Chapter

Antiseptic and Antibiotic Prophylaxis for Cataract Surgery

Sara Crespo Millas, Salvatore Di Lauro and David Galarreta Mira

Abstract

Prophylaxis for eye infections is important to avoid catastrophic consequences such as infectious endophthalmitis. There are different options as prophylaxis in cataract surgery. Prophylaxis with antiseptics is more and more important in ocular surgery and possesses several advantages compared to antibiotic prophylaxis. Povidone-iodine (PVI) 5% in the conjunctival sac and PVI 10% on periocular skin for 3 minutes is recommended prior to any cataract surgery to reduce the risk of postoperative endophthalmitis. Intracameral cefuroxime (1 mg/0.1 ml) at the end of the surgery is also useful in reducing the risk of infectious endophthalmitis. Nevertheless, there is no scientific evidence supporting the use of topical antibiotics in the postoperative period.

Keywords: cataract surgery, prophylaxis, antiseptic, antibiotic, endophthalmitis

1. Introduction

Infectious endophthalmitis after cataract surgery is an uncommon but devastating complication [1–4]. Infectious prophylaxis is essential in any eye surgery to prevent the infectious endophthalmitis. There are two forms of prophylaxis: antiseptic and antibiotic prophylaxis. The correct use of antibiotics is critical to avoid any unnecessary microorganism resistance able to reduce the already limited therapeutic options available to treat eye infections. Prophylaxis with antiseptics is more and more important in ocular surgery and possesses several advantages compared to antibiotic prophylaxis.

2. Antiseptics

The ideal antiseptic may have a wide spectrum of antimicrobial activity, including pathogens in biofilms, limited inactivation by organic compounds, good penetration including in the necrotic tissue with limited systemic absorption, without risk of acquired microbial resistance, good local and systemic tolerance, ability to aid cicatrization, may be easy to use and cheap [5, 6].

Povidone-iodine (PVI) is the most widely used antiseptic for ocular surgery. The PVI is a disinfectant and antiseptic of intermediate level [5, 6]. It is used in different concentrations (between 0.1 and 10%) depending on the country, but the most frequent concentrations are 5% in the conjunctival sac and 10% in periocular skin [5, 6].

The concentration of free iodine is already maximum with PVI 0.01–1%, obtaining minimum bactericide time. Nevertheless, free iodine is inactivated by the interaction with bacteria and organic compounds and with those concentrations it is necessary to repeat the PVI administration to maintain the bactericide effect [6]. PVI 2.5–10% generates enough free iodine reserve concentration to avoid the need for repeated administrations with a contact time of 3 minutes [1, 6].

PVI has well-known toxicity on the corneal epithelium and is directly related to the concentration and contact time [6]. PVI is toxic in vitro for epithelial cells, fibroblasts and endothelial cells in animal models. Nevertheless, repeated exposure during cataract surgery at 0.25% concentration is not toxic for the endothelium [6]. The application of PVI 5% is also safe for the endothelium [6].

Allergic reactions to PVI are rare and frequently reported by the patient and not confirmed [7]. Most frequently, contact dermatitis appears and is incorrectly classified as an allergy. There are no reports of anaphylactic reactions after topical ophthalmic use of PVI [8]. Iodine contrast allergy does not mean allergy to PVI [9]. In cases of real PVI allergy, there are alternative antiseptics available such as chlorhexidine.

Chlorhexidine is a cationic biguanide able to damage the bacterial cellular wall and cytoplasm. It is considered as a low-level disinfectant with lower microbicide activity compared with PVI, especially over viruses [10]. Furthermore, it is not sporicidal and not able to act on biofilms. Nevertheless, it is equally valid for infectious prophylaxis in ocular surgery, especially in cases with confirmed PVI allergy [6, 10].

Topical application on periocular skin must not exceed 0.5% considering the risk of accidental exposure to the corneal epithelium which may cause damage to the corneal epithelium. The recommended concentration for conjunctival irrigation of aqueous chlorhexidine is 0.05 acetate and 0.1% gluconate [10]. Alcoholic chlorhexidine must be avoided because it is toxic to corneal epithelium, stroma and endothelium [10]. Aqueous chlorhexidine is well tolerated, offering low epithelial toxicity [10]. A rare resistance to chlorhexidine of some *Staphylococcus* species has been described [11].

