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RESEARCH ARTICLE

MANAGEMENT OF POST-OPERATIVE ENDOPHTHALMITIS: A REVIEW

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Abstract

Postoperative endophthalmitis is one of the most feared complications for ophthalmologists, and the number of infections after intraocular procedures have been increasing. Nonetheless, a prompt intervention can result in the recovery of vision. In the past, endophthalmitis after cataract surgery was accountable for the majority of cases but is becoming less frequent due to the progress of surgical techniques and demographic developments with a steadily increasing number of intravitreal injections. In this review, we have focused on the epidemiology, existing risk factors, various clinical features, management strategies, and prophylaxis pertaining to postoperative endophthalmitis following cataract surgery.

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Introduction:-

Endophthalmitis following cataract surgery is rare but continues to be a serious complication following cataract surgery. Over the years, the improvement in various preoperative and perioperative measures include use of antiseptic and appropriate surgical draping techniques[1]. Despite this major improvements in surgical techniques related to cataract surgery that have occurred over the past 20 years, endophthalmitis after cataract surgery remains a devastating complication of this procedure[2]. It is a sight-threatening intraocular inflammation that may be due to a noninfectious process or may be caused by an infectious organism. It is a term used to describe intraocular inflammation that involves the vitreous cavity and the anterior chamber of the eye and can involve other adjacent ocular tissues such as the choroid or retina, sclera or cornea[3]. In infectious endophthalmitis, the organism might reach the eye from other infected sites in the body through hematologic seeding and in these cases it is labeled endogenous endophthalmitis. More commonly, the organism is exogenous and gains access to the intraocular environment[4]. The majority of cases of postoperative endophthalmitis involve infections caused by gram-positive organisms that are normal inhabitants of the lid and conjunctiva. It is felt that such bacteria gain access to the intraocular space either through direct inoculation during surgery or due to some problem with the surgical wound postoperatively[2].

According to the Endophthalmitis Vitrectomy Study (EVS), postoperative endophthalmitis is divided generally into two types: acute and chronic. Acute postoperative endophthalmitis is defined as infections within 6 weeks of surgery; on the other hand, chronic postoperative endophthalmitis is known to occur after 6 weeks of surgery[5]. The term chronic postoperative endophthalmitis (CPE) was first coined in 1986 in a case series of 15 patients by Meisler et al.[6]. The inflammation is usually indolent and may persist for months. It is often misdiagnosed as noninfectious iritis where it improves initially with topical corticosteroid therapy while flaring whenever corticosteroids are

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tapered or stopped[7]. This is in contrast to acute postoperative endophthalmitis, which presents as a single episode of severe inflammation with an acute onset that usually follows surgery by a few days but can be delayed more than a week in some cases. As such, acute and chronic postoperative endophthalmitis are two clearly different clinical entities[4,6,7].

Epidemiology of Postoperative endophthalmitis:

Postoperative endophthalmitis (POE) is an uncommon complication of any ocular surgery. The reported incidence of post-operative endophthalmitis ranges from 0.01% to 0.367%, with incidence varying among different surgical procedures and across studies and different countries[3,8,9]. Most of postoperative endophthalmitis studies were conducted on cases after cataract surgery, being the most commonly performed surgery in ophthalmology. In culture positive cases of endophthalmitis, the ocular surface and adnexa are considered to be the primary sources of bacteria. Speaker et al. noted an association between external bacterial flora and bacteria isolated from vitrectomy specimens in 82% of their patients[10]. Similarly, in the EVS study group, isolates from intraocular and conjunctival specimens were indistinguishable in 67.7% of cases[11]. West et al. reported the overall incidence of endophthalmitis as 0.215% among a cohort of older patients in the US between 1994 and 2001, noting a trend toward increasing rates of infection toward the end of the study period[2].

