

Intracameral Vancomycin: Rationale and Experience

During routine cataract surgery, injecting vancomycin in the bag, underneath the IOL, appears to help safely and effectively prevent endophthalmitis following cataract surgery.

BY HOWARD V. GIMBEL, MD, MPH, FRCSC

The prevention of endophthalmitis has been the impetus for many innovations in cataract surgery.¹ Although used for more than a decade, intracameral vancomycin for the prophylaxis of postoperative endophthalmitis is challenged by the drug's limited spectrum of activity and pharmacodynamics. Fourth-generation fluoroquinolones may be more effective against both gram-positive and gram-negative bacteria, and their intracameral safety is now being established. This article describes the results my colleagues and I have obtained with the routine, in-the-bag injection of vancomycin for preventing endophthalmitis in 36,047 consecutive eyes over a 16-year period. We previously reported early data and established this strategy's safety regarding corneal toxicity.²

PERSONAL EXPERIENCE

James Gills, MD, of Tarpon Springs, Florida, began using vancomycin in irrigating solutions in 1987 (a practice we followed in 1988), and his incidence of endophthalmitis dropped from 0.2% to 0.01%.³

In 1990, we started using a therapeutic dose of vancomycin as a concentrated bolus (1 mg of vancomycin in 0.1 mL of balanced salt solution [BSS; Alcon Laboratories, Inc., Fort Worth, TX]) injected under the IOL and into the capsular bag at the end of the case rather than a more dilute solution continuously infused in the irrigating solution. My reasoning was that infection was most likely to start in the aqueous fluid that the IOL sequesters in the bag and that, if the drug were placed in that location, it



Figure 1. These graphs show the incidence of endophthalmitis at the Gimbel Eye Center prior to the administration of intracameral vancomycin as a bolus under the IOL.

would not wash out as quickly as it would from the anterior chamber.

I placed incisions on the steep meridian, so there was a mixture of superior scleral tunnel incisions under a limbus-based conjunctival flap and temporal clear corneal incisions. I sutured fewer than 0.5% of the incisions. I started patients on Maxidex or Tobradex (both from Alcon Laboratories, Inc.) drops q.i.d. 1 day preoperatively and had them continue the drops immediately after surgery.

RESULTS

With Garamycin (Schering-Plough Corporation, Kenilworth, NJ) in the irrigating solution (1985 to 1987), the year-to-year incidence of endophthalmitis at the Gimbel Eye

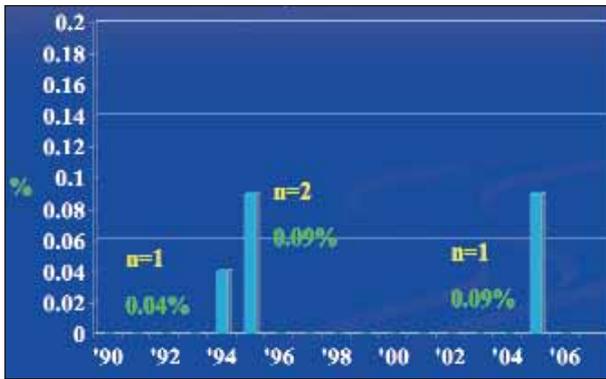


Figure 2. This graph shows the incidence of endophthalmitis (0.01%) in 36,047 consecutive eyes from 1990 to 2006 using intracameral vancomycin as a bolus under the IOL.

Centre in Calgary, Alberta, Canada, ranged from 0.02% to 0.15%. This rate remained relatively unchanged after we replaced vancomycin with Garamycin in the irrigating solution (1988 to 1989) (Figure 1).

In a series of 36,047 consecutive eyes from 1990 through 2006 in which we placed vancomycin as a bolus under the IOL, three eyes developed what was probably toxic endophthalmitis (Figure 2). These patients presented with anterior chamber fibrin but without pain on the first postoperative day. We managed the eyes aggressively with anterior vitrectomy through a posterior capsular capsulorhexis using the original cataract incision and an intravitreal injection of vancomycin 1 mg in 1 mL of BSS. All three eyes were culture negative and regained a BCVA of 20/20.

A fourth eye developed anterior segment inflammation and pain on the second postoperative day, although there was no hypopyon or fibrin. Conservative therapy achieved initial

improvement, but then the eye developed a fibrinous veil. It was not managed with the anterior vitrectomy approach like the other three cases. On day 7, the patient was referred to a retinal specialist who, on the eighth day, performed an anterior chamber tap and injected an antibiotic. Visual acuity improved to 20/40, but the recovery was unsatisfactory. Pars plana vitrectomy and antibiotic injection were therefore performed on the 10th postoperative day. The patient's visual acuity 8 weeks later was 20/25. Although cultures were all negative, this case was most likely a low-grade infectious endophthalmitis (Table 1).

