

Focus



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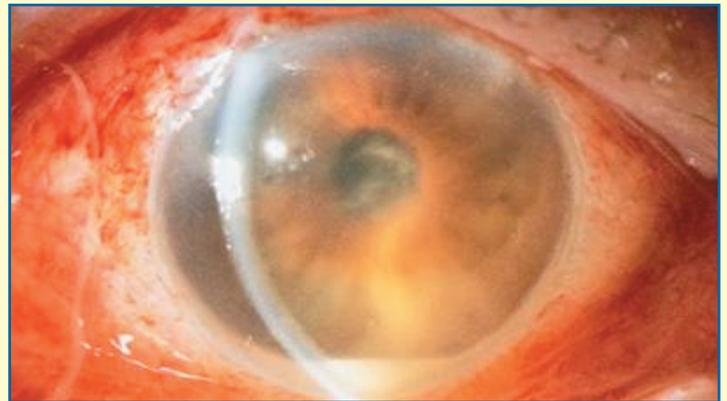
Antibiotic prophylaxis of post-operative endophthalmitis in cataract surgery

Post-operative endophthalmitis (PE) is a rare but dreaded complication of cataract surgery. The evidence suggests that it arises when bacterial flora from the lids and conjunctiva are introduced into the anterior chamber either at the time of surgery or in the early post-operative period. Current strategies for endophthalmitis prophylaxis focus on eliminating conjunctival bacteria with peri-operative topical antibiotics and antiseptics and on inhibiting the proliferation of microorganisms that have gained access to the anterior chamber through the use of high dose intracameral or subconjunctival bactericidal antibiotics.

A survey of 800 consultant ophthalmologists' practices in the UK conducted between October and November 2005 revealed the following preferences for antibiotic prophylaxis of PE: subconjunctival antibiotics 77%, intracameral antibiotics 17%, and single dose topical antibiotics 17%.¹ It is likely that prescribing patterns of antibiotic prophylaxis for PE will change in the near future in the light of recent developments in this field.

Intracameral antibiotics

In March 2006, the interim results of a prospective randomised controlled trial of intracameral cefuroxime for PE prophylaxis following cataract surgery were fast-tracked to publication owing to the significance of the findings.² In this study, which involved 24 centres in nine countries in Europe, 16,603 patients were randomised to receive one of four prophylactic regimens prior to cataract surgery: 1) no antibiotics, 2) intracameral cefuroxime 1mg in 0.1ml normal saline as a bolus injection at the end of surgery, 3) a topical regime of levofloxacin 0.5% starting 1 hour pre-operatively, or 4) a combination of intracameral cefuroxime and levofloxacin drops. All patients received a 6-day course of topical levofloxacin post-operatively. Final data analysis revealed that the absence of intracameral cefuroxime was associated with a 4.92-fold increase (95% confidence interval [CI], 1.87-12.9) in the risk of total PE (proven and suspected) and an even larger increase in risk for confirmed cases. The incidence rates for total PE was 0.35% when no antibiotic prophylaxis was given (background rate), reducing to below 0.08% with the use of



intracameral cefuroxime. Thus, the findings of this landmark study give resounding support to the use of intracameral cefuroxime for PE prophylaxis in cataract surgery.

Are there any limitations to the use of intracameral cefuroxime as endophthalmitis prophylaxis in cataract surgery?

The adverse effects of this treatment have not been fully elucidated to date, although it appears to have minimal effect on corneal endothelial function and post-operative macular thickness based on available evidence.³ Hypersensitivity reactions to cefuroxime appear to be extremely rare but cross-reactivity between penicillin and the cephalosporins is a cause for concern and intracameral cephalosporin-induced anaphylaxis has been reported.⁴ The potential for dosage errors and the introduction of contaminants into the eye also exists, especially if the drug is prepared for injection in the operating theatre rather than a sterile pharmacy. Cefuroxime reconstituted in normal saline becomes unstable after 24 hours at room temperature and after seven days when frozen so there is a degree of inconvenience attached to its use.⁴ At present, a single dose sterile preparation of cefuroxime is not commercially available.

Perhaps the greatest limitation of cefuroxime as the choice of antibiotic for PE prophylaxis relates to its spectrum of activity. As a third generation cephalosporin it has much better gram negative cover than first generation agents like cefazolin,

but at the expense of its gram positive potency. Since the widespread use of intracameral cefuroxime in Sweden, the proportion of cases of PE due to cefuroxime resistant organisms has increased from 7% to 60% in Sweden, with enterococcus accounting for a staggering 25% of cases compared to only 2% in the Endophthalmitis Vitrectomy Study.⁵ Although cefazolin lacks sufficient gram negative potency, it is probably better suited to the microbial spectrum seen in PE than cefuroxime, which according to most reports is 90-100% gram positive. Two retrospective observational studies from Spain have reported marked reductions in PE rates with the use of intracameral cefazolin of the same order of magnitude as the ESCRS study.^{6,7}

Vancomycin has been a popular choice for intracameral delivery during cataract surgery since the early 1990s and offers an alternative to the cephalosporins. It is a bactericidal antibiotic with 100% coverage of gram positive PE-causing organisms. Furthermore, it is the only antibiotic that has been shown to maintain bactericidal levels in the anterior chamber for in excess of 24 hours following intracameral bolus injection, although there is no definitive evidence that it protects against PE.⁸ The addition of vancomycin to the irrigating fluid during cataract surgery is a practice that should be abandoned as it has been shown to have no significant effect on the incidence rate of PE or aqueous contamination after cataract surgery and it fails to achieve sustained bactericidal levels of antibiotic in the anterior chamber. The potential for contributing to vancomycin resistance through its prophylactic use is a significant concern and both the American Academy of Ophthalmology and the Centers for Disease Control and Prevention in the USA advise against its use in cataract surgery.

