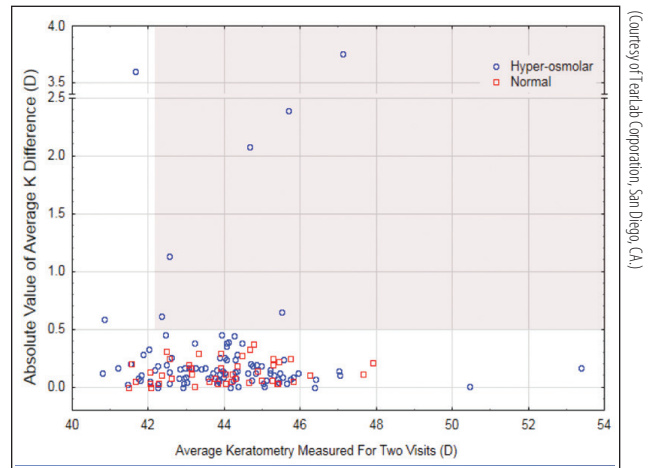
Dr. Donnenfeld: My staff and I perform TearLab Osmolarity testing on patients identified with the disease on every subsequent visit. Is there any reason not to perform osmolarity testing on follow-up visits?

Dr. McDonald: No. This is the best way to determine if the patient is responding to treatment.

Dr. Holland: Just as with internal medicine, patients with hypertension, for example, get follow-up visits with their internist to check their blood pressure, we likewise check the efficacy of our treatments for dry eye patients.

Dr. Donnenfeld: If the patient's osmolarity score is improving, but he or she is still symptomatic, what does that mean? How does it affect our course of therapy?

Dr. Harman: Studies have shown that symptomatic improvements lag behind the improvement in osmolarity figures. Again, this is why it is helpful to have these numbers, so we can reassure patients that the treatment is working, even if they are not feeling the effects yet.



(Courtesy of TearLab Corporation, San Diego, CA.)

Figure 1. This chart shows the absolute difference in average K readings in osmolar (normal) and hyperosmolar eyes measured between visits. There was a difference of 0.50 D in the average K readings in 8% of the hyperosmolar eyes compared with none in the normal eyes. Also, 10% of the hyperosmolar eyes received an IOL implant that was 0.50 D greater than necessary. Based on these figures, approximately one out of every 10 patients will have an incorrect IOL calculation due to hyperosmolarity during keratometry readings.

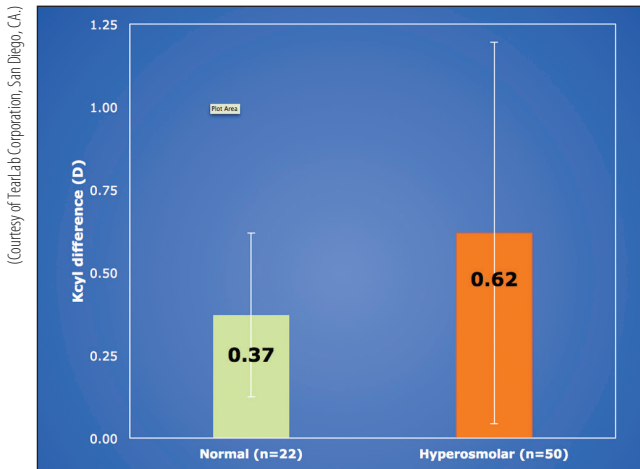
Dr. Donnenfeld: Because tear osmolarity readings can vary from visit to visit depending on many factors (ie, the patient's diet, external environment, etc.), I base my treatment therapy on the continuity of osmolarity over time. It is not the only sign I rely on; we have to evaluate every patient on an individual basis over time.

Dr. Srinivasan: I agree. The more I perform tear osmolarity testing, the more I identify hyperosmolar patients.

Dr. Holland: More than half of the cataract population will have dry eye disease.⁴

Dr. Donnenfeld: So, it is very reasonable to conduct tear osmolarity testing on all cataract surgery patients, because we know the surgery will worsen preexisting conditions. In my experience, the patients who know they have dry eye disease before surgery are not the ones who complain about the symptoms after surgery; it's the patients who were asymptomatic preoperatively who will blame the surgery for causing the symptoms. This is another reason to identify dry eye disease prior to surgery.

