

Update on Risk Factors and Prophylaxis of Endophthalmitis after Cataract Operation

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Endophthalmitis is a devastating complication occurring in a few cases after cataract surgery but resulting in profound morbidity. Thus every eye surgeon should remain vigilant to avoid it. The options of povidone iodine application to skin and conjunctiva, suturing the wound to make it leak proof, use of IOL injectors, intracameral cefuroxime or moxifloxacin, post operative levofloxacin/ gatifloxacin / moxifloxacin has profoundly reduced the incidence of endophthalmitis.

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Endophthalmitis is an inflammatory reaction occurring as a result of intraocular colonization by bacteria, fungi or rarely parasites. Commonly it is exogenous i.e. microbial entry from ocular surface through open wound/foreign bodies (e.g. post-traumatic) or through contaminated instruments/ intraocular lenses (IOLs) (e.g. post-operative). Rarely endophthalmitis may be endogenous (septicemic) in origin.

Pathophysiology: In approximately 30-45% of cataract operations, intraocular contamination occurs with facultative pathogenic bacteria from the ocular surface without the development of endophthalmitis¹⁻³. However, immune mechanisms of eye are effective in limiting the inflammatory process in most of the cases.

Whether the endophthalmitis will occur or not and its final picture depends on various factors: Firstly the characteristics and quantity of pathogens. Secondly patient's body resistance. Last but not least is the delay in initiation and the quality of treatment.

In microbial endophthalmitis, the first phase is the incubation period, which lasts 16-18 hours and is mainly determined by generation time of the pathogen e.g. Staphylococcus (Staph) aureus up to 10 min, Propionibacterium (P) >5 hours and specific characteristics of the pathogens (e.g. toxin production). Next is the invasion by macrophages and lymphocytes (acceleration phase) which is followed by the destruction phase in which the inflammatory mediators

especially cytokines not only recruit further leukocytes but directly result in retinal injury^{4,5}.

Microbial spectrum: Pathogens causing post-phaco-emulsification (phaco) endophthalmitis are⁵:

In approximately 50% of cases Coagulase-negative staphylococci (CNS).

In approximately 15% Staphylococcus (Staph) aureus.

In approximately 15% Streptococci (S) including β and α haemolytic, *S. pneumoniae*.

In approximately 15% Gram negative e.g. *Pseudomonas* (*Ps*) *aeruginosa*, *Haemophilus influenzae* etc.

In approximately 5% Fungi (*Candida*, *Aspergillus*)

The most important pathogens causing acute post-cataract endophthalmitis are Streptococci, Staph aureus, CNS, and Gram negative rods. In chronic postoperative endophthalmitis pathogens are⁵. *Propionibacterium acnes*, Diphtheroids, CNS and fungi. In an Indian study, *Nocardia* species⁶ and in a Pakistani study Staph aureus was the commonest pathogen isolated in endophthalmitis cases⁷. *Ochrobactrum anthropi* has also been found to cause chronic pseudophakic endophthalmitis⁸.

Incidence: After introduction of phaco and clear corneal incision (CCI), with only povidone iodine prophylaxis, incidence of endophthalmitis is 0.3-0.5% in Europe^{9,10} and 0.015% in USA. The European Society of Cataract and Refractive Surgery (ESCRS) study has found the lowest observed incidence rates were for the group which received both intracameral cefuroxime and perioperative topical levofloxacin¹¹. These rates were 0.049 percent for presumed endophthalmitis and 0.025 per cent for proven endophthalmitis. Incidence of acute endophthalmitis after cataract surgery has been found to be 0.05% in an Indian study⁶ and following intraocular surgeries 0.60% in a Pakistani study¹².

RISK FACTORS

ESCRS study¹⁰ findings: Endophthalmitis incidence was approximately 6 times greater with clear corneal incision (CCI) than with scleral tunnel incision (CSI). Wound leak on first post op day¹³ has been implicated as important factor. Thus suturing of the wound to produce leak proof incision after CCI was found preferable¹⁴. The endophthalmitis risk was reduced by 5 fold in superior CSI compared to temporal CCI¹⁵.

Patients receiving silicone IOLs were 3.13 times more likely than any other material IOL and those experiencing intraoperative capsular or zonular complications were 4.95 times more liable to develop infection. Rate of complications is higher if operated by junior staff.

Use of Injectors for IOL: Use of injectors for IOL has been found to reduce the risk of developing infection¹⁶.

Diabetes Mellitus: About 15 -20 % of all patients who develop post operative endophthalmitis after cataract operations are diabetic^{17,18}. If glycemic control is poor or diabetic retinopathy is present¹⁷, prognosis is usually worse.

Immune suppression: Patients on topically or systemically administered immuno suppressants (corticosteroids, antimetabolites) at the time of operation have a significantly higher risk of endophthalmitis¹⁹.

Altered bacterial flora: Atopic and those having rosacea have preponderance of Staph aureus²⁰. Preferably they should be given anti Staph prophylaxis prior to and after surgery²¹.

PROPHYLAXIS

1. Operating Theatre: All instruments for surgery should be thoroughly washed and sterilized with autoclaving. Single use of tubing and other disposables is ideal if cost allows. Tubing is preferably sterilized with ethylene oxide gas sterilizer.

Bottles of solutions containing BSS (balanced salt solution) etc. should never be kept or used for more than one operating session. Any air vent applied to these bottles should be protected by a bacterial filter.

