Dropless Cataract Surgery Update
(Intraoperative intravitreal antibiotic and steroid)

Cathy Schanzer, MD, FACS
Cataract Surgery Technology

- Equipment: peristaltic vs venturi phaco, Zepto capsulotomy, MiLoop nuclear fragmentation, iris and capsular hooks, pupil stretching devices, CTR, OVDs
- Preop: Biometry, topography, OCT, ECC
- Femtosecond laser (↓ US Energy)
- Premium IOLs improve vision
- Technology to eliminate astigmatism
Current Drop Regimen

- Topical antibiotic drops
- Topical anti-inflammatory drops
  - Steroid
  - NSAID
Cataract Surgery Fears

- Endophthalmitis
- CME
Topical antibiotics

- Prophylaxis against most common organisms
- Penetration varies: drug concentration in the eye
- Treating ocular surface: threat is inside the eye
- Vitreous is where infection takes place
Topical Anti-inflammatory

- Inflammation is guaranteed from surgery
  - Increases with additive surgery i.e.: glaucoma, IFIS, PKP
- Goal with anti-inflammatory
  - Decrease pain, photophobia, edema, CME
  - Faster visual recovery
Problems with Topical Medications
Problems with Topical Medications

toxicity
Problems with Topical Medications
Problems with Topical Medications

- **COST $$$$$$$**: Purchase price too high, unable to afford.
- Insurance limitations, i.e. pre-authorization & unauthorized substitutions → excessive phone calls and unfilled prescriptions.
- Pharmacy inventories → back orders, delay in obtaining drugs.
Problems with Topical Medications

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<tr>
<th>NDA (Branded)</th>
<th>ANDA (Generic)</th>
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<td>$802 million and 12 years to get a single drug to market&lt;sup&gt;1&lt;/sup&gt;</td>
<td>$4 million and 3-6 years to bring generic drug to market&lt;sup&gt;2&lt;/sup&gt;</td>
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<th>FDA Approval Requirements</th>
<th>Chemistry</th>
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Animal Studies

Clinical Studies

Bioavailability

} Bioequivalence in bottle*
Generics

- 1999 ACSRS Survey
- Observations of corneal melting after routine anterior segment surgeries
- Topical generic diclofenac (Falcon) identified and recalled
- ASCRS press release on NSAID Adverse Reaction Report
- Similar reports with other NSAIDs
Problems with Topical Medications

- Dosing/convenience/compliance
  - Family members often have to help, i.e. leave work to place drops
  - Elderly can’t remember to administer the drops
  - Administer drops at same time thereby diluting one with the other

- Studies Show
  - 50% of patients took < ½ of prescribed medicine
  - 20% took < ¼
Problems with Topical Medications

- Physical limitations
  - rheumatoid arthritis
  - kyphosis
  - torticollis
  - scoliosis
  - tremor
Problems with Topical Medications

- Accuracy

  - excessive drops placed in eye -> need refill

  - more on face than in the eye
Problems with Topical Medications

“Eye-Drop Phobia”
ADDRESSING THE MAIN POINTS WITH COMPOUND MEDICATIONS

PATIENTS
- Costs
- Multiple drops
- Recovery time
- Outcomes

PHYSICIANS & STAFF
- Costs
- Call backs
- Compliance
- Turnover & outcomes
Goals with Intraocular Medications

- Prophylaxis against infection
- Control inflammation
- Greater patient convenience
- Better therapeutic compliance
- Cost effective
- Easier communication with Patient
Endophthalmitis Prophylaxis

- Perioperative povidone-iodine
- Lid speculum and drape to isolate lashes
- Sterile prep
- Medications
Post Operative Endophthalmitis

- Risk factors
  - prior vitrectomy, PKP, glaucoma surgery
  - DM, trauma, dialysis, immune compromised
  - Blepharitis
  - inadequate prep and drape (betadine)
Postoperative Endophthalmitis

Endophthalmitis

- Bacterial: typical onset days to weeks after surgery
  - Gram negative: quick & aggressive
- Fungal: delayed, insidious onset
- Sterile: phacoanaphylactic, response to IOL materials or chemicals
Postoperative Endophthalmitis Prevention

