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The impact of the dry eye syndrome on the quality of life in elderly patients-minireview

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Abstract

Dry eye syndrome (DES) is a multifactorial surface ocular disease often seen in elderly patients with a high impact on the quality of life. There are a lot of risk factors related to DES such as older age, female gender, postmenopausal estrogen therapy, lack of omega 3-fatty acid in the diet, medication (antihistamines), connective tissue illnesses, radiation therapy, corneal refractive surgery, cataract surgery, hematopoietic stem cell transplantation, vitamin A deficiency, hepatitis C, androgen deficiency, cicatricial pemphigoid. The diagnosis of DES implies classical and emerging examinations. There are several types of DES. It is very important to establish the type because the treatment is according to the cause. The treatment is based on artificial tears, topical steroids, Cyclosporine A, lubricants, punctual plugs and Fatty acids Omega 3.

Key words: *dry eye syndrome, risk factors, type, dry eye treatment, quality of life,*

Introduction

Dry eye syndrome (DES) is a multifactorial surface ocular disease often seen in elderly patients. Lately it has become very common all over the world with a high impact on the quality of life. Some authors described the syndrome as a public health problem (1).The Tear Film and Ocular Surface Society (TFOS) Dry Eye Workshop (DEWS) II changed the old definition of DES introducing the term of loss of „homeostasis"(2) in the mechanism of appearance. Therefore, nowadays the definition of DES implies the instability and hyperosmolarity of the tear film, ocular surface damage and neurosensory abnormalities associated with the loss of „homeostasis"(3). In practice, DES is also called keratoconjunctivitis sicca or dysfunctional tear syndrome.

Epidemiology

It is estimated that all over the world there are 25-30 million patients with DES (4), with a frequency of 5 % to 34% (5).Some studies performed globally showed even a frequency of 50%.(2). In United States the frequency of the illness is almost 17% (6) but in Korea, Taiwan and Japan is 30% (7,8,9,10). In women, the prevalence increased with the onset of menopausal period (5). In general, the prevalence raised with the age being 18.6% in patients older than 75 years (3,11) and women are 50% more likely to develop DES comparative with man (11). Almost 20% of patients with rheumatoid polyarthritis developed DES (12,13).

Risk Factors

There are a lot of risk factors related to DES. The American Academy of Ophthalmology revealed as mostly consistent risk factors the following: the older age, female gender, postmenopausal estrogen therapy, lack of omega 3-fatty acid in the diet, medication (antihistamines), connective tissue illnesses, radiation therapy, corneal refractive surgery, cataract surgery, hematopoietic stem cell transplantation, vitamin A deficiency, hepatitis C, androgen deficiency, cicatricial pemphigoid (6). Mark et al suggested as risk factors: the Asian ethnicity, medication (beta blockers, diuretics, tricyclic antidepressants, Parkinson medication), diabetes mellitus, human immunodeficiency virus, systemic chemotherapy, sarcoidosis, ovarian dysfunction (14). Other studies found that oral cavity cancer, chronic fatigue syndrome,

Helicobacter Pylori were associated with DES (15,16). Particularly in elderly patients the autoimmune rheumatic disease represent a risk factor for DES, such as: Sjogren syndrome, rheumatoid polyarthritis, systemic lupus erythematous, systemic sclerosis, dermatomyositis and polymyositis (17,14). A study from Taiwan revealed that high temperature, carbon monoxide and nitrogen dioxide were strongly associated with DES (18,19). On the other hand the use of glaucoma medication, asthma, fibromyalgia and presbyopia were considered by some studies risk factors in the appearance of DES (20,21,22). Some authors suggest that staring for a long time at computer screens induce a decreased blink rate with the development of DES (14).

