Antibiotics in Cataract Surgery

BY SAMUEL MASKET, MD; ROGER F. STEINERT, MD; AND FRANCIS S. MAH, MD

Endophthalmitis, cystoid macular edema, and corneal decompensation are all serious complications of cataract surgery. Recent innovations in pre-, intra-, and postoperative drug regimens are intended to decrease the incidence of such problems. I asked three respected ophthalmologists to discuss some of these new pharmacologic ideas.

—William J. Fishkind, MD, Section Editor

SAMUEL MASKET, MD

Preventing infection after cataract surgery requires ophthalmologists' attention to four matters. First, they must reduce the number of microbes on the ocular surface and at the lid margins. Doing so may require particular effort when the patient suffers from chronic blepharitis and other conditions. Second, surgeons must avoid intraocular contamination during the cataract procedure by carefully draping the lid margins and eyelashes and by limiting surgical complications, particularly capsular rupture. Third, ophthalmologists must avoid intraocular contamination after surgery through the hermetic sealing and firm stability of the cataract incision. Finally, as a fail-safe, surgeons must destroy any microbes that enter the eye during or after the cataract procedure. It is here that intracameral and topical antibiotics play a significant role.

I employ chemprophylaxis for all four of the aforementioned categories. I instruct patients with blepharitis to cleanse their eyelids and apply bacitracin ointment at bedtime for 1 week, when I recheck their eyelids and lid margins. Assuming this regimen was effective, I then proceed with surgery in my usual fashion.

Very occasionally, I encounter patients who are immunologically incompetent, who have lost an eye to infection after surgery, who have an indwelling Jones lacrimal tube, or who have a prosthetic fellow eye. I would instruct all of these patients to apply bacitracin ointment to their eyelids for 1 week preoperatively and would receive treatment with systemic moxifloxacin 400 mg orally q.d. for 2 days prior to surgery, on the day of surgery, and for an additional 2 days after surgery. Their postoperative course would otherwise be routine.

Because silicone punctal plugs may harbor microbes or allow the formation of a biofilm, I remove them prior to surgery and then treat the patient routinely.

For me, routine preoperative prophylaxis involves topical Vigamox (moxifloxacin hydrochloride 0.5%; Alcon Laboratories, Inc., Fort Worth, TX) q.i.d. 1 day preoperatively and 1 hour prior to surgery in a "cocktail" with an NSAID and viscous anesthetic mixture. I prepare the skin with povidone-iodine 10% and place a 5% concentration on the anesthetized ocular surface.

I add vancomycin 20 mg to the 500-mL BSS (Alcon Laboratories, Inc.) infusate employed during the phacoemulsification. At the close of surgery, after sealing the incision and testing it with fluorescein dye at measured physiologic IOP, I add 50 µL of undiluted Vigamox to the anterior chamber. Using the agent directly from an unopened bottle in this manner is possible, because it has a pH of 6.8 and near isotonicity, and because it is sterile and not preserved. No other currently available product may be used for this purpose. Finally, I instruct patients to apply topical Vigamox q3h on the day of surgery and q.i.d. for an additional 5 days and then to cease its use abruptly so long as there is epithelial sealing of the incisions.

ROGER F. STEINERT, MD

Without firm scientific data, which may never be possible in the arena of endophthalmitis, I use the following regimen for routine cataract surgery based on logic, incomplete science, and my estimation of risks and benefits.

Starting 3 days preoperatively, patients use Zymar (gatifloxacin ophthalmic solution 0.3%; Allergan, Inc., Irvine, CA) and Acular LS (Allergan, Inc.) q.i.d. On the day of surgery, they receive two doses of Zymar approximately 30 minutes preoperatively along with dilating drops. I apply Betadine (The Purdue Frederick Company, Stamford, CT) to the skin around the eye and place 5% Betadine solution on the globe. I do not use an antibiotic in the infusion fluid or intracamerally at the end of surgery. I instill topical Zymar at the end of the procedure.

