Bacterial Endophthalmitis Prophylaxis for Cataract Surgery: An Evidence Based Update of Incidence, Risk Factors and Common Prophylactic Techniques

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Introduction

Cataract extraction with posterior chamber intraocular lens implant is the most commonly performed surgical procedure throughout the world. With the advancements in surgical technique such as phacoemulsification and micro incision cataract surgery, this surgical procedure has become efficacious and predictable. However the possibility of serious postoperative infection and loss of vision still remain a serious unsolved problem in this era.

Incidence

Endophthalmitis is the most devastating complication of intraocular surgery. A review of 30,002 cases at a major teaching institute showed an incidence of culture proven cases of endophthalmitis in 0.072 % following extra capsular cataract surgery, 0.051 % following parsplana vitrectomy, in 0.11 % cases following penetrating keratoplasty, and in 0.061 % of cases following a glaucoma filter. At the beginning of the 20th century (1910) the incidence of endophthalmitis after cataract operations was 10 %. In the era of extracapsular cataract surgery via a limbal or scleral incision and wound closure with sutures with observation of proper sterilization techniques and improved hygienic conditions (1970-1990) the infection rate declined to 0.12 % in Europe and 0.072 % in the US.

<table>
<thead>
<tr>
<th>% Incidence</th>
<th>Country</th>
<th>Year</th>
<th>Reference</th>
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<tbody>
<tr>
<td>0.22</td>
<td>USA</td>
<td>1991</td>
<td>Menikoff et al; Ophthalmology 98:1761-68; 1991</td>
</tr>
<tr>
<td>0.72</td>
<td>USA</td>
<td>1991</td>
<td>Kattan HM et al; Ophthalmol 1991</td>
</tr>
<tr>
<td>0.3</td>
<td>FRANCE</td>
<td>1992</td>
<td>Salvanet et al J.Fr. Ophthalmol. , 1992</td>
</tr>
<tr>
<td>0.148</td>
<td>GERMANY</td>
<td>1999</td>
<td>Schmitz et al; Ophthalmology 1999</td>
</tr>
<tr>
<td>0.1</td>
<td>NETHERLANDS</td>
<td>2000</td>
<td>Versteegh MFL et al. Documents Ophthalmologica ; 2000</td>
</tr>
<tr>
<td>0.198</td>
<td>AUSTRALIA</td>
<td>2003</td>
<td>Morley et al, Br.J.Ophthalmol ; 2003</td>
</tr>
<tr>
<td>0.1</td>
<td>NORWAY</td>
<td>2003</td>
<td>Sandvig KU et al, JCRS. ; 2003</td>
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</table>

In a study of Medicare beneficiaries in the US greater than 65 years of age admitted for cataract surgery in 1984, the risk of hospitalization in the year after surgery for endophthalmitis was 0.12 % following ECCE and phacoemulsification which was reduced to 0.08 % in the year 1986 when cataract surgery was largely performed as an outpatient technique. However since the introduction of phacoemulsification and clear corneal incisions the incidence has increased between 0.3 % to 0.5 % (Table 2).

Table 2. Review of literature showing increased incidence in Endophthalmitis

<table>
<thead>
<tr>
<th>Country</th>
<th>Year</th>
<th>Reference</th>
<th>Incidence %</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>2005</td>
<td>Jensen et al; Am.J. Ophthalmol</td>
<td>0.29 %</td>
</tr>
<tr>
<td>IRELAND</td>
<td>2005</td>
<td>Kahn et al; JCRS Vol 31</td>
<td>0.5 %</td>
</tr>
<tr>
<td>UK</td>
<td>2007</td>
<td>Molan et al; JCRS Vol 33</td>
<td>0.099 %</td>
</tr>
<tr>
<td>SWEDEN</td>
<td>2007</td>
<td>Lindstorm et al; Ophthalmology:114.</td>
<td>0.048 %</td>
</tr>
<tr>
<td>EUROPE</td>
<td>2007</td>
<td>ESCRS Endophthalmitis Study Group, JCRS;33</td>
<td>0.05-0.35 %</td>
</tr>
</tbody>
</table>

The trend of increased incidence of endophthalmitis seen in the past decade have coincided with the popularization of clear corneal incision. However the association between the clear corneal incision and increased incidence of endophthalmitis is not clear. One proposed mechanism is the ingress of ocular surface fluid into the anterior chamber in the immediate postoperative period from a physically unstable potentially leaking wound. The negative pressure gradient allows pericocular fluid with bacterial flora to enter the anterior chamber. The technique of clear corneal incision made cataract surgery possible under topical anaesthesia which replaced block anaesthesia. Ellis MF et al have reported an increased incidence of endophthalmitis with use of topical anaesthesia. Forced blinking and voluntary contraction of the extraocular muscles which are possible after surgery performed under topical anaesthesia, (due to lack of akinesia) can result in IOP variations, preceeded by wound leakage. This creates a negative pressure gradient, sucking in ocular surface fluid into the anterior chamber.

Risk Factors For Endophthalmitis Following Cataract Surgery.