Pathophysiology

The anatomical structure of the tear film consists in three layers. The inner mucin layer is composed of gel and soluble mucins produced by specialized conjunctival goblet cells that adhere the tear film to epithelial cells. It facilitates the aqueous layer to extent uniformly over cornea (23).The middle layer is the aqueous layer secreted by lacrimal and accessory glands to offer eye hydration and lubrication and helps in the removal of foreign bodies (24). The outer lipid layer produced by Meibomian and Zeiss glands to reduce tear evaporation (25,26,27). Cher et al (28) proposed a two-tiered model in which the mucin and aqueous interact in a muco-aqueous layer. Georgiev et al (29) showed that lipids produced from the Meibomian glands cannot inhibit the rate of evaporation. Moreover there are some studies that revealed other functions of the outer lipid layer such as: spreading the tears between blinking, providing a low surface tension for tear film and viscoelasticity properties (30,31,32). Tear production is under the control of sympathetic and parasympathetic stimulation of the lacrimal glands, which in turn is controlled by a neural reflex arc coming from the ocular surface (33). Cox et al (34) consider that the innervation of the Meibomian glands and goblet cells is also under parasympathetic control. The conjunctival epithelium includes immune cells such as natural killer, dendritic cells, macrophages, CD4+ and CD8+ T cells antimicrobial defense but also in DES. All these layers associated with the innervation provide tear film stability. Therefore, every factor which can influence the stability may induce DES as a consequence of disruption of the lacrimal functional unit composed by all the structures implicated in the ocular surface. During last years, the pathophysiology of DES has experienced a real change. Several studies showed that inflammation is another major factor implicated in DES mediated by the lymphocytes T within the conjunctiva (35,36,37,38).

The risk factors may induce tear hyperosmolarity which is the trigger for the pro-inflammatory effect on the ocular surface epithelium, by activating stress signaling pathways, increase the inflammatory mediators (cytokines, chemokines and matrix metalloproteinases) and the CD4+ T cells. The result will be the barrier disruption, neural sensitization, glandular secretion disfunction and apoptosis, including goblet cells. As a consequence, will appear tear instability and surface desiccation (39). All these inflammatory mediators upregulate each other, increasing the inflammatory cascade. There are studies which revealed increased level of inflammatory mediators in other ocular surface disease (atopic and vernal keratoconjunctivitis, keratoconus, recurrent corneal erosions, ocular burns) (40,41,42,43,44,45).

Clinical features

Conceding the severity of DES, the patient may complain of mild or episodic discomfort to severe and constant symptoms associated with visual symptoms such as: burning sensation, itchy eyes, aching sensations, heavy eyes, fatigued eyes, sore eyes, dryness sensation, red eyes, photophobia and blurred vision. Another common symptom is something called a foreign body sensation — the feeling that grit or some other object or material is "in" the eye. Surprisingly, the patients can have watery eyes because dryness on the eye's surface sometimes will over-stimulate production of the watery component of your tears as a protective mechanism. But this "reflex tearing" does not stay on the eye long enough to correct the underlying dry eye condition. In addition to these symptoms, dry eyes can cause inflammation and (sometimes permanent) damage to the surface of the eye.

Slit lamp examination will reveal increased thickness of the free palpebral margin and the obstruction of Meibomian glands orifices with solid granulose material. The inflammation of the Meibomian glands (meibomitis) and of the free margin (blepharitis) may be part of the clinical aspect (5). In advanced stages may appear

conjunctival and corneal scars, phylamentous keratitis, recurrent corneal erosions, corneal ulceration and even corneal perforation.

Dry eye examination

Clinical features and the impact on life quality require a correct examination of the dry eye. Classical and emerging examinations are able to confirm a positive diagnosis of dry eye.

Classical examination

[1]Epithelial staining

Fluoresceine, Bengal Rose or Green Lissamine can be used as a staining dye in order to establish ocular surface anomalies, tear film quality or dry eye severity (46). Fluorescein is the most frequent dye used in the evaluation of dry eye. It is useful to identify corneal epithelial defects at which level cornea will stain. The staining can show different aspects characteristic of dry eye especially in elderly patients. Bengal Rose is best to be used as an adjunct dye because of its lack of sensitivity and specificity (47). Machado et al (48) showed that Bengal Rose is toxic for the cornea that is why is seldom used and that Green Lissamine is not toxic for the cornea and has a better tolerability.