The fluoroquinolones are bactericidal antibiotics with broad spectrum activity against gram positive and gram negative infections. As increasing resistance in ocular bacterial isolates to the second generation agents ciprofloxacin and ofloxacin is becoming apparent, in particular against enterococcus, coagulase negative staphylococcus and streptococcal species, the third generation agent levofloxacin and the fourth generation agents moxifloxacin and gatifloxacin are being more widely used. Although no published data exist to support the efficacy of intracameral moxifloxacin in PE prophylaxis, at high intracameral concentrations its coverage of gram positive infections might be comparable to vancomycin. It shows excellent in vitro activity against ocular gram positive and gram negative isolates.⁴ Another potential advantage of moxifloxacin is that it is available in a single dose self-preserved preparation (Vigamox, Alcon) that appears to have no deleterious effect on the corneal endothelium following cataract surgery.⁹ Moxifloxacin is not currently licensed for ophthalmic use in the European Union but is due to be approved in the near future.

Subconjunctival antibiotics

Subconjunctival antibiotics, in particular cefuroxime and gentamicin, are popular for PE prophylaxis in the UK.¹ Kamalarajah and colleagues, on behalf of the British Ophthalmological Surveillance Unit (BOSU), found in a prospective case-control study of 214 cases of presumed PE following cataract surgery that the administration of subconjunctival antibiotics (gentamicin or cefuroxime) at the end of cataract surgery protected against PE (odds ratio 0.18,

confidence interval 0.09-0.36).¹⁰ In a retrospective population-based case-control study of 205 cases of PE in Western Australia from 1980 to 2000, Ng et al found that subconjunctival antibiotics reduced the risk of PE by 54%.¹¹ Thus, it appears on the basis of this evidence that subconjunctival antibiotics confer some protection against PE.

Topical antibiotics

In contrast to the small percentage of ophthalmologists in the UK using pre-operative topical antibiotics for cataract surgery (6%), this is an almost universal practice in the United States in spite of the lack of supporting evidence. A recent survey of members of the American Society of Cataract and Refractive Surgery revealed that 52% of cataract surgeons prescribe three days of pre-operative antibiotic drops, 20% give drops one day pre-operatively and 22% administer them pre-operatively on the day of surgery.¹²

Moshirafar and colleagues in the United States reported a PE incidence rate of 0.07% in a retrospective uncontrolled multi-centre observational series of approximately 16,000 patients undergoing uncomplicated cataract surgery who received a topical regimen of gatifloxacin or moxifloxacin starting one hour pre-operatively.¹³ As the study was uncontrolled it was not possible to definitively attribute the low PE rate to the use of prophylactic topical antibiotics. Of note, in the ESCRS study the use of levofloxacin drops 0.5% starting one hour pre-operatively was not found to significantly reduce the risk of PE (incidence rate 0.25% vs. 0.35% with placebo) and no other prospective controlled clinical trials of topical antibiotic prophylaxis of PE have been published to date.

Although it was not designed to evaluate the effectiveness of using levofloxacin drops post-operatively to prevent PE, the high incidence of PE in the two groups not receiving intracameral cefuroxime (approximately 1:300) suggested that there was little benefit in using post-operative antibiotics. Indeed, there is no evidence to support the use of topical antibiotics following cataract surgery in spite of their almost universal use.

Conclusion

The evidence regarding antibiotic prophylaxis of PE in cataract surgery strongly supports the use of intracameral cefuroxime. However, it is not without its limitations and arguably if a department has a PE rate of lower than that achieved with intracameral cefuroxime in the ESCRS study, continuing with less evidence-based strategies might be justified. Without doubt, the strength of the evidence presented supports at a very minimum the use of subconjunctival antibiotics in all cases, particularly in view of the high incidence rate of PE without any prophylaxis as demonstrated in the ESCRS study. At present the evidence for topical antibiotic prophylaxis is weak, but the fourth generation fluoroquinolone moxifloxacin appears to offer an excellent alternative to cefuroxime, either in topical or intracameral form, and further prospective controlled trials are required to investigate its efficacy and safety in PE prevention. The continuing emergence of multi-drug resistant bacteria will ensure that antibiotic prophylaxis of post-operative endophthalmitis remains an active area of investigation.

Conor Murphy, PhD FRCOphth

St. Paul's Eye Unit, Royal Liverpool University Hospital, Liverpool.

References can be found at <http://www.rcophth.ac.uk/scientificfocus>