The various preoperative, intraoperative and postoperative events that increase the risk for developing endophthalmitis have been studied and analysed in detail. Mats Lundstrom et al (2007) reported the results of a prospective study evaluating incidence of endophthalmitis in relation to incision type and location. They performed a multiple logistic regression analysis of independent predictors for development of postoperative endophthalmitis. The variables analysed included 1) intraoperative posterior capsular rent and communication with the vitreous (P <0.001); 2) no intracameral cefuroxime (P < 0.001); 3) Age = 85 years versus 0 to 84 years; 4) clear corneal incisions versus superior scleral tunnel incisions. (P = 0.14); 5) temporal versus superior incisions (P = 0.14); 6) IOL material acrylic (and others) versus silicone (P = 0.33); other surgical procedures versus phacoemulsification with IOL implantation (P = 0.41). Trevin Wallin et al performed a cohort study of 27 cases of endophthalmitis at a single institution. Multivariate regression analysis of risks showed that the following were associated with risk for developing endophthalmitis 1) wound leak on the first postoperative day, 2) posterior capsular rent or zonular dehiscence at the time of the surgery 3) antibiotics started on the first postoperative day rather than on the day of surgery, 4) eye was not patched after surgery, 5) collagen shield soaked in cefazolin and dexamethasone not used at end of surgery and, 6) and the use of silicone rather than acrylic 10Ls. ESCRs Endophthalmitis study on the prophylaxis of postoperative endophthalmitis following cataract surgery tried to identify the risk factors and assessed the effect of preoperative antibiotic prophylaxis as well as intracameral cefuroxime on the incidence of endophthalmitis. The risk factors for endophthalmitis following phacoemulsification surgery assessed in this study and the significance of the evidence as indicated by the odds ratio is given below in Table 3.
Table 3. Risk factors for endophthalmitis following phacoemulsification surgery investigated in the ESCRS study \(^{14,70}\).

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Odds Ratio</th>
</tr>
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<tbody>
<tr>
<td>1. Intracameral injection of Cefuroxime – given or not given</td>
<td>4.92</td>
</tr>
<tr>
<td>2. Clear corneal (and position) versus scleral tunnel incision</td>
<td>5.88</td>
</tr>
<tr>
<td>3. Type of wound closure – Suture or Sutureless</td>
<td>No evidence found</td>
</tr>
<tr>
<td>4. Insertion of IOL – injector or forceps</td>
<td>Not retained as a risk factor</td>
</tr>
<tr>
<td>5. Type of IOL material</td>
<td>3.13</td>
</tr>
<tr>
<td>6. Diabetic or non-diabetic</td>
<td>No evidence found</td>
</tr>
<tr>
<td>7. Immunosuppression or not</td>
<td>No evidence found</td>
</tr>
<tr>
<td>8. Complications of surgery</td>
<td>4.95</td>
</tr>
</tbody>
</table>

There are only few data on the incidence of endophthalmitis between inpatient and out patient surgery respectively. Various studies give no evidence of any difference in incidence \(^{71,72}\).

The clear corneal incision is thought to have contributed to the increase in the number of endophthalmitis cases following phacoemulsification.

Unsutured clear corneal cataract wounds have been implicated in the rising rates of bacterial endophthalmitis after cataract extraction over the past several years. However, the relationship is not certain \(^{16}\).

Many studies reveal an increased incidence of postoperative endophthalmitis after clear corneal cataract incisions. John and Moblith \(^{21}\) reported incidences of acute endophthalmitis of 0.29 % and 0.02 % after cataract extraction with clear corneal and scleral tunnel incisions respectively representing an almost 15 fold increase in risk. Lertsumikal et al \(^{22}\) reported a 3.5 fold increased risk of postoperative endophthalmitis with clear corneal temporal incisions compared with superior scleral incisions. Nagaki et al \(^{23}\) noted a 5.6 fold increase in risk of endophthalmitis with clear corneal incisions compared with scleral tunnel incisions. Colleaux and Hamilton \(^{24}\) reported a 2.6 fold increase in risk of endophthalmitis with clear corneal incisions, though not statistically significant. However, a large study from the Bascom Palmer Eye Institute reports no greater incidence of endophthalmitis with clear corneal incisions than with scleral incisions \(^{25}\).

The suggestion of increased risk of acute endophthalmitis with self-sealing clear corneal incision raises the question whether it might be possible for surface bacteria to traverse the clear corneal incision during the postoperative period.

One proposed mechanism is the ingress of fluid into the anterior chamber secondary to hypotony in the immediate postoperative period from physically unstable, potentially leaking wounds. This negative pressure gradient then allows periocular fluid with bacterial flora to enter the anterior chamber \(^{26}\). Studies have shown that 20.5 % of eyes had markedly low intraocular pressure (IOP) (5 mm Hg or less) 30 minutes postoperatively in unsutured 3 mm clear corneal incision cataract extraction \(^{27}\). Experimental models show an incompetence of clear corneal incision with intraocular contamination under conditions of low IOP \(^{28}\). It has been found that blinking and eyelid squeezing produce a sudden increase in IOP by 10 mm and 90 mm Hg respectively followed by 8 mm Hg undershoot after lid opening. A well pressurized operated eye may be able to withstand deformation brought on by these physiological compressive forces, but a hypotonic eye gives way to deformation and compression. This leads to progressive gaping of external incision, with the corneal tunnel pulling surface fluid into the tunnel and finally the internal incision gapes causing a precipitous efflux of aqueous. The elastic recoil of the globe creates a momentary state of relative vacuum in the anterior chamber producing a suction effect which sucks in the escaped aqueous-surface fluid flooding the conjunctiva and corneal tunnel into the anterior chamber. Thus a blink rate of 6 to 12 per minute causes scleral microincision events per minute until the IOP rebuilds to a point at which the eye ball can resist deformation from physiologic forces \(^{29}\). Ex-vivo wound gaping at 10 mm or less of intraocular pressure have been demonstrated by optical coherence tomography in rabbits and human cadaver eyes establishing the fact that the cataract incision is unstable at IOP 10 mm or less \(^{35}\).

