Povidone – Iodine in Ophthalmology

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Povidone-Iodine (PVI) is routinely used in cataract surgery for postoperative infection prophylaxis. It has also found applications in other fields of ophthalmology. In view of the important and diverse applications of povidone-iodine, it is important for us to be familiar with the chemistry and mechanism of action of this widely used drug. The aim of this paper is to throw light in the diverse uses of povidone-iodine and its applications in ophthalmology.

What is Povidone-Iodine?

The possible effect of iodine on the eye was first appreciated in 1951 when a reduction in ocular flora was reported following the application of iodine solution to the skin. Iodophors were reported to reduce skin flora around the eye in 1970, and only later was the specific combination of povidone and iodine utilized for direct ophthalmic use.

Iodophors are developed by complexing iodine with surfactants like nonionic detergents, quaternaries and macromolecules. The detergents act as stabilizers and carriers combining detergent property with antibacterial activity. Iodophors are non-irritating, non-staining and water miscible in all dilutions.

Povidone - Iodine (Betadine) is a complex polymer of iodine with polyvinyl pyrrolidone (a high-molecular weight, water soluble polymer), a complex that enhances the bactericidal activity of iodine. Iodine is slowly released from the complex, providing antimicrobial action. Most commercially available solutions of povidone-iodine have 1% available iodine.

Povidone-iodine is readily available world wide, either as a powder or as a 10 percent solution.

The spectrum of antimicrobial activity of povidone-iodine covers bacteria, viruses, and even spores. Most bacteria are killed within 30 seconds. Povidone-iodine has been shown to be a superior antiseptic agent for surgical preparation of skin. It has also been shown to be effective on the cervix and vagina in gynecological cases.

Depending on the type of application for ophthalmic use, the solution must be diluted to the appropriate strength. The diluents may be a balanced salt solution or other appropriate diluent. In the appropriate concentration, povidone-iodine is not toxic to the eye as are other iodine bearing compounds. It is a strong antiseptic with minimal secondary effects (i.e. red eye, allergic reactions) in healthy conjunctivas. It stains the area of application and rarely causes reactions like fever and generalized skin eruptions. It is important to avoid the detergent version of povidone-iodine generally used as a skin antiseptic, since this solution will adversely affect the cornea.

How Does Povidone - Iodine Work?

Povidone-iodine interacts strongly to the double bonds of saturated fatty acids in the bacterial cell wall and cell organelle membranes and also oxidizes amino acid and nucleotides. It causes pore formation and solid-liquid interfaces at the lipid membrane level of cell walls to loose cytosol material.

Bacteria generally adhere to the surfaces of infected tissue in biofilms on a glycoalcalyx material. Povidone-iodine can reach the biofilm and has been shown to...
cause the outer layers of the biomass to slough and be killed. It not only destroys a wide range of bacteria, but also inactivates and inhibits the release of bacterial exotoxins. The superficial location of bacteria may provide susceptibility to the effects of povidone-iodine.

**Role of Povidone-Iodine in Ophthalmology:**

Povidone-iodine has found several applications in ophthalmology. It has been employed preoperatively in an attempt to reduce the incidence of postoperative infections, including endophthalmitis. Other than its use in the prophylaxis of endophthalmitis, povidone-iodine used as a topical antimicrobial agent has been reported to be effective in treating conjunctivitis and keratoconjunctivitis. It has been used in the prevention of ophthalmia neonatorum.

Povidone-iodine has also been used as a means for decontamination of donor corneas. New investigations are underway to evaluate the effectiveness of povidone-iodine to treat corneal infections. Iodophors are used as hand washes, for preoperative skin preparation, as local antiseptics, in ringworm and in oral and vaginal moniliasis.

**Preoperative Infection Prophylaxis**

The best preoperative prophylaxis has not yet been found. However, povidone-iodine has played a very important role in the prophylaxis of post-cataract surgery endophthalmitis. In fact, till the results of ESCRs Endophthalmitis Study were made available povidone-iodine was the only prophylactic agent that had been shown to reduce the rate of post-cataract surgery endophthalmitis. Antiseptics like povidone-iodine lower preoperative bacterial colony counts and decrease incidence of postoperative endophthalmitis.

