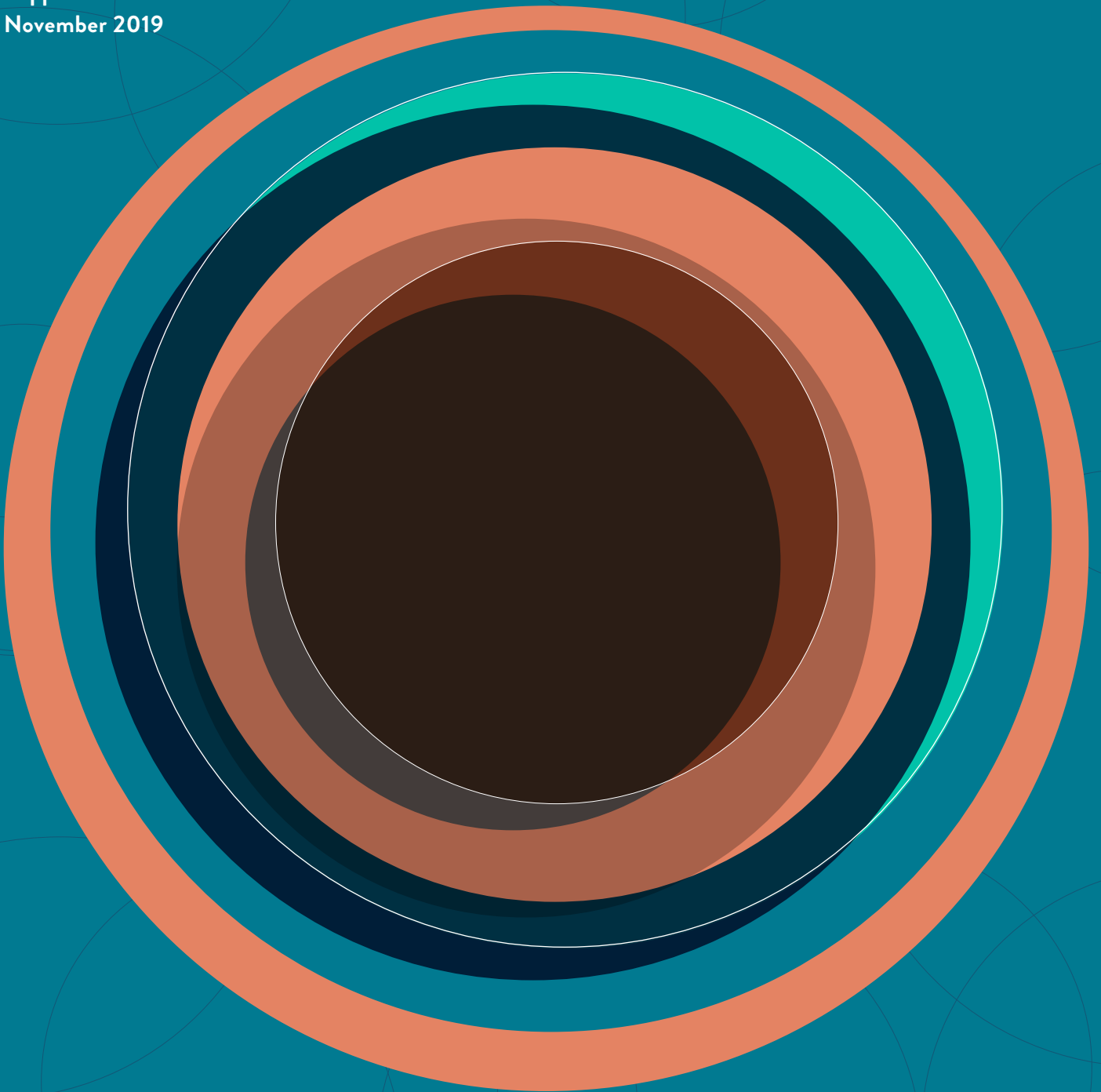




Supplement
November 2019



Education
FORUM



Ocular Surface Disease Diagnosis & Management: Special Focus on the Lipid Layer



Trends in OSD Treatment: 2018 ESCRS Clinical Survey Data

By José L. Güell, MD, PhD

The fourth annual ESCRS Clinical Trends Survey was conducted at the ESCRS Annual Meeting in Vienna, and almost 1,200 delegates responded to the survey. The goal of the survey is to assess current practice patterns, and below are some of the key results related to the diagnosis and treatment of ocular surface disease (OSD).

