Contact Lens Update
CLINICAL INSIGHTS BASED IN CURRENT RESEARCH

Dry eye update: new diagnostic and management strategies

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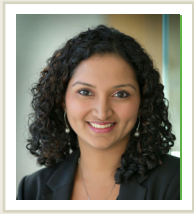

Sruthi Srinivasan is a clinical research manager at the Centre for Ocular Research & Education, and a research assistant professor at the School of Optometry and Vision Science, University of Waterloo, Canada.

Dry eye disease (DED) is a chronic condition affecting millions of people. The prevalence of DED is between 5% and 50%,[1] a wide range as there is no gold standard for diagnosis of this condition.[2-8] The Tear Film and Ocular surface Society (TFOS) Dry Eye Workshop II (DEWS II) report has recently updated the definition of DED as,

> "a multifactorial disease of the ocular surface characterised by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles."[1]

DED is a complex condition for which a single etiology is not known. The complexity of both the disease and its diagnosis makes it difficult to establish a single diagnostic test to diagnose DED. Hence, management strategies can also be challenging in certain cases of DED. This section provides an overview of the newest diagnostic tools for DED, as well as the latest approaches to management.

Patient questionnaires

Clinicians rely to a large degree on their case history, with the patient's input regarded as an important tool to diagnose and categorize patients with DED. Hence, symptoms of DED are a key factor in the diagnosis and management of DED. A variety of questionnaires are available for the evaluation of symptoms, which can aid in the diagnosis of DED and also monitor treatment effects. Of these, the TFOS DEWS II report recommends a positive score on a validated symptom questionnaire (either ≥ 6 on the Dry Eye Questionnaire (DEQ)-5 or ≥13 on the Ocular Surface Disease Index (OSDI)) for the diagnosis of DED.[9] Questionnaires can be completed while the patient is in the waiting room, and interpreting the questionnaire results can be rapidly undertaken, based on the questionnaire used.

It is also important to assess pain experienced in DED. Broadly, pain can be categorized into nociceptive and neuropathic pain. Nociceptive pain is signaled as a result of damage to tissues by noxious mechanical, thermal and chemical stimuli. In contrast, neuropathic pain is triggered by a lesion or disease of the somatosensory nervous system. This differentiation may improve clinical diagnosis and treatment efficacy of DED, as treatment for the pain and discomfort associated with DED is generally ineffective for ocular neuropathic pain.[10]

DED Diagnosis

Tear film instability and increased tear osmolarity are key mechanisms in dry eye, regardless of the underlying etiology.[1,11] Tear osmolarity is considered as a single biophysical measurement that captures the balance of inputs and outputs of the lacrimal system.[12] The ease of use and small tear sample required make newer in situ osmometers much more clinically accessible and the shorter contact time required to obtain tear samples is more

comfortable for the patient.

Newer electrical impedance osmometers, such as the TearLab osmometer (TearLab), measure osmolarity by measuring the number of charged particles within a sample and can provide results from a small tear sample in less than a minute.[13,14] The electrical impedance osmometer collects the tear sample by touching the tear meniscus with a small testing chip without the need for anaesthetic and without manipulation of the lids.

Another point-of-care tear osmometer that uses electrical impedance technology is the new i-Pen (I-MED Pharma Inc, OcuSOFT). Recent studies have not shown it to be as accurate in differentiating normal from dry eyes.[15,16] The iPen has a flexible conductimetric sensor, constructed using microelectronic techniques, which is placed on the palpebral conjunctival membrane to measure the electrical conductivity of the tear fluid.[17]

InflammaDry, a new rapid immunoassay by Quidel Corporation is an in-office test that allows for the identification of inflammatory DED and ocular surface disease. It detects elevated levels of matrix metalloproteinase 9 (MMP-9), an inflammatory marker that is considered to be elevated in the tears of DED patients.[18] A recent review on the role of ocular surface MMP-9 in DED and the implications of InflammaDry suggested that not all patients with symptoms of DED have increased (>40ng/ml) MMP-9 levels and that future studies are needed to clarify all the factors involved. This would allow eye care practitioners to understand how to best incorporate this in-office test into the dry eye testing routine to help in diagnosis and treatment decisions.[19]

The LipiView II (Johnson & Johnson Vision), Lipiscan (Johnson & Johnson Vision), Keratograph 5M (Oculus) EasyTearView+ (Easytear s.r.l.) and Ocular Surface Analyser (SBM Sistemi) are all instruments that have the capability of assessing the tear film and imaging the meibomian glands. These multi-functional devices provide space-saving options within eye care practices and it is likely that such devices will continue to be released that use a single platform to deliver multiple testing options.

DED management

Once diagnosed, a wide variety of management options exist to treat DED.[20] This article discusses some of the recent developments in the management of DED.

