

Prophylaxis of postoperative endophthalmitis after cataract surgery

Results of the 2007 ASCRS member survey

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An online survey of members of the American Society of Cataract and Refractive Surgery indicated a strong preference for preoperative and postoperative topical antibiotic prophylaxis, with most surgeons favoring latest generation topical fluoroquinolones. A significant percentage of surgeons reported being concerned about the risks of homemade intracameral antibiotic preparations, and there was a strong desire to have a commercially available antibiotic approved for intracameral injection. This is reflected in the fact that 77% of respondents were still not injecting intracameral antibiotics, but 82% would likely do so if a reasonably priced commercial preparation were available.

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The preliminary findings of the European Society of Cataract & Refractive Surgeons (ESCRS) endophthalmitis study,¹ announced in 2006, generated much controversy and confusion. The trial showed a several-fold decrease in the rate of infectious endophthalmitis with the use of intracameral cefuroxime.² The final results have been published.³

Twenty-four ophthalmology units in Austria, Belgium, Germany, Italy, Poland, Portugal, Spain, Turkey, and the United Kingdom participated in ESCRS' prospective randomized partially masked multicenter study. A total of 16603 patients were recruited as subjects. The study was based on a 2 × 2 factorial design, with intracameral cefuroxime and topical perioperative levofloxacin factors resulting in 4 treatment groups. Cefuroxime as 1 mg in 0.1 mL normal saline was injected into the anterior chamber

at the end of surgery. Levofloxacin 0.5% was administered as 1 drop 1 hour before surgery, 1 drop 30 minutes before surgery, and 3 drops at 5-minute intervals commencing immediately after surgery. All patients were prepped with povidone-iodine 5% drops 3 minutes before surgery, and all were prescribed levofloxacin 0.5% drops 4 times daily for 6 days starting the day after surgery.

Twenty-nine patients presented with endophthalmitis; of these, 20 were classified as culture-proven infective endophthalmitis. Patients not receiving intracameral cefuroxime prophylaxis incurred a 4.92-fold increase (95% confidence interval [CI], 1.87-12.9) in the risk for total endophthalmitis and a 5.86-fold increase (95% CI, 1.72-20.0) in the risk for proven endophthalmitis. In addition, the use of clear corneal incisions compared with the use of scleral tunnels was associated with a 5.88-fold increase (95% CI, 1.34-25.9) in total risk and a 7.43-fold increase (95% CI, 0.97-57.0) in the risk for proven endophthalmitis. The use of silicone intraocular lens optic material compared with the use of acrylic was associated with a 3.13-fold increase (95% CI, 1.47-6.67) in total risk. The presence of surgical complications increased the total risk 4.95-fold (95% CI, 1.68-14.6).

Believing that the evidence had become conclusive, the investigators terminated the study and recommended adoption of this prophylactic measure. Although this is the first prophylactic antiinfective regimen

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to have been proved effective by a prospective randomized controlled study, there is currently no commercially available antibiotic formulation for intracameral injection.

To better understand the implications and impact of the ESCRS study, the American Society of Cataract and Refractive Surgery (ASCRS) Cataract Clinical Committee surveyed the global membership of ASCRS about its current antibiotic prophylactic practices for cataract surgery.

MATERIALS AND METHODS

In January 2007, a link to an online survey was sent to the approximately 4000 ASCRS member e-mail addresses on file. The online anonymous survey consisted of 14 questions that took approximately 2 minutes to complete. The Appendix shows the questionnaire.

RESULTS

A total of 1312 members responded. A majority of respondents (69%) were from the United States, and the entire spectrum of low- to high-volume surgeons was well represented (Tables 1 and 2). All respondents were asked to list their rate of infectious endophthalmitis per 1000, and the results are shown in Table 3. Of note, 90% had an infection rate of 1/1000 or lower. Only 3% of respondents had a rate of 0.3% (3/1000) or higher.

Most surgeons (91%) used topical antibiotic prophylaxis at the time of cataract surgery (Table 4). Of ASCRS members prescribing topical antibiotics, 4th-generation fluoroquinolones (gatifloxacin or moxifloxacin) were preferred by 81%; other respondents preferred levofloxacin, ofloxacin or ciprofloxacin, and or another antibiotic agent (Table 5). It should be noted that topical fourth-generation fluoroquinolones are not commercially available in much of Europe. Eighty-eight percent of surgeons said they initiated topical antibiotics preoperatively (Table 4). Roughly one-half of them prescribed antibiotics 3 days before surgery, while the other half started them the day of surgery or 1 day before surgery (Table 6). Virtually all surgeons (98%) prescribed topical antibiotics postoperatively (Table 4). Approximately two thirds

Table 1. Distribution of respondents by practice location.

Location	Respondents
United States	910
Canada	52
Europe	138
Latin/South America	109

Table 2. Distribution of respondents by annual cataract volume.

Volume	Respondents
< 100 cases	143
100-300 cases	446
300-500 cases	361
> 500 cases	362

Table 3. Individual endophthalmitis rate.