The 2018 ESCRS Clinical Trends Survey revealed that the vast majority of respondents agree that mild-to-moderate dry eye significantly impacts keratometry and intraocular lens (IOL) calculations (Figure 1). However, routine examination of the ocular surface is inconsistent. Eighty-four percent of respondents routinely check the ocular surface in all or most of their preoperative laser vision correction (LVC) examinations, but only 76% perform an ocular surface check during preoperative cataract surgery examinations.

“Routine examination of the ocular surface is inconsistent”

ESCRS delegates believe that 20% of cataract patients present with ocular surface symptoms, and that 17% of their cataract patients present as asymptomatic before surgery but develop ocular surface problems after the surgery. This suggests that cataract surgeons will deal with significant ocular surface problems in approximately 40% of their patients, either preoperatively or both preoperatively and postoperatively.

Respondents of the 2018 ESCRS Clinical Trends Survey reported that they believed meibomian gland dysfunction (MGD) was present

“Most survey participants responded that they use diagnostic tests on a case-by-case basis even with conventional tests”

in only 40% of their patients who have dry eye disease, even though the actual prevalence of MGD is probably much higher.

When asked about diagnostic testing usage, most survey participants responded that they use diagnostic tests on a case-by-case basis even with conventional tests. Just under 15% of respondents said they use Schirmer's testing in every dry eye case, while over 70% said they rely on Schirmer's testing on a case-by-case basis. Fluorescein and tear break-up time testing is utilised by about half of the respondents. The survey revealed there is lots of room for growth in utilisation of meibography and osmolarity testing due to limited access to technologies, cost and lack of reimbursement.

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Financial disclosures: Alcon, Ophtec, Orca Surgical, Théa, Visiometrics, Zeiss.

How strongly do you believe that mild to moderate dry eye significantly impacts...

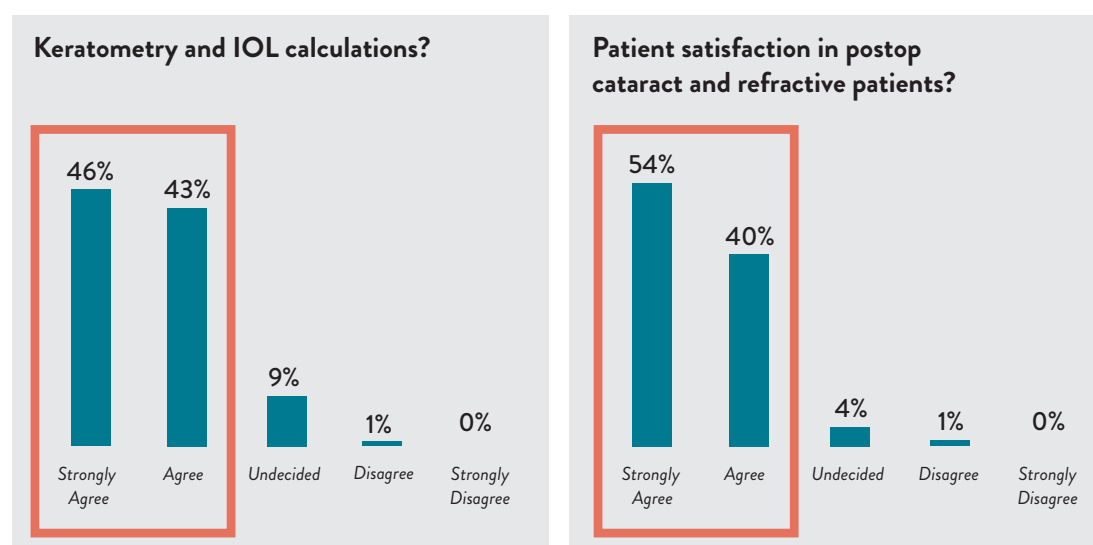


Figure 1: The vast majority of survey respondents believe that mild-to-moderate dry eye impacts keratometry and IOL calculations, as well as postoperative refractive surgery and cataract surgery patient satisfaction



Tear Film Instability: Aetiology, Incidence and Impact on Outcomes

By Béatrice Cochener-Lamard, MD, PhD

The ocular surface is the anatomical crossroads of the eye. It is integral to everything that affects vision. The health of the tear film is integral to patient comfort, visual function, surgical outcomes and more. The tear film is a barrier that provides protection against infection, provides oxygenation of the cornea and finally prevents dehydration of the cornea.

