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REVIEW

Prophylaxis of Ocular Infection in the Setting of Intraocular Surgery: Implications for Clinical Practice and Risk Management

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ABSTRACT

In this review we discuss the role of intraocular surgery preoperative prophylaxis. The correct choice of antimicrobial drug is variable in each surgical setting, according to the available strengths of evidence, the anatomical district involved, and the type of procedure. In the ophthalmic surgical field, there has been a progressive shift from antibiotic formulations, which are known to cause antibiotic resistance, to a new class of antiseptic compounds, which proved to be effective not only against bacteria, but also against fungi, protozoa, and viruses. Among these, povidone–iodine (PVI) is a water-soluble polymer that can form a complex with iodine, and the perioperative application of PVI 5–10% eye drop for 3 min is the gold standard for infection prophylaxis. A new formulation of 0.6% PVI eye drop is a new option for infection prophylaxis in the days before surgery. Chlorhexidine is a biguanide compound, which is a valid alternative with a good safety and efficacy profile and is the antiseptic of choice in patients with iodine allergy. New compounds that are currently being studied include polyhexamethylene biguanide (PHMB), picloxydine, ozone, hypochlorous acid (HOCl), and Biosecur. PHMB is a biguanide polymer that was found to be more effective than PVI in in vitro studies for reducing microorganisms and extending the duration of antisepsis, but to date, there are no formulations available on the market for preoperative ocular surgery in which it is present as main ingredient. Ozone is a molecule with oxidizing effect, which showed interesting preliminary results but is not effective against virus, *Staphylococcus aureus* and *Candida albicans*. HOCl has a natural bactericidal propriety but its applicability to prophylaxis of ocular infection in the setting of ocular surgery is not established. Biosecur is a non-toxic organic alcohol-free compound that exhibited

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bactericidal and fungicidal effect versus all common microorganisms and is currently available as an ocular spray.

Keywords: Antisepsis; Disinfectant; Antibiotic resistance; Ocular surgery; Endophthalmitis; Risk management; Public health

Key Summary Points

Why carry out this study?

Preoperative prophylaxis is essential to minimizing surgery-related infections and can be achieved with a new class of antiseptic compounds that showed effects against bacteria, fungi, protozoa, and viruses.

Newly introduced formulations with lower concentration of povidone–iodine or chlorhexidine are used in the preoperative days to reduce the conjunctival bacterial load.

In vitro/vivo studies are assessing the efficacy of new compounds, including PHMB, picloxydine, ozone, hypochlorous acid, and Biosecur.

A correct risk management protocol for infection prophylaxis may reduce healthcare-acquired infections and the related medical–legal disputes.

What was learned from the study?

Prophylaxis of infection represents a crucial step of intraocular surgery. Povidone–iodine is a compound well studied in the literature, and it is broadly used even if at different concentrations. Chlorhexidine is becoming more used as published studies demonstrate good safety and efficacy profiles with reduced patient discomfort. Moreover, there are new compounds such as picloxydine, ozone, hypochlorous acid, and Biosecur that showed very interesting preliminary results.

INTRODUCTION

Preoperative prophylaxis is the standard of care before ophthalmic surgery to reduce the risk of postoperative infections [1, 2]. Different strategies for ocular antisepsis are adopted preoperatively to decrease the number of pathological microorganisms residing in the ocular surface at the time of surgery. The survey of the European Observatory of Cataract Surgery suggested a considerable level of heterogeneity among European countries in the use of antiseptics both before and in the operating room [3]. Grzybowski et al. compared various endophthalmitis prophylaxis patterns around the world and concluded that there is no global consensus regarding endophthalmitis prophylaxis with cataract surgery [4].