Similarly an anterior chamber compression performed by the surgeon to treat post operative high IOP spikes can lead to ingress of fluid into the anterior chamber by a similar mechanism \(^{39}\).

There has also been reports on an increased incidence of post cataract endophthalmitis associated with clear corneal temporal incisions in comparison to the superior...
scleral tunnel incision. However, review of literature does not convincingly confirm this opinion. Results of studies performed by Colleaux et al and Miller JJ et al showed that there was no significant difference in incidence and no relation between wound construction, and its location with the incidence of postoperative endophthalmitis.

Appropriate wound construction will help to prevent deformation under hypotonic conditions. It has been demonstrated that cataract tunnel incisions that are square or nearly square in surface architecture are significantly more resistant to external deformation than those that are rectangular. In addition, Langerman-style, deeply grooved pre incision has been shown to resist deformation. Ernest et al also have shown that square cataract wounds are more stable than rectangular wounds. Square wounds in cadaver eyes 3.2 mm x 3.2 mm were stable up to an external pressure of 525 pounds / square inch (psi) compared to rectangular incision (3.2 mm x 2.0 mm) which leaked at 14 psi.

Furthermore, it is essential that the cataract incision is not subject to inordinate stretching and distortion during the surgical procedures as this can lead to instability of incision closure; the cornea being less tolerant than the sclera. The unsleeved, rigid round tubes used for bimanual microphaco distort the small slit incisions, increasing chances of postoperative leak.

It is also necessary to monitor all incisions and determine at the end of the case whether the wound is marginal in any way. A marginal wound might leak after stromal hydration ends which occurs in 15 minutes to 20 minutes. Wounds which are more than 1.75 mm long at any point, wound in which the peripheral edges are torn during wound creation or during the procedure, cases with Descemets’ detachment, wounds that require an inordinate amount of stromal hydration and appear stretched or otherwise not well constructed are all examples of “marginal wounds”.

In these cases the risk for contamination is potentially increased, and suturing the wound as well as use of appropriate topical antibiotics is necessary.

Any incision suspected of incompetence (including side-port paracentesis) should be considered for suturing, bandage lenses etc. To enhance wound sealing, the wound should be stromal hydrated. The roof as well as sides of the incision should be hydrated. After surgery the IOP should be established at a physiologic level by injection of fluid into the anterior chamber to ensure proper apposition of internal wound. Seidel’s testing should be done on all incisions to establish proof of closure.

The patient’s periocular bacterial flora is the source of microbes in endophthalmitis. Therefore careful draping of the eyelids margins and chemoprophylactic antisepsis is likely to reduce the chance of anterior chamber contamination during surgery.

For the future we might consider methods to standardize the clear corneal incision to create architecturally consistent and truly self sealing incision. Biologic tissue adhesives may play a future role.

In a case control study of postoperative endophthalmitis cases in Sweden between 1994 and 2000 by Wejde et al, it was observed that silicone intraocular lenses carried a higher risk than heparin surface modified PMMA implants. Likewise in the ESCR study, the type of IOL material was found to be a risk factor which was significantly associated with endophthalmitis. Patients receiving a silicone intraocular lens were 3.13 times more likely to develop endophthalmitis than patients receiving an acrylic (or other materials) IOL. Several other studies provided a comprehensive summary of clinical and experimental data supporting an association between silicone IOLs and post cataract endophthalmitis.

Results from an Asian study population reported by Wong TY & Chee SP et al showed that silicone IOLs were associated with 4.3 fold higher risk, of developing post cataract endophthalmitis and a 8 fold risk for culture positive cases. However a randomised trial from Japan showing that silicone IOLs were not associated with an increased risk had a biased, unbalanced study design and hence a proper assessment of risk, would not have been possible. The use of injector system to introduce the intraocular lens into the capsular bag provides both surgical conveniences and offer protection by keeping the IOL from touching the ocular surface, which is the main source of the offending microorganisms. However this association has not been substantiated by other authors. The ESCR Endophthalmitis study also assessed this risk factor and
proved that there is no difference in incidence of endophthalmitis whether injectors or forceps were used for IOL insertion. Several studies \(^{68,73,76}\) and lately the results of the ESCRS endophthalmitis study \(^{14}\) have conclusively proved that patients experiencing surgical complications (posterior capsular rent, zonular dialysis etc) during phacoemulsification had a 4.95 times higher risk of infection. Other factors, such as duration of surgery, tissue trauma, choice of viscoelastic, and irrigating solutions, degree of surgical experience of the surgeon, sex of the patient, age, diabetic status, outpatient versus inpatient surgery were analysed in detail and was not found to be associated with a higher risk of developing post cataract endophthalmitis.

