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DRY EYE: A CRITICAL REVIEW

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ABSTRACT

Our understanding of keratoconjunctivitis sicca (KCS), also known as dry eye syndrome, has been changed over recent years. Until lately, the condition was thought to be merely due to aqueous tear insufficiency. Today, it is understood that KCS is a multifactorial disorder due to inflammation of the ocular surface and lacrimal gland, neurotrophic deficiency and meibomiangland dysfunction.

KEYWORDS: Until lately, the condition was thought to be merely due to aqueous tear insufficiency.

INTRODUCTION

Dry eye occurs when there is inadequate tear volume or function, resulting in an unstable tear film and ocular surface disease. It is an extremely common condition, particularly in postmenopausal women and the elderly. Dry eye disease is a multifactorial disease of the ocular surface and tear film accompanied by increased osmolarity of the tear film and inflammation of the ocular surface. Sjögren syndrome is an autoimmune inflammatory disease of which dry eyes is a feature.

Xerophthalmia describes a dry eye associated with vitamin A deficiency. Xerosis refers to the extreme ocular dryness and keratinization that occurs in eyes with severe conjunctival cicatrization.

AIM AND OBJECTIVES

1. To review the concept of dry eye disease.

2. To understand the etiopathogenesis & management of dry eye disease.

MATERIAL AND METHODS

Material has been collected from modern textbooks research articles and electronic databases.

PHYSIOLOGY OF DRY EYE?

Tear film constituents

The tear film has three layers

1. Lipid layer secreted by the meibomian glands.
2. Aqueous layer secreted by the lacrimal glands.
3. Mucous layer secreted principally by conjunctival goblet cells. The constituents are complex, with as many as a hundred distinct proteins identified.

Spread of the tear film

The tear film is mechanically distributed over the ocular surface through a neuronally controlledblinking mechanism. Three factors are required for effective resurfacing of the tear film

1. Normal blink reflex.
2. Contact between the external ocular surface and the eyelids.
3. Normal corneal epithelium.

LIPID LAYER

- **Composition**

The outer lipid layer is composed of a polar phase contain ing phospholipids adjacent to the aqueous-mucin phase and a non-polar phase containing waxes, cholesterol esters and triglycerides.

- **Functions**

1. To prevent evaporation of the aqueous layer and maintain tear film thickness.
2. To act as a surfactant allowing spread of the tear film.
3. Deficiency results in evaporative dry eye.

AQUEOUS LAYER

- Secretion: Secretion of tears has basic (resting) and much greater reflex components.The latter occurs in response to corneal and conjunctival sensory stimulation, tear break-up

and ocular inflammation and is mediated via the fifth cranial nerve. It is reduced by topical anaesthesia and falls during sleep. Secretion can increase 500% in response to injury.

- **Composition**

1. Water, electrolytes, dissolved mucins and proteins
2. Growth factors derived from the lacrimal gland, the pro- duction of which increases in response to injury.
3. Pro-inflammatory interleukin cytokines that accumulate during sleep when tearproduction is reduced.

- **Functions**

1. To provide atmospheric oxygen to the corneal epitheliume Antibacterial activity due to proteins such as IgA, lysozyme and lactoferrin.
2. To wash away debris and noxious stimuli and facilitate the transport of leukocytes after injury.
3. To optically enhance the corneal surface by abolishing minute irregularities.

MUCOUS LAYER

- Composition: Mucins are high molecular weight glycoproteins that may be transmembrane or secretory in type.Secretory mucins are further classified as gel-forming or soluble. They are produced mainly by conjunctival goblet cells but also by the lacrimal glands.
- Functions

1. To permit wetting by converting the corneal epithelium from a hydrophobic to a hydrophilic surface.
2. Lubrication

MECHANISM OF DISEASE

The four core inter-related mechanisms thought to be responsible for the manifestations of dryeye are tear instability, tear hyperosmolarity, inflammation and ocular surface damage.

Inflamma- tion in the conjunctiva and accessory glands as well as the ocular surface is present in 80% of patients with KCS and may be both a cause and consequence of dry eye, amplifying and perpetuating disease. The presence of inflammation is the rationale for

specific anti- inflammatory measures such as steroid therapy. There is a strong association between dry eye syndrome and reduced levels of systemic androsterone sulphate and epiandrosterone sulphate.

