Evidence summary: Wound infection: iodophors and biofilms

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Question

What is the best available evidence in the effectiveness of iodophors to denature biofilm in wounds?

Clinical bottom line

Mature microbial cells that form a biofilm in chronic wounds and contribute to poor healing generally have reduced susceptibility to antimicrobial treatment (see *ES 7020 Wounds Infection: Biofilms defined and described*). If full eradication is not achieved with therapy, biofilms quickly re-proliferate[1]. Evidence from *in vitro* studies currently suggests that povidone-iodine (PVP-I) in solution[2-5] or impregnated wound dressings[2,6] and cadexomer-iodine wound dressings[2,7] can be effective in inhibiting the development of common bacterial biofilms and in reducing existing biofilm. *In vitro* studies that achieved total irradiation of existing bacterial biofilms used iodophors at 10% concentration[2,4]. There is insufficient research conducted in clinical settings, and it has been proposed that *in vitro* findings (particularly with respect to minimum inhibitory concentrations) may not be predictive of performance within the micro environment of a chronic wound[1].

Effectiveness in inhibiting development of biofilm

- One *in vitro* study found a cadexomer iodine dressing was more effective than control filter paper in preventing development of *P. aeruginosa*, *S. aureus* and mixed species bacteria biofilm[7]. (Level IV)
- In another *in vitro* study, supplementing culture plates with 1.4% PVP-I inhibited the development of *S. epidermidis* and *S. aureus* biofilm. Supplementing culture plates with PVP-I at sub-inhibitory concentrations (0.17%, 0.35% and 0.7%) significantly ($p<0.001$) reduced development of *S. epidermidis* and *S. aureus* biofilm[3]. (Level III)

Effectiveness in reducing bacterial biofilm

- In a study in which *S. aureus* and *P. aeruginosa* biofilm was grown *in vitro*, exposure to 1% povidone-iodine solution led to small reductions in bacterial counts (no statistical significance reported) compared to no bacterial reduction with exposure to flucloxacillin or ciprofloxacin. However, after eight consecutive days' treatment, there was only a 2-log reduction in bacterial levels[2]. (Level III)
- In the same *in vitro* study, a PVP-I dressing (Inadine®, therapeutic dose 10%) and a cadexomer iodine paste dressing (Iodoflex®, therapeutic dose 10%) achieved complete eradication of bacteria in young biofilm samples (3 days) and more mature biofilm samples (7 days) compared to no or minimal reductions associated with exposure to silver-based dressings[2]. (Level III)
- In the same study, another iodine-impregnated dressing (Betadine®) achieved slight reduction in *S. aureus* counts but was not effective in reducing *P. aeruginosa* counts in the *in vitro* biofilm samples[2]. (Level III)
- In another *in vitro* study, 30 minutes of incubation in 10% PVP-I solution there was a greater than 5 log reduction in cultures of *S. epidermidis*; however a clinically significant number of viable cells remained. Alcohol preparations and 3% and 5% hydrogen peroxide were superior to PVP-I in reducing bacterial biofilm[4]. (Level III)
- Significant reduction ($p<0.001$) in optical density of multi-bacterial biofilm attained from chronic wounds was achieved with sub-inhibitory concentrations of PVP-I solution compared with saline control in an in vitro study[5].
- One *in vitro* study found an iodine-impregnated dressing was significantly ($p<0.0001$) more effective than a silver-impregnated dressing at eradicating *S. aureus* and *P. aeruginosa* biofilms. In cultures exposed to iodine dressings, there was a 3-log reduction in bacterial levels within 8 hours and no viable bacteria after 24 hours exposure[6].

Adverse effects

One systematic review reporting 27 RCTs found no substantial difference in adverse reactions between iodine and other methods of local wound care. No major adverse events were reported[8]. (Level I) However, iodine should not be used with patients who have the following conditions[9,10]: (Level IV)

- known or suspected sensitivity to iodine;
- impaired renal function;
- a history of any thyroid disorders;
- pregnancy or breast-feeding;
- povidone iodine should not be used in in newborns and infants less than 6 months of age and cadexomer iodine is not recommended for use in children under 12 years[11];
- extensive burns to the body; or
- before and after treatment with radio-iodine until permanent healing has been achieved.