Risk factor of POE:

Risk factors mainly can be divided into preoperative, intraoperative and postoperative risk factors. Preoperative factors include age below 44years old, male sex, living in a rural area and immunosuppressive conditions such as diabetes mellitus[12,13]. The main preoperative risk factors for POE are acute or chronic eyelid inflammatory diseases like blepharitis, active conjunctivitis, meibomitis, lacrimal drainage system infection or obstruction. Intraoperative risk factors are disruption of the integrity of the barrier between the anterior and posterior chambers due to posterior capsular tear, zonular dialysis, and vitreous loss, and wound abnormalities, prolonged surgery, contaminated irrigation solutions, improperly cleaned phacohandpieces and instruments. Postoperative risk factors include improper ocular hygiene, wound leak, and contaminated eye drops[14].

Microbiology

Acute post cataract endophthalmitis (PCE) can be caused by a diverse group of organisms. Gram-positive, coagulase-negative staphylococci are the most common, making up about 70 percent of culture-positive cases. Other common organisms include Gram-positive cocci such as Staphylococcus aureus (6.8 to 10.2 percent), as well as Streptococcus (8.2 to 11.5percent) and Enterococcus species (2.5 to 6.8 percent)[15]. Cutibacterium acnes, the organism formerly known as Propionibacterium acnes, is a slow-growing, facultative anaerobic, Gram-positive bacteria that can cause chronic postoperative endophthalmitis[16]. Gram-negative bacteria make up about 5 percent of cases, with some notable species being Klebsiella pneumonia, Pseudomonas aeruginosa and Enterobacter species[13,15]. The Endophthalmitis Vitrectomy Study found that approximately one-third of cases were culture negative[17]. Anand et alhave noted that Gram-negative bacteria accounted for 41.7% of postoperative endophthalmitis followed by Gram-positive bacteria (37.6%) and fungi (21.8%). In another series, fungi were the leading cause of endophthalmitis accounting for 57.5% of all cultures followed by Gram-negative bacteria (15.9%)[3].

Clinical Presentation

By definition, acute post-cataract endophthalmitis occurs within six weeks of surgery, typically within a few days,while cases that occur more than six weeks after surgery are deemed chronic endophthalmitis. Most patients present with symptoms including blurred vision (93.1 percent of cases), redness (80.6 percent), pain (75.4 percent), and eyelid swelling (33.1 percent)[14]. On examination, eyes often have a corneal edema and conjunctival chemosis. The anterior chamber shows inflammatory cell, hypopyon, (seen in 85% of cases)flare and fibrin, and posterior synechiae may be present (Figure 1). In the posterior segment, vitritis often obscures the fundus, and sometimes retinal hemorrhages,periphlebitis(can be an early sign) occur. Significant media opacity often requires ultrasonography to grossly examine the posterior segment (Figure 2).

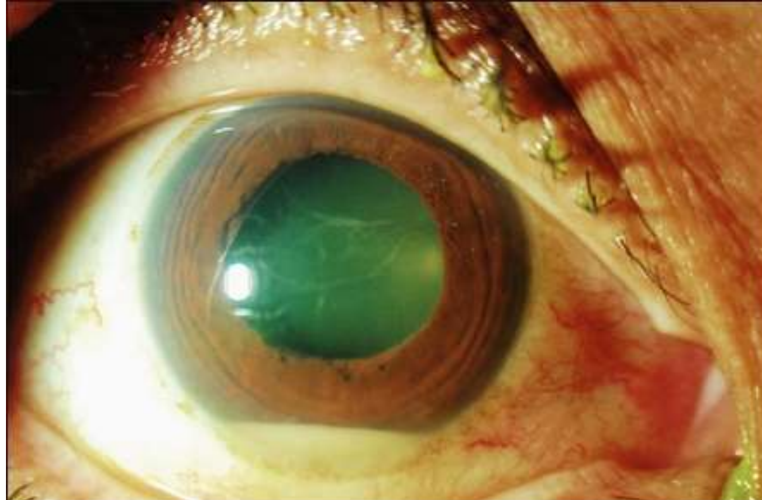

Figure 1:- This eye developed pain and decreased vision four days after uneventful cataract surgery. The subconjunctivalhemorrhage is from the tap-and-inject procedure. Conjunctival injection and hypopyon are visible.

