Pre-soaked IOLs make for an efficient drug delivery system

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in Heidelberg

PRE-SOAKING intraocular lenses in an antibiotic could be a better way to provide endophthalmitis prophylaxis, said Guy Kleinmann MD at the 22nd Congress of the German-speaking Society for Intraocular Lens Implantation, Interventional and Refractive Surgery (DGI).

“Topical fourth-generation fluoroquinolones do not succeed in reaching the minimum inhibitory concentration required to inhibit the growth of 90 per cent of microorganisms (MIC90) for S. epidermidis in the anterior chamber for more than a few minutes after application, studies show. The problem is that we are using protocols that are not efficient. Soaking IOls for 24 hours prior to implantation resulted in high antibiotic concentration levels for 12 hours after surgery,” Dr Kleinmann said.

He began with a pilot study in rabbits in which he pre-soaked the hydrophilic acrylic C Flex IOL (Rayner) for 24 hours in gatifloxacin (Zymar, Allergan) or moxifloxacin (Alcon, Vigamox), both fourth-generation fluoroquinolone antibiotic agents that are frequently used after ophthalmic surgery. After IOL implantation, Dr Kleinmann measured the antibiotic concentration in the anterior chamber two, four, and six hours after implantation. There was no other source of antibiotic used during or after cataract surgery.

The pilot investigation revealed that the antibiotic concentration in the anterior chamber was well above the level required to kill off S. epidermidis (2.0 mcg/ml), for six hours following implantation. In larger rabbits’ study, Dr Kleinmann compared the antibiotic concentration in the anterior chambers of eyes that received 24-hour pre-soaked IOL implanta tions with another set of rabbits that received regular unsoaked IOls and antibiotic drops according to a very strict postoperative drop protocol, given every two hours. Group one IOls were soaked with gatifloxacin, group two with moxifloxacin, group three eyes received a regular IOl with postoperative gatifloxacin drops, and group four received regular IOls followed by moxifloxacin drops.

At four, eight, and 12 hours postoperatively, eyes that received antibiotic drops were below the MIC90 level, in spite of being redropped every two hours. By sharp contrast, the soaked IOls, in particular those soaked with gatifloxacin, showed very high concentrations of antibiotic, lasting well up to 12 hours postoperatively. Results form similar studies on topical drops corroborate those obtained in this study, Dr Kleinmann noted.

No toxicity observed with antibiotic-soaked IOls

He observed no clinical signs of toxicity after 24 hours in the pre-soaked or repeat drop groups. To further assess safety for the IOls, however, Dr Kleinmann conducted a trial in which he placed four IOls in the two different solutions (two in gatifloxacin, two in moxifloxacin) for a duration of five weeks.

The gatifloxacin IOls were clear, and scanning electron microscopy revealed no damage. The IOls soaked in moxifloxacin, a yellow solution, appeared yellow after five weeks soaking, however. They began to clear after 10–14 days of soaking in BSS solution.

In a further in-vitro study, Dr Kleinmann addressed the soaking time, pre-soaking C-flex lenses for one week, 24 hours, and 10 minutes, in either gatifloxacin or moxifloxacin.

Dr Kleinmann noted that lenses soaked for one week released a mildly increased amount of antibiotic into the anterior chamber, compared to the 24-hour tested gold standard. He noted a longer release time for moxifloxacin. Ten-minute soaking achieved around one third of the amount of antibiotic released compared to the 24-hour concentration.

In a final set of three subgroups, the investigator implanted IOls soaked for 15 minutes with moxifloxacin in one group, IOls soaked for 15 minutes with gatifloxacin in the second, and used intracameral injections of gatifloxacin (100mg/0.1ml) in the third group of rabbit eyes using un-soaked lenses.

The intracameral injection group showed a high antibiotic concentration peak two hours after surgery. This concentration fell rapidly but remained above 2 mcg/ml. The 15-minute-soaked IOls showed somewhat higher concentrations of antibiotic than the eyes that received drops from his previous study. The results, overall, were not as good as expected, he maintained.

Most cases of postoperative endophthalmitis are being attributed to the external surface flora, inoculation of bacteria during surgery and during the first hours after the surgery while the surgical wound lack of stability and bacterial IOl adhesion considered the main means of bacterial entry into the eye. Preventive antibiotic treatment, although not proven directly to be effective until recently, is very popular, he said.

The ophthalmic literature supports the notion that bacterial resistance to fluoroquinolones is directly related to the under- or incomplete treatment with oral antibiotics. This can easily account for the significant increase in resistance to ciprofloxacin encountered in 37 per cent as shown in Recchia FM et al paper (Arch Ophthalmol 2005; 123:341-6).

Topical protocols of the fourth-generation fluoroquinolones did not succeed in reaching the MIC90 for S. epidermidis in the anterior chamber for more than a few minutes after the application. In fact many different studies showed that fluoroquinolones applied topically stay effective for 5-10 minutes after application, dropping well below the MIC90 level by one hour.

Dr Kleinmann is planning a trial that combines intracameral injections of antibiotic with pre-soaked IOls, to evaluate any change in antibiotic release over time.

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