About 14 % to 21 % of patients who develop bacterial endophthalmitis are diabetics \(^{78,79}\). However preexisting diabetes with controlled metabolic status has not been identified as an independent risk factor. If a diabetic with poor control and preexisting diabetic retinopathy develops infection, the visual prognosis becomes very grave \(^{79}\). Endophthalmitis in diabetic patients is usually caused by gram negative organisms more often than in non diabetics \(^{78}\). Immunosuppression in patients undergoing phacoemulsification carries a higher risk for infection and hence vigilant prophylactic measures have to be employed in this category of patients \(^{80}\).

### Prophylaxis For Post Cataract Endophthalmitis:

Thomas Ciulla et al \(^{41}\) published the results of a systematic literature review and evidence rating of the commonly used cataract surgery bacterial endophthalmitis prophylaxis measures published between 1966 – 2000. They tried to rate each practice depending on its relevance to the clinical outcome and on the basis of availability of evidences justifying its use. Outcomes were graded as shown in Table 4.

### Role of Normal Ocular flora

A variety of potentially infective microorganisms confront the cataract surgeon preoperatively. The main sources of bacteria include the lids, conjunctiva, ocular adnexa, irrigating solutions and medications, surgical instruments including IOL, respiratory tract and skin flora of the surgeon and his assistants and operating room air \(^{41}\). The patients’ own skin and conjunctival flora are the most significant among them, being the most difficult organism to contain.

The bacterial flora of normal human conjunctiva has been extensively studied and reported. Various staphylococcal species and corynebacterium predominate this flora, while streptococcal species and gram-negative organisms are less frequently seen \(^{42,43}\). The bacterial isolation rates and species from conjunctiva and lids of patients undergoing cataract surgery was studied by Behrens-Bauman et al \(^{44}\). The bacterial isolate from lids (84.6 %) was about twice that from the conjunctiva (36.7 %). Speaker et al \(^{45}\) used gene material for performing genetic analysis of bacteria by restriction enzyme endonuclease. Their study revealed that bacterial isolates from vitreous in 82 % of cases of acute postoperative endophthalmitis were genetically similar to bacteria isolated from lids, conjunctiva and nares of the patient. These studies suggest that indigenous conjunctival microorganisms are the most likely bacteria to enter the eye at time of surgery resulting in postoperative endophthalmitis. Therefore minimizing normal ocular microorganisms in the lids and conjunctiva preoperatively is an important step in the prevention of endophthalmitis.

Ariyasu et al \(^{46}\) showed that in 8 out of the 13 patients studied (62 %) for aqueous contamination of bacteria at the end of the surgery, the species and antibiotic sensitivities of the organisms were identical to those of bacteria cultured from the patient’s lids and conjunctiva preoperatively.

70 % of the bacterial isolates in the Endophthalmitis Vitrectomy Study (EVS) \(^{46,47,48}\), a multicentered
randomised prospective clinical treatment trial involving 420 endophthalmitis patients who were seen within 6 weeks of cataract surgery and secondary IOL implantation. Confirmed microbiological growth was demonstrated in 69.3% of cases. 70% were gram positive coagulase negative staphylococcus and 9.9% were Staph.aureus. Postoperatively cultured eyelid isolates were indistinguishable from intraocular isolates in 71 (67.7%) among 105 comparisons studied by pulsed – field gel electrophoresis, an established molecular strain typing technique.

It has been clearly demonstrated that viable organisms are introduced into the eye at the time of surgery, and bacteria may be isolated from the aqueous in a quarter or more eyes undergoing cataract surgery. Dickey JB et al reported that anterior chamber aspirates obtained at the conclusion of cataract surgery were culture positive in 13 of the 30 eyes studied (43%) and the most commonly associated organism was coagulase negative staphylococcus in 44% of eyes. It has also been reported that viable organisms can be isolated from the aqueous even when there has been an attempt at ocular surface disinfection with povidone-iodine or preoperative prophylaxis with topical antibiotics.

Although several studies have clearly demonstrated viable organisms from ocular surface contaminating the aqueous during cataract surgery, not all cases reported with positive cultures developed endophthalmitis. This proves that a low dose of bacterial innoculum occurring after cataract surgery can be cleared by the eye without developing endophthalmitis. The risk of contamination of aqueous during cataract surgery remains the same whether extracapsular cataract surgery, SICS or phacoemulsification is performed.

Given the ability of surface flora to enter the eye, prophylactic measures should aim at decreasing the bacterial load on the ocular surface, and achieving bactericidal concentrations of antibiotics to provide adequate coverage against the bacterial innoculum during cataract surgery.

**Role of Preoperative Cultures In Cataract Surgery**

Evidence proving that the patient himself was the major source of most postoperative infections prompted the technique of routine preoperative cultures from the ocular surface and attempts to contain or alter this flora with topical antibiotics. The role of routine preoperative conjunctival culture and sensitivity in predicting the risk of postoperative endophthalmitis has been extensively studied. Its reliability in eyes without any ocular inflammation is doubtful. In 35% of cases the conjunctival culture and sensitivity results obtained at the time of surgery were different from the results obtained the previous day. The conjunctival culture and sensitivity at the time of surgery may be negative even though the cultures had been positive 24 hours preoperatively and the reverse is also true (negative conjunctival culture and sensitivity preoperatively with positive cultures at time of surgery).

95% of routinely cultured eyes are positive for organisms causing endophthalmitis. However, very few of these culture positive eyes really go on to develop endophthalmitis even when the bacteria are of a particularly virulent nature.

