Benefits and Risk of Topical Corticosteroids in the Management of Ocular Inflammation

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Abstract
Ocular inflammations need to be managed at the earliest stage to minimize damages to delicate ocular tissue and to prevent loss of vision. Topical steroids are the strongest and fastest acting anti-inflammatory agent to control ocular inflammation and should be used judiciously to attain maximum benefits without any side effects.

Key words: Ocular inflammation, Topical corticosteroid
**Introduction**

Inflammation is a cascade of reactions occurs in our body in response to disease, trauma or following surgery resulting in cellular membranes damage, release of inflammatory mediators and triggering of a cascade of events that characterized by vasodilatation, oedema, exudation of proteins, cellular infiltration, pain and fever. In-fact this is the initial part of healing process in response to an assault in our body, fever goes off, pain reliefs and wound heals gradually without any anti-inflammatory agents. Inflammation is a harmless process for most of the body part except delicate structure like brain and eyes. We have to intervene to control inflammation in our eyes otherwise uncontrolled or inadequately controlled inflammation result in temporary or permanent vision loss.

**Corticosteroids the fastest and strongest anti-inflammatory agent**

Topical corticosteroids are the strongest and fastest acting anti-inflammatory agent use to control ocular inflammation in disease and following trauma and as a prophylaxis of inflammation after eye surgery. Topical administration of corticosteroids for ocular conditions is preferred over systemic administration due to higher drug concentrations in ocular tissue with minimal systemic adverse effects [1]. Therefore topical corticosteroids are the first line therapy for treating ocular inflammation since 1940s[2].

**Mechanisms of action of topical corticosteroids**

Topical corticosteroids act locally have anti-inflammatory, immunosuppressive effects and can prevent corneal scar formation. They exert their anti-inflammatory activity by inhibiting cyclooxygenase and lipoxygenase pathways and thereby inhibit arachidonic acid, prostaglandins and other potent inflammatory mediators. The immunosuppressive effects include decreasing the number and functionality of leucocytes. Topical corticosteroids prevent capillary proliferation, fibroblast proliferation, collagen deposition and scarring of healing tissue. Therefore topical corticosteroids are very effective in prevention of corneal scar formation in inflammation in disease and following cataract, corneal transplantation and corneal refractive surgery [3-10].
Side effects of topical corticosteroids

Most of the side-effects of topical steroids are related to the potency, duration of action and ability to penetrate through the cornea. There are two main types of ophthalmic corticosteroids: ketone-based and ester-based molecules. The side effects such as posterior sub-capsular cataracts and increased intraocular pressure are minimal or absent with the ester-based formulation like Loteprednol and occasionally seen with the ketone formulation such as Prednisolone and Dexamethasone. Formulations with acetates are more lipophilic and penetrate through the cornea better than those formulated with phosphates, which are relatively hydrophilic [10-15].

Loteprednol is very safe and highly effective and almost as strong as prednisolone with fewer side effects. Complications of topical steroids include the formation of a geographic ulcer if given in the presence of a dendritic herpetic keratitis, increased intra-ocular pressure and posterior sub-capsular cataract formation on prolong use of strong topical corticosteroid [12]. After 4-6 weeks of topical steroid therapy 5-6% of normal population develops a marked increase of intraocular pressure [11]. Therefore right choice of topical steroid for the clinical condition is very important to avoid side effects. Patient with high intraocular pressure, enlarged optic nerve cup and glaucomatous field visual field defects need careful administration of topical corticosteroids; monitoring of intraocular pressure is very important and may need anti-glaucoma agent to minimize side effects [11-15].

Safe use of topical corticosteroids in ophthalmology

Topical corticosteroids are potent and relatively inexpensive and have side effects judiciously used topical steroids are the best anti-inflammatory agent in ophthalmology. Through knowledge of steroids is desirable to choose the best one for each patient and balance the benefits and risks of steroids while treating ocular conditions. Prescribe adequate dosages; and never prescribe under dosages because of fears of side effects. Inadequate dose leads failure to gain complete control of inflammation and flare-up of inflammation on tapering the steroids. Long term moderate dosing of a steroid is more likely to result in a cataract than initial treatment with high doses of a strong steroid that is tapered gradually and switched to a lower-strength steroid for maintenance. The best approach is to use the most potent steroid as
quickly as possible and taper to a lower-strength steroid for on-going management. This way improves compliance and lowers the overall dosage, side effects, cost, and exposure to preservative in the medications [11-15].

