Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

HHS Public Access

Author manuscript

Clin Exp Ophthalmol. Author manuscript; available in PMC 2018 July 01.

Published in final edited form as:

Clin Exp Ophthalmol. 2017 July ; 45(5): 481–488. doi:10.1111/ceo.12910.

Pathogens and antibiotic sensitivities in endophthalmitis

Geraldine R Slean, MD[1], **Neal H Shorstein, MD**[2], **Liyan Liu, MD**[3], **John F Paschal, MD**[4], **Kevin L Winthrop, MD**[5], and **Lisa J Herrinton, PhD**[3]

[1]Department of Ophthalmology, California Pacific Medical Center, San Francisco, California, USA

[2]Departments of Ophthalmology and Quality, Kaiser Permanente, Walnut Creek, California, USA

[3]Division of Research, Kaiser Permanente Northern California, Oakland, California

[4]Department of Ophthalmology, Kaiser Permanente, Pasadena, California, USA

[5]Division of Infectious Diseases, Department of Ophthalmology, Oregon Health and Sciences University, Portland, Oregon, USA

Abstract

BACKGROUND—Antibiotic prophylaxis in cataract surgery is intended to minimize endophthalmitis. We describe pathogenic organisms, antibiotic sensitivities, and antibiotic prophylaxis in culture-proven endophthalmitis cases.

DESIGN—Retrospective consecutive case series, community-based setting.

SAMPLES—215 cases of endophthalmitis after cataract surgery performed during 2007–2012 in Kaiser Permanente, California.

METHODS AND MAIN OUTCOME MEASURES—Descriptive analysis of isolated organisms and antibiotic sensitivities in relation to antibiotic prophylaxis in culture-proven endophthalmitis cases.

RESULTS—The majority of culture-confirmed organisms (N=83) were Gram-positive (96%), most notably coagulase-negative *Staphylococci* (CoNS) (N=34, 52%), of which all that underwent testing were sensitive to vancomycin (N=32). Among 19 cases that had received only topical antibiotic prophylaxis, 7 (37%) were resistant to the antibiotic given: 50% of cases (5 of 10 isolates) that had received ofloxacin were resistant to this antibiotic, 40% (2 of 5 isolates) that had received gatifloxacin were resistant. In contrast, 100% of cases (N=4) that had received aminoglycosides were susceptible. Few culture-confirmed cases occurred in patients who received intracameral antibiotic (N=4).

CONCLUSIONS—In cases where fluoroquinolones were administered as antibiotic prophylaxis, isolates demonstrated a degree of bacterial resistance. The majority of endophthalmitis cases isolated following topical antibiotic prophylaxis only and were attributed to Gram-positive organisms, while few occurred in association with intracameral antibiotic.

Correspondence: Lisa Herrinton, PhD, Kaiser Permanente Division of Research, 2000 Broadway, Oakland, CA 94612, lisa.herrinton@kp.org, +1 510-891-3714.

Conflict of interest: None

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Keywords

Cataract surgery; endophthalmitis; topical antibiotics; intracameral antibiotics; sensitivities; resistance

INTRODUCTION

Historically, the incidence of endophthalmitis after cataract surgery has ranged from 0.03% to 0.70%.[1,2] The most common causative organisms are Gram-positive, such as coagulase-negative *Staphylococcus* (CoNS), *Streptococcus viridans* or *Staphylococcus aureus*.[3] Gram-negative organisms,[4] such as *Pseudomonas* or *Haemophilus*, are less common; fungi are rare.[1,4,5]

The injection of intracameral antibiotics has been shown to decrease the rate of endophthalmitis in cataract surgery.[1,6–12] Topical antibiotics are intended to reduce conjunctival bacterial load which is predominantly composed of CoNS.[4,13,14] We showed a 42% reduction in endophthalmitis associated with intracameral antibiotic compared with topical antibiotic, whereas no use of antibiotic prophylaxis was associated with a 95% increase in risk compared with use of topical antibiotic.[12] The use of topical antibiotics alone, however, is associated with concerns about inadequate bacterial eradication,[13,15,16] inadequate minimum inhibitory concentration,[17,18] and insufficient effect on lowering the risk of endophthalmitis.[6,19,20] Nevertheless, this method of antibiotic administration is still more common in the U.S.A.[21]

We described the pathogenic organisms, their antibiotic sensitivities, and type of antibiotic prophylaxis in 215 endophthalmitis cases diagnosed in Kaiser Permanente California from 2007 to 2013 to measure the effectiveness of antibiotic agent and route of administration.

METHODS

The study was approved by the Kaiser Foundation Research Institute Institutional Review Board. Detailed methods are provided elsewhere [12] and summarized here.

