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Review article

Current advances in dry eye disease diagnosis and treatment

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ABSTRACT

Dry eye disease (DED) is a disorder of the ocular surface caused due to hyperosmolarity and insufficient production of tears to moisturize the eye, which leads to less lubrication and ocular surface inflammation and results in visual disturbance and discomfort to the eye. Long-time use of computers, laptops, and mobiles causes less blinking, making the eye's mucin layer thinner, leading to tear-film instability and DED. Tens of millions of people are getting affected by DED worldwide. It is also known as Sjogren's syndrome, which impacts the lacrimal gland of the eyes, decreases tear secretion, and causes the development of aqueous tear film in the eyes and meibomian gland dysfunction. Here we have discussed the various diagnosis methods used for identifying DED and also the emerging technologies for the diagnosis of DED. The treatment options are discussed as per the disease's severity, including novel therapies like autologous serum, topical corticosteroids, and anti-inflammatory agents.

Keywords: Dry eye disease, Tear film, Inflammation, Sjogren's syndrome.

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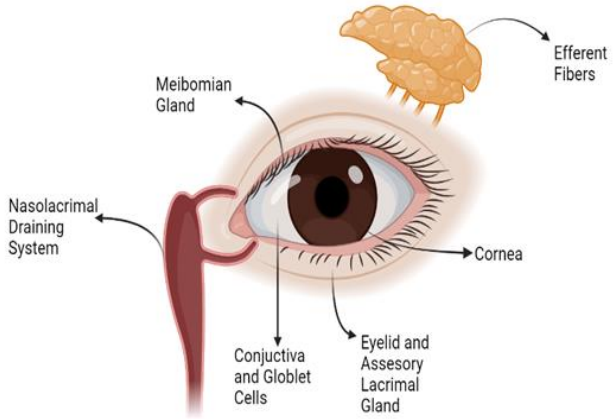
INTRODUCTION

A multifactorial eye illness called DED is characterized by tear film instability brought on by hyperosmolarity and inadequate tears to lubricate the eye, which causes ocular surface inflammation, impairs vision, and hurts the ocular surface. The resultant hyperosmolar stress may, directly or indirectly, causes inflammation of the eye surface that damages tissue and causes the loss of goblet and epithelial cells. This worsens surface wettability, which in turn causes early tear film instability. Tear hyperosmolarity, neurosensory variables, lack of lubrication, and inflammatory mediators are the causes of pain in DED, while abnormalities on the ocular surface are the origin of visual complaints. [1]. DED can considerably impact daily activities, social and physical functions, workplace productivity, and overall quality of life [2]. Increased tear evaporation affects the interpalpebral layer of the eye and produces discomfort in the eye. Visual disturbance, dryness, red eyes, and blurred vision are the symptoms of this disease. The aqueous deficiency type that mainly causes dry eye is also known as Sjogren's disorder. The Asia Dry Eye Society states that dry eye is diagnosed when subjective symptoms such as unstable tears are observed [3]. The inner mucin layer, outer lipid layer, and the middle aqueous layer, which interacts with the corneal epithelial surface, make up the tear film's three unique layers [4].

Figure 1: The Lacrimal Functional Unit (LFU)