Dry eye is increasingly prevalent, and environmental and lifestyle factors are partially responsible. Our way of life today promotes oxidative stress. Pollution, air conditioning, UV radiation, vitamin A deficiency, over-exposure to screens and tobacco use are all risk factors for loss of ocular surface homeostasis. Oxidative stress caused by these lifestyle factors results in excessive production of reactive oxygen species (ROS), which disturb the osmotic balance of the lipid layer, dehydrate epithelial cells and lead to apoptosis – keratitis and mucocyte destruction.

Evaporation is normally responsible for 33% of the total lacrimal flow. When ROS are introduced, evaporation of the lacrimal flow will increase by at least 75%, dehydrating the aqueous layer, the mucin layer and the epithelial cells.¹ (Figures 1 and 2)

What we know today about dry eye syndrome is that symptoms are not only functional. Sometimes there are visual disturbances; other times there is no expression, and it goes undiagnosed. We are all familiar with the vicious cycle of dry eye syndrome; it is a chronic and multifactorial disease.

DRY EYE AND SURGERY

When we think about the ramifications of dry eye in the context of refractive surgery, classically we've been talking about corneal laser surgery. We should keep in mind that now cataract surgery is refractive surgery, so we are looking at a whole new population of patients for whom we should be mindful of the presence of dry eye – those who opt for intraocular surgery because they are contact lens intolerant.

In corneal surgery, there is a direct attack on the cornea with nerve dissection and scar response. Contact lens intolerance, allergies, excessive digital screen exposure and wound management issues also lead to the same risk. This is why it is so important to detect dry eye or the predisposition to dry eye prior to surgery when it is asymptomatic. The cornea must be prepared, and the patient must be warned that the surgery will likely temporarily increase and aggravate their dry eye postoperatively.

When the eye's surface is healthy, there is a normal regulation. When you do the surgery, you increase the tear secretion, there is an increase in local defences and mucus secretions by the activation of the conjunctiva and the corneal nerve endings. However, if it becomes pathologic in terms of surface or tear gland, the nervous exhaustion is over-stimulated and becomes ineffective. This leads to

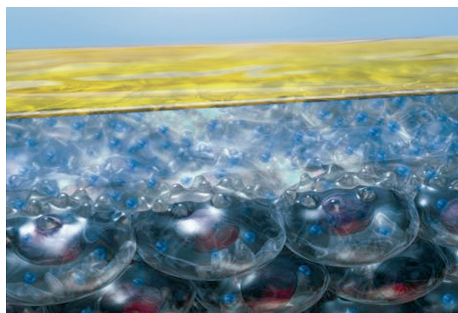


Figure 1: Water evaporation normally represents 33% of total lacrimal flow



Figure 2: Oxidative stress leads to evaporation of 75% or more of the lacrimal flow

paradoxical tearing, and that can lead to neurogenic inflammation. Most of the time in the case of PRK, LASIK and SMILE, repair and restoration happen naturally.

PATIENT COMFORT

Dry eye typically compromises patient comfort. Generally, that explains why the patient is not comfortable right after surgery from a few days for PRK to more than a few days for cataract surgery. In other cases, patients experience neuropathic pain, which results from chronic dryness after LASIK. There is no organic lesion; and autostimulation of a Loop of Boucle means the loop that will never heal. Most of the time, all of these functional symptoms will combine into a visual impairment.

Compromised visual performance is another consequence of dry eye. Visual performance will change; it can even lead to more than 1D of difference if there is huge variation between blinks. The optical power of tear film is 6-to-20 μm . Normally, there is 0.10D variation between two blinks. If the tear film is unstable, the variation between two blinks is more than 1D.

What are the consequences of dry eye? Epithelium growth, diffuse lamellar keratitis, refractive regression and infectious keratitis can all be induced by ocular surface disease. Moreover, OSD penalises daily activities – especially near vision activities – and has been linked to absenteeism in the workplace, depression, and even retinal disorders.

CONCLUSION

In conclusion, dry eye is the number one complication for refractive surgery, and can affect quality of life.

