Minimizing the risk of postoperative endophthalmitis requires the elimination of or a significant reduction in the bacterial flora that are found on the ocular surface at the time of surgery and during the immediate postoperative period. The major source of bacteria that cause endophthalmitis is a patient’s own eyelids and conjunctiva. Applying povidone-iodine at the time of surgery can decrease ocular bacteria. Topical antibiotics administered for several days and immediately prior to surgery provide an additional killing of bacteria beyond the effects of povidone-iodine, although a prospective randomized study has yet to prove that the use of topical antibiotics reduces the risk of endophthalmitis. Regardless, almost all ophthalmologists prescribe topical antibiotics for patients undergoing intraocular surgery.

Ophthalmologists also use antibiotics postoperatively to minimize the risk of bacteria’s entering the eye via the surgical wound. This is of particular concern with clear corneal incisions, because the wound may not be watertight. In addition, frequently applying a topical antibiotic may allow the drug to achieve levels in the aqueous that are high enough to kill the bacteria that contaminate the anterior chamber at the time of surgery. According to a rabbit study, Vigamox (Alcon Laboratories, Inc., Fort Worth, TX) administered in both the pre- and postoperative period can prevent the development of endophthalmitis following inoculation with Staphylococcus aureus.

The ideal topical antibiotics for minimizing the risk of postoperative endophthalmitis must have the following characteristics: broad-spectrum coverage of both gram-positive and gram-negative bacteria; bacteriocidal properties for quick kills of bacteria upon contact; and excellent penetration to achieve intraocular levels that are sufficiently high to kill the offending bacteria. The agent must also be nontoxic to the ocular surface and cost effective.

Several classes of antibiotics are currently available in the US and include the combination therapy of polymixin B and trimethoprim, the aminoglycosides, and the fluoroquinolones. Many ophthalmic ointments are also available, including erythromycin and the combination therapy of bacitracin and polymyxin B. Of all of these antibiotics, fluoroquinolones, in my opinion, may be the most appropriate antibiotics for endophthalmitis prophylaxis. The greatest advantages of these drugs over other classes of antibiotics are that they provide broad-spectrum coverage, are bacteriocidal and nontoxic, and penetrate the anterior chamber well. In contrast, other antibiotics such as polymixin B and trimethoprim are bacteriostatic, and aminoglycosides carry some risk of toxicity.

Among the commercially available topical ophthalmic fluoroquinolones, ciprofloxacin and ofloxacin have limited gram-positive coverage. The newer fluoroquinolones—specifically Quixin (Santen Inc., Napa, CA), Zymar (Allergan, Inc., Irvine, CA), and Vigamox—have enhanced activity toward gram-positive pathogens while maintaining broad-spectrum coverage against gram-negative organisms. They interfere with both topoisomerase II and IV, and bacterial resistance appears to be lower since mutations of both enzymes are necessary.
After reviewing the published literature for the most desirable properties of commercially available antibiotics, I found some minor differences between them. In general, the three most recently FDA-approved antibiotics (Quixin, Zymar, and Vigamox) are excellent antibiotics. Some of their important characteristics include low resistant rates, high efficacy and kill time, reduced surface toxicity, and effective aqueous penetration. This article discusses the off-label use of the approved products Quixin, Zymar, and Vigamox.

**ANTIBIOTIC SUSCEPTIBILITY**

Several recently published studies have demonstrated excellent efficacy for Quixin, Zymar, and Vigamox against common ocular pathogens. One potential limitation in susceptibility is that the determination is based on the serum level of the drug and not its tear or aqueous level. For that reason, although an antibiotic may be considered resistant, it may still be effective at killing bacteria given the high level of the medication in the tear film compared with the serum. Another limitation is the variations in resistance pattern based on geographic location. Consequently, a comprehensive study involving multiple sites throughout the US will have much more reliable data than one from a single center. For instance, the Tracking Resistance in the United States Today (TRUST) study is a surveillance report of more than 70,000 isolates that were collected from over 200 institutions since 1999. In this comprehensive study, 99% of *Streptococcus pneumoniae* remained susceptible to Quixin despite more than 9 years of extensive systemic use. Currently, ocular isolates are collected and analyzed to determine trends in resistance for the commonly prescribed topical antibiotics in the TRUST study.

**EFFICACY IN KILLING BACTERIA**

Fluoroquinolones as a class effectively kill bacteria, unlike bacteriostatic antibiotics, which inhibit bacterial growth. A fluoroquinolone's efficacy is dependent upon its concentration; the higher the concentration, the greater the kill rate. Frequent dosing of the medication during a short period of time may therefore be more appropriate than infrequent long-term use.