In particular, povidone–iodine (PVI) solution is considered the most effective antiseptic to reduce postoperative endophthalmitis rates [1, 5, 6]. In 1984, Apt et al. first demonstrated the effect of PVI on the conjunctiva with a reduction of nearly 90% of the ocular surface flora [7]. There is evidence from several studies that the bacteria residing in the lids, tear film, and adnexa are the main agents responsible for infection. In fact, most common microorganisms implicated in postoperative endophthalmitis are coagulase-negative staphylococci (CNS), especially *Staphylococcus epidermidis* and *Staphylococcus aureus* [8, 9]. These organisms are the most common in patient's own flora from the eyelid and conjunctiva [10]. Using molecular epidemiological techniques in the case of endophthalmitis, microbes isolated from the vitreous were found to be genetically indistinguishable from conjunctival organisms isolated from the patient's eyelid in more than 80% of cases [8]. In this scenario, preoperative prophylaxis plays a key role in the prevention of postoperative endophthalmitis. In 2013, the European Society of Cataract and Refractive Surgeons (ESCRS) published the "Guidelines for Prevention and Treatment of Endophthalmitis Following Cataract Surgery," highlighting unequivocally the clinical benefit of the use of the intracameral injection of cefuroxime at the end of cataract surgery thanks to the fivefold reduction in postoperative endophthalmitis rates [11]. At the same time, the use of PVI applied as ophthalmic solution to the cornea, conjunctival sac, and periocular skin immediately prior to surgery is considered mandatory. Surgical disciplines, including ophthalmic surgery, play a key role in healthcare-acquired infections and related medical malpractice cases. Intraocular procedures expose an unavoidable risk of endophthalmitis, and therefore ophthalmic surgery is highly involved in medico–legal controversies, showing a litigation/conviction ratio higher than in other specialties.

Currently, there is no universal consensus regarding the use of ophthalmic preparations in the form of eye drop, spray, or medicated wipes in the days before the surgery [11]. This review aims at highlighting the recent evidence and controversies in the field of preoperative prophylaxis of infection during ophthalmic surgery. Furthermore, since surgical disciplines, including ophthalmic surgery, suffer from the risk of healthcare-acquired infections and are highly involved in medico–legal controversies, a particular focus will be placed on this issue.

This review is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

TRADITIONAL USE OF ANTIBIOTICS

Preoperative prophylaxis with topical antibiotics has been widely used in the past. The main class of antibiotics studied is fluoroquinolones, and all studies demonstrated a reduction in conjunctival bacterial load. Specifically, multiple studies showed a synergic effect between the use of topical levofloxacin 0.3% on the preoperative day and PVI irrigation to reduce the conjunctival bacteria load [12, 13]. Moxifloxacin and gatifloxacin showed similar results and the application four times a day, both one day and three days before surgery, was equally effective in the reduction of colony-forming units (CFU) [14, 15]. Although the efficacy is well established, comparative studies of both moxifloxacin and gatifloxacin against PVI 5% have shown no significant effects on further reduction in the bacterial colonization rate [16, 17].

Regarding the relationship between topical therapy with preoperative antibiotics and endophthalmitis, an observational and cross-sectional study focused on the incidence of this complication after cataract extraction on 464,996 operations reported that short-term topical antibiotics given as add-on prophylaxis did not confer a clear-cut benefit in addition to intracameral antibiotics to reduce the rate of endophthalmitis [18].

Hence, preoperative topical antibiotics do not add any clear supplementary efficacy over PVI alone to reduce the incidence of endophthalmitis. Additionally, the routine use of preoperative fluoroquinolones may select a fluoroquinolone-resistant conjunctival flora [19, 20]. For these reasons, the preoperative use of topical antibiotics is not advisable.

ANTISEPTICS AND DISINFECTANTS

In the last few years, trends in endophthalmitis prophylaxis have changed significantly. Different drugs have been adopted for ocular antisepsis to decrease the overgrowth of pathological microorganisms before the surgery. Antiseptics are biocides or products that destroy or inhibit the growth of microorganisms in or on living tissue. Antiseptics have shown numerous advantages over antibiotics. First, they have a wide range of mechanisms that makes them active not only against bacteria, but also against fungi, protozoa, and viruses [21, 22]. In addition, they do not have a selective mechanism of action, and this makes antiseptics less susceptible to the development of resistance by microorganisms. Finally, their effectiveness is not affected by the presence of a biofilm [23].

Thanks to these characteristics, antiseptics have established themselves as leaders in preoperative prophylaxis in ophthalmic surgery as well. The following sections will describe the antiseptics used in preoperative prophylaxis, in vitro and in vivo evidence of their efficacy, and the main comparison studies (Table 1).