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Financial disclosures: Clinical investigator and consultant for Alcon, Cutting Edge, Dompé, Horus, Hoya, J&J, Santen, Théa, Zeiss.



Step-Wise Assessment of ADDE and EDE in Daily Practice

By Carina Koppen, MD, PhD

As dry eye disease diagnostic tools become increasingly sophisticated and effective, the Tear Film & Ocular Surface Society's (TFOS) Dry Eye Workshop guidelines suggests that diagnosing dry eye disease (DED) and classifying its subtypes is still possible by combining information on symptoms and signs. The complexity of the DEWS II guidelines can be intimidating, but if you break them down into manageable bites, they are easy to digest.

STEP 1: TRIAGING QUESTIONS

First, start with triaging questions to rule in dry eye or rule out other masking conditions. Once you suspect dry eye, move on to a risk factor analysis. DEWS II recommends using a questionnaire, for example the Ocular Surface Disease Index (OSDI) questionnaire, which pertains to symptoms of discomfort, impact on visual performance and triggering situations. The OSDI has been validated to discriminate between normal, mild to moderate, and severe DED as defined by the physician's assessment and a composite disease severity score. Questionnaires provide an easy and fast tool for diagnosis and follow-up, and having the patients fill out a questionnaire in the waiting room doesn't require any extra chair time.

Next, a thorough slit-lamp examination is a crucial part of the diagnostic process. Systematic examination from the outside to the inside of the eye should be performed. Take note that during this exam, you might notice lid-parallel conjunctival folds (LIPCOF) indicative of DED, frothy tears as seen in meibomian gland dysfunction (MGD) and you will miss superior limbic keratoconjunctivitis (SLK) and cicatrising conjunctivitis if you don't look in the fornices.

“ Diagnosing DED is still a matter of combining information on symptoms and signs

STEP 2: TBUT TESTING

Next, instil a drop of fluorescein to determine the tear break-up time (TBUT). A TBUT of less than 10 seconds suggests tear film instability, and less than 5 seconds suggests definite dry eye. With one application of fluorescein, you can see the dark spots of the tear film breaking up and you can see the staining of the corneal epithelium.

Ocular surface stains are used to assess the integrity of the superficial cell layers of the ocular surface. Fluorescein is the one used most commonly; rose bengal and lissamine green highlight other aspects of the ocular surface. To document the intensity of staining and the distribution pattern, it is advisable to use a semi-quantitative index, for example the van Bijsterveld score.

Every ophthalmologist should have fluorescein next to the slit lamp. Whether you should have an osmolarity test at your disposal is a matter of choice. Hyperosmolarity is a hallmark sign of DED and a maximum osmolarity of more than 308 mOsm and/or an inter-eye difference of more than 8 mOsm suggests DED. The main challenge is the detection of

“ ...there are standardised meibomian gland structure and function tests that... provide more objective evaluation in comparison to manual expression

mild dry eye. Values of osmolarity can fluctuate, so it is advised to test at least both eyes once, but it is more effective if you perform several tests per eye.

STEP 3: SUBTYPE CLASSIFICATION

At this stage, we want to classify the DED patient by subtype. Traditionally, we have thought of this as evaporative (EDE) vs. aqueous deficiency dry eye (ADDE). However, it is not an either/or situation. Once a patient gets trapped in the vicious cycle of DED, there will be elements of both subtypes present. For EDE, we will have to look at the tear lipid layer and at the meibomian glands; for ADDE, we will examine tear volume by looking at the tear meniscus height.

With respect to MGD, if you look for it, you will often find it. MGD is a chronic diffuse abnormality of the meibomian glands, characterised by terminal duct obstruction and/or qualitative/quantitative changes in the glandular secretions. MGD can have many appearances; traditionally we would look at the orifices on the eyelid margins and squeeze the glands to test their functionality. Today, there are standardised meibomian gland structure and function tests that, in combination with computer analysis, provide more objective evaluation in comparison to manual expression.

For instance: meibography, which is a non-contact technique using infrared photography, provides a useful, quick and patient-friendly method for obtaining information on the meibomian gland structure. Also, interferometry provides measurement of lipid layer thickness: LLT ≤ 60 nm has a 90% specificity for MGD. Having access to both of these tests helps evaluate the most common cause of DED.

