BEST PRACTICES FOR ENDOPHTHALMITIS PROPHYLAXIS

A comprehensive review.

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Modern phacoemulsification stands as a paragon of safe, effective, and highly successful surgical procedures. No operation is entirely without risk, however, and postoperative endophthalmitis, although uncommon, remains a dreaded complication. Approaches to endophthalmitis prophylaxis differ by country and region, and data on the efficacy of traditional measures are inconsistent. In this article, Dr. Grzybowski provides a comprehensive review of best practices for preventing endophthalmitis.

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In 2007, the ESCRS conducted a pivotal study of the perioperative prophylaxis of postoperative endophthalmitis.[1] Carried out in 24 ophthalmology units and eye clinics across nine European countries, the randomized, controlled, multicenter study found that the intracameral (IC) injection of cefuroxime decreased the risk of endophthalmitis following phaco cataract surgery by a factor of five.

The ESCRS published guidelines in 2013 that detail preventive measures and treatment options for postoperative endophthalmitis.[2] Ophthalmologists are advised to perform surgical procedures in specially designed operating theaters equipped with proper airflow systems and use sterile or single-use equipment. Health care professionals are also instructed to adhere to rigorous hygiene practices, including washing their hands with antiseptic soap and wearing masks, gowns, and sterile gloves.

FUNDAMENTAL 1 STRICT HYGIENE AND ANTISEPTIC MEASURES

The ESCRS guidelines mandate antisepsis of the periocular skin area, cornea, and conjunctival sac with topical povidone-iodine. A 5% to 10% povidone-iodine solution is applied to the skin's surface and left in place for at least 3 minutes. If a contraindication (eg, allergy or hyperthyroidism) exists, a 0.05% chlorhexidine solution may be used instead. For antisepsis of the conjunctiva and cornea, a 5% povidone-iodine solution should remain in the conjunctival sac for no less than 3 minutes. Solutions containing detergents should be avoided to prevent corneal damage. In accordance with the recommended protocol, 1 mg of cefuroxime in 0.1 mL saline (0.9%) is administered via an IC injection at the conclusion of surgery.[2]

Cefuroxime acts as a broad-spectrum antibiotic, effectively targeting most gram-positive and gram-negative organisms commonly implicated in postoperative infectious endophthalmitis. Notable exceptions include methicillin-resistant *Staphylococcus aureus*, methicillin-resistant *Staphylococcus epidermidis*, *Enterococcus faecalis*, *Pseudomonas aeruginosa*, and *Pseudomonas acnes*.

The ESCRS guidelines hold that administering topical antibiotics before or after surgery does not offer distinct advantages over the preoperative application of chlorhexidine or povidone-iodine coupled with the IC administration of antibiotics at the conclusion of surgery. The prophylactic efficacy of chlorhexidine against endophthalmitis, however, requires further investigation. The selection of postoperative antisepsis currently hinges on the surgeon's appraisal of the patient's postsurgical state and evaluation of any ensuing complications. Intravenous antibiotic prophylaxis is not endorsed because of its weak penetration into an eye that is not inflamed. Oral antibiotic prophylaxis is reserved for instances of severe coexisting atopic disease when the lid margins are habitually colonized with *S aureus*. In the event of a penetrating injury, the same antibiotic should be administered both systemically and intravitreally.[3-11]

FUNDAMENTAL 2 PREOPERATIVE PREPARATIONS

Povidone-iodine. This antiinfective is widely used as a surgical scrub for skin disinfection, in the preparation of patients for ophthalmic surgery, and as an intraocular injection. Extensive studies have been conducted on the medication's ophthalmic use, and level 1 evidence supports the application of a 5% to 10% povidone-iodine solution to the ocular surface and eyelids 3 minutes before cataract surgery.[12-14]

Povidone-iodine has demonstrated antimicrobial properties against various bacteria, fungi, protozoa, and viruses. Its antimicrobial activity is predicated on the direct delivery of diatomic-free iodine to the surface of target cells. In the context of bacteria, povidone-iodine targets the cytoplasmic membrane and cytoplasm, leading to swift bacterial eradication. Free iodine iodinates and oxidizes proteins, enzymes, and other vital molecules, thereby compromising their biologic function. It is noteworthy that, unlike antibiotics, povidone-iodine lacks a specific targeting mechanism for microorganisms and may affect host cells.[12-14]

