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Ocular surface diagnostics in clinical practice – from classical tests to advanced imaging

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Summary: The ocular surface is a complex anatomical and functional system comprising the eyelids, conjunctiva, cornea, and overlying tear film, together with neurosensory regulatory mechanisms. Disruption of ocular surface homeostasis leads to irritation, transient visual disturbance, and epithelial alterations. The most common clinical manifestation of this process is dry eye disease [1, 2]. This paper outlines current diagnostic methods for the ocular surface, detailing a practical sequence for patient evaluation, the clinical utility of advanced imaging techniques, and the limitations of most commonly used tests. It is a review synthesizing findings from key consensus reports and review articles indexed in PubMed.

Key words: ocular surface, dry eye disease, tear film, meibography, interferometry, anterior segment optical coherence tomography (AS-OCT).

Introduction

Proper functioning of the ocular surface is essential for maintaining epithelial integrity and tear film stability, ultimately ensuring visual comfort. Disorders of this system are among the most common problems encountered in ophthalmic practice and may lead to symptoms of irritation, visual fluctuations, and a reduced quality of life for patients [1, 2].

Advances in our understanding of the pathophysiology of ocular surface diseases have contributed to significant progress in diagnostic methods. Contemporary diagnostic approaches rely on the combined evaluation of clinical symptoms and objective parameters that reflect the condition of the ocular surface, tear film, and meibomian glands. Imaging techniques that enable a more objective and reproducible assessment of ocular surface disorders are also gaining increasing importance [1, 3, 4].

The aim of this paper is to present current diagnostic methods used in the evaluation of the ocular surface and to discuss their significance in daily clinical practice.

Methodology

This article presents a narrative review of the literature. It is based on the TFOS DEWS II report and selected publications addressing ocular surface assessment, dry eye disease, and meibomian gland dysfunction [1–4].

Results

Medical history

The diagnosis of ocular surface disorders should begin with a detailed medical interview with the patient. A thorough history includes information on the nature, duration, and severity of ophthalmic symptoms, environmental factors, occupational conditions, concurrent ocular and systemic diseases, as well as chronic local and systemic medications. Special attention is warranted in patients with chronic conditions, especially autoimmune diseases (e.g., rheumatoid arthritis, Sjögren's syndrome), dermatological disorders, and allergies. Taking a comprehensive patient history is also key to identifying conditions that can mimic dry eye disease, such as neuropathic pain, allergic conjunctivitis, or exposure keratopathy [1, 2].

The medical history is supplemented by standardized questionnaires assessing symptom severity, primarily OSDI (Ocular Surface Disease Index) and DEQ-5 (Dry Eye Questionnaire-5), as recommended by the TFOS DEWS II report. While these tools do not replace a clinical examination, they allow for a systematic evaluation of the patient's subjective symptoms, support the diagnostic process, and enable the monitoring of treatment efficacy during follow-up visits [1, 2].

Biomicroscopy

Although a detailed medical history and standardized questionnaires provide essential information on the nature and severity of symptoms, diagnosing ocular surface disorders requires confirmation through physical examination. Slit-lamp biomicroscopy plays a key role at this stage, enabling the evaluation of anterior segment structures and the identification of potential abnormalities. In addition to traditional clinical assessment, devices integrated with or compatible with the slit lamp are increasingly used to perform non-invasive evaluations of the tear film and ocular surface. In such cases, a proper examination sequence must be maintained. According to the TFOS DEWS II recommendations, the evaluation should begin with non-invasive methods, while more specific and invasive tests should be performed later, as they can affect subsequent measurements and reduce their reliability [1, 2].

Tear film stability

A tear break-up time (TBUT) shorter than 10 seconds indicates disruption of ocular surface homeostasis and often correlates with visual instability. This parameter can be assessed using either a non-invasive method (Non-Invasive Break-Up Time – NIBUT) or following fluorescein instillation (Fluorescein Tear Break-Up Time – FTBUT) [1–3].

