The Ocular Application of Povidone-Iodine

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The use of antiseptic agents to prevent blindness was not a self-evident development. It evolved over a number of years to the point that one antiseptic agent – povidone-iodine – is now used throughout the world, every day, to prevent blindness.

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.[1] Iodophors were reported to reduce skin flora around the eye in 1970,[2] and only later was the specific combination of povidone and iodine utilised for direct ophthalmic use.

Why was povidone-iodine chosen as an antimicrobial agent?

- *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 by 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; and so it is available throughout the world in some form
- Finally, especially important for use in developing areas, it is not expensive.

Pre-operative Use

Ophthalmic surgeons have come to appreciate the possibility of reducing post-operative infections, including endophthalmitis, by effective pre-operative preparation. However, even by the 1980s, pre-operative preparation of the eye had not been scientifically validated. A series of investigations were then conducted to evaluate various aspects of this preparation – to reduce the bacterial flora of the eye. By far the most effective measure was to place a drop of 5% povidone-iodine ophthalmic solution on the eye before surgery. Bacterial colonies were reduced by 91% and species by 50%. This decrease was significantly better than in the control group. This 1984 study was the first controlled trial of the ophthalmic use of povidone-iodine conducted.[3]

We then investigated the possible benefit of using povidone-iodine 5% solution placed on the eye just before the operation, in addition to a combination ophthalmic antibiotic solution (neomycin, polymyxin B, and gramicidin) used as an outpatient medication for three days before surgery.[4]

The combination reduced the mean number of bacterial colonies per eye from 1745 to 2 after use of both medications ($p < 0.01$). For species, the corresponding reduction was from 2.4 to 0.2 after both medications were used ($p < 0.01$). After use of both agents, 83% of eyes became sterile. This effect was the greatest reduction of bacteria ever produced in a controlled study to that time. A subsequent study showed that the synergistic effect of the antibiotic used three days pre-operatively, combined with povidone-iodine applied on the operating table before surgery, proved better than using povidone-iodine alone as an outpatient and before surgery.[5]

Is this technique effective in preventing endophthalmitis?

A 1991 study in New York of 8000 patients undergoing cataract surgery showed that the use of povidone-iodine solution placed on the eye just before surgery reduced the endophthalmitis rate from 0.24% to 0.06% ($p < 0.03$).[6] The resulting potential reduction in blindness in the United States alone can be estimated, assuming 1.8 million cataract surgeries per year and a 50% frequency of legal blindness after endophthalmitis. This would mean about 1600 American patients annually who would have been blind in the operated eye were it not for the pre-operative application of povidone-iodine. The actual figure would be much larger if one were to include all intraocular surgeries and extend the patient base to the entire world.

Post-operative Use

We then considered the effect that povidone-iodine would have if used after ocular surgery. The effect of 2.5% povidone-iodine solution placed on the eye immediately at the completion of the operation was compared with the similar use of a combination antibiotic (neomycin, polymyxin B, and gramicidin).[7] At 24 hours after surgery, povidone-iodine significantly reduced the colony forming units ($p=0.035$), but the combination of neomycin, polymyxin B, and gramicidin did not ($p=0.17$). The colony counts increased in the first 24 hours in the antibiotic treated eyes ($p=0.013$), but not in the povidone-iodine treated eyes. At 24 hours, the povidone-iodine treated eyes had a lower species count ($p=0.034$) than the antibiotic treated eyes.

Subsequently, patients were studied who used povidone-iodine 2.5% or 1.25% solution compared with a similar group using the antibiotic combination eyedrop three times a day for a week after ophthalmic surgery.[8] No ocular infections occurred. While the species counts increased in both groups over the post-operative week, they increased less in the povidone-iodine treated eyes ($p = 0.011$) and were lower than the untreated control group ($p=0.01$). However, in the antibiotic treated group the species count was not less than the controls ($p=0.29$).

Prevention of Ophthalmia Neonatorum

It has been estimated that ophthalmia neonatorum blinds more than 10,000 babies per year throughout the world. While prophylaxis using silver nitrate or other agents can be effective, it often is not utilised in areas where the prevalence of ophthalmia neonatorum is highest, primarily due to expense. Developing countries often cannot afford the cost of neonatal prophylaxis. Since povidone-iodine solutions can be prepared locally from stock solutions or powders, it is very inexpensive (about US$0.10 for a 5 ml bottle) and available worldwide.

A pilot study in California showed that povidone-iodine significantly reduced the bacterial ocular flora in normal neonates.[9] In 1995, a multi-year trial of povidone-iodine 2.5 % ophthalmic solution, used for ophthalmia neonatorum prophylaxis in more than 3000 neonates in Kenya was reported.[10] The study compared the effectiveness of povidone-iodine with silver nitrate and erythromycin. In Kenya, where prophylaxis had not been generally utilised because of expense, ophthalmia neonatorum occurred in as many as 23.2% of newborns. The trial found povidone-iodine to be more effective than the other two agents and was less toxic. Based on this report, povidone-iodine is now being used increasingly for neonatal prophylaxis in much of the world.

Treatment of Infections

All the studies mentioned have been concerned with prevention.

Would povidone-iodine be effective in treating an ongoing ocular infection?

There had never been a controlled randomised trial of the use of povidone-iodine to treat ocular infections. While conjunctivitis often is innocuous in the developed world, in developing areas, the infection can lead to corneal scarring and blindness from a number of causes, including a lack of appropriate antibiotics, malnutrition, vitamin A deficiency, trachoma, rubeola, and trauma.

To investigate the use of povidone-iodine in the treatment of paediatric conjunctivitis, 459 children were studied in Manila, Philippines.[11] This trial is believed to be the largest controlled investigation of conjunctivitis treatment ever reported. Povidone-iodine 1.25% ophthalmic solution, applied four times daily, was compared with the effect of an antibiotic combination (neomycin-polymyxin-B-gramicidin). As determined by 'time to cure', povidone-iodine was 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 1.25% ophthalmic solution can, therefore, be used to treat bacterial and chlamydial conjunctivitis, especially in emerging countries where topical antibiotics are unavailable or costly.

New investigations are underway to evaluate the effectiveness of povidone-iodine to treat corneal infections. These studies have the potential of decreasing the frequency of blindness from corneal infections and subsequent corneal scarring – the most frequent cause of preventable paediatric blindness in developing countries.

Practical Application

Povidone-iodine is readily available worldwide, either as a powder or as a 10% solution. Depending on the type of application, for ophthalmic use, the solution must be diluted to the appropriate strength. The diluent may be a balanced salt solution or other appropriate diluent.

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.

In summary, povidone-iodine ophthalmic solution has been proven effective before (5% solution) and after ocular surgery (1.25%), at birth (2.5%), and for some forms of conjunctivitis (1.25%). 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.

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(See also page 32)

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