In vitro studies, animal models, and clinical research have evaluated the potential toxicity of povidone-iodine in ophthalmic applications. Corneal epithelial and endothelial cells have been shown to tolerate repeated irrigation with 0.25% povidone-iodine during cataract surgery. In vitro studies found that 12-hour exposure to 0.05% povidone-iodine did not manifest toxicity to cultured bovine endothelial cells.[12-14] In a rabbit model, intravitreal injections of 0.1 mL of 0.1% and 0.3% povidone-iodine were well tolerated, as evaluated by electroretinography and histologic examination.[12-14] Randomized controlled trials of povidone-iodine with a specific focus on the primary endpoint of endophthalmitis rates are scarce. Nonetheless, a substantial nonrandomized parallel trial found that the application of 5% povidone-iodine to the conjunctiva before surgery reduced the incidence of endophthalmitis from 0.24% to 0.06%.[15] Studies have also assessed the concentration, dosage, and other facets of povidone-iodine application to the conjunctiva and anterior chamber contaminated with known bacterial concentrations as surrogate measures for diminishing the risk of endophthalmitis.[16]

Topical antibiotics. The use of topical antibiotics varies worldwide. In Sweden and Denmark, national guidelines advise against administering topical antibiotics before and after cataract surgery in standard cases. Most surgeons follow this advice. Postoperative topical antibiotics are commonly prescribed for 5 to 7 days in most European countries, but the agents' preoperative use has declined in recent years. For example, French national guidelines do not endorse the administration of topical antibiotics before surgery, and numerous surgeons in Poland and Germany have abandoned the practice.[3-11]

FUNDAMENTAL 3 INTRAOPERATIVE TECHNIQUES

Surgical complications such as wound leak, posterior capsular rupture, vitreous loss, and zonular complications are associated with an increased incidence of postoperative endophthalmitis. Elderly patients (especially those older than 85 years of age), patients with clear corneal versus scleral tunnel incisions, and those without an IC injection of cefuroxime are also at increased risk of infection.

The type of IOL implanted is another risk factor for endophthalmitis. Patients with silicone IOLs are more likely to develop this form of inflammation than those who receive IOLs made of acrylic or other materials.[1,2] The highest incidence of endophthalmitis reported in the literature occurred after secondary IOL implantation, and the lowest incidence occurred after pars plana vitrectomy, although postoperative endophthalmitis developed after cataract surgery in most instances.[3-11]

The selection of prophylactic IC antibiotics varies globally. Cefuroxime, moxifloxacin, and vancomycin are the most common agents.

Cefuroxime. The ESCRS Study provided substantial evidence to support the use of IC cefuroxime in prophylaxis.

Moxifloxacin. This fourth-generation fluoroquinolone has demonstrated potent, concentration-dependent activity against gram-positive bacteria, gram-negative bacteria, and atypical organisms. The increasing resistance to fluoroquinolones of coagulase-negative staphylococci, however, is a growing concern. Several retrospective studies have shown a low relative risk of endophthalmitis in patients who received IC moxifloxacin compared to those who did not receive IC antibiotic prophylaxis.[17] A randomized controlled trial analyzed the use of moxifloxacin in a small surgical population.[17] Several retrospective studies have shown a lower relative risk of endophthalmitis in patients who received IC moxifloxacin compared to those who did not receive any form of IC antibiotic prophylaxis.[17]

IC moxifloxacin is usually administered undiluted or at a dose of 500 mg. In India, moxifloxacin hydrochloride is used extensively for IC antibiotic prophylaxis.[17]

Vancomycin. IC vancomycin has been used in cataract surgery worldwide. Large retrospective analyses reported significant reductions in the incidence of endophthalmitis with IC vancomycin. In 2014, however, severe instances of bilateral ischemic retinal vasculitis following IC vancomycin were noted, along with subsequent reports of hemorrhagic occlusive retinal vasculitis (HORV) associated with IC vancomycin.[17] HORV is marked by painless vision loss and other specific ophthalmic findings after an otherwise uneventful postoperative period.[18] The HORV Task Force documented cases of HORV following IC vancomycin, underlining the challenges of diagnosis and management.

