



Endophthalmitis Prophylaxis

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Endophthalmitis Prophylaxis

Antiseptic Rules

Endophthalmitis Prophylaxis

- In intravitreal injections (IVI)
- In cataract surgery

Prophylaxis in Intravitreal Injections (IVI)

IVI; Prophylaxis

Outcomes are bad because of the organisms

- **Strept. viridans is 3-4 x higher after IVI compared to other surgeries,
? due to oral flora.**
- **Vision: often HM.**

- McCannel, Retina 2011
- Chen, Retina 2011
- Kim, Archives 2011
- Shah, Ophthalmology 2011

IVI; Prophylaxis

Masks and 'no talking'

- **Bacterial dispersion from oropharynx.**
- **Significant reduction in bacterial dispersion and endophthalmitis with masks and 'no talking' policy.**

- OKelly, Br J Anaesth 1993
- Wen, Archives 2010
- Abell, Br J Ophthalmol 2012
- Garg Dollin, Retina 2016

IVI; Prophylaxis

The preparation matters

Ranibizumab prefilled syringes

- Japan: 2014
- USA: 2016

IVI; Prophylaxis

10-center retrospective study Suspected Endophthalmitis

	Conventional	Prefilled
Injections	165,347	78,407
Cases	43	12
Incidence	0.026%	0.015%
Odds Ratio	0.59	$p=0.1$

IVI; Prophylaxis

10-center retrospective study Culture +ve incidence

	Conventional	Prefilled
Injections	165,347	78,407
Cases	22	2
Incidence	0.013%	0.0026%
Odds Ratio	0.19	$p=0.025^*$

IVI; Prophylaxis

10-center retrospective study VA

	Conventional	Prefilled	<i>p</i>
Average lines lost	4.45	0.38	0.006*
Average VA	1.13 LogMar (20/250)	0.42 LogMar (20/50)	0.000*
VA≤C.F.	27.9%	0.0%	0.05*
Odds Ratio	0.19	$p=0.025^*$	

IVI; Prophylaxis

Topical Antibiotics (TA)

Prospective, USA, 273 injections

Gatifloxacin 1x4x3 (preop)

- +ve conjunctival culture:

TA:	21%	
No prophylaxis:	48%	$p=0.005^*$

- After PI:

TA:	8%	
No prophylaxis:	4%	$p=0.324$

Antibiotics confer no additional benefit to PI

- Moss et al. Ophthalmology 2009

IVI; Prophylaxis

Topical Antibiotics (TA)

Retrospective study, Canada, 15,895 IVI

Endophthalmitis: 9 cases (0.057%); 3 culture +ve

- TA: immediately after: 2/2370 (0.084%)
- TA: for 5 ds: 5/8259 (0.061%)
- No TA: 2/5266 (0.038%)

Higher incidence of endophthalmitis with TA compared to no TA

- Cheung et al., Ophthalmology 2012

IVI; Prophylaxis

Topical Antibiotics (TA)

DRCR net: prospective

- 6/4694 (0.13%) with TA vs
- 1/3333 (0.03%) without TA (p=0.25)

Larger retrospective studies of 117,000 injections

- TA increased incidence
- TA did not improve visual income
- TA increased resistance

So, TA are unnecessary for IVI

- McCannel, Retina 2011
- Chen et al, Retina 2011
- Bhavsar et al, Archives 2009, 2012
- Storey et al, Ophthalmology 2013
- Storey, Grafes 2016

IVI; Prophylaxis

Povidone Iodine (PI) 5%

- Only agent shown to reduce the rate.
- *Speaker, Ophthalmology 1991*
- Still up to 1/4 have preop +ve cultures



IVI; Prophylaxis

Povidone Iodine (PI) 5%

- Inexpensive and widely available.
- Some patients hate it.

IVI; Prophylaxis

Chlorhexidine

- Broad spectrum antiseptic, the most effective antiseptic mouthwash to date
- Used as a mouthwash 0.2%.
 - Do not irrigate brain, meninges, and eyes.
- Aqueous solution is different.



IVI; Prophylaxis

Aqueous Chlorhexidine (AC)

- AC may be better tolerated compared to PI in some patients.
- Similar efficacy with microbiological testing.
- No large RCT.
- Not the standard of care.
- May be more expensive.

IVI; Prophylaxis

No paracentesis?!

IVI; Prophylaxis

USA 2009-2010: 27,736 IVI

23 cases of endophthalmitis (0.08%).

- Bladed lid speculum, conjunctival displacement, hemisphere of injection and type of anti-VEGF did not affect the risk.

IVI; Prophylaxis

Summary

- Masks and "no talking" policy.
- Prefilled syringes: lower rates.
- Routine topical antibiotics: useless, potentially harmful.
- Topical PI is very useful.
- AC may be useful alternative to PI in some eyes.
- No paracentesis.