In daily clinical practice, FTBUT remains the most widely used method for evaluating tear film stability due to its accessibility, simplicity, and speed. The test is performed after instilling fluorescein into the conjunctival sac and involves measuring the time elapsed from the last blink to the appearance of the first dry spots on the cornea (areas no longer covered by the fluorescein-stained tear film). A longer tear break-up time reflects greater tear film stability, with values exceeding 8–10 seconds considered normal [2, 3]. NIBUT is also gaining increasing importance, as it eliminates the potential influence of fluorescein on test results. The method uses specialized equipment and software to analyze distortions in a projected image reflected off the ocular surface

– most commonly a grid pattern or Placido rings – enabling an automated, objective evaluation of tear film stability without the use of dyes.

Ocular surface staining

Diagnostic staining is one of the essential tools used to evaluate epithelial damage and ocular surface integrity. The most commonly used dye is fluorescein, routinely applied in ophthalmic examinations to assess the corneal epithelium and measure TBUT. The dye is typically instilled using a moistened diagnostic strip or as drop solutions, after which the ocular surface is observed under cobalt blue light. Areas of epithelial damage or defects stain intensely green, which may indicate ocular surface disorders – including dry eye disease – as well as other corneal conditions. In addition to fluorescein, lissamine green is also used. It is particularly effective for highlighting conjunctival damage and areas with insufficient ocular surface protection. Lissamine green is better tolerated by patients and shows lower toxicity than the historically used rose bengal, which is now applied much less frequently [1–3].

Evaluation of tear volume

The Schirmer test remains the classic method for evaluating secretion of the aqueous component of the tear film, particularly when significant tear deficiency or an autoimmune condition such as Sjögren's syndrome is suspected. The procedure involves placing a standardized filter paper strip into the lower conjunctival fornix for 5 minutes, followed by measuring the length of the wetted area in millimeters. A result of less than 10 mm after 5 minutes may suggest impaired tear secretion. Despite its long-standing clinical use, the diagnostic value of this test is limited by high variability of results and susceptibility to external factors and reflex tearing [3].

Quantitative tear film assessment is supplemented by the analysis of the tear meniscus, observed along the lower eyelid margin. While its height can be evaluated during a slit-lamp examination, more objective imaging modalities are increasingly preferred, such as anterior segment optical coherence tomography (AS-OCT), which allows for precise measurement of meniscus height.

Both the Schirmer test result and tear meniscus evaluation should be interpreted in the context of patient-reported symptoms and other diagnostic parameters, including ocular surface staining and tear film stability, as current guidelines view them primarily as components of a comprehensive ocular surface homeostasis assessment [1–3].

Tear osmolarity

Tear film osmolarity is an important diagnostic parameter, as it reflects the balance between tear production and evaporation. Osmolarity measurement is performed using specialized osmometers that analyze a small tear sample collected from the inferior tear meniscus. Modern devices require only a few tens of nanoliters of sample volume, allowing them to be used even in patients with severe tear deficiency. An osmolarity value below 300 mOsm/L and an interocular difference of no more than 8 mOsm/L are considered normal. Elevated osmolarity indicates a loss of tear film homeostasis and supports the diagnosis of dry eye disease, with its magnitude correlating with the severity of ocular surface damage [1, 5].

Despite its documented diagnostic utility, tear osmolarity testing remains underutilized in Poland, primarily due to the limited availability of the necessary measuring equipment.

Ocular surface inflammatory markers

The evaluation of inflammatory markers is gaining increasing importance in the diagnosis of dry eye disease. The most commonly utilized marker is matrix metalloproteinase-9 (MMP-9), elevated levels of which indicate an active inflammatory process and ocular surface barrier disruption. In clinical practice, the InflammaDry test is used for the rapid detection of elevated MMP-9 concentrations in tears [1].

The test is performed prior to the administration of topical anesthetics and diagnostic dyes. A tear sample is collected from the palpebral conjunctiva, with results obtained in approximately 10 minutes. The test is qualitative, with a positive result corresponding to an MMP-9 concentration exceeding 40 ng/mL. The presence of elevated MMP-9 levels indicates an inflammatory etiology of ocular surface disorders and may serve as a rationale for initiating anti-inflammatory therapy. However, it should be noted that false-positive results may occur in conditions such as allergic conjunctivitis and ocular-surface infections.

