The Management of Ocular Discomfort

Treating the Pain

Sarah B. Muenk MD
Cataract and Eye Consultants of Michigan
It Hurts: How to Begin Anatomically

Surface / Cornea - abrasions, infections, erosions, dry eye

Surrounding Structures - contact dermatitis, cellulitis, zoster

Intraocular - uveitis, angle closure

Headache Syndromes - cluster, migraine, tension

Neurologic / Other - trigeminal neuralgia,

Quality, Duration, Frequency, Factors Reproducing
Using and Prescribing Pain Medications

- Want to relieve suffering

- Pain is emotional, subjective and influenced by experience

- Many of these medications interact with medications or supplements patient is already on
  - Always need a medication list from the patient
  - Includes OTC and Herbs
  - Ask the name of the patient’s physician and when they last saw him/her
  - Allergies

- Can always ask for help from patient’s physician (rheumatologist/neurologist)
Surface/Corneal pain

- Abrasion
- Bacterial Ulcer
- Foreign Body
- Dry Eye/ Keratoconjunctivitis Sicca
- Viral Infections
- Allergic Conjunctivitis
- Contact lens related pain
Inflammatory pain and Glaucoma

- Blepharitis
- Uveitis
- Giant Cell Arteritis
- Posner-Schlossman
- Uveitis-Glaucoma-Hyphema Syndrome
- Angle closure and Neovascular glaucoma
Neurologic pain and Vascular causes

- Migraine
- Optic Neuritis
- Cluster Headache and Hemicrania
- Pseudotumor
- Trigeminal Neuralgia
- Orbital Ischemic Syndrome, Orbital Varix
- Horner’s, Nerve Palsy
Topical Medications

- Artificial Tears and Ointments
- Proparacaine
- Diluted proparacaine
- NSAIDS
- Steroids
- Restasis/ Cyclosporine
- Cycloplegics
Topical Anesthetics

Anesthetics prevent the temporary increase in sodium permeability that occurs during nerve-impulse conduction. Without the ability of the nerve cell to generate action potentials, the nerve impulse is blocked and sensation is eliminated.

Canadian study of corneal injury patients in the ER with 33 participants, 15 using 0.05% proparacaine had pain reduction that was significantly better and were more satisfied overall.

Signs of abuse are persistent corneal epithelial defect or neurotrophic ulcer, deep ring-shaped stromal infiltrate, folds in Descemet's membrane, anterior segment inflammation, ulceration and even perforation, dense cataract, corneal or scleral melting, secondary glaucoma and iritis.
Can you use them?

- Benoxinate 04%, Proparacaine 0.5%, Tetracaine 0.5%

- Diagnostic use only? Diluted/limited use in Postoperative pain in refractive procedures? Contraindicated for long-term use should not disqualify its short-term application?

- Topical anesthetics disrupt surface microvilli of the epithelial cells, causing decreased stability in the tear film. Anesthesia also lessens mucous adherence, shortens tear breakup time, decreases the blink rate and blocks the reflex-tearing pathway, resulting in inadequate tear production in response to noxious stimuli.

A central persistent epithelial defect with underlying stromal haze in a ring like distribution in a patient with a history of minor trauma then topical anesthetic abuse. The prominent corneal neovascularization approaching the visual axis. Peripheral thinning at the limbus is present for nearly 360 degrees. VA is Hand Motion, required a PKP
Keratoconjunctivitis Sicca
Replacing the tear film to relieve symptoms

- Dry eye is underdiagnosed and undertreated
- Artificial tears and ointments for more of a long-term chronic pain relief
- Prevalence of Hyperosmolarity in a General Patient Population (Interim analysis of TearLab prevalence study, 16 sites across Europe and the United States so far)
  - Overall, 60% of the patients had dry eye and 62% reported symptoms of DED
- Can take time for patients to notice a difference and therefore compliance can be a problem
Other Topical Therapies to Improve Comfort

- Bandage Contact Lens: corneal ulcers, epithelial defects especially chronic, neurotrophic keratitis, chemical burns, after corneal surgery, erosions, basement membrane disease.

  Close monitoring and antibiotics. Low BC, silicone hydrogels

- Pressure Patching: requires a very tight patch and cannot use drops

- Punctal occlusion, plugs or cauterization

- Clean Compresses - hot or cold for blepharitis, chalazia, allergic conjunctivitis and dermatitis

PROSE device in patient with severe KCS. Prosthetic Replacement of the Surface Ecosystem with vaulted area to fill with lubrication or medicine. $5,000 per eye, 1-2 weeks to customize
Topical NSAIDs

- Block cyclooxygenase (COX) in the arachidonic acid metabolism pathway

- Results in decreased prostaglandin syntheses

- Prostaglandins serve as mediators of the inflammatory response associated with pain and allergic reactions

- Also increase permeability of blood-ocular barrier, alter IOP, cause miosis and hyperemia

- Ketorolac (Acular, Acuvail), Diclofenac (Voltaren), Bromfenac (Xibrom, Bromday), Nepafenac (Nevanac)

- Used to treat surgical inflammation, pain, prevent miosis photophobia and CME
The appeal of using NSAIDs in the treatment of ocular inflammation revolves around avoiding the recurrent complications associated with corticosteroids, and NSAIDs' beneficial effects include stabilizing intraocular pressure, inducing analgesia and reducing the risk of secondary infection.

