

Dry eye

Speaker - Dr. Teja Thirukovela (PG –MS ophthalmology)

Moderator – Dr.R.Sudha

Proff and HOD

Department of ophthalmology

 When you blink, a film of tears spreads over the eye. This keeps the eye's surface smooth and clear. This tear film is important for good vision.

- Dry eye disease (DED), also known as dry eye syndrome (DES) or keratoconjunctivitis sicca (KCS), is characterized by
- Ocular irritation and
- Visual disturbance
- resulting from alterations of the tear film and ocular surface.

EPIDEMIOLOGY

- Absence of consensus on a single reliable diagnostic test.
- Questionnaire based tests reveal a prevalence of 5% to 16% or from 27% to 33%

DEWS II DEFINITION

 The 2017 report for the International Dry Eye Workshop (DEWS II) was a 2-year effort with 12 subcommittees made up of 150 experts from 23 countries. The DEWS II report updated the definition of dry eye as follows:

DEWS II DEFINITION

"Dry eye is a multifactorial disease of the ocular surface characterized by

- a loss of homeostasis of the tear film,
- and accompanied by ocular symptoms,

in which

- tear film instability and hyperosmolarity,
- ocular surface inflammation and damage,
- and neurosensory abnormalities
- play etiological roles."

- The definition emphasizes the multifactorial nature of DED,
- Where loss of homeostasis of the tear film is the central pathophysiological concept.
- It also recognizes the role of neurosensory abnormalities in the development of DED

In simple terms-

Our eyes need tears to stay healthy and comfortable.

- If your eyes do not produce enough tears or
- When your eyes do not make the right type of tears or tear film,
- Or If the tears evaporate quickly ,

It can cause dry eye

- The effects of DED can vary from
- minor inconvenience to
- rare sight-threatening complications

- Complications:
- Eye infections. Your tears protect the surface of your eyes from infection.
 Without adequate tears, you may have an increased risk of eye infection.
- Damage to the surface of your eyes. If left untreated, severe dry eyes may lead to eye inflammation, abrasion of the corneal surface, corneal ulcers and vision loss.
- Decreased quality of life. Dry eyes can make it difficult to perform everyday activities, such as reading.



TEAR PRODUCTION AND DRAINAGE

- The lacrimal gland is located in the superolateral aspect of the eyelid below the eyebrow(s).
- It secretes watery (aqueous) tears and produces about 0.2 ml of tears in 24 hours.
- Aqueous tears flow downward and inward toward the tear drainage system at the inner canthus.



- In addition to aqueous tears, several glands located in the conjunctiva and eyelid margins secrete oily and <u>sticky (mucous) tears</u>.
- The meibomian glands are located within the tarsal plate of the eyelid and secrete oily tears.
- The glands of Zeiss, Moll, Wolfing, and Krause secrete sticky tears.



- These three types of tears provide moisture and protection to the surface of the eye(s).
- With each blink, tears are pushed across the eye toward the puncta located at the medial junction of the upper and lower eyelids.
- From the puncta, tears are pushed into the canaliculi and then into the lacrimal sac.



 They are drained from the lacrimal sac and nasolacrimal duct to the inside of the nose and down the throat

Layers of the tear film



- The tear film has three distinct layers.
- The <u>outermost layer</u> is secreted by the meibomian glands. This <u>lipid</u> layer prevents evaporation of the underlying tear layers, keeping the cornea continually moist.
- The <u>middle layer</u> consists of <u>aqueous</u> tears from the lacrimal gland. These tears provide nutrients that help sustain the health of the cornea.
- The *innermost layer* is composed of mucous, which provides stability to the tear film as well as lubrication and also functions to trap and remove debris.

Factors effecting the eye

Internal mileu

- Low blink rate,
- Wide lid aperture,
- Aging,
- Low androgen levels,
- High estrogen levels,
- And systemic drugs affect

External mileu

- Low relative humidity,
- Air conditioning,
- Air travel,
- High wind velocity,
- And other occupational environmental factors,
- Such as video display terminal use

Reduced aqueous tear flow Increased evaporation of the aqueous part of tears

Increased evaporation

Tear film instability

Tear Hyperosmolarity

Pathophysiology

Damages ocular epithelium

Apoptotic cell death Loss of goblet cells Deficient mucus production

Cascade of inflammatory pathways

Progression of Disease

- In the early stages of DED- Inflammation and mechanical irritation stimulates reflex secretion from the lacrimal gland and increased blink rate.
- Over time, damage to the ocular surface leads to <u>reduction in corneal sensation</u> <u>and impaired reflex tearing.</u>
- In advanced cases, chronic <u>conjunctival damage can lead to metaplasia and</u> <u>keratinization.</u>





Ocular manifestations

- Typical complaints include
- Burning,
- Itching,
- Foreign body sensation,
- Stinging,
- Dryness,
- Photophobia,
- Ocular fatigue, and
- Redness.

