Product focus: Nanocrystalline silver and diabetic foot management

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Article points

1. Diabetic foot ulcerations are prone to microbial infection.
2. Dressings containing nanocrystalline silver release very high levels of Ag^+ into the wound on initial contact.
3. The presence of Ag^+ creates a zone of inhibition and has a proven bactericidal effect.
4. The appropriate targeting of wounds suitable for nanocrystalline silver dressings, along with frequent wound reassessment, can result in better clinical outcomes and a cost-efficient use of resources.

Key words

- Foot ulceration
- Nanocrystalline silver
- Microbial infection

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The medical management of diabetes is clinically demanding; typically, a holistic approach is adopted. A key challenge in this therapy area is to prevent and manage the onset of foot problems and ulceration. Should foot ulceration occur, current practices to treat the ulcer include debridement, dressing the wound and pressure relief. An important additional consideration is the active prevention and treatment of infection as this will help contribute to wound closure over a shorter time period than might otherwise be expected. It is well documented that failure to achieve rapid closure of this type of wound is associated with a higher risk of developing an infection, which, in the more severe cases, may lead to amputation (Lipsky et al, 2005).

The recent medical and public focus on infection control strategies in modern hospital and community environments has attained high levels of visibility owing to the publicity surrounding the emergence of organisms that are difficult to eradicate. Additionally, the incidence of MRSA infections has increased in spite of new management approaches and this has been complicated by the appearance of community strains that show a higher level of virulence attributed to their toxin production (Crum, 2005; Grundmann et al, 2006). These new strains are causing clinical infections in much younger populations (Reichert and Birrell, 2005). A quote from a recent Royal Society of Medicine symposium concluded that Gram-negative organisms were 'turning nasty', especially *Pseudomonas*, *Enterobacter* and *Acinetobacter* species, which are found in many chronic wounds and burns (Hawkey and Nathwani, 2006). The development of bacterial resistance associated with the long-term, inappropriate use of antibiotics or topical antibacterial agents, including silver, requires continuous vigilance. To date, however, in the treatment of chronic wounds, resistance has not occurred with the use of silver dressings (Landsdown and Williams, 2007).

Owing to the speed at which infections can develop in diabetic foot ulcers and the associated risks of prolonged hospitalisation, development of osteomyelitis and subsequent amputation, choosing an appropriate evidence-based antimicrobial delivery system as an intervention is considered by many practitioners to be essential. This is in line with current guidelines for antibiotic use, where hard, broad and early use is increasingly recommended (Hawkey and Nathwani, 2006). In terms of assessing outcomes of topical antimicrobials, if the chosen product strategy is effective, it should be possible to see beneficial signs of improvement within a relatively short period of time. This is illustrated in the case study presented

to the right (*Figures 1–3*). At this point, clinical judgement should be used to decide whether or not the treatment should be continued or stopped.

In vitro evidence can provide an indication as to the relative clinical performance of topical antibacterials. It is possible in laboratory tests to show quantitatively that silver dressings can affect the viability of micro-organisms. If an antibacterial dressing is to act as an intervention, the rapid death or disablement of pathogens is an important goal as such organisms can potentially cause wound and systemic invasion in a matter of hours (Dalhoff, 1985). In addition, it is necessary to differentiate between bactericidal and bacteriostatic effects. Edwards-Jones (2006) showed that zone of inhibition tests can be confusing and demonstrated that even when a zone of inhibition is observed with products containing low concentrations of silver, it does not necessarily depict bactericidal action. In the presence of blood and chloride, only the nanocystalline silver containing dressings gave a zone of inhibition with a proven bactericidal effect.

However, it is the in vivo performance of antimicrobial dressings that is a true test of their clinical efficacy. Since chloride ions (for instance from saline solution) and physiological proteins bind to the silver ions (Ag^+) within silver dressings, thus removing the antibacterial agent, there must be enough Ag^+ released and replenished to impact significantly on the bacterial flora inhabiting the complex and dynamic biological environment of a chronic wound. In addition, bacteria themselves have evolved active efflux systems that act as protective mechanisms to remove antibacterial agents such as Ag^+ ions from the cell cytoplasm (Malliard and Stephen, 2006). This is one mechanism by which resistance can develop. It is therefore important to consider the biologically available silver ion levels and not just total silver levels when looking at overall effectiveness in terms of bactericidal activity. Chopra (2007) concludes that some silver-containing dressings appear to provide an alternative to antibiotics in the topical management of wound infection. However, dressings that release lower levels of Ag^+ are likely to be more problematic in terms of selection for resistance, especially if the silver concentration is sub-lethal. Clinicians should choose dressings that release high levels of Ag^+ and demonstrate rapid bactericidal activity.