- Treat pre-existing conditions
- Proper sterilization of instruments
- Disinfecting and isolating the eye
- Careful wound construction
- Antibiotics
Postoperative Endophthalmitis

Endophthalmitis Treatment

- Intraocular specimen for stain and culture
- Antibiotic: IV, intravitreal, topical, subconjunctival
- Vitrectomy
- May use steroids to control inflammation
Postoperative endophthalmitis Incidence

- 70/10,000 (.7%) overall with ATB drops only
- 23/10,000 (.23%) betadine scrubs
- 4/10,000 (.04%) intracameral ATB (ESCRS)

- 4.92 (5 fold) reduction with cefuroxime (1mg/.1ml)
Intracameral vs Intravitreal Placement

- **Intracameral Injection**
  - anterior chamber volume turnover (250 ul@2.5ul/min)
  - two hour max retention in A/C
  - AC placement of steroid particulate causes pseudo-hypopyon
  - TM outflow altered by drug-particulate blocks TM->IOP spikes
  - corneal endothelial toxicity depending on concentration
Intracameral vs Intravitreal Placement

- Intravitreal depot
  - bound into protein matrix-very tiny particulate size
  - drug retention & release gradually
  - high safety, no zonular damage
  - floaters up to 80% POD#1, 20% POW#1
Intraocular ATB for Infection Prophylaxis

- Narrow spectrum vs broad spectrum
- Ocular compatibility: critical for high safety
- Iso-osmotic and iso-tonic
- pH balanced
- Soluble medication
- Stability in formulation: long shelf life
- Ease of handling: transfer to sterile field, prep by surgical staff for delivery
Intraocular ATB for Infection Prophylaxis

- Different ATB require different pH
- Concentrations vary based on target therapy
- Binders and stabilizers critical to avoid precipitation
- Osmolarity and tonicity different for each drug
Intraocular ATB for Infection Prophylaxis

- Multiple studies: 100,000+ procedures
- Lower incidence of endophthalmitis with intraocular injection compared to topical
- Well tolerated intraocular delivery
- Various methods of delivery
- ESCRs Endophthalmitis study: 4/10,000
Intraocular Medications & Proactive Control

- Combination ATB & steroid into one injection
- Trimoxi or Trimoxivanc by Imprimis Pharmaceuticals
- Triamcinolone 15mg/ml
- Moxifloxacin 1 mg/ml
- Vancomycin 10 mg/ml
  - Highly efficient delivery into the vitreous
  - Inexpensive compared to pharmacy drugs
  - Produced by compounding pharmacy
    - Regulated & accredited, meets FDA protocols
SURFACTANT SOLUBILIZING PROCESS (SSP)

- Mixing process allows for unique combination of insoluble ingredients into a suspension
- Micronized particle size for a consistent suspension
- Optimized for the isotonicity and pH most compatible with the eye
Our proprietary, SSP technology® allows for the unique combination of these drugs. The resulting small, consistent particulate size enables injection through a 27-30 gauge needle or cannula.

The formulations have been optimized for the isotonicity and pH most compatible with the eye.

*Dropless Therapy® is the only available solution for a single injection of anti-infective and anti-inflammatory prophylaxis.*
Quality assurance from an imprimisrx® pharmacy

- Pharmacy Compounding Accreditation Board (PCAB)-Accredited Facility
- Meets or exceeds U.S. Pharmacopeia (USP) 797 guidelines
- Daily quality monitoring,
- Quarterly facility monitoring and inspections
- Endotoxin, potency and sterility testing of each sterile batch prior to distribution
- Cleared test results included with every order
Intravitreal Triamcinolone

Intravitreal administration of triamcinolone demonstrates sustained vitreous drug levels.

- Intravitreal triamcinolone suspension has a half-life of 18.6 days and is typically effective for approximately 3 months in nonvitrectomized eyes.
- The eye clears intravitreal medications relatively rapidly. To increase the duration of action, a crystal structure like triamcinolone is needed.
- Intravitreal dexamethasone has a relatively short half-life of 3.5 hours.