CONCLUSION

Industry is working on solutions to facilitate more widespread access to these exciting diagnostic technologies. A number of these devices have been introduced into the market that can perform meibography, interferometry, measurement of tear meniscus height and non-invasive TBUT, in just a few minutes. These advances suggest that the time is right to consider stepping beyond the essential basic tools when it comes to diagnosing DED.

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Financial disclosures: Horus: speaker; Théa Pharma: consultant; Ursapharm: speaker.



Diagnosing Lipid Layer and Meibomian Gland Deficiencies

By Jose Manuel Benitez del Castillo, MD

The official definition of meibomian gland dysfunction (MGD) explains that it is a chronic, diffuse abnormality of the meibomian glands, commonly characterised by terminal duct obstruction and/or qualitative/quantitative changes in the glandular secretions that may result in alteration of the tear film, symptoms of eye irritation, clinically apparent inflammation and ocular surface disease.¹ MGD is progressive and can get worse over time, thus early intervention is key.^{2,3} When meibomian gland orifices are obstructed they become dilated, then tortuous, and finally they atrophy. If there is no intervention, over time functioning meibomian glands will be lost.

When diagnosing MGD at the slit lamp, you must look at the lid margin and see hyperaemia, telangiectasia and occluded orifices. The key in diagnosing MGD is pressing eyelids to see the quality and quantity of the meibum secretion. You will see liquid and transparent secretions (Figure 1), or solid and yellow secretions (Figure 2). It is important to press the lids because you may have a patient who has what is referred to as non-obvious obstructive MGD, which means they are very symptomatic but have no signs at the level of the lid margins. If you don't press the eyelid, you won't diagnose non-obvious obstructive MGD.

NEW TOOLS

Meibography, interferometry, optical coherence tomography (OCT), confocal microscopy, evaporimetry and infrared thermography are among the new tools available to help diagnose the presence and extent of MGD, and I will discuss meibographers and interferometry.

When we perform meibography with one of the available systems, such as Eye Top Topographer (Schwind Sirius), Keratograph 5M (Oculus), and BG-4M/DC-4 (Topcon), we are using various grading systems to classify the meibomian glands. The most frequent one used is the meiboscore.⁴ Grade 0 indicates no loss of meibomian glands; grade 1 indicates loss of less than one-third of the total area of the meibomian glands; grade 2 indicates loss of between one- and two-thirds of the total area; and grade 3 indicates loss of over two-thirds of the total area. This classification does not take into account the tortuosity of the glands.

“MGD is progressive and can get worse over time, thus early intervention is key

We recently published a study aimed at assessing the relationship between meibomian gland loss (MGL) and relevant ocular surface clinical parameters, as well as the influence of age in this relationship. A total of 161 participants (mean age; 42 ± 17 years) were enrolled in this study.⁵ Infrared meibography was performed using Keratograph 5M. Participants were divided into five groups according to total meiboscore, and the ocular surface parameters of each MGL group were studied. In addition, the relationship between MGL and the ocular surface parameters was established including age as a covariant. Both eyelids were taken into account, since no association between the MGL from upper and lower eyelid was found (k value=0.2; $p=0.3$) despite being significantly correlated ($r=0.3$; $p<0.001$).

No statistically significant differences were found in symptomatology among different MGL groups. Statistically significant differences were found among MGL groups in tear osmolarity ($p=0.02$), bulbar redness ($p=0.04$), corneal and conjunctival staining ($p=0.01$ and $p=0.004$, respectively). Despite this, only corneal staining showed a significant correlation with MGL when age was a covariant ($r=0.2$; $p=0.04$). We concluded that MGL higher than 50% seems to be accompanied by signs on the ocular surface. Furthermore, age demonstrated to be a relevant factor when assessing MGL. For this reason, future studies should compare age-matched groups in order to know the contribution of the MGL on the ocular surface and establish valid cut-off values for dry eye diagnosis.