Table 1 Published studies on antiseptic ophthalmic formulations for the preoperative period before ocular surgery

Ophthalmic solutions	Manufacturer	Composition	Dosage	Publications	Main results
Iodim	Medivis, Catania, Italy	0.6% Povidone-iodine	One drop three times a day for three days, and one drop on the day of surgery	Reibaldi et al. [37] Tognetto et al. [38]	Reduction by 82% of the number of bacterial-growth-positive swab cultures, decreasing from 74% at the baseline to 14% after prophylaxis No cases of bacterial growth of post-injection needle cultures (2% in the control group)
Dropsept	Iromed Group s.r.l, Roma, Italy	Chlorexidine 0.02%, Vitamin E and D-a-Tocopherol polyethylene glycol 1000 succinate	No in vivo studies	Tognetto et al. [49] Caruso et al. [50]	Effective bactericidal activity on *S. aureus*, *S. epidermidis*, and *E. coli*. No effect on the growth of *P. aeruginosa*. Antiviral activity against *HAdV-2* and *HCoV-OC43* and amoebicidal activity
CHX 0.1%	Not specified	Aqueous 0.1% chlorhexidine gluconate	One drop three times before the injection, a few minutes apart	Oakley et al. [43]	Endophthalmitis rate after 4322 IVI procedures comparable with those published using PVI preparations
(I) Vitabact (II) Medibact (III) Bactavit	(I) Théa Pharma GmbH (II) Medipack, Pakistan (III) Rompharm, Georgia	Picloxydine dihydrochloride 0.05%	Not specified	Budzinskaya et al. [62]	Microflora growth was not detected in 80% of swabs taken next day after the end of the treatment
Ozodrop	FB VISION S.p.A., San Benedetto del Tronto (AP) Italy	Ozonized oil 0.5% in liposomes plus hypromellose	Two drops four times a day for three days	Spadea et al. [67]	Reduction of > 90% in microbial load in more than 90% of the samples
Ocudox	Alfa Intes, Casoria, Napoli, Italy	Hypochlorous acid	3 min application before surgery	Kanclerz et al. [71]	HOCl group reporting a higher number of positive swabs compared to povidone–iodine

Table 1 continued

Ophthalmic solutions	Manufacturer	Composition	Dosage	Publications	Main results
Oftasecur	OFFHEALTH, Florence, Italy	0.2% Biosecur, 0.15%, hypromellose, 1%, phospholipids S80	Four times per day for four days before surgery	Vagge et al. [74]	Significant reduction in conjunctival bacterial including both Gram-positive (especially *S. epidermidis*) and Gram-negative bacteria

Vitabact (Théa Pharma GmbH; Ciba Vision; Novartis Crop, Novartis; Excelvision, O.C.A.); Medibact (Medipak); and Bactavit (Rompharm)

POVIDONE–IODINE (0.6% AND 5–10%)

Povidone-iodine (PVI), also known as polyvinylpyrrolidone, is a water-soluble polymer with a high molecular weight that can form a complex with iodine [24]. Free iodine released from the complex provides antimicrobial action with a significant decrease in the microbial flora, bacteria, viruses, fungi, and protozoans [7, 25, 26]. A typical chemical property of this iodophor is that the concentration of free iodine increases with the dilution of PVI due to a weakening of the chemical bonding between iodine and povidone [27]. In clinical practice, different studies revealed the safety and tolerability profile of PVI on the ocular surface; however, due to corneal endothelial cell toxicity it cannot be used inside the eye [28, 29]. Despite different concentrations of PVI having been used, the ESCRS recommends applying PVI 5–10% to reach bactericidal efficacy to the cornea, conjunctival sac, and periocular skin for a minimum of 3 min before surgery [11, 30]. Ta et al. demonstrated that PVI at 5% used for 1 min is quicker, less toxic, and equally effective than PVI at 10% in preparation for ocular surgery. In addition, the rate of aqueous humor contamination at the end of surgery did not differ significantly between groups [27]. Results from another study showed that repeated irrigation of the operative field with 0.25% PVI during cataract surgery achieved a very low bacterial contamination rate in the anterior chamber [31]. To date, the use of PVI formulations has become the single most effective method of preoperative antisepsis. However, PVI at 5% cannot be used as preparation for ocular surgery during the preoperative days due to its irritant effects related to the duration of exposure; on the contrary, if used at lower concentrations (0.5–1%) it is less toxic and relatively safe [32]. This low concentration needs only a few seconds to kill bacteria, but unfortunately, has a short duration of cytotoxic effect, requiring frequent applications [33, 34].

