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REVIEW ARTICLE

DRY EYE SYNDROME: AN INCREASING PROBLEM WITH AGING

ABSTRACT

Dry eye syndrome is a multifactorial and prevalent ocular disease in elderly population that results in decrease quality of life. Dry eye syndrome is defined as a disease of tear film layer due to reduced tear production and/or tear film instability. Age-related alterations including eyelid laxity, meibomian gland disease and orifice metaplasia, decrease in tear volume result in dry eye. All ages may be suffered from Dry eye syndrome can be seen secondary to another eye diseases or systemic disease. This review will summarize the current knowledge about dry eye and therapeutic interventions being used to treat Dry eye syndrome.

Keywords: Dry eye syndrome; Aging; Sjögrens syndrome

DERLEME MAKALE

KURU GÖZ SENDROMU: YAŞLANMA İLE ARTAN BİR PROBLEM

Öz

Kuru göz sendromu yaşlı popülasyonda sık görülen ve yaşam kalitesinde azalma ile sonuçlanan multifaktöryel bir hastalıktır. Kuru göz sendromu azalmış gözyaşı üretimi ve/veya gözyaşı film tabakasının kararsızlığı nedeni ile gelişen gözyaşı film tabakasının bir hastalığıdır. Göz kapaklarında gevşeklik, meibomian bez hastalığı ve bez orifislerinde metaplazi, gözyaşı haciminde azalma gibi yaşa bağlı değişimler kuru göz ile sonuçlanmaktadır. Kuru göz sendromu tüm yaşları etkileyebilmekte ve göz veya sistemik hastalıklara sekonder ortaya çıkabilmektedir. Bu derlemenin amacı Kuru göz sendromu ile ilgili güncel bilginin ve günümüz tedavi yöntemlerinin özetlenmesidir.

Anahtar sözcükler: Kuru göz sendromu; Yaşlanma; Sjögren sendromu

INTRODUCTION

Dry eye syndrome (DES) is a multifactorial and prevalent ocular disease in elderly population that results in decrease quality of life. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface.(1) DES is defined as a disease of tear film layer due to reduced tear production and/or tear film instability. All ages may be suffered from DES can be seen secondary to another eye diseases or systemic disease. Tear production is controlled by the LFU consisting of the ocular surface (conjunctiva, cornea, accessory lacrimal glands, and meibomian glands), the main lacrimal gland and the interconnecting innervation. (2) Any of these structures may be affected in DES.

Epidemiology

The Tear Film and Ocular Surface Society (TFOS) epidemiology subcommittee reviewed the prevalence, incidence, risk factors, natural history, morbidity and questionnaires reported in epidemiological studies of DES.(3) In 2007 Dry Eye Workshop (DEWS) group reported the prevalence of DES ranged from %5-30 in individuals over the age of 50.(4) Race is an important factor in the prevalence estimates of abnormal tear function. DES's prevalence especially meibomian gland disease (MGD) appears to be higher in Asian than in Caucasian populations, increases with age, and women having a higher prevalence of dry eye than men.(5, 6) The Beaver Dam Eye Study established in a Caucasian population aged 48-91 that 13.3% (95% CI 12.0 -14.7%) of individuals developed symptomatic DES over 5 years and 21.6% (95% CI 19.9-23.3%) over 10 years.(7) Incidence was higher in women (25%) than men (17.3%) over the 10-year period after adjusting for age. Age was a risk factor for increased incidence, with an odds ratio of 1.2x (1.1-1.3) for each 10-year increment.(7)

The Singapore Malay Study and the Spanish Salnes Eye Study showed a higher rate of MGD in men.(8, 9) Interestingly DES is the relatively high prevalence rates reported in younger subjects and

in school children, which support the potential risk factors such as digital device use. The Women's Health Study, a study in which 25 665 postmenopausal women provided that women who use HRT, especially estrogen alone, are at increased risk of dry eye syndrome.(10)

Pathophysiology

Dysfunction of LFU results in bad quality and poor maintained tear film that causes ocular irritation symptoms and damage to the ocular surface. (11,12) The tear film is highly stabil and the stabil preocular tear film is important for cornea. In response to hyperosmolarity and surface cooling occurring in MGD-related DES, where the lacrimal gland is healthy, DES with a "wet dry eye". (13) In TFOS-DEWS II report, tear film osmolarity is a central factor in the pathogenesis of aqueous deficiency and evaporative dry eye. (14) The risk factors for DES can be classified as high, moderate and low level of evidence. High level evidence risk factors including; age, female sex, postmenopausal estrogen therapy, antihistamines, collagen vascular disease, corneal refractive surgery, irradiation, hematopoietic stem cell transplantation, vitamin A deficiency, hepatitis C and androgen insufficiency, moderate level evidence risk factors including; medications such as tricyclic antidepressants, selective serotonin reuptake inhibitors, diuretics, beta-blockers, diabetes mellitus, HIV/HTLV1 infection, systemic chemotherapy, cataract surgery with a large incision, keratoplasty, isotretinoin, low air humidity, sarcoidosis, ovarian dysfunction and low level evidence risk factors are smoking, hispanic ethnicity, anticholinergic drugs such as anxiolytics, antipsychotics, topical anti-glaucomatous medications, alcohol, menopause, botulinum toxin injection, acne, gout, oral contraceptives, pregnancy. (15-18)

