

Diagnosis of Dry Eye Syndrome and Treatment Options, Overview

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Abstract: Current study aiming to overview the Dry eye disease (DED) in clinical perspectives, through discussing the etiology and risk factors of DED, and most importantly was to review the diagnostic procedures used in DED diagnosis and proper treatment approaches. We conducted the literature search in following electronic database MEDLINE/PubMed, EMBASE, for published studies up to March, 2017. We have included most evidence based articles which were discussing the Dry eye disease (DED) treatment, diagnosis, etiology and any clinical association to DED. The therapy of dry eye has actually advanced from tear substitution alone to a reasonably based restorative formula. If the signs and symptoms are moderate, artificial tears of different kinds are advised. Cover health is valuable in the therapy of hyperevaporative dry eye, while collagen or silicon plugs can be utilized for partial occlusion of the efferent lacrimal ducts to treat severe hyposecretory dry eye.

Keywords: Dry eye disease (DED), treatment, diagnosis, Dry Eye Syndrome.

1. INTRODUCTION

Dry eye disease (DED) is defined as a multifactorial disease of the tears and ocular surface area that results in symptoms of pain, visual disruption, and tear film instability with prospective damage to the ocular surface area. It is accompanied by increased osmolarity of the tear film and subacute inflammation of the ocular surface ⁽¹⁾. DED is one of the most frequently encountered ocular morbidities. Quarter of patients who visit ophthalmic centers report signs of dry eye, making it a growing public health issue and among the most common conditions seen by eye care professionals ⁽²⁾. Literature have revealed that dry eye is an inflammatory disease that has numerous functions in common with autoimmune disease. Historically, the term "Keratoconjunctivitis sicca" can be credited to the Swedish ophthalmologist Henrik SC Sjögren ⁽³⁾.

DED is seen with increased frequency in patients with autoimmune diseases, which affect around 8% of the population, of whom 78% are women ⁽⁴⁾. Dry eye disease also impacts postmenopausal ladies and the senior ^(5,6,7). The frequency of DED is approximated to be 7.4% to 33.7% depending on which study is pointed out, how the disease is identified, and which population is surveyed ⁽⁷⁾. The Beaver Dam population-based research study discovered the DED frequency rate to be 14% in grownups 48 to 91 years of age ⁽⁶⁾. The research study likewise found that DED impacts more ladies than guys (16.7% versus 11.4%, respectively). Dependable epidemiological research studies from the large Women's Health Study and Physician's Health Study show that the occurrence of symptomatic dry eye in the United States is about 7% in women and 4% in guys over the age of 50 years ⁽⁵⁾. These numbers translate into approximately 3.2 million ladies and 1.05 million males with DED in the United States ⁽⁸⁾. Estimates of those affected by DED of any intensity total up to roughly 20 million or more in the United States alone ⁽⁹⁾. Worldwide epidemiological research studies report similar or higher rates around the world ^(8,9).

Increasing age, perimenopausal phases in females, hormonal diseases, and particular medications are simply a few factors that can lead to dryness on the ocular surface ^(10,11). Other factors consist of long-lasting contact lens smoking cigarettes, wear, and laser refractive eye surgical treatment ⁽¹²⁾. Activities like extended computer system usage, enjoying television, and reading can trigger and/or intensify dry eye signs ⁽¹³⁾.

Current study aiming to overview the Dry eye disease (DED) in clinical perspectives, through discussing the etiology and risk factors of DED, and most importantly was to review the diagnostic procedures used in DED diagnosis and proper treatment approaches.

2. METHODS

We conducted the literature search in following electronic database MEDLINE/PubMed, EMBASE, for published studies up to March,2017. We have included most evidence based articles which were discussing the Dry eye disease (DED) treatment, diagnosis, etiology and any clinical association to DED. We then manually searched the references of the original studies and reviews to identify any potential studies omitted by our search concerned topic. And we applied restriction to only English language with human subjected studies to be included in our study.

