Pharmaceutical Treatment of Anterior Segment Inflammatory Conditions (2 hours)

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Summary

As optometry's role evolves, so does the conditions that we manage. Pharmaceutical agents have offered the ability to treat ocular surface inflammation in effective ways. This course will discuss causes of ocular surface inflammation and strategies to manage them with the appropriate pharmaceutical agents.

Learning Objectives

1) Understand underlying mechanism of inflammation
2) Discuss strategies for treating acute inflammation
3) Understand strategies for treating chronic inflammation
4) Discuss anterior segment conditions that are inflammatory in nature
5) Understand systemic association with some inflammatory conditions
6) Understand appropriate pharmaceutical treatment of the ocular conditions

Course Summary

1) Pathophysiology
    a. Receptors in the nucleus of the cell promotes production of inflammatory mediators
    b. Phospholipase activation
    c. Cyclooxygenase – 1 and cyclooxygenase – 2
        1. Constitutively
            a. Continues at a constant level
            b. COX-1 – important for gastrointestinal function
        2. Facultatively
            a. Increases with inflammation
            b. COX-2 – is up regulated with inflammation
    ii. Phospholipid bilayer and phospholipase A2 – original molecules that begin the production of end products
    iii. Arachidonic acid
    iv. Prostaglandins and thromboxane – inflammatory end products
2) Topical Corticosteroids
    a. Topical corticosteroids
        i. Binds to steroid receptor in cell cytoplasm
        ii. Enters the nucleus of the cell and promotes production of anti-inflammatory mediators and inhibits the production of inflammatory proteins

iii. Promotes lipocortin-1 production inhibiting phospholipase A2
iv. Inhibits COX-1 and COX-2
v. Suppresses cyclooxygenase production
vi. Up-regulate anti-inflammatory proteins
vii. Down-regulate inflammatory proteins
viii. Ester vs. ketone steroids
ix. Side-effects – increased intraocular pressure and cataract formation
    1. Treat intraocular pressure increases with

b. Topical corticosteroids
    i. Frequency of dosing is dependent on severity
        1. More severe case will require higher dosing schedule to remediate intraocular inflammation
    ii. Loteprednol etabonate – available in various concentrations
        1. Alrex (0.2%)
            a. Approved for allergic conjunctivitis
            b. Lowest concentration of loteprednol available
        2. Lotemax (0.5%)
            a. Approved for post operative inflammation
        3. Lotemax gel (0.5%)
            a. Gel provides additional surface retentation
        4. Lotemax SM (0.38%)
            a. Submicron technology allows more efficient tissue penetration
        5. Zylet (loteprednol etabonate and tobramycin)
            a. Antibiotic/steroid combination
        6. Inveltys (1%)
            a. Approved for postoperative inflammation
            b. Mucous penetrating particle (MPP) technology allows targeted tissue penetration of the pharmaceutical
        7. Eysuvis (0.25%)
            a. Approved to treat signs and symptoms of dry eye
            b. Mucous penetrating particle (MPP) technology allows targeted tissue penetration of the pharmaceutical
    iii. Fluorometholone
        1. Flarex (0.1%) – fluorometholone acetate
        2. FML (0.1%) – fluorometholone alcohol
    iv. Dexamethasone
        1. Tobradex (Tobramycin 0.3%/Dexamethasone 0.1%)
        2. Tobradex ST (Tobramycin 0.3%/Dexamethasone 0.05%)
            a. Contains a xanthum gum vehicle that helps increase tissue penetration
    v. Prednisolone acetate
        1. Discuss branded versus generic
    vi. Difluprednate

1. Understand vehicle
2. Consistent concentration throughout the bottle
3. Dosing efficacy at qid in affected eye has been shown to be equal to eight times a day with prednisolone acetate
4. Be cognizant of IOP increase

c. Cycloplegics
   i. Inhibits response of ciliary body
   ii. Adds comfort to patient
   iii. Cyclopentolate, homatropine, scopolamine, atropine

d. Pain control
   i. Consider oral non-steroidal anti-inflammatory agents
   ii. Consider oral narcotics
      1. Codeine and hydrocodone
      2. Understand how these medications are commercially available
      3. Discuss appropriate considerations when treating with oral pain medications

