



PERSPECTIVE ADVANCEMENTS IN UNDERSTANDING AND MANAGING DRY EYE DISEASE

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Accepted on: 12-01-2011; Finalized on: 04-03-2011.

ABSTRACT

Dry eye, can also be known as keratoconjunctivitis sicca, either due to insufficient tear production or excessive tear evaporation, both resulting in tear hyperosmolarity that leads to symptoms of discomfort and ocular damage. Additionally, the severity of dry eye symptoms appears to be correlated to lipid layer thickness. In normal tears there is a correct balance and appropriate quantity of lipid layer, aqueous layer and mucin layer constituents deficiency of any of the three layer of the tear film, defective spreading of the tear film, systemic diseases and some systemic and topical medications can disturb the ocular surface or tear film and cause dry eye disease. Current treatment of dry eye is mostly restricted to management of symptoms and thereby mainly includes replacing or conserving tears. New findings demonstrated that a chronic immune mediated inflammatory process plays an essential role in the pathogenesis of the dry eye disease. This article is designed to educate researchers, health care practitioners and managed care professionals about current and emerging treatments for dry eye syndrome. Recent developments in the etiology of dry eye have triggered the development of new treatment strategies, status and effectiveness of current and emerging therapies. After reading this publication, the readers will be able to describe the etiology of dry eye syndrome, or keratoconjunctivitis sicca (KCS), and risks of untreated disease, treatment of KCS and design appropriate management of disease for patient care.

Keywords: Dry eye syndrome, keratoconjunctivitis sicca (KCS), tear film.

INTRODUCTION

Dry eye syndrome, also known as keratoconjunctivitis sicca, is a common condition reported by patients who seek ophthalmologic care. Knowledge of the pathophysiology of dry eye has made significant strides in recent years; today, what was once thought to be a simple matter of the eye not producing sufficient tear flow is understood within the ophthalmologic community to be a multifactorial disease. Many family physicians and payers, however, may still perceive dry eye to be little more than an irritation and thus may not be aware of emerging specific potent therapies. Research has shown that dry eye is a complex condition, the hallmark of which is inflammation of the ocular surface and tear-producing glands¹. Keratoconjunctivitis sicca (KCS), or dry eye disease, is one of the most common complaints seen by ophthalmic specialists. In the current scenario of aging population and increasing environmental factors it is becoming even more prevalent. Dry eye is not a trivial complaint. The symptoms cause significant discomfort and substantially reduce the sufferer's quality of life. Available data suggests that it is a significant problem in the older age group. In a community study in Sweden the prevalence rate of 15% was found in the general population aged 55-72 years. This was done on the basis of symptoms of dry eye disease and positive finding on Schirmer's test, tear film break up time or rose bengal staining. Hyperosmolarity is a precipitating event for both aqueous tear deficient (ATD) and evaporative dry eye (EDE), leading to the pathological changes associated with dry eye: for ATD, the tear flow rate at which critical

osmolarity occurs will depend on evaporation rate and for EDE, the rate of evaporation that results in critical osmolarity will depend on the tear flow rate². An integrated unit has been formed by the ocular surface, lacrimal gland, and the central nervous system which provides appropriate feedback to maintain ocular surface wetting¹. Some of the medical conditions with which dry eyes are also associated are such as rheumatoid arthritis, lupus, scleroderma and Sjogren's syndrome³.

The modern definition of dry eye disease is based on the concept of the three layers of the tear film devised by Holly and Lemp⁴. Also, secondary factors such as pathological changes to the eyelids, cornea, or conjunctiva, can themselves disturb the normal function of the tear film. Neurotransmitters, hormones, and immunological processes play an important role in the regulation of the tear production by the lacrimal gland⁵. Various environmental factors like contact lenses, pollution, working at video display terminals can affect the tear film^{6, 7}. This multiplicity of causes and effects make a global definition difficult. However, the following definition has been proposed: Dry Eye is a disease of the ocular surface attributes to different disturbances of the natural function and protective mechanism of the external eye, leading to an unstable tear film during the open eye state. It can occur in all age groups. Dry eye syndrome is especially prevalent in people over age 65. It is estimated that 10 to 15 percent of Americans in this age group have one or more symptoms of this disease. In serious cases, dry eye syndrome can lead to photophobia and vision loss⁸.