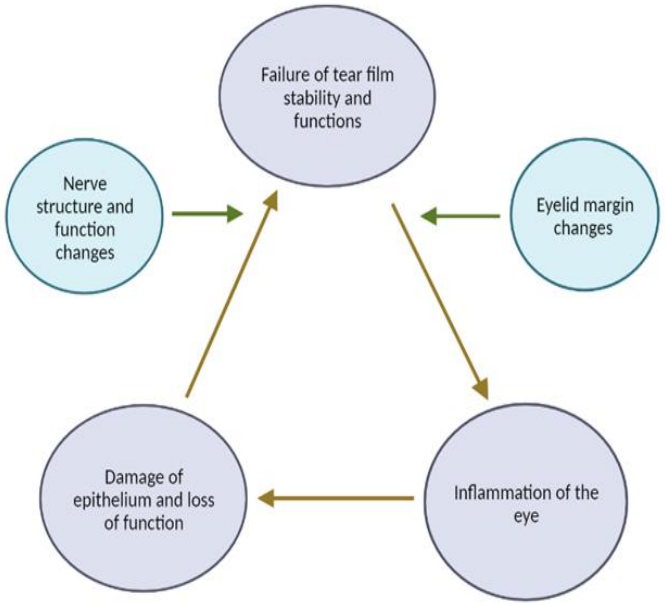
Mucins mostly release from the deepest layer of the tear film glycocalyx, and membrane-associated mucins are released by the goblet cells and help to keep the cornea's surface moist[5]. Nerve impulse activity in the ocular surface's sensory neurons can be caused

due to inflammation, which can change, tear production, and blinking [6]. At the same time, numerous variables contribute to DED, including meibomian gland dysfunction (MGD). DED may develop into an unreversible chronic inflammatory condition if the early disease is not treated. The lacrimal functional unit is given in **Figure1**

Epidemiology

In the world, 6 to 34% of the population is affected by dry eye disease. Most commonly over aged people over 50 years are generally affected by DED and 70% are women [7]. More than 80% of individuals with Sjogren's syndrome experience dry eyes, lacrimal gland damage, decreased tear production, and the development of an aqueous tear film. Other factors are air pollution, which causes DED more in metropolitan areas than in rural areas. Long-time use of computers, laptops, and mobiles causes less blinking, making the mucin and lipid layers thinner and leading to tearing film instability and gradually DED. The deficiency of vitamin-A causes visual impairment. Steven-Jonson syndrome and meibomian gland dysfunction are also identified as the cause of DED in patients. According to a report, DED may be related to seasonal environmental factors [8]. The key pathological factors contributing to the various circle of DED are given in **figure 2.**

Figure 2: Key pathological factors contributing to the various circle of DED



Current methods of diagnosis of DED

There are many methods of diagnosis for dry eye disease used for identification of and the condition of the disease and its signs and symptoms for easy detection of DED. All the current diagnostic methods are discussed below.

Schirmer test

Schirmer described a test in 1903 to measure tear production [9]. We can measure total tear secretion in Schirmer Test I, including basal tears and reflexes. The Schirmer strips are placed without contacting the cornea by avoiding injecting anesthetic drops into the lower conjunctival sac of the temporal lobe. The wetting strip length is recorded after 5 minutes in millimeters (mm). 8mm to 33mm is the normal mean test value, but more than 10mm length of the wetting strip is accepted as the normal value [10]. In terms of diagnosing dry eyes in a study, it is found that with anesthesia the Schirmer test I is more reliable than without anesthesia. It has been found that when the eyes of the patients are closed, more reliable results are found because the stimulation of eyelashes and the tear turnover rate might be affected by the eyelid margin. It has been discovered that a one-minute Schirmer test can lessen and even prevent eye pain. Schirmer assessment is most useful in severe DED cases [11].

Fluorescent Staining

In DED, fluorescein sodium can be a handy tool for the identification of the defects of corneal epithelium. The corneal surface will become stained if the cell-to-cell connection is disrupted, this staining shows the varied patterns of superficial punctate epithelial erosions on the cornea that are associated with the specific causes of DED. Fluorescein staining cannot provide straight evidence of dry eye. It cannot be regarded as a particular assessment because epithelial degradation can result through refractive surgery or from constantly wearing contacts. Eyecare professionals often put a drop of anesthesia with fluorescein. Generally, only 2-5µl of fluorescein drops should be instilled in the eye using a micropipette. Quick evaporation is another issue with Fluorescein [12].