**Dosages and tapering of topical corticosteroids**

Young patients often have more inflammation than older patients; patients who have had previous surgery or have existing inflammatory disease needs a lot more drug than patients with none of those risk factors. Selection of the best molecule, dose, frequency, and delivery route suitable for the patient is very important. At induction strongest steroid and doses; taper only when there are no signs of inflammation and maintain minimum effective strength and dose on tapering. Do not taper when the eye is just starting to improve or stabilize otherwise prolongation of inflammation and prolongation of steroid therapy will result. Once started it should be continued till the disappearance of cells, flare, keratic precipitates, cystoid macular oedema, injection or any other sign of inflammation [10-15].

**Synergistic use of topical nsaidsand topical steroids to control ocular inflammation**

Ophthalmic NSAIDs are useful in controlling pain and inflammation and there is no risk of suppression of immune system or raise of intraocular pressure. These agents can be combined with topical steroids for synergistic effect and to minimize side effects of steroids. Flurbiprofen, Ketorolac, Bromfenac and Nepafenac ophthalmic solution are very useful in management and prevention of inflammation, mydriasis and cystoid macular oedema related to ocular surgeries [16,17].

**Use of topical corticosteroids in ophthalmology**

**Pre-operative use topical steroids**

A patient with past history of uveitis undergoing cataract surgery needstopical steroids days to weeks prior to cataract surgery. Preoperative administration of NSIDs such as Flurbiprofen, Ketorolac are very effective in maintaining intraoperative mydriasis [16].
Post operative uses of topical corticosteroids

Topical steroids have been used to control inflammation after cataract surgery with intraocular lens implantation since the time of Sir Harold Ridley. Topical corticosteroids are extensively used for managing inflammation following cataract, refractive surgery and keratoplasty. Topical NSIDS like Ketorolac tromethamine, Nepafenac, Bromfenac are also used in combination with topical steroids. Fibrinous uveitis following cataract surgery is best managed by topical application of Prednisolone acetate. Topical steroids are also used in following Glaucoma surgeries, Pterygium excision and posterior segment surgeries like Vitrectomy, Retinal detachment surgeries etc. [16 -22].

Eye lids and conjunctivitival diseases

Eye lid conditions resulting from allergic and hypersensitivity, drug, cosmetic reactions, and toxic Blepharitis application of topical corticosteroids are very useful.

In the management of vernal, phlyctenular, atopic conjunctivitis and in chemical burns topical steroids are very useful. Seasonal and perennial allergic conjunctivitis are effectively treated with mast cell stabilizers and antihistamines but takes several days for symptomatic relief. Mild steroids Fluromethanol or Loteprednol relief discomforts very quickly which limits school or job performance [23-25]. Topical corticosteroids are indicated when cornea is involved in adenoviral epidemic keratoconjunctivis [26-28].

Topical steroids use in corneal conditions

Punctuate epithelial opacification, disciform keratities, interstitial keratitis and superficial vascularisation in Herpes simplex keratitis. Topical corticosteroids are also used in the management of immune complex infiltrates in Staphylococcus, Herpes, Varicella, adenoviral epidemic keratoconjunctivitis and contact lens users [29,30]. Peripheral ulcerative keratitis in Mooren ulcer and connective tissue diseases topical steroids are very effective [29].
Topical steroid use in dry eye
An aqueous tear deficiency dry eye patient with redness, Blepharitis, or ocular allergy needs induction therapy with a topical steroid for short period and then artificial tear and cyclosporine for the long term therapy. Loteprednol is very useful for acute flare-ups triggered of dry eye conditions by travel, allergies, respiratory infection, or exposure to environmental irritants [31-32]

Topical steroid use in scleral diseases
Prednisolone acetate ophthalmic solution for Episcleritis and Scleritis and sometimes in combination with oral steroids [33-34].