Considering all four of these cases, although the first three presented as toxic endophthalmitis, the incidence in this series (at one center) is 4:36,047 or 0.011%.

DISCUSSION

Most anterior segment ophthalmologists use broad-spectrum antibiotics either subconjunctivally or intracamerally during surgery. Both in vivo and in vitro studies have shown intracameral vancomycin to be effective for endophthalmitis prophylaxis.⁴⁻⁸ A number of investigators have suggested that vancomycin used intracamerally can significantly reduce the risk of endophthalmitis.⁹⁻¹⁶ A survey conducted by the ASCRS showed that at least 35% of ophthalmic surgeons were using intracameral antibiotics.¹⁷ Of the surgeons surveyed, 80% used vancomycin, and more than 40% used gentamicin.

The AAO-CDC Task Force on Vancomycin Prophylaxis in Ophthalmic Surgery recommends the prudent use of vancomycin in routine cataract surgery because of the potential for resistance to the drug and the lack of evidence for its effectiveness in preventing postoperative endophthalmitis.¹⁸ Recent in vivo and in vitro studies, however, have shown that

TABLE 1. CASE SUMMARIES OF ENDOPTHALMITIS

Year	Incision	IOL/OVD	1 Day Postoperatively	Treatment	BCVA	Culture
1994	Scleral 5.5 mm	812A/Healon GV	4+ cell and flare Hypopyon cell and flare	Posterior continuous curvilinear capsulorhexis Anterior vitrectomy antibiotics	6 days 20/20	Negative
1995	Clear corneal 3.2 mm	SI30NB/Healon GV	4+ cell and flare Hypopyon 20/70	Posterior continuous curvilinear capsulorhexis Anterior vitrectomy antibiotics	5 weeks 20/20	Negative
1995	Clear corneal 3.2 mm	SI30NB/Healon GV	4+ cell and flare Hypopyon cell and flare	Posterior continuous curvilinear capsulorhexis Anterior vitrectomy antibiotics	7 weeks 20/20	Negative
2005	Clear corneal 3.2 mm	SA60AT/Healon 5	8 days postoperatively 4+ cell and flare Hypopyon cell and flare	Anterior chamber tap Pars plana vitrectomy antibiotics	8 weeks 20/25	Negative

Note: The 812A lens (Pfizer, Inc., New York, NY); Healon GV, Healon 5, and the SI30NB lens (Advanced Medical Optics, Inc., Santa Ana, CA); the SA60AT lens (Alcon Laboratories, Inc., Fort Worth, TX).



Figure 3. The surgeon injects vancomycin into the bag, under the IOL.

resistance to vancomycin is unlikely in cataract surgery and that the drug continues to be quite effective in inhibiting bacterial colony-forming units.⁹⁻¹²

To determine what constitutes a prudent use of vancomycin, one should consider the pharmacokinetics of the drug. Vancomycin is a time-dependent antibiotic and requires prolonged contact with microbes in the anterior chamber to be effective. When injected at 20 μm per 1 mL of BSS, the antibiotic has a half-life of approximately 2 hours.^{14,15} Because aqueous turnover occurs within 1 to 2 hours, vancomycin may be most effective if injected in the bag, under the IOL, with the optic's edge well covered by the anterior capsule (Figure 3). This method of injection should result in a sustained release of vancomycin at therapeutic levels—important because vancomycin is relatively slow at killing organisms and may require 8 to 12 hours to reduce the inocula.

The improvement in outcomes in the recent ESCRS study using cefuroxime as a bolus at the end of surgery seems to confirm that a bolus of antibiotic with even a slow kill rate placed in the anterior chamber (where aqueous turnover is shorter than the kill time of the antibiotic) effectively lowers the incidence of endophthalmitis after cataract surgery.¹⁹

The lower incidence in our series compared with the cefuroxime group in the European series (one per 10,000 compared to six per 10,000) may not be because of the difference in the antibiotic used. Rather, it may be related to a one-center series versus a multicenter study, differences in pre- and postoperative routines, variations in surgical technique (such as the capsulorhexis' diameter compared with the optic of the IOL), whether or not the viscoelastic was removed from under the IOL with the I/A tip placed under the IOL, whether the bolus of the drug was placed under the IOL into the capsular bag or just into the anterior chamber, and the possible additional confounding factor of environmental and host resistance.

