Fourth generation fluoroquinolone proposed for endophthalmitis prophylaxis

Peter Barry

THE results of the ESCRS Endophthalmitis study have left little doubt that intracameral antibiotics are currently the most effective means of preventing the intraocular infections following cataract surgery. However, there remains considerable debate about which antibiotic should be used.

“That study did not show us which antibiotic was the best because they only used one antibiotic,” noted Steve Arshinoff MD, University of Toronto, Toronto, Canada and McMaster University, Hamilton, Ontario, Canada.

Fourth-generation fluoroquinolones have shown comparable results with other agents, including vancomycin, cefazolin, and the fourth generation fluoroquinolone, moxifloxacin (Alcon). He added that while there is not yet a large mass of a clinical evidence base for moxifloxacin’s superiority to cefuroxime, research has shown that it has a longer half-life, a broader spectrum of activity and is as well tolerated as the older agent. It is also easier to prepare for intracameral use, he pointed out.

He noted that the efficacy of glycopeptides, such as vancomycin, and cephalosporins, like cefazolin and cefuroxime, is time-dependent because their aqueous concentrations decrease to a fourth of their initial values within one hour. In contrast, the efficacy of fluoroquinolones is concentration-dependent, so the agents are more effective.

In addition, studies have shown that the maximum intracameral dose achievable with cefuroxime will result in less than a one log unit kill of beta-lactam-sensitive Staphylococcus aureus over three hours. By comparison, the achieved intracameral dose of moxifloxacin will achieve more than a three log unit kill of fluoroquinolone-resistant Staphylococcus aureus over the same time period.

Broader spectrum

As regards spectrum of activity, even vancomycin has a five per cent resistance rate and cefuroxime is ineffective against a broad range of pathogens including MRSA and enterococci. Fourth-generation fluoroquinolones, meanwhile, are effective against all of those organisms and have one agent has been proven effective.

Moxifloxacin is also easier to prepare for intracameral use than glycopeptide and cephalosporin antibiotics because it doesn’t require the use of 0.22 Millipore filter and the process of dilution is much simpler. Furthermore, its faint yellow colour makes it easy to identify in a surgical scenario.

Dr Arshinoff noted that he has used the agent in over 2,000 cataract procedures and has had no cases of endophthalmitis. He added that moxifloxacin is also inexpensive. One bottle of Vigamox® provides enough moxifloxacin for 40 cases.

Safety demonstrated in trial

In a related presentation, Samuel Masket MD described the results of a study that demonstrated the high safety profile of moxifloxacin. In the randomised placebo-control clinical trial, the antibiotic appeared in some respects to be less toxic than BSS.

The study involved 59 eyes of cataract patients older than 18 years with no other ocular pathology. They were randomised to receive an intracameral injection of either 50 µL of undiluted moxifloxacin 0.5 per cent or 50 µL of BSS during the final step of the surgery, explained Dr Masket, UCLA, Los Angeles, California US.

During three months of follow-up there was no difference between the two groups in terms of visual acuity, endothelial cell count, or corneal thickness. However, mean IOP in the moxifloxacin group was significantly lower compared to the BSS group (p=0.02). In addition, a trace of corneal oedema was evident in only one eye receiving moxifloxacin and no eyes receiving BSS. Furthermore, no eyes in either group had aqueous flare and none had more than trace evidence of aqueous cells.

Masket said that adding intracameral moxifloxacin 0.5 per cent to topical post-operative therapy might further reduce the risk of endophthalmitis following cataract surgery. However, he acknowledged that an efficacy study similar to the ESCRS investigation would be necessary to determine prophylactic value of intraocular moxifloxacin.

“There is no increased safety risk associated with the use of intracameral moxifloxacin 0.5 per cent compared to BSS within three months following cataract surgery. Intracameral moxifloxacin 0.5 per cent appears safe for use during cataract surgery for the prophylaxis of endophthalmitis,” he added.

Efficacy remains unproven

In the discussion that concluded the session, some attendees expressed concern that the widespread use of intracameral antibiotics in cataract surgery would lead to the emergence of resistant strains. Dr Arshinoff maintained that the risk of that occurring was practically nonexistent.

“If you give this to every person in the world during cataract surgery you might get one resistant strain induction. The risk is extremely low. Even the Centre for Disease Control now accepts that risk of inducing resistant strains with these antibiotics for eye surgery is close to zero,” he said.

Peter Barry MD, the lead investigator of the ESCRS study, asked why surgeons should be using antibiotics for which the efficacy has not been proven in human eyes when there is already an antibiotic available whose efficacy is established.

Dr Masket responded by pointing out that cefuroxime has to be prepared for intraocular use by surgeons and their assistants, raising the risk of TASS and dosage errors. Dr Barry replied that this is also true of moxifloxacin.

“One of the problems with acceptance of intracameral cefuroxime is that it doesn’t come prepared for that use. We at the ASCRS have approached the FDA hoping that they will allow the production of pre-mixed solutions of cefuroxime but there’s no chance unless we repeat the studies,” Dr Masket said.

Dr Arshinoff added that however good a prophylactic therapy is, it is always possible to do better and research should not stop just because one agent has been proven effective.

“The main thing I can do is give intracameral antibiotics, whether it is cefuroxime or moxifloxacin probably doesn’t make a great deal of difference because the rates of infection will be very low. In the same way, if it is shown that giving antibiotic eye drops is just as good, then I’ll do that. I just want to achieve a good result,” he said.

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