In dry eye the rate of tear turnover at the ocular surface slows, causes a reduction in lacrimal gland tear flow⁹. Although the exact mechanism of this delayed tear clearance is unknown, it has been well documented in the literature^{10,11}. Decreased tear turnover, known as delayed tear clearance, increases tear osmolarity, which activates inflammatory pathways at the ocular surface. The inflammation decreases corneal sensitivity, which disrupts the neural feedback mechanism between the ocular surface and lacrimal glands. A recent Japanese study revealed a 17% rate of positive symptoms of dry eye. Most other studies reveal a prevalence rate between 11 and 17%. These studies found that symptoms of dry eye disease are more frequent above 50 years of age; however, they found no association of symptoms with sex. Song et al. found many of the properties of dry eye pathology by depriving mice of neurturin, a neurotrophic factor that aids in the development of specific postganglionic parasympathetic neurons and trigeminal sensory nerves¹². Recent studies have shown that immunological changes play a role in the pathogenesis of the dry eye even in post infectious and age related conditions.

High-risk populations for dry eye syndrome¹³⁻¹⁶

- Inflammatory disease (vascular, allergy, asthma)
- Autoimmune diseases (lupus, colitis)
- Postmenopausal women
- Diabetes mellitus
- Thyroid disease
- Sjogren's syndrome
- Corneal transplantation
- Previous keratitis or corneal scarring
- Extracapsular or intracapsular large-incision cataract surgery
- Laser in situ keratomileusis (LASIK)
- Systemic medications (diuretics, antihistamines, psychotropics, cholesterol-lowering agents)
- Contact lens wear
- Environmental conditions (allergens, cigarette smoke, wind, dry climate, air travel, chemicals, some perfumes)

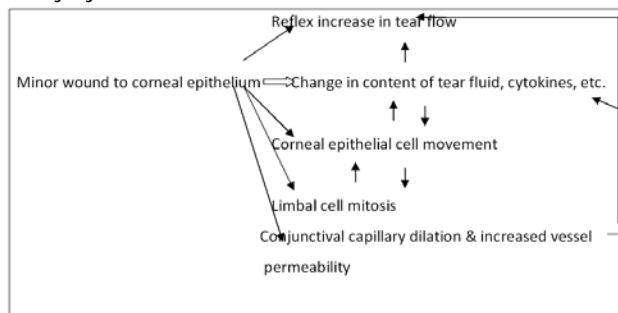
Symptoms of keratoconjunctivitis sicca¹⁷

- Dry sensation Foreign body or "gritty" sensation
- Redness Blurred vision
- Irritation/redness Contact lens intolerance
- Increased frequency of blinking Tearing
- Mucous discharge Burning/stinging

THE OCULAR SURFACE AND TEAR FILM

Tear film, corneal epithelium, conjunctiva, lacrimal glands, and the eyelids act as a functional unit in anatomic continuity and share feedback mechanism. This connectivity causes them to react to a stimulus as a single unit¹⁸. This is exemplified by the simultaneous reaction elicited amongst the various components by a single unit as shown in Fig. 1.

Figure 1: Flow chart showing various pathological changes in dry eye



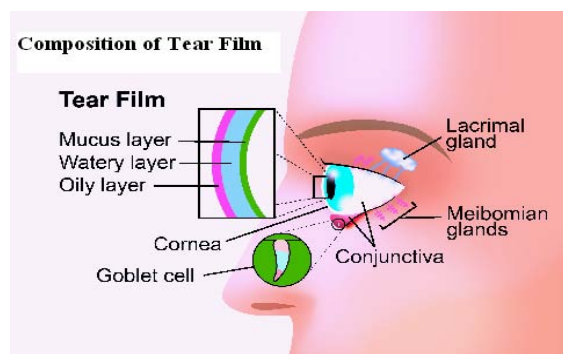
The relationship between ocular surface and tear film

