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## Dry eye disease as a common ocular disorder – current knowledge and management

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## **Abstract**

### **Introduction and purpose**

Dry eye disease is one of the most common ocular surface diseases. It is a multifactorial disease that contributes to symptoms impairing daily functioning. Dry eye syndrome occurs in up to half of the population. Therefore, proper diagnosis and treatment are necessary.

### **The state of knowledge**

One of the most common causes is meibomian gland dysfunction, which leads to impaired homeostasis and easy evaporation of tears. Environmental factors such as air pollution and stimulants also influence the occurrence of dry eye syndrome. All these factors lead to bothersome symptoms such as impaired visual acuity, itching, pain or burning. Patients also complain of a feeling of sand under the eyelids or photophobia. These patients' diagnoses are based mainly on history and ophthalmologic examination. Also, the Schirmer test or fluorescein staining can be used. It is essential to quickly apply treatment, which is mainly based on Artificial tears. Artificial tears are primarily a symptomatic treatment, while they are first-line therapy. In addition, treatment can include serum drops, anti-inflammatory drugs, or supplementation with omega-3 and omega-6 acids.

### **Summary**

Dry eye disease affects many people, especially the elderly. Symptoms may impair normal functioning. Untreated dry eye syndrome can also lead to many complications. Therefore, a proper diagnosis, primarily based on a basic ophthalmological examination, and individually

tailored treatment are necessary. New treatment methods are described in the literature, and they seem to be promising.

**Keywords:** Dry eye disease, dry eye syndrome, blurred vision, treatment, artificial tears

## **1. Introduction and purpose**

Dry eye disease (DED), also known as dry eye syndrome (DES) or ocular surface disease (OSD) [1] is one of the most common ocular surface disorders [2]. Depending on the scientific society, DED is defined slightly different. Currently, the most accurate definition is "Dry eye is a multifactorial disease of the ocular surface characterized 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." [3]. Due to the widespread occurrence of dry eye problems, it is essential to discuss the underlying causes of DED, as well as the epidemiology, diagnosis, and, most importantly, treatment methods. This paper will briefly discuss the pathogenesis, followed by the management and latest treatment guidelines for DED.

## **2. The state of knowledge**

### **2.1. Epidemiology**

Up to 50% of the general population is estimated to suffer from this condition, and some authors claim that even up to 75% of people may suffer from dry eye syndrome [4]. However, some data present a much lower prevalence, estimated at around 7% of the US population. In addition, the prevalence of DED increases with age and is more common in women than in men [5].

### **2.2. Etiology**

It has been shown that external (extrinsic) factors such as smoking or caffeine use, low humidity, air pollution, and contact lens use can be factors causing DED [6, 7]. In addition, DED can be caused by intrinsic factors. Intrinsic factors are internal factors such as inflammation of the eyelid margins (blepharitis), meibomian gland dysfunction (MGD) [8] or systemic diseases such as autoimmune disorders (e.g., Sjogren Syndrome), rheumatoid arthritis, or Diabetes Mellitus [1, 6]. An interesting possible factor that can cause DED is gut dysbiosis [1, 9].

### **2.3. Pathogenesis**

Risk factors can contribute to quantitative impaired tear secretion and/or qualitative abnormalities, i.e., abnormal tear film composition (homeostasis disorder) [1]. Therefore, two basic types of DED are distinguished. Evaporative Dry Eye (EDE) is the qualitative type of DED. It is caused by dysfunction in the lipid component of tears. The meibomian glands primarily secrete the lipid component, and meibomian gland dysfunction (MGD) is one of the main causes of EDE. Infrequent blinking or the use of contact lenses can also cause disturbances in the lipid layer. Disorders in the lipid layer lead to faster evaporation of tears [8]. Aqueous-deficient dry eye (ADE) is the quantitative type of DED. There are two types of ADE: Non-Sjogren ADE, which is caused, among other things, by lacrimal deficiency or systemic drugs, and Sjogren ADE, which is caused by primary or secondary Sjogren's syndrome [10]. ADE results in abnormalities in the aqueous phase of the tear film and quantitative tear disorders, which lead to dryness [1, 11-13]. Chronically, this can contribute to persistent inflammation of the ocular surface and several symptoms [14].

### **2.4. Symptoms**

Individuals with DED present with many symptoms that often do not correlate with signs of DED [6, 13]. Furthermore, these complaints can be so bothersome to the patient that they can lead to a significant reduction in quality of life and even to mental problems [5, 6]. Patients mainly report ocular burning or itchiness, even blurred vision, dryness, or a feeling of a foreign body or sand under the eyelids. They also complain of eye redness and photophobia [1, 15].

### **2.5. Diagnosis**

Diagnosis is mainly based on clinical symptoms and an essential ophthalmologic examination. Sometimes, Schirmer's test can be conducted, especially in quantitative tear secretion disorder. Fluorescein clearance tests (FCT) are other tear film evaluation methods. In addition, fluorescein can be used in Fluorescein staining, in which corneal epithelial loss and tear film breakage can be assessed [16]. Other tests can be tear breakup time (TBUT) or tear osmolarity [6, 17].

