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Microbial profile and antibiotic susceptibility trend in postoperative endophthalmitis: a 12-year review

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Abstract

Objective: To identify the microbial profile and susceptibility pattern of pathogens responsible for culture-proven postoperative endophthalmitis, and to investigate possible trends in both pathogens and antibiotic sensitivities.

Methods: The retrospective study was conducted at Aga Khan University Hospital, Karachi, and comprised record of ophthalmology patients from January 1, 2005, to December 31, 2016. Culture and sensitivity reports of vitreous and aqueous humor samples from all the patients were retrieved from the medical record section of the hospital. SPSS 19 was used for data analysis.

Results: Of the samples of 202 patients with a mean age of 58.2±15.8 years, 106(52.5%) were culture-positive. Of them, 55(51.8%) had gram-negative bacteria, 41(38.6%) had gram-positive bacteria, and 10(9.4%) had fungi. Among gram-positive bacteria, coagulase-negative staphylococcus was the principal isolate 18(17%) and among gram-negative bacteria, it was pseudomonas species 20(18.8%). Spectrum of gram-positive sensitivities included vancomycin 100%, gentamicin 91.5%, amikacin 100%, ciprofloxacin 68%, chloramphenicol 100%, and tetracycline 84.6%. Among gram-negative organisms, the sensitivities were ciprofloxacin 52.9%, ofloxacin 66.6%, ceftazidime 91.8%, amikacin 100%, tobramycin 100% imipenem 91.6%, gentamicin 81.2% and tetracycline 75%.

Conclusions: Vancomycin and ceftazidime were the best empirical antibiotic selection to treat postoperative endophthalmitis.

Keywords: Endophthalmitis, Microbiology, Antibiotic susceptibility, Postoperative.
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Introduction

Postoperative endophthalmitis is considered the most common form of endophthalmitis, and mostly occurs after cataract surgeries and intravitreal injections with reported incidence rates ranging from 0.012% to 1.3%¹ and 0.016% to 0.053%² respectively. If untreated, or treated inappropriately, it can rapidly progress to blindness. Therefore, it is very important to promptly commence appropriate empirical intravitreal antibiotic treatment followed by targeted antibiotic therapy once the final microbiological culture and sensitivities are available through culture of intraocular fluids.^{3,4} Moreover, it is also crucial to identify emerging causative bacterial strains resistant to routinely-used antibiotics, and to assess the microbial spectrum of newer antimicrobial therapies.⁴

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There have been a few large-scale studies in Western literature on the types of infectious agents causing postoperative endophthalmitis.⁴⁻⁷ However, from Pakistan, limited data is available on antimicrobial susceptibility of aetiological agents of postoperative endophthalmitis. Hence, there is a need to develop such guidelines and to identify most common antibiotics from antimicrobial susceptibility data for empirical therapy of postoperative endophthalmitis.

The current study was planned to identify the frequently occurring pathogens causing postoperative endophthalmitis and the pattern of susceptibilities of the bacterial isolates to the commonly-used antibiotics.

Materials and Methods

The retrospective descriptive case series was conducted at the Department of Ophthalmology, Aga Khan University Hospital (AKUH), Karachi. Data of culture and sensitivity reports of vitreous and aqueous humor samples from all

the patients from January 1, 2005, to December 31, 2016, were retrieved from medical records after approval was obtained from the institutional ethics review committee. Data related to cases of clinically diagnosed postoperative endophthalmitis. Culture-positive cases were included, while those which failed to show any growth of organism on standard culture media were excluded. No restriction was applied related to the type of surgery or procedure that resulted in endophthalmitis. Samples from vitreous and aqueous humor had been inoculated in sterile container and cultured in the AKUH microbiology laboratory. The samples were inoculated directly onto different media, including blood, chocolate, MacConkey agar, sabouraud agar and thioglycolate broth. Blood and chocolate agar plates were incubated at 5-10% carbon dioxide (CO₂) atmosphere. MacConkey agar, sabouraud agar and thioglycolate broth were incubated at 37°C in ambient air. The cultures were examined after 24 and 48 hours of incubation.

