An Updated Review of Post-Cataract Surgery Endophthalmitis

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ABSTRACT

Cataract extraction is the most performed ophthalmic surgery in the world. Although the meres of effective prophylaxis have significantly evolved following the improvement in the understanding of the aseptic techniques and applying the protocols for surgical prophylaxis as well as the introduction of modern technology and antiseptics, there is still minor probability of an infectious complication after the surgical intervention. Post–cataract surgery endophthalmitis is a grave complication that can result in severe vision loss and, occasionally, loss of globe integrity. [1] The currently reported incidence of post–cataract surgery endophthalmitis is from 0.06% to 0.36%.[2,3,4]. This literature review is performed in order to compile the updated data on the given issue and enhance eye-care specialists' theoretical knowledge on post-operative endophthalmitis through the materials that are provided in the article.

Keywords: Cataract extraction

Introduction

One of the most feared complications after cataract surgery is the increased vulnerability to postoperative endophthalmitis. This mostly starts when a corneal incision is made in the anterior chamber of the eye to remove the cataractous lens, which might lead to the invasion of bacterial flora. Of postoperative endophthalmitis cases, 15-30% have a grave prognosis on the visual outcome and medical care expenditures [5]. The unfavorable visual outcomes of postoperative endophthalmitis in cataract surgery ranges from decreased visual acuity less than 0.10 (Decimal) to the loss of the eye. Undeniably, endophthalmitis causes loss of quality of patient life in addition to the heavy load on the healthcare organizations as it is frequently followed by further hospitalization and even surgical intervention [6].

Etiology

According to the Endophthalmitis Vitrectomy Study (EVS), the main source of infection is the microflora of the surface of the patient's conjunctiva [7]. The most common causes of acute postoperative endophthalmitis are coagulase-negative staphylococci, in particular Staphylococcus epidermidis (33–77%); Staphylococcus aureus (10–21%)(Table 1). In chronic endophthalmitis, Proprionibacterium acnes is the most likely causative agent .

Table 1 Pathogenic organisms common in acute postoperative endophthalmitis [8]

Prevalence (%)	Types of microorganisms
33-77%	CNS (coagulase-negative staphylococci)
10-21%	Staphylococcus aureus
9-19%	BHS (β-hemolytic streptococci), S. pneumoniae, ∂-hemolytic streptococci,

	including S. mitis and S. salivarius
6–22%	Gram-negative bacteria, including Ps. aeruginosa
Up to 8%	Fungi (Candida spp., Aspergillus spp., Fusarium spp.)

Risk factors for endophthalmitis include: – Extended surgery time for an inexperienced surgeon – Damage to the posterior lens capsule and vitreous during surgery – Patient with blepharitis prior to surgery – Intraocular lens surface as a breeding ground for microorganisms – Insufficient sterilization of instruments and operating field Should also note the role of sutureless surgical techniques in the development of postoperative endophthalmitis: the use of a tunnel sutureless corneal incision increases the incidence of endophthalmitis after cataract phacoemulsification due to the possibility of tear fluid absorption into the anterior chamber in the early postoperative period. According to the ESCRS guidelines, patients with a corneal tunnel are 5.88 times more likely to develop endophthalmitis than those with a corneoscleral approach [8].

The same guidelines reported that implantation of silicone intraocular lenses (IOLs) was 3.13 times more likely to develop endophthalmitis compared to lenses made of acrylic or other material, and surgical complications were associated with a 4.95-fold increase in this risk. Most implantable IOLs are currently made of hydrophobic acrylic, and silicone ones are rare due to infectious complications and the risk of lens damage when implanted through incisions smaller than 2.8 mm [9].

Clinical presentation

The main clinical manifestations of acute endophthalmitis, according to the EVS study, include: blurred vision (94% of patients), pain syndrome (74%), eyelid edema (34%), hypopyon (80%), redness of the eye (82%), clouding of the media of the eye (74%). Lysis of the vitreous body and its replacement with purulent masses cause a yellow-green reflex from the fundus of the eye (Fig.1).

