

# Overview of Available Antibiotics

When considering antimicrobial prophylaxis and treatment, how does one know what medication to use and how best to administer that therapy?

BY CHRISTINA RAPP PRESCOTT, MD, PhD

Prophylactic use of antimicrobials is standard practice in ophthalmic surgery; however, the technique and type of prophylaxis varies. In the United States, surgeons primarily use topical antibiotics, typically fourth-generation fluoroquinolones. In many other countries, including Australia and most of Europe, the primary method of antibiotic prophylaxis is intracameral first- or second-generation cephalosporins injected at the time of surgery. Using either of these two methods, the incidence of endophthalmitis following cataract surgery is generally reported to be less than 0.3%.<sup>1-4</sup> The question remains: how can we do better?

## INTRACAMERAL ANTIBIOTICS IN EUROPE

There is a trend in many countries, with the notable exception of the United States, toward the intracameral injection of antibiotics at the conclusion of cataract surgery. The landmark study of the European Society of Cataract and Refractive Surgeons (ESCRS) showed a 4.92-fold decrease in rates of endophthalmitis after cataract surgery when a single intracameral injection of cefuroxime was used compared with topical levofloxacin 0.5%.<sup>5</sup> The ESCRS study dramatically changed the practice patterns of many European ophthalmologists. In Europe, more than half of ophthalmologists now use intracameral antibiotic prophylaxis (1.0 mg/0.1 mL cefazolin or 1.0 mg/0.1 mL cefuroxime). Those ophthalmologists who do not use intracameral antibiotics are primarily concerned with compounding issues and would use intracameral antibiotics if commercially available.<sup>6</sup> One criticism of the ESCRS study is the relatively high rate of endophthalmitis in the control group (0.34% vs 0.07% in the treatment group).<sup>5</sup>

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## INTRACAMERAL ANTIBIOTICS IN THE UNITED STATES

Intracameral antimicrobial prophylaxis has multiple benefits, including reduced cost and increased patients’ compliance (because the surgeon is administering the medication). There is a question of safety especially with compounded antibiotics.

As illustrated by the recent meningitis outbreak that was linked to drugs from the New England Compounding Center, compounded medications are not subject to the same regulations as commercially available medications. One option is to use commercially available moxifloxacin (Vigamox; Alcon Laboratories, Inc.) intracamerally. One group in California reported a decrease in the endophthalmitis rate from 3.13 to 0.14 per 1,000 patients after starting intracameral antibiotic prophylaxis using cefuroxime, moxifloxacin, or vancomycin.<sup>1</sup>

A large multicenter clinical trial comparing the use of intracameral cefuroxime and moxifloxacin would be of interest to many ophthalmologists, especially those who do not have access to compounded medications.

## COMMERCIALLY AVAILABLE ANTIBIOTICS

Whether topical or intracameral, the appropriate antibiotic must be selected to minimize the risk of endophthalmitis. It is important to remember that any use of antibiotic eyedrops in surgical prophylaxis is off label. Although it is standard clinical practice to use antibiotic prophylaxis for cataract surgery, no randomized trial has proven the efficacy of any antimicrobial in this setting. The antimicrobial eye drops that are commercially available have been approved for the indication of bacterial conjunctivitis. The general categories of antibiotic ophthalmic drops include fluoroquinolones (besifloxacin [Besivance; Bausch + Lomb], ciprofloxacin, gatifloxacin, levofloxacin, moxifloxacin, and ofloxacin), other single agents (azithromycin [AzaSite; Merk & Co.], erythromycin, gentamicin, sulfacetamide, tobramycin), and mixtures (polymyxin B with either bacitracin, neomycin and bacitracin, neomycin and gramicidin, or trimethoprim).<sup>7</sup> The newest FDA-approved ophthalmic antibiotic is besifloxacin 0.6%, a fluoroquinolone, which was approved for bacterial conjunctivitis based on comparison to placebo.<sup>8</sup> As fluoroquinolone resistance develops, the need for a new category of ophthalmic antibiotics, rather than simply a new drug in the same category, becomes increasingly apparent.

## OTHER COMMERCIALLY AVAILABLE ANTIMICROBIALS

Although antibiotics are the most commonly prescribed ophthalmic antimicrobials, antivirals, antifungals, and medications targeting *Acanthamoeba* also play an important role in infection control. Ganciclovir ophthalmic gel 0.15% (Zirgan; Bausch + Lomb) was approved for treatment of herpes simplex keratitis first as an orphan drug in 2007, and it received full FDA approval in 2009. The FDA approval was based on noninferiority to acyclovir ophthalmic ointment 3%, which is not approved for use in the United States. In the United States, the only commercially available antifungal is natamycin 5% (Natacyn; Alcon Laboratories, Inc.), a tetraene polyene. There are no medications currently FDA approved for the treatment of *Acanthamoeba*.

## COMPOUNDED ANTIMICROBIALS

Antibiotic ophthalmic drops can be compounded at higher concentrations than commercially available, such as tobramycin 14 mg/mL (compared with commercially available 3 mg/mL) or made from systemic antibiotics not available as ophthalmic preparations commercially, such as vancomycin (14 mg/mL or 25 mg/mL) and amikacin (25 mg/mL). Two of the more commonly used compounded topical antifungals are amphotericin-B

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0.1% and voriconazole 1%. Successful treatment of acanthamoeba relies on compounded medications, including propamidine isethionate 0.1% eye drops, chlorhexidine 0.02%, and polyhexamethylene biguanide 0.02%.

## CONCLUSION

There are a limited number of commercially available antimicrobial ophthalmic drops, especially for pathogens other than bacteria. Therefore, compounding pharmacies play an important role in the prevention and treatment of infections. Multiple antimicrobials can be made into either topical eye drops or intracameral formulations by a compounding pharmacy. These compounded antimicrobials are currently used for treatment of severe ocular infections, including methicillin-resistant *Staphylococcus aureus*, *Acanthamoeba*, and fungal infections. These compounded antimicrobials are especially critical for the treatment of acanthamoeba. Unfortunately, many patients do not have access to or cannot afford medications from a compounding pharmacy. Hopefully in the future more categories of antimicrobials will become commercially available for ophthalmic use, which will help us care for all of our patients. ■

*Christina Rapp Prescott, MD, PhD, is an assistant professor of ophthalmology in the Division of Cornea, Cataract, and External Diseases at The Wilmer Eye Institute, The Johns Hopkins School of Medicine, Baltimore. She acknowledged no financial interest in any of the products or companies mentioned herein. Dr. Prescott may be reached at (410) 893-0480; cpresco4@jhmi.edu.*



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