3. RESULTS

○ *Review of etiological factors for DED:*

The last years brought about a significant enhancement in the understanding of the etiology as well as pathogenesis of DED. One major advancement in the understanding of DED is the recognition of the two distinct elements of the disease--tear evaporation as well as inadequate tear production-- and their roles individually or in DED⁽¹⁴⁾. Another enhancement is the identification of tear film instability as a typical attribute of the numerous stages of DED as well as the understanding that the density of the lipid layer might determine the stability of the tear film⁽¹⁵⁾. Additionally, admiration of the duty of inflammation in DED was among the most important factors that assisted in the understanding as well as therapy of DED. The findings of the organization of inflammation with decreased tear secretion as well as succeeding damage to the eye surface led to the proposition of a linked idea of DED⁽¹⁶⁾.

A number of risk factors for the growth of DED have actually been identified consistently in epidemiological research studies (**Figure 1**), such as enhancing age as well as women sex (especially postmenopausal females). In professional experience, menopausal as well as postmenopausal ladies both tend to have completely dry eye signs; this can be attributed to the considerable decline of tear manufacturing around the sixth decade of life in ladies⁽¹⁷⁾. Hormone studies suggest that sex hormonal agents affect eye surface conditions via their results on tear secretions, meibomian gland feature, and conjunctival goblet cell thickness. Conner as well as colleagues⁽¹⁸⁾ explained that women that were taking oral contraceptive pills had substantially greater goblet cell density than those that were not taking oral contraceptive pills. Krenzer and also colleagues reported that chronic androgen shortage is associated with meibomian gland dysfunction. Schaumberg and colleagues as well as Uncu and also colleagues reported that postmenopausal females that make use of hormone substitute treatment (HRT) have a higher occurrence of DED compared to those who have never ever made use of HRT^(19,20,21). Other factors that intensify and/or precipitate DED include long-term contact lens wear, as it desensitizes the cornea over years of get in touch with lens excitement. Specific systemic drugs, such as some antihistamines and antidepressants, have drying out negative effects, which can lead or worsen to completely dry eye^(10,21).

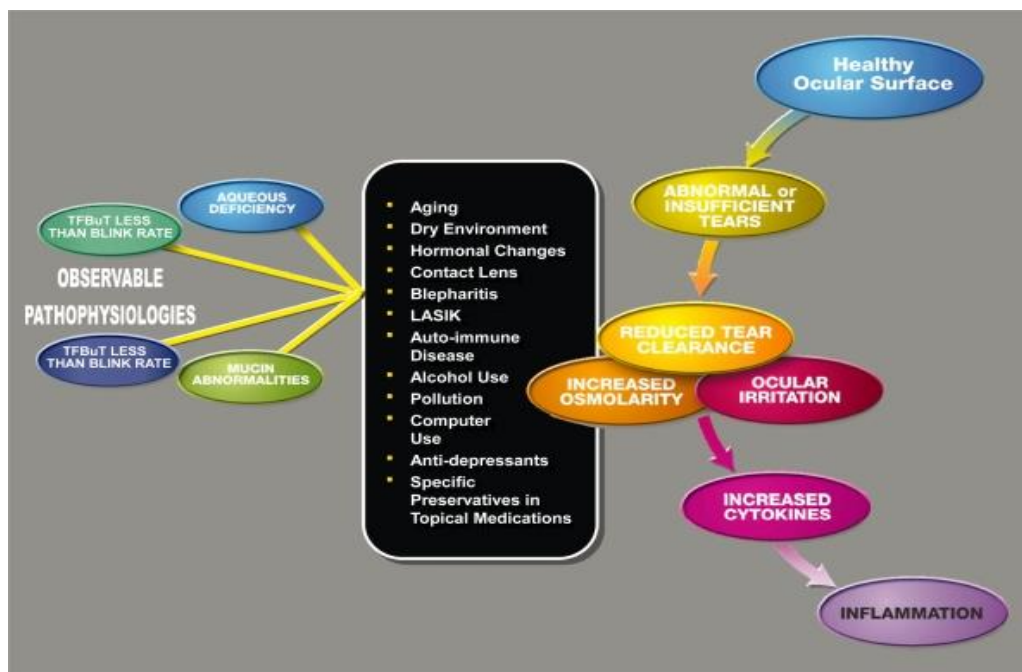


Figure 1: Dry eye disease progression, and etiological factors of abnormal tear film.

