Analyzing Antibiotic-Resistant Bacteria

In a retrospective, consecutive, observational case series, 64 cases of acute endophthalmitis occurring within 6 weeks after cataract surgery were identified over a 3-year interval at one vitreoretinal practice. Cultures from 33 of the 64 eyes tested positive for MRSA. Six of the 33 cultures that tested positive demonstrated MRSA infections. Those six eyes were started on fluoroquinolone antibiotics 2 to 3 days postoperatively. Corneal abnormalities were found in five of the six cases. Visual acuity at the last follow-up visit was no light perception in two eyes, hand movements in two eyes, and 20/30 in two eyes. One eye had no light perception vision and underwent enucleation within 3 days of presentation. All six organisms were sensitive in vitro to gentamicin and vancomycin. None of the organisms...
was sensitive to fluoroquinolone antibiotics, but investigators noted that not all of them were tested against fluoroquinolones.3

In an observational, prospective study, investigators collected preoperative conjunctival cultures from 1,940 consecutive patients undergoing cataract surgery during a 1-year period. Of these cultures, 4,391 microorganisms were isolated to identify the presence of antibiotic-resistant conjunctival bacteria. Investigators stated that 94.23% of the isolated microorganisms were gram-positive, and 5.31% were gram-negative. Of the 1,940 cultures, the most prevalent conjunctival bacteria were coagulase-negative staphylococci, which were present in 88.3% of cultures. Diphtheroids were harbored in 58.1% of patients, propionibacteria in 31%, streptococci in 23.1%, Staphylococcus aureus in 10.2%, haemophilus and gram-negative diplococci in 7.5%, other gram-negative rods in 4.5%, and enterococcus in 2%. The enterococci-staphylococci profile was the most resistant to antibiotics. Investigators concluded that the typical respiratory bacteria remained sensitive to chloramphenicol and ß-lactams, and other gram-negative rods were sensitive to aminoglycoside, quinolones, and certain ß-lactams.4

In an in vitro laboratory investigation, researchers examined in vitro antibiotic susceptibility patterns of conjunctival bacterial flora isolated before surgery from patients undergoing refractive surgery. Of 105 patients (105 eyes) scheduled for refractive surgery, 67.6% underwent LASIK with a femtosecond laser, 22.9% underwent LASIK with an automated microkeratome, 7.6% underwent LASEK, and 1.9% received a phakic IOL. Preoperative conjunctival cultures were obtained on the day of surgery before topical antibiotics, anesthetics, and povidone-iodine were administered. Coagulase-negative staphylococci were identified in 85% of patients, S. aureus was identified in 2.3%, and Streptococcus pneumoniae was identified in 1.2%. Five gram-negative bacilli were isolated, but no fungi or mycobacteria were isolated. Researchers concluded that gemifloxacin, moxifloxacin, and gatifloxacin were the most effective against conjunctival bacteria isolated from refractive surgery patients, and resistance to ofloxacin and levofloxacin is increasing among methicillin-susceptible coagulase-negative staphylococci (Table 1).5

### Table 1. Antibiotics Tested Against Bacterial Isolates

<table>
<thead>
<tr>
<th>Antibiotics Tested</th>
<th>MICs that would inhibit the growth of 90% of the bacterial isolates</th>
<th>MICs that would inhibit the growth of 90% of the bacterial isolates for methicillin-susceptible coagulase-negative staphylococci</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ofloxacin</td>
<td>0.5 µg/mL</td>
<td>32 µg/mL</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>0.19 µg/mL</td>
<td>4 µg/mL</td>
</tr>
<tr>
<td>Gatifloxacin</td>
<td>0.094 µg/mL</td>
<td>1 µg/mL</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>0.047 µg/mL</td>
<td>0.5 µg/mL</td>
</tr>
<tr>
<td>Gemifloxacin for methicillin-susceptible coagulase-negative staphylococci</td>
<td>0.023 µg/mL</td>
<td>0.25 µg/mL</td>
</tr>
</tbody>
</table>

Abbreviation: MICs, minimum inhibitory concentrations.