Therefore many use these “off-label”

### Figure 1. Approved Drugs for Inflammation after Cataract Surgery

<table>
<thead>
<tr>
<th>NSAID/Dosage</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acular: q.i.d. beginning 24 hours after surgery and through the first two postop weeks</td>
<td>Ocular itching due to seasonal allergic conjunctivitis, and for the treatment of inflammation after cataract surgery</td>
</tr>
<tr>
<td>Nevanac: t.i.d. one day prior to surgery, the day of surgery and for the first two postop weeks</td>
<td>Pain and inflammation after cataract surgery</td>
</tr>
<tr>
<td>Xibrom: b.i.d. one day prior to surgery and through the first two postop weeks</td>
<td>Inflammation post-cataract surgery</td>
</tr>
<tr>
<td>Bromday: q.d. one day prior to surgery and through the first two postop weeks</td>
<td>Inflammation and pain post-cataract surgery</td>
</tr>
<tr>
<td>Voltaren: q.i.d. the day after surgery, continuing for two weeks postop</td>
<td>Inflammation after cataract surgery and for temporary relief of pain and photophobia post-refractive surgery</td>
</tr>
</tbody>
</table>
NSAIDS-When to use them?

Pain Management

- Meibomian gland dysfunction and Dry Eye: Judicious use in dry eye and possibility of compromised healing

- To replace Steroid-induced elevated IOP

- Corneal abrasions and recurrent erosions: limited short term use

- In a randomized, double-masked, placebo-controlled, parallel-group study 223 adults with contact lens-associated GPC received either ketorolac or placebo, one drop, four times daily for 6 weeks. Improvement in papillae, itching, contact lens intolerance, other signs and symptoms of giant papillary conjunctivitis with ketorolac was clinically significant

- Post-operatively
Side Effects

Topical NSAIDS

Cornea

- Epitheliopathy, erosions and melts

- Caution with pre-existing corneal disease or systemic disease (Rheumatoid, DM)
  - Patients on systemic steroids
  - Herpetic infection

Glaucoma

- May interfere with IOP lowering effects of prostaglandin analogue
Topical Corticosteroids for Pain

- Mechanism of action higher in the inflammatory cascade

- Block both the cyclo-oxygenase and lipo-oxygenase pathways (responsible for leukotriene synthesis) thereby reducing inflammation

- Inflammation = Pain

- Short term use in many inflammatory conditions of the conjunctiva, cornea and anterior globe.

- Dry Eye patients may continue to complain of discomfort despite adequate aqueous replacement due to the inflammatory component

- Corticosteroids decrease ocular irritation symptoms, corneal fluorescein staining and improve filamentary keratitis
In a retrospective clinical series by Peter Marsh, M.D., and Stephen Pflugfelder, M.D., topical administration of a 1% solution of non-preserved methylprednisolone — given three to four times daily for two weeks to patients with Sjögren’s syndrome KCS — provided moderate to complete relief of symptoms in all patients. This therapy was even effective for patients with severe KCS who demonstrated no improvement with maximum aqueous enhancement therapies.
“Soft” vs “Hard” Steroids

Ketone Steroids

- Prednisolone, Dexamethasone, Flurometholone (FML, Flarex 0.1%), Medrysone and Rimexolone

Ester Steroids

- Loteprednol (Alrex 0.2%, Lotemax 0.5%)

In a summation of randomized studies, treatment with loteprednol etabonate (0.5% concentration) for less than 28 days resulted in a 2% incidence of elevated intraocular pressure, compared with a 7% incidence with prednisolone acetate (1% concentration) and 0.5% incidence with placebo.