Rose Bengal staining

The corneal portion or conjunctiva of the eye are the areas where the Rose Bengal (RB) staining is seen. These areas have an efficiency of membrane-connected mucins. It is a very effective device in estimating dry eyes, but due to its lack of specificity and sensitivity, it is best used as an adjunct. Rose Bengal staining is used in asymptomatic patients, and no clearly defined relationship is between the harm of ocular surface specific to the diagnosis of DED and a patient's symptoms. The method is toxic to the corneal epithelium. It is used less frequently than fluorescein because it might be uncomfortable during instillation without an anesthetic [13].

Lissamine green staining

Lassimine Green (LG) is a dye that helps to diagnose ocular surface damage. It is non-toxic to the corneal epithelium and tolerable than RB staining [14]. The 10 µm of 1% LG was found to be good for optimum accuracy, mainly when using a red filter. The Oxford plan, Van Bijsterveld method, and National Eye Institute Workshop rules are a few popular systems used to assess ocular surface staining. Although it is easy to use and reasonably priced, it requires a lot of time, which restricts its usefulness [15].

Tear function index

An additional method for assessing tear production is the tear function index. It is like the Schirmer test with the use of

anesthesia. Five minutes after placing 10µl of fluorescein, the wetted area length is measured with a standard color strip. The clearance rate of tears is determined by how quickly fluorescein dye fades in color. The proportion at which the fluorescein dye color disappears determines how quickly tears clear up [16]. Dry eyes are present when the index score is lower than 96; an index score of less than 34, suggests Sjogren's syndrome and less than 96 indicates dry eyes. The tear function index fails to account for tear fluid evaporation. Compared to the Schirmer test, it has been found to raise the specificity and improve the sensitivity in diagnosing DED [17].

Fluorescein clearance test

This test is a variant of the Schirmer test that can be done to test both tear secretion and drainage. It includes the application of proparacaine and Schirmer paper and 5µl of fluoresces (0.25% fluorescein and 0.4% benoxinate hydrochloride) [18]. Both the strip's soaking and the dye's removal are timed in increments of 10 minutes, a measurement of 3 mm or higher during the first interval of 10 minutes meets the definition of normal. Clearance is typical if the dye cannot be detected at the 20-minute mark. This dynamic examination examines the clearing of basal and reflex tears. The fluorescein clearance test is simple to execute and affordable Schirmer paper is used. Similar to the Schirmer test, it is time-consuming, irritating, and non-reproducible [19] .

Modern diagnostic technologies for DED

Optical coherence tomography (OCT)

OCT is the method for calculating the tear volume. Using OCT, the heights of the tear meniscus in aqueous-deficient Patients' rates of dry eyes were found to be significantly lower than in normal patients.Studies have established OCT to be a reliable, objective, and non-invasive process of measuring the tear lake [20]. Using OCT to evaluate tear film thickness is an intriguing potential benefit. OCT may help diagnose dry eyes and evaluate the effectiveness of a particular therapy using before-and-after data. The process, on the other hand, is costly, time-consuming, and frequently unreimbursed. OCT allows for the quick capture of the tear lake, although it is questionable whether this single measurement accurately captures the real tear film volume throughout the day due to the possibility of intraday changes. To determine the mean tear film thickness and tear lake volume serial OCT measurements may be required [21].

Reflective meniscometry

It is a non-invasive procedure for determining the shape and volume of the tear meniscus. A novel, portable digital viscometer with a slit-lamp mount was discovered to generate tear meniscus radius measurements that were comparable to those acquired through ocular coherence tomography (OCT). Even though there are many researches going on this new technique, it appears to be more affordable and promising than OCT [22].

Tear film stability analysis

When diagnosing dry eyes, it's crucial to consider the constancy of the tear film. The Japanese-developed tear film stability analysis system (TSAS) is a delicate video-keratography [23]. Using video-keratography, the TSAS takes ten topographic photographs of the corneal surface at one-second intervals. The TSAS measures areas of irregularity to quantify over ten seconds, dynamic changes in tear stability. Dry eye illness is more severe in those with more abnormalities. The surface asymmetry index and surface regularity index are two measurements that might be employed for this examination. Although the system is commercially available, research is scarce due to the technology's high cost and lengthy development [24].

