Clinical observations associated with proven and unproven cases in the ESCRS study of prophylaxis of postoperative endophthalmitis after cataract surgery

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PURPOSE: To describe cases of postoperative endophthalmitis in the European Society of Cataract & Refractive Surgeons (ESCRS) study of the prophylaxis of endophthalmitis, compare characteristics of unproven cases and cases proven by culture or polymerase chain reaction, and compare the characteristics with those in other reported series.

SETTING: Twenty-four ophthalmology units in Austria, Belgium, Germany, Italy, Poland, Portugal, Spain, Turkey, and the United Kingdom.

METHODS: Univariable and multivariable logistic regression models were used to analyze data for statistical association of signs and symptoms in cases with proven or unproven endophthalmitis. Specific data describing characteristics of the cases were compared between the 2 types of cases.

RESULTS: Data from 29 endophthalmitis cases were analyzed. Swollen lids and pain were statistically associated with proven cases of endophthalmitis on univariable regression analysis. Multivariable analysis indicated that swollen lids and an opaque vitreous were associated with proven cases. Five cases of endophthalmitis occurred in the cefuroxime-treated groups. No case of streptococcal infection occurred in the cefuroxime-treated groups. However, cases of infection due to streptococci showed striking differences in visual acuity and were associated with earlier onset. Characteristics in the 29 cases parallel results in previous studies, such as the Endophthalmitis Vitrectomy Study, although the addition of a control group in the ESCRS study elicited additional findings.

CONCLUSION: Swollen lids, pain, and an opaque vitreous were statistically associated with proven endophthalmitis cases in the ESCRS study.

The results and rationale for the European Society of Cataract & Refractive Surgeons (ESCRS) study of the prophylaxis of endophthalmitis after cataract surgery have been presented,[1–3] as has a description of the microbiologic and molecular methods used.[4] Intracameral injection of 1 mg cefuroxime in the 2 cefuroxime-treated groups resulted in a nearly 5-fold reduction in the rates of postoperative endophthalmitis over rates in study groups that did not receive the intracameral injection.[1] We present characteristics of each case of endophthalmitis in the study and compare the signs and symptoms in proven cases and unproven cases.

PATIENTS AND METHODS

Data from the cases of endophthalmitis in the ESCRS study of the prophylaxis of endophthalmitis after cataract surgery were reviewed for comparison of clinical characteristics. The clinical signs and symptoms in cases of proven endophthalmitis were compared with those in unproven cases. The data were compiled by time to diagnosis, visual acuity, microbiology results, and additional factors, including patient demographics, incision site, intraocular lens (IOL) material, surgeon experience, and surgical complications.

Proven endophthalmitis was defined as any case presenting with pain or loss of vision thought to be due to infection and in which infection was proven by Gram stain, culture, or polymerase chain reaction. Unproven or presumed

endophthalmitis was determined to be present when no test yielded a positive result.

Data in the results presented here refer to the randomization protocol used in the ESCRS study.[1] Group A, a control group, received an intensive placebo drop regimen perioperatively[1]; Group C received the active intensive perioperative antibiotic drop regimen (levofloxacin 0.5%).[1] In Group B, an intracameral injection of cefuroxime 1 mg was added to the regimen in Group A; in Group D, intracameral cefuroxime 1 mg was added to the regimen in Group C. All groups were prescribed a standard postoperative antibiotic drop regimen comprising topical levofloxacin 0.5%, 1 drop 4 times daily, for at least 1 week to prevent wound infection. In all, approximately one half (8108) of the intent to treat patients received an intracameral injection of cefuroxime 1 mg and one half (8103) did not.

The endpoint of the study was the diagnosis of endophthalmitis. The subsequent management of individual patients was at the discretion of the responsible surgeon. No aspects of subsequent treatment were randomized, and recording of the final visual outcome did not occur at a fixed time point after diagnosis. Therefore, postoperative visual acuities could not be subjected to statistical testing.