Acute post-cataract surgery endophthalmitis

Visual outcomes are often poor

- **30%: not more than C.F.¹**
- **50%: not more than 20/40¹**
- **34%: \leq 20/200²**

1 Endophthalmitis vitrectomy study, Arch 1995.

2 Gower et al, Ophthalmology 2015.

Effective postoperative endophthalmitis (POE) prophylaxis

A global imperative

- **World-wide rise in aging population.**
- **Increase in cataract surgery volume.**

Post-cataract surgery endophthalmitis

Incidence

- 19th century: 10%
- Before 1950s: 1%
- 1960s: 0.1%
- 1980s: 0.09%
- 2013-2017: 0.04% (8.5 million cases)*

*Pershing et al. Ophthalmology 2020

Post-cataract surgery endophthalmitis

Due to

- Antiseptic surgical protocols.
- Perioperative PI.
- Isolation of eyelids & lashes.
- Proper draping.
- Topical perioperative antibiotics?

Postoperative Endophthalmitis (POE) Prophylaxis

Topical Antibiotics (TA)

- Topical 4th generation fluoroquinolones: 0.07% POE

Morshifar et al, Ophthalmology 2007

POE Prophylaxis

Topical Antibiotics (TA)

Conjunctival culture, prospective comparative, USA: 60 patients

Gatifloxacin

- 1 day 1x4 : 67% +ve at baseline → 28% ($p < 0.001^*$)
- 1 hour 1x3 /5 min : 60% +ve at baseline → 37% ($p < 0.018^*$)
- Both regimens : 67% +ve at baseline → 18% ($p < 0.0001^*$)

So, 1 d & 1 h topical Gatifloxacin were effective in reducing frequency of conjunctival bacterial growth.

Both regimes → lower overall bacterial load.

Moss et al, Ophthalmology 2008

POE Prophylaxis

Topical Antibiotics (TA)

- Topical antibiotic prophylaxis is common in USA.
- However, it vanished in Europe: Intracameral antibiotics is the standard in Sweden, France, Denmark, Spain.

POE Prophylaxis

Intracameral antibiotics (ICA)

Rational

- Entry of periocular bacteria via instruments into the eye: 31%.¹
- Clear cornea wounds permit retrograde influx of external surface fluids during/after surgery until water-tight seal develops.
- Persistence of high concentration in AC for several hours.²

1 Balestrazzi et al, Eur J Ophthalmol 2012
2 Murphy et al, Br J Ophthalmol 2007

POE Prophylaxis

ICA: Drugs

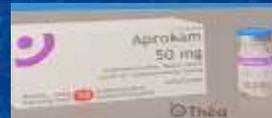
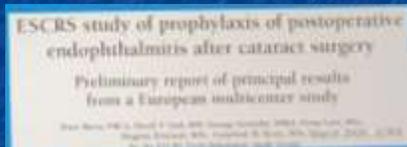
Class	Drug	Dose/0.1 ml
Complex glycopeptide	Vancomycin	1 mg
Cephalosporins	Cefuroxime (Zinnat, Zinacef) Cefazolin (Kefzol, Ancef)	1 mg 1-2.5 mg
G4 fluoroquinolones	Moxifloxacin (Vigamax) Gatifloxacin (Zymar)	500 ug 100 ug

POE Prophylaxis

ICA

Powerful evidence in favor of ICA prophylaxis

ESCRs multicenter study: 16,000 patients
Cefuroxime was effective in RCT
(24 centers)



Endophthalmitis:
● 0.07% with Cefuroxime
● 0.34% without Cefuroxime
>5-fold reduction

Available in Europe
Recommended by ESCRS
guidelines for POE prophylaxis

POE Prophylaxis

ICA

Author	ICA	Without	With	Country
1) Tan et al 2012	Cefazolin	19/29,539 (0.064%)	2/20,638 (0.01%)	Singapore
2) Herrinton et al 2015	Cefazolin	187/237,709 (0.07%)	28/63,241 (0.04%)	USA
3) Barreau et al 2012	Cefuroxime	35/2826 (1.24%)	1/2,289 (0.04%)	France
4) Jabbarvand et al 2016	Cefuroxime	28/139,440 (0.014%)	0/25,920 (0.0%)	Iran
5) Daien et al 2016	Cefuroxime	1393/1,479,158 (0.09%)	548/954,850 (0.06%)	France
Matsuura et al 2013	Moxifloxacin	8/15,958 (0.05%)	3/18,794 (0.01%)	Japan
Total		0.08%	0.04%	

POE Prophylaxis

ICA

Concerns with IC Cefuroxime:

- Limited spectrum of activity.
- Lack of commercially approved preparation in most countries (Aprokam)
- Risks of errors in dilution, concentration, dose: ME with overdose.
- Sterility.
- Risk of TASS: diluting fluid toxicity.
- Anaphylaxis: 2 cases reported.
- Increasing drug resistance: unlikely.
- Fusarium endophthalmitis followed use of compounded Cefuroxime in 8 consecutive cases from a single bottle of BSS.