Tear osmolarity

The level of tear osmolarity is higher in people with dry eyes, according to reports. The TearLab osmolarity system which is located in the USA can help in calculating osmolarity values and help in the diagnosis of DED. DED is defined as a value of osmolarity more than 308 mOsm/L A threshold value of 315 mOsm/L was found in another investigation for healthy dry eyes [25]. With higher sample sizes, this device can be better appraised. Studying the freezing temperatures of tear samples is another approach to determining tear osmolarity. The lower the freezing point, the greater the likelihood that the patient may experience dry eye because diluted samples freeze more quickly than concentrated samples because they do. This test must be finished quickly to prevent the tear sample from evaporating. Electrical impedance is used in the TearLab osmolarity system, which correlates well with the Clifton osmometer. Despite the positive results, more research on this needs to be done [26].

Treatment for DED

Patient education about the disease is important and should include information such as the fact that DED is a long-lasting disease with long-term treatment that may take time. Treatment of DED includes a step-by-step process and must take into account any concomitant meibomian gland dysfunction, (subclinical) ocular surface inflammation, and/or systemic disease, depending on how serious the problem is [27]. A crucial treatment element is avoiding aggravating variables, including cigarette smoke, air conditioning and dry heating air.

Treatment according to the severity level of DED

There are many treatments are available to treat dry eye disease. The treatment options as per the severity levels of DED are given in Table no 1.

Environmental measures to reduce DED and modification in lifestyle

Simple environmental approaches to improve moisture content include drinking enough water each day, abstaining from excessive alcohol, using humidifiers, limiting the use of forced hot-

air heating systems, and using air-conditioning, which can be counseled to the dry-eye patient by an eye care provider. It's important to note that tear-deficient dry eye (TDE) and evaporative dry eye are distinct medical disorders [28].

Level 1 severity

Table No 1: Treatment options as per the severity level of DED

Level 1 Severity	Environmental measures to reduce DED and modification in lifestyle	
	Dietary Modifications	Antioxidants as dietary supplements
	Hormone replacement for dry eye disease	
Level 2 Severity	Tear substitutes or artificial tear	
	Anti-Inflammatory agent	Topical Corticosteroids
		Topical Cyclosporin A
	Tetracyclines	
Level 3 Severity	Autologous Serum	

Dietary Modifications

Because vertebrates are unable to produce necessary fatty acids, they must be obtained through diet. Omega-3 fatty acids are 18-carbon omega-6 and are among the necessary fatty acids for eye [29]. Lactoferrin supplements have been shown to help individuals with aqueous-deficient dry eyes improve their tear stability and lipid layer interferometry grades. Similarly, accumulating data supports the treatment of dry eyes with antioxidants. It is currently unclear whether oral antioxidants improve both conjunctival health and tear stability [30].

Hormone replacement therapy for DED

Estrogen and androgenic receptors on corneal, conjunctival, and meibomian gland epithelia greatly affect the ocular surface function in both sexes. However, in postmenopausal women, it is still unclear whether androgen or estrogen shortage or their imbalance impairs the function of the ocular surface. Oestrogen, when provided at higher dosages and/or in combination with other hormonal supplements, can be harmful and/or cause inflammation. Oestrogen or androgen-based eye drops, including topical dihydroepiandrosterone, may represent a viable novel treatment [31].

Level 2severity

Artificial tear or tear substitutes

Artificial tear or tear substitutes are the cornerstones of dry eye treatment for all levels of severity. Although artificial tears are considered conventional and no major, controlled, randomized trials, have been conducted to assess the various types of tear substitutes on the market. Artificial tears have been demonstrated in small randomized studies to improve tear film stability, improve contrast sensitivity, reduce the optical quality of the surface and ocular Surface stress and improve quality of life [32]**.** In general, for ocular surface conditions, it should be suggested that products without the preservative benzalkonium chloride (an epitheliotoxin) be used. To treat meibomian gland dysfunction, artificial tears that include lipids such as triglycerides, castor oil and phospholipids are available [33].