Statistical Analysis

Logistic regression analysis was performed to determine whether any sign or symptom recorded for each patient when he or she presented with endophthalmitis was more frequently associated with proven or unproven cases. Each factor was screened individually using univariable binary logistic regression. All factors with a likelihood ratio test P value of 0.20 or less were made available for final multivariable logistic regression analyses. The likelihood ratio test statistical significance of each factor is reported with its odds ratio (OR) and associated 95% confidence interval (CI).

RESULTS

Of the 29 cases of endophthalmitis in the ESCRS study, 20 were proven and 9 were unproven. The median time to presentation with signs and symptoms was 4.5 days (4.0 days if the 1 late-presenting case at 132 days is discounted) in proven cases and 9.0 days in unproven cases; the median time overall was 5 days. Table 1 shows the distribution of cases grouped by time to onset; a greater proportion of proven cases occurred within the first 7 days postoperatively.

Table 1. Time to onset of signs and symptoms in 29 cases of endophthalmitis.

	Cases		
Days to Onset	Total	Proven	Unproven
1 3	9	8	1
4 7	9	7	2
8 14	7	3	4
>14	4	2	2

Table 2 shows the visual acuity and the signs and symptoms on presentation postoperatively. Table 3 shows the signs and symptoms by case and the results of univariable logistic regression analysis, which indicated that swollen lids and pain were the only sign or symptom significantly associated with proven cases.

After multivariable logistic regression modeling, swollen lids (P .04; OR 18.29; 95% CI, 1.07-311.42) and an opaque vitreous (P .05; OR 13.70; 95% CI, 1.06-177.16) were found to be significantly associated with the proven cases of endophthalmitis. A review of cases that did not have pain, swollen lids, or opaque vitreous, performed to determine whether there were common factors, showed that 1 unmixed case of infection due to *Propionibacterium acnes* was not associated with pain or swollen lids but was associated with an opaque vitreous. All 8 cases caused by streptococcal infection were associated with pain, hypopyon, and chemotic conjunctiva and with clear corneal incisions (Table 4). No commonality of microbial species with other factors was evident among cases, with further analysis impractical due to the small numbers involved.

Although postoperative visual acuities striking were not statistically tested, there was a difference in visual outcomes between cases of streptococcal and cases of staphylococcal infections, with the outcomes being far worse in streptococcal cases. The final visual acuity range in staphylococcal infections (11 cases, excluding 1 mixed case) was between 20/20 and 20/80, with no patient being legally blind (ie, 20/200 or worse); 3 of these cases received an intracameral cefuroxime injection. Conversely, the final visual acuity range in streptococcal infections (8 cases) was between 20/20 and no light perception; 5 of these patients were legally blind, all due to streptococci, and none of the 5 received intracameral cefuroxime (Table 4). All 8 cases with streptococcal infection were in the groups that did not receive intracameral cefuroxime.

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Table 4 shows the microorganisms isolated in the 20 cases of proven endophthalmitis, ordered by time to onset of signs and symptoms as well as the data from all 29 cases by treatment group, age, and sex. It also shows the distribution of risk factors identified as significant in the overall study results. These include site of incision, IOL optic material, surgeon experience, and presence of surgical complications.

Of the 29 endophthalmitis cases, 8 proven cases and 1 unproven case presented within 1 to 3 days postoperatively; all 8 cases were in Group A or Group C, which did not receive an intracameral injection of cefuroxime (Table 4). There was no case of early-onset (1 to 3 days) endophthalmitis in the 2 groups that received an intracameral cefuroxime injection. The early-onset cases included 6 isolates of streptococcal species and 2 isolates of *Staphylococcus epidermidis* and were generally associated with rapid and severe onset of symptoms.

Of the endophthalmitis cases presenting from 4 to 7 days, 7 were proven and 2 were unproven. Five of the 7 proven cases occurred in the groups that did not receive intracameral cefuroxime and 2 cases, in the groups that received intracameral cefuroxime.

