Adoption of Intracameral Antibiotic Prophylaxis of Endophthalmitis Following Cataract Surgery

An update on the European Society of Cataract and Refractive Surgeons (ESCRS) Endophthalmitis Study

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This is to certify that:

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ABSTRACT

Purpose:

The purpose of the study is to determine the use of intracameral cefuroxime at the end of cataract surgery across Europe since the beneficial results of reducing endophthalmitis rates by a factor of five were first reported by the European Society of Cataract and Refractive Surgeons Endophthalmitis Study Group in 2006.

Setting:

100 departments of ophthalmology were surveyed across Europe. They comprised both public and private hospitals and clinics.

Design:

A market research company, ASE, was employed to contact 250 cataract surgeons in Europe. They were provided with 500 names, emails and telephone numbers of ESCRS members. The number to be surveyed by country numbers was in proportion to the ESCRS membership in each country. The interviewees were randomly selected from this list.

Methods:

In a survey conducted by computer-assisted telephone interviews, participants responded to questions regarding their awareness of the results of the ESCRS endophthalmitis study and their current use or non-use of intracameral antibiotics in their cataract procedures. Those who routinely utilised intracameral antibiotics were asked which antibiotic they used and those who did not use intracameral antibiotics were asked why they did not. All were also asked whether they would use an approved single-unit dose of cefuroxime for intracameral use if one was commercially available at a reasonable price.

Results:

Seventy-four per cent of respondents said they always or usually use intracameral antibiotics in their cataract surgery procedures. The most frequently cited reasons for not using cefuroxime or other intracameral antibiotics was the lack of an approved commercial preparation and related anxieties regarding the risks of dilution errors and contamination. The great majority of those who did and those who did not currently use intracameral cefuroxime or other intracameral antibiotics said that they would use cefuroxime if an approved intracameral preparation were to become commercially available.

Conclusion:

In this survey of European ophthalmic surgeons, nearly three-fourths of respondents said that they have adopted the prophylactic use of intracameral antibiotics in their cataract procedures and over 90 per cent of respondents would use cefuroxime if an approved single-unit dose product were commercially available.
Introduction

The ESCRS endophthalmitis study, the results of which were published in 2006, showed a five-fold reduction in the endophthalmitis rate among patients randomly allocated to intracameral cefuroxime compared to those who did not receive intracameral antibiotics. The study’s findings appeared to confirm those obtained from data from the Swedish Cataract registry, which showed a reduction in endophthalmitis rate from 0.48 per cent to 0.06 per cent after the Swedish ophthalmologists adopted the use of intracameral cefuroxime in 1996.

Adoption of the prophylactic use of intracameral antibiotics following publication of the results of the ESCRS clinical trial has varied widely around the world. For example, a survey of American Society of Cataract and Refractive Surgery (ASCRS) and the European Society of Cataract and Refractive Surgeons (ESCRS) members which David Leaming MD, carried out in 2010 and presented at the XXVIII Congress of the ESCRs in 2011, showed that 60 percent of ESCRs respondents used intracameral antibiotics, compared to only 20 per cent of ASCRS respondents.

With regard to the ophthalmic surgeons in the United States those results showed no significant change from the survey which the ASCRS Cataract Clinical Committee conducted approximately one year after the ESCRS endophthalmitis study. It showed that only 23 per cent of over 1,300 ASCRS members who responded to the survey were injecting intracameral antibiotics. However, 82 per cent said that they would do so if a reasonably priced commercial preparation were available.

A survey of ophthalmic surgeons in the United Kingdom conducted in 2009 by Gore et al found that 55% of those surveyed were injecting intracameral cefuroxime. Of those using intracameral cefuroxime 48% switched after the publication of the ESCRS survey. The most common reason cited for not using intracameral cefuroxime was the dilution risks associated with preparing the drug in the absence of a commercially available preformulation.