Endophthalmitis Rate (per 1000)	Percentage
0	42
0.1-0.4	10
0.5-0.9	13
1	24
2-3	9
4-12	1

Table 4. Perioperative and postoperative use of antibiotic prophylaxis.

Regimen	Percentage	
	Use	Do Not Use
Perioperative topical antibiotics	91	9
Preoperative topical antibiotics	88	12
Intracameral antibiotics	30	70
Irrigation vs direct injection		
Irrigation bottle	48	
Direct injection	52	
Antibiotics at conclusion of surgery	90	10
Postoperative topical antibiotics	98	2

Table 5. Preferred perioperative topical antibiotic.*

Preferred Antibiotic	Percentage
Gatifloxacin or moxifloxacin	81
Ofloxacin or ciprofloxacin	9
Levofloxacin	3
Other	7

*Of those using a perioperative antibiotic

Table 6. Duration of preoperative topical antibiotic administration.*

Start Topical Antibiotics	Percentage
3 days before surgery	52
1 day before surgery	26
Upon arrival for surgery	22

*Of those using a preoperative antibiotic

(66%) started them on the day of surgery, while one third (34%) waited until the first day postoperatively. The latter group presumably included patients who were patched. Seventy-three percent of surgeons stopped the postoperative antibiotics by 1 week (Table 7); others used postoperative antibiotics for several weeks or tapered them over several weeks.

Ninety percent of surgeons were administering some type of antibiotic at the conclusion of surgery (Table 4). Of these, 83% applied topical antibiotic drops; roughly equal percentages of surgeons used a subconjunctival injection or an intracameral injection, and a small percentage used a collagen shield (Table 8).

Intracameral antibiotics were used by 30% of surgeons, who were equally divided between those injecting the antibiotic intracamerally and those placing it in the irrigating bottle (Table 4). Of those using intracameral antibiotics, 61% used vancomycin; other antibiotics used were cephalosporin, a quinolone, and other agents (Table 9). When intracameral antibiotics were used, most were prepared by the operating room nursing staff (77%); other respondents said the pharmacy or surgeon prepared the antibiotics (Table 10).

What impact did the ESCRS study have on ASCRS member practices by January 2007? Table 11 shows the effect on antibiotic use after the study results had been announced; 77% did not plan to start injecting intracameral antibiotic for a variety of reasons. Table 12 shows the reasons for not injecting an intracameral antibiotic; 89% said they believed that further study was needed.

The poll asked whether surgeons had ever experienced a complication using intracameral antibiotics.

Table 7. Duration of postoperative topical antibiotic use.

Stop Postop Antibiotic	Percentage
1 week or less (no taper)	73
Several weeks (no taper)	19
Several weeks (taper)	8

Table 8. Method of antibiotic administration at the conclusion of surgery.*

Delivery Method	Percentage
Topical application	83
Intracameral injection	15
Subconjunctival injection	13
Collagen shield	3

*Respondents could check more than 1 method; thus the percentages total more than 100.

Table 9. Intracameral antibiotic preferences.*

Intracameral Antibiotic	Percentage
Vancomycin	61
Injection	37
Bottle	63
Cephalosporin	23
Quinolone	22
Other	12

*Of those using an intracameral antibiotic

Table 10. Person who prepares the intracameral antibiotic.*

Prepares the Intracameral Antibiotic	Percentage
OR nursing staff	77
Pharmacy	18
Surgeon	5

OR = operating room

*Of those using intracameral antibiotic

Table 11. Impact of ESCRS study on use of intracameral antibiotics.

Intracameral Antibiotics (Direct Injection)	Percentage
Was already using before ESCRS study	16
Started or plan to after ESCRS study	7
Still not using	77

ESCRS = European Society of Cataract & Refractive Surgeons

Table 12. Reasons for not injecting antibiotics after release of ESCRS study results.*

Reason for Not Injecting Antibiotics*	Percentage
Further study needed	89
Concern about risk	45
Cost	11

*Asked of those not injecting intracameral antibiotic; because respondents could check more than 1 reason, the percentage exceeds 100.

Eighty-six percent of those using intracameral antibiotics said no. Fifty-seven respondents (14% of those using intracameral antibiotics) reported having had complications; Table 13 shows the reported complications.

Regarding the impact of the ESCRS study on the interest in intracameral antibiotic availability, 54% of respondents said they thought it was important to have a commercially available broad-spectrum antibiotic formulated for direct intracameral injection, 11% thought it was not important, and 35% were not sure. Forty-seven percent would use such a product, 18% would not, and 35% would consider using it depending on the cost.

DISCUSSION

It may be surprising that only 6% of respondents reported injecting intracameral cefuroxime, which the ESCRS study showed to be effective in reducing the rate of endophthalmitis. The study apparently did not have an impact on the practice of the 77% of respondents who said they still did not plan to institute the use of intracameral antibiotics of any kind. One can only speculate about the reasons for these findings based on the survey results.