Lower rates of IOP spikes and cataract formation with Lotemax and FML.
# Which Steroid to Pick
Tolerance, potency, side effects, infection risk

<table>
<thead>
<tr>
<th>Steroid Name</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Maxidex/dexamethasone</td>
<td>1. Treating inflammatory conditions of the conjunctiva, cornea and anterior segment, AND for corneal injury</td>
</tr>
<tr>
<td>2. FML/fluormetholone</td>
<td>2. Treating inflammatory conditions of the conjunctiva, cornea and anterior segment</td>
</tr>
<tr>
<td>3. FML forte</td>
<td>3. Treatment of corticosteroid-responsive inflammatory conditions of the conjunctiva, cornea, and anterior segment</td>
</tr>
<tr>
<td>4. Flarex/ fluorometholone acetate</td>
<td>4. Treatment of corticosteroid-responsive inflammatory conditions of the conjunctiva, cornea, and anterior segment</td>
</tr>
<tr>
<td>5. Lotemax/loteprednol</td>
<td>5. Treatment of corticosteroid-responsive inflammatory conditions of the conjunctiva, cornea, and anterior segment AND treating post-operative inflammation</td>
</tr>
<tr>
<td>6. Pred Forte/prednisolone</td>
<td>6. Treatment of corticosteroid-responsive inflammatory conditions of the conjunctiva, cornea, and anterior segment AND treating corneal injury</td>
</tr>
<tr>
<td>7. Prednisol/prednisolone sodium phosphate</td>
<td>7. Treating inflammatory conditions of the conjunctiva, cornea and anterior segment</td>
</tr>
<tr>
<td>8. Vexol/rimexolone</td>
<td>8. Treatment of anterior uveitis, treatment of post-operative inflammation</td>
</tr>
</tbody>
</table>
Conditions Often Requiring Steroids for Treatment and to Relieve Pain

- Moderate to severe Dry Eye
- HSV stromal keratitis (with a oral antiviral)
- Herpetic necrotizing keratitis
- Non-infectious / Sterile corneal ulcers
- Allergic keratoconjunctivitis—vernal and atopic
- Uveitis

19 y.o. man with a 'non-healing corneal ulcer'
Differential diagnosis of enlarged superior tarsal papillae includes:

- Giant papillary conjunctivitis,
- Vernal keratoconjunctivitis,
- Trachoma,
- Adult inclusion conjunctivitis

Pred forte q2hrs OD, cromolyn qid OU, cyclogyl bid OD, ciloxan BID OD, bandage CL OD

BCL removed, Cyclosporine 1%, allergist referral

2 months to fully heal
Topical Cyclosporine A as a Long Term Pain Therapy

- Alternative to steroids or as Adjunctive Therapy

- T-cell modulator, inhibiting T-lymphocytes

- Controls inflammation in dry eye disease, meibomian gland dysfunction, severe allergic keratoconjunctivitis, pre-operatively with refractive surgery, preventing corneal transplant rejection and fungal infections, for superficial keratitis after viral conjunctivitis, SLK, Thygeson’s

- Fewer Risks than steroids and safe for long-term use

  - No increase in IOP, no decreased wound healing, no effect on viral replication, does not cause cataracts

- Not a rapid acting relief therapy, need to discuss with patients, and may use combination therapy for approximately 1 month, tapering
Topical Mydriatic and Cycloplegic Agents

- Cyclopentolate, Homatropine, Atropine

- Ocular pain and photophobia induced by ciliary spasm in uveitis can potentially be reduced.

- There is thought that decreased vascular permeability may lead to lower amounts of inflammatory cells and protein in the anterior chamber (flare).

- Cyclopentolate may have a disadvantage as it has been shown to be a chemoattractant to inflammatory cells in vitro.

- Phenylephrine 10% has been shown to induce the release of pigment granules into the anterior chamber.

- Circulating levels of cycloplegics may exert an effect on muscarinic receptors throughout the body, initially causing dry mouth and flushing. Other more serious documented effects include urinary retention, tachycardia, somnolence, ataxia, hallucinations, and seizures.
Oral NSAIDS

- All drugs in drop form have some level of epithelial toxicity

- PO meds require a more thorough medical history: ETOH use, smoking, DM, pregnancy, anticoagulant use, liver or kidney disease, history of stomach ulcers

- Can be very useful in certain conditions: Episcleritis, scleritis

- Ocular Immunology and Uveitis Foundation in Boston studied 86 eyes in patients with a history of recurrent HLA-B27-associated uveitis, and the pre-NSAID and post-NSAID attack rates were compared. 66.8% reduction in recurrences of uveitis in this population of patients with recurrent HLA-B27-associated uveitis through the chronic use of oral NSAIDs, with complete freedom from steroid use.

- Vioxx, Celebrex
ORAL Narcotics

In contrast to current topical anesthetics, opioid analgesics can alleviate pain following a corneal abrasion without a negative effect on corneal wound healing.

Usually given for temporary acute severe corneal pain.

Post-operative, large abrasions

“Severe” is subject to interpretation

Only need a few days until epithelium is mostly healed over.

Tylenol #3, #4, Vicodin

Tylenol toxicity
Eye Pain as a first symptom of disease

- HZO
- Posterior Scleritis
- Retrobulbar Optic Neuritis
- Giant Cell Arteritis
- TMJ, Sinusitis
- Trigeminal neuralgia
- Orbital Pseudotumor