Topical steroids use in uveal diseases
In anterior uveitis management a strong steroid drop is very effective on hourly to six hours doses depending on severity. Frequent dosing, with tapering over the course of a month or more, seems to avoid prolonged treatment periods and significant reduction of relapses. Topical NSIDs like Bromfenac can be added during tapering for synergistic actions. Topical steroids are extensively used for treatment of uveal inflammatory conditions like Pars planitis, Endophthalmitis, Posterior uveitis and Sympathetic ophthalmitis 35-37].

Topical steroid use in retina
Topical steroids are use in the management of retinitis, retinal vasculitides, Choroiditis. Clinically significant pseudophakic acute cystoid macular edema is best treated by frequent application of Prednisolone acetate ophthalmic solution in combination with Ketorolac tromethamine ophthalmic solution [38].

Conclusion
Ocular inflammation needs to be controlled at the earliest stage to prevent irreversible damages to ocular tissue and loss of vision. Topical steroids are the best anti-inflammatory agent for fastest management of ocular inflammations and should not be avoided simply because of side effect.
Table: 1 Topical corticosteroids in order of potency

<table>
<thead>
<tr>
<th>Corticosteroid molecule</th>
<th>In-vitro relative anti-inflammatory activity</th>
<th>In-vitro relative potency</th>
<th>Brands</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluromethone</td>
<td>40</td>
<td>350</td>
<td>FML</td>
</tr>
<tr>
<td>Dexamethasone Sod.phosphate</td>
<td>25</td>
<td>400</td>
<td>Millox-DM (with moxifloxacin)</td>
</tr>
<tr>
<td>Loteprednoletabonate</td>
<td>25</td>
<td>550</td>
<td>L-PRED</td>
</tr>
<tr>
<td>Prednisolone acetate</td>
<td>4</td>
<td>600</td>
<td>Predmet</td>
</tr>
<tr>
<td>Difluprednate emulsion</td>
<td>60</td>
<td>1800</td>
<td>Diflu-P</td>
</tr>
</tbody>
</table>

Table: 2 Topical NSIDs Ophthalmic solutions.

<table>
<thead>
<tr>
<th>NSIDs</th>
<th>BRAND</th>
<th>INDICATIONS</th>
<th>ADVERSE EFFECTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bromfenac 0.09% solution</td>
<td>Bromonec</td>
<td>Inflammation following cataract extraction, CME</td>
<td>Transient burning/stinging Ocular Irritation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ocular pain following cataract surgery</td>
<td></td>
</tr>
<tr>
<td>Diclofenac 0.1% solution</td>
<td>Voveran Ophtha</td>
<td>Inflammation following cataract extraction, Pain and photophobia following corneal refractive surgery</td>
<td>Transient burning/stinging Ocular irritation, Corneal edema, Vision change</td>
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<tr>
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<td></td>
</tr>
<tr>
<td>Flurbiprofen sodium 0.03% solution</td>
<td>Flur</td>
<td>Prevention of intra operative miosis</td>
<td>Transient burning/stinging Ocular Irritation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketorolac tromethamine 0.5% solution</td>
<td>Acular</td>
<td>Seasonal allergic conjunctivitis Inflammation following cataract extraction, CME</td>
<td>Transient burning/stinging Ocular irritation</td>
</tr>
<tr>
<td></td>
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</tr>
<tr>
<td>Ketorolac tromethamine 0.4% solution</td>
<td>Acular LS</td>
<td>Pain, burning, and stinging following corneal refractive surgery</td>
<td>Transient burning/stinging Ocular Irritation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nepafenac 0.1% suspension</td>
<td>Nepalact</td>
<td>Pain and inflammation following cataract extraction, CME</td>
<td>Transient burning/stinging Ocular Irritation</td>
</tr>
</tbody>
</table>


References


Concepts. (http://www.intechopen.com/books/glaucoma-basic-and-clinical-concepts/steroid-induced-glaucoma)


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