The 7 cases with an onset of 8 to 14 days included 3 proven and 4 unproven cases. Of the proven cases, 1 occurred in a cefuroxime-treated group (Group B); in this case, *S epidermidis* was isolated and poor wound healing was reported. Of the unproven cases, 1 was in a cefuroxime-treated group and was associated with an operative complication.

The 2 late-onset proven cases (>14 days) occurred in control Group A, which did not receive cefuroxime, and included 1 case of *S epidermidis* and 1 of *Propionibacterium* species. Two late-onset unproven cases also occurred, both in Group A.

DISCUSSION

We describe the signs, symptoms, and characteristics of endophthalmitis cases in the largest series of patients evaluated for evidence-based prophylaxis of endophthalmitis after cataract surgery in a randomized clinical trial. Our data from the 16 211 intent-to-treat patients were unique in the inclusion of a control group to permit statistical evaluation of the specific intervention; that is, intracameral injection of 1 mg cefuroxime at the close of cataract surgery.

The report of the Endophthalmitis Vitrectomy Study (EVS), which was conducted from 1990 to 1994, describes a comparable series of patients with postoperative endophthalmitis.[5] Many characteristics in the EVS study align with findings in the ESCRS study (Table 5). There were more patients in the EVS study because all were presumed cases of endophthalmitis referred for treatment within a study protocol; however, prophylactic perioperative treatments varied, and recruitment was limited to 6 weeks postoperatively.

The median time to diagnosis in the United States–based EVS study and the European-based ESCRS study was similar (6 days and 5 days, respectively); the early-presenting patients in the control group are the likely reason for the shorter time in the ESCRS study. The majority of patients in both studies presented within 7 days after cataract surgery. In another series that comprised culture-proven endophthalmitis cases (73 eyes) only,[6] the mean time to presentation overall was 13 days (median 9 days); however, for the 42% of patients who presented within 7 days after cataract surgery, the mean time to presentation was 5 days. The somewhat longer time to presentation overall in that study was associated with the use of the clear corneal incision, whereas the EVS was associated with the scleral incision technique. In the ESCRS study, which used both surgical methods, 75% of proven endophthalmitis cases presented within 7 days.

The frequency of patients presenting with pain, swollen lids, and hypopyon is also comparable, although the EVS study did not analyze differences in signs and symptoms between proven cases and unproven cases. In the ESCRS study, hypopyon was present in 80% of proven cases and 56% of unproven cases, resulting in an overall incidence of 72%.

The percentage of culture-proven cases (69%) was identical in both studies and aligned with the 62% culture-positive cases described in an Asian report.[7] The frequency of total gram-positive microorganisms was almost identical (63% versus 62%) in the 2 studies, although streptococci were encountered more frequently in the ESCRS study. Streptococcal endophthalmitis resulted in earlier onset and notably worse outcomes than infection by staphylococcal species, a trend also reflected in EVS results and elsewhere.[8–10] In a series by Lalwani et al.,[6] *Streptococcus* species were identified in 8.2% of isolates overall, with most (83.3%) occurring in the early-presenting group. In the ESCRS study, 75.0% (6/8) of streptococcal cases presented within 3 days and 100% within 7 days. None of the eyes in the ESCRS study with the worst visual outcomes after streptococcal infection received intracameral cefuroxime. This indicates that the cefuroxime injection was an important factor in protecting patients against the development of postoperative streptococcal endophthalmitis with its associated destructive sequelae, which often result in a poor visual outcome. These cases of streptococcal infection reemphasize the importance of this pathogen in the etiology of postoperative endophthalmitis and suggest that proposed regimens for prophylaxis of endophthalmitis ensure microbiologic efficacy against this class of microbes.

Table 2. Signs and symptoms on presentation associated with the endophthalmitis cases.

