Intracameral Cefuroxime: Where Are We in 2013?

This method is gaining acceptance around the world as the best prophylaxis against endophthalmitis after cataract surgery.

BY PETER BARRY, FRCS

Let me begin by stating that, in my opinion, intracameral cefuroxime is mandatory for every cataract operation. To me, the reluctance worldwide to adopting intracameral cefuroxime for endophthalmitis prophylaxis after cataract surgery stems from the commercial unavailability of a single, sterile, FDA-approved unit dose for cataract surgery. The lack of an approved product raises genuine concerns among potential users regarding the possibility of errors in dilution, contamination, toxic anterior segment syndrome, and anaphylaxis in patients with a history of penicillin allergy. The weight of evidence supporting the practice, however, is growing.

ADDRESSING THE CONCERNS

Contamination

A report from Turkey described an outbreak of eight cases of *Fusarium* endophthalmitis, all occurring in patients who underwent surgery on a particular day in a specific OR and who received intracameral cefuroxime made up in that OR using a "kitchen pharmacy" and multidosing.[1] One would have to perform a lot of cataract operations without intracameral cefuroxime to cause eight cases of *Fusarium* endophthalmitis, all of which led to severe and permanent visual loss.

Error in Dilution

A report from Finland makes for frightening reading.[2] The standard practice was to use prophylactic, infusional vancomycin, but on this particular day, supplies had run out. The surgeons therefore sent a fax to the manufacturer of cefuroxime requesting instructions on its dilution for cataract surgery. The company, GlaxoSmithKline, obliged with a 3-page fax, but unfortunately, only 2 pages arrived. As a result, 16 patients, including one undergoing bilateral surgery, received 50 to 100 mg of intracameral cefuroxime (ie, 50-100 times the recommended dose). Eight of the 16 eyes suffered severe and permanent visual loss.

> "Cephalosporins can be safely prescribed for penicillin-allergic patients."

Penicillin, Cephalosporin Allergy

I find this concern to be overstated. Although the prevalence of penicillin allergy is estimated at 1% to 10%, a reported penicillin allergy is rarely a true allergy. On the other hand, there is a single case report of anaphylaxis attributed to intracameral cefuroxime from Spain.[3] The patient survived, but concerns were raised. Preoperative skin testing may be desirable but is simply impractical in most cataract surgical facilities. Withholding intracameral cefuroxime for fear of allergy, however, increases the risk of endophthalmitis by a factor of seven.[4]

Cephalosporins can be safely prescribed for penicillin-allergic patients. These drugs can essentially be divided into two groups. The first shares a common molecular side chain with penicillin (eg, cefazolin), which confers

TABLE. WHAT IS THE RATE OF ENDOPHTHALMITIS?			
Study	**No. of Patients**	**Rate With Intracameral Cefuroxime**	**Rate Without Intracameral Cefuroxime**
ESCRS study[6]	16,000	0.05%	0.35%
Swedish study[7]	225,000	0.048%	0.35%

an increased risk of allergic reaction among patients with a penicillin allergy. The second group, however, including cefuroxime and ceftazidime, does not share this molecular structure and thus does not increase the risk of allergic reaction.[5]

THE TRUE RATE OF ENDOPHTHALMITIS

A study by the European Society of Cataract & Refractive Surgeons (ESCRS) showed a rate of endophthalmitis of 0.35% in the control group, which was randomly allocated to no perioperative antibiotic and only received povidone-iodine prophylaxis.[6] This rate decreased to 0.05% in the study patients who were randomly assigned to receive intracameral cefuroxime at the end of the surgery. The background rate of 0.35% was heavily criticized, particularly in the United States, as extraordinarily high. If, however, one looks at the consecutive 225,000 patients from the published Swedish cataract registry, where the use of intracameral cefuroxime is routine, the rate of endophthalmitis with intracameral cefuroxime is almost precisely the same as the intracameral rate in the ESCRS study, 0.048%.[7]

Furthermore, if one extrapolates from the Swedish study those patients not receiving intracameral cefuroxime for whatever reason—most commonly a fear of allergy—the rate of endophthalmitis increases to 0.35%, which is precisely the same as in the ESCRS study's control group. I consider this background rate of 0.35% to be the reality (Table).

