Evidence summary: Wound infection: silver products and biofilms

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Author

Wound Healing and Management Node Group

Question

What is the best available evidence in the effectiveness of topical silver 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. If full eradication is not achieved with therapy, biofilms quickly re-proliferate[1]. Silver, in the form of salts (e.g. silver nitrate), creams (e.g. silver sulphadiazine) and impregnated wound dressings, has been used widely as an antimicrobial agent in wound management[2,3]. Current evidence from *in vitro* studies suggests that silver is effective in denaturing existing bacterial biofilm in the long term (7 days) when silver concentration levels at the bacterial site are maintained at greater than 5 µg/ml[2,4,5]. However, evidence suggests that silver products may not be as effective as iodine products in denaturing biofilm. Consideration should be given to the environment, patient, wound and local resources when selecting wound management products[6].

Effectiveness in inhibiting development of biofilm

- One RCT (n=36) found that after 4 weeks of treatment, a silver-impregnated dressing was significantly more effective (p=0.013) than a control alginate dressing at reducing the risk of clinical infection (assessed using an index that included development of biofilm) in colonised chronic leg and ulcers and pressure injuries[7]. (Level II) As other signs of clinical infection also decreased, it is likely the inhibition of biofilm development was achieved through the reduction in planktonic bacteria.

Effectiveness in denaturing existing bacterial biofilm

- One *in vitro* study compared the effectiveness of various silver products in denaturing immature biofilms from *S. aureus* strains. Silver sulphadiazine 1% (silver concentration 0.302%) and silver nitrate (silver concentration 0.302%) were associated with a 50 to 100 times reduction in biofilm colonies after 24 hours incubation. Eradication of bacterial film was not achieved[8]. (Level III)
- In the same study, no colony reduction was observed in samples of immature biofilms from *S. aureus* exposed to 0.698% sulphadiazine (without silver) and small colony reductions were observed with silver chloride (0.302% silver) exposure[8]. (Level III)
- In one in vitro study, silver sulphadiazine (10 µg/ml) was effective in completely eradicating mature *P. aeruginosa* biofilms within 24 hours, as compared with tobramycin (30µg/ml), which had minimal impact on the biofilm colony[2]. (Level III)
- In another *in vitro* study the threshold level of silver sulphadiazine for eradication of mature *P. aeruginosa* biofilms was determined to be a silver concentration exceeding 1-5 µg/ml, which was over 100 times more concentrated than thresholds to eradicate planktonic bacteria[2]. (Level III)
- An in vitro study investigating effectiveness of six different silver-impregnated dressings in denaturing *S. aureus* and *P. aeruginosa* biofilms found no reduction in bacterial counts in mature (7 day) biofilms after exposure for 7 days[4]. However, two of the six different silver-impregnated dressings (nanocrystalline silver and silver impregnated activated charcoal) achieved small reductions in *S. aureus* and *P. aeruginosa* counts in immature (3 day) biofilms after exposure for 7 days. These reductions were less pronounced than those achieved with iodine products[4]. (Level III)
- One *in vitro* study found a silver-impregnated dressing to be significantly (p<0.0001) less effective than an iodine-impregnated dressing at eradicating *S. aureus* and *P. aeruginosa* biofilms. In cultures exposed to silver dressings, there was a 3-log reduction in bacterial levels within 8 hours; however, bacterial levels increased significantly within the next 24 hours[9]. (Level III)
- In another *in vivo* study, a nanocrystalline silver-containing dressing maintained a reduction in biofilm bacteria over a 7-day period. In contrast, a silver carboxymethylcellulose dressing; a metallic silver with alginate dressing; and a metallic silver with starch copolymers on a polyurethane membrane dressing were all associated with an initial decrease in bacterial counts after one day, but this was not sustained over 7 days[5]. (Level III)

Adverse effects

One literature review presented evidence that high silver concentrations delivered to a wound may have a toxic effect on keratinocytes and fibroblasts and delay reepithelialisation[3]; however, other studies did not support this finding[10]. (Level IV)

