Changing Trends in the Microbiologic Aspects of Postcataract Endophthalmitis

Franco M. Recchia, MD; Brandon G. Busbee, MD; Robert B. Pearlman, MD; Cynthia A. Carvalho-Recchia, MD; Allen C. Ho, MD

Objective: To analyze the microbiologic spectrum and in vitro susceptibility profiles over the last 11 years of organisms isolated from the vitreous of patients with endophthalmitis following cataract surgery.

Methods: Records of 497 consecutive patients treated at 1 institution for clinically suspected endophthalmitis following cataract surgery from July 1989 through June 2000 were reviewed. Results of microbiologic culture and in vitro antibiotic susceptibility testing from the periods 1989 to 1994 and 1995 to 2000 were compared.

Results: Between the 2 periods, there was a significant increase in the incidence of gram-positive bacteria (92%-97% of bacterial isolates). There was a significant increase in resistance among all bacterial isolates to ciprofloxacin (23%-37%; \( P = .02 \)). There was increased resistance among coagulase-negative staphylococci to both ciprofloxacin (20%-38%) and cefazolin (19%-40%). Resistance to bacitracin, trimethoprim-sulfamethoxazole, and vancomycin remained unchanged. Vancomycin retained in vitro efficacy against more than 99% of gram-positive bacteria. Ceftazidime was effective against 100% of gram-negative bacteria tested.

Conclusions: The spectrum of pathogens causing postcataract endophthalmitis is changing, and resistance to antibiotics used for its prophylaxis has grown. These findings may affect the empirical treatment of postcataract endophthalmitis, as well as the use and choice of antibiotics in patients undergoing cataract surgery.


ENDOPHTHALMITIS REMAINS one of the most dreaded and devastating complications of intraocular surgery. In the modern era of cataract extraction, endophthalmitis still occurs with an approximate frequency of 1 in 400 to 1 in 1700 cases of cataract extraction\(^1\)\(^4\) and accounts for significant visual morbidity.\(^3\)\(^5\) Moreover, treatment of endophthalmitis requires additional intervention, necessitates additional office visits, and incurs additional costs.

Successful treatment of endophthalmitis requires prompt diagnosis and institution of antibiotic therapy appropriate for the infectious organism. The overwhelming majority of cases of endophthalmitis following cataract extraction are caused by bacteria. Coagulase-negative staphylococcal species (of which Staphylococcus epidermidis is the most common) are identified in up to 70% of cases with vitreous cultures positive for organisms.\(^6\) These causative organisms are the main constituents of skin and conjunctiva and have been recovered from the anterior chamber in up to 21% of patients undergoing uneventful cataract surgery.\(^8\)\(^9\)

With increasing and widespread use of topical antibiotics, especially fluoroquinolone antibiotics, however, there is justifiable concern over the emergence of resistant organisms.\(^10\)\(^11\) Diminishing efficacy of antibiotics against common and virulent pathogens presents a therapeutic challenge, as well as the potential for development of more serious infections. In the recent ophthalmic literature, several authors have reported increased in vitro resistance among bacteria-causing keratitis to antibiotics commonly used in their regions.\(^13\)\(^14\)

This study was undertaken to analyze the current microbiologic aspects of organisms isolated from the vitreous of patients with postcataract endophthalmitis. Specific aims were to analyze the current spectrum of infecting organisms, to document the effectiveness of commonly used topical antibiotics, and to evaluate changing trends in antibiotic resistance among infecting organisms.
Methods

Approval from the Wills Eye Hospital (Philadelphia, Pa) institutional review board and appropriate informed consent were obtained. Database searches of inpatient hospital admissions and all microbiologic laboratory records were performed to identify all patients treated for endophthalmitis at Wills Eye Hospital from July 1, 1989, through June 30, 2000. Patient records were reviewed in detail and the following data were recorded: demographics (age, race, sex); medical history (specifically history of diabetes mellitus or immunosuppression from systemic illness or immunomodulating medications); ocular history; and etiology of endophthalmitis. Diagnosis was made on the basis of vitritis and anterior chamber inflammation.