Fig.1 Acute-onset postoperative endophthalmitis with sutured corneal wound and hypopyon (arrow)

Chronic postoperative endophthalmitis may, in rare cases, occur months after the surgery [10]. Despite the great advances in the management of postoperative endophthalmitis, the prognosis is not usually favorable due to associated poor visual outcomes as less than 50% of the endophthalmitis patients are able to achieve a final visual acuity of 20/40 or better [6https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF1]. On the other hand, the prognosis is usually compromised by the increased incidence of bacterial resistance even with the growing era of optimal disinfectants and antibiotic delivery strategies [6].

Prophylaxis of Endophthalmitis

The basis for the prevention of postoperative endophthalmitis is compliance with the rules of asepsis and antisepsis. The use of local antibiotics in drops before surgery is not indicated due to low efficacy and lack of evidence [11].

Table 2. The main stages of antisepsis in the preoperative period

1. Mandatory treatment of the cornea and conjunctival sac with povidone-iodine
2. Mandatory treatment of the periorbital region with povidone-iodine
3. Use of medical overalls (gown, gloves, etc.) and a special ventilation mode in the operating room
4. Eye draping napkins, sealing eyelids and eyelashes (cutting is not recommended)

Povidone-iodine

Povidone-iodine displays a wide range of microbicidal activity against bacteria, fungi, protozoa, and viruses. They have a nonselective topical killing effect on microbes by disrupting cellular membranes. Numerous prospective studies have verified povidone-iodine as the only topical prophylactic antiseptic known to reduce endophthalmitis perioperatively with a three-fold to five-fold reduction rate due to its powerful reduction of conjunctival bacterial concentration with 96.7% bactericidal activity within one minute of irrigation [12]. Although the most applied concentration of povidone-iodine is 5%, there is no universal consensus on its concentration, period, and timing of application. Povidone-iodine is widely used in almost all ocular operations except in patients with hypersensitivity reactions [13].

Cefuroxime

Cefuroxime is the most widely used antibiotic during cataract surgery [14https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF22]. It is a second-generation cephalosporin that inhibits the formation of the peptidoglycan layer of the bacterial cell wall. Lower post-cataract surgery endophthalmitis rates with intracameral cefuroxime injection were reported in several retrospective and epidemiologic studies [14https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF22]. Unfortunately, cefuroxime is ineffective against MRSA and Enterococci [15https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF6].

Cefuroxime is registered in 24 European countries; it has not been approved by the FDA for intracameral prevention of post-cataract surgery endophthalmitis. It is formulated into single-use syringes (1 mg in 0.1 ml) for intraoperative use [14https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF22].

Intracameral cefuroxime has a wide safety margin and it is well-tolerated as reported by most studies with few associated side effects. Hypersensitivity reactions are fortunately uncommon; however, anaphylactic reactions (urticaria, bronchoconstriction, or life-threatening circulatory reactions) were recorded after intracameral cefuroxime application in patients with penicillin allergies [15https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF23]. The most described side effects resulting from accidental intracameral cefuroxime overdoses comprise macular edema, hemorrhagic retinopathy, serous retinal detachment, and corneal edema [16https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF24].

Moxifloxacin

Notably, moxifloxacin (a fourth-generation fluoroquinolone) possesses a very powerful concentration-dependent bactericidal effect on both gram-positive and gram-negative bacteria, as well as a considerable killing effect on atypical organisms. Moxifloxacin expresses broad-spectrum microbial coverage with a very good diffusion into the anterior chamber, and low adverse effects [17https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF25]. However, coagulase-negative staphylococci expressed increasing fluoroquinolone resistance, which can be overcome by increasing the administered intracameral dose [18https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF26]. Moxifloxacin inhibits topoisomerase I (DNA gyrase) and topoisomerase IV, enzymes required for replication, transcription, and repair of bacterial DNA during bacterial cell division [17https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF25]. Although the application of intracameral moxifloxacin has not

been investigated in randomized controlled trials, observational studies confirmed its efficacy with the overall reduction of endophthalmitis after cataract removal [19https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF27].

Moxifloxacin as a preservative-free formulation can be used either diluted or not for intracameral injection according to the concentration needed [20https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF28]. It has a very wide safety margin with no reported toxic effects on corneal endothelial cells, trabecular cells, and retinal pigment epithelial cells, even with previous exposure to inflammation and oxidative stress. However, allergic and anaphylactic reactions have been reported with preoperative topical application of moxifloxacin but hypersensitivity reactions are still very rare [21https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF29].