Hence routine preoperative cultures in eyes without any ocular inflammation are misleading and often inappropriately raise the suspicion for increased risk of infection. They also give the surgeon a false sense of security while operating on culture negative cases even when they do not give a true reflection of the patients’ own flora. Hence any decision to proceed with or cancel an intraocular procedure, or tailor antimicrobial prophylaxis based on culture results is unwarranted.

However, preoperative cultures from the conjunctiva and lid margins have a definite role in the presence of ocular surface inflammation such as blepharitis, canaliculitis, chronic conjunctivitis, dacryocystitis etc. These eyes carry an increased risk for developing postoperative endophthalmitis if taken up for intraocular surgery before eradicating the inflammation and obtaining a negative culture report after treatment.

**The Microbial Spectrum of Postoperative Endophthalmitis:**

The most important pathogens causing postoperative endophthalmitis from various studies on phacoemulsification is given in Table 5.

A study from India on the spectrum of aetiopathological agents in postoperative endophthalmitis and antibiotic susceptibility of bacterial isolates showed a higher
frequency of gram-negative organisms in 41.7 % of cases. The authors analysed 170 cases of postoperative endophthalmitis and reported on the frequency of various aetiological agents in their series: gram-negative organism 71/170 cases (41.7 %); gram-positive organism 64/170 cases (37.6 %) and fungi 37/170 cases (21.8 %). Table 6. gives the species identification in this series.

Table 6. Species Identification (AR Anand et al:2000.IJO)

<table>
<thead>
<tr>
<th>Gram Negative Organisms</th>
<th>Gram Positive Organisms</th>
</tr>
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<tbody>
<tr>
<td>PAeuroginosa 17.1 %</td>
<td>Staph epi 12.9 %</td>
</tr>
<tr>
<td>Other Pseudomonas</td>
<td></td>
</tr>
<tr>
<td>Species 8.8 %</td>
<td>S.Aureus 7.6 %</td>
</tr>
<tr>
<td>Non-fermenters 10.6 %</td>
<td>P.Acnes 5.9 %</td>
</tr>
<tr>
<td>Others 5.8 %</td>
<td>Enterococci 2.3 %</td>
</tr>
<tr>
<td>Polymicrobial Infection 3 (1.8 %)</td>
<td>Streptococcus 4.1 %</td>
</tr>
<tr>
<td>Others 4.8 %</td>
<td></td>
</tr>
</tbody>
</table>

This study emphasizes the importance of gram-negative bacilli and fungi in causing postoperative endophthalmitis which represents a failure to maintain absolute sterility during surgery. A proper perspective of the incidence and aetiology of postoperative endophthalmitis in India is not available at present and it points to a necessity of a reporting system nationwide.

Commonly Employed Prophylactic Measures:-

A variety of presurgical, intraoperative and postoperative prophylactic measures are employed in an attempt to decrease the incidence of endophthalmitis. Some of them do not have conclusive scientific proof to justify their use while others are backed by reliable supportive evidence. Prophylactic measures are broadly classified into 1) Preoperative 2) Intraoperative 3) Post operative.

(I) Preoperative preparation of the Eye

(a) Preoperative Eyelash Trimming: Review of studies published does not give conclusive evidence to support this age-old practice of 'trimming eyelashes' preoperatively. Available literature suggest that this procedure plays no role in reducing the ocular surface bacterial flora on the day of surgery 81,82.

(b) Saline Irrigation: of the conjunctival sac is used in an attempt to mechanically flush out bacteria from the ocular surface. David.A.Boes et al 83 have demonstrated that following saline irrigation of the conjunctival sac the surface contamination is actually increased because of two important factors (1) bacteria from lid and periorcular tissues are carried on to the ocular surface (2) washing out of organisms hidden with in the conjunctival crypts to the ocular surface. Thus the bacterial colony count literally doubles after irrigation of conjunctival sac and hence this practice should be avoided.

(c) Irrigation Of Lachrimal Passages: Preoperative irrigation of the lacrimal passages has no significant effect on the contamination of the aqueous aspirates 81. However this procedure should not be performed on the day of surgery as organisms from the lacrimal passages will get flushed out on to the conjunctival sac increasing the ocular surface bacterial load.

(d) Preoperative Chemical Preparation of the Ocular surface with Povidone – Iodine

The main aim of preoperative antiseptic prophylaxis is to reduce the risk of wound infection by reducing the total bacterial count in the area of the wound and its immediate surrounding environment.

1. For Periorbital Skin Antisepsis:
5 to 10 % Povidone – iodine solution should be allowed to act for a minimum of 3 minutes as the skin contains sebaceous glands. Povidone-iodine is contraindicated is the presence of allergy and hyperthyroidism 84.

2. For antisepsis of the conjunctiva and cornea: Povidone-iodine 5 % drop is instilled into the conjunctival sac and allowed to act for 3 minutes. 5 % Povidone-iodine decreases the colony forming units in the conjunctiva, kills bacteria, virus and fungi, and has
a synergistic effect with the topically administered antibiotic. Michael R. Keverline et al specifically assessed whether the commonly used combination of a fluoroquinolone with Povidone – iodine was complimentary or simply redundant. Their results show that this combination is a complimentary one for surgical prophylaxis. Fluoroquinolone resistant bacterial isolates were covered by Povidone-iodine, while fluoroquinolones were effective against S. Marcescens and Bacillus species that were less susceptible to Povidone – iodine. The results of this study are limited clinically by the inability to take into account the actual concentration of each agent that is present on ocular surface and anterior chamber with topical application.