Meanwhile, the ESCRS has published guidelines supporting the use of prophylactic intracameral antibiotics, specifically for cataract surgery advising the use of intracameral cefuroxime. The American Academy of Ophthalmology, state in their preferred practice guidelines for cataract surgery that “only intracameral antibiotics at the end of the case guarantees suprathreshold antibiotic levels for an extended period of time”.

ESCRS conducted this survey to determine the current uptake of the prophylactic use of intracameral antibiotics among European ophthalmic surgeons.

Materials and Methods:

ESCRS commissioned the UK based market research firm ASE to conduct up to 250 computer assisted telephone interviews. Based upon consultations with ASE it was agreed to select 250 surgeons from a list of 500 randomised from the ESCRs Membership database. The 500 selected were weighted by country according to each countries membership of
ESCRS. In the end 193 telephone calls were completed which was 77% of the targeted 250 calls. The number of completed calls tracked by country the numbers in the ESCR membership database. The final count included 100 surgeons from 31 European countries. The interviews were conducted in English. Participants were offered the option to complete the interview in Spanish, French, German or Italian but none of the respondents took up this option. After answering some qualifying questions re; type of practice, years in practice, clinical specialty the respondents were asked the following questions.

Are you aware of the ESCRs Endophthalmitis study?
Do you routinely use intracameral antibiotics at the time of cataract surgery?
What antibiotic do you use?
If no antibiotic used – why not?
Do you routinely use any other antibiotic at the time of surgery?
What antibiotic do you use?
Would you use an approved commercial preparation of cefuroxime if it were available?
Would you consider €20 per patient a reasonable cost for a commercial preparation?
If no – What would you consider a reasonable cost for a commercial preparation?
Do you use intracameral cefuroxime for any other intraocular surgery?

Results:

A total of 193 surgeons participated in the survey. Forty-three per cent were based in hospitals, 39 per cent were in private practice and the remainder were in university or government institutions. Most of the respondents were members of the ESCR (Table 1).

In their responses to the survey, 74 per cent said they always or usually use intracameral antibiotics for cataract surgery. Of those who used intracameral antibiotics, 82 per cent said they used cefuroxime, and 18 per cent used other agents, including vancomycin, moxifloxacin and gentamicin. (Table 2)

Among the 26 per cent of respondents who said that they rarely or never use intracameral antibiotics in their cataract procedures, 52 per cent said it was because they felt that there was no need to do so, and 26 per cent cited the lack of a protocol in their country or their clinic. 16 per cent said they were concerned about the possibility of adverse events and 10 per cent cited lack of a commercially prepared product. Six per cent said that they were worried about contamination risks. (Table 3)
In their response to the question of whether they would use a commercial single-dose preparation of cefuroxime if one became available, 73 per cent said they would, 14 per cent said they would not, and 13 per cent said they might use it on occasion. Of the 14 per cent (27) respondents who would not use a commercial preparation 12 were already using intracameral cefuroxime and were satisfied with the results. They saw no need to switch to a commercial preparation (Table 4).

Conversely, of the 73 per cent who said they would use it if it was commercially available, 29 per cent were not currently using intracameral antibiotics. Therefore, only 15 (8%) of the 193 surgeons interviewed would not use intracameral cefuroxime, whether or not it was commercially available.

With reference to a reasonable cost of a commercially prepared product the respondents were equally divided on the reasonableness of €20.00 per patient. Of the 45% who did not agree with a charge of €20.00 the vast majority believed the cost should be between €5.00 and €10.00.

Discussion:

In our survey of European ophthalmic surgeons, we were pleasantly surprised to find the relatively high figure of 74 per cent of respondents who always or almost always used intracameral antibiotics. Unfortunately we did not ask a specific question as to whether these same respondents had been using intracameral antibiotics prior to publication of the ESCR S study results. The rate of uptake among respondents to this survey was meaningfully higher than those obtained in previous surveys. Furthermore, if one includes those already using intracameral antibiotics but unwilling to change, over 90 percent of respondents would use an approved commercial single unit dose if one became available.

