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Investigations of the Dry Eye: An Overview

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ABSTRACT

Dry eye is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. Dry eye disease is caused by many factors that result in inflammation of the eye and the tear-producing glands, a disorder of the tear film due to tear deficiency, or excessive tear evaporation, which causes damage to the interpalpebral ocular surface. The database was collected from PubMed, PubMed Central (PMC), Cochrane library, Google scholar, and research gate. Recently, data from many studies have accumulated which show that dry eye is a lifestyle disease, it is becoming possible to prevent the onset by intervening with the daily habits, diet, exercise, and sleep. Future research will be needed to link clinical findings to the molecular biological findings in the tear film.

KEY WORDS: DRY EYE, SCHIRMER'S TEST, TEAR FILM, VISUAL DISCOMFORT, KERATOCONJUNCTIVITIS SICCA (KCS).

INTRODUCTION

Dry eye is a tear film disorder that occurs due to tear deficiency or excessive tear evaporation. The effect of dry eye can cause damage to the interpalpebral ocular surface, and it is also associated with a variety of symptoms reflecting visual discomfort.DES is also called kerato conjunctivitis sicca (KCS), keratitis sicca, sicca syndrome, xerophthalmia, dry eye disease (DED), ocular surface disease (OSD), or dysfunctional tear syndrome (DTS), or simply dry eyes. Dry eye patients experience difficulties in day-to-day life routine activities (Lemp 1995); thus, they compromise their quality of life. Kerato conjunctivitis sicca is a Latin word. Its literal translation is "dryness of the cornea and conjunctiva." It may be helpful to know that "sicca" is part of the English word "desiccate."

Dry eye disease (DED) is a chronic ocular pathology, and it is a major global health problem that manifests too many symptoms such as burning, photophobia, tearing, and grittiness. DES is connected with a reduced ability to do various activities that need visual concentration, such as reading, driving, and computer-related work.

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Around 25% of patients with this syndrome consult eye care professionals.The dry eye syndrome in which the eyes do not produce enough tears is also known as "Sjogren's syndrome. (Miljanović et al 2007 and Stern,et al 2004).

A report by van Setten et al. has suggested a link between seasonal environmental conditions and DED. In that study, almost half of responders stated that seasonal weather conditions significantly impacted their symptoms, notably wind and sunshine. In contrast, the summer and the winter were most commonly associated with dry eye complaints (Prydal, J.I.,et al 1992). Dry eye disease is characterized by instability of the tear film due to insufficient tear production or poor quality of tear film, which results in increased evaporation of the tears. Dry eye, therefore, can mainly be divided into two groups, namely,

Cause Of Dry Eye Syndrome: Insufficient tears cause damage to the interpalpebral ocular surface and are associated with symptoms of discomfort. Dry eye can be a side effect of some medication, including antihistamines, nasal decongestion, certain blood pressure medicines, Parkinson's drugs, birth control pills, anti-depressants, skin disease on or around the eyelids dry eye.

1) Aqueous production deficient dry eye disease
2) Evaporative dry eye disease

A dry eye can make it more challenging to perform some activities, such as using a computer or reading for an extended period. In addition, it can decrease tolerance for dry environments, such as the air inside an airplane.In this article, we address the management of the patients once the dry eye diagnosis has been made. Based on the existing literature and a consensus among the members of our study group, the opportunity of a dynamic therapeutic strategy according to the clinical results obtained during the disease is suggested. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface. The prevalence of dry eyes reported in North India is higher, ranging from 18.4% to 54.3%, with the majority of the patient falling within the age groups of 21-40 years (Phadatare, et al 2015 and Kallarackal ,et al 2002). The overall incidence ranges from 5% to 35% due to environmental pollution, climate conditions, life expectancy, lifestyles, and increased opioid consumption. This article aims to focus on the treatment necessary to improve the ocular surface conditions and long-term control of the disease.

