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- To review drug families and mechanism of action affecting dry eye disease (DED)
- To promote evaluation of patient systemic medical history as it related to ocular surface disease and the potential impact it may have
- To demonstrate cases where oral medications have exacerbated the dry eye disease process
- To educate practitioners on the need to educate patients about the influential nature of oral medications and dry eye
- To discuss collaborative care with other specialties and alternative treatment options

Many commonly prescribed oral medications can cause or exacerbate dry eye disease. This course discusses which drugs are the biggest offenders, what patients are at greatest risk and how to mitigate the effects for iatrogenic dry eye disease brought on by oral medications. Cases will be presented to illustrate discussion points.

- I. Review of etiologies of dry eye disease
- II. Common medications impacting dry eye disease
  - a. Ophthalmic
  - b. Systemic
- III. The Role of Medications in Dry Eye Disease (5 Hypotheses)
  - a. Hypothesis #1 If a Systemic Medication Causes Dry Mouth, It May Also Cause or Aggravate Dry Eye
    - i. Comparison between the ocular and oral mucosa
      1. Oral
        - a. Parotid gland
        - b. Submandibular
        - c. Sublingual

d. Minor salivary glands

2. Ocular

a. Lacrimal glands

b. Meibomian glands

c. Goblet cells

ii. Both the mouth and eyes are supplied by **acinar exocrine glands** that produce proteins, electrolytes, and enzymes in an aqueous medium

iii. Both the mouth and external eye are lined by **stratified squamous epithelium**

iv. Pharmacologically both systems react in a very similar manner, with **cholinergic** and **anticholinergic agents** probably giving the most drying effects both for the eye and mouth

b. Hypothesis #2 Polypharmacy Plays a Role in the Causation or Aggravation of Dry Eye

i. **Polypharmacy** is the use of five or more prescription drugs

ii. Polypharmacy is the primary cause of dry mouth

iii. Effects are worse in an aging population

iv. Most understood drug interactions involve **only 2 drugs**

v. Schein et al. study of 2,481 individuals

1. Ages 65–84 years

2. Found a strong correlation between the addition of each new class of drug known to have a sicca effect

c. Hypothesis #3 Systemic Medications May Induce Dry Eye

i. The Beaver Dam population-based, age-adjusted, cumulative

10-year dry eye study examined 3,722 individuals

- ii. A recent cross-sectional survey on over 26,000 males over the age of 50 showed an increased prevalence of dry eye when treated with medications for depression and prostatic disease.

d. Hypothesis #4 Topical Ocular Medications May Also Induce Dry Eye

- i. Potential additional effects on evaporation from topical medication should increase the total incidence of dry eye
- ii. Complications from topical medications may result from:
  1. Higher drug concentrations
  2. Greater frequency of application
  3. Preservative effects
  4. Higher incidence of drug-induced blepharitis
  5. Drug-induced ocular surface inflammation

e. Hypothesis #5 Long-Term Topical Ocular Medications with the Preservative, Benzalkonium Chloride (BAK), Can Cause Dry Eye

- i. Disagreement as to whether or not long-term BAK can cause dry eye.
  1. Some feel that changes described from long-term BAK use can be normal aging changes or not due to the preservative and they ask for better designed, long-term studies.
  2. There is no doubt that topical preservatives can cause ocular surface toxicity, which may take a number of forms, one of which includes DED.

#### IV. Allergy medications

a. Concomitant condition (allergy and DED)

b. Medications

i. Ocular

1. Mast cell stabilizers

2. Antihistamines/Mast cell stabilizers combination

ii. Systemic

1. Antihistamines

a. Over-the-counter (OTC)

b. Doctor prescribed

i. Cetirizine

ii. Desloratadine

iii. Loratadine

iv. Olopatadine

v. Tripelennamine

c. Intended effect

d. Side effect/adverse event potential

e. Effect of DED

2. Decongestants

a. Over-the-counter (OTC)

b. Doctor prescribed

c. Intended effect

d. Side effect/adverse event potential

e. Effect of DED

V. Anti-depressants

- a. Prevalence of anti-depressant prescriptions in the United States
  - i. Demographic overlap between dry eye patients and those taking anti-depressants
    - 1. Women>Men
    - 2. Aging population
- b. Concomitant relationship between depression and dry eye disease
  - i. Supportive studies
- c. Commonly prescribed medications
  - i. Citalopram
  - ii. Fluoxetine
  - iii. Paroxetine
  - iv. Sertaline
- d. Antidepressants:
  - i. Intended effect
  - ii. Side effect/adverse event potential
  - iii. Effect of DED

VI. Anti-hypertensives

- i. Most commonly prescribed anti-hypertensives
  - 1. Beta-agonists
    - a. Acebutolol
  - 2. Alpha-agonists
    - a. Atenolol
  - 3. Antiarrhythmic agents (beta blockers)
    - a. Carvedilol

- b. Labetalol
- c. Nadolol
- d. Pindolol
- e. Clonidine
- f. Prazosin
- g. Oxprenolol
- h. Propranolol

- ii. Intended effect
- iii. Side effects or adverse potential
- iv. Effect on DED

## VII. Retinoids

- a. Drug classification
  - i. Vitamers of vitamin A
  - ii. Used to regulate epithelial cell growth
  - iii. Generations
    - 1. First
      - a. Retinol
      - b. Retinal
      - c. Tretinoin
      - d. Isotretinoin
      - e. Alitretinoin
    - 2. Second
      - a. Etretinate
      - b. Acirectin
    - 3. Third

- a. Adapalene
- b. Bexarotene
- c. Tazarotene

iv. Used to treat:

- 1. inflammatory skin disorders
- 2. skin cancers
- 3. disorders of increased cell turnover
- 4. photoaging
- 5. skin wrinkles

v. Toxicity considerations

- 1. Medical signs
  - a. Systemic
  - b. Ocular
    - i. DED

VIII. Hormone Replacement Therapy/Birth Control medication

a. Initiating the conversation with patients about hormone-related medications

i. Estrogen therapy

- 1. Studies report higher risk of DED

ii. Progesterone-estrogen therapy

- 1. Studies report increased risk relative to the general population, but less so than estrogen alone

iii. Birth control medication

- 1. Risk associated

IX. Drugs secreted in the tears

- a. Aspirin
- b. Chloroquine
- c. Clofazimine
- d. Docetaxel
- e. Ethyl alcohol
- f. Hydroxychloroquine
- g. Ibuprofen
- h. Isotretinoin