Feeling the Burn - The Pharmacist's Role in Treating Dry Eye

ACTIVITY DESCRIPTION
Dry eye disease is a common ocular condition affecting millions of Americans. With this condition, there is most often an insufficient amount of tears to lubricate and nourish the eye. Tears are essential for ensuring the health of the front surface of the eye and maintaining clear vision. Dry eye can cause irritation and lead to complications of the ocular surface, thus appropriate diagnosis and treatment is essential. Topical treatment includes numerous over the counter drops as well as prescription medications. A majority of the patients have milder or episodic symptoms, which will respond to the over-the-counter artificial tear supplements. Since patients frequently self-treat, pharmacists should have an understanding of the symptoms and treatments for dry eye and be prepared to discuss treatment options with patients who do not adequately respond to artificial tears. This program not only gives the pharmacist a solid knowledge base to make appropriate treatment recommendations for patients presenting with the signs and symptoms of dry eye but also identifies the point when a timely referral to an eye care specialist is appropriate.

TARGET AUDIENCE
The target audience for this activity is pharmacists, pharmacy technicians, and nurses in hospital, community, and retail pharmacy settings.

LEARNING OBJECTIVES
After completing this activity, the pharmacist will be able to:
- Review the basics of dry eye including symptoms and causes
- Describe the FDA approved over-the-counter and prescription medications available to treat dry eye disease to include mechanism of action and side effects
- Outline key considerations regarding appropriate over-the-counter or prescription treatment and/or for referring patients to an eye care provider when appropriate

After completing this activity, the pharmacy technicians will be able to:
- Review the basics of dry eye including symptoms and causes
- Describe the FDA approved over-the-counter and prescription medications available to treat dry eye disease to include mechanism of action and side effects

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Dr. Fritz’s optometric interests include the management of ocular disease (diabetic retinopathy, macular degeneration, etc.), glaucoma, pediatrics, and contact lenses. She enjoys humanitarian work, and has traveled to El Salvador, in order to provide eye care to the impoverished in remote villages. She is a member of the Gold Key Optometric Honor Society, the Beta Sigma Kappa Optometric Honor Society, the American Optometric Association, and the Pennsylvania Optometric Association. Dr. Fritz resides in Lewisburg, PA with her husband.

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Feeling the Burn – The Pharmacist's Role in Treating Dry Eye

Objectives

• Review the basics of dry eye including symptoms and causes.
• Describe the FDA approved over-the-counter and prescription medications available to treat dry eye disease to include mechanism of action and side effects.
• Outline key considerations regarding appropriate over the counter or prescription treatment and/or referring patients to an eye care provider when appropriate.

Anatomy and Tears

Anatomy

• Lacrimal gland
  • Located superior temporal to each eye
  • Produces and secretes the aqueous component to tears
• Puncta
  • Small openings on nasal aspect of eyelid that drain tears from eye
  • Upper and lower puncta for each eye
  • From puncta tears drain into canaliculi (small ducts), to lacrimal sac, and finally into the nasolacrimal duct
Anatomy

- Meibomian glands (MGs)
  - Small sebaceous glands
  - Located on upper and lower eyelid margins between lashes and orbit
- Importance
  - Secrete an oil (meibum) that makes up the lipid component of tears
  - With each blink MGs are squeezed to excrete lipid layer to tears

Tears

- Layers of the tear film
  - Mucin layer (inner layer)
    - Necessary for the tears to adhere to eye
    - Produced by corneal and conjunctival cells
  - Aqueous layer (middle layer)
    - Provides hydration and nutrients
    - Involved in wound healing and corneal renewal
    - Secreted by lacrimal gland and its accessory glands
  - Lipid layer (outer layer)
    - Makes up 90% of tear film volume
    - Slow tear evaporation, enhances tear spreading, and provides a smooth optical surface
    - Secreted by the MGs

Tears

- Function of tears
  - Lubrication
  - Provide a smooth optical surface for clear vision
  - Supply nutrients and oxygen to the anterior surface of eye
  - Flush out foreign material and microbes
  - Promote healthy epithelium maintenance and wound healing
  - Protect against pathogens

Dry Eye Disease
Definition of Dry Eye

- According to the International Dry Eye Workshop
  - “Multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface.”