Setting

Kaiser Permanente is a closed, staff model, integrated healthcare delivery system with capitated payment that provides comprehensive care to 6.5 million Californians, representing one-third of covered individuals in the catchment area. The health plan uses an electronic health record to store detailed clinical information. Clear cornea phacoemulsification using the Alcon Infiniti is performed at 21 surgical centers in Northern California and at 17 surgical centers in Southern California. Surgeons have autonomy in choosing their chemoprophylaxis regimen for infection prevention.

Study Population

This study is a retrospective consecutive case series of endophthalmitis cases that occurred within 315,246 eligible non-complex phacoemulsification procedures (in 204,515 patients) at surgical centers following at least 6 months of health plan enrollment. The study period

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

began on January 1, 2005 and ran through December 31, 2012, with follow-up for endophthalmitis continuing for another 90 days through March 31, 2013. Cases were excluded if there was a prior diagnosis of endophthalmitis, if phacoemulsification was combined with corneal transplant or glaucoma surgery, if the planned procedure was complex, or if procedures were performed by retinal or oculoplastics specialists.

Data Collection

Postoperative infectious endophthalmitis was defined as occurring between the first post-operative day and 90 days after phacoemulsification. Preliminary cases of endophthalmitis were defined using diagnosis codes, or having an eye fluid specimen submitted to microbiology within 90 days of phacoemulsification. Endophthalmitis cases were later validated using detailed medical record review using a defined protocol which required a diagnosis recorded by a retina specialist within 90 days of surgery and evidence of intravitreal antibiotic therapy. We did not require microbiological confirmation, although positive cultures were noted. The review included the operative report, first follow-up visit, visits to retina specialists, and microbiology results.

Topical antibiotic orders and dispensings were obtained from the computerized pharmacy management information system, the gold standard, from which we obtained details regarding the following ophthalmic antibiotic preparations: gatifloxacin (Zymar or Zymaxid, Allergan, Parsippany, NJ), ofloxacin (Floxin, Daiichi Sankyo, Tokyo, Japan; Ocuflox, Allergan, Parsippany, NJ), polymyxin B/neomycin/dexamethasone (Maxitrol, Alcon, Hunenberg, Switzerland), polymyxin B sulfate/trimethoprim sulfate (Polytrim, Allergan, Parsippany, NJ), and gentamicin sulfate (various manufacturers) or tobramycin (Alcon, Hunenberg, Switzerland). We included dispensings recorded 90 days before phacoemulsification due to the timing of pre-operative visits, during which surgeons wrote the order for topical antibiotic to be filled in advance of the surgery. Agents dispensed up until the day after phacoemulsification were included to allow for late orders and dispensings while clearly separating prophylactic and therapeutic indications.

Intracameral injection was coded using batch processing of operative notes (N=315,246). Batch processing of intracameral injection information was performed without knowledge of endophthalmitis status to prevent investigator bias in adjudicating the cases. The positive and negative predictive values of the algorithm used to ascertain intracameral agent were 99.9% (95% CI, 99.4–100%). As the present case series is restricted to endophthalmitis cases, we allowed ourselves to re-examine the operative reports to confirm intracameral injection and agent. Two of the 215 cases previously classified as receiving an intracameral injection following batch processing for the prior study were reclassified as receiving topical agent only following chart review for this study.

Culture date, organism isolated, and antibiotic susceptibility testing results were obtained from clinical microbiology data. The majority of samples were obtained from the vitreous (N=94, 53%). All samples were sent for gram stain and culture. The culture media used was Trypticase™ soy agar with 5% sheep blood and chocolate agar (Becton Dickinson, Franklin Lakes, NJ). Antimicrobial susceptibility testing was performed in the laboratory using BBL™ Sensi-Discs™ (Becton Dickinson, Franklin Lakes, NJ) which are based on the

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Kirby-Bauer method. Interpretation of bacterial growth followed Clinical and Laboratory Standards Institute (CLSI) guidelines, or Sensi-Disc recommendations when CLSI guidelines were lacking (such as the interpretation of *Staphylococcus* species in the setting of bacitracin). Although sensitivity to moxifloxacin was not performed, sensitivity to gatifloxacin was considered a substitute for moxifloxacin sensitivity. *Staphylococcus* or *Streptococcus* species that are susceptible to gatifloxacin (or ciprofloxacin or ofloxacin) are considered susceptible to moxifloxacin as the latter has the most Gram-positive activity. Resistance to oxacillin was also deemed representative of clinical resistance to cephalosporins in *Staphylococcus* species.