## **2.6. Treatment**

Analyzing the available literature and the Tear Film and Ocular Surface Society's Dry Eye Workshop II (TFOS DEWS II) guidelines [18], several treatments for dry eye syndrome stand out, which will be briefly presented in this chapter. First and foremost, the elimination of risk factors, health care, diet, and lifestyle are essential. In a study conducted by Kawashima et al., it was shown that lifestyle changes have a statistically significant effect on subjective symptoms in dry eye syndrome [19]. In addition, one should take care of blepharitis by using eyelid margin hygiene, which can help reduce dry eye symptoms (especially in DED with MGD etiology) [12]. Nevertheless, the most common treatment for DED is Artificial tears (ATs) [20].

### **2.6.1. Artificial tears (ATs)**

According to TFOS DEWS II (Jones et al.) [18], Artificial tears (ATs) are the first-line treatment for dry eye syndrome. However, this treatment method is only symptomatic and does not address the pathogenesis and main problem [18]. Currently, there are many AT products available. They are based on various substances that alleviate symptoms and/or contribute to increased tear production. Prominent among them are ingredients such as hyaluronic acid (HA), carboxymethylcellulose (CMC), dextran, polyvinyl alcohol and many other active substances [18, 21]. A meta-analysis by Yang et al. showed that drops containing hyaluronic acid compared to non-hyaluronic acid contribute to greater tear production [21]. In addition, there is a group of drops containing lipids. They mainly prevent tear evaporation, so they are useful, especially for EDE of MGD etiology [18, 22]. Moisturizing preparations in the form of ointments or gels are also available. However, due to blurred vision, they are usually recommended for use before bedtime [23].

### **2.6.2. Autologous serum (AS)**

Autologous serum drops, compared to ATs, contain many biochemical components that also occur naturally in tears. According to Pan et al., these include lysozyme, transforming growth factor- $\beta$  (TGF- $\beta$ ), fibronectin, and immunoglobulin A (IgA). In addition, they show similar effects to ATs in terms of moisturizing the ocular surface [24]. According to data cited in article by Pan et al., AS can be used to treat Dry Eye Disease of various etiologies, including non-sjogren as well as Sjogren. In addition, they are also used in patients with corneal damage or after surgical procedures [18, 24].

### **2.6.3. Anti-inflammatory agents**

Depending on the severity of symptoms and the etiology, it is sometimes necessary to use an anti-inflammatory agent in addition. In ophthalmology, corticosteroid drops such as loteprednol or methylprednisolone are commonly used. Nevertheless, it should be borne in mind that with time of use, there is a risk of increased intraocular pressure [12, 23]. Cyclosporine-containing drops are also used, especially in patients who need prolonged use of anti-inflammatory agents [23].

### **2.6.4. Omega-3 and omega-6 fatty acids**

Liu et al. conducted a study on cell cultures containing Immortalized human meibomian gland epithelial cells (IHMGECs) that were subjected to omega-3 and omega-6 acids. It was shown that omega-3 and omega-6 acids caused an increase in triglycerides and small neutral lipid-containing vesicles, which may contribute to improved lipid composition [25]. Nevertheless, in a meta-analysis by Downie et al. of the use of omega-3 fatty acids vs placebo or no treatment, there was a low level of evidence for the effect of omega-3 in reducing DED symptoms, a medium level of evidence for an increase in aqueous tear film production [26]. In contrast, due to their anti-inflammatory effects, omega-3 and omega-6 acids can be used to aid in treating and preventing blepharitis, or MGD [27].

### **2.6.5. Vitamin-D**

According to Rolando et al., the vitamin D receptor (VDR), as well as hydroxylase, is distributed in different parts of the eyeball. Of the many potential actions of vitamin D,

the immunomodulatory or anti-inflammatory effect is relevant here. Hence, it can be speculated that vitamin D metabolism influences biochemical processes in the eyeball [15]. Rolando et al., in a review paper, present an interesting study by Kurtul et al. in which it was shown that vitamin D deficiency could contribute to lower scores on the Schirmer test or tear break-up time (TBUT) [15, 28]. Demirci et al. also link vitamin D deficiency to dry eye disease [15, 29]. Nevertheless, we still need more research on this topic.

#### **2.6.6. Other therapeutic methods**

There are many other treatments for dry eye syndrome in the literature, depending on the etiology and the patient's clinical condition. Sometimes, the above treatment methods need to be improved, and further treatment regimens are necessary. In the case of lacrimal gland hypofunction, peripheral neurostimulation, scleral lenses, amniotic membranes, or stem cell therapies may be used. In MGD, on the other hand, Intense Pulsed Light (IPL) or even Manuka Honey [5, 13, 30, 31].

### **Summary**

Dry eye syndrome can be called a disease of civilization. It affects many people, especially in the elderly. The etiology of DED is multifactorial, and sometimes the cause is impossible to determine. This leads to bothersome symptoms that prevent normal functioning, especially in people who work in an office or at a computer [1, 32]. For this reason, proper diagnosis and treatment are necessary. Above all, quick diagnosis and implementation of treatment play the most crucial role. Treatment should be selected according to the severity of the disease and the age and preferences of the patient. New treatment methods are described in the literature, and they seem to be promising.

### **Author's contribution**

Conceptualization, WM, and BR; methodology, BR, MG and MP; software, ŁM and BK; check, MP, MS and BK; formal analysis, WM, and BK; investigation, ŁM, MG, and BR; resources, WM, and BR; data curation, WM; writing - rough preparation, WM and BR; writing - review and editing, WM, BR, BK, MP, ŁM, MS, MG; visualization, MS, MG; supervision, BR; project administration, WM;

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