Microbiological Spectrum and Antibiotic Sensitivity in Endophthalmitis

A 25-Year Review

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Purpose: To identify the spectrum and susceptibility pattern of pathogens responsible for culture-positive endophthalmitis referred to a single institution and investigate possible trends in both pathogens and antibiotic sensitivities over the past 25 years.

Design: A retrospective, laboratory-based study of consecutive microbiological isolates.

Participants: A total of 988 consecutive culture-positive endophthalmitis isolates from 911 eyes.

Methods: All culture-positive endophthalmitis isolates collected from 1987 to 2011 were identified. Susceptibility rates to a variety of antibiotics were calculated. Chi-square test for trend was used to detect changes in spectrum or susceptibility over time.

Main Outcome Measures: Microbial spectrum and susceptibility pattern over time.

Results: A total of 988 isolates were identified from 911 eyes. The average patient age was 67±18 years, and 55% of the patients were female. The most prevalent pathogens were coagulase-negative staphylococcus (39.4%), followed by *Streptococcus viridans* species (12.1%) and *Staphylococcus aureus* (11.1%). Gram-negative organisms and fungi accounted for 10.3% and 4.6% of all isolates, respectively. With the exception of 2 isolates, *Enterococcus faecium* and *Nocardia exalbida*, all the other 725 (99.7%) gram-positive bacteria tested were susceptible to vancomycin. Of the 94 gram-negative organisms tested against ceftazidime, 2 were of intermediate sensitivity and 6 were resistant. For 8 antibiotics, increasing microbial resistance over time was observed: cefazolin ($P = 0.02$), cefotetan ($P = 0.006$), cephalothin ($P<0.0001$), clindamycin ($P = 0.04$), erythromycin ($P<0.0001$), methicillin/oxacillin ($P<0.0001$), ampicillin ($P = 0.01$), and ceftriaxone ($P = 0.006$). For 3 antibiotics, increasing microbial susceptibility was observed: gentamicin ($P<0.0001$), tobramycin ($P = 0.005$), and imipenem ($P<0.0001$).

Conclusions: Coagulase-negative staphylococcus remains the most frequently identified cause of endophthalmitis. Vancomycin and ceftazidime seem to be excellent empiric antibiotics for treating endophthalmitis. Although a statistically significant trend toward increasing microbial resistance against a variety of antibiotics, including cephalosporins and methicillin, was observed, a significant trend toward decreasing microbial resistance against aminoglycosides and imipenem also was detected. *Ophthalmology 2014;■:1–9 © 2014 by the American Academy of Ophthalmology.*

Endophthalmitis remains one of the most challenging and devastating complications faced by the ophthalmologist. Accurate diagnosis and appropriate and timely treatment are required to prevent irreversible loss of vision.[1–3] The microbial spectrum and sensitivity pattern of endophthalmitis depend on the cause, geographic location, and population studied.[2,4] In the acute setting of endophthalmitis, empiric intravitreal antibiotics against both gram-negative and gram-positive bacteria are the mainstay of treatment.[3] The current recommendation for empiric therapy is a combination of vancomycin and ceftazidime given intravitreally.[3] Numerous studies have evaluated the efficacy of third- and fourth-generation fluoroquinolones against endophthalmitis isolates and noted the increasing resistance of bacteria to these agents, as well as to methicillin/oxacillin.[4–8] New antibiotics continue to be developed as infecting organisms adapt and become resistant to older antibiotics.

Despite ongoing attempts and evolving strategies to prevent it, the incidence of endophthalmitis after intraocular surgery has remained rather stable, ranging from 0.04% to 0.13%, since the transition to prominently extracapsular cataract extraction techniques.[9–13] Current accepted standards for prevention of endophthalmitis include the use of 5% povidone iodine solution in the preparation before surgery, a simple measure that has conclusively been shown to lower the incidence of endophthalmitis after cataract surgery.[14] In the landmark European Society of Cataract and Refractive Surgeons trial and several other prospective and retrospective studies, intracameral antibiotics at the end of cataract surgery also have been associated with a lower incidence of endophthalmitis.[15–18] The use of perioperative topical antibiotics and antibiotics in the irrigating solutions during surgery remains controversial. Critics of prophylactic antibiotic use cite the potential for increasing

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the risk of bacterial resistance, a phenomenon that has been demonstrated in the setting of prophylactic topical antibiotics with intravitreal anti-vascular endothelial growth factor injections.[19,20]

Monitoring the causative organisms of endophthalmitis and their resistance is important in detecting trends to guide changes in our empiric management of endophthalmitis or reaffirm current practices. The purpose of this study was to characterize the spectrum of pathogens responsible for culture-positive endophthalmitis and investigate possible trends of changes in the microbial spectrum and antibiotic susceptibility patterns over the past 25 years.

Methods

This was a retrospective, noncomparative, consecutive laboratory-based microbiologic series of all culture-positive aqueous or vitreous samples submitted to the microbiology laboratory at the New York Eye and Ear Infirmary between January 1, 1987, and December 31, 2011. Approval was obtained by the institutional review board at the New York Eye and Ear Infirmary, and the tenets of the Declaration of Helsinki were adhered to.