Diurnal variation

- Patients commonly describe a diurnal pattern of aqueous tear deficiency
- with progression of symptoms over the day and decompensation
- in particular environmental conditions, such as low humidity in airline cabins, climate control, and the use of video display terminals.
- Conversely,
- Night time exposure and inflammatory conditions often present with worst discomfort upon awakening

Signs

- Common Signs Of DED Include
 Conjunctival Injection
- Decreased Tear Meniscus,
- Photophobia,
- Increased Tear Debris, And Loss Of
- Corneal Sheen
- Found More Commonly In The Exposed Interpalpebral Fissure.
- Paradoxical Epiphora In DED Is
 Usually A Result Of Reflex Tearing.



DRY EYE CLASSIFICATION





Aqueous Tear-Deficient Dry Eye

- Sjögren described KCS in 1933. Consequently, defective lacrimal tear secretion is subdivided into
- Non-Sjögren's tear deficiency (NSTD)
- Sjögren's syndrome tear deficiency (SSTD).
- NSTD has no association with systemic autoimmune disease, which is a cardinal feature of SSTD.

Sjögren's Syndrome Tear Deficiency

 Sjögren's syndrome is a clinical condition of aqueous tear deficiency combined with dry mouth.

Sjögren's syndrome

Primary (patients without a defined connective tissue disease)

Secondary (patients who have a confirmed connective tissue disease).

Primary SSTD

- Aqueous tear deficiency combined with symptoms of dry mouth,
- presence of autoantibodies to
- Ro(SSA) or La(SSB) antigens,
- decreased salivary secretion,
- presence of lymphocytic foci on minor salivary gland biopsy.

Seconday SSTD

- Asociated with rheumatoid arthritis,
- Systemic lupus erythematosus, polyarteritis nodosa,
- Wegener's granulomatosis,
- systemic sclerosis,
- primary biliary cirrhosis,
- mixed connective tissue disease.



Non-Sjögren's Tear Deficiency

NSTD can occur from

- Primary lacrimal gland deficiencies,
- Secondary lacrimal gland deficiencies,
- Obstruction of lacrimal gland ducts,
- Or reflex hyposecretion

a)Primary lacrimal gland deficiencies

Primary lacrimal gland deficiencies include

- Age-related DED,
- Congenital alacrima,
- And familial dysautonomia (riley–day syndrome)
- The most common form of NSTD is age-related DED
- (Which is associated with ductal and interacinar fibrosis and obstruction within thelacrimal gland, possibly as a result of low-grade chronic inflammation)

- Infiltration And Damage To The Lacrimal Gland
- Destruction Or Denervation Of Lacrimal Tissue
- Reflex Hyposecretion Of Tears
- Causes Of Decreased Ocular Surface
 Sensation Leading To Dry Eye
- Damage To Afferent Sensory Fibers
- Decreased Corneal Sensation And Blink Rate
- Systemic Medications
- Menopause

Infiltration and damage to the lacrimal gland

- In benign lymphoepithelial lesion of godwin ("mikulicz's disease"),
- Lymphoma,
- Sarcoidosis,
- Hemochromatosis,
- Amyloidosis,
- (Hiv/aids),
- And graft-versus-host disease

Destruction or denervation of lacrimal tissue

- Surgical Or Radiation-induced Secondary
 Obstruction Of The Lacrimal Gland Ducts
- Trachoma
- Ocular Cicatricial Pemphigoid,
- Mucous Membrane Pemphigoid,
- Erythema Multiforme/Stevens–johnson Syndrome,
- Chemical Burns,
- And Thermal Burns.

