

Preoperative povidone iodine: weighing the risks

BY JENNIFER KIM AND NIALL PATTON

Following on from our recent online survey, the authors examine the potential risks and benefits of diluting the concentration preoperative povidone iodine.

Povidone iodine (PI) is an iodophore that has an established use as a broad-spectrum antiseptic, mainly for the treatment of contaminated wounds and for preoperative preparation of the skin, mucous membranes and the ocular surface [1]. More recently, studies have reported its promising role in the treatment of adenoviral conjunctivitis [2]. PI has many potential advantages over other antiseptic medications including broader antibacterial spectrum, lack of identifiable bacterial resistance and significantly lower price [3]. It is well recognised that postoperative endophthalmitis is caused by gram-positive organisms in more than 90% of cases, most of which comes from commensal bacteria on the ocular surface which enter the eye as a result of surgery. Bacterial contamination to the eye can originate from the eyelid, periorbital skin and conjunctiva, and it is assumed that the conjunctiva is the primary source of commensal bacteria that increases the risk of developing endophthalmitis [4]. PI solution has been shown to be effective against these organisms, and a preoperative application of PI 5-10%, to the ocular surface is commonly used worldwide to prevent postoperative endophthalmitis [5].

Bactericidal activity of PI is dependent on its concentration, nature of the microorganism and exposure time [6,7].

“Bacterial contamination to the eye can originate from the eyelid, periorbital skin and conjunctiva”

A guideline produced by the American Academy of Ophthalmology (AAO) recommends PI 5% applied to the conjunctival cul-de-sac for three minutes before surgery [8]. Similarly, the European society of Cataract and Refractive Surgeons (ESCRS) recommends PI 5-10% application for at least three minutes before surgery [9]. However, there is limited guidance available on the exact regimen and PI is used in different ways with varying concentrations, volumes and exposure time. A prospective randomised double-blind study carried out by Ferguson et al. compared the number and species of bacterial colonies cultured from swabs taken from conjunctival fornices irrigated preoperatively with either PI 1% or PI 5%. With higher concentration, greater decrease in median colony forming units was observed, particularly in the presence of heavier initial bacterial load [10]. Whilst multiple studies have demonstrated superior functional properties of higher concentration PI [6,11], its possible adverse effect on corneal integrity remains a concern in clinical practice. Application of PI can also cause patient discomfort and transient changes in visual function (acuity and contrast sensitivity). The recent *Eye News* survey revealed that two thirds of respondents routinely dilute 10% betadine (50:50) for preoperative prep, reflecting the potential concerns highlighted. Increasing corneal toxicity with both higher PI concentration and exposure has been demonstrated in few studies, but it is worth noting that most of these findings were based on in vitro and animal models [12,13]. It is also reassuring to note that patient discomfort and visual dysfunction was transient and application of PI after an anaesthetic drop renders it pain free. A prospective, consecutive study at a single centre in Australia evaluated adverse events and visual outcomes associated with PI 10% left in contact with ocular surface for three minutes revealed no complications attributable to PI [14]. More recently,

studies have demonstrated that bactericidal effect of dilute PI applied multiple times is comparable to conventional higher concentrations of PI. An experimental study by Silas et al. reviewed microbial growth of *Staphylococcus epidermis*, 24 hours following treatment with PI solutions ranging between 0.1% to 10%. PI concentrations greater than 2.5% were effective in eliminating the organism with a single application, as well as three 30-second applications of PI at 0.7% [15].

PI is a complex of polyvinylpyrrolidone (povidone, PVP) with iodine. PI may cause allergic contact or irritant dermatitis (type 4 hypersensitivity), the latter mainly occurring after prolonged occlusive skin contact under pressure. Although povidone itself is considered not to cause contact hypersensitivity, some of its non-iodinated co-polymers (PVP-eicosene, PVP hexadecane) have been reported to rarely cause contact dermatitis (<1/10,000) [16]. Contrary to popular belief, allergies to shellfish and iodine contrast do not increase the risk of reaction to PI used in ophthalmic surgery [17]. In addition, antibody-mediated allergic reaction (Type 1 hypersensitivity) and immunoglobulin (Ig) E-mediated anaphylaxis is more likely to be against povidone rather than iodine, an essential element which is present in many body tissues. For the vast majority of respondents to the *Eye News* survey, chlorohexidine (CHG) was the most popular alternative antiseptic to use in patients with ‘iodine-allergy’. CHG is particularly effective against gram-positive bacteria and also active against gram-negative organisms, facultative anaerobes, aerobes and yeasts. Comparable bactericidal effects to PI have been demonstrated in CHG, although one study showed a higher positive value in bacterial culture collected from eyelids in the CHG group [18]. However, CHG can also lead to significant corneal damage including CHG-related keratitis [19,20], and special care must be taken when applied to the

periocular area.

PI remains an antiseptic of choice for many practising surgeons in the UK. Current evidence suggests that both PI 5% and 10% can be used safely with little lasting impact on the corneal integrity. True anaphylactic reaction to PI is unlikely, although it has been reported in the literature. Chlorhexidine is most widely accepted as a suitable alternative in these cases, however, care must be taken as it can lead to significant corneal damage.