Postoperative endophthalmitis, which is a rare, but sometimes devastating complication of cataract surgery, remains one of the most feared problems after intraocular surgery. Literature review suggests that there had been a gradual decline in the incidence of postoperative endophthalmitis till the early 1990s. However many publications seem to indicate that the incidence of post-cataract surgery endophthalmitis is on the rise with some studies reporting the occurrences between 0.07 % and 0.3 %. Most surgeons believe that this increase in frequency of endophthalmitis is due to increasing popularity of sutureless clear corneal surgery. Nagaki et al. reported that the relative risk for endophthalmitis was 4.6 times higher with temporal clear corneal incisions than with sclerocorneal incisions. Schmitz et al. found a 0.1 % incidence of endophthalmitis with clear corneal incisions and 0.07 % with scleral tunnel incisions.

Bacteria causing postoperative endophthalmitis most likely originate from the normal bacterial flora of the patient's own conjunctiva and eyelid. In 75 % to 95 % of reported cases, the causative organisms are gram-positive cocci. Normal conjunctival flora comprises predominately of coagulase negative staphylococci, i.e., Staphylococcus epidermidis (95.4 %). Less frequent bacteria are Staphylococcus aureus (14.8 %), anaerobes (44 %), (Corynebacterium species), Streptococcus species (4.4 %) and gram-negative rods (7.8 %). (i.e. E Coli, Pseudomonas aeruginosa). The Endophthalmitis Vitrectomy Study determined that, of 69 % of patients with confirmed microbiology growth, 70 % were infected with coagulase negative micrococcus, mostly Staphylococcus epidermidis, 10 % with Staphylococcus aureus, 9 % with streptococci, 2 % with enterococci, 3 % with other gram positive species and 6 % with gram negative species. Anaerobic or microaerophilic organisms such as Propionibacterium acnes are more commonly found in chronic and late intraocular inflammations. Because gram-positive cocci are the main cause of acute postoperative endophthalmitis, methods intended to reduce conjunctival bacterial flora should be effective against these bacteria.

The goal of preoperative chemical preparation of the eye (e.g. with povidone-iodine) is to minimize the number of microorganisms on the skin and eye immediately before the first incision and it is also desirable to reduce the bacterial flora in the conjunctival sac. Several studies have been conducted to reduce preoperative bacterial load on the conjunctiva. In 1984, Apt and Isenberg et al showed that povidone-iodine dilutions decreased the number of colonies by 91 % and decreased the number of species by 50 %. These findings were statistically significant compared to the untreated fellow control eyes. In another German study, povidone-iodine showed a significantly lower
incidence of culture positive endophthalmitis, compared with silver protein solution. Speaker and Menikoff et al. found evidence for an association between prophylaxis with povidone-iodine and lower incidence of postoperative endophthalmitis. Povidone-iodine decreases the conjunctival load of propionibacterium acne also, which is a common cause of chronic postoperative endophthalmitis.

For skin asepsis, a 10 percent povidone-iodine solution is widely used. In the periorbital region with many sebaceous glands the antiseptic should be administered about 10 minutes before surgery to act sufficiently. There is a wide variation in the technique and concentration of povidone-iodine application in the conjunctival sac.

Povidone-iodine may be applied a) directly, flushing the upper and lower fornices of the conjunctival sac, or b) as instillation of eye drops before an intraocular procedure. Irrigation of conjunctival sac may be more effective in reducing the conjunctival bacterial load and possibly decreased susceptibility to endophthalmitis. This was suggested in a prospective, randomized, controlled trial of 200 eyes undergoing anterior segment surgery treated with topical ofloxacin. The study group that underwent irrigation of the fornices with 10 ml of povidone-iodine had fewer positive conjunctival cultures than the control group that received two drops of povidone-iodine preoperatively. In this study 26% of study eyes had positive conjunctival cultures immediately before surgery and 18% had positive cultures at the end of surgery as opposed to 43% before surgery and 32% after surgery in the control eyes.

Preoperative conjunctival fornix irrigation with 5% rather than 1% povidone-iodine results in greater decrease in colony forming units, especially with heavier initial bacterial load (greater than 100 colony-forming units before irrigation with povidone-iodine). This was demonstrated in a prospective, randomized, double blind study of 105 patients in the United Kingdom where a statistically significant drop of 96.7% colony-forming units was seen in the 5% povidone-iodine group as compared with the 40% decrease in the 1% povidone-iodine group when there was heavier initial bacterial load. The efficacy of povidone-iodine in reducing conjunctival contamination is comparable to a 3-day course of topical antibiotics.

