



# The Susceptibility of Bacterial Endophthalmitis Isolates to Vancomycin, Ceftazidime, and Amikacin: A 23-Year Review

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**Purpose:** To investigate the in vitro susceptibility of gram-positive (GP) and gram-negative (GN) endophthalmitis bacterial isolates to vancomycin (VAN), amikacin (AMK), and ceftazidime (CEF) over a 23-year period.

**Design:** Retrospective noncomparative laboratory case series.

**Participants:** Culture-positive bacterial isolates derived from endophthalmitis patients.

**Methods:** Laboratory records of bacteria isolated from endophthalmitis specimens collected from January 1, 1993, to December 31, 2015, were reviewed for incidence and standard susceptibility testing.

**Main Outcome Measures:** The in vitro susceptibilities of bacteria cultured from endophthalmitis to VAN, AMK, and CEF.

**Results:** Patients with endophthalmitis had positive results from cultures for bacteria in 665 cases. Coagulase-negative staphylococci (CoNS) were the most common bacteria (54.6%), followed by streptococci (Strep) (20.8%), *Staphylococcus aureus* (10.2%), other GP bacteria (7.4%), and GN bacteria (7.1%). All GP organisms were susceptible to VAN, with the exception of 2 isolates. The in vitro susceptibilities of bacteria to AMK were CoNS, 95.3%; *S aureus*, 75.0%; Strep, 8.0%; GN, 95.7%; and other GP bacteria, 81.1%. The in vitro susceptibilities of bacteria to CEF were CoNS, 58.5%; *S aureus*, 54.4%; Strep, 84.1%; GN isolates, 93.6%; and other GP bacteria, 52.8%. There was no significant difference between AMK (95.7%) and CEF (93.6%) for GN coverage. For CoNS, *S aureus*, and other GP bacteria, AMK provided better coverage than CEF ( $P < 0.05$ , Fisher exact test); however, CEF seemed to provide better coverage ( $P < 0.001$ , Fisher exact test) for Strep than AMK did.

**Conclusions:** Based on standard in vitro susceptibility testing, VAN remains an optimal antibiotic choice for the treatment of GP endophthalmitis. AMK and CEF seem to provide equal GN coverage, but AMK seems to provide better coverage for CoNS, *S aureus*, and other GP bacteria, but not Strep isolates. *Ophthalmology Retina* 2016;■:1–4 Published by Elsevier on behalf of the American Academy of Ophthalmology

Bacterial endophthalmitis is a rare and typically severe intraocular infection that can occur following either intraocular surgery or traumatic injury to the eye, or can result from metastatic spread from an endogenous infection. Prompt treatment is mandatory to minimize severe vision loss and ocular morbidity. Samples of intraocular fluid are sent for culture while broad-spectrum intravitreal antimicrobial therapy is started. In cases of endophthalmitis with positive results from cultures, antibiotic therapy is tailored to the cultured microbe after culture results are available.<sup>1,2</sup>

Both to continue to optimally treat bacterial endophthalmitis and to minimize the risk of postprocedure endophthalmitis with prophylactic antibiotics, an understanding of endophthalmitis microbial spectra and antibiotic-susceptibility patterns is important. This information is important in either influencing a change in management or confirming that current practices are optimal.

Vancomycin (VAN) is established as first-line therapy in the treatment of gram-positive (GP) bacterial

endophthalmitis, whereas amikacin (AMK) or ceftazidime (CEF) are typically used for gram-negative (GN) coverage.<sup>2</sup> There are few reports of VAN-resistant GP bacteria in endophthalmitis.<sup>3</sup> Given the increasing concern with the emergence of VAN resistance in systemic bacterial infections, using an antibiotic combination where both antibiotics are effective against GP isolates would be beneficial and may indeed become a factor in determining the choice of the second antibiotic. The purpose of this study was to investigate the in vitro susceptibility of GP and GN endophthalmitis bacterial isolates to VAN, AMK, and CEF over a 23-year period.

## Methods

This was a retrospective, noncomparative laboratory case series. The microbiology laboratory records of bacterial cultures isolated from bacterial endophthalmitis from culture results that were positive for bacteria at the Charles T. Campbell Eye Microbiology

Table 1. Bacteria Isolated from the Intraocular Fluid of Patients Diagnosed with Endophthalmitis

Isolate	Number of Isolates	Percentage of Isolates
Coagulase-negative staphylococci	363	54.6
Streptococci	138	20.8
<i>Staphylococcus aureus</i>	68	10.2
Other gram-positive bacteria	49	7.4
<i>Propionibacterium acnes</i>	15	2.3
<i>Bacillus cereus</i>	13	2.0
Diphtheroids	12	1.8
Remaining gram-positive bacteria	9	1.4
Gram-negative isolates	47	7.0
<i>Haemophilus</i> species	8	1.2
<i>Serratia marcescens</i>	8	1.2
<i>Pseudomonas aeruginosa</i>	7	1.1
<i>Moraxella</i> species	3	0.5
Other gram-negative bacteria	21	3.2
Total	665	