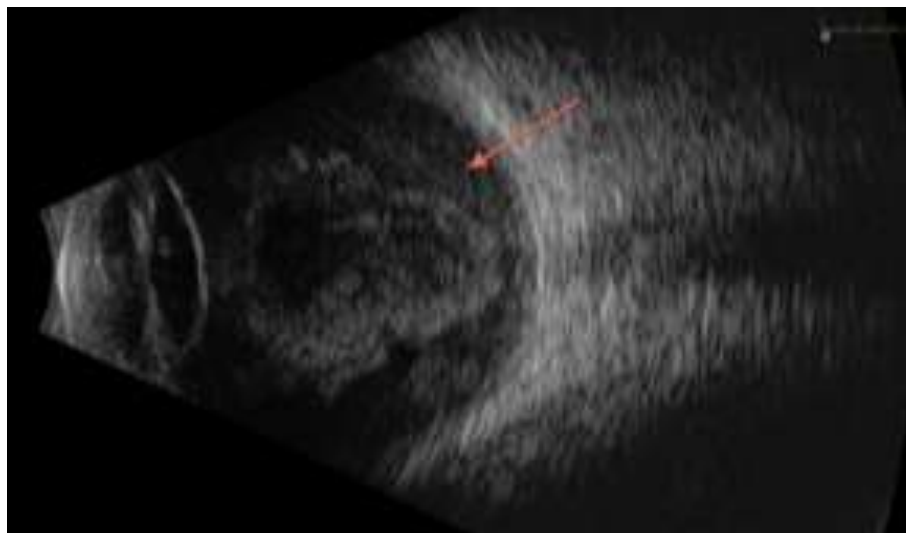

Figure 2:- B-scan ultrasonography demonstrating significant vitreous debris in an eye with acute endophthalmitis.

In chronic cases, patients may present with indolent, persistent uveitis that can be mistaken for recurrent postoperative inflammation.Patients with chronic endophthalmitis often have milder symptoms than acute cases, and eyes may have initially responded to topical steroids before getting worse. Some findings suggestive of a chronic PCE include granulomatous precipitates on the cornea and intraocular lens without an obvious hypopyon, as well as the presence of white intracapsular plaques.

Diagnostics

Ideally, identifying the causative organism could help tailor the antimicrobial used, and might give some idea about prognosis[18–20]. Cultures are helpful for guiding prognosis but may not be critical to management[18].

Nonetheless, the current standard practice is to culture the vitreous from a vitreous tap procedure. However, sometimes you can’t obtain a vitreous tap. An anterior chamber tap is often easy to obtain but has a lower yield rate[19].

Polymerase chain reaction testing of samples may improve diagnostic yield[20].A new methodology called whole-genome-sequencing is being investigated for pathogen detection. With WGS, it’s possible to screen for all non-human DNA in the sample, making it a powerful tool for identifying causative organisms in PCE[14].

Management of POE

1) **Ocular fluid biopsy**

For aqueous tap, a 30-gauge needle attached to a tuberculin syringe is inserted through the limbus into the anterior chamber and 0.1 ml of aqueous humour is aspirated. A vitreous specimen may be obtained either by a needle tap or by vitreous biopsy with a vitreous cutter. In a tap, a large bore needle (22G) is inserted into a sclerotomy site and the vitreal cavity under direct visualization and 0.2 cc of vitreous removed. If no fluid vitreous can be obtained with a needle tap, a vitreous biopsy must be performed to prevent the aspiration of formed vitreous[21].

In a vitreous biopsy, a syringe attached to the aspiration port of the vitreous cutter hand-piece is used to remove 0.3 to 0.4mL of undiluted vitreous, by using the automated cutting mechanism of the probe and slow, manual aspiration into the syringe. When done as part of vitrectomy, the infusion port is then turned on to prevent globe collapse[14].

2) **Povidone-Iodine**

Perioperative topical agents are widely used toreduce the bacterial load on the ocular surface.Since instrumentation that enters the eye is likelyto have some contact with the ocular surface route, sterilization of the ocular surface reducesthe risk of introducing infectious organisms[22]. Povidone-iodine used in a concentration of 5–10%preoperatively is effective in reducing bacterialcounts on the conjunctiva[23].

