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Intracameral moxifloxacin for endophthalmitis prophylaxis?

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in Berlin

INTRACAMERAL injection of the fourth-generation fluoroquinolone moxifloxacin (Vigamox®, Alcon) at the end of cataract procedures provides a safe and effective prophylaxis against endophthalmitis, according to a series of presentations at the XXVI Congress of the ESCRS.

Steve A Arshinoff MD FRCSC said that he has been routinely using intracameral moxifloxacin since 2004, and during that time, he has had no cases of endophthalmitis in over 3,000 cataract procedures.

He noted that although the ESCRS Endophthalmitis study has established that intracameral injection of the antibiotic cefuroxime at the end of cataract procedures can reduce the rate of postoperative endophthalmitis by 80 per cent, the study did not establish whether cefuroxime was the best agent to use.

Oliver Schein (Wilmer Institute Baltimore, MD) stated (Ophthalmology Times 15 06 08) "The ideal agent for intracameral antibiotics would have bactericidal activity and provide adequate ocular concentrations at the close of surgery and for 24 to 48 hours postoperatively. Cefuroxime, and other current drugs, do not do that," said Dr Arshinoff, University of Toronto, Toronto, Ontario, Canada. However, cefuroxime works on a time-dependent mechanism, so its duration of activity is important.

He added that the fourth-generation fluoroquinolones moxifloxacin might represent a better choice. The agent has several theoretical advantages over cefuroxime, including a longer half-life, concentration dependent activity, making it less dependent upon duration of activity, and a broader spectrum of cidal efficacy, he noted. It is also well tolerated in the eye.

Unlike cefuroxime, fourth-generation fluoroquinolones are effective against MRSA and Gram-positive enterococci and have only encountered resistance with some ciprofloxacin-resistant species of pseudomonas. In addition, studies have shown that cefuroxime at its concentration at 45 minutes after intracameral injection achieves less than one log unit kill of fluoroquinolone sensitive staphylococcus. By comparison, moxifloxacin will achieve more than a three log unit kill of resistant staphylococci at its concentration at 75 minutes post intracameral injection.

Moxifloxacin is also easier to prepare for intracameral use than cefuroxime, because it doesn't require the use of a millipore filter and the process of dilution is much simpler. Dr Arshinoff noted that to prepare the antibiotic for intracameral injection he first draws 2.0ml of moxifloxacin eye drop solution from a bottle of topical Vigamox, and then 8.0ml of BSS into a 10cc syringe. He then rotates the syringe in his hand until the solution is thoroughly mixed. He or his circulating nurse then place 0.5 cc of the solution into medicine cups, on e for each case.

When injecting the solution into the eye, after assuring that the main incision is sealed and the eye pressurised, he inserts a syringe containing 0.3ml of the antibiotic preparation into a side port incision and places the tip of the needle under the distal edge of the capsulorhexis. To prevent any of the solution from being expelled as he withdraws the needle, he injects a small amount of remaining antibiotic just as the needle's tip comes out through the incision.

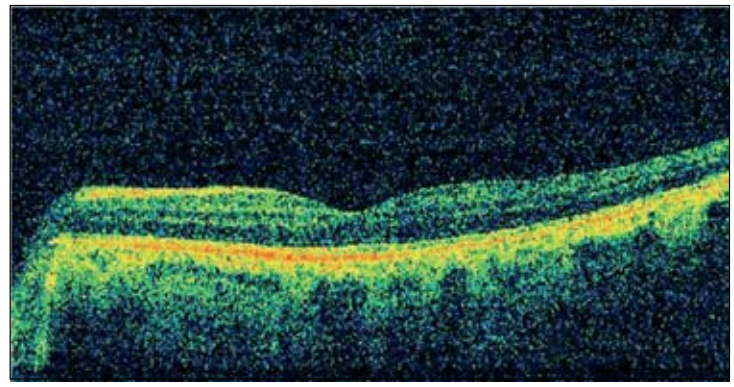
Dr Arshinoff noted that studies have shown that intracameral moxifloxacin is gentle to endothelial cells (Espiritu et al, JCRS, 2007; 33:63-68) and that its use results in low endothelial cell loss postoperatively and has no detrimental effect on macular thickness as measured by OCT (Brothers Arbisser et al, JCRS, 2008; 34:1114-1120).

He also pointed out that he has not seen any fibrin on the first postoperative day in the eyes of any of his cataract patients in whom he has injected moxifloxacin intracamerally at the end of the cataract procedures. He added that he has become convinced that, except in cases of TASS, the presence of fibrin in the anterior chamber in the first few days postoperatively generally indicates a subclinical infection rather than simply an inflammatory response to surgery.