Data Analysis

The approach to this descriptive analysis was informed by the work of Moloney and Park (2014).[4] Crude counts are presented in relation to antibiotic prophylaxis and identified organism.

RESULTS

As described in our previous publication,[12] one-third of endophthalmitis cases were under 70 years of age, one-third were aged 70–79, and one-thid were 80 and older. 16% of cases had a history of diabetic retinopathy, and 4.2% experience intraoperative posterior capsular rupture. In addition 78% received topical antibiotic prophylaxis alone, 13% intracameral with or without topical prophylaxis, and 9% had no record of either approach. Among the 215 endophthalmitis cases, 38 (18%) were not cultured. Of the 177 cases that were cultured, 94 (53%) had no growth.

Of the 83 cases with organisms identified (47% of those cultured) (Table 1), 80 were Gram-positive. CoNS was the predominant organism in the series, accounting for 43 (52%) culture-confirmed cases.

Among the Gram-positive organisms, information on sensitivity to any antibiotic was recorded for 68 (85%). Information on antibiotic sensitivity is summarized in Table 2. Among the 34 CoNS isolates with sensitivity testing, 58% (7 of 12 isolates) were sensitive to gatifloxacin, 57% (8 of 14) to ofloxacin and to polymyxin, 79% (11 of 14) to bacitracin and to trimethoprim, and 100% (N=32) to vancomycin. . *Streptococcus viridans* (13 of 14 isolates were tested) was 100% sensitive to cefazolin (N=4), ceftriaxone (N=9), cephalothin (N=3), ofloxacin (N=8), bacitracin (N=8), and clindamycin (N=6). Fifty percent (2 of 4 isolates) were sensitive to trimethoprim, 100% (N=10) to vancomycin, and 86% (6 of 7) to gatifloxacin. Other *Streptococcus* species (5 isolates, including 3 *S. pneumoniae*, 1 *S. agalactiae*, and 1 unspecified species) were 100% sensitive to ceftriaxone (N=2), bacitracin (N=2), cefazolin (N=1), cephalothin (N=1), clindamycin (N=4), and vancomycin (N=5). Fifty percent were sensitive to ofloxacin (1 of 2 isolates) and gatifloxacin (1 of 2)..

All *Staphylococcus aureus* isolates (MRSA, N = 7; MSSA, N=5) were susceptible to vancomycin. Only 33% (1 of 3) of MRSA isolates were sensitive to gatifloxacin or bacitracin, while 0% (N=3) were sensitive to ofloxacin or polymyxin. In addition, 100% (N=3) were sensitive to trimethoprim. MSSA isolates were 100% sensitive to gatifloxacin

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

(N=2) and trimethoprim (N=3). Sixty-seven percent of MSSA isolates (2 of 3 isolates) showed sensitivity to ofloxacin or bacitracin. All *Streptococcus* isolates (*Streptococcus viridans*, *Streptococcus aureus*, and other *Streptococcus* species) were resistant to polymyxin.

Enterococcus (5 isolates) was 100% sensitive to vancomycin. *Enterococcus* is intrinsically resistant to cephalosporins, clindamycin, trimethoprim, and aminoglycosides. Three isolates were tested for sensitivity to gatifloxacin (a moxifloxacin surrogate), and 1 was resistant.

Among the culture-confirmed cases where a topical antibiotic was the sole prophylactic agent, 45 had sensitivities measured to one or more antibiotics that are relevant to cataract surgery (Table 3). Among 10 isolates where topical ofloxacin had been prescribed and the organism was tested, 5 (50%) were sensitive to ofloxacin. Among 5 isolates where topical gatifloxacin had been prescribed and the organism was tested, 3 (60%) were sensitive to gatifloxacin. Among isolates where topical aminoglycoside (tobramycin or gentamicin) had been prescribed and the organism tested, 100% were sensitive to tobramycin and gentamicin. In summary, of 19 cases that had received topical antibiotic prophylaxis and had sensitivity testing performed, 7 (37%) were resistant to the antibiotic given.

Pathogens were identified in only eight cases of endophthalmitis following intracameral injection, and only 3 cases had pertinent antibiotic sensitivity data. Two cases received intracameral moxifloxacin and topical gatifloxacin, of which one was associated with culture of CoNS (resistant) and the other *S. viridans* (sensitive). The third case, also *S. viridans*, received intracameral cefuroxime with topical gatifloxacin, to which the pathogen was sensitive. All cases who received intracameral antibiotic were sensitive to vancomycin. Three cases of endophthalmitis were associated with culture of a Gram-negative organism (Table 1). *Kingella* species was recovered in one case where topical gatifloxacin was the sole prophylactic agent; this case was not tested for antibiotic sensitivities. *Pseudomonas aeruginosa* was cultured from an eye that received no antibiotic prophylaxis and was sensitive to all agents tested (ceftazidime, ciprofloxacin, gentamicin). *Moraxella* species was recovered from an eye that had been injected with intracameral cefuroxime and supplemented with topical ofloxacin but was not tested for sensitivities. No fungal organisms were recovered despite routine plating of specimens on Sabouraud's medium.