[2] Schirmer test

It is the most widely used test for evaluating dry eye. Even though the test is irritative, invasive and in some cases unreliable. This may induce a high risk of underdiagnosis of dry eye (49,50). The test gives information about tear production. There are two tests, Schirmer I (with or without anesthesia) and Schirmer II which only measures reflex tears comparative with the first one which measures total tear secretion. Normal test values vary from 8 mm to 33 mm but is considered normal value greater than 10mm (51,52). Lin et al (52) revealed that much more reliable results seems to offer the Schirmer test without anesthesia.

[3] Fluorescein clearance test

The test offers information about tear secretion and drainage. It combines Schirmer test with the use of proparacaine and 5μL of Fluoress® (0.25% fluorescein with 0.4% benoxinate hydrochloride). A normal value is considered to be equal or more than 3 mm at the first 10-minute interval. The disadvantages of the test consist in the fact that is time-consuming, irritating, and not reproducible (53).

d. Tear break-up time

The test measures stability of the tear film. It is performed at slit lamp, by instillation of fluorescein in the conjunctival inferior fornix and asking the patient not to blink. The positive diagnosis of dry eye is confirmed if a dry area appears before 10 seconds (54). Vanley et al (54) demonstrated that it is a quick test, is unexpansive but is not reproducible and it is inaccurate.

Emerging examinations

- Reflective meniscometry

Is a noninvasive technique giving quantitative information about tear meniscus curvature (19). The exam needs a portable slit-lamp mounted digital meniscometer.Yokoi et al (55) showed that the results are similar to those obtained by ocular coherence tomography (OCT).

b. Ocular coherence tomography

Is a noninvasive technique to measure the meniscus height. Savini et al (56) showed that tear meniscus height was found to be significantly lower in dry eye patients compared with controls using ocular coherence tomography (OCT.) Messner et al (57) revealed that a major advantage of OCT is the capacity to measure tear film thickness. One study found highly reproducible measurements using ultrahigh resolution OCT (57). Werkmeister et al (57) revealed that the normal value of central tear film thickness was 4.79±0.88μm.

c. Tear normalization test

Is a simple, inexpensive and noninvasive test. It consists in the examination of visual acuity before and after the instillation of no viscous artificial tears drops based on the fact that this kind of drops improve temporary the visual acuity in DES (58).

[4] Biomarkers

Analyzing tear biomarkers in order to establish the diagnosis of dry eye gained a lot of popularity lately. High level of inflammatory biomarkers, especially matrix metalloproteinase 9 suggest the presence of DES (59,60). Furthermore, allergy biomarkers such as lactoferrin and immunoglobulin E in the tear film will be very useful in the diagnosis of dry eye. Lee et al (61) showed high level of cytokine (interleukin-17, interleukin-6, and tumor necrosis factor-alpha) in patients with dry eye and Sjogren syndrome compared with patients with dry eye without Sjogren syndrome and controls.

[5] Tear osmolarity

Is a technique used to quantify osmolarity and be useful in the diagnosis of dry eye. Versura et al (62) demonstrated that patients with dry eye have a high level of tear osmolarity as a result of the ocular surface damage and inflammation. In dry eyes the osmolarity value is higher than 308 mOsm/L .

[6] Ocular Surface Thermographer

It is a device in order to measure the tear film temperature based on the fact that diurnal changes in corneal temperature may indicate ocular surface abnormality or corneal pathology.[63]

Types of Dry eye

DES can be caused by deficient tear production or by increased evaporative loss. Both groups can be divided into several types: lipid anomaly dry eye, allergic and toxic dry eye, cicatricial condition, autoimmune condition, lid surfacing anomalies and marginal dry eye.

Lipid anomaly dry eye

Lipid anomaly dry eye is an evaporative DES and appears as a result of Meibomian gland disfunction (64). Is the most frequent type.