When we looked at symptoms, there was a correlation with osmolarity, but no correlation with tear film break-up time and Schirmer. We tried

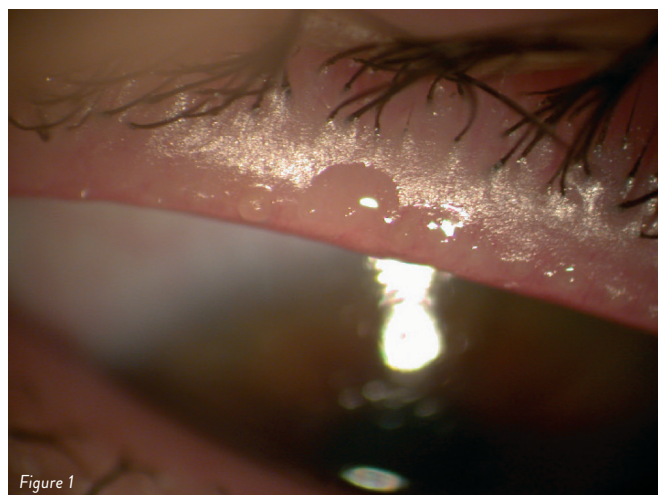


Figure 1

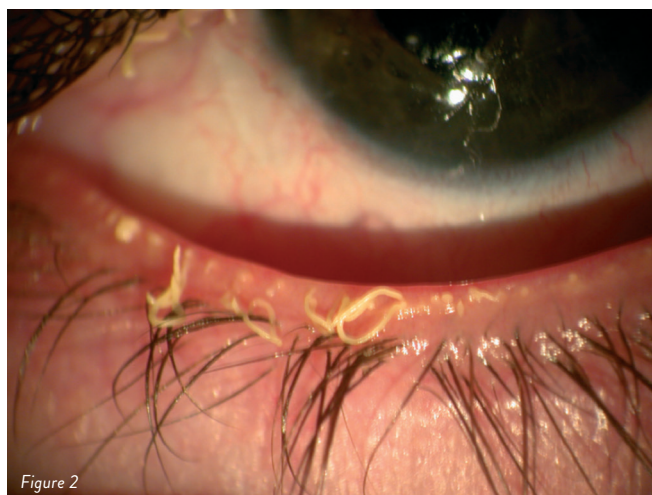


Figure 2

Diagnosing MGD: Press the lid margins; you will see liquid and transparent secretions (Figure 1), or solid and yellow secretions (Figure 2)

to correlate the tear film lipid thickness with the meiboscore and no correlation was found. So, we decided instead of looking only to atrophy, we developed a software for measuring the tortuosity, the length of the glands, the width and more. We were really disappointed that we found no statistical correlation with other parameters.

In my opinion, the reason we found no correlation with other parameters is because patients with low meiboscores (in the 0, 1 and 2 range) still have glands and they may increase the meibum production; also, these patients may increase the tear fluid production by the lacrimal gland. This compensates for the decreased lipid layer, so these patients won't have symptoms and signs of dry eye.

INTERFEROMETRY

The LipiView interferometer (Johnson & Johnson Vision) works according to the principle of white light interferometry, and the tear film is measured using an interferometry colour assessment by specular reflection. The unit of measurement is interferometry colour units, which is an index of thickness and is estimated on the basis of the observed mean interference colours.

In one study, LipiView was able to diagnose MGD with a sensitivity of 65.8% and specificity of 63.4% on the basis of a cut-off value of 75 nm for lipid layer thickness.⁶ With this instrument, you can also gain information about the blinking pattern; many patients with MGD, have incomplete or partial blinks.

CONCLUSION

Are meibographers and interferometers necessary for MGD diagnosis? No, but they can be helpful. Ultimately, the diagnosis is made at the slit lamp and by pressing the lids with your fingers.

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Financial disclosures: Abbvie, Allergan, Alcon, Angelini, Bausch + Lomb, Brill, Dompé, Esteve, Farmamix, Horus, Novartis, Santen, Syntentis, Théa.

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Exploring Treatment Options for the MGD Patient

By Serge Doan, MD

When you see signs and symptoms of meibomian function disease in patients who present with dry eye complaints or in patients who are being seen for a preoperative consultation, be aware that there are several effective strategies to treat meibomian gland dysfunction (MGD). In my opinion, it may not be necessary to treat all degrees of MGD before surgery, but every surgical patient who has MGD must be made aware of this before surgery.

The first step in the process is to inform these patients that they have dry eye and that it is probably going to increase after the surgery. If they have signs such as corneal or conjunctival staining, inflammation of the ocular surface and/or meibomian gland atrophy, they must be treated according to the severity of their symptoms. When there is lid margin anterior inflammation, you must think about bacterial superinfection and the possibility of infection after the surgery. In instances where there is major meibomian gland atrophy, there is a very high risk of having postoperative dry eye.