The disease of the glands in the eyelids, such as meibomian gland dysfunction, can cause dry eye. The International Dry Eye Workshop (2007) defined dry eye as a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It also causes increasedosmolarity of the tear film and inflammation of the ocular surface . Dysfunction of the lacrimal functional unit causes changes in the composition of the tear fluid and tear film stability, (Niederkorn, J.Y., 2007. and Johnson, M.E. and Murphy, P.J., 2004) leading to inflammation of the ocular surface. The eye does not produce adequate tears as the anti-inflammatory component of the eye is lacking, and irritation of the eye is not controlled. This causes activation of.

Prevalence: The prevalence of Dry Eye Disease increases with age.Dry eye disease is a common ocular condition that affects a large proportion of the population, particularly those over 50. 5.6 Surveys indicated the prevalence of Dry Eye disease ranging from 5% to >30 percent in different age groups throughout nations and globe, depending on the individual's geographical location, climate, and lifestyle (Lemp, M.A., 2008 Schiffman, R.M.,et al 2000 and Giannaccare, Get al 2018) It.

Diagnosis: Many ocular surface diseases produce similar symptoms to those associated with dry eye, including foreign body sensation, mild itching, irritation, and soreness. Identifying characteristics of the causative factors, such as adverse environments (e.g., air travel, sitting near an air conditioner vent, low humidity), prolonged visual efforts (e.g., reading, watching TV or computer use), or ameliorating circumstances

Patient History: Symptoms: Presenting complaints: Irritation, tearing, burning, stinging, dry or foreign body sensation, mild itching, photophobia, blurry vision, contact lens intolerance, redness, mucous discharge, increased frequency of blinking, diurnal fluctuation, and symptoms inflammatory cells, including T-lymphocytes, by the immune system of the body. T-cells release cytokines, which cause inflammation of the ocular surface and glands, thereby resulting in abnormal tears and dry eye symptoms.[18,19] An increase in osmolarity of the aqueous layer is suggested as a global feature of DES and is known to trigger inflammation, damaging the ocular surface.

observed a significant gradualhike in the last ten years in the ageing population, refractive laser surgeries & more frequent use of contact lenses. However, exploring other reasons computers, smartphones, and tablets stand remarkably out. The prevalence of DED is influenced by geographic location, climatic conditions, and lifestyle of the people and ranges from 5% to 35% (Giannaccare, Get al 2018). (symptomaticrelief with the help of artificial tears) helps diagnose dry eye. Supporting clinical observations and tests are used to confirm the diagnosis. Most patients have multiple factors contributing to dry eye. Many conditions, such as neurotrophic keratitis after herpes simplex virus infection or LASIK induce decreased tear production and increased evaporative loss. that worsen later in the day. Duration of symptoms. Exacerbating conditions: e.g., wind, air travel, decreased humidity, prolonged visual efforts associated with reduced blink rate such as reading or watching TV.

Ocular history details the following:

- Topical medications used, their frequency, and their

effect on symptoms: e.g., frequent "eyewash," artificial tears, anti-histaminic, glaucoma medications, vasoconstrictors, corticosteroids
- Contact lens wear: type of CL, wearing schedule, and care
- Allergic blepharoconjunctivitis or other types of chronic allergic eye disease

Investigation Of Dry Eye

The physical examination includes: visual acuity measurement with correction, external eye examination, and slit-lamp biomicroscopy. The purpose is to:
- Document the signs of dry eye
- Assess the presence and severity of deficient aqueous tear production and increased evaporative loss
- Determine other causes of ocular irritation

Proptosis
- Eyelids: incomplete closure/malposition, incomplete or infrequent blink, erythema of the eyelid margins, abnormal deposits, or secretions, trichiasis, entropion, ectropion
- Adnexa: enlargement of the lacrimal glands

External Examination:
- Gait: as in rheumatoid arthritis
- Hands: joint deformities characteristic of rheumatoid arthritis
- Skin: e.g., scleroderma, florid acne, facial changes consistent with rosacea, Slit Lamp Examination
- Cranial nerve functions: e.g., trigeminal, and facial nerve