Aqueous Tear deficiency

Aqueous Tear deficiency is the result of multiple causes linked with autoimmune diseases.: Sjogren syndrome and cicatricial pemphigoid. Sjogren syndrome is an autoimmune disease associated with lacrimal and salivary gland lymphocytic infiltration with T cell, B cell, dendritic and natural killer cells (65). In elderly patients we often diagnose this syndrome. Cicatricial pemphigoid is another autoimmune disease which is associated with dry eye, loss of vision and conjunctival vascularization. Dart et al (66) and McCluskey et al (67) demonstrated that in this type of DSE the treatment has to control the conjunctival inflammation combined with general administration of steroids or methotrexate, infliximab or intravenous immunoglobulin therapy.

Allergic and toxic dry eye

Is the form of DES related with allergy or toxin. The main cause is allergic conjunctivitis that is why this form may appear also in pediatric patients (68,69).

Cicatricial condition dry eye

This form of DES has two common causal entities: xerophthalmia and trachoma. Both diseases appear in urban areas where the patients have poor hygiene, low level of life or improper administration of A vitamin (70,71).

Blinking anomalies

Is caused by reduced or incomplete blinking. Is often present at persons who stay in front of the computer or watching TV for several hours, especially in elderly patients. Ousler et al (72) showed that in dry eye patients rate of blinking was shorter comparative with the normal ones.

Marginal dry eye

Appears in patients who have a normal tear function only in some condition. So, in improper conditions (air conditioning, contact lenses use, alcohol ingestion) the lacrimal film may be damaged (73).

Dry eye treatment

The purpose of the treatment is to improve the comfort of the patient and quality of life and to regain the ocular surface homeostasis (74). Several treatments were proposed during last years according the type of DSE, clinical features and causal mechanism. Additionally, it is mandatory to treat Meibomian gland disfunction and the systemic causal illness.

Artificial tears

Artificial tears were by far the most used drugs for several years, providing tear stability, less ocular stress and contrast sensitivity (19). An important progress in the evolution of artificial tears was the elimination of Benzalkonium chloride (BAK) the common preservative used in eye drops and which was responsible for the ocular surface damage. There are studies which showed that osmolarity balanced artificial tears (carboxymethylcellulose sodium) were the preferred treatment in patients with moderate to severe dry eye and liposomal spray for patients with lipid layer deficiency (75,76). Single-dose application units is preferred in case of DES to prevent the possible contamination. This is very important in elderly people because many of them have glaucoma with antiglaucomatous drugs as treatment.

Autologous serum eye drops

Higuchi et al (77) and Geerling et al (78) revealed the efficiency of autologous serum eye drops in the treatment of dry eye. It is created from human serum which contains cytokines, fibronectin, epidermal growth factor, vitamin A, substances whose role in maintaining the integrity of corneal and conjunctival epithelium is very well known (79).

Cyclosporine A

The effect of Cyclosporine A is to restore the ocular surface by stopping the T cell activation pathway and decreasing the cytokine level and increasing the Goblet cells number in corneal epithelium (80). You-Kai et al (19) and Straub et al (81) showed a real improvement after twice daily administration.

Punctum plug

The obstruction of the lacrimal punctum with plugs is another way to prolog the lubricants effects and conserve natural tear (82).

Anti-inflammatory agents (steroids)

De Paiva et al (83) demonstrated that the steroids and Doxycycline suppress the activity of metalloproteins and inflammatory cytokines from the ocular surface. Follow-up of the patients is very important taking into consideration the possible adverse effect of topical steroids such as glaucoma and cataract formation (84).

Fatty acids Omega 3

Nowadays, fatty acids Omega 3 are considered to be a potential progress in the treatment of DES. Liu et al (85) showed that they act directly on human Meibomian gland epithelial cells in order to improve the quality and quantity of intracellular lipids, by this inducing the tear film stability and influencing the quality life of this patients.

Conclusion

Dry eye disease is a frequent entity, especially present in elderly people. The early diagnosis and management is mandatory in order to improve the quality of life at this patients.

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