On the day of surgery, immediately postoperatively,

patients receive Pred Forte (Allergan, Inc.), Acular LS, and Zymar q4h. They continue taking these three medications q.i.d. for 1 week. At that point, patients discontinue the Zymar and decrease their dosing of Pred Forte and Acular LS to b.i.d. for the next 2 weeks. They then administer Pred Forte and Acular LS q.d. for 3 more weeks. This therapeutic regimen lasts longer and is more intense than that followed by many cataract surgeons, but it is geared toward the third standard deviation outlier. I almost never have a case of postoperative rebound iritis or cystoid macular edema (CME).

FRANCIS S. MAH, MD

The use of the antiseptic povidone-iodine 5% solution in the conjunctival cul-de-sac prior to surgery is the cornerstone of endophthalmitis prophylaxis.[1]

Although there is no consensus on which antibiotic to use or the method of application in cataract surgery, ophthalmologists generally agree that perioperative antibiotics are the standard of care.[2-6] Outside of ophthalmic surgery, studies have demonstrated the efficacy of antibiotics in the prevention of postoperative infections. In these nonophthalmic surgeries, antibiotics are most efficacious when administered no more than 1 hour before surgery. Moreover, 30 minutes prior to starting the incision is the optimal time to begin intravenous antibiotic prophylaxis.[7] Because there are no clinical trials in ophthalmology helping to guide surgeons as to when to start prophylactic antibiotics, I defer to the general surgical literature and begin topical antibiotics starting 1 to 2 hours prior to surgery.

For ophthalmic procedures, I think it is prudent to use topical antibiotics until the epithelium is intact following cataract surgery. Although tapering steroids and other anti-inflammatory medications is typical, it is important not to taper antibiotics due to the real risk of developing and selecting for bacteria that are resistant.[8] I therefore have patients start using topical antibiotics at least 30 minutes to 1 hour prior to surgery and continue the medication at the full FDA-approved dosage until their epithelium has healed, roughly 3 to 10 days, without tapering the antibiotic.

Factors in the choice of antibiotic include the medications' peak concentrations in the ocular tissues and the minimum inhibitory concentration (MIC) of the key bacteria that cause endophthalmitis.[9] Today's fluoroquinolones generally have the desirable combination of the lowest MICs and the highest concentrations in ocular tissues when used topically.[9] Gatifloxacin and moxifloxacin are the most potent (lowest MICs) and reach the highest concentrations in the cornea and the anterior chamber (highest peak concentrations).[9] It is my opinion that cataract surgeons should use one of these two agents for perioperative cataract surgery prophylaxis.

A study by the ESCRS generated earnest discussion among cataract surgeons regarding the future of prophylaxis.[2] Although the study's results were dramatic, valid criticism of the research includes its use of levofloxacin 0.5% as the topical antibiotic instead of an agent that acquires higher concentrations while providing more potency. Another issue is the study's use of cefuroxime as the intracameral agent instead of a drug that could have better pharmacokinetic and pharmacodynamic characteristics. Further criticism relates to the relatively high rate of endophthalmitis seen in this study (> 1:400 cases) and the potential long- and short-term adverse events, including toxic anterior segment syndrome and anaphylaxis from administering intracameral antibiotics that are not commercially prepared.[2] Although my colleagues and I have conducted some animal studies, I am not currently using intracameral antibiotics of any kind for prophylaxis.