○ **Diagnosis of DED:**

Several tests and procedures contributing in the diagnosis of DED, with variation on specificity and sensitivity we assumed the most important ones and we discussed each test in details for more evidence-based review.

A. Schirmer test:

Explained in 1903 by Schirmer, this test is still one of the most typically made use of measures of tear manufacturing⁽²²⁾. Variations of the Schirmer examination have been created. The Schirmer I check steps overall tear secretion, consisting of basic and also reflex tears. Without instilling anesthetic decreases, the Schirmer strips are inserted into the temporal lower conjunctival cavity, staying clear of contact with the cornea, and also the length of wetting strips is tape-recorded in millimeters after 5 minutes. Normal mean test worths range from 8 mm to 33 mm, yet an accepted typical worth is greater than 10 mm^(22,23). In a research comparing Schirmer I with and also without anesthesia, with anesthesia was found to be more dependable and unbiased in regards to detecting dry eyes than without anesthetic⁽²⁴⁾. Nonetheless, if the medical professional chooses to perform the Schirmer I test without anesthesia, it has been located that patients with eyes shut have an even more trusted outcome due to the fact that the eyelid margin and eyelash excitement can alter the tear turnover rate⁽²⁵⁾. A variation is the Schirmer II test, which uses topical anesthetic and only measures response tears utilizing excitement with a cotton suggestion applicator. A much shorter one-minute Schirmer test was discovered to lower eye pain in addition to conserve time⁽²⁶⁾. The Schirmer examination is more reproducible in more advanced cases of completely dry eye disease⁽²⁷⁾. Even more, even the position of the eye throughout the Schirmer test shows up to affect the results, with inferior gaze creating an incorrectly higher outcome. The Schirmer test is one of the most extensively utilized devices in diagnosing completely dry eye, the extensive nature of the examination, the truth that the majority of patients discover the test invasive as well as annoying, and its unreliable and also largely irreproducible nature may explain a high risk of underdiagnosis^(26,27).

B. Fluorescein staining in diagnosis of DED:

Fluorescein salt can be used to determine corneal epithelial flaws as well as can be a beneficial device in reviewing completely dry eye. The corneal surface will discolor whenever there is a disruption of cell-to-cell joints. The discoloration could reveal corneal surface punctate epithelial disintegrations in patterns that follow particular root causes of completely dry eye. Disintegrations seen in the lower third of the cornea, for example, can symbolize lid-related exposure concerns such as poor or irregular blink or lagophthalmos. Considering that epithelial disintegrations can originate from other sources like refractive surgical treatment, call lens usage, exposure-related factors like thyroid orbitopathy, previous eyelid surgical treatments, or infections, this type of staining can disappoint straight proof of dry eye, neither can it be considered a really sensitive or specific step^(28,29). Usually, ophthalmologist impart a ready decrease of anesthetic mixed with fluorescein. Early in the slit-lamp examination, this large quantity can mask corneal discoloration. Ideally, only 2 - 5 μ L must be instilled utilizing a micropipette. One more concern with using fluorescein decreases is that, in some offices, the professional instills some version of this decline beforehand to check the patient's intraocular pressure. By the time the patient is taken a look at by the eye doctor, the fluorescein has actually either evaporated, the preservative caused some surface poisoning, or the methods by which the technician checks the intraocular stress can create refined epithelial damage. Ideally, to evaluate effectively whether a patient has dry eye, the patient ought to be evaluated before any decreases or screening is done to establish a standard look. The patient may have to be examined at various times of the day in order to contrast morning versus late afternoon searchings for. When the patient is asymptomatic versus symptomatic, it is also essential to compare evaluations on days. One research study did discover poor repeatability of the visibility or lack of substandard corneal staining in dry eye patients⁽²⁶⁾.

C. Examination of the conjunctiva:

Temporal lid-parallel conjunctival folds (LIPCOFs) in straight gaze are an outcome of enhanced rubbing between the lids as well as the conjunctiva. They are regarded as a vital indication of dry eye, with a level of sensitivity of 84.9% as well as a specificity of up to 90%⁽³⁰⁾. They can be merely, swiftly, as well as noninvasively determined making use of the slit light. LIPCOFs are classified according to Höh et al. right into three qualities⁽³¹⁾ (**Figure 2**).