Vancomycin

The glycopeptide vancomycin antibacterial mechanism of action depends on binding to pentapeptides to prevent peptidoglycan polymerization, and hence weakens the bacterial cell wall. Although vancomycin has powerful bactericidal activity against S. epidermidis, S. aureus (both methicillin-sensitive and methicillin-resistant strains), and most strains of Streptococcus, it expresses a very weak effect on gram-negative bacteria, including the pseudomonads. Recently, intracameral vancomycin has been greatly recommended by the American Society of Cataract and Refractive Surgery for endophthalmitis prophylaxis during cataract surgery [22https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF30].

Up till now, there is no prepared, single-use syringe for intraocular application of vancomycin. Therefore, in order to apply it intracameral, vancomycin powder 500 mg and 1000 mg vials are reconstituted by dissolving the powder in a balanced salt solution to give a final concentration of 10 mg/1 ml from which 0.1 ml (1 mg) can be injected intracamerally [23https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF31]. Application of vancomycin intracamerally has a wide safety margin. Nevertheless, cases of severe, bilateral, ischemic retinal vasculitis and hemorrhagic occlusive retinal vasculitis have been reported in the form of delayed-onset, painless vision loss following cataract surgery. Vasculitis is supposed to be a type III hypersensitivity reaction rather than direct drug toxicity [24https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF32].

Despite the powerful effect of vancomycin on S. epidermidis and S. aureus, its routine use in postoperative prophylaxis of endophthalmitis should be restricted except in patients with life-threatening allergies to beta-lactam antibiotics. Vancomycin can be administrated either intravenously, as an intracameral injection, or topically as an irrigating solution [25https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF33]. Vancomycin is proposed to be the antibiotic of choice for both prophylactic and therapeutic intracameral injections of endophthalmitis in many parts of the world with 100% sensitivity of the gram-positive bacteria [26https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF34].

Corticosteroid Therapy

Topical corticosteroid therapy is believed to offer help in postoperative endophthalmitis management in order to reduce the immune-inflammatory response with the subsequent tissue damage. The antimicrobial alone may induce aggravating inflammatory responses to dead organisms plus those induced by the living organisms. Therefore, corticosteroids are strongly indicated in collaboration with optimal antibiotic cover to reduce the anterior segment inflammation except in cases of suspected fungal infection. Corticosteroids suppress inflammation by inhibition of macrophages and neutrophil migration, as well as inhibition of phospholipase A2 leading to decreased prostaglandin synthesis and reduced capillary permeability. Furthermore, stabilization of lysosomal membranes by corticosteroids inhibits neutrophils, mast cells, macrophages, and basophils degranulation

[27https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF19].

The most practicable choice is the instillation of topical prednisolone acetate 1% for several days up to several weeks. Subconjunctival injection of 4 mg dexamethasone is administered at the time of initial intravitreal antibiotic therapy. Oral corticosteroid (prednisone 30 mg twice daily for 5-10 days), is also recommended beginning postoperative day one. However, the timing, dosing, and route of steroid administration are controversial and highly dependent on the organism
responsible. [25https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF33].

Management

Acute Postoperative Endophthalmitis

Systemic antibiotics have a controversial role in the treatment of postoperative endophthalmitis. The systemic amikacin and ceftazidime were reported to have no effect on the final visual outcome this is because these drugs fail to cross the blood ocular barrier [36]. On the other hand, systemic ciprofloxacin versus moxifloxacin had reported a faster resolution of hypopyon and a decreased need for repeat intravitreal antibiotics in patients with acute postoperative endophthalmitis because these drugs cross the blood ocular barrier [28https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF38].