The ocular surface is the interface between the eye and the outer world. It must function optimally to provide a refractive surface to enable the sharpest vision, and also react quickly to resist injury and protect the ocular structure. It is also important to realize that the ocular surface has to maintain the integrity in the face of continuous challenges by the shearing forces of blinking, air currents, humidity variation and foreign bodies, as also attacks by microorganisms. This causes the ocular surface and each of the components to be in a highly dynamic state to meet the changing needs created by changing environmental conditions¹⁸.

From all the components of the ocular surface, the tear film can be considered as an extra cellular matrix, playing a complex and active role with surrounding tissue. It functions to provide nutrients and communication pathways, distributes regulatory factors and provides a pathway for cells to reach the epithelium¹⁹.

Tear clean, lubricate and nourish the surface of the eye, as also provide physical and immune protection against infection. The tear film-air interface is the most powerful refractive surface of the eye. A small change in the tear film stability and/or volume will result in a significant change in the quality of the image at the retina; thus maintenance of a stable tear film is essential to vision²⁰. The tear film composition has been described having three layers as indicated in Fig. 2. There is now evidence that it is two layered structure where under the lipid layer lies an aqueous mucin gel, in which the mucus have a decreasing gradient of concentration from the epithelium to the surface^{5,21}.

Figure 2: Structure of eye along with the composition of tear film



Importance of the lipid layer in tear

The chief function of the lipid layer, however, is to retard water evaporation from the surface of the open eye²⁴. Studies suggest that normally, much of the tear film lipid layer is a structure that remains stable over a series of blinks, folding concertina-like, as it approaches the lower lid margin in the down-phase of the blink and unfolding in

the up-phase, with little mixing of lipid within the lipid layer or between the lipid layer and the reservoirs^{25,26}. When this dynamic stability of the tear film is disturbed there is functional disturbance such as variability of functional visual acuity and increased optical aberration^{18, 25}.

Table 1: Function of various layers of precorneal tear film^{22,23}

| | Mucin Layer | Aqueous Layer | Lipid Layer |
|----------|---|---|---|
| Source | Conjunctival goblet cells, conjunctival and corneal epithelial cells | Main and accessory lacrimal glands | Meibomian glands |
| Function | <p>Formation of glycocalyx renders the ocular surface hydrophilic.</p> <p>Allows the viscosity of tears to change as per the shear rate of blinking.</p> <p>Maintains the dioptric integrity of the tear film in the inter-blink interval.</p> <p>Prevents adhesion of foreign bodies to the ocular surface.</p> <p>Heavily glycosylated proteins, mucins</p> <ul style="list-style-type: none"> • Immunoglobulins • Antimicrobial proteins | <p>Creating the proper environment for the epithelial cells.</p> <p>Provides essential nutrients and oxygen to the cornea.</p> <p>Allows cell movement over the ocular surface.</p> <p>Provides many of the growth factors necessary for ocular surface health.</p> <p>Contains lysozyme, which is an anti-bacterial substance.</p> | <p>Prevents the evaporation of tears.</p> <p>Enhance stability of the tear film.</p> <p>Lipid layer act as vapour barrier</p> |