Case Type/#	VA	Sign or Symptom: Corneal Edema	Hypopyon	Opaque Vit	Vit Condensation	Chemotic Conj
Proven						
28	<20/200	✓	✓	✓	N	✓
10	20/200	✓	✓	✓	—	✓
22	<20/200	✓	✓	✓	✓	✓
21	20/40	✓	✓	—	—	✓
27	<20/200	✓	✓	✓	✓	✓
9	<20/200	—	✓	✓	✓	✓
14	<20/200	✓	✓	✓	✓	✓
3	20/40	—	✓	—	N	✓
17	<20/200	✓	✓	✓	N	—
4*	<20/200	✓	—	—	—	✓
12*	<20/200	✓	✓	✓	N	—
6	20/60	✓	✓	✓	✓	✓
2	<20/200	✓	✓	✓	—	✓
25	<20/200	✓	✓	✓	✓	—
18	<20/200	✓	✓	N	N	—
5	20/200	✓	—	N	—	✓
24	20/200	✓	✓	✓	✓	✓
8*	<20/200	✓	✓	—	—	—
20	20/120	✓	—	—	✓	—
29	20/80	—	—	✓	✓	—
Nonproven					—	—
16	20/80	✓	✓	—	—	✓
15*	20/200	✓	—	—	✓	✓
19	20/200	✓	—	—	✓	—
1*	20/200	✓	✓	—	✓	✓
11	<20/200	—	—	✓	—	—
13	<20/200	✓	✓	—	—	—
26	<20/200	—	✓	✓	—	—
7	<20/200	✓	✓	N	N	—
23	<20/200	✓	—	N	✓	—

✓ = sign/symptom present; — = sign/symptom not present; Conj = conjunctiva; N = presence or absence of sign/symptom not documented; Pupil Memb = pupillary membrane; VA = visual acuity; Vit = vitreous
*Patient received intracameral cefuroxime at close of surgery

Five cases of endophthalmitis (3 proven, 2 unproven) occurred in the ESCRS study groups that received an intracameral cefuroxime injection. One unproven case involved an intraoperative complication. In another series,[11] approximately one half of the endophthalmitis cases were also associated with intraoperative complications. One proven case in a cefuroxime-treated group, which presented 13 days postoperatively, was associated with poor wound apposition. This occurred in a patient whose occupation was hospital based, raising the possibility that a postoperative nosocomial infection with a less susceptible strain of *S epidermidis* occurred at the wound site. The isolate was termed resistant to cefuroxime by previous definitions.[4] Another isolate in the cefuroxime-treated groups was identified as *Staphylococcus warneri* in a patient presenting 4 days after surgery with visual acuity worse than 6/60, swollen lids, and corneal edema, but no hypopyon or vitreous condensation. This isolate was lost to sensitivity testing for cefuroxime, although culture results indicated susceptibility to several antibiotics, including methicillin, but resistance to penicillin and gentamicin. Ocular isolates of *S warneri* are described in the literature, identified from corneal/external eye infections in patients with chronic blepharitis, purulent conjunctivitis, and suppurative keratitis[12] and in hospitals, neonatal units, and food.[13–15] The third isolate in cefuroxime-treated groups was *S epidermidis*, determined to be sensitive to cefuroxime.

Table 2. (Cont.)