**Postoperative Infection Prophylaxis:**

When the timing of the bacterial penetration of the eye is considered, there are two main intervals during which the eye is at risk. The first is during the actual operation, when the ocular tissues have been incised. The second important interval during which the eye is at risk is in the immediate postoperative period. During that time the surgical wound is somewhat exposed to the environment. Five percent povidone-iodine solution applied at the conclusion of surgery significantly decreased the number of colony-forming units immediately postoperatively and at 24 hours following surgery, thereby decreasing bacteria that may enter the surgical wound postoperatively. This may be a particularly significant prophylactic measure since compromised clear corneal wound architecture have been implicated in the recent spurt in the incidence of post-cataract surgery endophthalmitis.

**Prevention of Ophthalmia Neonatorum**

Povidone-iodine has been recommended for prophylaxis against ophthalmia neonatorum, especially in developing countries. In a study by Isenberg et al. in 1995, it was demonstrated that prophylaxis with a 2.5 percent ophthalmic solution of povidone-iodine resulted in fewer cases of ophthalmia neonatorum over all and notably fewer cases of chlamydial conjunctivitis than prophylactic treatment with either erythromycin or silver nitrate. Povidone-iodine has many potential advantages over these currently used drugs, including a broader antibacterial spectrum. In a concentration as low as 0.1 percent, povidone-iodine is effective against Neisseria gonorrhea; in a concentration as low as 1 percent, it is effective against C. trachomatis; and in a concentration of 0.5 percent or lower, its antiviral spectrum includes the human immunodeficiency virus and herpes simplex virus.

Povidone-iodine turns the surface of the eye brown for a few minutes, a characteristic that can serve as an indicator that it has been properly applied. The possibility of misapplication is greater with the other two agents because they are colourless. With povidone-iodine, unlike antibiotics, bacterial resistance has not been encountered. Finally, it is cheaper than the other agents. In many developing countries, where
ophthalmia neonatorum is more common, no prophylaxis is used mainly because of the expense and lack of availability.

**Treatment of Ongoing Ocular Infections:**

In addition to the role of povidone-iodine in prevention of infections, its role has also been explored in the treatment of ongoing ocular infections.

A study was conducted by Isenberg S J. et al in 2002 to investigate the use of povidone-iodine in the treatment of paediatric conjunctivitis in 459 children in Manila, Philippines. Povidone-iodine 1.25 percent ophthalmic solution, applied 4 times daily, was compared with the effect of an antibiotic combination (neomycin – polymyxin B-gramicidin) and was found to be as effective in the treatment of bacterial conjunctivitis, marginally more effective against chlamydial conjunctivitis (P = 0.057) but equally ineffective against viral conjunctivitis. Povidone-iodine still continues to be highly germicidal when used at the lower concentration of 1.25 percent than 2.5 percent. Because povidone-iodine ophthalmic solution can be prepared from powder and stock solutions meant for other antiseptic purposes, it is not only inexpensive but also widely available in developing countries. Povidone-iodine 1.25 percent ophthalmic solution can therefore be considered as treatment for bacterial and chlamydial conjunctivitis, especially in developing countries where topical antibiotics are often unavailable or costly.

**Conclusion**

Povidone-iodine is frequently chosen as an antimicrobial agent in view of its various advantages. In the appropriate concentration, it is not toxic to the eye as are other iodine bearing compounds. It has a very broad antimicrobial spectrum, including bacteria, viruses, and fungi, given enough contact time in vitro. Resistance to bacteria is rare. The medication turns the eye brown for a few minutes proving that it has been applied. It is widely available as a solution or powder. Since it is not expensive, it is widely used even in developing countries.

Povidone-iodine is an effective disinfectant significantly reducing both the contamination levels of the conjunctival sac as well as the incidence of post-cataract surgery infection. Investigations of its use in treating other types of ophthalmic infections are continuing. The use of povidone-iodine in ophthalmic practice continues to reduce the incidence of blindness in children and adults throughout the world.

**References**