DISCUSSION

We assessed infective organisms and antibiotic sensitivities in 215 endophthalmitis cases relative to the route of administration and antibiotic agent used for prophylaxis. Consistent with other reports, about half of the cases submitted for microbiological testing were confirmed with an infective organism.[1] Among those that were culture-confirmed, 96% were Gram-positive, with *Staphylococcus* species (including MRSA and MSSA) accounting for 66% of organisms and MRSA itself making up 8% of isolates. Our finding that only 4% of isolates were Gram-negative corresponds to previous reports.[1,3,4] Sensitivity results from our study correspond to prior literature showing that both MRSA and MSSA have greater *in vitro* sensitivity to gentamicin than fluoroquinolones.[22,23] Our results also support prior

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

reports that *Streptococcus* species is highly susceptible to ceftriaxone and vancomycin,[24] and that *Enterococcus faecalis* is highly sensitive to vancomycin.[25]

Postoperative, culture-confirmed endophthalmitis can develop despite antibiotic prophylaxis for several reasons: (1) delayed wound healing;[26] (2) lack of sufficient penetration or dosing of a topical agent; and (3) antibiotic resistance. Corneal wounds in phacoemulsification are subject to incompetence, allowing fluid to enter the eye.[27,28] It is logical to expect that the probability of infection is increased if an organism enters through the wound in the hours or days following a decline in antibiotic concentration below the organism's minimum inhibitory concentration (MIC). Topical agents reach relatively low levels of concentration in the anterior chamber[17,18,29,30] and are subject to peaks and troughs. Therefore, in addition to the practice of intracameral injection, wound construction and stromal hydration are important in the goal to maintain a watertight wound.[31]

Our earlier report described an important difference in effectiveness between topical aminoglycosides (tobramycin, gentamycin) and topical fluoroquinolones (gatifloxacin and ofloxacin).[20] Although aminoglycosides are highly effective against Gram-positive and Gram-negative species *in vitro*,[3] recent animal studies indicate poor penetration into the eye's anterior chamber.[23,29,32,33] Our findings are consistent with prior animal evidence: among 6 endophthalmitis isolates that had received topical aminoglycoside prophylaxis and were tested, 100% were sensitive. In contrast, only 50% of 10 isolates that had received topical ofloxacin prophylaxis were sensitive to ofloxacin, while 60% of 5 isolates that had received topical gatifloxacin prophylaxis were sensitive to gatifloxacin. Resistance to fluoroquinolones has been confirmed in other studies[3,22,23,34,35] and calls into question the recommended usage of these antibiotics for routine prophylaxis.

We have separately reported the effectiveness of intracameral injection, compared with topical antibiotic, for preventing endophthalmitis.[12] We found the use of intracameral antibiotics to be associated with a significantly lower rate of endophthalmitis following cataract surgery (intracameral compared with topical: odds ratio 0.58 with 95% confidence interval 0.38–0.91). This result is similar to other reports.[1,6–9] This supports the importance of administering a high concentration (compared to MIC90 of most causative organisms) of antibiotic directly into the anterior chamber.[36, 37] Studies suggest that topical antibiotics may not add any additional clinical benefit to intracameral injection.[9,19,21]

Vancomycin would appear to be an excellent choice for intracameral injection given that over 96% of organisms recovered in our setting were sensitive to that agent. Tempering the enthusiasm for vancomycin are prior recommendations from the CDC reserving vancomycin for non-routine infections and recent reports linking intracameral vancomycin to hemorrhagic occlusive retinal vasculitis.[38, 39] Although exceedingly rare, the condition most commonly results in a devastating loss of vision. This latter concern prompted the American Society of Cataract and Refractive Surgery to issue an advisory warning.[40] Intracameral cefuroxime and moxifloxacin are similar to each other in reducing endophthalmitis rates.[21]. Although neither of these agents are available as government approved, manufactured products in the United States, cefuroxime is available in the European Union as Aprokam

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

(Thea pharmaceuticals, Keele, UK) and moxifloxacin is available in India as Promox (Aurolab, Tamil, Nadu, India).