The disinfective effect of Povidone – iodine depends on the exposure time and appropriate concentration. A marked reduction in its disinfective action has been observed in the presence of organic material such as serum. Thus Povidone iodine had a definite antiseptic effect against resident flora, although it does not achieve the effect of totally eradicating it. It was also observed that it had no toxic effect on the ocular surface.

Preoperative administration of Povidone – iodine was associated with a low incidence of intraoperative bacterial contamination of aqueous humor, and was observed to decrease the incidence of endophthalmitis. Application of Povidone – iodine solution had a greater bactericidal effect when used in conjunction with preoperative course of topical antibiotics.

Schmitz et al in their questionnaire survey of 469 ophthalmic surgical institutions in Germany came to the conclusion that preoperative use of povidone – iodine on the conjunctiva significantly reduced the risk of endophthalmitis. However the survey gave no indication of the method of application, concentration of Povidone – iodine or its contact time with the ocular surface. The evidence based analysis of available Medline literature (1966 – 2000) performed by Ciulla et al confirmed the beneficial effect of Povidone – iodine antisepsis (EbM 111 = moderately important to clinical outcome).

Speaker MG et al performed an open labelled non-randomised parallel trial for 11 months where 5% Povidone – iodine was used in one set of 5 operating theatres while silver protein solution was used in another set of 5 operation theatres. In all cases the surgeons continued to use their systemic antibiotics. The Povidone – iodine group showed a lower incidence of endophthalmitis in comparison with the silver protein group (0.06 % vs 0.24 %). There were no adverse reactions to the use of Povidone – iodine. A similar trend was noticed by Bohignan et al who demonstrated a reduction in the incidence of endophthalmitis from 0.08 % to 0.03 % following the introduction of antisepsis with 5% Povidone – iodine. However considerable toxic effects have been reported if Povidone – iodine enters the anterior chamber.

Application of a cotton pad soaked with 10 ml of 5% Povidone – iodine one hour prior to the surgery, clamped against the closed lids was associated with fewer positive conjunctival cultures just prior to surgery and at conclusion of the procedure.

Thus the available clinical studies show that only Povidone – iodine in 5 % concentration can be recommended as an effective preoperative antiseptic. The optimum concentration of Povidone – iodine for use as preoperative antiseptic is still not established. Although 5 % solution is effective, studies showing significant reduction in conjunctival colony count when 1.25 % was used may lead to its use for preoperative antisepsis.

**Preoperative Antibiotic Prophylaxis**

Given the ability of the surface flora to contaminate the anterior chamber during cataract surgery, preoperative prophylaxis aims at reducing the bacterial load on the ocular surface. This is achieved using preoperative topical antibiotics and achieving sufficient bacterial concentration of the antibiotic in the aqueous to provide adequate coverage against the bacterial inoculums during surgery. Antibiotics have been used for years by ophthalmic surgeons before, during and after cataract surgery as a prophylaxis against infection. Estimates suggest that 30 % of antibiotic usage in ophthalmic practice is for prophylaxis in surgical patients. Economic factors, adverse reactions, emerging bacterial resistance to the drug, emergence of new strains of antibiotic resistant microorganisms have rekindled concerns about inappropriate antibiotic usage. The degree to which the ocular flora will be reduced depend on the choice of antibiotic, frequency and duration of its administration, and the bacterial species present.
An antibiotic with a broad spectrum of antibacterial activity, excellent penetration into the cornea and anterior chamber, low toxicity and resistance and that which is compatible with other drugs is the ideal antibiotic for prophylaxis. It should be able to address the potential pathogens effectively and must be available at the site prior to inoculation with organisms. Appropriate time schedule for applications and adequate dosages are absolutely essential for maximizing efficacy.

Allan and Mangiarcine compared the incidence of post cataract endophthalmitis with and without the use of prophylactic topical antibiotics and their results suggest that preoperative antibiotic prophylaxis reduces the incidence of endophthalmitis. The difference in effect of preoperative antibiotic administration of Ofloxacin and Tobramycin on bacterial isolates from the conjunctiva was studied by Hara and Yasuda et al. Aerobic species were cultured from 24% Tobramycin treated eyes whereas only 3.6% of bacteria were cultured from Ofloxacin treated eyes, thus showing a marked decrease in positive isolation rate after Ofloxacin treatment.

Changes in the bacterial isolation rates during preoperative preparation was again studied by Hara and Yasuda. Isolation of aerobic bacteria reduced from 17% to 3% and a lower incidence of P.acnes was observed in eyes after conjunctival irrigation with Povidone-iodine than when Benzetonium chloride solution was used (9% Vs 30%). It is interesting to note that isolation of P.acnes actually showed an increase from 10% prior to conjunctival irrigation to 30% after conjunctival irrigation.

Application of preoperative prophylactic antibiotics appear rational to reduce the bacterial load on the ocular surface. Various antibiotics like chloramphenicol, aminoglycosides, vancomycin, fusidic acid, polymyxin-bacitracin, neomycin and current use of topical fluoroquinolones have been tried. However there has been no consensus on the choice of antibiotic and its optimum dosing for preoperative prophylaxis.