Stability of the tear film maintains stable vision. Although patients with dry eye disease often describe fluctuation of vision, particularly when reading or using video display terminals, measured Snellen acuity is not decreased until significant ocular surface damage is present. This maintenance of Snellen acuity as measured by a stable optotype occurs because the patient is able to blink frequently enough to read the chart during the examination. Novel techniques of measuring visual acuity have been developed by Tsubota that determine functional visual acuity (FVA)¹⁸. The technique rapidly presents optotypes in such a fashion that the patient can not compensate by blinking, thus determining ambient visual function. The technique confirms visual functional alteration in dry eye and has been used to monitor some therapies of dry eye¹⁸. Mathers and Lane have put forward the concept that a stable tear film is one in which a minimum amount of tears evaporate. The evaporation rate is determined primarily by the status of the lipid layer and the protein constituents of the tear film (primarily lipocalin), the mucin coating of the epithelial cells, and the aqueous component of lacrimal secretions, the lipid layer being the key^{27, 28}. There is some evidence that evaporation is affected by lipid layer thickness, but it is currently not known specifically how lipid composition alters either the stability or thickness of the lipid layer, despite the fact that thicker TFL correlates with better tear stability²⁹. It has been proposed, though, that the polar lipids act as a surfactant that helps spread the non polar lipids over the aqueous component of the tear film, provide a barrier between the two layers, and provide a structure that supports the non polar phase, which is responsible for creating a seal that decreases evaporation from the tear film^{25, 30, 31}.

Tear film regulation and function

In normal tears there is a correct balance and appropriate quantity of lipid layer, aqueous layer and mucin layer constituents. Between blinks, tear film thins by evaporation and lipid molecules from the outer layer begin to migrate through the aqueous layer to the ocular surface. These increases the surface tension of the tear film and eventually causes it to the break up and form a dry spot. At this point, a neural signal is issued that stimulates additional tear secretion³². The next blink then repairs the rupture by removing the lipid molecule that migrated to it, restoring a thick aqueous layer. Thus, with respect to tear function and regulation, the compositional aspect, which involves the ocular surface epithelia (corneal and conjunctival) and external adnexae, and the hydrodynamic aspect, which involves eyelid blinking and closure, constitute key elements in regulation and maintenance of a stable tear film⁷.

Omega-3 EFAs also plays an important role in the synthesis of meibum, (oil secreted by meibomian glands). People with omega-3 EFA deficiency typically have a thicker meibomian gland secretion. The use of omega-3 EFA supplements results in clearing and thinning of meibomian gland secretions which in turn improves symptoms of dry eye³³. The spreading of the tear film on the ocular surface to form the complexly structured preocular tear film is the consequence of blinking³⁴. The sequential operation of the orbicular and levator muscles of the lids spread the tear fluid and reconstruct the tear film architecture distributed by the evaporation of water and by environment contamination during the inter blink period. The movement of the lids exerts a significant pressure on the bulbar surface at each blink, with a



retropulsion of the eye of 0.7 to 1 mm (up to 2 mm on forced blinking)^{35, 36}. If not protected by an efficient viscoelastic tear film, the applied shear forces can damage the ocular surface epithelia³⁷.

Dysfunction of the ocular surface and tear film

Deficiency of any of the three layers of the tear film, defective spreading of the tear film, systemic diseases and some systemic and topical medications can disturb the ocular surface or tear film and cause dry eye disease^{18, 38}. The National Eye Institute classification of dry eye has two major divisions: Aqueous layer deficiency and evaporative deficiency. This helps in separating patients according to the main causative factor of the disease³⁹.

The vicious cycle of increased evaporation and dry eye

Tear evaporation has a definitive role in ocular surface disease. It triggers the vicious cycle of evaporative dry eye and also has a role in build up and maintenance of the vicious cycle of damage in tear deficiency dry eye⁴⁰.

DIAGNOSIS OF DRY EYE⁴¹⁻⁴³

Each form of dry eye has certain global features in common, including

1. A set of characteristic symptoms
2. Ocular surface damage
3. Reduced tear film stability
4. Tear hyperosmolarity

The global features of dry eye disease can be identified by the following type of diagnostic test:

Diagnostic tests

The poor correlation between reported symptoms and clinical signs, along with the aforementioned limitations of clinical tests, make it difficult to diagnose dry eye in its mild form. For patients with mild irritation symptoms an unstable tear film with normal aqueous tear production can be detected by a rapid TBUT, and by ocular surface dye staining a minimal pattern or no pattern may be detected. One or more of the following tests can be used for diagnosis, in patients with moderate to severe aqueous tear deficiency: TBUT, ocular surface dye staining pattern (rose bengal, fluorescein, or lissamine green), or Schirmer wetting test.