Reflex hyposecretion of tears

- Reflex sensory block (damage to the afferent arm)
- reflex motor block (damage to the efferent, or secretomotor arm)

Causes of decreased ocular surface sensation leading to dry eye

- topical anesthetic use,
- contact lens wear,
- diabetes mellitus,
- aging,
- and neurotrophic keratitis

Damage to afferent sensory fibers occurs after

- incisional corneal surgery (penetrating or anterior lamellar keratoplasty, radial keratotomy, and limbal cataract incision)
- and after damage to the first division of the trigeminal ganglion from
- trauma, tumor,
- and herpes simplex or zoster,
- resulting in reduced tear production

Decreased corneal sensation and blink rate are

- Laser-assisted in situ keratomileusis (LASIK) and
- Photorefractive keratectomy

Menopause

TABLE 4.23.1 Medications Associated With Dry Eye Disease

Mechanism of Action	Class	Medications
Anticholinergic	Antimuscarinics	Tolterodine tartrate (Detrol) Scopolamine
	Antihistamines (sedating compounds are associated with greater dryness)	Chlorpheniramine (Chlor-Trimeton) Diphenhydramine (Benadryl) Promethazine (Phenergan)
	Antiparkinsonian	Benzotropine (Cogentin) Trihexyphenidyl (Artane)
	Antidepressants MAO inhibitors	Amitriptyline (Elavil) Nortriptyline (Pamelor) Imipramines (Tofranil)
	Antipsychotics	Doxepin (Sinequan) Phenelzine Chlorpromazine (Thorazine) Thioridazine (Mellaril)
	Antimanics Antiarrhythmics	Fluphenazine (Prolixin) Lithium Disopyramide (Norpace) Mexiletine (Mexitil)
Antiadrenergic	Alpha-agonists Beta-blockers	Clonidine (Catapres) Methyldopa (Aldomet) Propranolol (Inderal) Metoprolol (Lopressor)
Diuretic	ThiaziDED	Hydrochlorothiazide
Other	Nonsteroidal anti- inflammatory drugs Cannabinoids	Ibuprofen (Advil) Naproxen (Naprosyn, Aleve) Marijuana

b)Secondary lacrimal gland deficiency

Systemic medications are a common source for the inhibition of efferent lacrimal gland stimulation

 through anticholinergic activity or decreased secretion through systemic dehydration


Evaporative dry eye disease



Mebomian gland dysfunction(MGD) and blepheritis







In MGD

Bacterial Colonization By Normal Lid Commensals

- Directly Altering Secreted Lipids
- Indirectly Cause Inflammation.

Dermatological Association

- Conditions, Such As Seborrheic Dermatitis, Atopic Dermatitis, And Acne Rosacea,
- A Disorder Resulting In Vascular Dilation, Telangiectasias, And Plugging Of Sebaceous Glands Of Both Facial And Eyelid Skin.

Secondary MGD

- Use of 13-cis retinoic acid (isotretinoin) for treatment of acne,
- Ingestion of polychlorinated
 biphenyls in contaminated cooking
 oil,

- With cicatricial changes in conditions, such as
 - Chemical/thermal burns,
 - Trachoma, pemphigoid,
 - Erythema multiforme/stevensjohnson syndrome,
 - Acne rosacea,
 - Vernal keratoconjunctivitis,
 - And atopickeratoconjunctivitis.

Exposure

Excessive exposure of the ocular surface leads to increased evaporative loss of tear causing evaporative DED.

- Impaired or reduced blinking
 - Psychological, psychiatric, mechanical, neurological,
 - Or traumatic impairment of eyelid function

 Lagophthalmos, or an increased palpebral fissure width, resulting in an evaporative dry eye.

 Evaporative DED can be seen in thyroid eye disease secondary to proptosis or lid retraction.

Mucin Deficiency

Cicatrizing disease or surgical trauma

Local conjunctival damage from

Depopulation of mucin-producing goblet cells Anatomical abnormalities of the conjunctiva

Improper tear distribution

DED



Common systemic diseases and dry eye

- Sjögren's Syndrome- disruption of the lacrimal glands affects tear production, as the glands are responsible for secreting the aqueous (watery) layer of the tear film
- Rheumatoid Arthritis-disease also targets the eyes, interfering with normal tear production.
- Rosacea- Secondary MGD
- Systemic Lupus Erythematous (SLE) associated with sjogrens.
- Thyroid-related Disorders-prevents the eyelids from fully closing; as a result, the eyes can dry out.