For patients with endophthalmitis presumed secondary to recent cataract extraction, the following data were recorded: initial visual acuity, symptoms, timing of onset of symptoms, time to diagnosis, diagnostic and therapeutic interventions performed, intravitreal antibiotics used, results of aqueous and vitreous cultures, in vitro antibiotic susceptibility, and resistance of cultured organisms. Details regarding the cataract surgery (use of preoperative antibiotics, surgical technique, wound length, wound location, location and type of intraocular lens implant) were recorded where obtainable from operative reports.

Undiluted vitreous and aqueous specimens were obtained under sterile conditions and cultured by plating onto chocolate agar (37°C, in carbon dioxide), thioglycolate liquid, and enriched blood agar. Speciation was performed by standard biochemical testing methods. In vitro antibiotic susceptibility testing was performed by the Kirby-Bauer disk diffusion method in accordance with standards outlined by the National Committee for Clinical Laboratory Standards (Wayne, Pa).15,16

Two study periods (period 1, July 1989-December 1994; period 2, January 1995-June 2000), each spanning 5.5 years, were designated. Statistical comparison of rates of antibiotic resistance between the 2 periods was performed using a 2 by 2 contingency table (χ² analysis with 1 df or Fisher exact test where indicated). Linear graphs of trends in antibiotic resistance were calculated using a least squares method.

Results

Between July 1, 1989, and June 30, 2000, a total of 497 consecutive patients were treated at Wills Eye Hospital for endophthalmitis following primary cataract surgery. Demographic and baseline clinical characteristics for all 497 patients included in this study are shown in Table 1. The mean age was 73.6 years, 443 patients (89%) were white, and 287 (57%) were women. Seventy-eight patients (17%) had diabetes mellitus, and 24 (5%) had documented evidence of systemic immunosuppression.

Symptoms were documented in 81% of cases and included decreased vision (89%), pain (54%), redness (8%), floaters (3%), and photophobia (1%). Thirty percent of patients in the later study period developed symptoms within 3 days of surgery, compared with 22% in the earlier study period (P = .06).

Table 1. Demographic and Baseline Clinical Characteristics for All Patients Studied

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, mean (range)</td>
<td>73.6 (3-94)</td>
<td>73.2 (3-91)</td>
<td>74 (35-94)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>216 (43)</td>
<td>101 (40)</td>
<td>115 (48)</td>
<td>.08</td>
</tr>
<tr>
<td>Female</td>
<td>287 (57)</td>
<td>154 (60)</td>
<td>127 (52)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>443 (89)</td>
<td>230 (90)</td>
<td>213 (88)</td>
<td>.44</td>
</tr>
<tr>
<td>Nonwhite</td>
<td>54 (11)</td>
<td>25 (10)</td>
<td>29 (12)</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>78 (17)</td>
<td>39 (16)</td>
<td>39 (17)</td>
<td>.71</td>
</tr>
<tr>
<td>Absent</td>
<td>394 (83)</td>
<td>206 (84)</td>
<td>188 (83)</td>
<td></td>
</tr>
<tr>
<td>Immunosuppression†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>24 (5)</td>
<td>16 (7)</td>
<td>8 (4)</td>
<td>.14</td>
</tr>
<tr>
<td>Absent</td>
<td>448 (95)</td>
<td>229 (93)</td>
<td>219 (96)</td>
<td></td>
</tr>
<tr>
<td>Time to diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-3 d</td>
<td>99 (20)</td>
<td>38 (15)</td>
<td>61 (25)</td>
<td></td>
</tr>
<tr>
<td>4-7 d</td>
<td>184 (37)</td>
<td>92 (36)</td>
<td>92 (38)</td>
<td>.006</td>
</tr>
<tr>
<td>8-14 d</td>
<td>79 (16)</td>
<td>38 (15)</td>
<td>41 (17)</td>
<td></td>
</tr>
<tr>
<td>2-6 wk</td>
<td>70 (14)</td>
<td>41 (16)</td>
<td>29 (12)</td>
<td></td>
</tr>
<tr>
<td>&gt;6 wk</td>
<td>65 (13)</td>
<td>46 (18)</td>
<td>19 (8)</td>
<td></td>
</tr>
<tr>
<td>Initial VA‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20/400 or better</td>
<td>97 (20)</td>
<td>58 (24)</td>
<td>39 (17)</td>
<td></td>
</tr>
<tr>
<td>CF</td>
<td>95 (20)</td>
<td>46 (19)</td>
<td>49 (21)</td>
<td></td>
</tr>
<tr>
<td>HM</td>
<td>184 (38)</td>
<td>96 (40)</td>
<td>88 (37)</td>
<td>.06</td>
</tr>
<tr>
<td>LP</td>
<td>99 (21)</td>
<td>42 (17)</td>
<td>57 (24)</td>
<td></td>
</tr>
<tr>
<td>NLP</td>
<td>3 (1)</td>
<td>1 (0.4)</td>
<td>2 (1)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CF, counting fingers; HM, hand motions; LP, light perception; NLP, no light perception; VA, visual acuity.