After the publication of the ESCRS study's results, the administration at the University Hospital in Madrid, Spain, introduced a blanket policy of intracameral antibiotics in 2005.[8] The rate of endophthalmitis from 1999 to 2005, in the era before intracameral cefuroxime, from a total of 6,595 patients was 0.59%. In the 3 years following the universal adoption of intracameral cefuroxime (2005-2008), the rate dropped to 0.043% in a total of 7,057 patients, a greater than tenfold reduction in endophthalmitis.

In a similar study from France of 5,115 patients, all undergoing uncomplicated surgery, the rate of endophthalmitis before the introduction of intracameral cefuroxime was 1.238% in 2,826 patients between April 2003 and May 2006.[9] After the intracameral injection of cefuroxime became routine (June 2006 to June 2008), the rate dropped to one incident in 2,289 patients (ie, 0.044%), a dramatic reduction.

A large retrospective review of an Asian population over an 11-year period showed similar results.[10] Researchers analyzed 50,177 patients undergoing phacoemulsification and extracapsular cataract surgery. The antibiotic they used was cefazolin. Prior to instituting intracameral cefazolin, 19 of 29,539 patients developed endophthalmitis, a rate of 0.064%. After the use of intracameral cefazolin became standard, there were two cases of endophthalmitis in 20,628 patients, a rate of 0.01%. All patients also received subconjunctival gentamycin and dexamethasone; in addition, the non-intracameral group received subconjunctival cefazolin.

THE AMERICAN CONVERSION

For the first time, supporting evidence is available from the United States that the systematic intracameral injection of an antibiotic at the end of cataract surgery is associated with a lower rate of endophthalmitis.[11] At a large surgery center in Northern California, the rate of endophthalmitis in 2007 was 0.32%, similar to that of the control group in the ESCRS study. The center began to use intracameral cefuroxime routinely in 2007 unless there was anxiety about penicillin/cephalosporin allergy or posterior capsular rupture. From 2010 to 2011, all patients received intracameral antibiotics, including those with penicillin/cephalosporin allergy and especially those with a posterior capsular rupture.

The rate of endophthalmitis fell by a factor of 22 over a 5-year period of the study and appeared to be independent of the postoperative use of topical antibiotic drops. Nineteen cases of endophthalmitis occurred in 16,264 cataract procedures. The bacteriology and visual outcomes are strikingly similar to those in the ESCRS study. Eight of the 19 eyes were culture positive. Those due to coagulase-negative staphylococci achieved a good visual outcome, whereas those infected by streptococci, methicillin-resistant *Staphylococcus aureus*, and *Enterococcus faecalis* fared badly. Four of the patients in the last three groups ended up with no light perception, and none had received intracameral antibiotics.

I hope that this magnificent study will encourage the FDA to approve the intracameral route!

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CHANGING ATTITUDES

In a survey of the United Kingdom and Irish Society of Cataract and Refractive Surgeons after the publication of the ESCRS study's results in 2009, 63% of respondents were routinely using an intracameral antibiotic. Of the others, 67% said that they would do so if a commercial product were available.[12]

In a similar 2007 survey of members of the American Society of Cataract and Refractive Surgery, only 23% of respondents were routinely using an intracameral antibiotic, mostly infusional vancomycin. Of the nonusers, 82% said that they would switch if a commercial product were available.[13]

CONCLUSION

The use of intracameral antibiotics, particularly cefuroxime, is becoming more widely accepted, particularly in Europe. A recent decision by the European Medicines Agency to approve such a product in six European countries now and a further 12 in 2013 is to be welcomed. The availability of an approved product in Europe and the recent US study[11] are signs of change and indicate that the intracameral injection of antibiotics will become routine for cataract surgery. ■

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