Is it time to polish the silver again?

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To complete the *The Diabetic Foot Journal*'s silver anniversary editions we thought it was time to look again at the use of silver dressings in the management of diabetic foot ulceration. As a declaration of competing interests, and as a conscious decision, I have not spoken on behalf of a pharma or dressing company for over a decade. As the journal's editor, as much as this journal and the accompanying conferences are dependant on sponsorship and advertising for their survival, I wanted to retain my independence when it came to editorials and policy.

The history

Most, if not all of you, will be aware of the ancient history of silver use. Dating back to the ancient Egyptians, centuries BC, silver was used to purify water and reduce wound infections. In the middle ages, silver nitrate was used to cauterise wounds, much as we use it to shrink hypergranulation tissue today. As the awareness of postoperative infections rose, silver wire was sometimes used to close wounds. In the 20th century, colloidal silver, a liquid suspension of microscopic silver particles, was used as a disinfectant and was also used as an intravenous treatment of infection before the development of antibiotics. It has also been taken as an health supplement and as nose drops.

However, these uses carry a significant risk of argyriosis. Argyriosis develops when silver is deposited in the skin causing a blue-grey discolouration which can be permanent. Generally, this has no serious consequences other than a cosmetic problem but in the lens, retina and corneas it can lead to visual problems. In 1991, the United States Environmental Protection Agency, estimated that if the lifetime daily exposure to silver was less than5 µg/kg·per day then this is unlikely to lead to argyriosis. Topical silver, even on a large area for a long duration, is extremely unlikely to lead to such a problem. Temporary discolouration of the skin can occur with high dose silver dressings but this usually resolves when the dressing is discontinued.

Modern silver dressings

Modern silver dressings typically contain silver nanoparticles, usually embedded in a dressing matrix. This makes absorption of significant amounts of silver extremely unlikely. Silver resistance is similarly very unusual and when silver dressings started to become widespread in the late '90s, they were marketed as ways of reducing bacterial burden in stagnating wounds. Silver interrupts bacterial metabolism and can break down the barriers in the muco polysaccharides that comprise the "glue" of biofilms. The concept of critical colonisation became wildly discussed and gained a hold in psyche of wound care practitioners. Some believe it is a precursor of infection, some believe it means that biofilms reach a point where they inhibit wound healing, others are less convinced. I have always been in the latter camp. However, there are many in vitro studies which show that silver and other topical anti microbials can reduce the levels of bacteria within wounds and these led to the widespread use of silver dressings in the early part of this century.

Doubts have been raised about local toxicity to fibroblasts and keratinocytes leading to the inhibition of wound healing with silver containing dressings. The toxic concentration of silver is over 60 parts per million (ppm). The therapeutic window for silver ions to have effective bactericidal activity, is around a concentration of 30 to 40 ppm. Therefore, there is a narrow range for an ideal silver dressing to deliver more than 30 and less than 60 ppm over the duration of the use of the dressing. This quite difficult to achieve.

Through the '90s, multiple Cochrane and other reviews repeatedly concluded that there was not enough evidence for the use of newer or more expensive dressings, including silver dressings.

However, I have discussed this in previous editorials in this journal stating that a lack of evidence does not in itself mean a lack of efficacy, merely that the trials have not been published.

Despite these statements, the unmet need for a dressing to improve the generally poor outcomes and healing of chronic wounds meant that for a while it seemed that every slow-to-heal wound was treated with silver containing dressings. Unfortunately due to the heterogenous nature of these dressings, and indeed of the wounds we treat, it became difficult, or even impossible to determine if these dressings were improving wound care outcomes. Practitioners were applying silver dressings for many weeks at a time when manufacturers were recommending a shorter duration. The reputation of silver dressings became tarnished and unsurprisingly, in the face of rising cost pressures and multiple systematic reviews berating the lack of properly controlled outcome trials, prescribing managers, formularies and guidelines started to turn against silver dressings and they were either restricted to specialist use only or removed altogether.

Did overuse lead to under use?

Once the decision was made to remove silver containing dressings from wound formularies, my experience was that usage dropped away very rapidly. For a time almost no patients were referred with a foot ulcer and who had been managed with a silver containing dressing. New models of use were proposed, the most publicised of these being the two week challenge. Essentially, if the wound being managed is not healing effectively then try 2 weeks of silver and see if it improves. Brilliantly simple in concept, but was often seen more as a marketing tactic than a valid clinical model.

Time, however, has given us a chance to revisit silver's role in wound healing. The initial overuse of these products and their perceived lack of efficacy could be explained by over optimistic expectations of what might be achieved. Healing diabetic foot ulceration is a complex problem. Pressure, blood supply, metabolic control and adherence all play a major part and, in the main, dressings can only be expected to have a marginal impact on wound healing rates. Had we been more realistic about what dressings and, in particular, silver-containing dressings, could achieve, would we have avoided the dash to silver and the inevitable over correction? I think so. There is enough theoretical and research experience to demonstrate that if we use silver dressings for their original purpose, to minimise bacterial burden in chronic non-healing wounds, for a limited time, then they will achieve what we want. They may even improve healing rates, but proving this is very difficult. So perhaps the time has come to polish off the silver, but use it wisely, use it sparingly and know what to expect and, once again, silver dressings might take their rightful place among the most popular wound-healing products. ■