Dry Eye Categories

- Categories of Dry Eye Disease (DED)
  - Aqueous deficient
    - Decreased aqueous layer
  - Evaporative
    - Deficient lipid layer
  - Combination
  - Most cases of DED are a combination of both categories

Dry Eye Disease

- Chronic disease
  - Usually bilateral
  - Discomfort commonly out of proportion to clinical signs
    - Many patients do not realize they are actually suffering from a common eye disease
  - DED is expected to grow 10.2% over the next 10 years

Dry Eye Disease

- General symptoms
  - Ocular discomfort - burning, foreign body sensation, sandy/gritty feeling, tearing, eye pain, tired eyes
  - Mild diffuse redness
  - Transient blur
    - Can improve with blinking
  - Worse with computer or reading
    - Reduced blink rate (30%) with sustained visual attention
  - Worse toward the end of the day
Dry Eye Disease

- **Risk Factors**
  - Age
  - Female
    - Hormonal changes - menopausal and postmenopausal

- **Environmental Causes**
  - Climate (wind, low humidity, high temps)
  - Heat/air conditioning
  - Smoking

Dry Eye Disease

- **Ocular Causes**
  - Corneal irregularities
  - Conjunctival scarring
  - Frequent uses of eye drops with preservatives (e.g. glaucoma)
  - Contact lenses
  - S/p eye surgery
    - Cataract surgery
    - LASIK or PRK
    - Disruption to corneal nerves and interference with normal reflex tearing

Dry Eye Disease

- **Associated systemic condition**
  - Connective tissue and autoimmune diseases
    - Sjogren syndrome
    - RA
    - Wegener granulomatosis,
    - Systemic lupus erythematosus
    - Etc.
  - Vitamin A deficiency

Dry Eye Disease

- **Medications**
  - Oral contraceptives
  - Anti’s - Anticholinergics, Antihistamines, Antiarrhythmics, Antipsychotics, Antispasmodics
  - Tricyclic antidepressants, SSRIs
  - Beta blockers
  - Diuretics
  - Chemotherapy
Prevalence

- Overall 14.5% of the US population suffers from DED
  - Affecting nearly 30 million people
- Incidence increases with age
  - Affecting approximately 5% of the adult population aged 30-40
    - Affects 50% of contact lens wearers
  - 10-15% of adults over age 65
    - In women age 65-84 affects over 25%

Associated Ocular Conditions

Blepharitis

- Inflammation of eyelids
  - Causes red, irritated, and itchy eyelids
  - Formation of dandruff-like scales on eyelashes
- Common eye disorder
  - Caused by bacterial or skin condition (rosacea)
  - Not contagious
  - Not likely to cause permanent damage
  - Demodex mite

Meibomian Gland Dysfunction

- Oil (meibum) secreted from meibomian glands should be oily in appearance and composition
  - If it thickens then it cannot exit glands appropriately
  - Glands become clogged and no oil is released into tears
    - Can lead to chalazion (stye)
- Capped glands visible
  - No meibum released upon mechanical expression
  - Reduced TBUT
Ocular Rosacea

- Acne Rosacea
  - Papules on the cheek, forehead, and nose (including rhinophyma)
  - Flushing with certain triggers such as alcoholic beverages, caffeine, sun exposure
  - Affects sebaceous glands - including MGs
- Rosacea keratitis
  - Blepharitis, MGD, telangiectasia of lid margin
  - Recurrent hordeolum/chalazion (stye), and keratitis
  - Chronic ocular surface disease and dryness

Ocular Complications

- Superficial damage to corneal epithelium
  - Eye pain
  - Blurred vision
- Lid abnormalities
  - Lids act as windshield wipers spreading tears and pushing them nasally toward puncta
    - If not positioned properly (droopy), tears are not spread evenly and are also not drained into puncta correctly causing tearing
  - Exposure keratopathy
    - Incomplete lid closure or incomplete blink leads to corneal dryness, superficial damage and even ulcerations

Testing In Office

- Pt symptoms and history
- Examination
  - Inspect lid position / lid globe congruity
  - Staining with dyes that show damaged corneal/conjunctival epithelium
  - Thickness of tear prism
  - Tear break-up time (tear evaporation)
  - Quality of tear film
  - Inspect MGs and mechanical expression
  - Tear osmolarity

Prescription Treatment
Xiidra™

• Xiidra™ (lifitegrast 5%)
• FDA approved for the treatment of the signs and symptoms of dry eye disease.
  • New class of drug: lymphocyte function-associated antigen 1 (LFA-1) antagonist
• Preservative free single use vials (cannot re-cap)
• Dosing BID
• Onset of effect as soon as 2 weeks

Mechanism of Action

• The exact mechanism of action of lifitegrast in dry eye disease is not known.
  • Binds to a cell surface protein found on leukocytes and blocks the interaction (of LFA-1 with its cognate ligand intercellular adhesion molecule 1 [ICAM-1]).
  • This molecule may be overexpressed in corneal and conjunctival tissues in dry eye disease.
  • This interaction can contribute to the formation of an immunological synapse resulting in T-cell activation and migration to target tissues.
  • Inhibiting T-cell adhesion to ICAM-1 in a human T-cell line and may inhibit secretion of inflammatory cytokines

Xiidra™

• Side effects
  • Common: instillation site irritation, dysgeusia (unusual taste sensation), decreased visual acuity (occurred in 5-25%)
  • Other: blurred vision, conjunctival hyperemia, eye irritation, headache, increased lacrimation, eye discharge, eye discomfort, eye pruritus and sinusitis (reported in 1-5% in study)

