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The role of Keratosept® drops in perioperative prophylaxis in patients undergoing intravitreal injections

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HIGHLIGHTS

Instilling Keratosept (containing 3 antiseptics, dexpanthenol, and polyvinyl alcohol) 2 days before the procedure and 3 days after it will reduce the bacterial flora of the conjunctival sac before and after the injection and facilitate healing of changes in the conjunctival and corneal epithelium after povidone.

ABSTRACT

In ophthalmology intravitreal injections are one of the most commonly performed procedures. The most dangerous complication after the procedure is endophthalmitis. The most commonly used preventive measure is the application of povidone-iodine solution before and after the procedure. However, povidone has a cytotoxic effect on the epithelium of the eye surface. Therefore, it is advisable to in still Keratosept eye drops (containing 3 antiseptics, dexpanthenol, and polyvinyl alcohol) 2 days before the procedure and 3 days after to sterilize the surface of the eye before and after the injection and to facilitate the healing of changes in the conjunctival and corneal epithelium after the procedure.

Key words: Keratosept, intravitreal injections, povidone-iodine

Intravitreal injections are currently among the most commonly performed procedures in ophthalmology. They are used to treat age-related macular degeneration (AMD), diabetic macular edema, retinal vein occlusion, retinopathy of prematurity, and other conditions associated with intraocular neovascularization and retinal edema. As with any intraocular procedure, intravitreal injection carries risks, including transient elevation of intraocular pressure, intraocular hemorrhage, traumatic cataract, retinal vascular occlusion, retinal vasculitis, and endophthalmitis [1]. Endophthalmitis is the most serious of these complications and occurs after approximately 0.042–0.075% of injections [2]. Despite prompt treatment with intravitreal antibiotics, with pars plana vitrectomy performed when indicated, it is associated with a poor visual prognosis. Several studies have reported poorer visual outcomes after injection-related endophthalmitis than after postoperative endophthalmitis following cataract surgery [3].

Most cases are caused by bacteria originating from the ocular surface. Gram-positive organisms predominate, particularly staphylococci, including *Staphylococcus aureus* – both methicillin-susceptible and methicillin-resistant strains – and *Staphylococcus epidermidis*, as well as streptococci, especially *Streptococcus pneumoniae* and viridans group streptococci. Less frequently isolated pathogens include *Haemophilus influenzae*, *Moraxella lacunata*, *Escherichia coli*, *Pseudomonas aeruginosa*, and species of *Serratia*, *Proteus*, *Enterobacter*, *Klebsiella*, and *Corynebacterium* [4–6]. Overall, staphylococci and streptococci account for the vast majority of cases.

Since intravitreal injections were introduced into clinical practice, various strategies have been used to prevent endophthalmitis. Initially, topical antibiotics were administered for several days before and after the procedure, but this practice has largely been abandoned. The agents most commonly used were aminoglycosides and fluoroquinolones, although their activity against Gram-positive and Gram-negative bacteria varies among individual drugs and across fluoroquinolone generations [6, 7]. Moreover, peri-injection topical antibiotic use promotes the selection of antibiotic-resistant ocular-surface bacteria [8–10].

Given the lack of evidence that peri-injection topical antibiotics reduce the risk of endophthalmitis and their role in promoting antimicrobial resistance, ocular-surface antisepsis immediately before intravitreal injection is now the cornerstone of prophylaxis. The most commonly used agent is 5% povidone-iodine; 0.05% aqueous chlorhexidine may be considered when povidone-iodine cannot be used. Both antiseptics exhibit broad activity against Gram-positive and Gram-negative bacteria [11–14]. Povidone-iodine, however, may cause concentration- and exposure-dependent toxicity to the corneal epithelium, resulting in superficial punctate epitheliopathy or, less commonly, epithelial defects [15]. Such ocular-surface injury may compromise epithelial barrier integrity and cause pain, irritation, and foreign-body sensation. It may also reduce patient comfort and delay ocular-surface recovery after the procedure. Antiseptic formulations that maintain broad antimicrobial activity while causing less ocular-surface toxicity are therefore desirable.

Keratosept® eye drops (Bruschettini Srl, Italy) are a recently introduced ophthalmic antiseptic formulation. The product contains three antiseptic agents: 0.05% hexamidine diisethionate, 0.0001% polyhexanide hydrochloride (PHMB), and 0.01% disodium edetate. It also contains 5% dexpanthenol, a provitamin B_5 (the alcohol analogue of pantothenic acid) with epithelial-supporting and wound-healing properties, and 1.25% polyvinyl alcohol, which provides film-forming, lubricating, viscoelastic, mucoadhesive, and protective effects. Clinical microbiological studies have demonstrated antimicrobial activity against staphylococci, streptococci, and *Candida spp.* [16–18], microorganisms commonly implicated in post-procedural endophthalmitis [6]. Antimicrobial activity against *Pseudomonas aeruginosa* appears to be less pronounced following a single exposure [16, 20]. In vitro, complete eradication of this organism was observed only after 24 h of incubation with Keratosept [16]. Clinical studies have also shown Keratosept to be better tolerated than povidone-iodine [17, 18]. These findings are supported by experiments in cultured conjunctival and corneal epithelial cells, which demonstrated no significant cytotoxic effects under the tested exposure conditions [19]. These studies also demonstrated greater conjunctival epithelial cell viability, faster healing of corneal epithelial defects, and more rapid closure of experimentally induced cell-free gaps in Keratosept-treated cultures than in untreated control cultures [19].

Should povidone-iodine therefore continue to be used for endophthalmitis prophylaxis?

Povidone-iodine is used worldwide for the prevention of endophthalmitis after intravitreal injections. Its use is also recommended by the Polish Ophthalmological Society and the American Academy of Ophthalmology [20, 21]. The product information for intravitreal agents such as Eylea and Lucentis likewise recommends ocular-surface antisepsis with povidone-iodine. Its continued use therefore remains well justified. A remaining concern is its potential toxicity to conjunctival and corneal epithelial cells, which, together with procedure-related mechanical and chemical irritation, may contribute to postprocedural ocular discomfort. Administration of Keratosept for 2 days before and 3 days after the procedure may help reduce the conjunctival bacterial load during the peri-injection period and support recovery of the ocular surface after exposure to povidone-iodine. However, these potential benefits should be confirmed in appropriately designed clinical studies.

The incidence of endophthalmitis is lower after intravitreal injection than after cataract surgery. This difference may be partly attributable to the very small scleral entry site created by the injection needle, together with the oblique transscleral tract and its subsequent coverage by the conjunctiva, all of which may limit bacterial ingress into the eye. Nevertheless, endophthalmitis following intravitreal injection may be associated with a poorer visual prognosis than postoperative endophthalmitis after cataract surgery [3]. Because the risk remains clinically relevant [1–3], adjunctive use of Keratosept as part of peri-injection care may help reduce the conjunctival bacterial load and support ocular-surface recovery. Whether it also reduces the incidence of endophthalmitis requires confirmation in appropriately designed clinical studies.

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The content presented in the article complies with the principles of the Helsinki Declaration, EU directives and harmonized requirements for biomedical journals.