Other methods to increase the concentration of antibiotic in the anterior chamber include improved formulations of topical agents and bottles (such as medication concentration, pH, and instillation volume) that could improve corneal penetration, particularly in regards to aminoglycosides.[41] Intraocular lenses soaked in antibiotics and antibiotic nanoparticles may also hold a future role in endophthalmitis prevention.[42,43]

Although this study accessed endophthlamitis cases from a large population, 18% of the cases were not cultured. This is a consequence of the study being set in a community-based population. The setting was both a limitation and a strength, in that it represents real-world care in a diverse population. The cases were obtained as a consecutive case series from a well-characterized population and represent the distribution of organisms in our underlying geographic region. Nonetheless, caution must be exercised in applying these findings to other geographic regions, where the distribution of pathogens and their sensitivities may differ.

In summary, Gram-positive organisms, and CoNS in particular, were the predominant organisms associated with endophthalmitis in this series. More than 50% of CoNS showed resistance to fluoroquinolones. *S. viridans*, which accounted for the next most prevalent organism, was predominantly sensitive to fluoroquinolones. Topically applied fluoroquinolones have been associated with increased likelihood of emergence of antibiotic resistance.[44,45] While pathogens were generally susceptible to aminoglycosides *in vitro*, our previous report suggests that these are not effective in endophthalmitis prophylaxis, most likely due to poor ocular penetration.

Acknowledgments

Funding sources: This research was funded by a grant from the National Eye Institute (R21 EY022989) and the Garfield Fund, along with resources provided by the Kaiser Foundation Community Benefit program.

We would like to thank Susanne Gardner, Pharm D and Jeffrey M. Schapiro, MD for their insightful contributions to this manuscript. We would also like to recognize the support of the Garfield Memorial Fund.

REFERENCES

1. Kessel L, Flesner P, Andresen J, et al. Antibiotic prevention of postcataract endophthalmitis: a systematic review and meta-analysis. Acta Ophthalmol. 2015; 93:303–317. [PubMed: 25779209]
2. Taban M, Behrens A, Newcomb RL, et al. Acute endophthalmitis following cataract surgery: a systematic review of the literature. Arch Ophthalmol. 2005; 123:613–620. [PubMed: 15883279]
3. Gentile RC, Shukla S, Shah M, et al. Microbiological spectrum and antibiotic sensitivity in endophthalmitis: a 25-year review. Ophthalmol. 2014; 121:1634–1642.
4. Moloney TP, Park J. Microbiological isolates and antibiotic sensitivities in culture-proven endophthalmitis: a 15-year review. Br J Ophthalmol. 2014; 98:1492–1497. [PubMed: 24939423]
5. Behndig A, Cochener B, Güell JL, et al. Endophthalmitis prophylaxis in cataract surgery: overview of current practice patterns in 9 European countries. J Cataract Refract Surg. 2013; 39:1421–1431. [PubMed: 23988244]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

