Intracameral Antibiotics in the Shadow of Hemorrhagic Occlusive Retinal Vasculitis
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This month’s issue of Ophthalmology, (see www.aaojournal.org/article/S0161-6420(16)31231-3/fulltext) highlights the rare but devastating complication of hemorrhagic occlusive retinal vasculitis (HORV) associated with the use of intracameral vancomycin for the prevention of acute postoperative endophthalmitis after cataract surgery (POE).1 The dramatic fundus images and poor visual outcomes are enough to give any surgeon pause. For surgeons hesitant about using intracameral antibiotics (ICAs), HORV may represent confirmation that ophthalmologists should avoid ICAs altogether. Concerns over the use of ICAs include a perceived lack of evidence supporting this method, a low baseline rate of endophthalmitis without ICAs, the safety of ICAs, and issues around optimal antibiotic stewardship.2

Nevertheless, the evidence in support of the efficacy and safety of ICAs is compelling. Numerous reports over the last 15 years confirm the findings from the seminal European Society of Cataract and Refractive Surgeons prospective trial,5 including studies from Sweden, Spain, Japan, the United Kingdom, France, Australia, Israel, Iran, India, South Africa, Singapore, Ireland, and the United States.6–22 Javitt23 offered an excellent summary showing that baseline POE rates generally fall between 0.10% and 0.30%, and that rate is reduced 2.5-fold to between 0.03% and 0.07% with the introduction of ICAs.23 Haripriya et al24 recently reported the results of another large study from the Aravind hospital system of more than 600 000 eyes that showed a 3.5-fold reduction in baseline POE rates generally fall between 0.10% and 0.30%, and that rate is reduced 2.5-fold to between 0.03% and 0.07% with the introduction of ICAs.23

Is the risk of injecting an antibiotic into every eye undergoing cataract surgery worth the reduction in the risk of POE? If vancomycin were the only ICA available, the description of HORV by Witkin et al1 would make anyone hesitant to consider its regular use, although HORV seems to be an extremely rare condition. As reported in the American Society of Cataract & Refractive Surgery (ASCRS) surveys of POE prophylaxis, many surgeons have used intracameral vancomycin routinely.22,32 In Kaiser Permanente Colorado, a closed network with excellent patient follow-up, 45 000 cases were performed with vancomycin in the irrigation bottle with incision hydration, and there were no reported cases of HORV.34 Others have reported the safe use of intracameral vancomycin in almost 25 000 eyes.11,14 It is possible that cases of HORV were either misdiagnosed or not recognized in prior studies of intracameral vancomycin, perhaps in part because HORV is so uncommon. Nonetheless, after the creation of a joint task force with member solicitation of large cataract and retina societies, Witkin et al1 report HORV in 36 eyes of 23 patients worldwide spanning an 11-year period. By contrast, it has been estimated that the expanded use of ICAs could prevent 2000 cases of POE annually in the United States alone.23 Although HORV is likely extremely rare compared with POE, the uniformly poor outcome and bilateral risks reported with vancomycin-associated HORV should point surgeons toward intracameral alternatives such as cefuroxime or moxifloxacin, whose efficacy and safety have been broadly reported.

Safety is always a primary concern, and there are risks of injecting any medication into the eye, including anaphylactic reactions. Two cases of anaphylaxis have been reported in the literature that were associated with intracameral antibiotic injection, cefuroxime in both cases.33,35 But it should be noted that even topical antibiotics, including fourth-generation fluoroquinolones, are not immune to the risks of anaphylaxis.37 Toxicity to the
cornea or retina, both transient and permanent, also has been reported after intracameral injection of compounded drugs. Although injectable manufactured products are commercially available in some countries, there is no such Food and Drug Administration-approved drug available in the United States as of the writing of this editorial. The closest alternatives to commercially manufactured products are compounded agents obtained from a Food and Drug Administration-registered outsourcing facility. These pharmacies must follow section 503B of the Drug Quality and Security Act and conform with current good manufacturing practices. Results of Food and Drug Administration inspections are available on the government website. Drugs may be purchased in bulk, without an individual prescription, in those states that allow it.

The cost effectiveness of ICAs has been studied. Because labor costs and drug prices vary across nations, the cost of ICAs will also vary. In the United States, the costs of compounded ICAs appear reasonable compared with the costs of popular topical fourth-generation fluoroquinolones, with one pharmacy providing intracameral moxifloxacin for $33/vial, whereas the average United States sale price for branded topical moxifloxacin is $170/bottle. In fact, ICAs result in cost savings since there are significant expenses associated with treating POE cases, which are prevented with effective prophylaxis associated with ICAs. Although some have switched from expensive branded topical antibiotics to generic topical options after the introduction of ICAs, others have reported outstanding clinical outcomes without the use of topical antibiotics.

Some also have questioned whether “intracameral antibiotic use is contrary to the basic tenet of antibiotic stewardship,” with the potential development of resistant organisms. Ironically, concerns over resistant organisms and antibiotic stewardship are more appropriately directed toward the common practice of prescribing topical antibiotics for infection prophylaxis. Intracameral antibiotics involve a 1-time, highly concentrated dose of antibiotics injected into a physiologically isolated space. By contrast, topical antibiotic use involves the repeated and sometimes sporadic installation of antibiotic onto a bacteria-rich ocular surface, with systemic communication via the nasolacrimal drainage system, given over several days. As one might expect based on concepts of microbial exposure, topical antibiotic therapy has been shown to induce resistant bacteria, whereas there is no evidence ICAs have a similar effect. Perhaps most importantly, ICAs actually have been shown to be effective in preventing POE, whereas the widespread use of topical antibiotics for preventing POE has little supporting evidence.

In summary, the evidence in favor of intracameral antibiotic injection for the prophylaxis of endophthalmitis outweighs that for topical application. As to which antibiotic to choose, the recent report by Witkin et al should prompt a re-evaluation of the role of vancomycin in routine endophthalmitis prophylaxis. The choice between the remaining most popular current options, cefuroxime and moxifloxacin, may depend on the historical infection profile of the surgery center and sourcing capabilities.

References

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