3) **Pars plana vitrectomy (PPV)**

The removal of the vitreous and replacement with aqueous humor following PPV in inflamed eyes is said to help by decreasing inflammatory processes consequent to increased free cortisol levels and anti-inflammatory cytokine production and complement fixation[24]. In endophthalmitis, PPV helps by providing more material for microbiologic workup especially in cases in which fungal aetiology is suspected, better dispersion of antibiotics in the vitreous, clearance of the media and better posterior segment visualization, removal of vitreous membranes which may be a source of late traction and subsequent detachment, removal of inflammatory mediators and toxins and most importantly, removal of source of infection[25,26].

Eyes having hazy media, PPV might create further complications such as retinal breaks and retinal detachment due to pull on the thin, necrotic retina. PPV is done either with two or three ports. With the cutting rate kept high, a vitreous sample of 0.2 to 0.5 mL is first manually aspirated into a syringe attached to the aspiration port of the cutter, with the infusion turned off. Infusion is then turned on and core vitrectomy is performed. The intraocular lens is not sacrificed for most cases of acute POE. Recently more extensive PPV has been advocated with better visual results seen when compared to the EVS. In a series of 47 eyes with complete vitrectomy, 91% achieved 20/40 final visual acuity compared to 53% seen in the EVS[27].

4) Intravitreal antibiotics

Intravitreal injection of antibiotics remains the main stay of POE till date. A combination of antibiotics with both gram-positive and gram-negative coverage is the quickest way to ensure delivery directly to the infected tissues. The most commonly employed empirical antibiotics are Vancomycin 1.0 mg/0.1 mL to cover gram positive organisms and either Ceftazidime 2.25 µg/ 0.1 mL or Amikacin 400 µg/0.1 mL for gram negative organisms. Ceftazidime is more popular owing to the reports of macular infarction with aminoglycosides[28]. These antibiotics are popular after the EVS demonstrated 100% susceptibility of gram positive organisms to Vancomycin and 89.5% susceptibility of gram negative organisms to Ceftazidime and Amikacin[36].
In India, low susceptibilities of Gram-negative bacteria to amikacin and ceftazidime have been observed (68% and 63% respectively).

Vancomycin resistance is rare but is a potential problem as reported by Bains et al[29].Another study from South India by Vedantham et al demonstrated poor susceptibilities to both Vancomycin and Amikacin[30].

After showing a lot of promise, fluoroquinolones are not being widely used as intravitreal agents in endophthalmitis due to widespread resistance[31]. Empirical antifungal agents such as Voriconazole or Amphotericin-B are injected in cases of suspected fungal endophthalmitis[14].

5) Systemic antibiotics

EVS, the administration of intravenous antibiotics (amikacin plus ceftazidime or amikacin plus ciprofloxacin), did not confer any advantage in the form of difference in visual acuity or media clarity when given in addition to intravitreal antibiotics[14].

Engelbert et al found that amikacin does not penetrate well into the vitreous cavity and ciprofloxacin does not adequately cover gram positive organisms which commonly cause POE. Use of intravenous imipenem which has good vitreous penetration and coverage, was found to confer no additional benefit[39].

Several reports are available on good intraocular penetration of oral moxifloxacin and gatifloxacin with 90% minimal inhibitory concentrations (MIC90) achieved against many Gram-positive and Gram-negative microbes with the notable exception of Pseudomonas aeruginosa and Bacteroides fragilis[32].

However Vedantham et al have reported that despite good intraocular penetration of oral Moxifloxacin, the spectrum of coverage did not appropriately encompass the most common causative organisms in endophthalmitis, especially Staphylococcus epidermidis[21]. However, the broad antimicrobial coverage and convenient oral administration ensure that when needed, oral fourth generation fluoroquinolones are useful adjuncts to intravitreal antibiotics[14].

6) Topical Antibiotics:

Topical antibiotics are commonly used for the prophylaxis of endophthalmitis following cataract surgery, despite the fact that the clinical evidence for their efficacy is limited[3].