FIRST-LINE TREATMENTS

Among the first-line treatments for MGD are lid hygiene/massage and lipid tear layer substitution. Lids must be warmed for five

“Artificial tears and emulsions are an option for MGD treatment, but there are real challenges to substituting the lipid layer

minutes to effect softening of the meibum, so it can be expelled during lid massage. There are limitations to this process, because it must be avoided after LASIK and cataract surgery.

In the case of anterior blepharitis, it is helpful to prescribe lid hygiene. You can remove crusts with lid preparations, tea tree oil wipes or baby shampoo using a special brush similar to a toothbrush. You can also consider treating demodex, which the literature suggests will have an effect on the super-infection of the lids.¹

Artificial tears and emulsions are an option for MGD treatment,



Figure 1: Thermal pulsation safely heats meibomian glands, then presses the glands to release built up meibum secretions

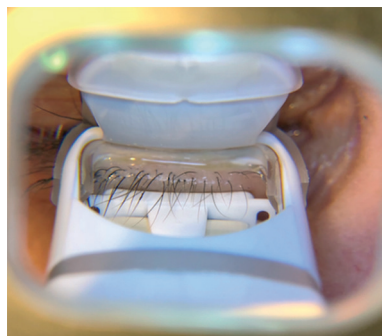


Figure 2: Handheld instrument mechanically warms the meibomian glands through the lids.

but there are real challenges to substituting the lipid layer. The lipid layer has a hydrophobic layer that inhibits the evaporation of the tears, as well as a second thinner layer, the polar interface, which is very important for the adherence and stability of the hydrophobic lipid layer on to the aqueous tear layer, and there are numerous challenges to recreating this interior polar interface layer.

Antibiotics and omega-3s are among the available second-line MGD treatments. With respect to antibiotics, the classic treatment is oral tetracyclines, but it has numerous contraindications and requires ongoing use. For these reasons, I prefer to use oral or topical azithromycin; it has a long half-life and only needs to be taken twice a day for three days once or twice per month. The downside of relying on antibiotics, is that if you prescribe them preoperatively there could be increased risk of bacterial resistance in the lids. Oral omega-3 substitution is an option, but it is controversial, with a recent study calling into question its effect on meibum quality.²

“ In instances where there is major meibomian gland atrophy, there is a very high risk of having postoperative dry eye

DIFFICULT CASES

In more difficult cases, there are other options worth considering. For instance, the LipiFlow thermal pulsation system (Johnson & Johnson Vision) is a 12-minute in-office process that safely heats meibomian glands beneath the eyelids and then presses the glands to release built up meibum secretions (Figure 1). Several studies support the efficacy of thermal pulsation, including one showing that thermal pulsation improved MGD symptoms and signs more effectively than doxycycline; and another by Cynthia Matossian, MD, showing that patients who did not have thermal pulsation prior to surgery had more MGD signs and symptoms postoperatively.^{3,4}

Another option is the hand-held iLux system (Tear Film), which also mechanically warms the meibomian glands through the lids; but in this case, once the pent-up meibum is softened it is expressed manually (Figure 2).

Another very interesting and effective option is intense pulsed

light (IPL) therapy, a therapy derived from dermatology that is available for ophthalmic use as the E-Eye (E-Swin), the M22®/Q (Lumenis) and the Eye-Light (Topcon). We are not sure how IPL works to reduce the MGD burden, but we do know that it does. Speculation suggests that IPL might have an effect on the vessels, it might heat the glands, it might stimulate a remodeling and remodelling of the fibroblasts and/or it might have also anti-inflammatory or anti-infectious effects and modulate nerve function. Two noteworthy placebo-controlled studies show impressive IPL effect on tear break-up time and signs and anti-inflammatory effect and you can have a decrease of these inflammatory cytokines in the tears after IPL, respectively.^{5,6}

CONCLUSION

In conclusion, if your patient has postoperative dry eye, you should think about MGD and blepharitis, but remember that you have to rule out aqueous deficient dry eye and treat it, rule out inflammation and treat it, rule out mucous-related evaporative dry eye and treat it and always rule out neuropathic pain because it can be a major problem after cataract surgery.

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Financial disclosures: Consultant for Alcon-Novartis, Allergan, Bausch & Lomb, Horus, Johnson & Johnson, Santen, Théa.

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Supplement
November 2019



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