*Values are expressed as number (percentage) of cases unless otherwise indicated. There was no statistically significant difference (P > .05) in demographic variables between the 2 periods. In the latter period, a significantly greater number of patients were diagnosed with endophthalmitis within 3 days of cataract surgery (P = .006), and there was a trend for initial visual acuity to be light perception or worse (P = .06).

†Data available for 472 patients (245 in period 1 and 227 in period 2).
‡Data available for 478 patients (243 in period 1 and 235 in period 2).
Time from cataract surgery to diagnosis was ascertained in all cases. This interval ranged from 12 hours to 25 months. In 13% of patients, the diagnosis of endophthalmitis was made more than 6 weeks following cataract surgery. A significantly greater number of cases were diagnosed within 3 days of surgery in the latter half of the study (25% vs 15%).

Overall, initial visual acuity was counting fingers or better in two fifths of patients and hand motions or better in four fifths. Three patients had an initial visual acuity of no light perception. There was a trend toward worse initial visual acuity in the latter half of the study; 25% of patients in the period 1995 to 2000 had a visual acuity of no light perception compared with 17% in the period 1989 to 1994.

In 175 (35%) of the 497 cases, no organism was cultured from the vitreous (Table 2). The probability of obtaining a vitreous culture positive for organisms declined with increasing time to diagnosis. For example, 86.3% of cultures positive for organisms occurred in cases diagnosed within 10 days of surgery. By contrast, nearly half of cultures negative for organisms occurred in patients diagnosed more than 2 weeks following surgery. The rate of culture positivity increased significantly (from 60%-70%; P=.04) between the 2 periods. Of the 322 cases (65%) with vitreous cultures positive for organisms, fungi were identified in 7 (1.4% of total cases) and bacteria were identified in 315 (63.3% of the total cases). In 9 cases, 2 bacteria were isolated. Thus, a total of 324 bacteria were identified.

The vast majority of isolates were gram-positive bacteria. In the most recent period (1995-2000), gram-positive bacteria accounted for 95% of all isolates and 97% of bacteria. In both cases, this represented an increase over the preceding period. The largest subgroup (56%) was the coagulase-negative staphylococci, consisting of 7 different species: Staphylococcus epidermidis (91%), Staphylococcus warneri (4%), Staphylococcus haemolyticus (2%), Staphylococcus hominis (1%), Staphylococcus aureus (13% of all isolates overall), Enterococcus, Propionibacterium acnes, other gram-positive species (consisting of 32 isolates of various Streptococcus species and 5 isolates of Clostridium diphtheriae). The gram-negative isolates included: Serratia, Enterobacter, Pseudomonas, Moraxella, Flavobacterium, Xanthomonas, Proteus, and Morganella.

