

DRY EYE DISEASE

Background

1. Definition:
 - Also known as dry eye syndrome, keratoconjunctivitis sicca, and dysfunctional tear syndrome
 - Multifactorial disease of tears and ocular surface
 - Results in discomfort, impairment of vision, and possible damage to ocular surface.
2. General Information:
 - classified into two general groups:
 - Decreased tear production
 - Increased tear evaporation

Pathophysiology:¹

1. Pathology of Disease
 - Complex and multifactorial etiology
 - Two primary mechanisms: Decreased Production (Aqueous deficient); Increased Evaporation (Evaporative)
 - Overlap of mechanisms commonly exists
 - Dysfunction of any component of the lacrimal functional unit (lacrimal glands, eyelids, cornea, conjunctiva, meibomian glands and related nerves)
 - Dry eye due to decreased tear production (two types)
 - Sjogren's syndrome –inflammatory infiltration of lacrimal glands leading to cell death and tear hyposecretion
 - Non-Sjogren's type – tear deficiency due to lacrimal gland dysfunction without systemic findings
 - Most common is age-related due to progressive blockage of lacrimal gland
 - Conjunctival scarring conditions – trachoma, mucous membrane pemphigoid, erythema multiforme and ocular burns
 - Lacrimal gland infiltration – sarcoidosis, lymphoma, graft versus host disease, episcleritis and AIDS
 - Reflex hyposecretion
 - Corneal sensation impairment
 - Corneal Surgery
 - Contact lens use
 - Diabetes Mellitus
 - Post-infectious (herpes simplex, herpes zoster)
 - Motor impairment
 - Cranial nerve VII alteration
 - Anticholinergic medications
 - Multiple Neuromatosis

- Dry eye due to increased tear evaporation
 - Most commonly caused by dysfunction of meibomian gland, which is responsible for producing lipid component of tear film
 - Meibomian Dysfunction
 - Local disease
 - Systemic dermatologic disease
 - Rosacea
 - Seborrheic dermatitis
 - Vitamin A deficiency
 - Medication Toxicity
 - Congenital Aplasia
 - Distichiasis (aberrant eyelash growth)
 - Decreased blink function (i.e. Parkinson's disease, contact wear)
 - Structural abnormalities of eyelid position
 - Exophthalmos
 - Lid deformity
 - Poor apposition
 - Surface disorders (i.e. allergic conjunctivitis)
 - Frequent use of eye drops containing medications or preservatives
 - Ocular allergy syndromes
2. Incidence, Prevalence:^{2,3}
 - Prevalence increases with age; 0.4-0.5% overall; affects 5 to 30% of population age ≥ 50 y/o; women more than men
 - Expected to increase as population ages
3. Risk Factors:
 - Age
 - Female gender
 - Hormonal changes: decreased androgen states
 - Systemic diseases: Diabetes mellitus, Parkinson disease
 - Contact lens use
 - Systemic medications⁴:
 - antihistamines,
 - anticholinergics,
 - tricyclic antidepressants,
 - estrogens,
 - isotretinoin,
 - SSRIs,
 - amiodarone,
 - nicotinic acid,
 - beta-blockers,
 - diuretics,
 - interferon,
 - anti-androgen agents,
 - narcotics,

- antiparkinson medications,
 - phenothiazines,
 - benzodiazepines
 - Ocular medications (especially those with preservatives): glaucoma medications and artificial tears
 - Nutritional deficiency: Vitamin A, Omega-3 fatty acids
 - Decreased corneal sensation
 - Ophthalmic surgery (especially corneal refractive surgery)
 - Low humidity environments
 - Genetic predisposition (Sjogren's syndrome)
 - Occupational factors: sustained visual attention, upward/horizontal gaze (computer use)
4. Morbidity / Mortality³
- Morbidity: Severe cases may lead to corneal scarring and loss of visual acuity
 - Increased problems in affected population:
 - reading
 - performing professional work
 - computer use
 - daytime / nighttime driving

Diagnostics^{1,4,6}

1. History:
 - Chief complaints include:
 - Dryness
 - Red eyes
 - General irritation
 - Gritty sensation
 - Burning sensation
 - Foreign body sensation
 - Blurred vision
 - Excessive tearing
 - Light sensitivity
 - Pain or soreness
 - Eye fatigue
 - Mucus discharge
 - Contact lens intolerance
 - Review of Systems (searching for systemic disease – i.e. Sjogren's)
 - Joint pains
 - Rash
 - Dry mouth
2. Physical Examination
 - Assess conjunctival injection; should be symmetric in both eyes
 - Assess blink rate
 - Evaluate complete eye closure
 - Evaluate cranial nerves
 - Excessive tearing; can be a paradoxical sign of dry eye