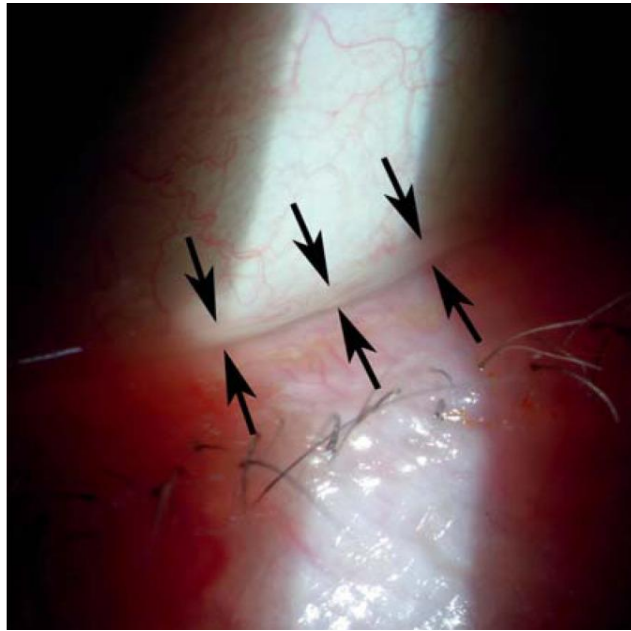


Figure 2: Lid-parallel conjunctival folds

D. Examination of the ocular surface helps in diagnosis of DED:

The surface area of the eye is checked out making use of the slit light and also essential stains. The normal dyes in medical method are fluorescein and lissamine environment-friendly. Fluorescein discolorations both the precorneal tear movie and also epithelial disintegrations in the conjunctiva and also cornea. Lissamine green highlights superficially harmed cells with a defective mucin layer⁽³²⁾ (Figure 3).

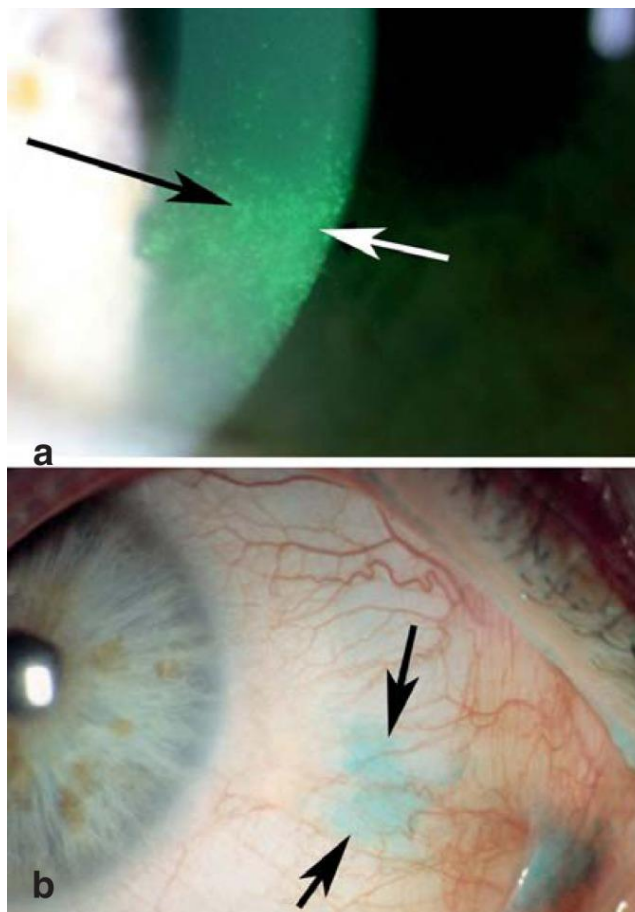


Figure 3: Vital staining of the ocular surface in a patient with dry eye disease

With all dyes, the strength of staining and the color distribution pattern are examined semiquantitatively. Tarnishing in the location of the palpebral crack is suggestive of dry eye. Several indices are available for the analysis of discoloration, such as the van Bijsterveld Index (**Figure 4**), the Oxford Grading Scale, and the CLEK plan ⁽¹⁾.