Xiidra™

• Contraindications
  • None
• Pregnancy category
  • “There are no available data on Xiidra™ use in pregnant women to inform any drug associated risks.” “There are no data on the presence of lifitegrast in human milk, the effects on the breastfed infant, or the effects on milk production.” (FDA label)
• Pediatric use
  • Safety and efficacy in those below age 17 years have not been established
Restasis®

- Restasis® (cyclosporine 0.05%)
- FDA approved to increase tear production
- Restasis can be re-capped
- Dosed BID
- Usually takes 3-4 months to reach full therapeutic effect
  - Some doctors may Rx mild ophthalmic steroid concurrently for 1 month to speed onset of therapeutic effect

Restasis®

- Mechanism of Action
  - The exact mechanism of action for Restasis® is unknown
    - Partial immunomodulator
      - Limits T lymphocyte activation
  - Anti-inflammatory
    - Preventing T-cells from releasing cytokines
    - By affecting the inflammatory cascade, the ocular surface and the lacrimal gland both recover, promoting normal tear production.

Restasis®

- Side effects
  - Common: ocular burning (reported by 17%)
  - Other: conjunctival hyperemia, discharge, epiphora, eye pain, foreign body sensation, stinging, pruritus, and visual disturbance (more often blurring) (occurred in 1-5%)

Restasis®

- Contraindications
  - Pts with active ocular infections, hypersensitivity to any ingredients
- Pregnancy category
  - Category C
  - Cyclosporine is known to be excreted in human milk following systemic administration but excretion in human milk after topical treatment has not been investigated.
- Pediatric use
  - Safety has not been established in those below age 16.
Counseling Points

- Xiidra™ and Restasis®
  - Rx for Xiidra™ and Restasis® should be written as 90 day supply or dispense 180 vials.
  - Preservative free vials are approved for 1 time use
  - It can take several months to reach full therapeutic effect
  - Burning upon instillation is normal
  - These drops are for long term management of DES, they are not a cure

Ophthalmic Steroids

- Mild Topical Corticosteroids
  - Pulse dosing = 1gtt QID x 1 month
  - Safe to use for short period of time, with monitoring
  - Loteprednol etabonate
    - Ester based - low chance of steroid response
    - Lotemax® 0.5%
    - Lotemax® gel
    - Alrex® 0.2%
  - Fluorometholone
    - FML® suspension (must shake) - liquifilm 0.1%
    - FML Forte® 0.25%
    - FML® ointment 0.1%

Doxycycline

- Used to treat MGD associated with ocular rosacea
  - At low doses mechanism of action is anti-inflammatory
- Dose
  - 100 mg BID x 1 month
  - then 50 mg QD 1-3 months
- Pregnancy: Category D
- Not approved for those under 8 yrs of age
- Side Effects: GI upset, Photosensitivity, Pseudotumor cerebri

Treatments from Eye Care Provider
Punctal Plugs

- Insert plug into puncta to slow/stop tear drainage into lacrimal sac
  - Your own tears stay on eye longer
- Come in different materials, shapes, and sizes
  - Collagen - temporary, they dissolve over time
  - Silicone or Acrylic - can be removed (umbrella plugs)
- Typically inserted into lower first, and if necessary upper puncta
- For very severe cases can permanently occlude with cautery

Over-The-Counter Treatment

Artificial Tears (ATs)

- Lubricating eye drops
- Recommend QID dosing to start then taper PRN
- Side effects: Slight blur and burn upon instillation
- Different formulations to treat different categories of dry eye
  - Lipid based artificial tears
  - ATs for aqueous deficiency
    - Refresh®
    - Blink®
    - Systane®

Artificial Tears

- Lipid based ATs
  - Replenishes the complete tear film
  - Provides a protective lipid barrier
    - Systane® Balance
    - Refresh Optive® Advance
    - Soothe® XP
    - Retaine® MGD™
Artificial Tears

- Preservative-free (PF) options
  - Refresh Optive® PF, Thera® Tears PF, Systane® Ultra PF,
- Same vial can not be used for more than 24 hours!
- When to recommend...
  - For those patients with sensitive eyes
  - If using ATs more than QID
  - S/P LASIK surgery - patients use ATs every few hours at first
  - Patients on prescription eye drops

Artificial Tears

- Gel and ointments
  - Systane® Gel
  - Refresh Liquigel®
  - Refresh P.M.® - ointment
  - More viscous than ATs = increased contact time
  - Common dosing QHS
  - Can use PRN as pt can tolerate blur from instillation
  - Side effects: cause blur upon installation for several minutes