Managing lid conditions

For the treatment of blepharitis, topical hypochlorous is now available as Avenova from NovaBay[21,22] and also as Hypochlor from OCuSOFT.[23] These products are designed for the removal of microorganisms and debris on and around the eyelid margins.[21,23,24]

Intense pulsed light (IPL) has been extensively studied and reported to have a beneficial effect on erythema and telangiectasia.[25] Light energy absorbed by hemoglobin converts to heat and causes the destruction of superficial blood vessels (thrombosis). In meibomian gland dysfunction (MGD), the destruction of abnormal erythematous blood vessels decreases the inflammatory mediators, therefore removing a main cause of inflammation from the eyelids and meibomian glands.[26]

Also available is LipiFlow (Johnson and Johnson), which provides thermal pulsation therapy[27] to rapidly melt the meibum and improve the MGD that is prevalent in several patients with dry eye. A recent study showed a single LipiFlow® treatment effect, with improved gland function and dry eye symptoms, can be sustained for up to 12 months.[27] Another device which heats the meibomian glands is the MiBo Thermoflo (MiBo Medical Group).[28] This device massages the outer area of the eyelids with continuous controlled heat.

BlephEx™ (Rysurg) is used as an in-office blepharitis treatment. The handheld device is fitted with a single-use,

disposable sponge on its tip, which spins/rotates, effectively helping the clinician to microexfoliate the lid margins and lashes and is a less invasive method to mechanically remove debris and biofilm at the lid margins.[29]

Prescription therapies

Cyclosporine is an immunomodulatory drug with anti-inflammatory properties, with other actions relevant to managing DED.[30,31] Cyclosporine is an inhibitor of T-cell proliferation and thereby inhibits T-cell-mediated immune responses.[32] The availability of Restasis multidose™ (Cyclosporine Ophthalmic Emulsion) 0.05% was announced by Allergan recently. The unit dose format received FDA clearance in October 2016 and has been available since March 2017. It is one of the first FDA-approved, preservative-free prescription eye drops available in a multi-dose bottle with a patented unidirectional valve and air filter technology.[33] Patients who find the single-dose unit difficult to handle may welcome the multi-dose bottle.

A new topical dry eye therapeutic agent – Lifitegrast ophthalmic solution 5.0% (Xiidra, Shire) hit the US market in 2016. Lifitegrast is approved by the FDA for the treatment of signs and symptoms of DED. It is a small molecule integrin antagonist, made to mimic intercellular adhesion molecule 1's (ICAM-1's) binding domain to lymphocyte function-associated antigen-1 (LFA-1) and serves as a competitive antagonist to block binding between LFA-1 and ICAM- 1. This results in inhibition of T cell migration into target tissues, reduction of cytokine release, and reduction of further T cell recruitment.[34,35] Lifitegrast was studied in four 12-week, randomized, double-blind, vehicle-controlled clinical trials in a total of 2133 adult patients with DED.[36-38] These trials showed improved patient-reported symptoms of DED, as measured by the symptom score and corneal fluorescein staining. The recommended dosage of one drop of solution instilled twice a day appears to be safe and effective in treating the signs and symptoms of DED.

Novel device

An intranasal neuro-stimulation device (TrueTear Intranasal Tear Stimulator, Allergan), recently approved by the FDA, could be a useful treatment for DED. This portable, handheld device stimulates the production of tears that can return the ocular surface to a more normal condition. This device features a reusable base with a disposable tip that is inserted into the nose to contact the anterior nasal mucosa. The tip transmits a series of low-voltage electrical pulses to the trigeminal nerve, triggering the nasolacrimal reflex to stimulate natural tear production.[39]

ProKera amniotic membranes (BioTissue) is another alternative to speed up the healing of severe DED. The application of the amniotic membrane is a suture-free, in-office procedure.[40] It is made by clipping a piece of amniotic membrane tissue in between two rings made out of a clear, flexible material. The amniotic membrane used here is thin and clear like the tissue on the surface of the eye and protects damaged tissue when inserted.

Conclusion

Although there are several novel approaches in the diagnosis and treatment of DED, to date, there is no single test known to conclusively diagnose DED. At the present time a "combination of subjective and objective dry eye tests" is necessary to determine the underlying etiology to arrive at a diagnosis. With the lack of association between the symptoms and signs of DED, poor test reproducibility of objective tests, variability with season and time of day, and even variability between eye care examinations, DED is an complicated disease process, and we are only starting to understand its intricacy. Researchers are working towards the development of simple, less cumbersome, clinician friendly, inexpensive, reliable, repeatable, and highly specific and sensitive diagnostic tools for DED. This may then lead to more specific management strategies for DED that could restore the homeostasis of the ocular surface.

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