The Prevention of Endophthalmitis After Cataract Surgery

Specific measures can help to avoid this rare but serious complication.

BY LUIS CORDOVÉS, MD

Postoperative endophthalmitis after cataract surgery has become a rare event, but, when it occurs, it often results in severe and irreversible visual loss (Figure 1). Many surgeons consider clear corneal phacoemulsification under topical anesthesia a routine and fast procedure; nonetheless, we should not disregard measures needed to avoid this dreaded complication.

The low incidence of postoperative endophthalmitis makes it difficult to perform scientifically sound studies on prevention or prophylaxis because these require very large population samples. The only measures to date shown by scientific evidence to reduce the rate of endophthalmitis after cataract surgery are the use of preoperative povidone-iodine and intracameral cefuroxime. This does not imply that other interventions are useless, but it has not been possible to study and evaluate each individual factor involved in cataract surgery.

The recently published European Society of Cataract and Refractive Surgeons (ESCRS) guidelines for prevention and treatment of endophthalmitis following cataract surgery1 provide a thorough review of prophylactic measures, and this article attempts to summarize the most important facts. The full ESCRs Endophthalmitis Guidelines are available in several languages at http://www.escrs.org/endophthalmitis/default.asp.

PATIENT PREPARATION

It is probably more common than we care to admit that the surgeon first meets the cataract surgery patient at the operating table. If he or she finds blepharitis, atopia, or a prosthetic fellow eye, it is then too late to take adequate prophylactic measures.

For this reason, the surgeon or a well-trained assistant must identify and treat the risk factors for endophthalmitis before the day of surgery. Routine use of preoperative topical antibiotics, once popular, has declined. Theoretically, the bacterial load on the ocular surface would be reduced by this practice, yet no study has shown that topical antibiotics effectively prevent endophthalmitis. In these high-risk patients, a short course of fusidic acid or another antistaphylococcal antibiotic plus a lid scrub (but not on the day of surgery) seem reasonable.

It is also wise, well before the day of surgery, to obtain adequate informed consent and to warn patients about the signs and symptoms of this rare infectious complication, encouraging patients to seek prompt care in the event that symptoms appear.

PREOPERATIVE ANTISEPSIS

Topical povidone-iodine, an antiseptic agent with broad-spectrum bactericidal activity, has become the standard of care for ocular surface preparation prior to cataract surgery (Figure 2); its use is supported by a prospective comparative (although not randomized) study2 and by ample clinical and laboratory evidence.
Investigators have examined the value of different povidone-iodine concentrations, but the routine often chosen by ophthalmologists is povidone-iodine 5% applied to the cornea, conjunctival sac, and periocular skin for a minimum of 3 minutes.

Although this is a short time, in a busy operating room it seems like a lifetime. In the ESCRS endophthalmitis trial, each clinical participant received a stopwatch to regulate the time. In a standard surgical practice, it may be wise to give an initial prep with povidone-iodine in an area outside the operating room, such as in a patient waiting area. Before applying povidone-iodine, a drop of local anesthetic is applied, and the patient is instructed to keep his or her eyes closed, thereby avoiding a dry corneal epithelium. The anesthetic should cut the stinging sensation brought on by the povidone-iodine. In rare cases of true allergy to povidone-iodine, 0.05% aqueous chlorhexidine may be used.

Ocular surface flora are substantially reduced with povidone-iodine use, but complete sterilization of the ocular surface should not be expected, and continued bacterial contamination of the aqueous humor is reported in the literature. Povidone-iodine application at the end of surgery is not recommended because of its toxicity to corneal endothelial cells in the event of inflow into the anterior chamber due to postoperative pressure changes.

CLEAR CORNEAL INCISIONS

The adoption of clear corneal incisions is thought to have led to an increased incidence of endophthalmitis after phacoemulsification surgery, but improvement in incision technique and the use of prophylactic intracameral cefuroxime have likely since then contributed to a reduction of this risk.

### TABLE 1. ENDOPHTHALMITIS INCIDENCE IN ESCRS STUDY GROUPS (INTENT TO TREAT)

<table>
<thead>
<tr>
<th>GROUP A</th>
<th>GROUP B</th>
</tr>
</thead>
<tbody>
<tr>
<td>No intracameral cefuroxime</td>
<td>Intracameral cefuroxime</td>
</tr>
<tr>
<td>No topical levofloxacin</td>
<td>No topical levofloxacin</td>
</tr>
<tr>
<td>Incidence rates (%)</td>
<td>Incidence rates (%)</td>
</tr>
<tr>
<td>Total: 0.345</td>
<td>Total: 0.074</td>
</tr>
<tr>
<td>Proven: 0.247</td>
<td>Proven: 0.049</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>GROUP C</th>
<th>GROUP D</th>
</tr>
</thead>
<tbody>
<tr>
<td>No intracameral cefuroxime</td>
<td>Intracameral cefuroxime</td>
</tr>
<tr>
<td>Topical levofloxacin</td>
<td>Topical levofloxacin</td>
</tr>
<tr>
<td>Incidence rates (%)</td>
<td>Incidence rates (%)</td>
</tr>
<tr>
<td>Total: 0.247</td>
<td>Total: 0.049</td>
</tr>
<tr>
<td>Proven: 0.173</td>
<td>Proven: 0.025</td>
</tr>
</tbody>
</table>