These tests should be performed in the above mentioned sequence, because the Schirmer test can disrupt tear film stability and cause false-positive ocular surface dye staining. Other tests helpful in evaluating selected patients, but some have limited availability include tear osmolarity, fluorescein clearance, impression cytology, tear function index, and tear protein analysis (including lactoferrin, lysozyme, immunoglobulin, and albumin)¹³. Corneal sensation should be assessed when trigeminal nerve dysfunction is suspected⁴⁴. A laboratory and clinical evaluation for autoimmune disorders should be

considered for patients with significant dry eyes, other signs and symptoms of an autoimmune disorder (e.g., dry mouth, rash, arthritis, colitis, or renal dysfunction), or a family history of autoimmune disorders.

TREATMENT OF DRY EYE

1. House-hold remedies⁴⁵

Several aspects are to be considered while treating dry eye patients.

- Like controlling the humidity by using a humidifier in the living and working areas, particularly the bedroom. Ideally, the humidity should remain at 40 to 50 percent.
- Four drops of preservative free artificial tears in each eye every day.
- Reduction or discontinuation of systemic drugs for allergies, insomnia and nervous disorders.
- As in mild dry eye good lid hygiene should be advised.
- As suggested washing the faces with a Turkish face cloth twice a day, followed by a 30-73 second warm tap-water compress using a face cloth over both closed eyelids, also benefits such patients. After the warm (as opposed to hot) tap-water compress, the lower lid margin of each eye should be wiped once with a tightly wound dry cotton-tipped applicator. The heat and mild friction created with a single wipe from side to side removes excess oils, mucous and debris from the lower lid margin. Also, this will draw reflex tearing from the lacrimal gland, if it's available. Even a small amount of reflex tearing will decrease the need for artificial tear solutions.
- Moist chamber spectacles can also be considered when patient compliance is not a problem.

2. Current treatment strategies

Current treatment of dry eye is largely palliative, mostly restricted to management of symptoms. Therapy mainly includes replacing or conserving tears⁴⁶. With the understanding of the new pathogenesis of the dry eye disease process is improving, new strategies are emerging in the treatment of this condition.

a. Tear substitution

Tear replacement by topical artificial tears and lubricants is currently the most widely used therapy for dry eyes, and a variety of components are used to formulate a considerable number of commercially available preparations. Tear substitutes are used to increase humidity at the ocular surface and to improve lubrication with the secondary benefit of visual improvement. Topographic studies have shown that after instillation of artificial tears, the surface regularity index, the surface asymmetric index⁴⁷ and potential visual acuity is better in a patient with dry eye. As the drop is washed off within a few minutes⁴⁸, tear substitutes have been improved by the addition of absorptive polymers in their formulations. Among the various available tear molecules,



carboxymethyl cellulose seems to have the highest retention rate on the ocular surface.

Most commercially available preparation contains preservative that provides stability and prevents contamination. Use of tears with preservatives on long term in an already compromised ocular surface can aggravate the surface damage. The common preservatives used are benzalkonium chloride, chlorbutanol and thiomersal. Tears with preservative are preferred in condition, which require a artificial tears on a short term basis^{49, 50}. The introduction of preservative-free tears is the single most important contribution in the formulation of tears substitutes. However, these are expensive and require patient compliance.

b. Tear preservation

Punctal occlusion is one of the most useful and practical therapies for conserving tears. This technique increases tear volume, and the retention of aqueous tears also may increase the concentration of biologically active constituents in tears^{51, 52}.

c. Decreasing tear viscosity

Patients with clinically observable stagnant mucus tend to develop filamentous and/or coarse mucus plaques. Acetyl cysteine in 10-20% concentration can decrease the viscosity of the mucin and lead to an alleviation of symptoms. The solution; however are irritating, costly and malodorous⁵³.

