Why Use Intracameral Gatifloxacin?

A potential agent for antimicrobial prophylaxis in cataract surgery.

BY BRIAN C. K. AU, MD, AND ROBERT W. SNYDER, MD, PHD

Various sources report a recent increase in the incidence of infectious endophthalmitis following clear corneal cataract surgery.[1-3] These reports have renewed interest and investigation into more effective methods of preventing postoperative endophthalmitis. Our preference is intracameral gatifloxacin.

THE CASE FOR INTRACAMERAL ANTIBIOTICS

One option for combating endophthalmitis may be intracameral antibiotics. The ESCRS Endophthalmitis Study Group recently advocated intracameral cefuroxime as a means of reducing the incidence of endophthalmitis after cataract extraction.[4,5] The group's results may serve as a "proof of concept" for the utility of prophylactic intracameral antibiotics. Because the incidence of endophthalmitis in the ESCRS study's intracameral group (0.292%) was considerably higher than has been reported with the use of fourth-generation topical fluoroquinolones in the US (0.07%),[6] however, further study is needed before advocating the routine use of intracameral antibiotics.

In addition to cefuroxime, vancomycin has been studied for intracameral use. Because bacteria continually develop resistance to antibiotics, we believe that ongoing research is needed to identify the most effective antibiotics to stay ahead of this evolutionary process. The selected antibiotics should be (1) safe for intraocular administration, (2) broad spectrum, and (3) bactericidal, dose-dependent killing agents with fast kill curves.

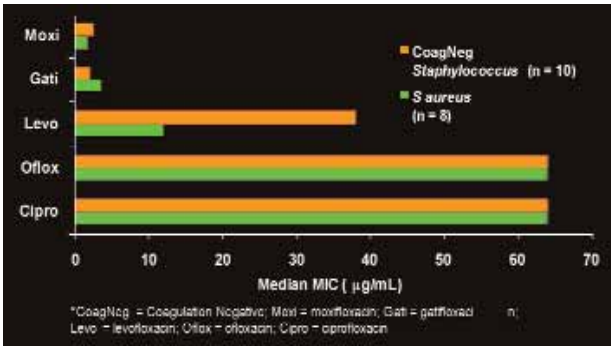

Figure 1. Fourth-generation fluoroquinolones are far more effective than third-generation agents. The isolates from bacterial endophthalmitis resistant to various agents are indicated. (Data adapted from Mather R et al.[8])

WHY FOURTH-GENERATION FLUOROQUINOLONES ARE SUPERIOR

Fourth-generation fluoroquinolones have rapid, concentration-dependent bacteriocidal action, steep kill curves, high aqueous solubility, and a broad spectrum of action against both gram-positive and gram-negative species. The agents gatifloxacin and moxifloxacin have demonstrated superior susceptibility profiles against ocular flora compared with levofloxacin (a third-generation fluoroquinolone) as well as ciprofloxacin and ofloxacin (second-generation fluoroquinolones)[7,8] (Figure 1).

We recently conducted two studies in order to determine if gatifloxacin could safely be used for intracameral prophylaxis.

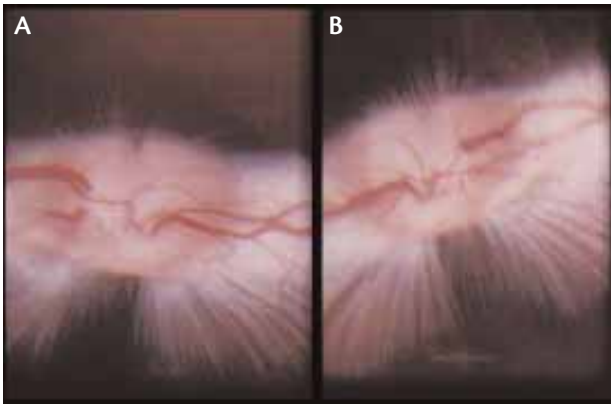

Figure 2. Retinal photographs show the right (A) and left (B) optic nerves of a rabbit 29 days after treatment with intracameral gatifloxacin.

SAFETY OF INTRACAMERAL GATIFLOXACIN

Our intraocular toxicity studies in rabbits found intracameral gatifloxacin, up to a concentration of 320 µg/mL, to be nontoxic to the retina and the anterior segment.[9] We monitored toxicity by slit-lamp examination, IOP, and ultrasonic pachymetry on postoperative days 1, 3, and 28, followed by histologic examination. We also tested for intravitreal toxicity by injecting up to 160 µg of gatifloxacin. We monitored retinal toxicity by fundus photography, electroretinogram (ERG), and visually evoked potential on postoperative days 1 and 28, followed by histologic studies of the retina. Our results revealed no significant changes in IOP or pachymetry in any eyes up to the 28th postoperative day. Moreover, we saw no abnormalities in the fundus/optic nerve photographs (Figure 2), ERG, visually evoked potential, or histologic studies of all eyes in both the intracameral and intravitreal subgroups. Kazi et al[10] also found that intravitreal gatifloxacin of up to 400 µg was nontoxic and well tolerated in rabbit eyes, based on pre- and postinjection ERG changes recorded up to postoperative day 14.

Along with Eric Donnenfeld, MD, and colleagues, we conducted a small study of the safety of intracameral gatifloxacin in 40 human subjects undergoing unilateral cataract extraction. We found no evidence of intraocular toxicity with a 100 µg/0.1 mL dose.[11] We evaluated patients' BCVA, IOP, corneal clarity, dilated fundus examination, and ultrasonic pachymetry at 1 day, 1 week, 1 month, and 3 months postoperatively. Patients' mean preoperative BCVAs improved from 20/74 to 20/24 postoperatively at 1 week and to 20/22 at both 1 and 3 months. Seven of 40 patients had as high as grade 2 corneal edema on the first postoperative day, but all patients had clear corneas on subsequent examinations. A mean increase in IOP of 6 mm Hg on the first postoperative day ($P<.001$) had normalized on subsequent examinations. We found no significant changes in ultrasonic pachymetry or retinal pathology in any patients, and none developed endophthalmitis. Intracameral gatifloxacin therefore appears to be safe and well tolerated at a concentration of 100 µg/0.1 mL at the conclusion of cataract surgery.

Since we conducted these preliminary studies, intravenous gatifloxacin (Tequin; Bristol-Myers Squibb Company, Princeton, NJ) is no longer marketed in the US. If an unpreserved gatifloxacin becomes available in the future, these studies could be the basis of further research.

CONCLUSION

We believe that our studies provide preliminary evidence to warrant a larger clinical trial to verify the safety of intracameral gatifloxacin. Future trials should aim at establishing the safety of broad-spectrum, fast-killing intracameral antibiotics that stay ahead of microbial resistance.

Currently, of course, the prophylactic use of intracameral fluoroquinolones in cataract surgery is considered off label and, as such, should be driven by the judgment of the individual physician and by evidence-based literature. ■

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