6. Endophthalmitis Study Group ESCRS. Prophylaxis of postoperative endophthalmitis following cataract surgery: results of the ESCRS multicenter study and identification of risk factors. J Cataract Refract Surg. 2007; 33:978–988. [PubMed: 17531690]
7. Seal DV, Barry P, Gettinby G, et al. ESCRS study of prophylaxis of postoperative endophthalmitis after cataract surgery: Case for a European multicenter study. J Cataract Refract Surg. 2006; 32:396–406. [PubMed: 16631046]
8. Arshinoff SA, Bastianelli PA. Incidence of postoperative endophthalmitis after immediate sequential bilateral cataract surgery. J Cataract Refract Surg. 2011; 37:2105–2114. [PubMed: 22108106]
9. Shorstein NH, Winthrop KL, Herrinton LJ. Decreased postoperative endophthalmitis rate after institution of intracameral antibiotics in a Northern California eye department. J Cataract Refract Surg. 2013; 39:8–14. [PubMed: 23036356]
10. Anijeet DR, Palimar P, Peckar CO. Intracameral vancomycin following cataract surgery: An eleven-year study. Clin Ophthalmol. 2010; 4:321–326. [PubMed: 20463800]
11. Matsuura K, Miyoshi T, Suto C, et al. Efficacy and safety of prophylactic intracameral moxifloxacin injection in Japan. J Cataract Refract Surg. 2013; 39:1702–1706. [PubMed: 24054967]
12. Herrinton LJ, Shorstein NH, Paschal JF, et al. Comparative Effectiveness of Antibiotic Prophylaxis in Cataract Surgery. Ophthalmol. 2016; 123:287–294.
13. Coskun M, Altintas AG, Anayol MA, et al. Evaluation of efficacy of topical povidone-iodine and different types of fluoroquinolones in the sterilization of bacterial flora on the conjunctiva. J Ocul Pharmacol Ther. 2011; 27:589–592. [PubMed: 21834670]
14. Ta CN, Chang RT, Singh K, et al. Antibiotic resistance patterns of ocular bacterial flora: a prospective study of patients undergoing anterior segment surgery. Ophthalmol. 2003; 110:1946–1951.
15. Inoue Y, Usui M, Ohashi Y, et al. Preoperative disinfection of the conjunctival sac with antibiotics and iodine compounds: a prospective randomized multicenter study. Jpn J Ophthalmol. 2008; 52:151–161. [PubMed: 18661264]
16. He L, Ta CN, Hu N, et al. Prospective randomized comparison of 1-day and 3-day application of topical 0.5% moxifloxacin in eliminating preoperative conjunctival bacteria. J Ocul Pharmacol Ther. 2009; 25:373–378. [PubMed: 19492956]
17. Yalvac IS, Basci NE, Bozkurt A, Duman S. Penetration of topically applied ciprofloxacin and ofloxacin into the aqueous humor and vitreous. J Cataract Refract Surg. 2003; 29:487–491. [PubMed: 12663011]
18. Yamada M, Mochizuki H, Yamada K, et al. Aqueous humor levels of topically applied levofloxacin in human eyes. Curr Eye Res. 2002; 24:403–406. [PubMed: 12434310]
19. Råen M, Sandvik GF, Drolsum L. Endophthalmitis following cataract surgery: the role of prophylactic postoperative chloramphenicol eye drops. Acta Ophthalmol. 2013; 91:118–122. [PubMed: 22151787]
20. Friling E, Lundstrom M, Stenevi U, Montan P. Six-year incidence of endophthalmitis after cataract surgery: Swedish national study. J Cataract Refract Surg. 2013; 39:15–21. [PubMed: 23245359]
21. Chang DF, Braga-Mele R, Henderson BA, et al. Antibiotic prophylaxis of postoperative endophthalmitis after cataract surgery: Results of the 2014 ASCRS member survey. J Cataract Refract Surg. 2015; 41:1300–1305. [PubMed: 26189384]
22. Deramo VA, Lai JC, Winokur J, et al. Visual outcome and bacterial sensitivity after methicillin-resistant *Staphylococcus aureus*-associated acute endophthalmitis. Am J Ophthalmol. 2008; 145:413–417. [PubMed: 18191097]
23. Major JC, Engelbert M, Flynn HW, et al. *Staphylococcus aureus* endophthalmitis: antibiotic susceptibilities, methicillin resistance, and clinical outcomes. Am J Ophthalmol. 2010; 149:278–283. [PubMed: 19926069]
24. Kuriyan AE, Weiss KD, Flynn HW, et al. Endophthalmitis caused by streptococcal species: clinical settings, microbiology, management, and outcomes. Am J Ophthalmol. 2014; 157:774–780. [PubMed: 24418264]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