†Courtesy of the ESCRS

**ANTIBIOTICS IN CATARACT SURGERY**

**Preoperative topical antibiotics.** Preoperative topical antibiotics reduce the bacterial load on the ocular surface, but there are no studies proving that they effectively prevent endophthalmitis. The aim of achieving therapeutic concentrations in the anterior chamber of the eye is probably of little use, as most of the antibiotic is washed out once surgery starts.

There is growing concern that topical antibiotic use may select resistant strains, particularly when these agents are used for several days and in a repeated manner, as with frequent intravitreal injections. In that setting, Moss and colleagues found that antibiotic use conferred no additional benefit in combination with povidone-iodine over povidone-iodine alone.

The experience from the large Swedish cataract register and from the ESCRS study do not support the additional use of topical antibiotics (see below under Postoperative Antibiotics).

**Intracameral antibiotics.** An intracameral injection of an antibiotic at the end of cataract surgery delivers the highest and most precise dose within the therapeutic range at the site where it is needed.

Intracameral cefuroxime use was introduced in Sweden in 1996 by Per Montan and colleagues at St. Erik’s Eye Hospital, Stockholm, and most Swedish surgeons quickly...
The Swedish cataract register has collected data from a large number of patients supporting the efficacy and safety of intracameral cefuroxime injection. The ESCRS study on prophylaxis of endophthalmitis after cataract surgery, a prospective, randomized clinical trial, evaluated the effects of an intracameral injection of 1 mg cefuroxime at the close of surgery and of an intensive pulsed perioperative topical application of levofloxacin in a 2 X 2 factorial design. That landmark study scientifically proved that intracameral cefuroxime reduced the risk of contracting postoperative endophthalmitis by approximately fivefold. Topical levofloxacin had no statistically significant effect (Table 1).

Many sites in multiple countries have reported a significant drop in endophthalmitis rates after the introduction of intracameral cefuroxime (Table 2). Of special relevance is the fact that the baseline rates in these studies were in the same range as those for Group A of the ESCRS study (Table 1), which was heavily criticized for its high background endophthalmitis rate.

The microbiologic spectrum of postcataract endophthalmitis varies by geographical area. In countries such as India and China, gram-negative and fungal cases are more common than in Europe. No reports of cefuroxime use have been published from these areas, but this regimen may be less effective there because of variation in the population of infective organisms, and perhaps other options may be considered.

The use of intracameral cefuroxime rather than another intracameral antibiotic has been questioned for several reasons. *Pseudomonas* spp, *Enterococcus* spp, methicillin-resistant *Staphylococcus aureus*, and methicillin-resistant *Staphylococcus epidermidis* are resistant to cefuroxime. *Enterococcus* and *Pseudomonas* spp are not common as causative organisms in postoperative endophthalmitis in Western countries, but, when other causative microorganisms (mainly coagulase-negative staphylococci) are eradicated by the use of cefuroxime, these are the infectious agents we are going to face. However, their absolute number in the Swedish series does not seem to have increased. Methicillin-resistant *S. aureus* and methicillin-resistant *S. epidermidis* did not constitute significant problems in the ESCRS study, but resistance patterns must be cautiously followed. It remains to be proven whether other antibiotics (eg, moxifloxacin) are more effective in these potentially resistant cases.

As for the lack of a commercially available product for intracocular use, this issue has been resolved in Europe with the European Medicines Agency’s approval of Aprokam (known as Prokam in Spain; Thea Pharmaceuticals). This product contains cefuroxime 50 mg powder, which is to be diluted with 5 mL sodium chloride 9 mg/mL (0.9%) solution for injection. The vial is intended for single use of an injected dose of 1 mg cefuroxime in 0.1 mL volume intracamerally at the end of cataract surgery.

In regard to patients with a penicillin allergy, the risk of cross-reactivity between penicillin and cefuroxime (and ceftazidime) is low because the molecules do not share R1 side chains. In Sweden, every patient receives intracameral cefuroxime unless he or she has a distinct allergy to cephalosporins, not penicillin. On the other hand, cefazolin, which has also been used for intracameral injection, may show cross-allergenicity with penicillin.