Anti-Inflammatory agent

The most efficient anti-inflammatory drugs used in the treatment of DED are corticosteroids. Loteprednol etabonate 0.5% ophthalmic suspension was found to be more efficient in reducing the number of indications and symptoms of DED in a randomized, 4-week, double-masked research involving 64 persons with DED [34]. In another trial, the patients on fluorometholone and artificial tears had lower symptom severity than patients on artificial tears alone in a 4-week randomized, open-label investigation of 32 patients with DED [35].

Topical Corticosteroids

In the treatment of DED, corticosteroids are an effective anti-inflammatory medication. Injections of unpreserved corticosteroid eyedrops spaced 2 to 4 weeks apart have been demonstrated to alleviate the clinical symptoms and signs of moderate to severe dry eye disease in randomized, controlled clinical investigations [36]. Symptoms regressed significantly (43%) or totally (100%) after two weeks of treatment. After the therapy was stopped the discomfort and clinical symptoms in patients were reduced for several weeks. Long-term therapy caused difficulties in a few patients (increased intraocular pressure, cataract), hence eyedrops of corticosteroids are only indicated for short-term use [37].

Topical Cyclosporine A

Increased tear production is induced by cyclosporin A, presumably due to local parasympathetic neurotransmitter release [38]. Treatment with 0.05 % eyedrops twice daily improved keratopathy, enhanced Schirmer test scores, and reduced symptoms like foreign body sensation, blurry vision, epiphora and ocular dryness. In the United States, as a long-term therapeutic option, 0.05% cyclosporin A eyedrops are readily available. In Germany, dispensing pharmacies can prescribe cyclosporin A as an extemporaneous substance [39].

Tetracyclines

A controlled investigation of tetracycline analogs effectively treats DED [40]. Doxycycline dosages range from 40 to 400 mg per day, whereas minocycline dosages ranging from 50 to 100 mg per day are preferred mostly for DED. Tear film instability symptom was improved even at low doses. Due to a considerably higher likelihood of side effects (mostly gastrointestinal and skin issues) with larger dosages, a lower dose for 6 to 12 weeks is advised. These derivatives have also been discovered to reduce corneal epithelial cell death in aqueous deficit dry-eye models by lowering matrix metalloproteinase-9 (MMP-9) protein levels [41].

Level 3severity

The use of autologous serum (AS) in DED is explained by the discovery that serum contains the same vitamins and growth agents present in tears. Using AS has a clear advantage over using artificial tears, which are deficient in such essential components. Children and adults alike frequently experience eye diseases. Eyedrops containing the patient's serum (autologous serum eyedrops)

are used in concentrations ranging from 20% to 100%. They are rich in growth factors that are anti-inflammatory and epitheliotropic. Using AS eye drops to treat dry eyes is especially beneficial [42]. This becomes the best way of management of severe DED [43].

CONCLUSION

DED is a multifactorial illness that, if ignored, may become treatment-resistant and cause long-term harm to the ocular surface. We have compiled recent research addressing significant developments in diagnosing and treating DED in this review. The advancements in DED diagnosis may now find the irregularities of each tear film layer. There are now just a few clinically useful examination techniques for DED, and more research and development should be done in the future. With the development of precise diagnostic techniques, an accurate diagnosis of DED is possible.

Further research in developing new drugs and novel delivery systems still needs to be done to treat DED effectively. Long-term anti-inflammatory medications and cyclosporine eye drops will benefit moderate or severe DED. Lifestyle therapies, such as nutrition therapy, anti-aging techniques, and exercise, may help treat dry eyes in addition to ophthalmic solution-based methods.