For each positive culture identified, the age, gender, and eye were recorded, when available, in addition to the date of specimen submission, type of specimen (aqueous or vitreous sample), organisms isolated, and each isolate's antibiotic sensitivities to a variety of antibiotics. Antibiotic sensitivity testing was performed using the Kirby–Bauer disk diffusion method before June of 1998. After June 1998, antibiotic sensitivity testing was performed using the Vitek automated system, initially using Vitek 1 (bioMérieux, Inc, Marcy-L'Étoile, France) and then Vitek 2 (bioMérieux, Inc) after 2005. An isolate's antibiotic sensitivity was recorded as susceptible, intermediate, or resistant and was determined using guidelines from the Clinical and Laboratory Standards Institute.

The microbiology laboratory along with the Department of Ophthalmology at the New York Eye and Ear Infirmary determined the spectrum of antibiotics tested against individual pathogens on the basis of available ophthalmic antibiotics and current literature regarding bacterial sensitivities and resistances. The "percentage susceptible" was calculated as the number of susceptible isolates over the total number of isolates times 100 and grouped into five 5-year intervals from 1987 to 2011 when possible. Statistical analysis was performed using the chi-square test for trend when appropriate. For antibiotic sensitivities that were in use for $\leq$12 years, analysis for trend was performed using data from consecutive 3-year intervals. Because the fourth-generation fluoroquinolones moxifloxacin and gatifloxacin were introduced to the ophthalmic marketplace in 2003, susceptibility testing was unavailable for these agents from 1997 to 2003. In addition, the Vitek 2 stopped testing for ofloxacin in 2006 and used ciprofloxacin as a representative antibiotic for this generation of fluoroquinolone antibiotic. Since 1992, methicillin sensitivity testing was performed using oxacillin according to Clinical and Laboratory Standards Institute guidelines.

Results

A total of 988 endophthalmitis isolates were cultured from 911 eyes over the 25-year study period. A total of 618 of the isolates were obtained from a vitreous sample only, 201 were obtained from an aqueous sample only, and 169 were obtained from both aqueous and vitreous samples. Sixty-three eyes yielded 2 isolates, and 7 eyes yielded 3 isolates. The average number of endophthalmitis isolates per year was 40±18 (median, 39; range, 12–74). The average patient age was 67±18 years, and 55% of the patients were female; 50.5% of the isolates were obtained from the right eye. Fifty samples did not include age data, 15 samples did not include gender, and 12 samples did not include laterality.

Spectrum of Organisms

Overall, 85.1% of isolates were gram-positive, 10.3% were gram-negative, and 4.6% were fungal. The most common pathogens were *Staphylococcus epidermidis* (30.3%), followed by *Streptococcus viridans* species (12.1%), *Staphylococcus aureus* (11.1%), and other coagulase-negative staphylococci (9.1%). Among the gram-negative organisms isolated, *Enterobacteriaceae* (3.4%) and *Pseudomonas aeruginosa* (2.5%) were encountered most frequently. *Candida* was the most frequently isolated fungus (2.8%). A detailed overview of endophthalmitis isolates is provided in Table 1.

Table 1. Endophthalmitis Isolates from 1987 to 2011

Isolates	N	% Total
Gram-positive	841	85.1
Staphylococcus epidermidis	299	30.3
Streptococcus viridans group*	120	12.1
Staphylococcus aureus	110	11.1
Other coagulase-negative *Staphylococci*†	90	9.1
Propionibacterium acnes	87	8.8
Streptococcus pneumoniae	51	5.2
Enterococcus species	22	2.2
Bacillus species‡	15	1.5
Other *Streptococcus* species§	16	1.6
Corynebacterium species	13	1.3
Gemella species	7	0.7
Other gram-positive bacteria	11	1.1
Gram-negative	102	10.3
Enterobacteriaceae‖	34	3.4
Pseudomonas aeruginosa	25	2.5
Fastidious gram-negative¶	27	2.7
Branhamella catarrhalis	7	0.7
Other gram-negative bacteria#	9	0.9
Fungi	45	4.6
Candida species**	28	2.8
Aspergillus species††	6	0.6
Other fungi‡‡	11	1.1
Total	988	100

*S. *acidominimus*, S. *constellatus*, S. *gordonii*, S. *intermedius*, S. *mitis*, S. *oralis*, S. *parasanguinis*, S. *salivarius*, S. *sanguis*, S. *uberis*.
†S. *auricularis*, S. *capitis*, S. *chromogenes*, S. *cohnii*, S. *haemolyticus*, S. *hominis*, S. *lugdunensis*, S. *saprophyticus*, S. *simulans*, S. *warneri*, S. *xylosus*.
‡B. *cereus*, B. *subtilis*.
§Beta-hemolytic *streptococcus*, S. *agalactiae*.
‖*E. coli*, *Enterobacter* sp., *K. pneumonia*, *Proteus* sp., *Serratia* sp., *S. sonnei*.
¶*Acinetobacter* sp., *Haemophilus* sp., *Moraxella* sp., *Neisseria* sp.
#A. *hydrophila*, A. *xylosoxidans*, C. *indoltheticum*, *Burkholderia* sp., *F. meningosepticum*.
**C. *albicans*, C. *glabrata*, C. *dubliniensis*, C. *guilliermondii*, C. *parapsilosis*, C. *tropicalis*, C. *lusitaniae*, C. *zeylanoides*.
††A. *niger*, A. *flavus*, A. *fumigatus*.
‡‡*Acremonium* sp., *Fusarium* sp., *Metarhizium* sp., *Penicillium* sp., *Rhodotorula* sp., *Cryptococcus* sp., *Wangiella* sp., unknown fungus.