EFFECT OF ENVIRONMENTAL FACTORS

As well as the basic classification, DEWS draws attention to the effect of the environment on the type of dry eye with which a patient presents. These can be both internal, such as age, hormonal status and behaviour patterns, and external, such as the exacer- bation of evaporative factors in an atmosphere with low relative humidity.

SJOGREN SYNDROME

Sjögren syndrome (SS) is an autoimmune disorder characterized by lymphocytic inflammation and destruction of lacrimal and salivary glands and other exocrine organs. The classic clinical triad consists of dry eyes, dry mouth and parotid gland enlargement.

CLINICAL FEATURES

SYMPTOMS

1. feelings of dryness, gritti- ness and burning
2. Stringy discharge
3. Transient blurring of vision
4. Redness
5. Crusting of the lids

SIGNS

1. Conjunctiva - Redness.
2. Cornea - Punctate epithelial erosions that stain well with fluorescein
3. Tear film - In the normal eye, as the tear film breaks down, the mucin layer becomes contaminated with lipid but is washed away. In the dry eye, the lipid-contaminated mucin accumulates in the tear film as particles and debris that move with each blink.

INVESTIGATIONS

The aim of investigation is to confirm and quantify a clinical diagnosis of dry eye. The reliability of tests improves as the severity of dry eye increases. The tests measure the following parameters:

- Stability of the tear film as related to its break-up time (BUT).

- Tear production (Schirmer, fluorescein clearance and tear osmolarity).
- Ocular surface disease (corneal stains and impression cytology).

Schirmer test

The Schirmer test is a useful assessment of aqueous tear production. The test involves measuring the amount of wetting of a special (no. 41 Whatman) filter paper, 5 mm wide and 35 mm long. The test can be performed with or without topical anaesthesia. In theory, when performed with an anaesthetic (Schirmer 2) basic secretion is measured and without anaesthetic (Schirmer 1) it measures maximum basic plus reflex secretion. In practice, however, topical anaesthesia cannot abolish all sensory and psychological stimuli for reflex secretion.

Thetest is performed as follows

- Excess tears are delicately dried. If topical anaesthesia is applied the excess should be removed from the inferior fornix with filter paper.
- The filter paper is folded 5 mm from one end and inserted at the junction of the middleand outer third of the lower lid, taking care not to touch the cornea or lashes
- The patient is asked to keep the eyes gently closed.
- After 5 minutes the filter paper is removed and the amount of wetting from the fold measured.
- Less than 10 mm of wetting after 5 minutes without anaes- thesia or less than 6 mmwith anaesthesia is considered abnormal.

Results can be variable and a single Schirmer test should not be used as the sole criterion for diagnosing dry eye, but repeatedly abnormal tests are highly supportive.

Other investigations done in dry eyes

1. **Fluorescein clearance test** and the tear function index may be assessed by placing 5 µlof fluorescein on the ocular surface and measuring the residual dye in a Schirmer strip placed on the lower lateral lid margin at set intervals. Delayed clearance is observed inall dry eye states.
2. **Tear film osmolarity** measurement techniques are available and are emerging as an accurate means of diagnosis. The threshold value that distinguishes between a healthy eye and an eye with dry eye syndrome varies from 305 mOsm/l and 316 mOsm/l, depending on the degree of tear film instability. Tear osmolarity may not correlate with ocular

symptoms, but it does correlate with effective treatment when evaluated in the long term.

3. **Tear constituent** measurement. Tear samples can be assayed for the presence of markers known to be elevated (e.g. matrix metalloproteinase-9) or decreased (e.g. lactoferrin) in dry eye.
4. **Phenol red thread test** uses a thread impregnated with a pH- sensitive dye. The end of the thread is placed over the lower lid and the length wetted (the dye changes from yellow to red in tears) is measured after 15 seconds. A value of 6 mm is abnormal. It is comparable to the Schirmer test but takes less time to perform.
5. **Tear meniscometry** is a technique to quantify the height and thus the volume of thelower lid meniscus.
6. **Impression cytology** can determine goblet cell numbers.
7. **Slit lamp examination:** This test checks the amount of tears your eyes produce. The provider shines a light into each of your eyes and uses a microscope to examine youreyes and eyelids.

TREATMENT

DEWS have produced guidelines based on earlier International Taskforce Guidelines for Dry Eye, in which suggested treatment options depend on the level of severity of disease graded from 1 to 4.