Several formulations were used as preoperative prophylaxis prior to cataract surgery. In 2021 Musumeci et al. demonstrated that 0.6% PVI eye drop (IODIM, Medivis, Catania, Italy) used for 3 days in patients who underwent cataract surgery were effective in reducing the conjunctival bacterial load [35]. Accordingly, Pinna et al. showed that 0.6% PVI eye drop had rapid in vitro antimicrobial activity against common etiologic agents of ocular infection, such as *S. epidermidis*, *S. aureus*, and *P. aeruginosa* [36]. In vivo non-prospective studies reported the effectiveness of 0.6% PVI eye drop treatment in reducing the conjunctival bacterial load [37, 38]. According to published results, PVI eye drop at low concentrations (0.6%) is efficacious in preoperative prophylaxis, allowing for the eradication of conjunctival bacteria and ensuring satisfactory ocular tolerability.

CHLORHEXIDINE (CHX)

Chlorhexidine is a biguanide compound whose activity is dependent on the pH of the environment; the optimal range is between 5.5 and 7.0 [21]. CHX is a cationic molecule able to bind to negatively charged bacterial membrane phospholipids [39]. Antimicrobial CHX effect is dose dependent; in particular, it presents bacteriostatic activity at low concentrations (0.02–0.06%) and bactericidal activity at higher concentrations (> 0.12%) [40]. Overall, it has a wide spectrum activity against Gram-positive and Gram-negative bacteria, some yeasts, and some viruses [41]. The ESCRS supports the use of CHX 0.05% for ocular surface preparation as measures for ocular antisepsis in patients with iodine allergy [11]. Merani et al. reported that CHX 0.05% or 0.1% was well tolerated and associated with a low rate of post-intravitreal injection endophthalmitis [42]. Additionally, Oakley et al. reported an endophthalmitis rate of 0.023% in 4322 intravitreal injections using aqueous chlorhexidine gluconate (0.1% Pfizer, New York) [43]. This is comparable with the published rates of PVI [44].

However, it is important to use an aqueous solution of CHX gluconate rather than preparations containing alcohol or detergents, which have been shown to cause epithelial, stromal, and endothelial toxicity, and in the most severely affected cases, permanent stromal scarring or bullous keratopathy [45, 46]. The current understanding of CHX bacterial activity profiles shows resistance among methicillin-resistant *Staphylococcus aureus* and other staphylococci. Furthermore, it is inactive against *Enterobacteriaceae*, *Pseudomonas aeruginosa*, all *Actinobacteria spp*., and all spores [23]. In 1999, CHX was used in Sweden in combination with intracameral cefuroxime in cataract surgery with a postoperative endophthalmitis rate that was stable at around 0.02% [47, 48]. At the same time, in Australia the use of CHX instead of PVI before intravitreal injections did not record changes in the endophthalmitis rates [42].

Dropsept (Iromed Group s.r.l, Rome, Italy), a new preparation based on CHX 0.02%, Vitamin E and D-a-Tocopherol polyethylene glycol 1000 succinate, was recently introduced. An in vitro study by Tognetto et al. showed a good antiseptic activity against *E. coli*, a weaker activity against the staphylococci strains and *P. aeruginosa*, while *Candida albicans* was not affected [49]. Similar in vitro results were shown by Caruso et al., with effective bactericidal activity on *S. aureus*, *S. epidermidis*, and *Escherichia coli*, but with no inhibitory effect on the growth of *P. aeruginosa*. In addition, Dropsept showed antiviral activity against HAdV-2 and HCoV-OC43 and amoebicidal activity [50]. These in vitro results are very interesting and promising, but in vivo studies using Dropsept or CHX at a concentration of 0.02% have yet to be performed to confirm its effectiveness in the prophylaxis of post-surgical endophthalmitis as well as its ocular tolerability.