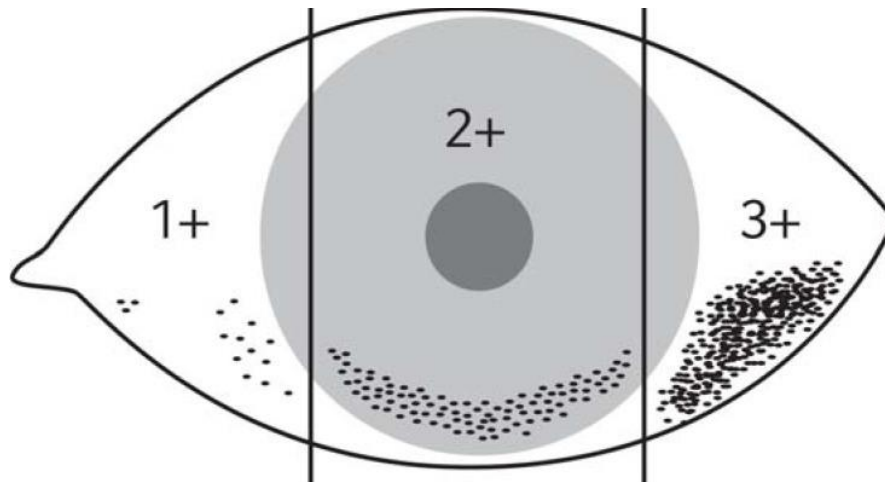


Figure 4: Semiquantitative assessment of surface staining.

E. Diagnosis of DED using Tear function index:

The tear function index is another approach of examining tear manufacturing as well as resembles the anesthetized Schirmer test. Five minutes after instilling a 10 μ L decline of fluorescein, the size of the wetted location is measured as well as its intensity is compared to a standard shade strip. The tear clearance rate is based on the price at which the shade of the fluorescein color fades. The tear feature index is then determined by separating the worth of the Schirmer test with anesthetic, which reflects the tear drain, by the tear clearance rate ⁽³³⁾. An index score less than 96 suggests completely dry eyes as well as an index rating less than 34 indicates Sjogren's syndrome ⁽³⁴⁾. A downside of this examination is that it cannot account for dissipation of tear fluid. Additionally, instillation of fluorescein boosts the tear volume and could work as a stimulant as a result of its prospective to create irritation as well as tear excitement ⁽³⁵⁾. The tear function index has actually been shown to enhance level of sensitivity as well as specificity in diagnosing completely dry eyes contrasted with the standard Schirmer step or tear clearance rate alone ⁽³⁴⁾. The tear feature index is economical and reasonably easy, it is taxing as well as subjective, which limits its practical application in an office setup.

F. Optical coherence tomography (OCT) for detection of DED:

An additional means to gauge the tear lake is by OCT. Tear meniscus heights were discovered to be dramatically reduced in aqueous-deficient completely dry eye patients compared to controls utilizing OCT. In an additional research, the tear crescent volume was measured with OCT after punctal occlusion ⁽³⁶⁾. The outcomes showed that completely dry eye patients with punctal plugs have higher tear curve heights. Researches have actually shown that OCT is a reproducible, objective, as well as noninvasive instrument for determining the tear lake ^(37,38). Of intriguing potential value is the capacity to measure tear movie thickness utilizing OCT. One study found extremely reproducible measurements utilizing ultrahigh resolution OCT. The typical main tear film density was $4.79 \pm 0.88 \mu\text{m}$, with an intraclass correlation coefficient of 0.97. OCT cannot just help in the diagnosis of dry eyes but could additionally evaluate the success of specific therapies based upon before and also after dimensions ⁽³⁸⁾.

o Treatment options for dry eye disease (DED):

The primary step in managing the disease is to determine the underlying etiology and also to try to remove it and/or treat it. Later, and despite the etiology, the pillar first-line therapy is external augmentation of the tear film with topically carried out fabricated tear replacements. Currently, there are numerous formulations on the market attempting to improve tear movie security and increase TFBuT; however, numerous have actually been found to just temporarily soothe the signs and symptoms of dry eye ⁽³⁹⁾ as opposed to recover the ocular surface or treat the underlying root cause of the disease. Man-made splits are normally buffered services that contain electrolytes, surfactants, chemicals (not all formulas), as well as a thickness agent that is planned to enhance the residency time of the decrease ⁽⁴⁰⁾. Although a lot of man-made splits have comparable components, they differ in the sort of lube used, in their chemical residential properties, as well as in the kind (or the absence thereof) of the chemical used ⁽⁴¹⁾.