d. Stimulation of tears

A number of medications have been used to stimulate the lacrimal glands to produce tears. These include mucolytic agents (bromhexine and ambroxol), cholinergic agents (carbachol, bethanecol, pilocarpine) and eledosin. Oral bromhexine and its derivative ambroxol have demonstrated variable results in clinical trials but have sometimes been associated with side effects such as generalized nausea, sweating and rashes and therefore have not achieved widespread use. Topical eledosin, extracted from the salivary gland of Mediterranean octopus *Eledone moscata*, has been found to increase tear volume and tear flow. Topical application of pilocarpine has been found to have no effect on the stimulation of tear secretion in animal experiments. Unlike oral pilocarpine, which objectively increases tear production and flow, and improves symptoms of dry eyes? Stimulation of tear production is not a widespread therapeutic strategy due to the scarcity of prospective studies and their potential side effects when given orally. These agents may not be useful when the disease process has already caused extensive damage to the lacrimal gland parenchyma or blocked the lacrimal ducts through conjunctival scarring. Stimulation of previously inflamed lacrimal glands and conjunctiva could deliver pro-inflammatory tears to the ocular surface, worsening the disease. Improvement in reports of DES symptoms and an increase in tear production have been reported after six months of omega-6 EFA treatment⁵⁴.

NEW METHODS OF TREATMENT OF DRY EYE DISEASE

The therapies describe above only improve the signs and symptoms of dry eye. New findings have demonstrated that a chronic immune-mediated inflammatory process plays an essential role in the pathogenesis of dry eye disease. Increased inflammatory cytokines have also been demonstrated, as has been lack of hormonal support or altered innervations.

The following are the main anti-inflammatory, immunomodulatory, or hormonal therapeutic agents tested or under investigation for the treatment of dry eye.

1. Cyclosporine A

Chronic immune-mediated inflammatory process appears to play an essential role in the pathogenesis of dry eye disease. Topical cyclosporine A (CSA), a potent suppressor of T-cell function stimulates aqueous tear production⁵⁵. It is effective in reducing lymphocyte infiltration, facilitating apoptosis of lymphocytes in the lacrimal glands and conjunctiva, while suppressing apoptosis of lacrimal gland and conjunctival epithelial cells, contributing to reduction in the underlying inflammation⁵⁶. Studies have shown that significant improvement in dry eye signs and symptoms when cyclosporine is used in a concentration of 0.05% and 0.1% compared with vehicle⁵⁷. One study concludes that long term use of topical CSA ophthalmic emulsions at doses that are clinically efficacious for treating dry eye disease will not cause any systemic side effects⁵⁸. Eun Chul Kim, et al., compared the efficacy of vitamin A (retinyl palmitate) and cyclosporine A 0.05% eye drops in treating patients with dry eye disease. Both vitamin A eye drops and topical cyclosporine A 0.05% treatments found to be effective for the treatment of dry eye disorder⁵⁹.

2. Topical corticosteroids⁶⁰

This therapy is useful for short-term treatment to reduce the initial inflammation. Long-term use would be hampered with the significant risk of side effects like raised intraocular pressure, cataract formation, and secondary infections. Topical steroids (preferably non-preserved) are therefore, more suitable for acute management of dry eye exacerbations.

3. Sodium hyaluronate⁶¹⁻⁶⁷

In study, sodium hyaluronate eye drops did not improve subjective symptoms in 104 dry eye patients, whereas it did improve fluorescein staining scores in these patients. This was followed by several other recent studies that showed that hyaluronate eye drops were useful in improving subjective symptoms as well as the ocular health of dry eye patients, treating lipid tear-deficient patients and treating Sjogren's syndrome patients. Sodium hyaluronate also seemed to have protective effects on the corneal epithelium.