FUNDAMENTAL 4 POSTOPERATIVE CARE

Topical antibiotics. Despite a lack of definitive evidence supporting the use of topical antibiotics for prophylaxis, the practice remains widespread. A 2021 survey by the ASCRS found that most respondents used topical antibiotics both peri- and postoperatively.[19] It remains unclear, however, whether the reduction in conjunctival flora achieved through topical antibiotics effectively lowers endophthalmitis rates. The ESCRS

study found no significant difference in endophthalmitis rates between patients receiving perioperative topical levofloxacin and those who did not.[1,2] Similarly, a systematic review and meta-analysis of randomized controlled trials and observational studies did not find sufficient evidence to endorse the use of postoperative topical antibiotics following ocular surgery.[20]

It is essential to recognize that the drug concentration attained with IC administration significantly surpasses that achieved with topical administration. Some studies have explored the supplemental effect of topical or systemic antibiotics in combination with IC cefuroxime. The administration of topical agents, however, has not shown uniform benefits.[1-4] It is imperative for ophthalmologists to strive to minimize the use of topical antibiotics and, when required, administer them at maximal doses and elevated frequencies to avert the emergence of drug resistance.

Antiseptics. Povidone-iodine, chlorhexidine, and other antiseptics may serve as alternatives to antibiotics. Povidone-iodine is the gold standard among antiseptics in ophthalmology owing to its wide-ranging antimicrobial action against various microorganisms. The agent, moreover, does not induce resistance or cross-resistance to antibiotics.

Chlorhexidine is larger and less potent against specific bacteria, such as *P aeruginosa*. Use of this antiseptic has also been correlated with bacterial resistance, particularly methicillin-resistant *S aureus*.

Generally, povidone-iodine is thought to be less irritating than chlorhexidine; high concentrations of chlorhexidine can be toxic to the corneal epithelium. Anaphylaxis after topical povidone-iodine administration has never been reported, and adverse skin reactions to the agent are exceedingly rare, rendering it a safe and well-tolerated solution for ophthalmic application.

FUNDAMENTAL 5 EMERGING TRENDS AND TECHNOLOGIES

The effectiveness of povidone-iodine rests on the release of free iodine from the solution and its subsequent infiltration of microbial membranes, causing cell death. The bactericidal impact of povidone-iodine can be realized in 15 to 120 seconds, depending on the concentration used. Safe and effective concentrations of povidone-iodine range from 0.005% to 10%.[13] Recent studies have shown that even diluted povidone-iodine solutions can wield a bactericidal effect.[14] For instance, cleansing the ocular surface with a 0.25% povidone-iodine solution, even when diluted 25 to 50 times in the operative field, still manifested a bactericidal impact.[14] The diluted solutions required less time to eliminate bacteria because the dilution aids in the release of free iodine.

Further investigation has substantiated the efficacy of iodine solutions in curtailing bacterial contamination during cataract surgery.[13] Periodic irrigation of the operative field at 20-second intervals with diluted iodine solutions (eg, 0.025% povidone-iodine and 0.0025% polyvinyl alcohol iodine) throughout cataract surgery resulted in a markedly low rate of bacterial contamination within the anterior chamber.[14] This suggests that iodine solutions could serve as a viable alternative to preoperative antibiotics for prophylaxis against postoperative endophthalmitis in cataract surgery.

Beyond prophylaxis, studies have evaluated the application of povidone-iodine for the treatment of postoperative endophthalmitis. Research has demonstrated that repeated irrigation of the operative area with 0.25% povidone-iodine during vitrectomy diminished vitreous contamination without evident ocular toxicity.[12,14] This indicates that povidone-iodine might be a safe and effective approach for the prevention and treatment of postoperative endophthalmitis. Additional studies of this potential application are warranted. The ability of povidone-iodine to reduce bacterial contamination coupled with its relatively low ocular toxicity positions it as a promising option to enhance surgical outcomes. ■

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