2. Antisepsis: After extracapsular cataract extraction, 85% of endophthalmitis cases have been traced to the patient by comparing DNA profiles of vitreous isolates of bacteria with those collected from the lid and skin flora of the patient.²² The goal of pre-operative antisepsis is to reduce the total bacterial count in the wound area.

For peri-orbital skin antisepsis, a 5-10 % povidone-iodine solution applied for a minimum of 3 min is recommended. In case of allergy to it, an aqueous solution of chlorhexidine (0.05%) can be used^{23, 24}. For antisepsis of conjunctiva and cornea, 5 % solution of povidone-iodine (a 10% solution of povidone-iodine can be diluted 1:1 with BSS or isotonic saline) applied

for 3 min reduces the number of bacteria from 10 to 100 fold²⁵⁻²⁹. It can, however, cause problems if it gets into the anterior chamber³⁰.

Large bottles of diluted povidone -iodine or chlorhexidine should be avoided and single-use sachets or vials be used as both antiseptics can become contaminated with *Ps. aeruginosa*. Covering the eye lashes with adhesive tape³¹ (Opsite etc), prevents them from coming in the surgical field.

3. Antibiotics

• Pre Operative

Topical: Lower endophthalmitis rate has been observed following use of topical ofloxacin compared to topical ciprofloxacin³². Levofloxacin reaches higher concentrations in the anterior chamber than ofloxacin and ciprofloxacin³³⁻³⁵. In ESCRS study¹⁰ patients were administered one drop of 0.5% levofloxacin one hour and one drop 30 min before surgery and three drops at five - minute intervals immediately following surgery. Moxifloxacin (Vigamox, Megamox etc) has been found to penetrate the eye significantly better than ofloxacin³⁶. Quinolones are more effective against methicillin-sensitive coagulase-negative staphylococci than methicillin-resistant coagulase-negative staphylococci and the fourth generation fluoroquinolones appear to be more potent, affecting even coagulase-negative staphylococcal strains resistant to second generation fluoroquinolones³⁷.

A few recommend that reserve/latest antibiotics should not be used for routine preoperative prophylaxis while others routinely use moxifloxacin. In an online survey of ophthalmologists practicing in Canada, it was found that topical antibiotics, of which moxifloxacin was the most common (32%), were used preoperatively by 78%³⁸. Corneal precipitation of fluoroquinolones may provide an advantageous drug depot but delay healing and result in corneal perforation in approximately 10% of cases³⁹. No significant difference in antibiotic effects between moxifloxacin and levofloxacin on most bacterial strains(except for *Serratia marcescens*) has been found however levofloxacin seemed to be safer than moxifloxacin in human corneal epithelial cells⁴⁰.

Systemic: In our set up many people use systemic antibiotic prophylaxis to cover mild/undiagnosed systemic infections however others recommend that routine cataract surgery does not require oral systemic antibiotic prophylaxis unless the patient has severe atopic disease.

• Intra-Operative

Addition to irrigating solution: Though a large number of surgeons have been using antibiotics like gentamicin and vancomycin, added to the irrigating solution, it has not been found to decrease incidence of endophthalmitis⁴¹⁻⁴³. Onset of action of vancomycin, in vitro is observed only after three to four hours while the half-life of the drug in anterior chamber is three hours. In addition there is risk of aminoglycoside retinal toxicity and development of resistance.

As an intracameral injection in 0.1 ml at the end of surgery: All Swedish cataract surgeons routinely give an intracameral injection of 1 mg cefuroxime in 0.1 ml at the end of phaco surgery and over 400000 patients had been given cefuroxime intracamerally till August 2007. ESCRS study found that risk of endophthalmitis following phaco was reduced by five fold by an injection of cefuroxime at the end of surgery^{10, 11}. There is a small risk of allergic reaction to cefuroxime in patients with known allergy to penicillin⁴⁴. In these patients an antihistamine tablet 15 minutes before surgery may be considered. In patients with known allergy to cephalosporins, cefuroxime should not be used and vancomycin may be used instead.

For intracameral use at the end of the operation moxifloxacin has been found to be safe in an animal model⁴⁵ and humans⁴⁶ as far as anterior chamber reaction, pachymetry, and corneal endothelial cell density is considered and also effective (68% of Staph. epidermidis endophthalmitis were sensitive)⁴⁷. Espiritu presented his experience of intracameral injection at the end of operation, in Asia Pacific Academy of Ophthalmology, Lahore in Jan 2007. 0.1 ml of solution can be taken directly from the eye drop bottle as it is preservative free and isotonic with the aqueous. Author has injected moxifloxacin in more than 1500 cataract (90 % phaco) operations in the last one and a half years and is satisfied with its safety and efficacy.

Subconjunctival injection: Subconjunctival antibiotic injection prophylaxis has been used over the last 30 years but has not been found effective^{5,48}. 125 mg of cefuroxime given by subconjunctival route gave levels of 20 µg /ml in the anterior chamber, which is far lower than that (3000 µg /ml) which occurs when injected by the intracameral route. Gentamicin, used by many, has no activity against streptococci and *Propionibacterium acnes*.

• Post Operative

ESCRS study recommended that to maintain an adequate level of levofloxacin in the anterior chamber, it may be considered continuing to dose every one to two hours topically post operatively on the day of surgery and from the next day on four times daily⁴⁹. Use of the preoperatively applied topical antibiotic is recommended four times a day for upto two weeks. 1.25 per cent povidone - iodine has been recommended post operatively as it significantly reduced conjunctival bacterial count²⁸. In Canada online survey revealed that postoperative topical antibiotics, of which moxifloxacin was the most common (30%), were used by 97% of ophthalmologists³⁸.

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