Evolution of the Intracameral Regimen

James P. Gills, MD
Affiliate Professor of Ophthalmology
University of South Florida
Consulting Professor of Ophthalmology
Duke University Medical Center

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Antibiotic Prophylaxis
40 years of History

- Began by using antibiotics in irrigating solution 40 years ago
  - Vancomycin
    - 1/10,000 endophthalmitis
  - Controlled dosage with postop A/C injection
    - 35 years
    - Vancomycin / Ceftazidime

Present Dosage – 8 years
- Dosage of 0.1cc is equal to:
  - Vancomycin 33.3mcg
  - Dexamethasone 99mcg
  - Ceftazidime 20mcg
- Irrigated into an anterior chamber
  - Already formed, collapsed and reformed again
  - With 1/10th cc of antibiotic solution
  - Day 1 – Rare Ray or Cell in AC

James P. Gills - Results
- 75,000 routine cataract procedures
  - Over 15 years
- Each patient received dosage of 0.1cc equal to:
  - Vancomycin 33.3mcg
  - Dexamethasone 99mcg
  - Ceftazidime 20mcg
- No topical antibiotics
- No incidents of endophthalmitis
Richard Mackool, MD - Results

- 75,000 consecutive cataract implant procedures
  - Over 14 years
  - Performed by 40 ophthalmologists
  - 30,000 Mackool pts. / 45,000 other surgeons
- Each patient received:
  - 0.1mg intracameral vancomycin in 0.1cc of BSS at the end of procedure
- No Cases of endophthalmitis

Howard Gimbel, MD - Results

- 44,554 routine cataract procedures
  - Over 22 years
- Each patient received:
  - Bolus of Vancomycin in the bag and AC
- 4 Cases of presumed but not proved endophthalmitis = 0.0089%

Samuel Masket, MD - Results

- 5,000 routine cataract procedures
  - Over 6 years
- Each patient received:
  - 0.50ml of Vigamox® in the AC at the close of cataract surgery
- No incidents of endophthalmitis

Samar Basak, MD - Results

- 12,192 routine cataract procedures
  - Over 5 years
- Each patient received:
  - 0.1ml of 0.5% Moxifloxacin (Vigamox®) in the AC at the end of cataract surgery
- No incidents of endophthalmitis
- No case of TASS or other major reaction
Vigamox / Moxifloxacin

- Toxicity profile/efficacy are key issues
- Off the shelf Vigamox (moxifloxacin 0.5%)
  - Offers potential advantages
- Broad spectrum bactericidal activity
  - Sterile, self-preserved formulation (without BAK)
  - Ease of administration – no dilution or mixing
  - Formulated at pH 6.8 and osmolality 290mOsm/kg which is compatible with the human anterior chamber fluid (pH 7.4/osmolality 305mOsm/kg).
- Prior non-controlled study of 65 human eyes from Esp et al (JCRS Jan 07)
- Kowalski, et al - AJO Intracameral safety in rabbits
- Arshinoff Study (ASCRS Poster 2007)

Topical Antibiotics No Benefit

- With Intravitreal injections
  - Topical Antibiotics vs. No Antibiotics
  - Topical antibiotics associated with greater incidences of endophthalmitis compared with not giving antibiotics.
  - Use of Topical antibiotics has never shown to be a benefit in preventing endophthalmitis


Postulate

1. Natural defense mechanism of the anterior chamber fights infection
   - Experimentally bacteria injected into AC of animals and cleared naturally (dose dependent)
2. Antibiotics stun or kill most bacteria
3. Vancomycin
   - Gram positive bacteria
4. Ceftazidime
   - Gram negative bacteria

Topical antibiotic drops may produce resistant bacteria if used for a long period of time

Thus, topical drops antibiotic should be avoided
**Intraocular Implants & Cataract Surgery**

**New Drug Device**

- 3 mm long x 0.5 mm diameter
- 9 week duration
- Drug released over 60 days
  - Consistent dose of 5 micrograms per day
- Intraocular implant testing in rabbits
  - Low, medium and high ranges tested
Dissolution Profiles of Formulas Containing Diclofenac

Dissolution Profile of Formulas Containing Diclofenac

Safety Testing Studies

- Cytotoxicity
- Sensitization
- Systemic toxicity injections
- Pyrogen testing
- Four week systemic toxicity implants
- Genotoxicity studies (bacterial and mouse lymphoma)
- Blood micronucleus studies

Safety Testing Studies

- Intracutaneous implant testing
- Intraocular implant testing in rabbits
  - Dose Range: Low, medium, & high ranges tested (150 - 1500 µg)
- IOL Implant study (device vs drop therapy)
Analytical Characterization

- UV/Vis spectroscopy
  - Drug/matrix characterization
  - Drug release rate testing
- HPLC
- GC/MS for residuals

Initial Clinical Testing

- Testing in a small group of humans resulted in quiet eyes with no signs of inflammation.
- Swelling of the polymer resulted in movement of the first devices tested.
  - A mild corneal edema was observed in one patient
  - Two patients had the device removed due to movement in front of the visual axis.
- Device has been resized to compensate for swelling and is now implanted in the capsular bag. No further problems have been observed.

Regulatory Steps

- Requires a New Drug Application (FDA)
- Demonstration of safety and efficacy
  - Already approved drug/new device
- Submit data
  - Process parameters (SOP’s)
  - Analytical and Stability
- Initial Small Scale Clinical Trial (US)