Slit-Lamp Examination:
- Eyelashes: trichiasis, distichiasis, deposits
- Anterior and posterior eyelid margins: abnormalities of meibomian glands (e.g., orifice metaplasia, reduced expressible meibum, atrophy), the character of meibomian gland secretions [e.g., turbid, thickened (tooth-paste sign), foamy, deficient], vascularization crossing the mucocutaneous junction, keratinization, scarring
- Puncta: position, patency, the position of plugs if present
- Tear film: height of the meniscus, debris, increased viscosity, mucus strands, and foam
- Conjunctiva: Inferior fornix and tarsal conjunctiva: e.g., mucous threads, gross scarring, stellate scar (in healed trachoma), erythema, papillary reaction, enlarged follicles, keratinization, fornix shortening, symblepharon (especially the medial symblepharon) Bulbar conjunctiva: e.g., punctate staining with rose Bengal, fluorescein, or Lissamine green dyes; follicles, Herbert's pit (healed trachoma), hyperaemia; localized drying; Bitot's spot, keratinization.
- Cornea: localized inter-palpebral drying, punctate epithelial erosions, superficial punctate staining with rose Bengal or fluorescein dyes, filamentary keratopathy, epithelial defects, mucous plaques, keratinization, pannus formation, localized Dellen, thinning, infiltrates, ulceration, scarring, neovascularization, evidence of cataract, corneal or keratorefractive surgery.

Diagnostic Test: For patients with mild irritation symptoms: a reduced tear break-up time (TBUT) may indicate an unstable tear film with normal aqueous tear production. There may be minimal or no dye staining of the ocular surface. For patients with moderate to severe symptoms: the diagnosis can be made by using one or more of the following tests:

- Tear break-up time (TBUT) test – to evaluate tear-film stability.
- Ocular surface dye staining(Fluorescein/rose Bengal/ Lissamine green) test: to evaluate ocular surface disease (KCS).
- Schirmer test: to evaluate aqueous tear production,these tests should be performed in this sequence because the Schirmer test can disrupt tear film stability and cause false-positive ocular-surface dye staining.

Device/Tool Used

1)Schirmer'sTest-

Itwas performed to evaluate basal and reflex tear secretion. In Schirmer's, I test a filter paper strip (35 x 5 mm) to measure the quantity of tear production in 5 minutes.

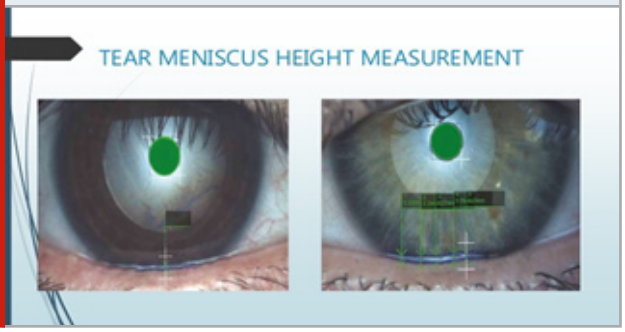
Figure 1: Schirmer Test

2) Ocular surface analyzer (OSA)-: is a more scientific device for analysingtear film that allows for quick detailed structural research of the tear composition and all the layers: lipid, aqueous, and mucin. OSA also helps identify the type of Dry Eye Disease and determine which layers can be treated with a specific treatment related to the kind of deficiency (Titiyal, J.S.,et al 2018) It is a non-invasive integrated system for analyzing the ocular surface using sophisticated software that gives a quick judgment of treatment mode. The following parameters can measure by using the ocular surface analyzer.

a) Interferometer- Thetechnique used studies surface reflection pattern and dynamics of the lipid layer. The instrument was focus on the patient's eye, and magnification was medium with 100% focus. Depending on the lipid layer's thickness and regularity, it may appear like marble appearance, amorphous structure, and mattewhite pattern.

Figure 1: The interferometry Procedure.

Figure 2: The arrow indicated tear meniscus height.



b) Tear meniscus height– To evaluate the size of the tear meniscus on the upper and lower lid. Focus on the lower lid of the patient's eye and increase or decrease focus till the tear meniscus becomes clear and visible and capture the picture. The tear meniscus height was marked, and the value was recorded.