Topical silver products should not be used for patients with silver sensitivities and silver sulphadiazine products are not recommended for patients with sulphur sensitivities[3]. (Level IV)

Other considerations

One *in vitro* study identified that the threshold of silver concentration required to eradicate mature bacterial biofilm was higher than concentrations available in most commercial silver-impregnated dressings[2]. (Level IV). To ensure appropriate levels of silver (greater than 5µg/ml or 11mg/cm^2) are delivered to the infected wound research recommends:

- Elemental silver dressings (e.g. silver hydroalginate, nanocrystalline silver) generally have higher concentrations of silver than ionic silver dressings (8–20% versus 0.02 to 1.5%) and sustain silver ion release for longer[4,5,11]. (Level III and IV)
- Sustained release products may maintain silver at greater concentrations for longer[3,5]. (Level III and IV)
- Consider using dressings with the highest available concentration of silver ions[2]. (Level IV)
- Consider more frequent change of silver impregnated wound dressings in the presence of high exudate[2]. (Level IV)

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 silver. The evidence in this summary comes from:

- One non-blinded RCT in which confidence intervals were not reported[7]. (Level II)
- Five *in vitro* studies[2,4,5,8,9]. (Level III)
- Two evidence-based, non-systematic reviews[3,10]. (Level IV)

Best practice recommendations

Topical silver-impregnated dressings could be used to manage biofilms in chronic wounds. (Level B)

Denaturing of biofilms is more likely to be maintained through use of elemental silver dressings and sustained release silver products. (Level B)

NB: Related topics:

ES7020 Wounds Infection: Biofilms defined and described.

ES7369 Wound infection: Biofilms and Iodophors**.**

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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3. Toy L & Macera L. Evidence-based review of silver dressing use on chronic wounds. J Am Acad Nurse Pract 2011; 23:183–92. (Level IV)
4. Hill K, 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(6):1195-206. (Level III)
5. Kostenko V, Lyczak J, Turner K & Martinuzzi R. Impact of silver-containing wound dressings on bacterial biofilm viability and susceptibility to antibiotics during prolonged treatment. Antimicrob Agents Chemother 2010; 54:5120–31. (Level III)
6. Australian Wound Management Association Inc. Standards for wound management. 2nd ed: AWMA; 2010. (Level IV)
7. Beele H, Meuleneire F, Nahuys M & Percival S. A prospective randomised open label study to evaluate the potential of a new silver alginate/carboxymethylcellulose antimicrobial wound dressing to promote wound healing. Int Wound J 2010; 7:262–70.(Level II)
8. Akiyama H, Yamasaki O, Kanzaki H, Tada J & Arata J. Effects of sucrose and silver on *Staphylococcus aureus* biofilms. J Antimicrob Chemother 1998; 42:629–34. (Level III)
9. Thorn R, Austin A, Greenman J, Wilkins J & Davis P. *In vitro* comparison of antimicrobial activity of iodine and silver dressings against biofilms. J Wound Care 2009; 18:343–6.
10. Wilkinson L, White R & Chipman J. Silver and nanoparticles of silver in wound dressings: a review of efficacy and safety. J Wound Care 2011; 20:543–9. (Level IV)
11. Teot L, Maggio G & Barrett S. The management of wounds using Silvercel hydroalginate. Wounds UK 2005; 1(2):70–7. (Level IV)

Audit criteria

1. The selection of a silver product for wound management is based on current evidence of effectiveness, with consideration having been given to the patient, wound, environment and local resources.
2. The dressing product selected is aimed at delivering appropriate levels of silver (greater than 5 µg/ml or 11 mg/cm).
3. The patient has no known silver or sulphur sensitivities.
4. The wound management plan is documented and updated on a regular basis (at least weekly).
5. If the level of exudate is high, the dressings are changed more frequently.
6. There is documented evidence of appropriate adjustments to the wound management plan when the wound is not responding according to expectations.

Keywords

Wound management; silver; silver sulphadiazine; biofilm