Endophthalmitis: Recommendations Based on the ESCRS Study

The adoption of intracameral cefuroxime is a safe and effective method to reduce postoperative endophthalmitis by a factor of five.

BY PETER BARRY, FRCS

The ESCRS endophthalmitis study[1,2] on the prophylaxis of endophthalmitis following cataract surgery with phacoemulsification was designed to answer one fundamental question: do perioperative antibiotics prevent endophthalmitis? If so, investigators also sought to determine how the agents should be administered—via intracameral injection, intensive topical drops, or both?

STUDY DESIGN

The study enrolled 15,971 subjects from 23 clinics in nine European countries. Half of the patients were randomly assigned to receive 1 mg of intracameral cefuroxime in 0.10 mL of normal saline solution at the end of the surgery. Additionally, all patients received, in a randomized, masked fashion, intensive topical levofloxacin or placebo drops commencing 60 minutes before the surgery and concluding 30 minutes after its completion. Each patient received a total of five drops.

Because withholding any prophylaxis from the control group was considered unethical, all patients received povidone-iodine preoperatively and topical levofloxacin drops q.i.d. for 6 days beginning on the first postoperative day. The study's objectives were the efficacy of the use of intracameral cefuroxime and intensive perioperative antibiotics versus placebo. The objectives did not include the use of povidone-iodine and routine levofloxacin for 1 week postoperatively. Preoperative antibiotic drops were not used in the conventional sense.

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The endpoint was the occurrence of infectious endophthalmitis, either clinically diagnosed or proven. All suspect eyes were subjected to a vitreous/anterior chamber tap for gram stain, culture, and polymerase chain reaction. Investigators considered infection proven if any of these three tests were positive.

INFECTIONS

In the study group that did not receive the perioperative antibiotic, the rate of endophthalmitis was high at 33 per 10,000 patients for presumed cases and 23 per 10,000 patients for proven cases. In the group that received intracameral cefuroxime, the incidence was six presumed cases per 10,000 patients and four proven cases per 10,000 patients. These results represent a fivefold reduction for both presumed and proven cases in patients who received intracameral cefuroxime.

TABLE 1. SIGNIFICANT RISK FACTORS FOR PRESUMED ENDOPHTHALMITIS

Key Risk Factor	*P* Value	Odds Ratio*	95% Confidence Limits for Odds Ratio	
			Lower Limit	Upper Limit
Cefuroxime injection† (present, absent)	.002	4.8	1.8	12.5
IOL optic material (other, silicone)	.002	3.3	1.2	7.1
Site of incision (scleral tunnel, clear corneal)	.021	5.8	1.3	25.4
Levofloxacin perioperative drops† (present, absent)	.462	1.3	0.6	2.8

**Odds ratios after adjustment for age, gender, and other factors within regression model.*
†Study objective factor.

In the group that did not receive intracameral cefuroxime, the investigators found eight staphylococcal and eight streptococcal infections. In the cefuroxime group, there were three staphylococcal and zero streptococcal infections.

VISUAL ACUITY

The final range of visual acuity for the 11 staphylococcal cases ranged from 20/20 to 20/80. No eye incurred legal blindness (ie, 20/200 or less).

For the eyes infected with *Streptococcus*, the final visual acuity range was 20/20 to no light perception. Five eyes in the non-cefuroxime group became legally blind, all due to streptococci.

RISK FACTORS

We analyzed an exhaustive number of potential risk factors. Table 1 shows those factors identified as significant for presumed endophthalmitis. They include a failure to inject cefuroxime (*P* =.002; odds ratio, 4.8), the use of a silicone as opposed to an acrylic IOL material (*P* =.002; odds ratio, 3.3), and the utilization of a clear corneal as opposed to a scleral tunnel incision (*P*=.021; odds ratio, 5.8). Regarding the last factor, only two out of 23 centers in the study routinely used the scleral tunnel incision. Theoretically, therefore, there could be a hospital/center effect, but this is unlikely. A subanalysis of the risk of silicone versus acrylic IOL material is ongoing and will soon be published by the ESCRS Endophthalmitis Study Group.[3] The use of intensive perioperative levofloxacin drops was not shown to be of clinical significance.

THE EFFECT OF INTRACAMERAL CEFUROXIME

The striking outcome of the ESCRS study was the beneficial effect of using 1 mg of intracameral cefuroxime in 0.10 mL of normal saline solution at the end of the surgery. This measure effectively achieved a fivefold reduction in endophthalmitis compared with the group that received no perioperative antibiotics. The 0.3% incidence of endophthalmitis in the latter group was high and surprised us all. We know that retrospective studies showing lower rates of infection are prone to underreporting and that poor results are often unpublished, but this outcome also raises the possibility that preoperative povidone-iodine combined with routine postoperative antibiotic drops q.i.d. for 1 week is not as effective a regimen as originally thought. It certainly appears inadequate compared with the beneficial effects of intracameral cefuroxime.

It is not likely that the ESCRS study will result in a major conversion by ophthalmologists from clear corneal to scleral tunnel incisions, although this has always been my standard practice. Rather, the data will likely result in stricter construction and sealing of the corneal wound for surgeons for whom it is preferred practice.

WHY CEFUROXIME?

My colleagues and I chose cefuroxime for the study, because it is effective against the majority of organisms that cause postoperative endophthalmitis. Importantly, its efficacy and safety have been shown in more than 400,000 Swedish patients.[4,5] The Swedish experience suggested cefuroxime's benefit, and the ESCRS study has proven it.

Although it may always be argued that other intracameral agents or alternative systems of drug delivery could be superior to cefuroxime, they will require safety studies and clinical trials to prove their superiority. Given the ESCRS study's results, it may well be impossi-

ble for any future clinical trial to deny an intracameral antibiotic to participants. A study to evaluate the comparative benefits of the newer fluoroquinolones applied topically versus using cefuroxime intracamerally would require an enormous and expensive trial, and it may be superfluous if intracameral cefuroxime can achieve the endophthalmitis rate of 0.05% that we have shown. Any such planned studies should also consider the ethics of using the newer fluoroquinolones or vancomycin for prophylaxis. Perhaps they should be considered reserve antibiotics for treatment.

SUMMARY

From the results of the ESCRS study, my co-investigators and I believe that intracameral cefuroxime should be adopted worldwide. Its use could save many thousands of eyes from potential blindness due to postoperative bacterial endophthalmitis following cataract surgery with IOL implantation. ■

Cefuroxime is not licensed for intraocular use. An exemption certificate was obtained for the purposes of the ESCRS endophthalmitis study.

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