3) Cyclosporine
   a. Commercially available as:
      i. Restasis
         1. 0.05% concentration
         2. Preservative free
            a. Single vials
            b. Multi-dose bottle
               i. Patented non-preserved system that maintains its sterility
      ii. Cequa
         1. 0.09% concentration
         2. Preservative free
         3. Single vials
         4. Micelle ocular delivery
   b. Is an immunosuppressive agent
   c. In patients whose tear production is presumed to be reduced due to ocular inflammation associated with keratoconjunctivitis sicca, cyclosporine emulsion is thought to act as a partial immunomodulatory
   d. What is the future for cyclosporine
      i. Generic formulations may arise
4) Lifitegrast
   a. Commercially available as Xiidra
      i. 5% concentration
      ii. non-preserved sterile unit dose vials
   b. It is a lymphocyte functioning antigen-1 (LFA-1) antagonist
   c. Intercellular adhesion molecule-1 (ICAM-1) is found on surface cells of the conjunctiva and cornea
   d. ICAM-1 is overexpressed in dry eye disease

e. LFA-1 and ICAM-1 binding is believed to be propogate inflammatory cascade on the ocular surface
    i. Is believed to do so by T-cell activation and migration to target tissues
f. Lifitegrast applied topically is believed to prevent the interaction between LFA-1 on T-cells and ICAM-1 on the ocular surface
g. Has been shown to improve both signs and symptoms of dry eye within a 12 week time period

5) Anti-histamine/mast cell stabilizing agents
    a. Mast cell is primed with IgE molecules
        i. Allergen binds to mast cells primed with IgE
        ii. Causes significant cross reaction and degranulation of mast cell
        iii. Releases pre-formed mediators – mainly histamine – immediate response
        iv. Also causes the release of other chronic inflammatory mediators
    b. Antihistamine/mast cell stabilizer combination
        1. Alcaftadine
            a. QD dosing regimen
        2. Azelastine
            a. BID dosing regimen
            b. Generic available
        3. Bepotastine
            a. BID dosing regimen
        4. Cetirizine
            a. BID dosing regimen
            b. 0.24% concentration
            c. Available in unit dose vials
        5. Epinastine
            a. BID dosing regimen
            b. Generic availible
        6. Ketotifen
            a. BID dosing regimen
            b. Over the counter
            c. Available under a number of names
        7. Olopatadine
            a. Available in three concentrations (now over the counter)
            b. 0.1% - bid dosing regimen
            c. 0.2% - qd dosing regimen
            d. 0.7% - qd dosing regimen

6) Inflammatory ocular conditions that require treatment with pharmaceutical agents
    a. Dry Eye
        i. Inflammation is a common finding in dry eye
        ii. Inflammation arises from a variety of sources
            1. Lid margin disease
                a. blepharitis
            2. Meibomian gland dysfunction

3. Aqueous deficiency
4. Measuring inflammation
    a. InflammaDry
        i. Measures whether matrix metalloproteinase 9 levels are above or below the normal range
        ii. MMP levels will guide the treatment and need for inflammation control
        iii. Can help provide guidance for punctal occlusion

b. Allergic Eye Disease
    i. Acute responses
        1. IgE mediated
        2. Allergen binds to IgE bound to mast cells
        3. Causes degranulation of mast cells releasing histamine
        4. Histamine binds to receptors on target tissues
    ii. Chronic responses
        1. Involves IgE but recruits significantly more chronic inflammatory mediators
        2. Often times involves corticosteroids to appropriately manage conditions
c. Corneal infiltrates
    i. Non-infectious
        1. Result of inflammation at the surface of the cornea
        2. Not the result of microorganisms breaching corneal integrity
        3. Often times results in opacities in the cornea
    ii. Infectious
        1. Direct result of a microorganism breaching the cornea
        2. Usually accompanied with corneal staining
        3. Can see anterior chamber reaction
d. Anterior Uveitis
    i. Conjunctival hyperemia more concentrated in the limbal region
    ii. Cells in the anterior chamber
    iii. Flare in the anterior chamber
    iv. Keratic precipitates
    v. Miotic pupil
    vi. Posterior synechiae
    vii. Decrease vision
    viii. Increased intraocular pressure
    ix. Sensitivity to light on pupil testing and during slit lamp evaluation
    x. Can be associated with systemic condition
e. Episcleritis
    i. Inflammation of the episclera
    ii. Often times idiopathic
    iii. Can be associated with systemic condition
f. Thygeson's SPK

i. Inflammation in the sup-epithelial region causing small corneal lesions with overlying staining noted
ii. Symptoms are variable
iii. Respond to steroid treatment