Figure 3: Patterned break-up time.

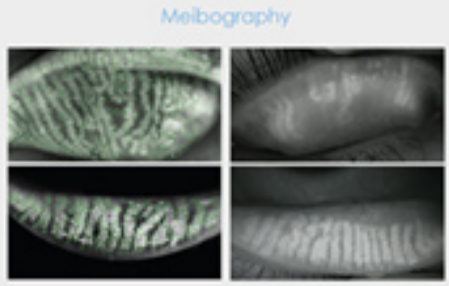
c) Non-Invasive break-up time– The stability of mucin layer and whole tear film measured by using non-invasive break-up time using grids projected onto the cornea.

c) Meibography– This is the clear picture analysis of the meibomian gland. Here we go for visualization of glands through transillumination of the eyelid with infrared light.

Ocular Surface Dye Staining: Fluorescein, rose Bengal, or Lissamine Green dyes are used to assess the extent of ocular surface damage. Fluorescein dye test: It stains corneal and conjunctival epithelial areas where there is sufficient disruption of intercellular junctions to allow the dye to permeate into the tissue.61 Saline-moistened fluorescein strips are used to stain the tear film. After instilling the dye, the ocular surface is examined through a Slit lamp microscope using a cobalt blue filter. Staining may become more apparent after 1 to 2 minutes. Mild fluorescein staining can be observed in normal eyes and may be more prominent in the morning. Exposure-zone punctate or blotchy fluorescein staining is observed in dry eyes, and staining is more easily visualized on the cornea than on the conjunctiva.

Rose Bengal staining: It may be performed using a salinemoistened strip. The saline drop used to moisten the strip should remain in contact with the strip for at least a minute to achieve an adequate concentration of rose Bengal to stain the ocular surface. Patients should be informed that the drop might irritate the eye. Rose Bengal staining is more intense on the conjunctiva than the cornea. The dye stains ocular surface cells that lack a mucous coating and debris in the tear film, (Baudouin, C., et al 2013) the staining may be easier to observe with a red-free filter. Lissamine green dye has a staining profile similar to that of rose Bengal, (Sarkar, S., et al 2007 and Cagini, C., et al 2017) and may cause less ocular irritation (Cagini, C.,et al 2017).

Figure 4: Meibography



Treatment: There are on the market variants of artificial tear buffered electrolyte formulations, surfactants, preservatives, which increase the patient's symptoms due to alleged cytotoxicity. As a result, using nutraceutical, preservative-free vitamins to cure conjunctival dryness is a safer option.

Figure 5: Intense regulated pulse light (IRPL):-

Intense Regulated Pulse Light (IRPL): Intense regulated pulse light therapy is well in trend new treatment particularly effective in treating meibomian gland dysfunction (MGD), which is the most common cause of our day-to-day ocular irritation saying it as dry eye (Figure-1). IRPL uses regulated pulse light to treat the meibomian gland dysfunction. IRPL is one of the therapies for chronic dry eye that can potentially regenerate the Meibomian gland structure. This treatment is effective as well as efficient in treating dry eyes. It is an easy-to-use and quick treatment device for Meibomian gland dysfunction. Patients are mostly satisfied after two sittings of this therapy. This device is portable and easy to handle.

IRPL targets all the following aspects of Meibomian gland dysfunction-

- Improves functioning of the Meibomian gland.
- It helps in unclogging Meibomian glands.
- Improves tear film quality and stability by restoring the tear film's lipid (oil) layer.

Intense pulse light (IPL) is a similar treatment as IRPL for dry eyes. Low pulse light uses. It is not a portable device and has drained before shifting. The intense pulse light (IPL) effect is less than low regulated pulsed light (IRPL). In this therapy, the pulse light energy gradually decreases, and the effect also gets reduced.