Sign or Symptom								
Pupil Memb	Swollen Lid	View of Fundus	View of Retinal Vessels	Loss of Red Reflex	Blurred Vision	Loss of Vision	Pain	Other
—	✓	—	—	✓	N	✓	✓	—
✓	✓	✓	✓	✓		✓	✓	✓
—	—	—	—	✓	✓	✓	✓	—
✓	✓	✓	✓	—	✓	✓	✓	—
—	✓	—	—	—	✓	✓	✓	—
✓	✓	—	—	—	✓	✓	✓	—
—	✓	—	—	—	✓	✓	✓	—
✓	N	✓	✓	—	—	—	✓	✓
—	—	—	—	—	✓	✓	✓	—
✓	✓	✓	✓	—	✓	✓	✓	—
✓	✓	—	—	N	✓	✓	✓	—
✓	✓	✓	✓	—	✓	—	✓	—
✓	✓	—	—	✓	✓	✓	✓	—
—	—	—	—	✓	✓	✓	✓	—
✓	—	—	—	✓	✓	✓	✓	—
✓	✓	✓	—	—	✓	✓	✓	—
—	—	—	—	—	✓	✓	✓	—
—	✓	—	—	—	✓	✓	—	—
—	—	✓	✓	—	✓	—	✓	—
✓		✓	✓	—	✓	✓	—	—
✓	—	—	—	—	✓	✓	—	—
—	✓	✓	✓	—	✓	✓	✓	—
✓	—	✓	✓	—	✓	N	—	—
—	—	N	N	✓	✓	✓	✓	✓
—	—	—	✓	—	✓	✓	—	—
✓	—	—	—	—	✓	✓	—	—
—	—	—	—	—	✓	✓	—	—
N	—	N	N	N	✓	✓	✓	—
—	—	—	—	✓	✓	✓	✓	—

Two cases of unproven endophthalmitis occurred in the cefuroxime-treated groups; an intraoperative complication was associated with 1 of the cases. Intraoperative complications were also associated with culture-negative cases in another series[16] in which endophthalmitis occurred after a variety of surgical procedures.

In the intent-to-treat patient population that received intracameral cefuroxime (Group B and Group D), the rate of total endophthalmitis was 0.062%. The rate in patients who did not receive cefuroxime (Group A and Group C) was approximately 5 times higher (0.296%). The baseline rates in ESCRS study groups not receiving cefuroxime may be compared with presumed postoperative endophthalmitis rates (0.215%,[17] 0.265%,[18] 0.286% and at times 0.330%[19]) in studies that included patient populations in referral centers or older patients or with rates associated with changing trends in surgical technique. Despite changes in surgical techniques and an increasingly elderly population, the rate of endophthalmitis after cataract surgery remained near 0.2% in a Western Australia study that spanned almost 2 decades.[20] These series presumably incorporated some form of perioperative prophylaxis and did not include control groups. A more contemporary analysis[21] found a 0.35% rate of postoperative endophthalmitis in a group of patients who did not receive intracameral cefuroxime. This is an especially relevant comparison to the ESCRS findings because topical antibiotic

Table 3. Presence or absence of each sign and symptom and results of univariable logistic regression analysis.

Parameter	Percentage†		Univariable Logistic Regression		
	Proven Cases	Unproven Cases	*P* Value	OR	95% CI
Sign					
VA 20/200 or worse	75	89	.41	0.38	0.04 3.79
Corneal edema	85	78	.64	1.62	0.22 11.89
Hypopyon	80	56	.18	3.20	0.58 17.72
Vitreous opaque	72	29	.06	6.50	0.94 45.11
Vitreous condensation	60	50	.65	1.50	0.27 8.45
Chemotic conjunctiva	65	33	.12	3.71	0.70 19.59
Pupillary membrane	55	38	.41	2.04	0.38 10.94
Swollen lids	63	11	.02	13.71	1.41 133.85
View of fundus	40	29	.59	1.67	0.26 10.79
View of retinal vessels	35	43	.71	0.72	0.12 4.16
Loss of red reflex	32	25	.73	1.38	0.21 8.98
Symptom					
Blurring of vision*	89	100	—	—	—
Loss of vision*	85	100	—	—	—
Pain	90	56	.05	7.20	1.01 51.39
Other	10	11	.93	0.89	0.07 11.28

CI = confidence interval; OR = odds ratio; VA = visual acuity
*Data unsuitable for logistic regression
†Percentage based on cases in which presence/absence documented

ointment or drops were not routinely used at those centers.