As presented in Table 3 and Table 4, in the latter half of the 1990s (period 2), vancomycin was the only antibiotic with consistent efficacy against gram-positive bacteria. Ceftazidime was tested against 15 of 17 gram-negative isolates and was effective against all 15 (100%) (Table 5). The aminoglycoside antibiotics (gentamicin, tobramycin, and amikacin) were not tested with sufficient frequency and consistency to allow statistically valid interpretation of their efficacy. Considerably more than one third of all vitreous isolates were resistant to ciprofloxacin and cefazolin. Ofloxacin came to be included in the standard panel of susceptibility testing in early 1995; 30% of all isolates (and 35% of coagulase-negative staphylococci) were resistant to ofloxacin.

Statistical comparison of the 2 study periods (Table 4) revealed a significant increase in resistance to ciprofloxacin. Among coagulase-negative staphylococci, resistance rose to both ciprofloxacin (20%-38%; \( P = .01 \)) and to cefazolin (19%-40%; \( P = .005 \)). Even accounting for the 8 isolates with no reported sensitivity profile, this increase in resistance remained significant. Resistance to bacitracin rose (from 4%-10%) but not to a statistically significant degree. Resistance to vancomycin and trimethoprim-sulfamethoxazole remained unchanged.

Endophthalmitis is a debilitating and costly complication of cataract surgery. Numerous studies have been conducted to identify risk factors, etiologies, and optimal therapies. The present findings of vitreous culture pos-
tivity (65%) and the preponderance of coagulase-negative staphylococci (54% of positive cultures) are consistent with those published as part of the Endophthalmitis Vitrectomy Study. In addition, the spectrums of antibiotic susceptibility of coagulase-negative staphylococci are nearly identical for corresponding periods. To our knowledge, the present study is the first, however, to demonstrate significant changes over the past decade in the in vitro susceptibility patterns of bacteria isolated from the vitreous of patients with endophthalmitis following cataract surgery.

We reviewed all cases of endophthalmitis treated over an 11-year period at Wills Eye Hospital, a tertiary care institution with a large referral base in the mid-Atlantic United States. Our data show a statistically significant increase, between the periods 1989 to 1994 and 1995 to 2000, in the resistance of gram-positive bacteria to ciprofloxacin and in the resistance of coagulase-negative staphylococci to ciprofloxacin and to cefazolin. The 2 study periods of equivalent length were designed to allow comparison with the results from the Endophthalmitis Vitrectomy Study, which spanned from 1989 to 1994. Resistance to bacitracin, vancomycin, and trimethoprim-sulfamethoxazole remained statistically unchanged. It is reassuring to find that vancomycin, which is the intravitreal antibiotic of choice for the treatment of gram-positive organisms, has maintained its high efficacy.

Davis et al reported an increase in resistance among coagulase-negative staphylococci to gentamicin and methicillin between the periods 1973 to 1981 and 1982 to 1986. The present study, involving newer antibiotics over a more recent and shorter interval, recapitulates the earlier findings of increasing resistance.

The present work has significance and relevance for any ophthalmologist who performs cataract surgery or who is involved in the perioperative care of patients with cataract. There are 2 important clinical scenarios on which this study may bear: (1) use of preoperative topical antibiotics and (2) treatment of postcataract endophthalmitis.