POLYHEXAMETHYLENE BIGUANIDE (PHMB)

Polyhexamethylene biguanide (PHMB) is a biguanide polymer used as a compound in preservative, disinfectant, and broad-spectrum antiseptic [51, 52]. Biguanides are potent chemical bases, and as a result, PHMB compounds have a high positive charge at physiological pH [53]. In the past, it was believed that the mechanism of action was mostly based on the disruption of microbial membranes [52, 54–56], but more recently, the ability to specifically bind and compress bacterial DNA, halting bacterial cell division, has been reported. This mechanical antibacterial method of action might contribute to the explanation of the minimal incidence of antibiotic resistance associated with the use of PHMB, despite considerable testing since its synthesis [52]. PHMB has been shown as effective against a broad range of infections, including *Acanthamoeba castellanii* [57], *S. epidermidis* [54, 57], and *E. coli* strains [52, 54]. The segregation of the polymer into endosomes, which appears to protect the nucleus from its negative effects, leaves mammalian cells mostly unaffected by it [52]. In addition, in comparison to other antimicrobials, PHMB resulted in quicker wound healing [58]. A prospective, randomized, double-masked controlled trial in 90 healthy volunteers was conducted to assess the safety and tolerability of preservative-free PHMB at three dosage levels (0.04%, 0.06%, and 0.08%). Except for corneal punctate keratopathy caused by PHMB 0.08%, which healed completely in 7–14 days, there was no tendency for an increased incidence of any mild adverse events (AEs) as PHMB concentrations rose [59]. Randomized clinical research found that PHMB was more effective than PVI at reducing microorganisms and extending the duration of antisepsis [60]. Ristau et al. showed a low incidence of endophthalmitis following intravitreal injections (IVIs) using polyhexanide as an antiseptic, which was equivalent to the incidence in earlier trials using PVI [61]. To the best of our knowledge, despite PHMB being present as a preservative in several eye drops, there are no formulations available on the market for preoperative ocular surgery that have it as main ingredient.

PICLOXYDINE DIHYDROCHLORIDE

Picloxydine dihydrochloride is another biguanide with significant antiseptic power. There are few studies in the literature showing its efficacy in the setting of ophthalmology. Budzinskaya et al. showed the efficacy of eye antiseptic picloxydine 0.05% against conjunctival bacteria in patients undergoing intravitreal injections [62]. Three different formulations containing Picloxydine are commercially available: Vitabact (Thea Pharma GmbH; Ciba Vision; Novartis Crop, Novartis; Excelvision, O.C.A.), Medibact (Medipak), and Bactavit (Rompharm). More studies on this molecule are needed to provide robust results.

OZONE

Ozone is a molecule with oxidizing effect that has been extensively studied for its antiseptic and antiinflammatory properties [63–66]. The mechanism of action is based on penetration of ozonides into the wall of the target pathogen and hydrolyzation, forming reactive oxygen species that alter the pathogen proteins, lipids, and DNA/RNA [67].

A specific ophthalmic formulation has been recently developed composed of ozonized oil 0.5% in liposomes plus hypromellose (Ozodrop, FB VISION S.p.A., San Benedetto del Tronto, Italy). Caruso et al. showed an inhibition of the growth of *S. epidermidis* and *E. coli* in vitro after 24 h, and *S. aureus* and *P. aureginosa* after only 7 days. Ozodrop did not exert any antiviral activity and antiamoebic effect [50]. Again in vitro, Tognetto et al. showed antimicrobial efficacy of Ozodrop against *S. epidermidis*, *E. coli*, and *P. aeruginosa*. Moreover, no activity was detected against *S. aureus* strains and *C. albicans* [49]. Focusing on the anti-Candida effect, Celenza et al. showed an antifungal effect on several Candida species [65]. Regarding clinical studies, Spadea et al. published the results of an interventional, non-randomized, clinical study on patients undergoing cataract surgery [67]. This study showed a reduction of $> 90\%$ in microbial load in $> 90\%$ of the samples presented in the group treated with Ozodrop, with optimal ocular tolerability. Liposomal ozonated oil has shown similar effects to other traditional antiseptics, with a wide antimicrobial power and a low rate of adverse events [49, 50]. Therefore, it may be an interesting option before ophthalmic surgery as an alternative to traditional compounds.