25. Kuriyan AE, Sridhar J, Flynn HW, et al. Endophthalmitis caused by Enterococcus faecalis: clinical features, antibiotic sensitivities, and outcomes. Am J Ophthalmol. 2014; 158:1018–1023. [PubMed: 25089354]
26. Maxwell DP, Diamond JG, May DR. Surgical wound defects associated with endophthalmitis. Ophthalmic Surg. 1994; 25:157–161. [PubMed: 8196919]
27. Fine IH, Hoffman RS, Packer M. Profile of clear corneal cataract incisions demonstrated by ocular coherence tomography. J Cataract Refract Surg. 2007; 33:94–97. [PubMed: 17189800]
28. Masket S, Belani S. Proper wound construction to prevent short-term ocular hypotony after clear corneal incision cataract surgery. J Cataract Refract Surg. 2007; 33:383–386. [PubMed: 17321386]
29. Cagini C, Piccinelli F, Lupidi M, et al. Ocular penetration of topical antibiotics: study on the penetration of chloramphenicol, tobramycin and netilmicin into the anterior chamber after topical administration. Clin Exp Ophthalmol. 2013; 41:644–647. [PubMed: 23433257]
30. Donnenfeld ED, Comstock TL, Proksch JW. Human aqueous humor concentrations of besifloxacin, moxifloxacin, and gatifloxacin after topical ocular application. J Cataract Refract Surg. 2011; 37:1082–1089. [PubMed: 21596251]
31. Fukuda S, Kawana K, Yasuno Y, Oshika T. Wound architecture of clear corneal incision with or without stromal hydration observed with 3-dimensional optical coherence tomography. Am J Ophthalmol. 2011; 151:413–419. [PubMed: 21236408]
32. Yao K, Zhang Z, Yang YH, Wu XD. Aqueous humor penetration of topically applied ofloxacin, ciprofloxacin and tobramycin. Zhonghua Yan Ke Za Zhi. 2003; 39:736–739. [PubMed: 14769225]
33. Gonzalez LS, Spencer JP. Aminoglycosides: a practical review. Am Fam Phys. 1998; 58:1811–1820.
34. Chiquet C, Maurin M, Altayrac J, et al. Correlation between clinical data and antibiotic resistance in coagulase-negative Staphylococcus species isolated from 68 patients with acute post-cataract endophthalmitis. Clin Microbiol Infect. 2015; 21:592.
35. McDonald M, Blondeau JM. Emerging antibiotic resistance in ocular infections and the role of fluoroquinolones. J Cataract Refract Surg. 2010; 36:1588–1598. [PubMed: 20692574]
36. Asbell PA, Sanfilippo CM, Pillar CM, et al. Antibiotic Resistance Among Ocular Pathogens in the United States: Five-Year Results From the Antibiotic Resistance Monitoring in Ocular Microorganisms (ARMOR) Surveillance Study. JAMA Ophthalmol. 2015; 133:1445–1454. [PubMed: 26502312]
37. Schelonka LP, SaBell MA. Postcataract endophthalmitis prophylaxis using irrigation, incision hydration, and eye pressurization with vancomycin. Clin Ophthalmol. 2015; 9:1337–1345. [PubMed: 26229425]
38. Witkin AJ, Shah AR, Engstrom RE, et al. Postoperative Hemorrhagic Occlusive Retinal Vasculitis: Expanding the Clinical Spectrum and Possible Association with Vancomycin. Ophthalmol. 2015; 122:1438–1451.
39. Balducci N, Savini G, Barboni P, et al. Hemorrhagic Occlusive Retinal Vasculitis After First Eye Cataract Surgery Without Subsequent Second Eye Involvement. Ophthalmic Surg Lasers Imaging Retina. 2016; 47:764–766. [PubMed: 27548454]
40. ASCRS, ASRS. [Accessed Nov 30, 2016] Clinical alert: HORV association with intraocular vancomycin. 2016. ascrs.org/sites/default/files/HORV-Alert-Final.pdf
41. Sharma C, Biswas NR, Ojha S, Velpandian T. Comprehensive evaluation of formulation factors for ocular penetration of fluoroquinolones in rabbits using cassette dosing technique. Drug Des Devel Ther. 2016; 10:811–823.
42. Garg P, Roy A, Sharma S. Endophthalmitis after cataract surgery: epidemiology, risk factors, and evidence on protection. Curr Opin Ophthalmol. 2017; 28:67–72. [PubMed: 27661662]
43. Schwartz SG, Flynn HW. Update on the prevention and treatment of endophthalmitis. Expert Rev Ophthalmol. 2014; 9:425–430. [PubMed: 26609317]
44. Schimel AM, Miller D, Flynn HW. Evolving fluoroquinolone resistance among coagulase-negative *Staphylococcus* isolates causing endophthalmitis. Arch Ophthalmol. 2012; 130:1617–1618. [PubMed: 23229711]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

45. Milder E, Vander J, Shah C, Garg S. Changes in antibiotic resistance patterns of conjunctival flora due to repeated use of topical antibiotics after intravitreal injection. Ophthalmol. 2012; 119:1420–1424.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 1

Pathogen profile in relation to route of antibiotic prophylaxis (intracameral, topical).

	Intracameral (IC) antibiotic		No IC, topical antibiotic only			No IC or topical agent	Total
Organism isolated	**With topical agent**	**Without topical agent**	**Topical ofloxacin**	**Topical gatifloxacin**	**Topical amino-glycoside**		
Gram-positive organisms							
Coagulase-negative *Staphylococcus*	3	1	16†	12†	3	9	**43**
Streptococcus viridians	2	-	4	5	1	2	**14**
Methicillin-resistant *S. aureus*	-	-	2	1	1	3	**7**
Methicillin-sensitive *S. aureus*	-	-	2	2	-	1	**5**
Other *Streptococcus* species‡	-	-	1	2	-	2	**5**
Enterococcus species§	-	-	2	1	1	1	**5**
Propionibacterium acnes	1	-	-	-	-	-	**1**
Gram-negative organisms							
Kingella species	-	-	-	1	-	-	**1**
Pseudomonas aeruginosa	-	-	-	-	-	1	**1**
Moraxella species	1	-	-	-	-	-	**1**
Total	**7**	**1**	**27**	**24**	**6**	**19**	**83**

†One case, shown in two columns, received both topical ofloxacin and topical gatifloxacin.

