ENDOPHTHALMITIS PROPHYLAXIS IN CATARACT SURGERY

Junaid S Wani MS, A R Nasti MS, Manzoor Q Keng MS, Sabia Rashid MS

The term endophthalmitis refers to intraocular inflammation predominantly involving the vitreous cavity and anterior chamber of the eye. Infectious endophthalmitis, inflammation associated with an infectious process is the most common form. Classically, most cases of infectious endophthalmitis develop after intraocular surgery. There are more than 2 million cataract surgeries performed each year in the United States. Fortunately, the incidence of postoperative endophthalmitis is relatively low, with an estimated five to ten cases per 10,000. Overall, the incidence of postoperative endophthalmitis for cataract surgery by extracapsular cataract extraction or phacoemulsification ranges between 0.07% and 0.12%. When endophthalmitis occurs, the outcome for the patient can be devastating. As such, there is much interest and need in minimizing the occurrence of endophthalmitis. There are few well-controlled studies of the risk factors or efficacy of preventive measures because of the low incidence of this condition. Pre-operative disinfection of the surgical site and meticulous attention to sterile technique are essential. The role played by perioperative antibiotics is uncertain.

Phage typing and DNA fingerprint analysis have shown that the organisms that cause postoperative endophthalmitis, despite their low virulence in other surgical settings, are those that reside on the patient's own eyelid flora and adnexa. Staphylococcus epidermidis is the most common infecting bacteria, followed by staphylococcus aureus and rarely, gram negative rods or even candida. Staphylococci bacteria are ubiquitous and S. epidermidis is considered normal flora on the skin and lid.

In the operating room, it is imperative to have a "sterile technique" but it is not uncommon for the anterior segment to become contaminated during cataract surgery. Reports suggest that bacteria can be isolated from anterior chamber fluid up to 43% of the time following cataract surgery. Despite this, endophthalmitis is still a rare occurrence. It appears that there may be a threshold inoculum necessary to cause endophthalmitis.

**Strategy:**

Given that the majority of organisms come from the patient's own flora, the most practical way to decrease the potential inoculum is to decrease the number of organisms on the lid margin or in the cul-de-sac. This can be effectively done using povidone-iodine, such as Betadine or povidone-iodine plus antibiotics. Povidone-iodine 5% has been shown to significantly decrease the incidence of endophthalmitis and is effective in reducing the number of organisms in the cul-de-sac.

Povidone-iodine releases free iodine, which kills organisms via oxidation. As an oxidizing agent, it requires time for killing, in vitro experiments suggest 1 to 2 minutes of contact time. It is advised to prepare the lid margin skin and place 5% Betadine directly into the cul-de-sac so that it has at least 1 to 2 minutes of contact time with the tissue. More diluted povidone-iodine solutions have adequate amounts of free iodine and are also effective, however, the less concentrated solutions are not as stable and must be made up fresh.

Preoperative antibiotics have been advocated in addition to using preoperative Betadine because antibiotics further decrease the number of organisms both on the lid margins and in the cul-de-sac. There are no controlled prospective studies that prove a decrease in the incidence of endophthalmitis with the use of preoperative antibiotics. Preoperative antibiotics have little intrinsic risk. The choice of antibiotic is most likely more controversial. The ideal antibiotic would have broad spectrum, would be non-toxic and would have a fast killing time. Using these criteria, the fluoroquinolones would be the best choice.
Among the fluoroquinolones, both ciprofloxacin HCL and Ofloxacin have been shown to have comparable spectra of activity\textsuperscript{11} and comparable kill times\textsuperscript{12} and are both relatively safe. Because Ofloxacin is more soluble (pH 7.0), it has better tissue penetration\textsuperscript{13}. Aggressive dosing of Ofloxacin (1 drop every 5 minutes five times preoperatively) can yield approximately 1 mm of Ofloxacin per milliliter of aqueous\textsuperscript{14}. Similar unpublished studies show results with 2 drops every 30 minutes two times. This is above the minimum inhibitory concentration (MIC) for many strains of S epidermidis. Therefore Ofloxacin is more favourable than Ciprofloxacin. Levofloxacin is the L-isomer of Ofloxacin. It may have more favourable MIC levels and attain higher tissue penetration, although the safety of the formulation has not been reported with regard to epithelial wound healing.

There are other measures that are generally accepted and recommended to reduce the inoculum. It has been traditionally advocated and is important to identify patients with active blepharitis, treat them and avoid intraocular surgery until their lid disease is controlled. Daily lid scrubs with an antibiotic or steroid ointment to the lids at bed time can be effective. In cases with concomitant ocular rosacea, tetracycline 250 mg four times a day for 1 month or doxycycline 100mg/day will help control the meibomianitis. Additionally, isolation of the lids with adhesive tape or plastic tape dressings is recommended. This prevents meibomian secretion or debris surrounding the hair follicles from contacting the surgical site.