The ozonized oil is an alternative antiseptic in liposomal formulation to improve eye tolerance. The mechanism of action is based on oxygenated compounds, lipidic peroxides and oxygen-reactive species able to damage pathogens through direct oxidation as by interaction with macromolecules, destroying them. Results in animal models and in patients where they show the ability to reduce the ocular surface flora before cataract surgery are promising [12, 13].

3. Antibiotics

Antibiotics have been used during the perioperative period as a prophylactic agent in multiple ophthalmic surgeries. Their use is limited because of the development of antiseptic agents and multiple disadvantages. In fact, antibiotics compared with antiseptics have the following limitations:

- Limited spectrum of antimicrobial activity

- Usually, microbiostatics not microbicides
- High risk of resistance
- Limited or absent activity against multi-resistant organisms
- No residual effect
- Low concentration in the eye
- Cytotoxicity
- Potentially high allergenicity

Antibiotics compared with antiseptics can be used not only topically but also systemically. Topical administrated antibiotics have been most commonly used in ophthalmology, but they did not show superiority compared with antiseptics as prophylactic agents [11].

Alternative administering ways such as systemic, subconjunctival or mixed with irrigation infusion fluid did not show advantages in preventing infections after cataract surgery [1]. Nevertheless, intracameral antibiotics are useful in preventing infectious endo-ophthalmitis after cataract surgery [1, 14]. Intracameral antibiotics can be used at relatively high concentrations and with an extremely low chance of developing microbial resistance [3].

3.1 Intracameral antibiotics

The use of intracameral antibiotics at the end of the cataract surgery is the only procedure that has shown efficacy in endophthalmitis prophylaxis. Generally, three antibiotics have been used: cefuroxime, moxifloxacin and vancomycin, each one of them with their particularities (**Table 1**) [2].

3.1.1 Cefuroxime

Cefuroxime was the antibiotic chosen for the study by the European Society of Cataract and Refractive Surgeons (ESCRS) [1] for its spectrum and experience of use. It is a second-generation cephalosporine that has demonstrated its safety at the doses used for intracameral injection. Although penicillin allergy is frequent, the cross-reactions with cefuroxime are rare. A meta-analysis has estimated that in patients with a history of allergy to penicillin, the general index of cross-reactivity with cephalosporin antibiotics is approximately 1% [15]. The risk of cross-reactivity with penicillin exists principally for first- and second-generations which have similar R1 lateral chains. The cefuroxime has not a similar R1 lateral chain and high risk of cross-reactivity with penicillin is practically negligible, although there are documented cases of anaphylaxis after intracameral use [3].

3.1.2 Moxifloxacin

Moxifloxacin is a fourth-generation fluoroquinolone that inhibits the bacterial topoisomerases II and IV. Intracameral moxifloxacin has not been evaluated in

Antibiotic and recommended dose	Spectrum	Resistances	Security
Cefuroxime 1 mg/0.1 mL	Wide spectrum gram-positive and limited to gram-negative	No efficacy against methicillin-resistant *Staphylococcus. aureus*	Secure at recommended dose. Possibility of toxic anterior segment syndrome at wrong concentrations
Moxifloxacin 250 μg/0.05 mL 0500 μg/0.1 ml	Wide spectrum gram-positive and negative. Good activity against atypical germs	No efficacy against methicillin-resistant *Staphylococcus aureus.* Cross-resistance with other quinolones	Use from the eye drops formulation, without approval for intracameral use
Vancomycin 1 mg/0.1 mL	Effective against the majority of gram-positive. Limited activity against gram-negatives	Rare resistance to gram-positive	Pharmaceutical preparation from intravenous solutions

Table 1.
Characteristics of the antibiotics more used in the prophylaxis in cataract surgery.

randomized clinical trials but the evidence in observational studies suggests that it is effective. A study with more than two million cataract surgeries from the same institution in India showed a general reduction in the number of postoperative endophthalmitis from 0.07 to 0.02% with the routine use of moxifloxacin [2].

There are no anaphylaxis cases reported after the intracameral use and the severe hypersensitivity reactions related to the moxifloxacin are probably rare [2].