- Blepharitis; often presents as visible erythematous or irritated eyelid edges
 - Entropion (inward turning of eyelids) and ectropion (outward turning of eyelids)
 - Assess visual acuity, evaluate for improvement after increased blink rate or use of lubricating drops
3. Diagnostic Testing
- Fluorescein stain to evaluate for corneal ulceration or other damage to the ocular surface
 - Slit Lamp Exam
 - Tear Breakup Time (best clinical test)– instill fluorescein into eye; distribute by blinking, patient then stares straight ahead
 - Via slit lamp – time between last blink and appearance of first break in fluorescent tear film
 - Under 5 seconds is abnormal
 - Tear flow – Shirmer test
 - Paper strip placed over lower lid margin in contact with ocular surface
 - Without anesthesia – maximal reflex tearing
 - Remove paper after 5 minutes
 - Less than 5 millimeters wetting distance abnormal
 - With anesthesia – basal tearing
 - Same parameters as above
4. Laboratory evaluation
- Evaluate for autoimmune disorders, specifically Sjogren’s

Differential Diagnosis

1. Key Differential Diagnoses
- Blepharitis
 - Ocular allergies
 - Viral conjunctivitis
 - Other microbial infections

Therapeutics

1. Acute/Long-Term Treatment^{4,5}
- Environmental modifications:
 - Humidify home air
 - Avoid air currents
 - Frequent breaks from visually demanding tasks
 - Avoid environmental triggers – smoke, low humidity
 - When possible, discontinue offending medications
 - Topical Lubrication – i.e. artificial tears (mainstay of treatment)
 - Multiple over-the-counter products exist with variable content parameters:
 - Electrolyte composition - potassium and bicarbonate most important

- Osmolarity/Osmolality – neutral versus hypo-osmolar
 - Hypotonic - used in patients with evaporative (hyperosmotic) disorders
- Viscosity – higher viscosity improves retention but causes more blurred vision
 - Lipid containing – used for patients with meibomian gland dysfunction (increase existing lipid tear film layer/decrease evaporation)
- Preservatives – preservative containing effective in mild disease
 - Preservative-free – moderate to severe disease requiring use of artificial tears more than 4 times daily
- Compatible solutes – used in patients with evaporative (hyperosmotic) disorders
 - Gels – use in severe disease and inadequate eyelid closure states
- Anti-inflammatory agents
 - Topical cyclosporine (Restasis[®])
 - For use in tear deficiency states
 - Only FDA approved pharmacological treatment for Dry Eye Disease
 - Safe for long-term use
 - Disease-modifying rather than merely palliative
 - Topical steroids – recommend prescribing for less than one month and in concert with ophthalmology referral
 - Loteprednol etabonate has less incidence of elevated ocular pressures than prednisolone acetate⁵
 - Oral tetracyclines – for patients with ocular rosacea / blepharitis
 - Oral Omega-3 fatty acid supplements – use in meibomian gland dysfunction and evaporative disorders
 - Decreases inflammation; produces more stable tear film
- Punctal Plugs – occludes lacrimal ducts
- Autologous blood serum drops – for refractory cases
 - Patient's centrifuged blood, mix with normal saline to 20% solution
 - Contain neurotrophic and epidermal growth factors (stabilize tear film)
- Accupuncture⁷
- Step-wise Approach⁵
 - Level 1
 - Education / Counseling
 - Environmental Management
 - Medication Elimination
 - Preserved tear substitutes, allergy eye drops
 - Level 2 (if Level 1 ineffective)
 - Unpreserved tears, gels, ointments
 - Steroids
 - Cyclosporine A

- Secretagogues (cholinergic agents treating aqueous-deficient disease)
 - Pilocarpine
 - Cevimeline
- Nutritional Supplements
- Level 3 (if Level 2 ineffective)
 - Tetracyclines (off-label)
 - Autologous serum tears
 - Punctal Plugs (following inflammation control)
- Level 4 (if Level 3 ineffective)
 - Topical Vitamin A (controversial)
 - Therapeutic Contact Lenses
 - Acetylcysteine (off-label)
 - Moisture goggles (efficacy limited; adherence issues)
 - Surgery (Tarsorrhaphy) – short-term closure of eyelids

Follow-Up⁶

1. Return to Office
 - Frequency depends on severity of disease, chosen therapy, and response to treatment
2. Consultation with ophthalmologist
 - Corneal infiltration or ulceration
 - Visual loss
 - Moderate or severe pain
 - Lack of response to treatment

Prognosis

1. No cure for dry eye disease
2. Most mild to moderate cases can be adequately controlled with current treatment modalities

Patient Education

1. Educate patient about chronic nature of disease
2. Provide specific instructions for treatment regimens
3. Inform patient that refractive surgery may worsen their condition
4. <http://www.nei.nih.gov/health/dryeye/dryeye.asp>

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