Ten ophthalmic OR nurses from two hospitals in Glasgow, Lanarkshire, United Kingdom, performed different protocols to dilute cefuroxime for intracameral injection. Oven-dried, analytical-grade potassium chloride was used as a surrogate for cefuroxime. Each group of nurses prepared solutions of 1.0 mg in 0.1 mL according to a protocol with which they were familiar and one with which they were unfamiliar. Ten samples were collected from each group of nurses for each protocol. Ten analytical chemists also performed both dilutions to act as a nonmedical comparison group. A total of 30 samples were obtained for each protocol. The median dose after dilution was 1.17 mg for the unfamiliar protocol and 2.05 mg for the familiar protocol. For the familiar protocol, the median dose was significantly higher (P < .001), and there was greater variability. Investigators noted that inadequate mixing in a 1-mL syringe was likely the cause for inaccuracy in the familiar protocol, which...
indicates that small-volume syringes should not be used for mixing. They concluded that the mathematical accuracy of a dilution protocol does not ensure dosing accuracy in a clinical setting.\(^6\)

To combat infections that arise from the bacterial colonization of a new IOL and the subsequent formation of an antibiotic-tolerant biofilm, researchers developed a polymeric hydrogel system that delivers specific levels of antibiotics over an extended period of time within the globe of the eye. Investigators loaded norfloxacin into cross-linked poly(2-hydroxyethyl methacrylate) gels, which were surface-modified with octadecyl isocyanate to produce a hydrophobic rate-limiting barrier controlling the release of norfloxacin. Octadecyl surface modification was characterized using scanning electron microscopy and X-ray photoelectron spectroscopy. A 15-minute modification reportedly led to a uniform surface coating and nearly a zero-order release of norfloxacin from the matrix. They concluded that norfloxacin released from coated, poly(2-hydroxyethyl methacrylate) kills *Staphylococcus epidermidis* in suspension and on a simulated medical implant’s surface.\(^7\)

**VANCOMYCIN**

In a retrospective study, researchers analyzed 16,606 cataract surgeries that were performed at the Warrington Hospital in North West England over an 11-year period. The surgeries were divided into two time periods. Period A consisted of surgeries that were performed between January 1, 1998, and December 31, 2000, prior to the introduction of intracameral vancomycin at the end of surgery. Period B consisted of surgeries that were performed between January 1, 2001, and December 31, 2008, after the introduction of intracameral vancomycin at the end of surgery. The incidence of endophthalmitis per 1,000 cataract surgeries was 3.0 during period A and 0.08 during period B. This reduction was statistically significant (Chi-squared test; \(P < .0001\)). The relative risk of developing endophthalmitis without intracameral vancomycin prophylaxis was 38, and the reduction in absolute risk was 292 cases of endophthalmitis per 100,000 cataract surgeries.\(^8\)

Following routine cataract surgery with phacoemulsification and the implantation of a PCIOL, 19 patients received injections of vancomycin 1 mg/0.1 mL saline solution. Aqueous samples were obtained by inserting a cannula into the anterior chamber through the sideport incision. In nine patients, group 1, aqueous sampling took place 1 minute after intracameral injections of vancomycin. In 10 patients, group 2, aqueous sampling took place between 18 and 24 hours postoperatively. Fluorescence polarization immunoassay was used to calculate the aqueous vancomycin concentration. The mean and median concentrations of vancomycin were 5,385 mg/L and 5,458 mg/L in group 1, respectively. In group 2, the mean and median concentrations of vancomycin were 41.1 mg/L and 40.6 mg/L, respectively. The concentration of vancomycin exceeded its minimum inhibitory concentration by a factor of four for up to 26 hours postoperatively.\(^8\)

In a prospective, controlled trial, 41 patients (50 eyes) with cataracts were randomized to receive 20 µg/mL of vancomycin and 8 µg/mL of gentamicin in the infusion fluid at the time of cataract surgery or no intracameral antibiotics. Follow-up was completed on 49 eyes. Optical coherence tomography was performed to measure macular thickness at 1 day and 1 and 5 weeks postoperatively. In patients who did not receive intracameral antibiotics, the central retinal thickness increased at 5 weeks from baseline by a mean of 12.3 ±27.5 µm (\(P < .001\)). In patients who received intracameral antibiotics, central retinal thickness increased at 5 weeks from baseline by a mean of 10 ±13 µm (\(P < .001\)). The mean contrast sensitivity was 1.26 in patients with increased macular thickness and 1.43 in those with no change (\(P = .001\)). Researchers noted no significant effect of intracameral antibiotics in the infusion fluid on macular thickness or visual function after cataract surgery.\(^9\)