4. Sex hormones⁶¹⁻⁶⁷

The relationship between hormone levels and tear production is obviously complex but it is still unclear how the different hormones regulate the functional activity of these tissues. Oestrogen receptors are found in the meibomian glands and androgen receptors in lacrimal glands, meibomian glands, cornea and conjunctiva. A strong role for androgen in maintaining an anti-inflammatory state of the ocular surface has been hypothesised. Investigations have shown that the systematic androgen therapy suppresses the inflammation and stimulate the functioning of the lacrimal glands in female mouse models of Sjogern's syndrome. Symptomatic improvement of dry eyes with systemic oestrogen deficiency has been reported. A clinical trial reported on the use of oestrogen as a potential therapy for dry eyes. Another study has shown increase in dry eye symptoms in post-menopausal woman on systemic oestrogen therapy.

5. Autologous serum⁶¹⁻⁶⁷

Autologous serum has been reported to be useful in the treatment of severe dry eyes and persistent epithelial defects, as they are known to deliver components such as vitamin A, EGF and TGF. Poon et al., used autologous serum in patients with keratoconjunctivitis sicca (KCS) and persistent epithelial defects (PED) in response to conventional treatment. Patient with autologous serum diluted 20% in saline for 4 weeks showed improvement in rose bengal and fluorescein staining. The obvious disadvantage is that the patient's serum needs to be drawn and the serum can be kept refrigerated only for a short period of time.

6. Botulinium toxin⁶¹⁻⁶⁷

Injection of Botulinium toxin into the orbicularis oculi of Sjogern's syndrome patient with severe xerophthalmia and blpherospasm has been shown to increase tearing, and its injection into the medial aspect of the eyelids of both normal controls and dry eye patient produced a decreased lacrimal drainage. Its actual clinical utility is yet to be evolved.

Table 2: Marketed formulations used in treatment of dry eye syndrome⁶⁸

| S. no. | Generic Name | Trade name |
|--------|----------------------------------|------------------------------|
| 1 | Bacitracin/polymyxin B | Polysporin |
| 2 | Cyclosporine ophthalmic emulsion | Restasis |
| 3 | Hydroxypropyl cellulose | Lacrisert |
| 4 | N-acetylcysteine | Mucomyst |
| 5 | Loteprednol etabonate | Lotemax |
| 6 | Pilocarpine | Salagen |
| 7 | Prednisolone acetate | Pred Forte |
| 8 | Sodium carboxymethyl cellulose | TheraTears (0.25 percent) |

STEPWISE MANAGEMENT OF DRY EYES

Step I Mild disease

- Artificial tears 3-4 times
- Moderate to severe disease
- Artificial tears 8-10 times a day
- Preservative free tears as often as the patient needs
- Lubricating ointment at bedtime
- Treatment of lid disease
- Treatment of Rheumatoid arthritis by methotrexate if disease is active.

Step II Punctal occlusion

- Silicone punctal plugs
- Punctal cautery if Schirmer's test is repeatedly low (< 1mm)

Step III

- Short course of preservative free methyl prednisolone
- Topical cyclosporine therapy

Step IV

- Autologous serum
- P2Y2 purinergic receptor agonists

CONCLUSION

The treatment of dry eye syndrome has relied predominantly on artificial tears and lubricants. This palliative approach generally has been successful at relieving the signs and symptoms of mild to moderate disease and, in rare cases, has slowed the progressive damage to the cornea and conjunctiva that occur over time with dry eye. Overall, decades of research has shown a strong correlation between dry eye symptoms and the state of the tear film lipid layer, as well as a clear connection between the status of the lipid layer and the osmolarity of the tear film. More recent work with supplementation of the tear film lipids has also shown effectiveness in stabilizing the TFL. Increasing research and advancing knowledge has identified an inflammatory component to dry eye syndrome and has focused treatment efforts at addressing this newly identified etiology. Topical cyclosporine emulsion 0.05 percent is the first and currently only FDA-approved targeted immunomodulatory or anti-inflammatory product to combat the underlying source of disease. Future investigation of the mechanism of interaction of the lipids, proteins, and electrolytes of the tear film should further improve our management of tear film instability and dry eye. All eye care professionals will need to diligently familiarize themselves with the latest research regarding dry eye management. Understanding the mechanisms of action and the standard time course of treatment will enable doctors to properly educate dry eye patients and ensure adherence to the treatment regimen.



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