3.1.3 Vancomycin

Vancomycin is a glycopeptide antibiotic that acts by binding pentapeptides, preventing peptidoglycans polymerization and weakening bacterial cellular walls [2]. The spectrum of action includes gram-positive coccus, the most frequent causal agent in infectious endophthalmitis. It has been used extensively in the past, but it has gradually been replaced by cefuroxime and moxifloxacin. Intracameral vancomycin 1 mg/0.1 ml is enough to achieve the minimal inhibitory concentration for almost all gram-positive coccus [2]. There are some reasons to avoid it: (1) risk of hemorrhagic/obstructive retinal vasculitis with devastating results on VA; (2) vancomycin is the treatment of choice in infectious endophthalmitis and the use as a prophylactic agent may limit its use if necessary; (3) risk of resistance [2, 11].

3.2 Topical antibiotics

There is no evidence that they are useful in preventing postoperative endophthalmitis when used in the preoperative and postoperative periods [1]. There is evidence that the use of topical antibiotics before surgery is not better than the use of PVI alone [4]. Furthermore, there is a higher risk of resistance and global costs are significantly increased [11]. Nevertheless, postoperative topical antibiotics are commonly used all

around the world, especially fluoroquinolones, tobramycin and the combination of polymyxin- neomycin- gramicidin [16].

4. Recommendations for infectious prophylaxis in cataract surgery

Infectious endophthalmitis after cataract surgery is uncommon (0.01-0.08%) [1]. Topical PVI in periocular skin and conjunctival sac and intracameral cefuroxime at the end of the surgery have been demonstrated to be effective as prophylactic measures [1].

Preoperative prophylaxis [1]

- PVI (level of evidence 2, clinical recommendation B): PVI 5% for cleaning of the cornea and conjunctival sac; PVI 10% on periocular skin; minimum recommended contact time: 3 minutes; in case of PVI allergy change to aqueous chlorhexidine 0.05% in the conjunctival sac

- Preoperative lid hygiene (level of evidence 3, clinical recommendation C): can be useful in patients with an increased population of *Staphylococcus aureus* (especially patients with rosacea and atopy)

- Preoperative topical antibiotics (level of evidence 3, clinical recommendation C): there is no evidence of endophthalmitis reduction which can result in resistance.

- Operating room, surgeon and patient preparation: standard protocols of sterilization and operating room preparation. It is important to isolate the eyelashes and eyelids with an adhesive cloth

Recent data suggests PVI 0.5–1% may have the same results as PVI 5% in the conjunctival sac avoiding corneal toxicity and being commercially available also in combination with hyaluronic acid [1]. Nevertheless, these concentrations must be used carefully and according to posology [4].

Intraoperative prophylaxis

- Intracameral antibiotic (level of evidence 1b; clinical recommendation A): cefuroxime (1 mg/0.1 ml) is the preferred antibiotic because: is active against bacteria most commonly involved in endophthalmitis; there is evidence of effectiveness in a European multicentric study; cross-reaction with penicillin is uncommon; availability of a commercial single dose formulation. In allergic patients' moxifloxacin (250-500 μg/0.1 ml) can be used.

In addition to intracameral antibiotics, it is important to confirm that the surgical wound is well sealed at the end of the surgery. In fact, periocular flora is responsible for the vast majority of postsurgical endophthalmitis [17] and if there is any doubt about wound tightness a surgical suture is recommended [18].

Postoperative prophylaxis

Postoperative topical antibiotics are extensively used but their use combined with intracameral antibiotics does not improve results [1, 16]. When used, it is

important to avoid a descending treatment regimen because of the risk of improving resistance [11, 18].

5. Conclusions

Topical antiseptics such as PVI have several advantages over antibiotics as prophylactic agents for infectious endophthalmitis after cataract surgery. PVI 5% in the conjunctival sac and PVI 10% on periocular skin for 3 minutes is recommended prior to any cataract surgery to reduce the risk of postoperative endophthalmitis. In patients with an allergy to PVI, chlorhexidine 0.02-0.1% in the conjunctival sac can be used. Intracameral cefuroxime at the end of the surgery is effective as a prophylactic measure, although in allergic patients intracameral moxifloxacin may be used. On the contrary, there is no evidence that postoperative topical antibiotics are useful.

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