Such reports underscore the value of the ESCRS study results in answering the call for randomized trials to contribute statistically valid data for strategies to reduce endophthalmitis rates as patient numbers increase worldwide.[17] In particular, because reported rates of anterior chamber contamination during cataract surgery are extraordinarily high (20% to 24%,[22] 29%,[23] 43%[24]), it should not be surprising to find baseline endophthalmitis rates in ESCRS control groups that reflect the higher range of reported rates. The lower endophthalmitis rates in cefuroxime-treated groups parallel those in other series in the literature; however, without predefined study protocols to address the significance of specific interventions, assumptions outside the ESCRS study remain speculative and clouded by the many factors at play in various surgical settings.

To date, intracameral cefuroxime remains the only prophylactic intervention proven to reduce rates of endophthalmitis after cataract surgery. Although fourth-generation fluoroquinolones have been promoted as a potential substitute for intracameral cefuroxime, recent reports describing steadily increasing resistance of endophthalmitis isolates to fourth-generation fluoroquinolones ring a cautionary note. From 1990 to 2004, in 111 ocular endophthalmitis isolates of coagulase-negative *Staphylococcus* (CNS), 67.6% being *S epidermidis*, the percentage of strains sensitive to moxifloxacin declined significantly from 96.6% (1990 to 1994) to 65.4% (2000 to 2004) (*P* .03), a 32.2% decline over a relatively short period.[25]

A significant increase in the prevalence of resistant isolates was also documented for moxifloxacin over this time period (*P* .007). The minimum inhibitory concentration required to inhibit the growth of 90% of organisms for moxifloxacin increased by a factor of 266, rising from 0.12 μg/mL (93.2% of isolates) during 1990 to 1994, to 4.00 μg/mL (100% of isolates) during 1995 to 1999, and to 32.00 μg/mL (100% of isolates) during 2000 to 2004. Overall, only 72.1% of the 111 CNS isolates recovered from patients with clinical endophthalmitis were considered sensitive to moxifloxacin ($\leq$0.5 μg/mL).[25]

In the ESCRS study, 2 to 3 of the 5 *S epidermidis* isolates tested showed reduced susceptibility to moxifloxacin.[4] This trend, together with reports describing postoperative endophthalmitis despite perioperative and postoperative use of fourth-generation fluoroquinolone drops,[26] the potentially unresolved questions of safe dosage[27] and cautionary statements that eyedrops such as moxifloxacin should not be injected directly into the eye (Alcon Laboratories, Vigamox product insert), suggest that further large-scale randomized trials are required to validate any substitutions of cefuroxime for intracameral injection at this time.

Table 4. Description of proven and nonproven endophthalmitis cases.