Artificial tears help in reliving the worsening of DED:

Artificial tears are the pillar of treatment for all seriousness grades of completely dry eye. Although man-made tears are regarded as typical, no large, randomized, regulated research studies have actually been carried out to evaluate the many various sort of artificial tears readily available in the marketplace. The licensing of artificial tears, most of which are marketed as CE products, is not based upon their scientific performance. Tiny randomized researches^(42,43,44,45) have actually revealed that fabricated tears could add in following;

- Increase tear movie stability
- Reduce eye surface area stress and anxiety
- Improve comparison sensitivity and also the optical quality of the surface
- Are able to boost quality of life

A great deal of preparations based on polyvinyl alcohol, povidone, hydroxypropyl guar, cellulose derivatives, as well as hyaluronic acid are offered. Depending on the extent of disease, a whole series of compounds from low-viscosity preparations to high-viscosity gels (carbomers) as well as ointments can be made use of. As a matter of principle, for ocular surface area disorders, products should be recommended that do not consist of benzalkonium chloride (an epitheliotoxin) as a chemical⁽⁴⁶⁾. For meibomian gland disorder, fabricated tears containing lipids such as triglycerides, phospholipids, as well as castor oil are available. In little randomized, regulated tests these brought about enhanced meibomian gland feature and also enhanced tear film security^(47,48,49,50).

Eyedrops made from the patient's own product (autologous serum eyedrops) are utilized in a focus of 20% to 100%. They include a plethora of epitheliotropic growth factors and anti-inflammatory substances. Autologous serum eyedrops are used especially in extreme cases of dry eye. Their manufacturing is regulated by the German Medicines Act and Transfusion Law⁽⁵¹⁾. A randomized, controlled study in patients with extreme completely dry eye disease revealed a considerable improvement in tear movie stability as well as subjective symptoms but no decrease in surface discoloration with autologous serum eyedrops compared with preservative-free fabricated tears⁽⁵²⁾.

Topical cyclosporine A treatment:

Cyclosporine A is an immunosuppressant that hinders the calcineurin-- phosphatase path by complicated formation with cyclophilin, as well as thus lowers the transcription of T-cell-activating cytokines such as interleukin-2 (IL-2)⁽⁵³⁾. Topical application of cyclosporine A leads to raised manufacturing of tear liquid, possibly by means of regional launch of parasympathetic natural chemicals⁽⁵⁴⁾. In randomized, controlled scientific trials, therapy with 0.05% eyedrops 2 x/ day brought about improvement in keratopathy, increased Schirmer test worths, lowered symptoms (fuzzy vision, ocular dryness, international body sensation, as well as epiphora), as well as a decrease in the use of man-made tears^(55,56). This clinical enhancement was related to a decrease in inflammatory cells as well as inflammatory pens on the ocular surface and a boost in the variety of goblet cells in the conjunctiva⁽⁵⁶⁾.

4. CONCLUSION

Patients with dry eye disease have high pain sensitivity and low pain resistance,104 which can use up a significant amount of chair time. What would certainly assist are easy, inexpensive, and highly sensitive and also specific tests that could reliably aid in the medical diagnosis of dry eye. This will certainly then result in even more certain treatments for dry eye disease that could target the resource of the dryness. For now, we are unfortunately entrusted various diagnostic examinations that are not yet commonly accepted and also are commonly not reproducible. The therapy of dry eye has actually advanced from tear substitution alone to a reasonably based restorative formula. If the signs and symptoms are moderate, artificial tears of different kinds are advised. Cover health is valuable in the therapy of hyperevaporative dry eye, while collagen or silicon plugs can be utilized for partial occlusion of the efferent lacrimal ducts to treat severe hyposecretory dry eye.

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