<table>
<thead>
<tr>
<th>Table: Recommendations for preventing endophthalmitis.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Identify and treat preoperative blepharitis</td>
</tr>
<tr>
<td>2. Reduce inoculum. Preoperative antibiotic Ofloxacin four times a day start 1 day preoperatively</td>
</tr>
<tr>
<td>3. Betadine 5% to cul-de-sac, lids and skin 2 minutes contact as a preoperative preparation</td>
</tr>
<tr>
<td>4. Isolate the lids</td>
</tr>
<tr>
<td>5. Although most cases of endophthalmitis arise from the host flora others are also important</td>
</tr>
<tr>
<td>6. Avoid prolene haptics</td>
</tr>
<tr>
<td>7. Administer postoperative topical antibiotics until the epithelium is healed</td>
</tr>
<tr>
<td>8. Consider oral Ofloxacin for special cases in which the risk is high</td>
</tr>
</tbody>
</table>

The role of intraoperative antibiotics remains controversial. A number of investigators have suggested that aminoglycoside and vancomycin used intracameral, or vancomycin alone, injected in the bag can significantly reduce the risk of endophthalmitis\textsuperscript{15, 16}. A survey conducted by the American Society for Cataract and Refractive Surgeons has shown at least 35% of Ophthalmic surgeons currently use intraocular antibiotics. Vancomycin was used by 80% and gentamicin by more than 40% of the surgeons surveyed\textsuperscript{17}. Although the anecdotal and retrospective analyses are appealing and show that the relative risk of endophthalmitis is reduced, there is no solid prospective evidence in the peer-reviewed literature to support this practice. Additionally, there is some potential for causing toxicity. Gentamicin has a narrow therapeutic safety range and significant retinal toxicity can occur above 100 mm/cc, while vancomycin can cause cystoid macular edema.

Vancomycin injected at 20 mm/cc has been shown to have a half life of approximately 2 hours, which is relatively short. This is important because vancomycin is relatively slow at killing organisms. Intracameral antibiotics may be appropriate; however, vancomycin does not appear to be the right choice. Ferro and colleagues showed that adding vancomycin and gentamicin did not statistically reduce the number of anterior segment aspirates that were positive for bacteria following cataract surgery\textsuperscript{18}.

Vancomycin requires actively growing bacteria to be effective and will not work unless the bacteria are in active phase. In lieu of vancomycin, one would more likely benefit from having an antibiotic that is fast killing, has broad-spectrum killing of both gram-negative and gram-positive organisms and one in which the antibiotic concentration can be augmented and maintained with supplemented topical antibiotics. In the future, perhaps a fluoroquinolone antibiotic with these preferred requirements will be found to be useful.

Postoperative subconjunctival injections of antibiotic have also been practiced for many years. The benefits could come from delivery of therapeutic levels of antibiotic to the anterior chamber, which would result in the reduction of bacteria numbers and prevent clinically significant endophthalmitis. In prospective studies, Christy was not able to show a benefit from subconjunctival antibiotic alone, but did have a benefit from subconjunctival plus preoperative topical antibiotic. More recent retrospective analysis by Colleaux and Hamilton revealed a statistically significant reduction in the incidence of endophthalmitis when subconjunctival antibiotics were used\textsuperscript{19}.

Gentamicin is toxic to the retina and there is significant concern among retina surgeons as to the safety of routine postoperative injections of gentamicin\textsuperscript{20}. Cefazolin alone has not been established as effective in scientific studies. However, subconjunctival injection of Cefazolin is probably much safer and deserves further evaluation. With the trend towards clear cornea and topical or intracameral anesthetic, the use of subconjunctival injection is less practical.

Postoperatively, endophthalmitis can still occur via contamination of the anterior segment while the wound is still open. This may be a problem with clear cornea and topical anesthesia, or even scleral wound incisions that may gape and take contaminated fluid back into the eye. Because of this, continued antibiotic therapy is advised until the epithelial barrier has been established. The ideal choice of antibiotic would again be one with broad spectrum, fast-acting relatively high solubility and relatively sustained tear film levels with low toxicity. Again, the fluoroquinolones are the best choice. Ofloxacin is the most favourable choice because it has the best solubility at pH7, relatively good penetration and persists in the tear film for relatively long periods of time. Levofloxacin may prove to be superior, however, toxicity studies remain to be completed.
Attention to adequate wound closure is also important. It is recommended to check the wound with fluorescein when the case is over, injecting balanced salt solution into the stroma to enhance the seal if necessary or placing a suture if there is persistent leakage or if the patient is expected to have compromised wound healing.

Prolene haptics can increase the risk of endophthalmitis by approximately 4 - 5 times. This is due to the ability of Staphylococcus to directly bind to prolene. The elimination of prolene haptics may be necessary to maximally reduce the risk of endophthalmitis. Additionally, a surgeon should avoid directly contaminating the IOL by not placing it on the eye or touching it to the lid margins.

In the report of Menu-Koff and colleagues, the highest risk for endophthalmitis (14 times) occurred with capsule rupture. In such high risk cases, the addition of antibiotics that reach therapeutic levels in the vitreous may be appropriate. Subconjunctival antibiotics are generally not believed to reach high enough vitreous levels. Systemic antibiotics have not been traditionally found to effectively cross the blood-aqueous barrier. More recently, the fluoroquinolones have been found to penetrate the eye well because of their increased lipid solubility. Ofloxacin seems to be approximately two times better than Ciprofloxacin. Oral Ofloxacin 400mg twice a day in conjunctival fashion with topical Ofloxacin has been shown to reach a concentration of approximately 2.7 mm/cc in the aqueous. In the higher risk cases, the addition of systemic Ofloxacin 400 mg twice daily for 3 days, with 2 days of topical Ofloxacin 0.3% every 2 hours is recommended. This regimen should not be adapted to all cases because of the increased resistance to fluoroquinolones and increased medical costs.

Sterile technique is an important prevention method. This includes following manufacturer's recommendation regarding sterilization and use of disposables. Excessive talking and coughing have been implicated as not being sterile in repeated cases and should be kept to a minimum.

BIBLIOGRAPHY