Dry eye today

- Smartphone use could not only aggravate subjective symptoms but also induce tear film instability and oxidative stress indices in the tears and at the ocular surface.
- Continuous use is found to be more detrimental than intermittent use or judicious use with enough breaks to avoid ocular fatigue.
- A difference of frequency of blinking, dry eye symptom scores and amount of tears was noted in various studies
- Following cessation of smartphone uses corneal epithelium and tear film improves
- Living in air conditioned moisture deficit environments also aggravates dry eye

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Faruqui S.¹, Agarwal R.², Kumar R.^{3*}

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¹ Saba Faruqui, Assistant Professor, Department of ophthalmology, LN Medical College and JK Hospital, Bhopal, Madhya Pradesh, India. ² Rahul Agarwal, Professor and Head, Department of ophthalmology, LN Medical College and JK Hospital, Bhopal, Madhya Pradesh, India. ^{3*} Rashmi Kumar, Associate Professor, Department of ophthalmology, LN Medical College and JK Hospital, Bhopal, Madhya Pradesh, India.

Background: CVS and dry eye disease due to computers, in general, is well documented, but specific literature on smartphone usage leading to these conditions is limited. This study aims to estimate the prevalence of dry eye and determine the effect of duration of use on the CVS symptoms in college-going smartphone users. Aims: (1) To find a correlation between smartphone usage and dry eye(2)To find the prevalence of dry eye disease in the smartphone using college students (3)To study whether the duration and pattern of smartphone usage has a bearing on the severity of CVS symptoms. Materials and Methods: 394 medical students using smartphones for over a year and without pre-existing dry eye disease or ocular surface pathology were included. Tear film parameters were estimated. The duration of use and smartphone settings were correlated with the prevalence of dry eye and computer vision syndrome symptoms. Results: The prevalence of dry eye was 20.81%. The average DED score was 1.56±0.234, and 1.35±0.248 respectively in the DED and non-DED group with a p-value of 0.0001. The most common CVS symptoms were fatigue (54% in DED,44% in non-DED) and heaviness in both groups (60.9% in DED, 45% in non-DED group.). Conclusions: There was a statistically significant increase in the DED symptom score and the prevalence of CVS symptoms with increasing duration of use and daily exposure to smartphones.

Keywords: Smartphone, Dry eye disease, Computer vision syndrome, Blue filters, Screen guard

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Relationship between Smartphone Use and Dry Eye Symptoms in Children

Nikita Dash, Deepak Choudhury, Sumita Mohapatra, Prasanta Kumar Nanda Department of Ophthalmology, Regional Institute of Ophthalmology, SCB Medical College, Cuttack, India

Corresponding Author:

Nikita Dash

Department of Ophthalmology R.I.O., S.C.B. Medical College Cuttack-753007, Odisha, India Email id: ndash18@gmail.com

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Smartphone use is a risk factor for pediatric dry eye disease according to region and age: a case control study

Jun Hyung Moon, Kyoung Woo Kim & Nam Ju Moon 🖂

BMC Ophthalmology 16, Article number: 188 (2016) Cite this article 12k Accesses 68 Citations 187 Altmetric Metrics

Abstract

Background

In 2014, the overall rate of smartphone use in Korea was 83 and 89.8 % in children and adolescents. The rate of smartphone use differs according to region (urban vs. rural) and age (younger grade vs. older grade). We investigated risk and protective factors associated with pediatric dry eye disease (DED) in relation to smartphone use rate according to region and age.

Afficie | PDF Available

The association between smartphone addiction and eve disease: A cross-sectional study

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Authors:



Ayman Baabdullah International Medical Center

AbdulmalikGhassan Abumohssin

YaraAedh Algahtani



King Abdulaziz University

Show all 6 authors



Conv link

Diagnostic tests

- Tear film breakup time (TBUT)
- Stain staining of interpalpebral region, corneal staining significant
- Schirmer's test –
- Fluorescein clearance test
- Larcimal gland function Tear lactoferrin
- Tear meniscus height
- Impression cytology



Schirmer's test

- Normal >15mm
- Low normal 10-15mm
- Borderline 6-10 mm
- Wetting < 6mm abnormal



The Aims For Treating Dry Eye Disease

- Reducing or alleviating signs and symptoms of dry eye
- Maintaining and improving visual function
- Reducing or preventing structural damage
- Restoring the health of the ocular surface

ALGORITHM FOR OCULAR IRRITATION



Treatment modalities

- Aqueous tear deficiency
- Evaporative dry eye
- Ocular surface inflammation

Aqueous Tear Deficiency

- Artificial tears-
 - first line of treatment-
 - increase available tears and,
 - through dilution, reduce tear hyperosmolarity.