As with any topical antibiotic, the goal is to eradicate the bacteria as quickly as possible. There is some recent evidence suggesting that the preservative benzalkonium chloride (BAK) may have a synergistic effect in improving an agent’s kill time. A recent in vitro study demonstrated that 0.005% BAK alone or 0.3% gatifloxacin with 0.005% BAK (Zymar) kills *Staphylococcus epidermidis* and *S. aureus* within 1 hour, compared with 4 hours for 0.5% moxifloxacin alone (Vigamox) (Figure 1). Another study demonstrated similar results, with Zymar eliminating all *Staphylococcus* within 60 minutes, whereas 50% of the bacteria treated with Vigamox remained.

Other clinical studies have confirmed the slow kill rate of Vigamox (Figure 2). In a study of 60 patients undergoing intraocular surgery, after a 1-hour application of Vigamox preoperatively, there was no effect on killing bacterial flora on the ocular surface. At baseline, 55% of eyes had positive cultures compared with 53% of the eyes after treatment with Vigamox for 1 hour. In contrast, my colleagues and I will report a study at this year’s ARVO Annual Meeting in which a 1-hour preoperative application of Zymar significantly decreased the rate of bacterial contamination of the conjunctiva in patients undergoing intraocular surgery from a baseline of 75% to 40%. These studies suggest that antibiotics preserved with BAK may be much more efficacious in the rapid killing of bacteria compared with antibiotics without BAK. Quixin, which is 0.5% levofloxacin and 0.005% BAK, and Zymar therefore may kill bacteria much quicker than Vigamox.

**Figure 1.** An in vitro laboratory study demonstrating time-kill for *S. epidermidis* and *S. aureus*. Both bacteria are killed 1 hour following exposure to Zymar, compared to 4 hours for Vigamox.

**Figure 2.** The percentage of bacteria eliminated from the ocular surface following a 1-hour application of antibiotics is shown.
In general, fluoroquinolones have an excellent safety profile, which is important given the millions of prescriptions written for this class of drugs every year. A concern with any topical ophthalmic medication is the preservative BAK. A study by Cha et al demonstrated in tissue culture that BAK can cause epithelial cell death that is dependent on concentration and duration of exposure. Although Vigamox does not have BAK, recently published research suggests that Vigamox may be toxic to the ocular surface. In a double-masked, prospective study, 28 eyes of 14 patients were randomized to receive either Zymar or Vigamox. The investigators reported that the eyes that received Vigamox had a significantly higher degree of conjunctival injection, discomfort, and corneal epithelial cell loss compared to eyes treated with Zymar. This finding was confirmed by an in vitro study, in which the exposure of corneal and conjunctival epithelial cells to different concentrations of Vigamox resulted in poor cellular migration and adhesion. Furthermore, eyes exposed to Vigamox achieved a significant reduction in the production of collagen type IV and fibronectin than eyes exposed to Zymar. Effects on cellular migration, proliferation, and production of collagen and fibronectin are important for wound healing and the health of the ocular surface. These in vitro findings were confirmed by animal studies, in which incisions were created in rabbit corneas and exposed to either Zymar or Vigamox. Eyes exposed to Vigamox demonstrated a decrease in collagen IV production, disorganized and slower wound healing, inhibition of cellular proliferation, and a loss of the normal structure of the basal lamina.

In contrast to the aforementioned studies, Burka et al conducted a prospective, masked, randomized study comparing Zymar and Vigamox in patients undergoing PRK. The investigators found that eyes treated with Vigamox healed faster and had smaller epithelial defects compared with those treated with Zymar. Of course, no corneal incision is created during the refractive procedure. In another PRK study, no difference was found with respect to hazy, visual acuity, or epithelial healing between eyes treated with Zymar and Vigamox. Finally, Walter and Tyler reported two patients with worsening and persistent corneal ulcers as well as endothelial cell dysfunction while on Vigamox. The patients' conditions resolved after the discontinuation of Vigamox and the initiation of Zymar and corticosteroid treatment.

Figure 3 summarizes the results of a study by Ong-Tone. Quixin, Zymar, and Vigamox all achieve levels above the minimal inhibitory concentration following typical preoperative application.

In summary, bacterial resistance against these fluoroquinolones is uncommon. As a class, these
fluoroquinolones are well tolerated with minimal toxicity, and they penetrate the aqueous humor well.

The choice of antibiotic depends on the clinical situation. To quickly kill bacteria, those drugs preserved with BAK, such as Zymar and Quixin, may be indicated. Vigamox has better penetration into the aqueous humor, however, and may be more appropriate in eyes for which bacterial contamination of the anterior chamber is likely, although some evidence suggests that the drug may impair wound healing.

Based upon the literature mentioned herein, the later generations of topical fluoroquinolones represent the best of the available antibiotics.

Christopher N. Ta, MD, is Associate Professor and Director of Residency Program, Cornea and External Diseases, Department of Ophthalmology, Stanford University School of Medicine, Stanford, California. He is consultant for Vistakon and Allergan, Inc., and has received unrestricted research and educational gifts from Allergan, Inc. Dr. Ta may be reached at (650) 725-5743; cta@stanford.edu.
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