Regarding the prevention of miosis, management of postoperative pain, and control of postoperative inflammation, the peer-reviewed literature demonstrates the superiority of using topical NSAIDs for 3 days prior to surgery compared with 1 day, which in turn is more effective than using the agents only on the day of surgery.[10-12] Considering that CME has a peak incidence of 4 to 6 weeks following routine uncomplicated surgery, it makes sense that an NSAID should be used for at least 6 to 8 weeks to cover the high-risk period. Patients at greater risk (eg, diabetics, uveitics, vasculopaths, and individuals whose surgery was complicated) should

(Continued on page 30)

(Continued from page 24)

probably use prophylactic NSAIDs for at least 8 to 12 weeks. The dosing should never exceed the FDA's recommended frequency, and ophthalmologists should carefully monitor the eyes of all patients who use NSAIDs for more than 4 weeks due to the risk of corneal and scleral melts. These postoperative melts are most likely in patients with neurotrophic keratopathy, severe dry eye disease, and moderate-to-severe ocular surface disease such as blepharitis and meibomitis.[10-12]

Studies have demonstrated the efficacy of diclofenac, ketorolac 0.5%, bromfenac 0.09%, and nepafenac 0.1% in the management of inflammation and pain after cataract surgery.[10-12] In clinical trials, diclofenac and ketorolac were efficacious in the management of CME. The newest NSAIDs, bromfenac and nepafenac, are reportedly more potent and more bioavailable after topical dosing. Nepafenac is the only prodrug.[10-12] Until there are prospective data showing the differences between the available NSAIDs, it makes sense to view the pain management, CME prevention, and anti-inflammatory efficacy as effects of the drug class. Several key differences are the dosing (ranging from b.i.d. to q.i.d.), the formulations (solution vs suspension), and the rate of burning and stinging in the FDA trials (0% to 40%).

Unless they are at high risk of scleral or corneal melts, as mentioned earlier, my patients all begin using a topical NSAID on the day of cataract surgery at the least or, ideally, 3 days preoperatively, and they continue taking the FDA-approved dose for 6 to 8 weeks postoperatively. Those of my patients at high risk of CME after cataract surgery begin using NSAIDs at least 3 days preoperatively and continue them for at least 8 to 12 weeks. ■

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1. Speaker MG, Menikoff JA. Prophylaxis of endophthalmitis with topical povidone-iodine. *Ophthalmology.* 1991;98:1769-1775.
2. Barry P, Seal DV, Gettinby G, et al. ESCRS study of prophylaxis of postoperative endophthalmitis after cataract surgery. *J Cataract Refract Surg.* 2006;32:407-410.
3. Jensen MK, Fiscella RG. Comparison of endophthalmitis rates over four years associated with topical ofloxacin vs ciprofloxacin. Poster presented at: The ARVO Annual Meeting; May 2002; Fort Lauderdale, FL.
4. Masket S. Preventing, diagnosing, and treating endophthalmitis. *J Cataract Refract Surg.* 1998;24:725-726.
5. Fisch A, Salvanet A, Prazuck T; The French Collaborative Study Group on Endophthalmitis. Epidemiology of infective endophthalmitis in France. *Lancet.* 1991;338:1373-1376.
6. Montan PG, Wejde G, Setterquist H, et al. Prophylactic intracameral cefuroxime. Evaluation of safety and kinetics in cataract surgery. *J Cataract Refract Surg.* 2002;28:982-987.
7. Bratzler DW, Houck PM, Surgical Infection Prevention Guidelines Writers Workgroup, et al. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. *Clin Infect Dis.* 2004;38:1706-1715.
8. Mah FS. Fourth-generation fluoroquinolones: new topical agents in the war on ocular bacterial infections. *Curr Opin Ophthalmol.* 2004;15:316-320.
9. Mah FS. New antibiotics for bacterial infections. *Ophthalmol Clin North Am.* 2003;16:11-27.
10. O'Brien TP. Emerging guidelines for use of NSAID therapy to optimized cataract surgery patient care. *Curr Med Res Opin.* 2005;21:1131-1137.
11. Lindstrom R, Kim T. Nepafenac: ocular permeation and inhibition of retinal inflammation: an examination of data and opinion of clinical utility. *Curr Med Res Opin.* 2006;22:397-404.
12. McColgin AZ, Heier JS. Control of intraocular inflammation associated with cataract surgery. *Curr Opin Ophthalmol.* 2000;11:3-6.