
ENDOPHTHALMITIS – MICROBIOLOGIC SPECTRUM AND ANTIMICROBIAL SUSCEPTIBILITY PATTERNS.

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Infection is a dynamic process – involving invasion of the body by pathogenic organisms. The significance of bacteria within wounds depends on whether it is

1. Contamination – the presence of bacteria without multiplication.
2. Colonization – the presence of multiplying bacteria with no host reaction.
3. Infection – the presence of multiplying bacteria with an accompanying host reaction.

The risk factors related to surgical infection are considered as either

1. Host-related
2. Surgery related
3. Microbial.

Endophthalmitis maybe

1. Post operative,
2. Post traumatic
3. Endogenous.¹

Infectious endophthalmitis is a problem of major concern in ophthalmology and the cornerstone of its management is speedy identification of the responsible agent and prompt institution of appropriate therapy. The dictum is that all unexpected inflammatory responses following intraocular surgery be considered endophthalmitis unless proven otherwise. For this it is vital to confirm the diagnosis by culturing the organism from intraocular samples.

Based on the clinical profile 3 forms of endophthalmitis are recognized.

1. The severe or fulminant form occurs within 4 days of surgery and is caused by gram-negative bacilli, streptococcus and Staphylococcus aureus.
2. The acute form develops between 5-7 days and is most likely to be caused by coagulase negative staphylococci.
3. Chronic endophthalmitis usually develops several months after the surgery and the organisms involved are fungi, coagulase negative staphylococci and Propionobacterium acnes.

Virulence and load of the causative organisms is another important determinant in outcome. The higher the load, the greater is the risk developing endophthalmitis. Postoperative endophthalmitis

following cataract extraction is considered the most common form of endophthalmitis accounting for upto 70% of infections endophthalmitis. In a one year study of OPD samples referred to our lab all samples were from post operative cases. (Table 1-2)

Diagnosis of an infectious etiology is usually made with vitreous and aqueous sampling by staining (Gram stain, Giemsa and calcofluor white) and culture. Aspirates are plated on blood agar, chocolate agar, brain heart infusion broth, thioglycollate broth and sabourauds dextrose agar. The latter are incubated at 37 C and 27 C.

Discharge from the conjunctival sac and the lid margin are not recommended due to poor yield, culture of an unrelated organism, and needless expense. But if a suture abscess is present, the removed suture should be cultured. The most important samples to culture are aspirates from the aqueous and vitreous. Though the vitreous yield is better than aqueous (50-70 % vs. 30-40%) on occasion only the aqueous has been positive for growth. Also in laboratories using polymerase chain reaction (PCR) for diagnosis, the aqueous has been found equally sensitive as vitreous.²

Studies have shown that diluted and undiluted vitreous samples as the vitreous cassette fluid have significant advantage compared with a single sample. The cassette fluid must be passed through a 0.22-micron Millipore filter for culture. Culture fluid alone has yielded a positivity rate of 44% and cassette fluid alone of 49%.³

In most recent studies approx 70-75% of eyes with suspected endophthalmitis are culture positive from intraocular specimens.² In our study only 44% were

A 1-year study at PD Hinduja National Hospital and Medical Research Centre (from OPD samples received from referral clinics in and around Mumbai).

Table 1.

total number of vitreous samples	62
positive	27
no growth	35
organisms seen on gram stain	37

Table 2

Gram positive organisms	15
Staphylococcus epidermidis(coagulase negative staphylococcus)	7
Staphylococcus aureus	3
Streptococcus species	3
Enterococci species	1
Diphtheroids	1
Gram negative bacilli	7
Pseudomonas aeruginosa	4
Acinobacter species	1
Klebsiella Pneumoniae	2
Filamentous Fungi	5
Aspergillus species	4
Fusarium	1

this organism despite our best efforts. Polymerase chain reaction with specific primers for P.acnes maybe useful in bacteriologically negative specimens by conventional methods.² Of note is that gram negative bacilli comprised 7 of 27 isolates (26%) higher than 6% found in some series but consistent with studies in other parts of India.^{1,4} We also found a relatively high incidence of fungal isolates - 5 out of 27 (19%) reflecting the local tropical habitat of this region. It has also been reported that secondary or anterior chamber lens implantation is associated with a possible shift toward gram positive organisms other than coagulase negative micrococci.

Antimicrobial Therapy

In endophthalmitis single intravitreal doses of ciprofloxacin, gentamicin and imipenem were administered to animals and pseudomonas endophthalmitis at 24 hours (early) and at 48 hours (late). With the early treatment the dose response relationship was linear with all 3 drugs. In contrast with the late treatment the same vitreal concentrations had no effect on bacterial counts despite the organisms being sensitive in vitro to these agents.⁵ Intravitreal corticosteroid therapy may play an important role in minimizing the inflammation and tissue damage especially associated with bacterial infection.⁶

Table3 : % susceptibility of isolates to various antimicrobials

Gram positive	ceftazolin	ceftazidime	chloramphenicol	gentamicin	amikacin	ciprofloxacin	vancomycin
Staph epidermidis	89	89	81	76	96	83	100
Staph aureus	97	97	88	82	98	92	100
Strep species	100	100	85	40	42	90	100
Enterococci	0	0	40	0	0	20	100
Diphtheroids	90	-	100	90	90	100	100
Gram negative							
Pseudo aeruginosa	0	65	26	40	65	40	-
Klebsiella species	26	60	35	36	61	55	-
Acinetobacter nitratum	0	100	100	0	0	100	-

microbiologically positive including those with fungal etiology. The reason is prior antibiotic therapy as all our samples were referred to us from various centres after varying periods of treatment. This is evident as in 10 samples, though organisms were seen on smear examination, they failed to grow in culture. Coagulase negative staph predominated this series and though Propionobacterium acnes has been reported in several studies we did not isolate

Pharmacokinetics and spectrum of activity of antimicrobial intravitreal drugs is an important consideration. Rapid concentration of bactericidal drugs and maintaining their levels without toxicity is a challenge. Dose, pH, ionization, protein binding, route of egress from the eye also affect the drug concentration. Ocular factors as surgical status of the eye, presence or absence of lens, vitreous, degree of

breakdown of the blood retinal barrier are the host factors to consider.

Systemic drugs

It is however now unequivocally established that most antibiotics given systemically do not reach the minimum inhibitory concentrations necessary to kill the organism in the vitreous **despite** a compromised blood ocular barrier in endophthalmitis. Some fluoroquinolones as ciprofloxacin, sparfloxacin and pefloxacin and a 3rd generation cephalosporin as ceftriaxone may achieve adequate concentrations but intravitreal administration of drugs is the **best** route to achieve bacterial killing.

In this study vancomycin was active against all gram-positive isolates tested (100%). Ceftazidime and amikacin were susceptible (65%) to the most common gram-negative isolate – *Pseudomonas aeruginosa*. Due to the high prevalence of gram-negative bacilli and fungi, empiric therapy should target coverage for these pathogens in appropriate settings. Ideally an attempt **must** be made to culture and recover the offending agent, but in the absence of lab support in addition to the expeditious administration of intravitreal vancomycin, an aminoglycoside as amikacin or an antipseudomonal cephalosporin as ceftazidime should be given empirically. With the 3rd generation cephalosporins the gram-positive spectrum is variable, especially with ceftazidime. However, the choice for non pseudomonal gram-negative bacilli should be cefotaxime or ceftriaxone. It is important to remember that the cephalosporins have no action against Methicillin Resistant *Staph aureus* (MRSA) or enterococci.

Imipenem should be kept in reserve for documented resistance to 3rd generation cephalosporins.

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James Allen