The Acticoat (Smith & Nephew, Hull) family of wound dressings have been designed to meet the needs currently associated with topical antibacterials. The unique wound contact layer of Silcryst™ nanocrystals is a critical component to their mechanism of action as a bactericidal intervention. During molecular deposition, the smaller the particles deposited on the surface of the substrate, the larger the surface area to volume ratio (*Figure 4* shows Silcryst™ nanocrystals as viewed via a scanning electron microscopy). When exudate bathes against this interface, it has been shown that more chemical reactions occur than with other products that release and replenish Ag^+ (Burrell, 2003).

The nanocrystalline silver layer of Acticoat releases 70–100 ppm of Ag^+ into the wound on initial contact, a concentration higher than other modern silver-releasing dressings (Burrell, 2003). It has been proposed that levels of at least 20 ppm are necessary in wounds to have a bactericidal effect (Wright et al, 1998). Although it is difficult to measure silver content in wounds, it is easier to measure the impact of topical therapies on levels of bacterial flora. Coutts et al (2004) demonstrated that Acticoat 7 can significantly reduce the

Case study. Acticoat Moisture Control: a new clinical option. Adapted from Bowering (2005).

Figure 1. Initial (day 1) presentation of a person with type 2 diabetes with extensive partial-thickness skin loss after debridement. Left leg amputated previously following complications arising from infected neuropathic ulcer.

Figure 2. Follow up (day 14). Wound after 14 days of treatment with ACTICOAT Moisture Control dressing, almost healed.

Figure 3. Follow-up visit at diabetic foot clinic, 4 weeks after initial presentation.

Page points

1. When seeking further clinical understanding and evidence, similarities can be found between burns and diabetic foot ulcers in terms of the risks associated with the development of infection in these two patient groups.
2. The author acknowledges that the treatment of diabetic foot ulceration may also involve the use of topical antimicrobials for the prevention of wound infections.
3. The presence of nanocrystalline silver in the Acticoat range of dressings allows the release and replenishment of Ag^+ at levels where they can act as both an effective barrier and a bactericidal intervention.
4. A recent review of the available silver-containing dressings concluded that those incorporating nanocrystalline silver have the most consistent bench-to-bedside evidence streams to support their efficacy.

total bacterial load in chronic wounds quantified from full-thickness skin biopsies before and after treatment. To date, no other modern silver-containing dressing has been proven to obtain similar reductions in vivo.

When seeking further clinical understanding and evidence, similarities can be found between burns and diabetic foot ulcers in terms of the risks associated with the development of infection in these two patient groups. Following use in burn treatment, Acticoat has been shown to reduce infection rates and the development of secondary bacteraemia. It can also lower the incidence of spreading cellulitis and antibiotics in several studies (Tredget et al, 1998; Fong et al, 2005). These studies also demonstrated significant cost savings.

It is important to differentiate between the first-line use of Acticoat in burns compared with its use in chronic wounds, where application follows clinical observations of the primary and secondary signs of infection. The author acknowledges that the treatment of diabetic foot ulceration may also involve the use of topical antimicrobials for the prevention of wound infections.

Conclusion

The presence of nanocrystalline silver in the Acticoat range of dressings allows the release and replenishment of Ag^+ at levels where they can act as both an effective barrier and a bactericidal intervention. The in vivo benefits of this approach allow rapid bacterial kill, and can contribute to the prevention of infection developing in both acute and chronic wounds.

A recent review of the available silver-containing dressings concluded that those incorporating nanocrystalline silver have the most consistent bench-to-bedside evidence streams to support their efficacy (Leaper, 2006). The appropriate targeting of wounds requiring interventional antibacterial treatment, along with frequent reassessment, can result in better clinical outcomes and the cost-effective use of nanocrystalline silver wound dressings. ■

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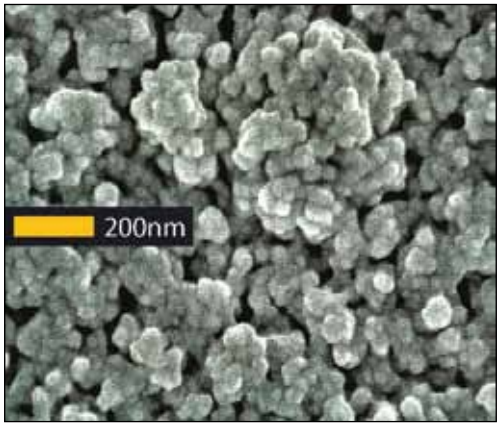

Figure 4. Scanning electron microscopy of the surface of the Articoat dressing demonstrating the large surface area created by the Silcryst™ nanocrystals.

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