Tear film interferometry

Interferometry enables evaluation of the lipid layer of the tear film through analysis of interference patterns formed on its surface. Based on the characteristics of light reflection, it is possible to indirectly assess the lipid layer – specifically its thickness, continuity, and dynamics, and consequently its capacity to hinder tear evaporation [2, 3]. One of the first clinically available devices utilizing this technology was the LipiView system, which enables quantitative measurement of lipid layer thickness between blinks. The result is expressed in Interferometric Color Units (ICU), with the analysis based on tear film imagery captured over several minutes. Additionally, this device evaluates blink dynamics, including the frequency of incomplete blinks, which can impair tear film stability [6, 7].

The clinical value of interferometry lies in its ability to evaluate lipid layer parameters that cannot be reliably assessed during a routine slit-lamp examination. An abnormal lipid layer pattern supports the diagnosis of meibomian gland dysfunction and evaporative dry eye disease, particularly when accompanied by a shortened tear break-up time and eyelid margin abnormalities [2, 3]. Interferometry is also useful for monitoring the efficacy of treatments aimed at improving meibum quality, eyelid margin hygiene, and thermal pulsation therapy for the meibomian glands. A limitation of the technique remains the dependence of results on blink quality, examination conditions, and measurement standardization [3].

Meibography

Meibomian glands produce the lipids that form the outermost layer of the tear film, whose primary function is to reduce tear evaporation.

Meibography, most commonly performed using infrared imaging, is the primary method for evaluating meibomian glands. This technique enables visualization of gland architecture after eyelid eversion using infrared cameras or dedicated imaging systems. The captured images allow assessment of gland morphology, including shortening, tortuosity, dilation, and the degree of atrophy.

Reviews dedicated to this technique emphasize that meibography has become one of the most important tools for phenotyping ocular surface diseases associated with meibomian gland dysfunction [8]. This examination carries not only diagnostic but also prognostic value. Advanced glandular atrophy may explain the limited efficacy of certain treatment modalities and indicate the need for more intensive management aimed at improving eyelid margin function [9].

Corneal topography and aberrometry

Contemporary ocular surface diagnostics increasingly incorporate the evaluation of optical parameters, which can be disrupted

by tear film instability. An unstable tear film may lead to transient changes in the regularity of the anterior corneal surface and an increase in higher-order optical aberrations, resulting in visual fluctuations despite relatively good visual acuity measured in a standard manner [3].

Corneal topography enables the assessment of surface regularity and symmetry, whereas aberrometry allows determination of the impact of tear film disturbances on the eye's optical quality. These investigations are particularly useful in patients reporting fluctuating vision, in evaluating candidacy for refractive procedures and cataract surgery, and in monitoring the efficacy of treatments aimed at improving tear film stability [3, 8].

Advanced ocular surface diagnostic platforms

Recent years have seen the growing popularity of integrated ocular surface diagnostic platforms such as Keratograph 5M, IDRA, C.Diag, LacryDiag, and LipiView. These systems enable simultaneous assessment of multiple tear film and ocular surface parameters, including NIBUT, tear meniscus height, lipid layer thickness, meibography, and blink dynamics. Their primary advantages include a high degree of test standardization, objective results, and the ability to perform a comprehensive patient assessment during a single visit. Although these devices offer clear diagnostic benefits, they are still not widely available across ophthalmic centers, mainly due to high acquisition and operational costs [10].

Conclusions

Assessment of the ocular surface requires a comprehensive approach that combines evaluation of patient symptoms with objective measures of tear film function and ocular surface integrity. Given the multifactorial nature of ocular surface disorders, no single test should be considered a standalone diagnostic tool.

Current best practice relies on a detailed medical history, slit-lamp biomicroscopy, and assessment of tear film stability and volume, complemented by ocular surface staining, tear osmolarity testing, and evaluation of the meibomian glands. Advanced imaging techniques, including interferometry, meibography, and anterior segment optical coherence tomography (AS-OCT), are playing an increasingly important role by improving diagnostic accuracy, facilitating treatment monitoring, and supporting clinical decision-making.

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