‡Three cases of *S. pneumonia*, one case of *S. agalactiae* (received topical gatifloxacin only) and one case of *Streptococcus* unspecified (topical ofloxacin only).

§Four cases of *E. faecalis* and one case of *Enterococcus* species unspecified (received topical gentamicin only).

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 2

Isolates and antibiotic sensitivities in 68 Gram-positive culture-confirmed endophthalmitis cases following phacoemulsification surgery (number sensitive / number tested).

Antibiotic	*Coagulase-negative Staphylococcus* N=34	Methicillin-resistant *Staphylococcus aureus* N=6	Methicillin-sensitive *Staphylococcus aureus* N=5	*Streptococcus viridans* N=13	*Streptococcus species* N=5	*Enterococcus* N=5
Cephalosporins						
Cefazolin	13/13	0/3	2/3	4/4	1/1	0/1[§]
Ceftazidime	6/17	0/3	0/1	1/2	1/1	0/1
Ceftriaxone	9/16	0/3	1/1	9/9	2/2	0/1
Cefuroxime	7/12	1/3	--	--	1/1	0/1
Cephalothin	15/15	3/3	1/1	3/3	1/1	0/1
Fluoroquinolones [†]						
Ciprofloxacin	11/18	0/4	1/1	0/3	1/1	1/3
Gatifloxacin (surrogate for moxifloxacin)	7/12	1/3	2/2	6/7	1/2	2/3
Ofloxacin	8/14	0/3	2/3	8/8	1/2	0/1
Aminoglycosides						
Gentamicin	19/19	4/4	3/3	3/5	0/1	0/1[§]
Amikacin	14/15	1/3	1/1	0/4	0/1	0/2[§]
Neomycin	13/14	0/3	3/3	0/8	0/2	0/2[§]
Tobramycin	5/5	0/1	1/1	1/1	--	--
Polypeptides						
Bacitracin	11/14	1/3	2/3	8/8	2/2	1/2
Polymyxin B	8/14	0/3	0/3	0/8	0/2	0/2

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Antibiotic	***Coagulase-negative Staphylococcus* N=34**	**Methicillin-resistant *Staphylococcus aureus* N=6**	**Methicillin-sensitive *Staphylococcus aureus* N=5**	***Streptococcus viridans* N=13**	***Streptococcus species* N=5**	***Enterococcus* N=5**
Other						
Clindamycin	27/32	0/6	2/3	6/6	4/4	0/1[§]
Oxacillin[≠]	18/30	0/6	3/3	2/5	2/3	0/1
Sulfisoxazole	11/14	2/3	2/3	1/3	1/1	0/1
Tetracycline	20/22	3/3	3/3	1/2	0/1	--
Trimethoprim	11/14	3/3	3/3	2/4	0/1	1/1[§]
Vancomycin	32/32	6/6	5/5	9/10	5/5	4/4

[†] *Staphylococcus* or *streptococcus* species which are susceptible to gatifloxacin (or ciprofloxacin or ofloxacin) are considered susceptible to moxifloxacin because moxifloxacin has the greatest Gram-positive activity.

[≠] If a *Staphylococcus* organism is sensitive to oxacillin, it is considered sensitive to all the cephalosporins. If it is resistant to oxacillin, it is considered resistant to all the cephalosporins.

[§] *Enterococcus* is considered intrinsically resistant to cephalosporins, clindamycin and trimethoprim. Organisms tested as sensitive to trimethoprim may have *in vitro* activity, but trimethoprim is not clinically effective against Enterococcus. In addition, aminoglycosides are not effective against *Enterococcus* even if *in vitro* testing suggests susceptibility; higher doses would be required and would need to be specifically tested.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 3

Isolates and antibiotic sensitivities in 45 culture-confirmed, Gram-positive endophthalmitis cases following phacoemulsification surgery with only prophylactic topical antibiotics (number sensitive / number tested).[†]

	Topical ofloxacin[‡] (N=21)	Topical gatifloxacin[‡] (N=18)	Topical aminoglycoside (N=6)
Oxacillin	10/18	9/15	3/5
Fluoroquinolones			
Ciprofloxacin	5/9	2/7	2/5
Gatifloxacin	8/9	**3/5**	0/1
Ofloxacin	**5/10**	5/6	1/3
Aminoglycosides			
Tobramycin	2/2	2/2	**2/2**
Gentamicin	11/11	7/9	**4/4**

[†]The table does not show cases whose antibiotic sensitivity was not tested or was tested to other antibiotics.

[‡]One case, shown in two columns, received both topical ofloxacin and topical gatifloxacin.