HYPOCHLOROUS ACID

Hypochlorous acid (HOCl) has a natural bactericidal propriety since it is generated as a portion of the cytotoxic myeloperoxidase in neutrophils [68]. In vitro studies demonstrated that HOCl triggers oxidation of nucleotides, deactivation of cell enzymes, interruption of cell membranes and prompt cell lysis [69]. Therefore, HOCl is potentially a highly active compound versus all infectious human pathogens. Furthermore, HOCl was not toxic when used on the ocular surface, making it an established adjuvant to manage eye infections [70]. However, its applicability to prophylaxis of infection in the setting of ocular surgery is not established. A study by Kanclerz et al. reported

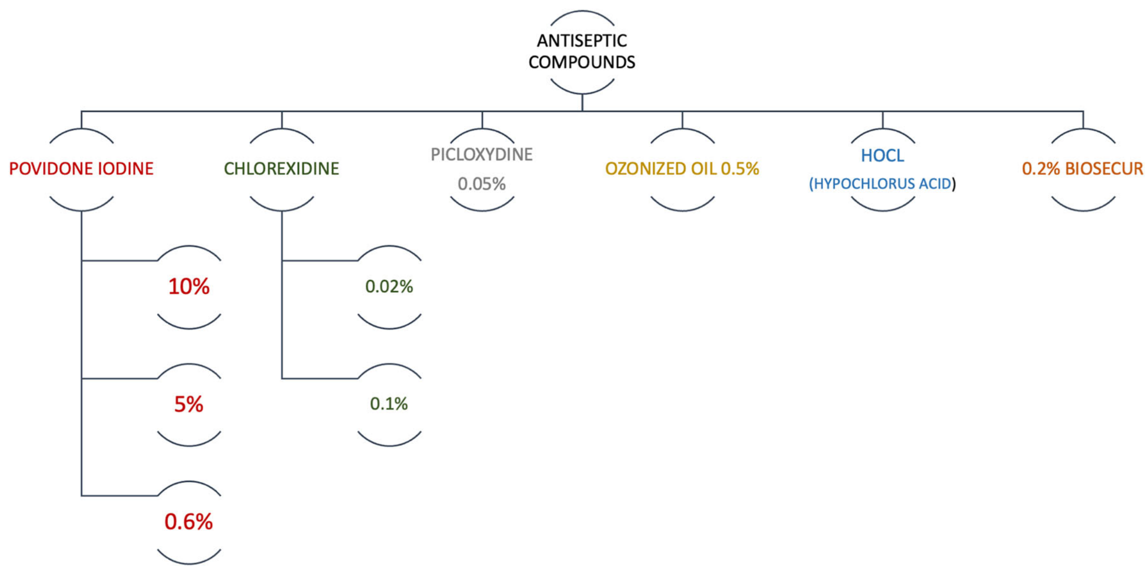

Fig. 1 Synoptic diagram representing the analyzed compounds

results of conjunctival swabs performed in patients undergoing cataract surgery that were randomized to either 10% PVI or HOCl solution; according to their results there was a significant difference, with the HOCl group reporting a higher number of positive swabs [71]. An advantage of the HOCl group was the significantly lower level of discomfort. Overall, more evidence is needed, and currently, there is an ongoing open-label, single-group clinical trial (*NCT04568213*) testing the effect of HOCl disinfection on ocular flora prior to cataract surgery [72].

BIOSECUR

Biosecur is a non-toxic organic alcohol-free compound containing citrus bioflavonoids suspended in glycerin. Mencucci et al. tested in vitro a liposomal commercial formulation, Oftasecur Ocular Spray (OFFHEALTH S.p.a., Florence, Italy) containing 0.2% biosecur, reporting bactericidal and fungicidal effects versus all common microorganisms at dilutions varying from 1:2 to 1:16 [73]. Moreover, Vagge et al. tested the compound in vivo in a prospective study on patients undergoing IVIs, reporting a significant decrease in conjunctival bacterial load after a 4-day prophylactic treatment [74] (Fig. 1).

TOXIC ANTERIOR SEGMENT SYNDROME RELATED TO ANTISEPSIS

Toxic anterior segment syndrome (TASS) is a condition characterized by an acute, sterile postoperative inflammation due to a noninfectious agent that penetrates the anterior segment perioperatively [75]. The likelihood of an antiseptic agent causing a TASS is very low according to published literature. However, there are a few reports in which residual antiseptic solution on surgical instruments has been described as the causative agent of TASS [76, 77].