Other considerations

A systematic review that reported cost-effectiveness as an outcome measure, determined that a course of treatment with PVP-I cost substantially less than other standard treatments and cadexomer iodine was more expensive; however, there was no consideration to the presence of biofilms or otherwise[8]. (Level I)

Characteristics of the evidence

This evidence summary is based on a structured literature and database search combining search terms that describe wound management, biofilm and iodophors. The evidence in this summary comes from:

- Four *in vitro* studies[2-6]. (Level III)
- One conference abstract reporting an *in vitro* study in minimal detail[7]. (Level IV)
- One discussion paper on biofilms[1]. (Level IV)
- A systematic review on use of iodophors in wound care that reported adverse events[8]. (Level I)
- Two opinion papers that included discussion on cautious use of iodophors in wound care[9,10]. (Level IV)

Best practice recommendations

- Povidone-iodine in solution or impregnated wound dressings could be used to manage bacterial biofilms in chronic wounds. (Level B)
- Cadexomer iodine dressing could be used to manage bacterial biofilms in chronic wounds. (Level B)

NB. Related topics:

ES7020 Wounds Infection: Biofilms defined and described

ES 7367 Wound infection: Iodophors

ES 7366 Wound Management: Hydrogen peroxide in wound care

Grades of recommendations

Grade A	Strong support that merits application
Grade B	Moderate support that warrants consideration of application
Grade C	Not supported

References

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2. Hill KE, Malic S, McKee R *et al.* An *in vitro* model of chronic wound biofilms to test wound dressings and assess antimicrobial susceptibilities. J Antimicrob Chemother 2010; 65:1195–206. (Level III)
3. Oduwole KO, McCormack DJ, Glynn AA *et al.* Anti-biofilm activity of sub-inhibitory povidone-iodine concentrations against Staphylococcus epidermidis and Staphylococcus aureus. J Orthop Res 2010; 28:1252–6. (Level III)
4. Presterl E, Suchomel M, Eder M *et al.* Effects of alcohols, povidone-iodine and hydrogen peroxide on biofilms of *Staphylococcus epidermidis*. J Antimicrob Chemother 2007; 60:417–20. (Level III)
5. Suman E, Madhavi R & Shashidhar Kotian M. Role of bacterial biofilms in chronic non-healing ulcers and effect of subinhibitory concentrations of Betadine and hydrogen peroxide on biofilms. J Hosp Infect 2009; 73:87–9. (Level III)
6. Thorn RMS, Austin AJ, Greenman J, Wilkins JPG & Davis PJ. *In vitro* comparison of antimicrobial activity of iodine and silver dressings against biofilms. J Wound Care 2009; 18:343–6. (Level III)
7. Brett D. Testing of cadexomer iodine against a variety of micro-organisms grown in single and mixed species biofilms. J Wound Ostomy Continence Nurs 2011; 38(3S):S2–S115 (Level IV)
8. Vermeulen H, Westerbos SJ & Ubbink DT. Benefit and harm of iodine in wound care: a systematic review. J Hosp Infect 2010; 76:191–9. (Level I)
9. Leaper DJ & Durani P. Topical antimicrobial therapy of chronic wounds healing by secondary intention using iodine products. Int Wound J 2008; 5:361–8. (Level IV)
10. Sibbald RG, Leaper DJ & Queen D. Iodine made easy. Wounds Int 2011; 2(2):S1–6. (Level IV)
11. Smith & Nephew. Cadexomer Iodine Ointment. http://wound.smith-nephew.com/au [accessed October 2012]

Keywords

Povidone iodine; PVP-I; cadexomer iodine; iodine; iodophor; biofilm.