Steroids and Infectious Keratitis

CYRIL DALMON, MD

UCSF December Course 2011

Outline

• Acanthameoba and Fungal Infection
  o Brief Discussion
  o Proctor approach

• Bacterial Keratitis
  o Review of the literature
  o Steroids for Corneal Ulcers Trial (SCUT)
  o Comments

Financial Disclosure

• I have no financial interest in any of the content or materials in this presentation

• Steroid for Corneal Ulcers Trial (SCUT)
  o Study funding from the National Eye Institute U10 EY015114
  o Alcon donated moxifloxacin and prednisolone phosphate
  o Leiter’s Pharmacy (San Jose, California) and Aurolab prepared the study medicine

Steroids and Acanthamoeba Keratitis

• Keenan et al. Cornea 2011.
  o Survey sent to all subscribers of The Cornea Society; 82 respondents
  o Frequency of steroid use (in select cases)
    ▪ 50% “some of the time”
    ▪ 10% “most of the time”
    ▪ 40% “never”
Steroids and Acanthamoeba Keratitis

- **Proctor Approach:**
  - Taper off steroids if already using on presentation (do not discontinue abruptly)
  - Obtain control of the infection (typically with monotherapy of PHMB or Chlorhexidine) – usually 6 months
  - Consider low dose topical steroids in select cases (usually milder) after 1 month on biguanide and clinical control

Steroids and Fungal Keratitis

- Limited published experience
- Most clinicians, and Proctor, do not recommend steroid use
- Consider topical steroids for corneal transplants secondary to fungal keratitis
  - Wait 2 weeks after surgery

Background – Steroids and Bacterial Keratitis

- Contentious and controversial topic, actively discussed since the 1950’s
- Anecdotal evidence and traditional teachings, relatively few studies in the literature

The Clinician Perspective

Which ulcer would you treat with topical steroids, if any?
### Steroids and Bacterial Keratitis

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Decrease immune-mediated tissue damage</td>
<td>• Potentiate infection</td>
</tr>
<tr>
<td>• Decrease scar formation</td>
<td>• Increase corneal thinning, perforation</td>
</tr>
<tr>
<td>• Improve visual acuity outcomes</td>
<td>• Elevate intraocular pressure</td>
</tr>
<tr>
<td></td>
<td>• Increase cataract risk</td>
</tr>
</tbody>
</table>

### Controversy in the literature

- **Dr. K Wilhelm. Ophthalmology 2002**  
  - Large review. Increased risk with steroids, advocated caution if used.

- **Dr. E Cohen. Arch Ophthalmol. 2009**  
  - Small prospective study was discontinued when a patient with *Pseudomonas* spp worsened with steroid use.

### Prospective Trials

- **Carmichael et al. BJO 1990**  
  - 40 patients

- **M Srinivasan et al. BJO 2009**  
  - 42 patients

  - 30 patients

- "A study on topical steroids in antibiotic-treated bacterial ulcers needs to be a multicenter study... The steroid and possibly the antibiotic regimen would need to be standardized... Serious infections have both the most potential benefit and risk but would need to be included...”  
  - Elisabeth Cohen MD
### Steroids for Corneal Ulcers Trial (SCUT)

- Randomized, double-masked, placebo controlled, clinical trial – 500 patients with bacterial corneal ulcers

- **Multicenter:**
  - Aravind Eye Hospitals
  - Dartmouth-Hitchcock Medical Center
  - University of California, San Francisco; F.I. Proctor Foundation

### SCUT – Study Design

- **Intervention**
  - 0.5% moxifloxacin every hour while awake for 48hrs, then reduced
  - 1% Prednisolone Phosphate/Placebo
    - Started at 48 hours
    - qid for 1 week
    - bid for 1 week
    - qd for 1 week

### SCUT – Primary Outcome

- Best Spectacle Corrected Visual Acuity at 3 months (LogMAR)
  - controlling for enrollment BSCVA

### SCUT – Secondary Outcomes

- BSCVA 3 weeks, 12 months
- Hard Contact Lens BSCVA 3 months
- Perforations
- Infiltrate/Scar size (Clinical)
- Infiltrate/Scar size (Photographic)
- Re-epithelialization time
SCUT – BSCVA at 3 months

No difference between steroid and placebo

P=0.82

Pre-specified subgroup analysis of severe ulcers

- Steroid use associated with significantly better visual acuity in the most severe ulcers
  - Vision of CF or worse (P=.03)
  - Lesion covering the central 4mm. (P=.02)
  - Deepest infiltrate (P=.07)

- Difference of 1.5 to 2 lines of visual acuity at 3 months with corticosteroids in severe ulcers

Steroids for Corneal Ulcers Trial (SCUT)

Table 5. Adverse Events by Treatment Group

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>No. of Patients</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vision</td>
<td>Placebo</td>
<td>Corticosteroid</td>
</tr>
<tr>
<td>Corneal perforation</td>
<td>15</td>
<td>7</td>
</tr>
<tr>
<td>Endophthalmitis</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>IOP &gt;35 mm Hg</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Systemic infection</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Mycobacterial infection</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nematodes</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Local allergic reaction</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Increase in IOP</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Increase in IOP &gt;50%</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>No healing of superficial ulcer by 21 d</td>
<td>27</td>
<td>44</td>
</tr>
<tr>
<td>IOP elevated &gt;30 mm Hg but &lt;35 mm Hg</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>Progressive corneal thinning</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>13</td>
<td>9</td>
</tr>
</tbody>
</table>

Abbreviation: IOP: intraocular pressure
*Patients may have had more than 1 such event.
+Significant at .05 level.

SCUT: Pseudomonas

- 1.5 lines worse acuity at presentation than other ulcers
  - Same acuity at 3 months
- 0.4 lines better with steroids (vs placebo)

- Note: Nocardia spp did poorly with steroids
SCUT - Comments

- 97% of patients from India
- Ulcers reflect prevalence of Southern India
  - *Nocardia* spp more common than in the U.S.
  - Most were Pneumococcus, Pseudomonas, Staph, Moraxella
- Infiltrates worse at baseline than prior studies
- Choice of treatment algorithm
  - Different antibiotic or steroid regimens may have had different outcomes

Summary

- **Bacterial Keratitis**
  - No difference with steroid use in safety or efficacy
  - There is some evidence supporting use of steroids in severe ulcers but more studies are needed

The Clinician Perspective

Which ulcer would you treat with topical steroids, if any?

Acknowledgements

<table>
<thead>
<tr>
<th>Aravind</th>
<th>Proctor/Dartmouth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muthiah Srinivasan</td>
<td>Stephen D. McLeod</td>
</tr>
<tr>
<td>Jeena Mascarenhas</td>
<td>Nisha R. Acharya</td>
</tr>
<tr>
<td>Revathi Rajaraman</td>
<td>Thomas M. Lietman</td>
</tr>
<tr>
<td>Meenakshi Ravindran</td>
<td>Jeremy Keenan</td>
</tr>
<tr>
<td>Prajna Lalitha</td>
<td>David V. Glidden</td>
</tr>
<tr>
<td></td>
<td>Kathryn J. Ray</td>
</tr>
<tr>
<td></td>
<td>Jack Whitcher</td>
</tr>
<tr>
<td></td>
<td>Catherine E. Oldenburg</td>
</tr>
<tr>
<td></td>
<td>Salena M. Lee</td>
</tr>
<tr>
<td></td>
<td>Michael E. Zegans</td>
</tr>
</tbody>
</table>
Sources

- Aileen Sy et al. Pseudomonas aeruginosa Keratitis: Outcomes and Response to Corticosteroid Treatment. Personal Correspondence.