RISK MANAGEMENT STRATEGIES

Infection prevention and control represent a fundamental goal in all medically invasive procedures. Modern medicine is facing a progressive spread of multiresistant bacterial clones that are difficult to eradicate due to the uncontrolled use of antibiotics in the last decades. In some surgical contexts, the preventive administration of systemic antibiotics (usually 30–60 min before the skin incision) is a well-accepted practice and considered necessary to reduce the risk of perioperative infections. In the field of ophthalmic surgery, on the contrary, there are many different practices of disinfection used in different countries [47].

Although the use of antibiotics is surely effective in the reduction of conjunctival bacterial flora [13], the prophylactic effect against infection being not so valuable must be considered. On the other hand, this practice has the risk of inducing resistant bacteria [31]. In this context, the introduction of chemical disinfectants is very helpful because they can work in an effective way while preventing the emergence of new antibiotic resistance [78]. PVI is widely used, and its safety has been strongly established. One of the advantages of PVI is that it does not induce antibiotic resistance and has a wide antimicrobial spectrum [78], so its use can be considered effective in reducing the risk of infections related to intraocular procedures. In addition to the advantages of safety and effectiveness in preventing infections and avoiding the selection of multiresistant bacteria, another important aspect of PVI is the lower cost compared with antibiotics. This aspect is very important and must be considered because health expenditure is continually growing worldwide. It is necessary for healthcare providers to choose the most efficient products that ensure safety and are economically cost effective. From this perspective, the evaluation of risk–benefit ratio led us to consider that the use of antibiotics in place of PVI can be considered not justified. Since the safety and effectiveness of PVI has been well acknowledged by several scientific studies [1, 35], ocular surgeons can use PVI without the risk of incurring medical claims for not having administered antibiotics.

From a medico–legal point of view, the occurrence of healthcare-acquired infections (HAIs) can be a potential source of liability for the surgeon and the healthcare facility. Furthermore, the increasing complexity of medical and surgical activity along with the evolution of the law in the matter of professional liability require medical treatments to be increasingly safer for the patient's health [79, 80]. HAIs are generally defined as infections of bacterial, fungal, or viral origin that are contracted in any healthcare setting (hospitals, outpatient clinics, dialysis centers, long-term care, home care, territorial residential facilities) and that at the time of admission to the facility or prior to the provision of care were neither clinically manifest nor incubating [81]. The Ministry of Health estimates that every year in Italy 450,000–700,000 infections occur in hospitalized persons (overall, a care-related infection occurs in 4–7% of hospitalizations) [82]. Concerning the surgical setting, it has been estimated that surgical wound infection is the most common cause of nosocomial infection with a doubled risk of death compared with patients undergoing the same procedures without developing infections [83]. It should be emphasized that the surgical disciplines are also those most involved in HAIs related medical malpractice cases. In intraocular procedures, infectious endophthalmitis due to bacterial or fungal infection is a potentially devastating complication [30, 84]. Furthermore, a study showed that ophthalmic surgery had a significant litigation/conviction ratio (83.3%), much higher compared with other branches. These data also underline the importance of implementing increasingly effective preventive measures to reduce medical–legal disputes that are, in some cases, particularly burdensome in health and economic terms [24]. The centrality of the prevention issue in the context of HAIs, including the proper application of asepsis measures, is further emphasized by the fact that in Italy the omission of such measures is one of the main elements in defining and circumscribing the healthcare liability that may result.

CONCLUSIONS

Ophthalmic surgery procedures are nowadays very commonly performed worldwide. Preoperative prophylaxis is therefore a crucial step to reduce infections; at the same time, there is the need to reduce antibiotic use due to continuously growing antibiotic resistance. In this scenario, antiseptic compounds are a valuable tool. PVI is well established in the literature and broadly used, although at different concentrations. CHX is becoming more used as published literature demonstrates a good safety and efficacy profile with reduced patient discomfort. Lastly, there are new compounds such as picloxydine, ozone, HOCl, and Biosecur that show very interesting preliminary results, but further studies are needed to confirm these outcomes.

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Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Data Availability. Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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