To evaluate the oxidative-stress parameters of intracameral cefuroxime and vancomycin in the cornea, the right eyes of 30 animal models were randomized into three groups: a cefuroxime group (\(n = 10\)), a vancomycin group (\(n = 10\)), and a control group (\(n = 10\)). Twenty eyes were injected with 0.1 mL of the two antibiotic agents, and 10 eyes were injected with 0.1 mL of balanced salt solution. Corneal thickness and clarity were measured before surgery and at 3 and 6 hours postoperatively. Corneal tissues were extracted and homogenized in 2 mL of physiological saline and kept at -80°C. Malondialdehyde and total thiol levels were measured with spectrophotometric methods, and a statistical analysis was conducted. Neither cefuroxime nor vancomycin caused corneal thickening or edema at

“Physicians should consider MRSA in patients with atypical conjunctivitis showing patchy necrosis of the conjunctiva and investigate any dimpled or eroded areas for evidence of deeper invasion.”

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3 and 6 hours after injection, and no anterior chamber reactions were observed in either group. In the cefuroxime group, the level of total thiol significantly decreased ($P = .001$), and the level of malondialdehyde significantly increased ($P < .001$). There were no biochemical changes in the vancomycin group compared with the control group.\(^{11}\)

In a prospective, interventional, hospital-based study, 400 patients (400 eyes) who underwent phacoemulsification between January 2004 and 2006 were nonrandomly assigned to two groups. Group 1 comprised 180 patients who received topical 0.3% ciprofloxacin eye drops q.i.d. for 1 day preoperatively and did not receive vancomycin in the irrigating solution during cataract surgery. Group 2 comprised 220 patients who underwent cataract surgery with 20 µg/mL of vancomycin in the irrigating solution but did not receive topical antibiotics preoperatively. Anterior chamber aspirates were obtained from both groups at the end of surgery. Statistical analysis was performed with a Chi-square test. Bacteria were cultured in 21.1% of eyes in group 1 and in 7.7% of eyes in group 2. Coagulase-negative \textit{Staphylococcus} was the most prevalent organism in both groups. Multiple organisms were identified in 2.2% of eyes in group 1, whereas none of the eyes in group 2 showed multiple organisms. None of the eyes in either group exhibited fungal contamination. One patient in group 1 developed endophthalmitis caused by \textit{Alcaligenes faecalis}. All patients were analyzed at a follow-up visit between 6 and 14 months postoperatively.\(^{12}\)

**COMPLEX CASES**

A 54-year-old man presented to the Cole Eye Institute in Cleveland with a complaint of severe pain and decreased vision in his left eye for a 2-day period. The patient had a BCVA of 20/25 in his right eye and 20/100 in his left eye. His left eye was swollen and displayed moderate eyelid erythema and diffuse injection. A slit-lamp examination revealed a corneal ulcer associated with a loose suture from cataract surgery that had been performed 2 years ago. The broken suture was removed, and the patient was started on topical antibiotic treatment, alternating between 50 mg/mL of cefazolin and 14 mg/mL of gentamicin every 30 minutes. Cultures of the ulcer revealed MRSA. The patient’s treatment regimen was changed to include 50 µg/mL of vancomycin, but the ulcer continued to progress. Three days later, the ulcer perforated, and the patient underwent an emergency corneal patch graft and lateral tarsorrhaphy. Preoperative cultures were negative, and the patient was treated with Zymar (Allergan, Inc.) q.i.d. and bacticain ointment. By 1 month postoperatively, the BCVA in the patient’s left eye was 20/30, and the ocular surface and patch graft were intact. Investigators reported that, to their knowledge, this was “the first reported case of suture-related MRSA keratitis after uncomplicated clear corneal cataract surgery.”\(^{13}\)

A 31-year-old man was referred to the Cabarrus Eye Center in Concord, North Carolina. He had developed necrotizing community-based MRSA conjunctivitis that caused palpebral conjunctival ulceration and destruction of postseptal soft tissue with invasion of extraconal fat. The authors of the report noted that, although the patient’s infection was severe, the external signs of eyelid disease were modest. He did not have any apparent risk factors for MRSA colonization. The patient was treated for 7 days with intravenous vancomycin and tobramycin sulfate as well as oral rifampin and then for 7 days with oral trimethoprim sulfa double strength with clinical resolution. The report’s authors stated that physicians should consider MRSA in patients with atypical conjunctivitis showing patchy necrosis of the conjunctiva and investigate any dimpled or eroded areas for evidence of deeper invasion.\(^{14}\)

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