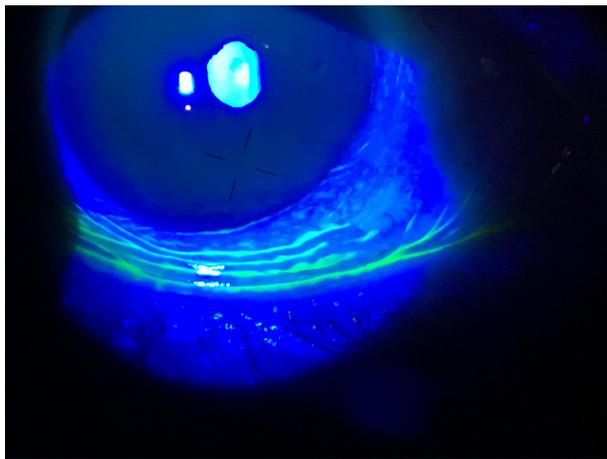
Symptoms of DES

Visual symptoms due to tear film instability and breakup, ocular discomfort, reduced lubrication, and neuropathic pain can be seen with DES. Slit



lamp examination may reveal duct dilatation and gland loss of meibomian glands, punctate epithelial keratopathy, filamentary keratitis, superior limbic keratoconjunctivitis, lid parallel conjunctival folds (LIPCOF) (Figure 1), and the lid margins changes.

Figure 1. The redundant conjunctival folds are located over the free edge of the lower eyelid and stained with fluorescein dye and cobalt light.



Classification of DES

Visual symptoms due to tear film instability and breakup, ocular discomfort, reduced lubrication, and neuropathic pain can be seen with DES. Slit

I. Aqueous-deficient dry eye (ADDE)

ADDE is included Sjögren syndrome dry eye (SSDE) and non-Sjögren syndrome dry eye (NSDE).

1. Sjögren Syndrome and Sjögren Syndrome dry eye

Sjögren syndrome (SS) is a chronic autoimmune disorder characterized by immune cell infiltration of exocrine glands and systemic complications due to autoantibody production, immune complex deposition and lymphocytic infiltration of many organ. (19, 20)

Sjögren syndrome occurs predominantly in women, with a female/male ratio of 9:1,

and it may lead to a very severe form of DES.(20-23) The lacrimal and salivary ducts are primary targets. Infiltration by T and B lymphocytes, dendritic cells, macrophages and other mononuclear cells, leading to tissue dysfunction or destruction. The loss of aqueous tear flow in Sjögren syndrome is a result of inflammatory cell infiltration of the lacrimal glands which leads to acinar and duct destruction. (19)

2. Non-Sjögren Syndrome dry eye:

- a. Age-related NSDE
- b. Congenital alacrima
- c. Familial dysautonomia
- d. Lacrimal gland infiltration (lymphoma, sarcoidosis, hemochromatosis, and amyloidosis)
- e. Viral infections (retroviruses, Epstein-Barr virus, human T-cell lymphotropic virus type 1, and human immunodeficiency virus (HIV), Hepatitis C virüs (HCV)
- f. Hematopoietic stem cell transplants with or without the development of graft-versus-host disease: infiltration and fibrosis of the lacrimal glands and conjunctiva as a result of T-cell interaction with fibroblasts (20-30).

II. Evaporative dry eye (EDE)

1. Lid-related evaporative dry eye (intrinsic EDE):

- a. Age-related meibomian gland changes: meibomian gland drop out score is increasing after 40 years of age.
- b. The influence of sex hormones on meibomian gland function: Sjögren syndrome, antiandrogen treatment and complete androgen insensitivity syndrome, is associated with MGD, altered meibum lipid profiles and evidence of decreased tear film stability.
- c. Meibomian gland dysfunction: This is the

most common etiology of EDE. It must be distinguished from other meibomian gland diseases.