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REFERENCES

1. A J Bron, 2017. TFOS DEWS II pathophysiology report. Ocul Surf, vol. 15, no. 3, Pages- 438–510, Doi: 10.1016/j.jtos. 2017.05.011.
2. S C Pflugfelder, 2008. Prevalence, burden, and pharmaco economics of dry eye disease. Am J Manag Care, vol. 14, no. 3 Suppl, Pages-102-106, Doi: 10.1016/j.jtos.20 12. 12.002.
3. M Sisto, D Ribatti, S Lisi, 2022. Molecular Mechanisms Linking Inflammation to Autoimmunity in Sjögren's Syndrome: Identification of New Targets. Int J Mol Sci, vol. 23, no. 21, Pages-13229, Doi: 10.3390/ijms232113229.
4. A J Bron, J M Tiffany, S M Gouveia, et al, 2004. Functional aspects of the tear film lipid layer., Exp Eye Res, vol. 78, no. 3, Pages-347–360, Doi: 10.1016/j.exer.2003.09.019.
5. L Zhou, 2012. In-depth analysis of the human tear proteome, J Proteomics, vol. 75, no. 13, Pages-3877–3885, Doi: 10.1016 /j.jprot.2012.04.053.
6. C Belmonte, 2017. TFOS DEWS II pain and sensation report. Ocul Surf, vol. 15, no. 3, Pages-404–437, Doi: 10.10 16/j.jtos.2017.05.002.
7. F Stapleton, 2017. TFOS DEWS II Epidemiology Report. Ocul Surf, vol. 15, no. 3, Pages-334–365, Doi: 10.1016/j.jtos. 2017.05.003.
8. G van Setten, M Labetoulle, C Baudouin, et al, 2016. Evidence of seasonality and effects of psychrometry in dry eye disease. Acta Ophthalmol, vol. 94, no. 5, Pages-499–506, Doi: 10.1111/aos.12985.
9. M S B Zeev, D Miller, R Latkany, 2014. Diagnosis of dry eye disease and emerging technologies. Clin Ophthalmol, vol. 8, Pages-581–590, Doi: 10.2147/OPTH.S45444.
10. N Li, X G Deng, M F He, et al, 2012. Comparison of the Schirmer I test with and without topical anesthesia for diagnosing dry eye. Int J Ophthalmol, vol. 5, no. 4, Pages-478–481, Doi: 10.3980/j.issn.2222-3959.2012.04.14.
11. D Serin, S Karsloğlu, A Kyan, G Alagözet, et al, 2007. A simple approach to the repeatability of the Schirmer test without anesthesia: eyes open or closed? Cornea, vol. 26, no. 8, Pages-903–906, Doi: 10.1097/ICO.0b013e3180950083.
12. K C Yoon, S K Im, H G Kim, et al, 2011. Usefulness of double vital staining with 1% fluorescein and 1% lissamine green in patients with dry eye syndrome. Cornea, vol. 30, no. 9, Pages-972–976, Doi: 10.1097/ICO.0b013e31820687dd.
13. D Khan Lim, M Berry, 2004. Still confused about rose bengal? Curr Eye Res, vol. 29, no. 4–5, Pages-311–317, Doi: 10.1080/02713680490516864.
14. L M Machado, R S Castro, B M Fontes, et al, 2009. Staining patterns in dry eye syndrome: rose bengal versus lissamine green. Cornea, vol. 28, no. 7, Pages-732–4, Doi: 10.1097/ICO.0b013e3181930c03.
15. P Hamrah, F Alipour, S Jiang,et et al, 2011. Optimizing evaluation of Lissamine Green parameters for ocular surface staining. Eye (Lond), vol. 25, no. 11, Pages-1429–1434, Doi: 10.1038/eye.2011.184.
16. G Savini, P Prabhawasat, T Kojima, et al, 2008. The challenge of dry eye diagnosis. Clin Ophthalmol, vol. 2, no. 1, Pages-31–55, Doi: 10.2147/opth.s1496.
17. S B Kaye, G Sims, C Willoughby, et al, 2001. Modification of the tear function index and its use in the diagnosis of Sjögren's syndrome. Br J Ophthalmol, vol. 85, no. 2, Pages-193–199, Doi: 10.1136/bjo.85.2.193.
18. P Prabhasawat, S C Tseng, 1998. Frequent association of delayed tear clearance in ocular irritation. Br J Ophthalmol, vol. 82, no. 6, Pages-666–675, Doi: 10.1136/bjo.82.6.666.
19. A Afonso, D Monroy, M E Stern, et al, 1999. Correlation of tear fluorescein clearance and Schirmer test scores with ocular irritation symptoms. Ophthalmology, vol. 106, no. 4, Pages-803–810, Doi: 10.1016/S0161-6420(99)90170-7.
20. R Altan Yaycioglu, S Sizmaz, H Canan, et al, 2013. Optical coherence tomography for measuring the tear film meniscus: correlation with schirmer test and tear-film breakup time. Curr