Intravitreal Moxifloxacin

Intravitreal moxifloxacin demonstrate sustained vitreous drug levels.

- Intravitreal injection of moxifloxacin is detectable at therapeutics levels in the vitreous at 12 hours.
- A single intracameral bolus injection of 500 µg/0.1 ml moxifloxacin in a rabbit model reaches prevention concentration levels for 6 hours.
- Intracameral moxifloxacin is difficult to ensure delivery of small amounts of antibiotic into the area behind the intraocular lens (IOL).

1. Trans Am Ophthalmol Soc. 2005 Dec; 103: 76-83. PMCID: PMC1447561 INTRAVITREAL CLEARANCE OF MOXIFLOXACIN Mohan N Iyer, MD, Feng He, PhD, Theodore G Wensel, PhD, William F Mieler, MD,*§ Matthew S Benz, MD, and Eric R Holz, MD


Allergy History to Trimoxivanc

- Rare due to privileged ocular barrier
- Allergy does not modify the use of the product
Intraoperative

- Loss of red reflex
Intravitreal Trimoxi and Trimoxivanc

- 3%-7% require supplemental topical steroids
- 10-14 days postop - 1 out of 15 have breakthrough inflammation
- Slight Redness (ciliary flush)
  - Good and stable vision
  - Some photophobia
  - No lid swelling
  - Quiet AC
- Quick to respond to topical PF1% or FML.1%
Intravitreal Trimoxi and Trimoxivanc

- No IOP elevations with <4mg triamcinolone
- Endophthalmitis rate <0.005% or 0.5/10,000 (10x less than topical)
- CME rate (OCT): 1.8% in healthy eyes
  - 8.6% in Diabetic Retinopathy
  - 8% with epiretinal membrane
Unplanned Initiation of Postoperative Topical Medications after Intravitreal Antibiotic-Steroid Injection during Cataract Surgery (ARVO 2017 Zeeshan Haq)

elevated IOP (>30mmHg) 11%
breakthrough inflammation 14%
CME 1%
Endophthalmitis 0%
20/25 or better 86%

N=90 eyes
Intravitreal antibiotic + steroid makes dropless cataract surgery possible
S. Galloway, MD  N=1575 eyes

CME incidence
2% overall
8.9% in pt with ERM  (2.9% if added NSAID)
2.7% in pt with DM
Patients Benefiting from Dropless Cataract Surgery

- Severe kyphosis
- Mentally retarded: combative/uncooperative
- Nursing home patient
- Severe RA (unable to squeeze eye drop btl)
- Impoverished patients w/o ins., $$, or samples
- Eye drop phobia
- Patients seeking a convenient alternative
DROPLESS THERAPY® PATIENT BENEFITS

- Support physically and/or mentally challenged patients
- Eliminate compliance challenges of proper dosing
- Lift burden from family members/caregivers assisting with instillation
- Put patients with “Eye Drop Phobia” at ease
- Avoid pharmacy issues: premature refills, generic switches, QID/BID dose alterations
- Help extended care patients in nursing facilities
- Aid patients without insurance, money or access to sample drops

- Osteoarthritis
- Rheumatoid Arthritis
- Scoliosis
- Parkinson’s
- Kyphosis
- Alzheimer’s
- Dementia
Postoperative Concerns

- Floaters in superior field
- “Bubble in vitreous (may look like IOL)
- Ciliary body hemorrhage (microhyphema)
Postoperative Concerns

- Tongue of vitreous comes into AC
- Inadvertant injection anterior to zonules, will reflux into A/C or remain hidden under the iris around the perimeter of the equator
White out” due to Steroid in Bergers Space
Dropless Cataract Surgery

- Effective
- Saves Time
- Saves Money
- Has good results
Injectable RX INNOVATION

- Dropless Therapy® formulations
- Enabled by SSP Technology®
- Injectable platform
- Antibiotic and steroid combinations

The three C’s:
- Cost
- Compliance
- Call-backs
Intraoperative administration of drugs virtually eliminates both non-compliance and patient errors, significantly lessening the surgeon’s concern and enhancing the patient’s experience with cataract surgery.
Thank You!!

Q&A