AR Anand et al studied the antibiotic susceptibilities of the bacterial isolates in 170 cases of postoperative endophthalmitis referred to their centre to commonly used antibiotics. Analysing the antibiotic susceptibilities of the gram-negative isolates it was seen that 55.5% were sensitive to gentamycin, 65.2% to cefotaxime, 68.1% to amikacin, 73.2% of the gram positive isolation were sensitive to gentamycin, 88.6% to cefotaxime, 88.4% to ciprofloxacin, 92.6% to ceftazidime and 100% to vancomycin. In this large series of postoperative endophthalmitis gram-negative bacilli followed by fungi accounted for the largest number of cases. A high degree of resistance of gram-negative bacilli to gentamycin, cefotaxime, amikacin, and ceftazidime was recorded.

The ESCRS Study showed the use of preoperative levofloxacin, which reached significantly higher concentrations in the anterior chamber than ofloxacin and ciprofloxacin, can prevent postoperative endophthalmitis. Although there appeared to be some benefit, the effect was smaller than for intracameral cefuroxime, and did not reach statistical significance. To maintain adequate bactericidal concentrations in the anterior chamber, levofloxacin should be continued every two hours on the day of surgery postoperatively.

In a retrospective observational series by Moshirfar et al on the rate of endophthalmitis after uncomplicated cataract surgery in 20,013 patients the effect of two 4th generation fluoroquinolones (Gatifloxacin 0.3% and Moxifloxacin 0.5%) prophylactic agents was compared. Estimated endophthalmitis rates of 0.06% for gatifloxacin and 0.1% for moxifloxacin was reported. The conclusion drawn by the authors is that older fluoroquinolones (Ofloxacin, Levofloxacin) should be used as prophylactic antibiotics and newer agents reserved for frank infection.

Fluoroquinolones achieve superior intraocular penetration after parenteral or even oral administration. Studies have shown that 200 mg of oflox achieves an aqueous level of 0.38 mg/l, two hours after oral administration, and an aqueous level of 0.33 mg/l after intravenous administration. A 750 mg single oral dose of ciprofloxacin at 17.5 and 5.5 hours after administration orally in 40 patients achieved a mean aqueous level of 0.53 ± 0.25mg/l. Oral prophylaxis with ciprofloxacin had been seriously considered. However the cost benefit ratio might not be favourable for using an expensive antibiotic for the very infrequent complication of postoperative endophthalmitis. Studies have shown that combining prophylaxis for three days by oral route with short term prophylaxis by the topical
route (1 hour prior to surgery) provided higher antibiotic concentrations in the aqueous than either modality alone. Combining prophylactic measures has not demonstrated a reduction in intraocular bacterial contamination in subsequently published reports. Antibiotic resistance patterns of ocular bacterial flora were analysed in a prospective study of patients undergoing anterior segment surgery by Ta et al. 78% of the coagulase negative staphylococcus were isolated in their series and 90% of the coagulase negative staphylococcus were susceptible to cefotaxime, levofloxacin, imipenam, meropenam, vancomycin and aminoglycosides except neomycin. 70% to 90% of coagulase negative staphylococcus were susceptible to cefazolin, neomycin, ciprofloxacin, oflox, norflox and chloramphenicol whereas only < 70% were sensitive to penicillin analogues, ceftaxidime, erythromycin and tetracyclines. This study clearly proves the superiority of vancomycin, aminoglycosides and levofloxacin as preoperative bacterial prophylaxis. However vancomycin the drug most effective against coagulase negative staphylococcus is not used as a preoperative prophylactic drug and its use is only reserved for frank infection.

Addition of Antibiotics to Irrigating Solution

With shift in surgical technique from extracapsular to phacoemulsification, antibiotic addition to the irrigating fluids was considered, but no significant difference in anterior chamber contamination was noticed in the questionnaire reporting surveys from various countries. 60% of the responding surgeons in Germany, 35% in the US, 16% in Newzealand, 8.5% in England and 8 in Australia used antibiotics in the irrigating fluids namely vancomycin and gentamycin. The result of this survey does not give an accurate indication due to poor response ratio and hence the results can be considered as crude comparative rates. Beigi et al and Montan et al have studied the anterior chamber contamination rates and compared it with and without the addition of vancomycin to the irrigating solution. Although a dramatic reduction in the anterior chamber contamination rate was demonstrated by Beigi et al, contradictory conclusions were drawn from the similar study by Montan et al.

The risks for developing aminoglycoside retinal toxicity and the danger of developing resistance are particularly disturbing as vancomycin is considered as a reserve drug and should not to be used for preoperative prophylaxis.

Intracameral Antibiotics at conclusion of Surgery

Intracameral application of antibiotics (cefazolin, cefuroxime, vancomycin and aminoglycosides) is not licensed by the regulatory authorities and hence this method of use is off-label at the surgeons discretion. A 3 year retrospective study of the use of intracameral cefazolin to prevent endophthalmitis in cataract surgery by Magela Garat et al showed a statistically significant reduction in the incidence of endophthalmitis (0.421% to 0.031%). Cefazoline was used in this study in view of its safety, effectiveness against gram positive organisms and cost factor. Similar results were published by Pedro Romero et al in 2006. Montan PG et al reported a lowered incidence of endophthalmitis from 0.26% to 0.06% when prophylactic intracameral cefuroxime 1 mg was used after cataract surgery. The use of 1 mg cefuroxime in 0.1ml at the conclusion of surgery is an accepted practice in Europe. Cefuroxime is a broad spectrum antibiotic effective against staphylococcal and streptococcal species (except Methicillin resistant staphylococcus aureus, Methicillin resistant staphylococcus epidermidis and enterococcus faecalis), gram-negative bacteria (except Pseudomonas aeruginosa and enterococcus faecalis), and Pneumococci. There has been no reports of corneal toxicity. However, severe anaphylactic reaction following intracameral use has been reported and hence its use is contraindicated in patients with allergy to cephalosporins.