The advisability of preoperative topical antibiotics before routine cataract surgery is controversial. More than 75% of ophthalmologists in the United States and abroad use preoperative antibiotics, of which the fluoroquinolones have grown increasingly popular. The theoretical advantage is reduction of conjunctival flora and eradication of organisms sensitive to the antibiotic given. However, complete sterilization of the conjunctiva is never achieved. In a recent, large survey of German ophthalmologists, use of topical preoperative antibiotics was associated with a significantly increased risk of development of infection. Furthermore, it has been speculated that widespread use of antibiotics may contribute to emerging bacterial resistance, presumably by selecting for genetically mutated strains. The real contribution of topical ocular antibiotic drops to this increased resistance, however, remains unclear. Our data suggest, for example, that 2 topical antibiotics commonly used during the study periods—ciprofloxacin and ofloxacin—would be effective against barely 60% of the coagulase-negative staphylococci that they are intended to eradicate. This modest benefit would have to be weighed against the cost, inconvenience, and potential adverse effects of the medication.

Empirical treatment of the patient suspected of having endophthalmitis typically includes antibiotics with activity against both gram-positive and gram-negative organisms. From our data, it appears that vancomycin remains effective against gram-positive bacteria in vitro and should remain the intravitreal drug of choice for antimicrobial treatment against these organisms. Cefazidime was effective against all 15 gram-negative bacteria against which it was tested in vitro. By contrast, while cefazolin and the fluoroquinolones may once have been effective in empirical therapy, their appropriateness as first-line agents should be reconsidered based on the present data.

Fourth-generation fluoroquinolones, introduced since the termination of the later study period, have been used with increasing frequency. However, substantive conclusions regarding their efficacy in the context of the present study cannot be made because of their relative novelty. Moreover, these newest antibiotics may not be in widespread use in all parts of the world.

The present study suffers the limitations of any retrospective review, particularly with respect to inconsistent details regarding patients’ perioperative course and manifestation. However, this study is primarily a microbiologic survey, and as such, its main strength is the unparalleled number of consecutive isolates analyzed in a consistent and standardized method over 11 years. Additionally, the study reinforces the importance and necessity of surveillance studies to monitor changing microbiologic patterns and to assess efficacy of contemporary therapies.

Two important clinical questions for further investigation are prompted by this study:

1. Is the use of preoperative topical antibiotics associated with increased chance of infection with a resistant organism? While, admittedly, a number of environmental, epidemiologic, humoral, and perioperative factors contribute to the development of endophthalmitis, the role of preoperative antibiotics cannot be minimized.

2. Does infection with a resistant bacterium portend a worse clinical outcome? For example, in experimentally induced endophthalmitis in rabbits, infection with...
multidrug-resistant strains of *S. epidermidis* caused significantly more intraocular inflammation and retinal destruction than did infection with sensitive strains.23

In summary, when prescribing any antibiotic, ophthalmologists must be aware of the suspected bacterial pathogens and the effectiveness of the antibiotic against these pathogens. The present data suggest that empirical treatment with intravitreal administration of vancomycin and cefazidime remains appropriate. The data further suggest diminished in vitro efficacy of ciprofloxacin and cefazolin against those pathogens responsible for the majority of cases of postcataract endophthalmitis. The diminished efficacy of frequently used antibiotics should be considered when deciding on empirical treatment for patients with suspected postcataract endophthalmitis. In addition, from a global, epidemiological standpoint, the current findings of emerging resistance should remind physicians to be judicious in their use of antibiotics in any patient, bearing in mind that indiscriminate use may potentially contribute to the undesirable consequence of increased resistance.

Submitted for Publication: October 10, 2003; final revision received August 12, 2004; accepted August 12, 2004.

Correspondence: Franco M. Recchia, MD, Division of Vitreoretinal Diseases and Surgery, Vanderbilt Eye Institute, 8018 Medical Center East, Nashville, TN 37232 (franco.recchia@vanderbilt.edu).

Funding/Support: This study was supported in part by the Heed Ophthalmic Foundation, Cleveland, Ohio (Dr Recchia).

Previous Presentation: This study was presented in part at the Association for Research in Vision and Ophthalmology (ARVO) Meeting; May 9, 2002; Fort Lauderdale, Fla, and the Retina Congress; October 1, 2002; San Francisco, Calif.

Additional Information: Dr Recchia had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

REFERENCES