Case Type/#	Days to Onset	Organism	Tx Group	Sex/Age (Y)	Incision Site	IOL Optic Material	Surgeon Experience (# of Surgeries)	Surgical Complications	Visual Outcome†
Proven									
28	1	*Streptococcus salivarius*	C	M/70	Clear corneal	Silicone	>500	No	20/60
10	2	*Streptococcus pneumoniae*	A	M/79	Clear corneal	Silicone	>500	No	<20/200
22	2	*Streptococcus pneumoniae*	A	M/75	Clear corneal	Silicone	>500	No	<20/200
21	2	*Streptococcus salivarius*	A	F/69	Clear corneal	Acrylic	>500	No	<20/200
27	2	*Streptococcus sanguis*	C	M/78	Clear corneal	Acrylic	>500	No	<20/200
9	3	*Staphylococcus epidermidis*	C	F/81	Scleral tunnel	Silicone	<100	No	20/25
14	3	*Staphylococcus epidermidis*	A	M/62	Clear corneal	Acrylic	>500	Yes	20/25
3	3	*Streptococcus oralis*	C	F/66	Clear corneal	Acrylic	>500	No	20/200
17	4	*Staphylococcus epidermidis*	A	F/79	Clear corneal	Silicone	>500	No	20/30
4*	4	*Staphylococcus warneri*	D	F/63	Clear corneal	Acrylic	100 500	No	20/80
12*	5	*Staphylococcus epidermidis*	B	M/81	Clear corneal	Acrylic	>500	No	20/80
6	5	*Staphylococcus epidermidis/ Streptococcus mitis*	A	M/67	Clear corneal	Silicone	>500	No	20/20
2	5	*Streptococcus suis*	A	M/68	Clear corneal	Acrylic	>500	Yes	20/30
25	7	*Staphylococcus epidermidis*	C	M/91	Clear corneal	Acrylic	>500	No	20/25
18	7	*Staphylococcus hominis or haemolyticus*	C	M/83	Clear corneal	Silicone	>500	No	20/40
5	8	*Staphylococcus aureus/ Propionibacterium acnes*	A	M/71	Clear corneal	Acrylic	>500	No	20/30
24	10	*Staphylococcus aureus*	C	M/69	Clear corneal	Acrylic	>500	No	20/60
8*	13	*Staphylococcus epidermidis*	B	M/73	Clear corneal	Silicone	>500	No	20/25
20	16	*Staphylococcus epidermidis*	A	F/69	Clear corneal	Silicone	>500	No	20/20
29	132	*Propionibacterium acnes*	A	F/68	Clear corneal	Silicone	>500	No	20/20
Nonproven									
16	3	—	C	M/71	Scleral tunnel	Silicone	100 500	No	20/40
15*	4	—	D	F/72	Clear corneal	Acrylic	>500	No	20/25
19	4	—	C	F/78	Clear corneal	Acrylic	<100	No	20/30
1*	9	—	B	F/82	Clear corneal	Silicone	>500	Yes	20/60
11	9	—	A	F/74	Clear corneal	Silicone	100 500	Yes	20/25
13	9	—	C	F/76	Clear corneal	Acrylic	>500	No	20/40
26	11	—	A	F/83	Clear corneal	Acrylic	>500	No	20/20
7	15	—	A	M/76	Clear corneal	Acrylic	>500	No	20/30
23	36	—	A	M/85	Clear corneal	Acrylic	>500	No	20/80

Tx = treatment
*Patient received intracameral cefuroxime at close of surgery (Groups B and D)
†Time between presentation and final visual acuity readings: range 3 weeks to 8 months

Formulated and manufactured as an injectable, cefuroxime meets safety standards for drugs intended for injection rather than topical use. The safety of intracameral cefuroxime is supported in large numbers of patients[28,29] as well as by optical coherence tomography after a 1 mg dose, after which no significant effect on postoperative macular thickness was found.[30]

In conclusion, comparison of the signs and symptoms in cases of proven and unproven postoperative endophthalmitis in the ESCRS study showed that swollen lids, pain, and opaque vitreous were statistically associated with the proven cases. Many characteristics of the ESCRS study parallel those of the EVS study and reports from other regions. Five endophthalmitis cases (3 proven, 2 unproven) occurred in cefuroxime-treated groups; 1 of these was associated with poor wound healing and another, with an intraoperative complication, similar to findings in other reported series. The rates of endophthalmitis in ESCRS study groups parallel those in a spectrum of reports that reflect the variety of surgical settings and patient populations described in the literature worldwide. The ESCRS study groups that received an intracameral injection of cefuroxime had a near 5-fold reduction in postoperative endophthalmitis. Intracameral cefuroxime remains the only prophylactic intervention to date with an evidence-based benefit in the reduction of endophthalmitis after cataract surgery.

Table 5. Comparison of ESCRS and EVS studies.

Parameter	Study	
	ESCRS	EVS
Number of cases	29	420
Positive cultures* (%)	69	69
Coagulase negative gm+	24	47
Other gm+	38	16
Total gm+	62	63
Gm	0	4
Mixed	7	3
Median time to presentation (d)	5	6
Presentation (%)		
Within 3 days	31	24
Within 4 7 days	31	37
Within 8 14 days	24	17
Beyond 14 days	14	22
Sign/symptom (%)		
Hypopyon	72	86
Pain	79	74
Swollen lids	46.5	34.5

EVS = Endophthalmitis Vitrectomy Study; gm+ = gram positive; gm = gram negative
*EVS, culture only; ESCRS, culture and polymerase chain reaction

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