In the ESCRS endophthalmitis study results the risk for contracting endophthalmitis following phacoemulsification cataract surgery was significantly reduced (five fold) by an intracameral injection of cefuroxime at the end of the surgery (P = 0.001) for presumed endophthalmitis and P = 0.005 for proven endophthalmitis. The lowest observed incidence rates was in the 4th arm of the study which received both intracameral cefuroxime and perioperative topical levofloxacin. In the ESCRS study despite prophylaxis,
some patients developed postoperative endophthalmitis. Cefuroxime resistance was also noticed in 3 isolates of coagulase negative staphylococcus. On sub-analysis the evidence of benefit of cefuroxime was weaker against Coagulase negative staphylococcus endophthalmitis than against streptococcal endophthalmitis. Cesar Ramon G Esperiter et al studied the safety of prophylactic intracameral moxifloxacin 0.5 % ophthalmic solution (Vigamox) in patients undergoing cataract surgery. They concluded that intracameral Vigamox 0.5 mg/ml appeared to be nontoxic in terms of visual rehabilitation, anterior chamber reaction, pachymetry and corneal endothelial cell density. This study effectively proved the safety of intracameral moxifloxacin. Further studies are required to test its efficacy in preventing endophthalmitis.

**Subconjunctival Antibiotic Injection**

Prophylaxis has been used over the last 30 years with no definite scientific evidence whether this prophylactic technique had any benefit. Subconjunctival antibiotic injections may achieve bactericidal aqueous humor levels for short periods postoperatively and thereby decrease the incidence of endophthalmitis. Significant incidence of contamination of corneoscleral incisions and aqueous humor at the end of the surgery has been demonstrated and bactericidal levels of antibiotics can penetrate the aqueous. Higher incidence of macular infarction after cataract surgery has been attributed to seepage of drug through the unstable cataract incision into the posterior segment.

**FLOW CHART ON PROPHYLAXIS GUIDELINES**

(Adapted from ESCR S multicentre study \(^{14,20}\) (2006), Healy et al \(^{112}\) (2004), Jensen et al \(^{113}\) (2005), Peyman et al \(^{63}\) (2004))

<table>
<thead>
<tr>
<th>PRE OP</th>
<th>ON OT TABLE</th>
<th>THE SURGEON</th>
<th>INTRA OPERATIVE</th>
<th>POST OPERATIVE</th>
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<tr>
<td>Topical Fluoroquinolones (Levofloxacin/Olofoxacin) qid 48 hours prior to surgery.</td>
<td>Topical antibodies with one drop 1 hour prior to surgery and 1/2 hour prior to surgery.</td>
<td>Conjunctival Candid in presence of lid, conjunctival or lacrimal infection.</td>
<td>Intracameral Cefuroxime 1 mg/0.1 ml saline.</td>
<td>Reapply preoperative prophylactic antibiotic 2 hourly on day 1 followed by 4 times daily for 2 weeks post operatively.</td>
</tr>
<tr>
<td></td>
<td>Povidone-Iodine 5 % drop on Conjunctival Sac and allowed to act for 3 minutes.</td>
<td>Sponge soaked in Povidone-Iodine 5 % kept over conj and cornea for 3 minutes.</td>
<td>Lid and Periorbital skin cleaned with 10 ml of 10 % povidone iodine and excess allowed to pool over into conjunctival sac.</td>
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There are no formal studies to establish the efficacy of this technique, but there are studies on endophthalmitis including EVS in which the subjects who received subconjunctival injection of antibiotic developed postoperative infection. Jenkins et al.112 who investigated the pharmacokinetics of cefuroxime when 125 mg was given by subconjunctival route demonstrated an aqueous concentration of 20 μg/ml which is much lower than the concentration achieved after intracameral injection (3000 μg/ml). Thus this prophylactic technique, although widely used for the last 30 years has little scientific basis to justify its usage.

Postoperative prophylaxis: In order to minimise the risk of infection until wound healing is secure, the continued use of the preoperatively administered antibiotic is advocated for up to 2 weeks. The frequency of application is every 2 hourly on the day of surgery and on 1st postoperative day followed by four times daily applications.

Conclusion

Thus the overall strategy of prophylaxis against post cataract Endophthalmitis is to adopt measures to reduce the patients own bacterial load on the lid, conjunctiva and periorcular tissues, measures to reduce microbial contamination of the anterior chamber and strategies to ensure that bacteriadal concentration of the antibiotic is present in the anterior chamber to tackles the bacterial inoculum. The flow chart given below summarises the essential prophylactic measures to be adopted to ensure zero post cataract Endophthalmitis rate.

References

40. Chithkara DJ, Manners T, Chapman F et al. Lack of effect of preoperative norfloxacin on bacterial contamination