Counseling Points

- Artificial tears
  - Use with contact lenses
    - Can use ATs PRN
    - Use ATs for Contacts or PF options if using frequently
  - Avoid all drops that say “get the red out”
    - Such as Visine® / Clear Eyes® or similar products
    - These drops are vasoconstrictors that do not treat dry eye but just make eyes look better
    - Rebound redness
  - Wait 10 minutes in between instillation of additional drops

Over-The-Counter Treatment

- Omega-3 Fish Oil
  - Treatment for moderate-severe MGD
  - Long-term treatment
  - 1,000 mg BID
  - May take 4-6 months to obtain significant therapeutic effect
Over-the-counter Treatment

- Warm compress
  - Used to treat meibomian gland disease
  - Heat oil (meibum) in clogged meibomian glands of eyelids so that oil can be liquified and naturally secreted into tears
    - Warm washcloth (clean)
    - Bruder mask from eye care provider
  - Use initially QID for 10-15 minutes
    - Then QD to BID as maintenance

Eyelid scrubs

- Used to treat anterior blepharitis (debris on eyelids)
- Use BID then QAM for maintenance
- Retail products available
  - OCuSOFT®, Systane™ Lid Wipes
  - Can also try cotton ball with diluted baby shampoo
  - Rub gently at lash margin

Counseling Points

- Many different treatments available
  - Treatments will be determined during eye exam based on pt history and clinical findings
  - Until patient can be evaluated by an eyecare provider, okay to supplement with OTC products
    - ATs QID and warm compresses BID helpful in most cases
  - Become knowledgeable about DED treatments to better educate patients about condition and possible treatments available
Counseling Points

- **Lifestyle modifications**
  - Stop smoking
  - Humidifier in house
  - Turn off ceiling fans
  - Take breaks with computer work or with long periods of reading (20/20/20 rule)

Counseling Points

- **Tearing can actually be a sign of dry eye**
  - Eyes feel dry
  - Corneal nerves send signals to lacrimal gland to produce reflex tears
  - Lacrimal gland pours out reflex tears
  - These new tears do not have the needed lipid component therefore they have poor adherence to the eye, leading to excess tearing
  - Recommend ATs QID then PRN for maintenance

Counseling Points

- **Recommendations to your patients/customers**
  - OTC products as first line of care
  - Ask about symptoms
    - Worse toward a specific time of day / activity - ATs PRN
    - Dryness upon awakening - gel BID
    - Does vision improve with blinking - Warm compress BID and ATs QID
  - Good recommendation is ATs QID then taper as symptoms are controlled

Counseling Points

- **Recommendations to your patients/customers**
  - Again... no “get the red out” products
    - Vasoconstrictors cause rebound redness
    - Instead recommend lipid based ATs
  - No contraindications for ATs use
  - DED is a disease that requires long term management
  - Many prescription and OTC treatments available
    - Pharmacists and eye care providers can help patients control symptoms of this growing ocular condition
Counseling Points

• If pt has eye pain, change in vision, moderate/severe redness, photophobia (or other ocular symptoms) pt should skip self treatment with OTC products and seek an eye care provider to be evaluated and treated appropriately!
Exam Questions

1. What is not a symptom of dry eye disease?
   a. Burning
   b. Itching - correct
   c. Tearing
   d. Foreign body sensation

2. What is the dosing for Xiidra?
   a. PRN
   b. QD
   c. BID - correct
   d. TID

3. Which ophthalmic drop does not come as preservative free?
   a. Restasis
   b. Xiidra
   c. Lotemax - correct
   d. Refresh

4. Which is a good recommendation for a patient suffering from occasional eye burning while working at the computer?
   a. Lipid based artificial tears PRN - correct
   b. Eye rinses BID
   c. Visine PRN
   d. Clear Eyes PRN

5. What is a good recommendation for a patient who has mild eye redness, a mild constant decrease in vision, and light sensitivity?
   a. Visine BID
   b. Warm compresses BID
   c. Make an appointment with an eye care provider - correct
   d. Lid scrubs
6. What is a good first recommendation for a patient who suffers from dry eye and has visible flaking on eyelashes?
   a. Artificial tears QID
   b. Lid scrubs BID - correct
   c. Restasis BID
   d. Xiidra BID

7. What is a common symptom of Xiidra and Restasis?
   a. Burning - correct
   b. Flashes
   c. Blurred vision
   d. Headache

8. What is the expected treatment length when a patient is using Restasis or Xiidra?
   a. 2 months
   b. 6 months
   c. 1 year
   d. Long term – correct

9. When might a patient start to notice the therapeutic effects of Xiidra?
   a. 1 day
   b. 1 week
   c. 2 weeks - correct
   d. 2 months

10. What patient should you recommend preservative free artificial tears to?
    a. After LASIK surgery
    b. Patient on 2 different glaucoma medications
    c. A patient using lipid based artificial tears 6x per day
    d. All of the above - correct