Epithelial Protection: Another pillar of DED therapy is epithelium protection, necessary to interrupt the vicious circle sustained by pro-inflammatory cytokines produced during epithelial damage. The protective physical and biological characteristics of some tears have been identified as a potential treatment to protect epithelial damage (Ohsumi, Y., 2014 and Coassin, M., et al 2005) Trehalose has been indicated as a possible therapeutic tool (Saettone, M.F., 1994 and Geerling, G. and Hartwig, D., 2002), able to interfere with the cellular metabolic dysfunction associated with DED and control inflammation. This naturally occurring sugar is a non-reducing disaccharide, found in high concentrations in many organisms, and is a key element involved in anhydrobiosis (ability to survive almost complete dehydration).

Lid Management: For complete ocular surface treatment, other aspects must be considered, most notably, the meibomian gland dysfunction (MGD)/blepharitis and nerve impairment. Several measures are necessary to control MGD/blepharitis, including lid hygiene, using warm/hot compresses and medicated wipes, topical or systemic antibiotic treatments, anti-inflammatory agents, and less viscous tear substitutes for increasing tear clearance. MGD and blepharitis are the consequence of MG disease: this can be isolated but is more frequently associated with skin alterations, indicating a general sebaceous dysfunction.

Nerve Treatment: The last pillar of DED is neurological impairment, responsible for the frequent lack of correlation between signs and symptoms in patients. There is still a lack of treatments able to address nerve structures, although human recombinant nerve growth factor (NGF) is now on the market for neurotrophic keratitis and is under investigation in the USA and Europe for DED treatment.

Other Management: The treatments of keratoconjunctivitis are varied. The treatment goals are to relieve the symptoms of dry eye, improve the patient's comfort, return the ocular surface, and tear film to the normal state, and, whenever possible, prevent corneal damage. Treatment may range from education, environmental or dietary modifications, artificial tear punctal plugs, and topical and systemic anti-inflammatory medications to surgery.

Artificial Tears: Artificial tears are lubricant eye drops used to treat the dryness and irritation associated with deficient tear production in KCS. The lubricant tears are available as OTC products and usually are the first line of treatment. Mild disease conditions require the application of lubricant drops four times a day, while severe cases need greater frequency (10–12 times a day) of administration. These OTC products mainly vary in their ingredients, indications, and availability of preservatives. Ingredients such as cellulose and polyvinyl derivatives, chondroitin sulphate, and sodium hyaluronate determine their viscosity, retention time, and adhesion to the ocular surface.

Polyunsaturated Fatty Acid Derivative Flaxseeds: Artificial tear buffer formulations of electrolytes, surfactants, preservatives are available on the market, that also enhance patient complaints because of known cytotoxicity. Nutraceutical, non-conservative supplements are therefore safer means of treating conjunctival dryness. Omega-3 fatty acids and their derivatives: flax-rich alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and chemical formulation (DHA), [18:3(n-3), are important acids for increasing a tear replacement in dry eyes.

Autologous Serum Eye Drops: Autologous serum eye drops contain different essential tear components such as hepatocyte growth, epidermal growth, vitamin A, and fibronectin necessary for maintaining a healthy ocular surface (Bron, A.J. and Mengher, L.S., 1989)

Nonsteroidal Anti-Inflammatory Drugs and Antibiotics: NSAID drops containing drugs such as diclofenac sodium and ketorolac reduce the inflammation associated with DES A topical ophthalmic aqueous solution of tetracycline has been developed for chronic DES. Tetracyclines are used in DES primarily for their anti-inflammatory effects rather than antibacterial actions (Foulks, G.N.,et al 2015)

Punctal Plugs: A small medical device called a "punctal plug" is inserted into the puncta of an eye to block the duct to prevent nasolacrimal drainage of tears from the eye and thereby dry eyes. Clinical studies have shown

that the punctal plugs, as means of occlusion, improve DED symptoms and signs (Teo, L. and Chee, E., 2012)

Vitamin A: Vitamin A is an essential nutrient present naturally in the tear film of healthy eyes. Vitamin A plays an essential role in producing the mucin layer, the most innermost lubricating layer of tear film that is crucial for a healthy tear film. Vitamin A deficiency leads to loss of mucin layer and goblet cell atrophy (Teo, L. and Chee, E., 2012)

Omega 3 Fatty Acids: Oral supplementation with essential fatty acids (EFAs) is suggested nowadays by ophthalmologists EFAs are the precursors of eicosanoids, locally acting hormones involved in mediating inflammatory processes (Teo, L. and Chee, E., 2012).