Intracameral moxifloxacin at the end of cataract surgery has also been used, with the theoretical advantages of a broader spectrum and a concentration-dependent mechanism of action. In the last report from the Swedish cataract register, patients who received intracameral

<table>
<thead>
<tr>
<th>Data Source</th>
<th>No Intracameral Cefuroxime (%)</th>
<th>Intracameral Cefuroxime (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESCRs⁸</td>
<td>0.35</td>
<td>0.05</td>
</tr>
<tr>
<td>Sweden⁷</td>
<td>0.39</td>
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</tr>
<tr>
<td>Great Britain</td>
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<td>France</td>
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<tr>
<td>United States</td>
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</tr>
<tr>
<td>South Africa</td>
<td>0.55</td>
<td>0.08</td>
</tr>
<tr>
<td>Portugal</td>
<td>0.26</td>
<td>0</td>
</tr>
</tbody>
</table>

†Courtesy of the ESCRs⁸

**TAKE-HOME MESSAGE**

- Postoperative endophthalmitis after cataract surgery has become a rare event, but, when it occurs, it often results in severe and irreversible visual loss.
- The only measures to date shown by scientific evidence to reduce the rate of endophthalmitis after cataract surgery are the use of preoperative povidone-iodine and intracameral cefuroxime.
- To ensure that substantial changes in the postoperative endophthalmitis microbial spectrum and microbial antibiotic sensitivities are not being overlooked, it is important that other geographical areas have registers similar to the Swedish register.
moxifloxacin had a postoperative endophthalmitis rate of 0.029%, similar to that for cefuroxime. In a recent Japanese survey-based report, the endophthalmitis rate with intracameral moxifloxacin use was 0.016%.

The availability of a commercial preparation of cefuroxime for intraocular use, as opposed to use of a moxifloxacin formulation from an eye drop bottle, along with an increasing rate of resistance to fluoroquinolones, makes the option of intracameral moxifloxacin less attractive.

Use of antibiotics in the irrigating solution is discouraged because not only the patient but also the staff are exposed to the antibiotic, which usually ends up down the drain of the surgical facility. Additionally, an unknown dose is delivered in this manner, as compared with the precise amount given by intracameral injection. Use of vancomycin in this way is particularly discouraged.

**Postoperative topical antibiotics.** As with preoperative topical antibiotics, there is no scientific evidence to justify the use of postoperative topical antibiotics. However, most surgeons advise their use until the cataract surgical wound has healed adequately, which is about 1 week. Retrospective studies support starting these drops early after cataract surgery; a common approach nowadays with clear corneal phacoemulsification under topical anesthesia. It is important not to taper the drops in order to discourage development of antibiotic resistance.

Data from the ESCRs study and from the Swedish cataract register (Table 3) suggest that pre- and postoperative topical antibiotic drops confer no added benefit over intracameral cefuroxime injection in reduction of postoperative endophthalmitis. Fourth-generation fluoroquinolones were not used, but the intensive pulsed levofloxacin regimen used in the ESCRs study achieved relatively high concentrations in the anterior chamber—although much lower than after an intracameral antibiotic injection—with no significant effect on endophthalmitis rate reduction.

**Subconjunctival antibiotics.** The adoption of topical anesthesia for cataract surgery has made subconjunctival antibiotic injection rather inconvenient. Some retrospective studies support their use, but the reduction of endophthalmitis rates when subconjunctival cefuroxime has been replaced by intracameral cefuroxime has tipped the balance toward the latter.

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**TABLE 3. ENDOPHTHALMITIS RATES AFTER INTRACAMERAL ANTIBIOTIC INJECTION ALONE AND WITH TOPICAL ANTIBIOTIC REGIMENS**

<table>
<thead>
<tr>
<th></th>
<th>Intracameral Antibiotics Only</th>
<th>Plus Preoperative Topical Antibiotics</th>
<th>Plus Postoperative Topical Antibiotics</th>
<th>Plus Pre- and Postoperative Topical Antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endophthalmitis Rate</td>
<td>0.025%</td>
<td>0.017%</td>
<td>0.019%</td>
<td>0.041%</td>
</tr>
</tbody>
</table>

*Adapted from Friling et al.

*No statistically significant benefit from add-on topical antibiotics.

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**FUTURE DIRECTIONS**

Prophylactic regimens (ie, intracameral antibiotics) will likely produce a change in the spectrum and antibiotic sensitivities of microorganisms involved in postoperative endophthalmitis. Data from the Swedish cataract register suggest that the incidence of endophthalmitis includes cases with microbes not covered by intracameral cefuroxime but that an absolute increase in the number of cefuroxime-resistant infections is not being induced.

To ensure that substantial changes in the postoperative endophthalmitis microbial spectrum and microbial antibiotic sensitivities are not being overlooked, it is important that other geographical areas have in place registers similar to the Swedish one and that may work hand-in-hand with the ESCRs-Euretina initiative.

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