Comment from Amar Alwitry

Another excellent article discussing the issues underlying practice variance. After reading this my thoughts remain unchanged. Infection endophthalmitis is a catastrophic complication and I need to do everything I can to avoid it. I feel the 10% concentration will deliver more antisepsis than the 5% and so it makes sense that I use it. I do not think the evidence is there to warrant dilution and the risk of endophthalmitis, which is real in my opinion, outweighs the theoretical risk of toxicity to the corneal epithelium which would surely be transient. I will leave the *Eye News* readership to reach their own conclusions.

References

1. Minims Povidone Iodine 5% w/v Eye Drops, Solution: Electronic Medicines Compendium.
2. Kovalyuk N, Kaiserman I, Mimouni M, et al. Treatment of adenoviral keratoconjunctivitis with a combination of povidone-iodine 1.0% and dexamethasone 0.1% drops: a clinical prospective controlled randomized study. *Acta Ophthalmologica* 2017;**95**(8):e686-e92.
3. Grzybowski A, Kanclerz P, Myers WG. The use of povidone-iodine in ophthalmology. *Curr Opin Ophthalmol* 2018;**29**(1):19-32.
4. Leong JK, Shah R, McCluskey PJ, et al. Bacterial contamination of the anterior chamber during phacoemulsification cataract surgery. *J Cataract Refract Surg* 2002;**28**(5):826-33.
5. Carrim ZI, Mackie G, Gallacher G, Wykes WN. The efficacy of 5% povidone-iodine for 3 minutes prior to cataract surgery. *Eur J Ophthalmol* 2009;**19**(4):560-4.
6. Hosseini H, Ashraf MJ, Saleh M, et al. Effect of povidone-iodine concentration and exposure time on bacteria isolated from endophthalmitis cases. *J Cataract Refract Surg* 2012;**38**(1):92-6.
7. Berkelman RL, Holland BW, Anderson RL. Increased bactericidal activity of dilute preparations of povidone-iodine solutions. *J Clin Microbiol* 1982;**15**(4):635-9.
8. Olson RJ, Braga-Mele R, Chen SH, et al. Cataract in the Adult Eye Preferred Practice Pattern(R). *Ophthalmology* 2017;**124**(2):1-119.
9. Barry P, Seal DV, Gettinby G, et al. ESCRS study of prophylaxis of postoperative endophthalmitis after cataract surgery: Preliminary report of principal results from a European multicenter study. *J Cataract Refract Surg* 2006;**32**(3):407-10.
10. Ferguson AW, Scott JA, McGavigan J, et al. Comparison of 5% povidone-iodine solution against 1% povidone-iodine solution in preoperative cataract surgery antisepsis: a prospective randomised double blind study. *Br J Ophthalmol* 2003;**87**(2):163-7.
11. Li B, Nentwich MM, Hoffmann LE, et al. Comparison of the efficacy of povidone-iodine 1.0%, 5.0%, and 10.0% irrigation combined with topical levofloxacin 0.3% as preoperative prophylaxis in cataract surgery. *J Cataract Refract Surg* 2013;**39**(7):994-1001.
12. Shibata Y, Tanaka Y, Tomita T, et al. Evaluation of corneal damage caused by iodine preparations using human corneal epithelial cells. *Jpn J Ophthalmol* 2014;**58**(6):522-7.
13. Jiang J, Wu M, Shen T. The toxic effect of different concentrations of povidone iodine on the rabbit's cornea. *Cutan Ocul Toxicol* 2009;**28**(3):119-24.
14. Nguyen CL, Oh LJ, Wong E, Francis IC. Povidone-iodine 3-minute exposure time is viable in preparation for cataract surgery. *Eur J Ophthalmol* 2017;**27**(5):573-6.
15. Silas MR, Schroeder RM, Thomson RB, Myers WG. Optimizing the antisepsis protocol: Effectiveness of 3 povidone-iodine 1.0% applications versus a single application of povidone-iodine 5.0. *J Cataract Refract Surg* 2017;**43**(3):400-4.
16. Vandergriff TW, Wasko CA, Schwartz MR, Hsu S. Irritant contact dermatitis from exposure to povidone-iodine may resemble toxic epidermal necrolysis. *Dermatol Online J* 2006;**12**(7):12.
17. Schabelman E, Witting M. The relationship of radiocontrast, iodine, and seafood allergies: a medical myth exposed. *J Emerg Med* 2010;**39**(5):701-7.
18. Yokoyama Y, Makino S, Ibaraki N. [Comparison in effectiveness of sterilization between chlorhexidine gluconate and povidone-iodine]. *Nippon Ganka Gakkai Zasshi* 2008;**112**(2):148-51.
19. Bever GJ, Brodie FL, Hwang DG. Corneal Injury from Presurgical Chlorhexidine Skin Preparation. *World Neurosurg* 2016;**96**:610.e1-e4.
20. Steinsapir KD, Woodward JA. Chlorhexidine Keratitis: Safety of Chlorhexidine as a Facial Antiseptic. *Dermatol Surg* 2017;**43**(1):1-6.

The survey referenced was undertaken among the *Eye News* readership in June 2019. You can read a breakdown of the results in the August/September 2019 issue, available online here: <https://www.eyenews.uk.com/education/medico-legal/post/ophthalmology-survey-results-augustseptember-2019>

See details of the next survey on page 45.

AUTHORS



Jennifer Kim,

Specialist Registrar, Manchester Royal Eye Hospital, Manchester, UK.



Niall Patton,

Consultant Ophthalmologist, Manchester Royal Eye Hospital, Manchester, UK.

Declaration of competing interests:

None declared.