Eye Res, vol. 38, no. 7, Pages-736–742, Doi: 10.3109/0 2713683.2013.774422.

21. N García, 2014. Basal values, intra-day and inter-day variations in tear film osmolarity and tear fluorescein clearance. Curr Eye Res, vol. 39, no. 7, Pages-673–679, Doi: 10.3109/02713683.2013.865757.

22. S Bandlitz, C Purslow, P J Murphy, H Pult, et al, 2014. Comparison of a new portable digital meniscometer and optical coherence tomography in tear meniscus radius measurement. Acta Ophthalmol, vol. 92, no. 2, Pages-112-8, Doi: 10.1111/aos.12275.

23. T Goto, 2003. A new method for tear film stability analysis using videokeratography, Am J Ophthalmol, vol. 135, no. 5, Pages-607–612, Doi: 10.1016/S0002-9394(02)02221-3.

24. R Montés Micó, Cáliz, J L Alió, et al, 2004. Wavefront analysis of higher order aberrations in dry eye patients. J Refract Surg, vol. 20, no. 3, Pages-243–247, Doi: 10.3928/1081-597X-20040 501-08.

25. E Szalai, A Berta, Z Szekanecz, et al, 2012. Evaluation of tear osmolarity in non-Sjögren and Sjögren syndrome dry eye patients with the TearLab system. Cornea, vol. 31, no. 8, Pages-867–871, Doi: 10.1097/ICO.0b013e3182532047.

26. A Tomlinson, L C McCann, E I Pearce, et al, 2010. Comparison of Human Tear Film Osmolarity Measured by Electrical Impedance and Freezing Point Depression Techniques. Cornea, vol. 29, no. 9, Pages-1036–1041, Doi: 10.1097 /ICO.0b013e3181cd9a1d.

27. J H Krachmer, P R Laibson, 1974. Corneal thinning and perforation in Sjögren's syndrome. Am J Ophthalmol, vol. 78, no. 6, Pages-917–920, Doi: 10.1016/0002-9394(74)90801-0.

28. Pflugfelder S, 2007. Management and therapy of dry eye disease: report of the Management and Therapy Subcommittee of the International Dry Eye WorkShop (2007). Ocul Surf, vol. 5, no. 2, Pages-163–178, Doi: 10.1016/s1542-0124(12)7 0085-x.

29. M Dogru, 2007. Lactoferrin in Sjögren's syndrome. Ophthalmology, vol. 114, no. 12, Pages-2366–2367, Doi: 10.1016/j.ophtha.2007.06.027.

30. B J Willcox, 2007. Caloric restriction, the traditional Okinawan diet, and healthy aging: the diet of the world's longest-lived people and its potential impact on morbidity and life span. Ann N Y Acad Sci, vol. 1114, Pages-434–455, Doi: 10.1196/annals.1396.037.