Lab, University of Pittsburgh Medical Center, a regional tertiary referral center, between January 1, 1993, and December 31, 2015, were reviewed. These data are used for determining susceptibility profiles for the in-house and community ophthalmology practices as mandated by the College of American Pathologists (Northfield, IL) for certification. These data are deidentified to protect the privacy of the patients. Clinical presentations, circumstances, and outcomes are not available in laboratory records. In vitro susceptibility to VAN, AMK, and CEF was assessed using the Kirby–Bauer disk diffusion method with serum breakpoint standard interpretations.<sup>4</sup> The intravitreal concentrations of the tested antibiotics are higher than can be achieved systemically, and thus the serum standards may overreport resistance.

Specimens were obtained from varying combinations of anterior chamber, vitreous humor, and vitrectomy samples. Study outcome measures included bacterial species identified, as well as the in vitro susceptibility of these identified organisms to VAN, AMK, and CEF.

## Results

### Endophthalmitis Isolates

A total of 665 bacterial endophthalmitis isolates were cultured over the 23-year study period.

### Spectrum of Organisms

In all, 92.9% of isolates were GP and 7.1% were GN. Coagulase-negative staphylococci (CoNS) were the most commonly cultured bacteria (54.6%), followed by streptococci (20.8%) and *Staphylococcus aureus* (10.2%). Other GP bacteria accounted for 7.4% of isolates. Among the GN bacteria isolated, *Serratia marcescens* (1.2%), *Haemophilus* species (1.2%) and *Pseudomonas aeruginosa* (1.1%) were the mostly frequently cultured organisms. An overview of the isolates cultured is provided in Table 1.

### Susceptibility of Gram-Positive Isolates to Vancomycin

All GP bacteria, with the exception of 2 isolates (*Lactobacillus* and *Fusobacterium varium*) were susceptible to VAN, including all CoNS, streptococci, and *S aureus* isolates (Table 2).

Table 2. Susceptibility of Gram-Positive Isolates to Vancomycin

Isolate	Number Susceptible	Percentage Susceptible (Number Susceptible/ Tested)
Coagulase-negative staphylococci	363	100.0
Streptococci	138	100.0
<i>Staphylococcus aureus</i>	68	100.0
Other gram-positive isolates	35	94.6
Total		99.7

### Susceptibility of Gram-Negative Isolates to Ceftazidime and Amikacin

A total of 93.6% of GN isolates were susceptible to CEF, and 95.7% were susceptible to AMK. Among the most commonly isolated GN organisms, all *S marcescens* isolates were susceptible to CEF and AMK. Among *Haemophilus* cultures, 87.5% were susceptible to CEF and 100% to AMK. Last, 85.7% of *P aeruginosa* isolates were susceptible to CEF and AMK. Table 3 includes the susceptibility of GN isolates to both CEF and AMK. Overall, 3 GN isolates were found to be resistant to CEF and 2 GN isolates were found to be resistant to AMK; these tallies both include a *Pseudomonas* isolate that was resistant to both antibiotics.

### Susceptibility of Gram-Positive Isolates to Ceftazidime and Amikacin

Next, to determine whether dual coverage of GP isolates is attainable with the use of either CEF or AMK, the susceptibilities of the cultured GP isolates to both CEF and AMK were reviewed. Overall, there was no significant difference between AMK (89.8%) and CEF (91.8%) for GN coverage. However, AMK provided better coverage than CEF for CoNS, *S aureus*, and other GP bacteria ( $P < 0.05$ , Fisher exact test). In contrast, CEF seemed to provide better coverage ( $P < 0.001$ , Fisher exact test) for streptococci than AMK did.

## Discussion

The prompt diagnosis and immediate initiation of treatment in infectious endophthalmitis is a critical factor in ensuring a successful outcome and minimizing ocular morbidity.<sup>5</sup> The appropriate empiric treatment of infectious endophthalmitis requires an understanding of the likely causative microbes, as well as their susceptibility profiles. Here we report the spectrum of endophthalmitis bacterial isolates cultured over a 23-year period at our institution. Notably, our sample size of 665 cultured isolates places this study among the largest reviews of endophthalmitis isolates reported. Our results show that GP bacteria account for most bacterial endophthalmitis cultured isolates (92.9%), with GN bacteria accounting for only 7.1% of cultures. These data are consistent with those of other recently published reviews of endophthalmitis isolates<sup>6–11</sup> (Table 4), with the exception of the data reported by Reddy et al<sup>12</sup> from Hyderabad, India. The high proportion of GN isolates observed in their study

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