That finding is particularly relevant given the recent introduction of a commercially produced single-unit dose of cefuroxime (Aprokam®, Thea), which has been approved by the European Medicines Agency (EMA) and has received approval in over 12 European countries at this writing.

The reluctance of some surgeons, particularly those outside of Europe, to adopt the use of intracameral antibiotics is not entirely unreasonable, since it has up to now required the use of off-label products that require additional preparation, often under conditions that are below the standards expected from industrial production facilities.

Many hospitals use compounding pharmacies for their off-label preparations and in the United States these facilities have lately acquired a poor reputation among physicians in general. Two years ago in the United States there was an outbreak of endophthalmitis in Florida among patients who had received intravitreal injections of bevacizumab that had been prepared at a compounding pharmacy. In 2012 there was an outbreak of fungal meningitis and other fungal infections in 678 patients who underwent epidural injection of steroids prepared at a single compounding pharmacy.
Moreover, eye surgeons using intracameral cefuroxime have had their share of mishaps. They include an outbreak in a hospital in Turkey of eight cases of Fusarium endophthalmitis among cataract patients who received intracameral cefuroxime from doses that had been prepared in the operating room using a “kitchen pharmacy” method.\(^\text{10}\)

Furthermore, in a hospital in Finland an incorrect dilution resulted in a series of patients receiving intracameral cefuroxime at 50-100 times the recommended dose. Eight of the 16 eyes suffered severe and permanent visual loss.\(^\text{11}\)

However, despite the risks, the United States Food and Drug Administration’s reluctance to approve new products will inevitably lead to clinicians opting for products from compounding pharmacies because they are convinced of their clinical superiority. Moreover, new evidence continues to accumulate in favour of the efficacy of intracameral antibiotics. Findings include the latest report from the Swedish Cataract registry\(^\text{12}\) which shows that during the years 2005 to 2010 the rate of endophthalmitis following cataract surgery among 464,996 operated eyes was only 0.029 per cent.

The numbers of endophthalmitis cases caused by strains resistant to intracameral cefuroxime has not increased in Sweden over the years although such strains now account for a higher proportion of cases.

Also impressive is the finding from a study conducted at a large surgery centre in Northern California. The patients who received intracameral injection over the course of the 5-year study had a 22-fold lower rate of infection.\(^\text{13}\)

The choice of cefuroxime as the preferred agent for intracameral antibiotic has met with criticism. Critics of its use point to the broader spectrum of activity afforded by fourth generation fluoroquinolones and vancomycin. However, those agents have serious drawbacks of their own.

In the case of fourth generation fluoroquinolones, widespread use in the United States of topical moxifloxacin as a prophylaxis against endophthalmitis have exposed the periocular flora of vast numbers of patients to the agent. In fact, microorganisms that have developed resistance to these antibiotics have already been implicated in cases of endophthalmitis.\(^\text{14}\) Alcon, the manufacturer of Vigamox specifically states that their product is for topical and not for intraocular use.\(^\text{15}\)

Proponents of vancomycin, meanwhile, point to the fact that it is effective against MRSA. However, screening at-risk patients i.e. those in long term nursing home care or recent inpatient hospital care for MRSA and treating them before surgery will eliminate most of the risk posed by such microorganisms. The Center for Disease Control in Atlanta, Georgia, US, have advised strongly against the routine use of vancomycin as a prophylaxis against endophthalmitis.
Conclusion:

The results of this survey indicate that the ESCRS endophthalmitis Study has had a strong impact on the practice of endophthalmitis prophylaxis among European ophthalmic surgeons. Around three-fourths of respondents said they currently use intracameral antibiotics and over 90 per cent said would do so if an approved preparation of cefuroxime was commercially available. The recent introduction of an approved commercially available single-unit dose of cefuroxime should therefore lead to an increased uptake of intracameral cefuroxime in cataract procedures by ophthalmic surgeons across Europe, with a concomitant reduction in the incidence of postoperative endophthalmitis.
References


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15. Alcon Laboratories Product Information 5.1 Warnings and Precautions