Prevention And Early Detection: Dry Eye Syndrome cannot be prevented, notably because most of the cases are due to the aging process. However, these guidelines are helpful to ease the discomfort and further complications (Teo, L. and Chee, E., 2012) To avoid excessive air movement: windy conditions – outside or inside To avoid hot, dry environments and add moisture to the air, a humidifier can be used to keep the air moist. Air conditioning is as bad as heaters for increasing the evaporation of your tears. To wear glasses on windy days and goggles while swimming: The wraparound style of glasses may help reduce the effects of the wind. In addition, goggles protect your eyes from chemicals in pool water that can dry your eyes.

To take frequent breaks: While watching TV, reading, or working at a computer. To position the computer screen below eye level: The computer screen below eye level keeps the eye open narrowly. This may help slow the evaporation of tears between eyes blinks. To stop smoking and avoid passive smoking: Smoke can worsen dry eyes symptoms.To use hot compresses and eye massage: Particularly for blepharitis, meibomianitis, and related conditions.100 To in still artificial tears/ lubricating gels: as soon as there is suspicion of dry eye disease and close follow-up to detect the dry eye disease early.

Follow Up: To assess the response of the therapy as a basis for altering/ adjusting treatment, as necessary. To monitor for structural ocular damage and to provide reassurance and constant counselling. The frequency and extent of the follow-up evaluation will depend on the severity of the disease, the therapeutic approach, and the response to the therapy. For example, patients with sterile corneal ulceration associated with dry eye may require daily follow-up. Level of care Primary level: at PHC, BPHC, and district level by non-ophthalmologist eye care providers (optometrists, ophthalmic assistants, or non- ophthalmologist physicians) To take proper ocular and medical history to identify the disease and associated risk factors. To start treatment in case of mild dry eye.

To guide and counsel the patient. To refer the patient promptly to the secondary/tertiary level in any doubt like Exacerbation of symptoms Blurring of vision, No response to artificial tears and any red eye/ lid abnormalities o Positive systemic history, like rheumatoid arthritis Secondary level: at district level by a comprehensive ophthalmologist or ophthalmologists of other subspecialties. To perform common dry eye tests to grade the severity of the disease. To treat mild to moderate dry eye. To refer the patient promptly to the tertiary level if any of the following occurs: Visual loss of Moderate or severe pain or Lack of response to the Corneal therapy infiltration or Tertiary ulceration level: at medical colleges, tertiary eye institutes, or by specialist ophthalmologists To treat and manage patients with dry eye disease at any level. To find out etiological factors responsible To treat any complications – in patients with severe dry eye. To train comprehensive ophthalmologists.

CONCLUSION

Clinicians should be aware of the extent of dry eye symptoms. A thorough history and investigation are necessary to identify the cause of dry eye. Useful clinical tests for assessing the condition's severity include Schirmer, Fluorescein dye, and tear break up time test. A proper and adaptable treatment will improve the ocular surface, including relief from symptoms and an effective improvement of the quality of life.Current knowledge about causes, symptoms, and diagnostic tests of KCS provides better opportunities for improving medication management. In addition, the development of new potential drugs and different colloidal delivery systems provides a ray of hope for more effective treatment of this widely prevalent and debilitating disease.

Recommendations: The future scope of the study is to incorporate screening for dry eye anomalies; advocacy for the same will be carried out through awareness sessions and educational materials to patient and practitioner.The conventional approach to dry eye management with tear substitutes is not enough in moderate to severe dry eyes. The newer treatment approach is to target the underlying risk factors of the dry eye instead of conventional symptomatic relief.

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