31. K J Blades, S Patel, K E Aidoo, et al, 2001. Oral antioxidant therapy for marginal dry eye. Eur J Clin Nutr, vol. 55, no. 7, Pages-589–597, Doi: 10.1038/sj.ejcn.1601186.

32. G Uncu, R Avci, Y Uncu, et al, 2006. The effects of different hormone replacement therapy regimens on tear function, intraocular pressure and lens opacity. Gynecol Endocrinol, vol. 22, no. 9, Pages-501–505, Doi: 10.1080/09513590600917 919.

33. S Barabino, M Rolando, M Nardi, et al, 2014, The effect of an artificial tear combining hyaluronic acid and tamarind seeds polysaccharide in patients with moderate dry eye syndrome: a new treatment for dry eye. Eur J Ophthalmol, vol. 24, no. 2, Pages-173–178, Doi: 10.5301/ejo.5000355.

34. N Freudenthaler, H Neuf, G Kadner, et al, 2003. Characteristics of spontaneous eyeblink activity during video display terminal use in healthy volunteers. Graefes Arch Clin Exp Ophthalmol, vol. 241, no. 11, Pages-914–920, Doi: 10.1007/s00417-003-0786-6.

35. S C Pflugfelder, 2004. A randomized, double-masked, placebo-controlled, multicenter comparison of loteprednol etabonate ophthalmic suspension, 0.5%, and placebo for treatment of keratoconjunctivitis sicca in patients with delayed tear clearance. Am J Ophthalmol, vol. 138, no. 3, Pages-444–457, Doi: 10.1016/j.ajo.2004.04.052.

36. E M Messmer, M Bulgen, A Kampik, et al, 2010. Hyperosmolarity of the tear film in dry eye syndrome. Dev Ophthalmol, vol. 45, Pages-129–138, Doi: 10.1159/000315026.

37. M A Lemp, 2011. Tear osmolarity in the diagnosis and management of dry eye disease. Am J Ophthalmol, vol. 151, no. 5, Pages-792-798.e1, Doi: 10.1016/j.ajo.2010.10.032.

38. A Yoshida, T Fujihara, K Nakata, et al, 1999. Cyclosporin A increases tear fluid secretion via release of sensory neurotransmitters and muscarinic pathway in mice. Exp Eye Res, vol. 68, no. 5, Pages-541–546, Doi: 10.1006/exer.1998. 0619.

39. L Baiza Durán, J Medrano Palafox, E Hernández Quintela, et al, 2010. A comparative clinical trial of the efficacy of two different aqueous solutions of cyclosporine for the treatment of moderate-to-severe dry eye syndrome. Br J Ophthalmol, vol. 94, no. 10, Pages-1312–1315, Doi: 10.1136/bjo.2008.150011.

40. W E Shine, J P McCulley, A G Pandya, et al, 2003. Minocycline effect on meibomian gland lipids in meibomianitis patients. Exp Eye Res, vol. 76, no. 4, Pages- 417–420, Doi: 10.1016 /s0014-4835(03)00005-8.

41. S Barabino, M Rolando, M Nardi, et al, 2014. The effect of an artificial tear combining hyaluronic acid and tamarind seeds polysaccharide in patients with moderate dry eye syndrome: a new treatment for dry eye. Eur J Ophthalmol, vol. 24, no. 2, Pages-173–178, Doi: 10.5301/ejo.5000355.

42. RM Werkmeister, 2013. Measurement of tear film thickness using ultrahigh-resolution optical coherence tomography. Invest Ophthalmol Vis Sci, vol. 54, no. 8, Pages-5578–5583, Doi: 10.1167/iovs.13-11920.

43. Shrivas, Y, 2021. Indigenous drugs for eye disorders in shatkalpa adhyay of kashyapa samhita. Journal of Medical Pharmaceutical and Allied Sciences, 10(3), 3038–3048, Doi: 10.22270/jmpas.V10I3.1153.

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