In addition, I believe there are three groups of cataract surgery candidates who deserve special attention for dry eye disease: (1) those with preexisting disease; (2) those in whom you are planning arcuate or limbal relaxing incisions, because these will worsen the condition; and (3)



(Courtesy of TearLab Corporation, San Diego, CA.)

Figure 2. This graph indicates the change in keratometry cylinder (Kcyl) between the first and second patient visits. Hyperosmolar patients demonstrated a wider variation in Kcyl between the visits compared with the control group ($P=.013$).

individuals requesting multifocal IOLs, because even mild dry eye disease will affect their postsurgical vision.

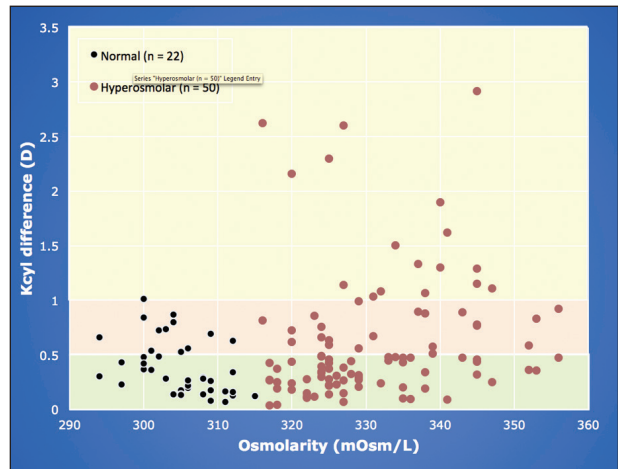
Dr. Holland: Another asymptomatic group is patients who also have a cataract that obscures fluctuating vision. They may have the cataract removed, but they are left with an unstable tear film and fluctuating vision that they think is a result of the surgery if the condition is not detected preoperatively.

Dr. McDonald: Yes, and they may even experience monocular diplopia from it.

DRY EYE DISEASE IN CATARACT AND REFRACTIVE SURGICAL PATIENTS

Dr. Donnenfeld: The ocular surface is extraordinarily important in keratometry, which is the rate-limiting factor in patients' biometric measurements. If the Ks are not accurate, we may implant the wrong IOL power or treat cylinder inaccurately (Figure 1). Thus, improving the tear film before performing keratometry will give us better results.

In fact, at a TearLab-sponsored symposium held during the 2014 ESCRS meeting in London, R. Doyle Stulting, MD, presented a study that evaluated the relationship of a hyperosmolar tear film on keratometry readings. The study, which has been submitted to the *Journal of Cataract & Refractive Surgery*, demonstrated that hyperosmolar patients ($n=75$) had a wider variation in keratometry calculations between visits relative to the normal osmolar group ($P=.13$) (Figure 2). In the



(Courtesy of TearLab Corporation, San Diego, CA.)

Figure 3. The difference in keratometry cylinder (Kcyl) values between the first and second patient visits. There was greater than 1.00 D of change in Kcyl values between the two visits in 17% of the hyperosmolar eyes, whereas only one eye in the normal control group had 1.01 D of change between visits.

hyperosmolar group, 17% of hyperosmolar eyes had more than 1.00 D of change in K cylinder values between the first and second visit (Figure 3). This study confirms the importance of evaluating osmolarity during surgical planning to ensure presurgical keratometry readings are not compromised by hyperosmolarity.

Dr. McDonald, how important is it to diagnose dry eye and treat it before doing refractive procedures?

Dr. McDonald: It is very important. If refractive surgical candidates are made aware that they have a pre-existing condition that may compromise their outcome, and they receive proper treatment preoperatively, they sail through their postoperative period uneventfully. With a healthy ocular surface, our complication and enhancement rates go down, and UCVA and BCVA go up.

Dr. Donnenfeld: I agree, it's a no-brainer. I think the greatest advance in ocular surgery in the past decade has been the realization of the importance of the ocular surface in surgical results. And a lot of the technologies we use today are predicated on having the healthiest ocular surface possible. ■

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