The cornerstone of the control of massive bacterial postoperative endophthalmitis is the simultaneous intravitreal injection of unpreserved dexamethasone and broad-spectrum antibiotics combination [29https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF19]. Vancomycin-ceftazidime is injected intravitreally as first-line treatment, and vancomycin-amikacin is used as a second-line [30https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF39]. Each agent is diluted in 0.1 mL of sterile water or saline. Ceftazidime is preferred over amikacin because of the small risk of macular infarction with injected aminoglycosides. Antibiotic concentrations in the vitreous decline rapidly following injection and most last only 24 to 48 hours. Thus, one injection of antibiotics may not maintain levels in the vitreous long enough to kill all bacteria. Repeat injection of vancomycin or ceftazidime may be indicated after 48 hours if there is persistent or worsening intraocular inflammation; the second injection of amikacin is avoided given concerns for retinal toxicity. The choice of antibiotic for repeat intravitreal injection is based on the culture result. [30https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF39]. However, the ESCRS emphasizes administrating adjunctive systemic antibiotic therapy for the management of acute postoperative endophthalmitis [31https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF36]. In cases of fulminant refractory acute postoperative surgery endophthalmitis with rapidly worsening visual acuity, complete vitrectomy operation is the fundamental option to debride ocular pus [32https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF7].

Delayed-Onset Postoperative Endophthalmitis

The treatment of chronic postoperative endophthalmitis is difficult because of delayed diagnosis due to variable clinical manifestations (Figure 2) with different differential diagnoses as well as different causative organisms [33https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF40]. Treatment usually involves partial capsulectomy associated with injection of intraocular antibiotics, but this regimen may lead to complete resolution in only 50% of the cases. Additionally, 70-90% of the cases were completely treated with total capsulectomy and IOL exchange or removal because the organisms were sequestered in the capsule
[33https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF40]. Therefore, intravitreal antibiotics injection, IOL extraction, and vitrectomy remain the best treatment options
[34https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8913541/ - REF41].

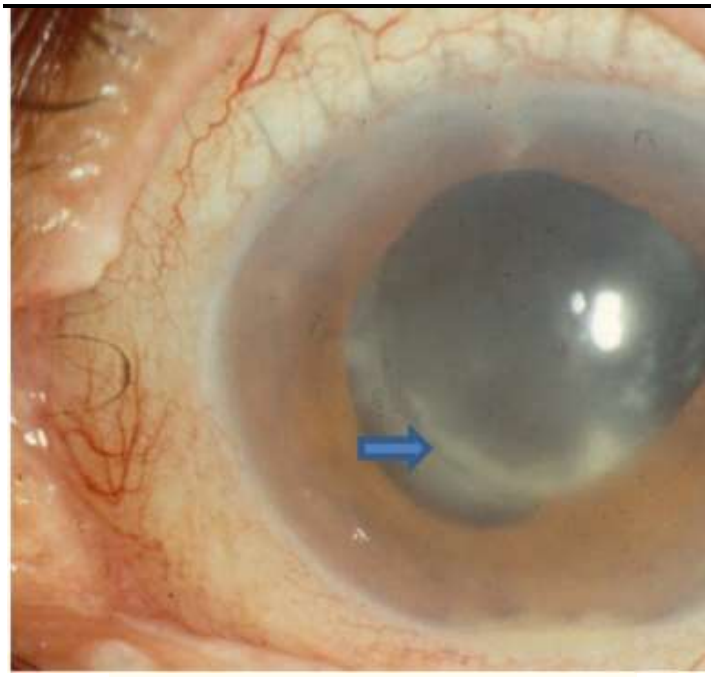

Fig. 2 Delayed-onset (chronic) postoperative endophthalmitis with small hypopyon and peripheral intracapsular infiltrates (arrow).

Conclusion

In order to reduce the risk of postoperative endophthalmitis, all patients undergoing cataract surgery should be evaluated for any potential risk factors. At the time of surgery, 5% povidone-iodine is the antiseptic agent of choice for the area surrounding the eye as well as the ocular surface. It is also suggested by Jagadesh C Reddy and co. that IC antibiotic should be included as a part of the standard operating protocol for cataract surgery[35]. This will marginally increase the cost of surgery, but the cost–benefit ratio is much higher in the event of endophthalmitis without its use. While waiting for such a policy decision, one should consider IC antibiotic during cataract surgery in the elderly (≥ 70 years), in immunodeficient people including those with diabetes, in people with one seeing eye, in events of longer duration (>30 minutes) surgery, and in events of posterior capsule rent. Moreover, we strongly recommend the Ophthalmologists to call patients for early follow-up after cataract surgery to detect any sign of endophthalmitis and treat it immediately and ensure patient compliance on post-surgery medication and precautions to reduce the serious complications caused by late diagnosis and treatment of postoperative endophthalmitis.

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