POE Prophylaxis

ICA

IC Vancomycin (1 mg/0.1 ml)

- Broad spectrum coverage of all G+ve bacteria; most common cause of POE.
- Choice of most American ophthalmologists in ASCRS surveys: 2007, 2014.
- Reported with good results for 15 ys; from Sydney.

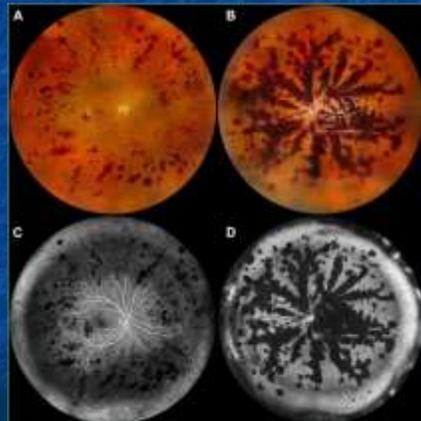
POE Prophylaxis

ICA

Concerns with IC Vancomycin:

Rare cases of hemorrhagic occlusive retinal vasculitis (HORV)

- Witkin et al reported 36 eyes of 23 patients (13 bilateral) with IC or IV Vancomycin during or shortly after (1-21 ds) cataract surgery.



Witkin et al, Ophthalmology 2015 & 2017

POE Prophylaxis

ICA

Concerns with IC Vancomycin:

Rare cases of hemorrhagic occlusive retinal vasculitis (HORV)

- Witkin et al reported 36 eyes of 23 patients (13 bilateral) with IC or IV Vancomycin during or shortly after (1-21 ds) cataract surgery.
- 61%: $\leq 20/200$.
- 22%: NLP.
- 56%: NVG within 1-2 M.
- Delayed (Type III) hypersensitivity.

Should be reserved for Rx of clinically suspected POE.

Witkin et al, Ophthalmology 2015 & 2017

POE Prophylaxis

ICA

IC Moxifloxacin (MF): 500 µg/0.1 ml.

- 4th G. fluoroquinolone; excellent ocular penetration.
- Potent activity at low concentration.
- Unpreserved Vigamox: safe and easy to use.
- Auromax (India): 0.1ml 0.5%.

POE Prophylaxis

ICA

ICMF

Aravind Eye Hospitals (2014-2016)

617,453: phaco & MSICS

	Topical Ofloxacin	ICMF	<i>P</i>
Phaco	75/104,894 (0.07%)	11/89,358 (0.01%)	<0.001*
MSICS	135/192,149 (0.07%)	52/222,508 (0.02%)	<0.001*
Total	214/302,815 (0.07%)	64/314,638 (0.02%)	<0.001*

ICMF reduced overall POE 3.5-fold (3-fold for MSICS, 6-fold for phaco)

HariPriya et al, Ophthalmology 2017

POE Prophylaxis

ICA

ICMF

- Chang et al reported 3.5-fold reduction in POE in over 1 million patients

Chang et al, Ophthalmology 2017

POE Prophylaxis

ICA

Comparison of ICMF & Cefuroxime in prevention of POE

- Prospective, comparative, interventional study.
- Prasade Eye Institute, India.
- Over 18 M: Oct 2016-Mar 2018.
- MSICS/Phaco.

POE Prophylaxis

ICA

Comparison of ICMF & Cefuroxime in prevention of POE

Drug Preparation

	Cefuroxime	MF
Commercial dispensing	250 mg powder	1 ml solution 0.5%
Preparation		
Step 1	+12.5 ml NS: 20 mg/ml	X
Step 2	+1 ml to reconstituted Cefuroxime = 10 mg/ml	X
Step 3	0.1 ml = 1mg	0.1 ml direct from vial

POE Prophylaxis

ICA

Comparison of ICMF & Cefuroxime in prevention of POE

Results

42,466 subjects

17,932 Cefuroxime	24,534 MF
Before IC 0.05%	Before IC 0.194%
After IC 0.017%	After IC 0.049%

Significant reduction in POE after ICA

No significant difference between the 2 drugs

POE Prophylaxis

Summary

- ICA during cataract surgery, although used in some parts of the world, remain controversial.
- Prophylactic antibiotics are associated with increased costs, risk to the individual patient (HORV), and risks to the population by contributing to the emergence of drug resistant organisms.

POE Prophylaxis

Summary

- Mounting evidence that ICA is an efficacious method for POE prophylaxis.
- Cefuroxime and MF seem to be equally efficacious.
- FDA approval of ICA prophylaxis would enhance acceptance.