Level 1

- Education and environmental/dietary modifications

i. Establishment of realistic expectations and emphasis on the importanceof compliance.
ii. Lifestyle review including the importance of blinking whilst reading, watching television or using a computer screen (which should be orientated below eye level to minimize palpebral aperture size) and themanagement of contact lens wear.
iii. Environmental review, e.g. increasing humidity may be possible for someenvironments.
iv. Instillation aids for eye drops (manufacturer-supplied or makeshift, suchas nut-crackers to hold plastic bottles) should be advocated for patients with reduced dexterity (e.g. rheumatoid arthritis).
v. Caution the patient that laser refractive surgery can exacerbate dry eye.

- Systemic medication review to exclude contributory effects and eliminate offending agents. Discontinuation of toxic/ preserved topical medication if possible.
- Artificial tear substitutes including gels and ointments

- Eyelid therapy - Basic measures such as warm compresses and lid hygiene for blepharitis. Reparative lid surgery (e.g. entropion, ectropion, excessive lid laxity orscleral show) may be considered as an early measure.

Level 2

- Non-preserved tear substitutes
- Anti-inflammatory agents such as topical steroids, oral omega fatty acids and otheragents such as topical ciclosporin.
- Tetracyclines (for meibomianitis, rosacea).
- Punctal plugs.
- Secretagogues, e.g. pilocarpine, cevimeline, rebamipide.
- Moisture chamber spectacles and spectacle side shields.

Level 3

- Serum eye drops. Autologous or umbilical cord serum.
- Contact lenses.
- Permanent punctal occlusion.

Level 4

- Systemic anti-inflammatory agents.
- Surgery

Eyelid surgery such as tarsorrhaphy

TEAR SUBSTITIUTES

Tear substitutes have a relatively simple formulation that cannot approximate the complex components and structure of the normal tear film. Their delivery is also periodic rather than continuous. Almost all are based on replacement of the aqueous phase of the tear film. There are no mucus substitutes and paraffin is only an approximation to the action of tear lipids. The optimal frequency of instillation varies with agent and with severity.

- Drops and gels

i. Cellulose derivatives (e.g. hypromellose, methylcellulose) areappropriate for mild cases.
ii. Carbomer gels adhere to the ocular surface and so are longer-lasting.
iii. Other agents include polyvinyl alcohol (PVA), which increases the persistence of the tear film and is useful in mucin deficiency, sodium hyaluronate, povidone, glycerine,

propylene glycol, polysorbate andothers.

iv. Diquafosol is a newer agent that works as a topical secretagogue.

- Ointments containing petrolatum (paraffin) mineral oil can be used at bedtime to supplement daytime drops or gel instillation.
- Eyelid sprays are applied to the closed eye and typically contain a liposome-based agent that may stabilize the tear film and reduce evaporation.
- Artificial tear inserts emplaced once or twice daily offer extended duration treatment and are preferred by some patients.
- Mucolytic agents - Acetylcysteine 5% drops may be useful in patients with corneal filaments and mucous plaques. Manual debridement of filaments may also be useful.
- Haemoderivative treatment has been used to manage severe ocular surface disease including graft-versus-host-related dry eye disease, Sjögren syndrome, post-LASIK dry eye persistent epithelial defects and recurrent erosions.

DISCUSSION

The pathogenesis of dry eye may be due to stress on the ocular surface (infection, environmental factors, stress, genetic factors, and antigens). Dry eye is a chronic disease, particularly among older people, but proper treatment decreases symptoms and, eventually, ocular damage.

CONCLUSIONS

Dry eye syndrome consists of a wide spectrum of disorders with different causes. A thorough history and investigation is necessary to identify the cause of dry eye. Useful clinical tests for assessing the severity of the condition include Schirmer, fluorescein dye, and tear break up timetests. Management depends on an accurate diagnosis and the severity of the condition.

Treatments that replenish deficient tears include gels, ointments in mild to moderate disease. Other treatment modalities such as topical steroids, immunomodulating drugs, antibiotics, bandage contact lenses, and amniotic membrane transplantation may be used in more severe cases. In severely dry eyes, surgical intervention such as punctal occlusion can be employed to minimize tear drainage. Certain conjunctival and lid operations can also be performed to treatspecific causes.

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