Antibiotic susceptibility was determined for all positive cultures using the Kirby-Bauer disc diffusion method. Antibiotic susceptibility testing of isolated bacteria was performed in vitro on ceftazidime (30µg), ciprofloxacin (5µg), tobramycin (10µg), amikacin (30µg), gentamicin (10µg), tetracycline (30µg), vancomycin (30µg) and chloramphenicol (30µg) using the Kirby-Bauer disc diffusion method. Bacterial susceptibilities were recorded as resistant, intermediate and sensitive. The antibiotic susceptibility was determined in accordance with the methods of the Clinical and Laboratory Standards Institute (CLSI).⁸

Overall, antibiotic sensitivities for gram-positive organisms and gram-negative organisms were calculated by finding the percentage of those organisms that were sensitive to each particular antibiotic.

Data was analysed using SPSS 19. Frequencies and percentages were used to express the sensitivities of particular antibiotics for the organisms.

Results

Of the samples of 202 patients with a mean age of 58.2±15.8 years, 106(52.5%) were culture-positive. Of them, 55(51.8%) had gram-negative bacteria, 41(38.6%) had gram-positive bacteria, and 10(9.4%) had fungi. Among fungi, 7(6.6%) were yeast and 3(2.8%) were molds. Out of gram-positive bacteria, the principal bacterial agent isolated was coagulase-negative staphylococcus (CoNS),

Table-1: List of bacterial strains isolated from vitreous specimen.

S#	GRAM POSITIVE ORGANISM	n (%)
1	Coagulase negative staphylococcus	18 (16.9)
2	Streptococcus species	11 (10.3)
3	Streptococcus group D	4 (3.7)
4	Bacillus species	3 (2.8)
5	Enterococcus species	2 (1.8)
6	Corynebacterium species	2 (1.8)
7	Staphylococcus aureus	1 (0.9)
	Total	41 (38.6)
	GRAM NEGATIVE ORGANISM	
1	Pseudomonas species	20 (18.8)
2	Pseudomonas aeruginosa	9 (8.4)
3	Enterobacter species	8 (7.5)
4	Acinetobacter species	8 (7.5)
5	Stenotrophomonas maltophilia	4 (3.7)
6	E coli	3 (2.8)
7	Haemophilus influenzae	3 (2.8)
	Total	55 (51.8)
	FUNGI	
	YEAST	
1	Candida tropicalis	4 (3.8)
2	Candida parapsilosis	3 (2.8)
	Total	7 (6.6)
	MOLD	
1	Aspergillus fumigatus	1 (0.94)
2	Aspergillus terreus	1 (0.94)
3	Fusarium species	1 (0.94)
	Total	3 (2.8)
	Total fungi (Yeast and molds)	10 (9.4)

while among gram-negative bacteria, *Pseudomonas* species (spp.) were the most common isolated organisms (Table 1).

Among the 41 gram-positive organisms identified, overall sensitivities noted were vancomycin 100%, gentamicin 91.5%, amikacin 100% ciprofloxacin 68%, chloramphenicol 100%, and tetracycline 84.6%. Among the 55 gram-negative organisms identified, overall sensitivities noted were ciprofloxacin 52.9%, ofloxacin 66.6%, ceftazidime 91.8%, amikacin 100%, tobramycin 100% imipenem 91.6%, gentamicin 81.2% and tetracycline 75% (Table 2).

Discussion

The study found that 52.5% of the identified endophthalmitis cases were culture-positive over a period of 12 years. Gram-negative organisms were most commonly isolated, followed by gram-positive bacteria. Fungi accounted for only 9.4% cases. The culture-positive rate is almost similar to rates in literature that range from 33.3% to 60%.⁹⁻¹¹

Table-2: Percentages of sensitivities of endophthalmitis-causing organisms to commonly used antibiotics.

S#	Gram Positive Organism	Amikacin	Chloramphenicol	Gentamicin	Erythromycin	Ciprofloxacin	Tetracycline	Vancomycin	Ofloxacin
1	Coagulase negative staphylococcus	100	100	88.8	90	55.5	88.8	100	NT
2	Streptococcus species	NT	100	NT	100	NT	NT	100	54.5
3	Streptococcus group D	NT	100	NT	NT	NT	NT	100	100
4	Bacillus species	100	100	100	NT	100	100	100	66.6
5	Enterococcus species	NT	100	100	00	NT	00	100	NT
6	Corynebacterium species	100	100	NT	NT	100	100	100	NT
7	Staphylococcus aureus	100	100	NT	100	100	100	100	NT
	Gram Negative Organism	Amikacin	Ceftazidime	Gentamicin	Tobramycin	Ciprofloxacin	Tetracycline	Levofloxacin	Imipenem
1	Pseudomonas species	100	90	70	100	15	NT	NT	100
2	Pseudomonas aeruginosa	100	100	100	100	100	NT	NT	100
3	Enterobacter species	100	100	87.5	NT	15	37.5	NT	100
4	Acinetobacter species	100	75	100	100	100	75	NT	50
5	Stenotrophomonas maltophilia	NT	100	NT	NT	NT	NT	100	NT
6	E coli	100	NT	33	100	33	00	NT	100
7	Haemophilus influenzae	NT	NT	NT	NT	100	100	NT	NT