In another study, 120 consecutive patients underwent intracameral injection of 0.1ml of moxifloxacin in the anterior chamber at the end of uncomplicated phacoemulsification and had completed three months of follow-up, reported Rakesh Bansal MD, Department of Ophthalmology, Government Medical College and Hospital, Chandigarh, India.

As in previous studies, moxifloxacin was well tolerated within the eye, Dr Bansal noted. The mean preoperative and postoperative endothelial cell counts were 2495cells/cc^2 and 2156 cells /cc^2, respectively, amounting to a mean cell loss of 13.5 per cent, he added. Furthermore, OCT showed no changes in macular thickness. Mild corneal oedema occurred in six patients, but cleared up within the first postoperative week. Moreover, none of the patients developed any sign of endophthalmitis.

Dr Bansal noted that there are other factors that are important in preventing postoperative endophthalmitis. They include a watertight wound architecture, and good hydration of the wound at the end of surgery. However, use of intracameral moxifloxacin and a drop of five per cent betadine before surgery is key in preventing the complication, he maintained. So far more than 500 eyes have been injected with intracameral moxifloxacin and none has developed endophthalmitis.



Courtesy of Purendra Bhasin MD

Post-op OCT

"With the use of antibiotics before and after surgery and intracamerally at the conclusion of surgery we can eliminate postoperative endophthalmitis. Fourth-generation fluoroquinolones have a broader spectrum of activity than cefuroxime so they are the drug of choice these days," he added.

The findings of another study supported Dr Bansal's findings. The prospective study involved 55 eyes of 55 cataract patients with no other ocular pathology who underwent intracameral injection of 0.1ml of 0.5 per cent moxifloxacin at the conclusion of phacoemulsification surgery, said Purendra Bhasin MD, Ratan Jyoti Netralaya, Ophthalmic Institute & Research Centre, Gwalior, India. "In our series of patients, intracameral injection of 0.1ml of 0.5 per cent moxifloxacin (Vigamox, Alcon) was found to be safe in terms of visual rehabilitation, the corneal endothelium, anterior chamber reaction, macular oedema and IOP," he said.

None of the patients in the study developed endophthalmitis in the six-month follow-up period. The BCVA at one month postoperatively was 20/30 or better in all eyes and remained stable throughout follow-up. In addition, mean endothelial cell counts fell by only two per cent, from a preoperative count of 2227cells/mm^2 to 2191/mm^2 at one month. Furthermore, aqueous activity on the first postoperative day was similar to that seen in most series of cataract patients, and was grade 1 in 30 eyes, grade 2 in 24 eyes, and grade 3 in one eye. In addition, OCT examinations on day one and day seven after surgery detected no signs of macular oedema.

The mean IOP was 16.0 mmHg preoperatively, 19.0 mmHg at day one, 17.0 mmHg at day seven, and 15.0 mmHg at one month postoperatively, Dr Bhasin said. In seven cases with grade IV hard brown cataracts there was stromal oedema at day one, which disappeared at day seven in all cases, he added. Moxifloxacin 0.5 per cent is taken directly from the vial into a 5ml syringe and then 0.1ml transferred into a tuberculin syringe which is then injected intracamerally by 25G Cannula under capsulorhexis margin. This avoids the steps of reconstitution and dilution of the drug which is necessary when cefuroxime or vancomycin is used. No case of endophthalmitis is recorded in more than 2000 phaco cases done until now in our hospital.

Moxifloxacin was used for endophthalmitis prophylaxis because it is preservative free, self preserved. Its osmolality of 290 mOsm/kg and ph 6.8 is compatible to the human aqueous. It has broad spectrum and its levels in aqueous exceeding MICs (Mean Inhibitory Concentration) for relevant species persists for minimum five hours and MPC, (Mutant Prevention Concentration) which is 8-10 times of MIC is maintained for three hours after surgery. This is important because it is observed that through clear corneal hydrated phaco incision there is influx of fluid into the aqueous in the early postoperative period. Therefore, presence of broad spectrum antibiotic maintained in right concentration in the aqueous in early postoperative period will decrease the incidence of endophthalmitis.

Peter Barry FRCS, Dublin, Ireland noted that the spectre of resistance is casting a shadow over the future of fourth-generation fluoroquinolones as a prophylaxis against endophthalmitis. The agents are now entering the food chain due to their use in animal husbandry, which may in turn lead to the generation of resistant strains of pathogenic bacteria.

Dr Arshinoff concurred with Dr Barry and said that the overuse of systemic administration of the agents in the human population is another cause for concern.

"Agriculture is a big problem for the potential induction of bacterial antibiotic resistance with all the antibiotics that we use. The other big culprit is the chronic use of Vancomycin orally in cases of clostridium difficile, often for years, increasing the likelihood of developing resistant strains," he added.

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