The study's control group did not reflect current prophylactic antibiotic practices for the majority of respondents. For example, 1 arm of the ESCRS study control group received topical levofloxacin immediately before and after surgery, which was the preferred

Table 13. Complications of homemade intracameral antibiotic (reported by 57 respondents).*

Complication	Percentage
Inflammation	56
Corneal endothelial injury	42
Infection	4
Other	23

*Respondents could check more than 1 complication; thus, the percentage exceeds 100.

topical agent of only 3% of ASCRS respondents prescribing topical antibiotics. The other arm was not treated with any preoperative antibiotic, which reflects what only 12% of ASCRS respondents reported doing. Only 34% of respondents said they waited until the day after surgery to initiate postoperative topical antibiotics, as was universally done in the ESCRS trial.

Based on this survey, the most common antibiotic prophylactic practices appears to be topical 4th-generation fluoroquinolones prescribed at least 1 to 3 days preoperatively and resumed immediately postoperatively. In contrast, the only topical antibiotic used in the ESCRS study was levofloxacin, which was administered shortly before surgery in half the patients, while the other half did not receive any preoperative antibiotic. Postoperatively, topical levofloxacin was not started until the first postoperative morning. We acknowledge there has never been a randomized controlled clinical trial demonstrating the prophylactic benefit of any preoperative or postoperative topical antibiotic. Nevertheless, the ESCRS study does not address whether intracameral cefuroxime was equal to, superior to, or of adjunctive benefit to the most commonly used topical antibiotic protocols.

Finally, the possible risks of administering "home-made" intracameral antibiotic mixtures were a significant concern to 45% of surgeons not currently using them. These risks might include dilution errors, bacterial contamination, or toxic anterior segment syndrome. Indeed, 14% of respondents using intracameral antibiotics said they believe they have experienced complications of the practice at some point. These concerns seem to be affirmed by the fact that more than 80% of ASCRS members would most likely inject intracameral antibiotics routinely if a commercially approved preparation were available at a reasonable cost.

Certainly, one cannot draw definitive conclusions from an online survey because there are many potential biases in the responses. Nonetheless, the results indicate that most surgeons use preoperative and postoperative topical fluoroquinolone antibiotics off label and presumably believe they are safe and effective. The ESCRS study has certainly had some impact because although only 16% of surgeons reported using a direct intracameral antibiotic injection before the study, a majority of surgeons said they would like to use this approach if a cost-effective commercial preparation were available. We believe that this is a strong message for the ocular pharmaceutical industry to consider.

CONCLUSION

A large online survey of ASCRS members indicated a strong preference for preoperative and postoperative

topical fourth-generation fluoroquinolone prophylaxis. With a significant percentage of surgeons concerned about the risks of homemade intracameral antibiotic preparations, there is a strong desire to have a commercially available antibiotic agent for this purpose. That 77% of respondents were still not injecting intracameral antibiotics but 82% would likely do so if a reasonably priced commercial preparation were available suggests that for most surgeons, the ESCRS study did not convincingly prove a strong enough benefit-risk ratio.

APPENDIX

ASCRS 2006 Antibiotic Questionnaire

1. **Annual cataract volume**
 < 100 cases 100–300 cases 300–500 cases
 > 500 cases
2. **Your location**
 United States Canada Europe
 Latin/South America/Mexico Africa Australia/Asia
3. **Your preferred perioperative topical antibiotic**
 Don't use
 Ofloxacin or ciprofloxacin
 Levofloxacin
 Gatifloxacin or moxifloxacin
 Other
4. **When do you start preoperative topical antibiotic?**
 Don't use
 3 days prior
 1 day prior
 Upon arrival at ASC
5. **Your use of intracameral antibiotics**
 Don't use
 Cephalosporin (eg, cefuroxime) direct injection
 Cephalosporin (infusion bottle)
 Vancomycin (direct injection)
 Vancomycin (infusion bottle)
 Quinolone (direct injection)
 Quinolone (infusion bottle)
 Other antibiotic (direct injection)
 Other antibiotic (infusion bottle)
6. **Who prepares your intracameral antibiotic?**
 OR nursing staff
 Pharmacy
 Surgeon
 Don't use intracameral antibiotic
7. **Do you administer antibiotics at the conclusion of surgery?**
 (check all that apply)
 Topical application
 Subconjunctival injection
 Collagen shield
 Intracameral injection
 None of the above
8. **When do you start postoperative topical antibiotic?**
 Don't use
 Day of surgery
 Postop day 1
9. **For how long do you continue postoperative topical antibiotic?**
 Don't use
 One week or less (no taper)
 Several weeks (no taper)
 Taper off during several weeks
10. **Estimate your number of infectious endophthalmitis cases per 1000 (current regimen) _____**
11. **Did you alter your regimen following the ESCRS study?**
 No—still do not inject intracameral antibiotic [check all that apply below]
 because of risk of mixing because of cost because more study needed
 No—was already injecting intracameral antibiotic
 Yes—have now started or plan to start injecting intracameral antibiotic
12. **Is it important to have a commercially available broad-spectrum antibiotic formulated for direct intracameral injection?**
 Yes
 No
 Not sure
13. **Would you use it?**
 Yes
 No
 Would depend on cost
14. **Have you ever had a complication from using "home-made" intracameral antibiotics?**
 Don't use them
 No, despite using them
 Yes; please check all that apply:
 Infection
 Inflammation
 Corneal endothelial injury
 Other

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