Autologous serum tears

- contain trophic factors and other proteins useful in ocular surface maintenance
- These can be useful as a preservative-free, biological tear substitute
- preparation is labor intensive.





- Punctal occlusion
- retards tear drainage,
- thereby increasing tear volume on the ocular surface and
- Hence lowering tear osmolarity
- *irreversibly* by cauterization
- <u>semi-permanently</u> with the use of nonabsorbable plugs.



- Secretagogues- require functional glandular tissue.
 - Oral pilocarpine (Salagen) and cevimeline (Evoxac) are M3 cholinergic agonists approved for use in dry mouth that also stimulate tear secretion.
- Various nutritional supplements no clear confirmation of their efficacy

Evaporative Dry Eye Disease

- Lid hygiene, in the form of warm compresses and lid massage
- The Lipiflow System,.
- Lid scrubs with dilute detergents decrease the seborrheic or bacterial load, thereby breaking the pro inflammatory cycle of MGD
- Systemic tetracyclines
- Topical erythromycin or azithromycin
- Lipid-like tear substitutes have become commercially available, which have been used with some success

- Correction of eyelid abnormalities that increase exposure of the ocular surface, such as lower lid ptosis and lagophthalmos, can stabilize a decompensated ocular surface
- In severe cases, a Partial or complete tarsorrhaphy or a conjunctival flap may be necessary to prevent decompensation of the cornea.
- The use of humidifiers, moisture chambers, glasses, or goggles increases periocular humidity and decreases surface evaporative pressure.

- New high-Dk (oxygen permeability), high-water-content contact lenses and new polymer lenses, accompanied by proper tear supplementation and hygiene, are effective in treating patients with DED with poor corneal wetting.
- In patients with severe DED, scleral contact lenses can promote lubrication and slow evaporation of tears from the ocular surface.

Ocular surface inflammation

Suppression of inflammation creates a supportive environment for reversal of DEDinduced cellular changes

- 1. Topical cyclosporine A
- 2. Lifitegrast 0.05% (decreases inflammation by inhibiting T-cell recruitment and activation)
- **3.** Judicious use of low-dose topical corticosteroids
- 4. Supplementing the diet with omega-3 fatty acids has been shown to decrease both signs and symptoms of DED
- 5. A number of drugs are currently being evaluated in clinical trials

Recent advances

- Lifitegrast 0.05% is the drug most recently (July 11, 2016) approved by the U.S.
 - Food and Drug Administration to address DED
- And is the only therapy approved to treat both the signs and symptoms of DED.
- Lifitegrast is a topical anti-inflammatory drug that blocks the binding of intercellular
- Adhesion molecule-1 (ICAM-1) to lymphocyte function associated antigen-1
- (LFA-1) on the T-cell surface.
- Lifitegrast decreases inflammation by inhibiting T-cell recruitment and activation

- Eye-platelet rich plasma (E-PRP) and plasma rich in growth factors (PGRF).
- Three to five times the platelet concentration compared to serum drops and aim to maximize the concentration of growth factors, cell adhesion molecules and alpha-granule released cytokines+
- result in substantial therapeutic effects on the ocular surface.

Intense pulsed light

- Intense pulsed light (IPL) involves targeting pigmented or vascular lesions with visible and infrared light, which, upon absorption, is converted to destructive heat
- off-label treatment for evaporative dry eye mediated by MGD



- Vectored Thermal Pulsation (LipiFlow™)
- evice that combines meibomian gland expression with heat,
- device applies heat over the palpebral conjunctiva of the upper and lower eyelids, while providing pulsatile external pressure



TearCare[®] System

- Procedure involves placement of single-use, flexible iLid™ published clinical trial applicators over each tarsal plate
- Which deliver constant, regulated heat at 41°C–45°C over a 12 minute treatment time
- D-uring which the patient is encouraged to blink normally to allow natural meibum expression .
- This is then followed by manual meibum expression by the physician immediately following removal of the iLid applicator



Intranasal tear neurostimulation (TrueTear[®])

 Designed to stimulate the mucosal nerves via small electrical currents to increase natural tear production via the nasolacrimal reflex pathway of the lacrimal function unit



Potential future dry eye treatments

- Lacritin-ocular specific glycoprotein
- **Lubricin-**mucin-like glycoprotein t
- Thymosin ß4-G-actin binding protein
- Amniotic membrane extract eye drops
- New Cyclosporine Formulations