Moss et al. studied the preoperative application of topical gatifloxacin. They compared two dosing regimens: one group received three doses of drug within 1 hour before surgery; the other group received four doses on the day before surgery in addition to three doses 1 hour before surgery. They found a significant reduction in bacterial load in both groups with no statistical difference between the two groups[33].

In an analogous approach, Inoue et al. compared levofloxacin with povidone-iodine and found a similar reduction in bacterial load with each treatment[22].

Solomon et al Hourly topical antibiotics (usually fluoroquinolones) that have good intraocular penetration after topical administration, are employed frequently[34].

Kowalski et al suggested that the topical application of fourth-generation fluoroquinolones may be protective against endophthalmitis[35].

7) Subconjuctival antibiotics:

Souli et al. showed that subconjunctival injections of vancomycin achieve adequate aqueous concentrations of drug, making it a valid prophylactic option for cataract extraction. However, some experimental studies provide conflicting evidence[36].

Barza et al. reported that vitreous concentrations of ceftriaxone, ceftazidime and vancomycin did not achieve therapeutic levels[37].

Although most cases of endophthalmitis involve infection within the vitreous cavity, it is not clear that therapeutic drug concentrations in the vitreous are absolutely necessary for prophylactic efficacy. Nonetheless, clinical outcomes suggest that, although subconjunctivalantibacterials may or may not achieve therapeutic intraocular concentrations, they do have a beneficial effect in preventing endophthalmitis[3].

8) Corticosteroid

To reduce the destructive effect of the significant inflammation that coexists with infection in endophthalmitis, many ophthalmologists use systemic, topical, subconjunctival, and intravitreal corticosteroids in combination with antibiotics, provided that no contraindications exist (e.g., diabetes mellitus, tuberculosis, fungal infection,etc)[4].

Pathengay et al Topical corticosteroid therapy is strongly recommended toreduce the anterior segment inflammation and its sequelae. It isstarted in conjunction with appropriate antibiotic therapy. Themost common choice is topical prednisolone acetate 1% instilledas frequently as practicable[1]. Subconjunctival injection of dexamethasone (usually 4 mg) is administered at the time of initial intravitreal antibiotic therapy[4].

Intravitreal corticosteroid was not included in the standard drug regimen in the EVS. The lack of a randomized clinical evaluation, the use of intravitreal corticosteroids remains controversial[4]. Aaberg et al found that the use of intravitreal dexamethasone (400 mg) had no statistically significant effect on visual outcome in a 10-year retrospective study of 54 culture-proved cases of acute postoperative endophthalmitis[5].

Vedantham et al There is at present no role for systemic steroids in POE. Steroids are generally avoided in suspected /proven fungal endophthalmitis[21].

9) Collagen Shields

A less common method of antibacterial administration is via a collagen shield. The collagen shield, which is a contact lens that dissolves on its own and is placed on the eye at the end of surgery, is used as a medication reservoir[3].

Wallin et al found that absence of a collagen shield was one of the risk factors for infection[38]. Regarding the penetration of antibacterial into the eye, Taravella et al found that the intraocular concentration of ofloxacin was higher in patients receiving a drugsoaked collagen shield than in patients receiving topical antibacterials alone[39].

PCE-Prophylaxis

Though much work has been done on endophthalmitis prophylaxis, povidone-iodine remains the primary way to prevent post-procedure endophthalmitis[40]. The use of intraoperative intracameral antibiotic injection is increasingly used as prophylaxis against PCE[41]. Large retrospective studies, using varying intracameral antibiotics including cefuroxime, Moxifloxacin and vancomycin, found a reduction in endophthalmitis in cohorts that received intracameral injections[42–44]. The use of intracameral vancomycin also carries the risk of the rare but potentially devastating hemorrhagic occlusive retinal vasculitis, as reported in some retrospective case series[45,46].

Conclusions:-

Endophthalmitis continues to be a serious complication of cataract surgery. Significant advances have been made, which have decreased the incidence of endophthalmitis and improved subsequent outcomes. Unfortunately, given the rarity of endophthalmitis, researchers will continue to have difficulty producing studies with sufficient power to fully investigate future treatment and prophylactic measures.

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