Another factor to consider relates to our center's preoperative

protocol. Whether diabetic or not, we ask our patients to minimize or eliminate their intake of simple sugars for a few days before and after surgery. The Endophthalmitis Vitrectomy Study found that diabetics tend to have more virulent organisms, to have a higher percentage of gram-negative isolates, and to be culture negative less often.²⁰

Although newer broad-spectrum drugs will probably become more commonly used intracamerally than vancomycin, there is little motivation for us to change protocols or drugs when we have not lost an eye or had patients lose vision to less than 20/25 due to infectious or toxic endophthalmitis in 36,047 cataract surgeries. ■

Howard V. Gimbel, MD, MPH, FRCSC, is Professor and Chairman, Department of Ophthalmology, Loma Linda University, Loma Linda, California. He is also Medical Director and Senior Surgeon at the Gimbel Eye Center, Calgary, Alberta, Canada. He acknowledged no financial interest in the products or companies mentioned herein. Dr. Gimbel may be reached at (909) 558-2182 or (403) 202-3329; hvjgimbel@gimbel.com.



- Gills JP. Filters and antibiotics in irrigating solution for cataract surgery. *J Cataract Refract Surg.* 1991;17:385.
- Gimbel HV, Sun R, DeBroff BM. Prophylactic intracameral antibiotics during cataract surgery: the incidence of endophthalmitis and corneal endothelial cell loss. *Eur J Implant Refract Surg.* 1994;6:280-285.
- Gills JP. Pharmacodynamics of cataract surgery. In: Gills JP, ed. *Cataract Surgery: The State of the Art.* Thorofare, NJ: Slack, Inc.; 1998:19-26.
- Olson RJ. Reducing the risk of postoperative endophthalmitis. *Surv Ophthalmol.* 2004;49(suppl 2):55-61.
- Busbee BG. Advances in knowledge and treatment: an update on endophthalmitis. *Curr Opin Ophthalmol.* 2004;15:232-237.
- Mamalis N, Kearsley L, Brinton E. Postoperative endophthalmitis. *Curr Opin Ophthalmol.* 2002;15:14-16.
- Benz MS, Scott IU, Flynn HW, et al. Endophthalmitis isolates and antibiotic sensitivities: a 6-year review of culture proven cases. *Am J Ophthalmol.* 2004;137:38-42.
- Gordon YJ. Vancomycin prophylaxis and emerging resistance: are ophthalmologists the villains? The heroes? *Am J Ophthalmol.* 2001;131:371-376.
- Seppala H, Al-Juhaish M, Jarvinen H, et al. Effect of prophylactic antibiotics on antimicrobial resistance of viridans streptococci in the normal flora of cataract surgery patients. *J Cataract Refract Surg.* 2004;30:307-315.
- Ta CN, Chang RT, Singh K, et al. Antibiotic resistance patterns of ocular bacterial flora: a prospective study of patients undergoing anterior segment surgery. *Ophthalmology.* 2003;110:1946-1951.
- Libre PE, Della-Latta P, Chin NX. Intracameral antibiotic agents for endophthalmitis prophylaxis: a pharmacokinetic model. *J Cataract Refract Surg.* 2003;29:1791-1794.
- Sobaci G, Tuncer K, Tas A, et al. The effect of intraoperative antibiotics in irrigating solutions on aqueous humor contamination and endophthalmitis after phacoemulsification surgery. *Eur J Ophthalmol.* 2003;13:773-778.
- Das T, Sharma S, Muralidhar AV, Endophthalmitis Research Group. Effect of vancomycin on *Staphylococcus epidermidis* adherence to poly(methyl methacrylate) intraocular lenses. *J Cataract Refract Surg.* 2002;28:703-708.
- Souli M, Kopsinis G, Kavouklis E, et al. Vancomycin levels in human aqueous humour after intravenous and subconjunctival administration. *Int J Antimicrob Agents.* 2001;18:239-243.
- Mendivil Soto A, Mendivil MP. The effect of topical povidone-iodine, intraocular vancomycin, or both on aqueous humor cultures at the time of cataract surgery. *Am J Ophthalmol.* 2001;131:293-300.
- Tipperman R. Pharmacologic considerations for cataract surgery. *Curr Opin Ophthalmol.* 2004;15:51-55.
- Masket S. Preventing, diagnosing and treating endophthalmitis (guest editorial). *J Cataract Refract Surg.* 1998;24:725-726.
- The American Academy of Ophthalmology information statements page. The prophylactic use of vancomycin for intraocular surgery. A joint statement of the American Academy of Ophthalmology and the Centers for Disease Control and Prevention. Available at: <http://www.aaao.org/aaao/education/library/information/vancomycin.cfm>. Accessed January 14, 2005.
- Barry P, Seal DV, Gettlin G, et al. ESCRS study of prophylaxis of postoperative endophthalmitis after cataract surgery: preliminary report of principal results from a European multicentre study. *J Cataract Refract Surg.* 2006;32:3:407-410.
- Results of the Endophthalmitis Vitrectomy Study. A randomized trial of immediate vitrectomy and of intravenous antibiotics for the treatment of postoperative bacterial endophthalmitis. Endophthalmitis Vitrectomy Study Group. *Arch Ophthalmol.* 1995;113:1479-1496.