NT =Not tested

For the successful management of endophthalmitis, implementation of empirical antibiotic therapy to cover the common organisms from data of microbial spectrum and its trend of susceptibility of different micro-organism causing endophthalmitis is very crucial. Studies have reported different microbiological spectrum of causative organisms and trend of susceptibility according to various clinical settings.¹² In our 12-year review of postoperative endophthalmitis, *Pseudomonas* spp and CoNS were the most frequently isolated aetiological organisms. All gram-negative bacteria were largely susceptible to amikacin and ceftazidime in vitro, whereas all gram-positive bacteria were susceptible to vancomycin, amikacin and chloramphenicol. A retrospective analysis in India found a culture-positive rate of 34.6% from a total of 1,110 cases.¹³ *Staphylococcus epidermis* was the most common isolate followed by *Pseudomonas* spp.¹³

Endophthalmitis can be successfully managed if there is an up-to-date local data on the most common causative micro-organisms involved and their response to routinely used intravitreal antibiotics. The antibiotic therapy for bacterial endophthalmitis should ideally be broadspectrum to cover most of the likely causative bacteria.

The current study showed higher resistance of postoperative endophthalmitis isolates to ciprofloxacin. This finding is consistent with studies.¹⁴ Resistance to fluoroquinolones has emerged as a major challenge as newer and more expensive drugs are being used as treatment options. High resistance rates of gram-negative

bacteria to fluoroquinolones (18%-29%) were also seen in a study from the region.¹³

We found no evidence of emerging resistance to vancomycin which is generally reserved as an empirical intravitreal antibiotic. Intravitreal vancomycin plus either amikacin or ceftazidime should be the firstline treatment for postoperative endophthalmitis in our setting as is the current practice in many other countries. Excellent susceptibility of gram-positive organisms to vancomycin was also demonstrated by a study.¹³ Susceptibility of gram-negative organisms, except *Acinobacter* spp., to ceftazidime varied between 90% and 100% in our study, which is in contrast to a study¹⁴ that reported susceptibility of only 60.9%.

Fungi accounted for 10% of all suspected cases of endophthalmitis in our study. *Candida* spp. was the most common fungus identified, in contrast to published studies that found *Aspergillus* spp. as the most common isolate.¹⁴⁻¹⁶ Fungal endophthalmitis is generally more difficult to manage and should be suspected if the infection is not responding to initial antibiotic therapy. Maintaining a high index of suspicion and instituting early aggressive treatment is essential. In its initial form, fungal endophthalmitis mimics bacterial endophthalmitis, with red, painful, swollen eyes and reduced vision, usually developing days to weeks after an intraocular procedure. However, it can also present as a sub-acute infection with reduced vision but without significant pain. Any underlying immunodeficiency state significantly raises the possibility of fungal aetiology. The treatment is

intravitreal and / or systemic antifungal therapy with or without pars plana vitrectomy. Infectious disease specialist should be consulted regarding the selection of the appropriate antifungal therapy and its route of administration.

The strength of the current study is that it provides a profile of organisms cultured from vitreous and aqueous samples and their antibiotic sensitivity patterns in a tertiary care centre over a long period of time. Such information can be used to institute early treatment and to observe evolving patterns of antibiotic resistance.

The main limitation of our study is its retrospective data. For majority of patients, we were not able to retrieve accurate information on details of surgical procedure, risk factors and visual outcomes which might interest readers. Another limitation is that it is a single-centre study. The situation in other centres may be different. Lastly, we did not analyse changes in the patterns of antibiotic resistance given the relatively small number of cases per year.

Conclusions

Pseudomonas spp. and CoNS were the most frequently identified cause of endophthalmitis. Vancomycin and ceftazidime seemed to be excellent empirical antibiotics for treating postoperative endophthalmitis. Gram-negative organisms were significantly more sensitive to aminoglycosides, imipenem and ceftazidime compared to ciprofloxacin. A high degree of susceptibility was observed with vancomycin, chloramphenicol, amikacin, tobramycin, gentamicin and imipenem.

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