i. High meibum delivery state meibomian seborrhea: It is uncommon. This is associated with seborrhoeic dermatitis and rosacea. Acne Rosacea is a disease of eye and skin and is usually seen with fairly skinned individuals. Rosacea may be difficult to diagnose and differential diagnosis. Visualize telangiectasia or facial flushing are the skin findings and in eyes chronic recurrent blepharokeratoconjunctivitis, punctate erosions, peripheral keratitis, MGD, or recurrent chalazia are common findings. Children with ocular rosacea often present with corneal involvement and asymmetry of ocular disease, and the potential for sight-threatening visual impairment should be considered.

ii. Low meibum delivery states-obstructive meibomian gland dysfunction: This is obstructive MGD and the most common type. TFOS Workshop on MGD, as follows and further details may be found in that report: "meibomian gland dysfunction (MGD) is a chronic, diffuse abnormality of the meibomian glands, commonly characterized by terminal duct obstruction and/or qualitative/quantitative changes in the glandular secretion. This may result in alteration of the tear film, symptoms of eye irritation, clinically apparent inflammation, and ocular surface disease". MGD can be seen primary or secondary also cicatricial or noncicatricial.

2. Disorders of lid aperture, congruity and dynamics
 - a. Nocturnal lagophthalmos
 - b. Incomplete lid closure or lid deformity

- c. An increase in palpebral fissure width or globe prominence exposes the tear film to greater evaporation

- d. Parkinson's disease and in progressive ophthalmoplegia

3. Ocular surface-related evaporative dry eye

- a. Allergic eye disease

- b. Vitamin A deficiency

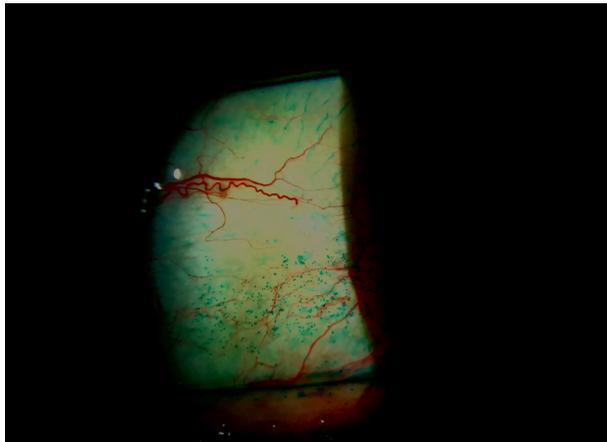
- c. Ocular surface disease due to topical agents (31-40).

Diagnosis of DES

Understanding characteristics of the causative factors, such as environments (air travel, sitting near an air conditioner vent, low humidity), prolonged visual efforts (reading, computer use), or symptomatic treatment with the use of artificial tears is helpful in diagnosing DES. A detailed review system examination must be done for any patient who has significant dry eye. Rheumatological system examination is important. For patients who are suspected of having Sjögrens syndrome, a serological examination (Sjögrens syndrome A antibody (SSA or anti-Ro), anti-Sjögren syndrome B antibody (SSB or anti-La), rheumatoid factor, and antinuclear antibody) should be ordered. Patients who might have thyroid eye disease should be tested for antithyroid peroxidase antibody and antithyroglobulin antibody. For standardization in clinical research, symptoms are typically taken through the use of questionnaire instruments that are most often self-administered by the patient or research subject without input from the clinician or researcher. Tear film breakup time, Schirmer test, ocular surface staining, tear film osmolarity, impression cytology, meibography, and in vivo confocal microscopy are the current diagnostic tests. (Figure 2).



Figure 2. Lissamine green staining of the ocular surface in a patient with dry eye syndrome secondary to Sjögrens Syndrome.



Treatment of DES

Staged Management And Treatment Recommendations For DES

First step of the management include education about the disease, modification of local environmental factors, dietary modifications (including oral essential fatty acid

supplementation), identification and potential modification/elimination of offending systemic and topical medications. As treatment, ocular lubricants of various types (if MGD is present, then consider lipid-containing supplements), and lid hygiene and warm compresses comprise the treatment of mild DES. If the above options are inadequate, the second step of the treatment of DES include non-preserved ocular lubricants to minimize preservative-induced toxicity, tea tree oil treatment for Demodex (if present) and inflammation, punctal occlusion and/or moisture chamber spectacles/goggles to tear conservation, and overnight treatments (such as ointment or moisture chamber devices). For inflammatory DES, such as Sjögrens Syndrome, the gold standart treatment options are anti-inflammatory agents including topical corticosteroid for limited-duration non-glucocorticoid immunomodulatory eye drops (such as cyclosporine and LFA-1 antagonist). For the severe DES, to protect the ocular surface, autologous/allogeneic serum eye drops, therapeutic contact lenses or some surgical procedures (tarsorrhaphy, amniotic membrane grafts) can be considered (41, 42).

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