Should one size fit all? An overview and critique of the VULCAN study on silver dressings

The VULCAN study results were published in 2009 supported by the HTA and published in the British Journal of Surgery (1). As a multicentre, prospective randomised controlled trial, its objective was to examine the efficacy and cost-effectiveness of antimicrobial silver dressings in treating venous leg ulcers. Patients were recruited from two different areas of the UK, South Yorkshire and Devon.

Silver dressings were compared with non-antimicrobial, low-adherent control dressings. A total of 304 patients were recruited, all with venous ulceration of the lower leg that had been present for more than 6 weeks, of whom 213 participated in the trial, and 91 underwent observation only. Participants were randomised to receive either an antimicrobial silver dressing ($n = 107$) or a control dressing ($n = 106$). Both dressings were applied underneath compression bandages or hosiery. The choice of dressing type was made by the treating clinician; the silver dressing was selected from an approved list (Aquacel® Ag, Acticoat™, Acticoat™ 7, Acticoat™ Absorbent, Contreet® Foam and Urgotul® SSD), and the control dressing was specified as any non-antimicrobial dressing from any manufacturer. Clinical assessment by the treating clinician was used to evaluate dressing effectiveness, with a primary outcome measure of complete healing at 12 weeks. Costs and resource use, quality-adjusted life-years (QALYs), cost-effectiveness, time to healing, and recurrence rates at 6 months and 1 year were used as secondary outcome measures.

The study authors found no significant differences between the two groups for the number of ulcers healed at 12 weeks (59.6% in the silver dressing group, and 56.7% in the control group), and overall median time to healing ($P = 0.408$). No significant difference between the two dressing types was found in either primary or secondary endpoints. Geographical differences were seen in treating clinician preference for dressing type – Urgotul® SSD was more commonly used in the north, whereas Acticoat™ 7 or Aquacel® Ag was more commonly used in the south. The authors concluded that no significant benefits in venous leg ulcer healing were associated with the use of silver dressings, and that these dressings were also associated with a greater incremental cost per patient (£97.85), compared with non-antimicrobial, low-adherent control dressings. This cost was determined from both the increased cost of the dressings themselves, and also from an increase in the number of dressing changes recorded in the silver dressing group.

The authors state that their findings of lack of benefit from silver dressings were robust, with no suggestion of particular benefit associated with any of the dressing types, or in particular patient subgroups (1). They comment that silver dressings are widely used within the NHS, and that introduction of new dressings should be investigated more carefully using large well-designed research studies before widespread use. They conclude that their results suggest no indication for the general and regular use of antimicrobial dressings to promote venous ulcer healing, and recommend the use of less-expensive low- or non-adherent dressings in these wound types.

This study provides some interesting and thought-provoking results, but it has a number of limitations. The main clinical indication for use of antiseptics (including silver) is to prevent the progression of 'critical colonisation', infection or recurrence of infection in those patients who have chronic wounds and are at increased risk (i.e. those with burns, who are immunocompromised, or those in whom patient or systemic factors mean that wounds are unlikely to heal), or to treat established localised or spreading infection in chronic wounds. Discontinuation is recommended when the signs of infection resolve, or the wound starts to heal, and indiscriminate or indefinite use of antiseptics is not recommended (2). The main indication of silver dressing use is not to promote wound healing (3). The VULCAN study therefore did not use these dressings as recommended. It also did not address how to manage patients with non-healing, critically colonised or infected ulcers, or those unable to tolerate compression. The researchers only considered one type of chronic wound (venous ulcers), which have a lower risk of infection than wounds such as burns and skin grafts, where silver dressings have had demonstrable benefits (4). Silver dressings were used for a prolonged time period (up to 12 weeks) on wounds which were not infected, which is contrary to current recommended best practice (5). The length of time of dressing use and number of changes were also inconsistent across the study.

The treating clinicians were also allowed free choice of silver dressing from an approved list of six different types (which offer very different properties), and the study does not report whether the dressing type chosen affected wound healing. As these dressing types are made differently, by different manufacturers and vary considerably in structure, composition and silver content (although all indicated for venous ulcers), one could argue that relying on clinician choice may introduce bias – particularly as some dressing types were indeed more popular than others. Urgotul® SSD was the most commonly used (39.6%), followed by Acticoat™ 7 (27.5%), and a distinct clinician preference was also observed between the two geographical areas of the study. A further potential bias is introduced by allowing free clinician choice of any non-antimicrobial dressing from any manufacturer. Demographic data and healing rates also differed geographically in the VULCAN study, with the northern population being younger overall and having greater co-morbidity associated with worse rates of healing – another factor that could introduce bias, which was acknowledged by the study authors. The fact that the study was conducted in only two geographical areas, which differed demographically, suggests that more comprehensive results would be obtained by using a greater number of study areas, which would give a less restrictive picture of healing rates in the general population.

The use of antiseptics on wounds is an issue which has been widely debated. The main argument for use of antiseptics on open wounds is to prevent and treat infection, therefore promoting the healing process. All chronic wounds are colonised by bacteria, and antiseptics may have advantages over antibiotics as they will not promote bacterial resistance. Silver is also toxic to bacteria in many of ways, damaging the bacterial cell wall and membrane permeability, blocking enzyme and transport systems and preventing transcription and cell division – which also reduces the likelihood of bacterial resistance developing (4). However, a comparative evaluation by Castellano *et al*. (6) found that, while silver dressings exhibited antimicrobial properties, with the highest concentrations of silver showing the greatest bactericidal effect, all silver dressings tested exhibited inferior bactericidal and bacteriostatic properties to other commonly used topical antimicrobial agents. While antiseptics are generally less likely to cause contact sensitivity (3), some silver-based antiseptics, like all antiseptics, have been found to exert cytotoxic effects on wound tissue, and to inhibit keratinocyte production (7,8), and there is concern that using them on open wounds may inhibit wound healing (3,9). This has not been realised in clinical practice. Antiseptics may not also be so effective against bacteria in open wounds, where their efficacy can be reduced by the presence of exudate, serum or blood. A review by Drosou and colleagues concludes, however, that silver compounds do not have a negative effect on wounds (3).

Clinical evidence for the use of silver dressings in wound care is still poor, with few large-scale randomised controlled trials in this area (4). The VULCAN study is therefore a valuable addition to the evidence base.

A 2010 Cochrane review on silver dressings concluded that there was insufficient evidence to determine the effectiveness of silver in dressing or topical form in promoting wound healing or preventing wound infection, based on a review of 26 randomised controlled trials. The reviewers concluded that silver-containing dressings and creams do not prevent wound infection or promote healing – although they admit that most of the studies used as a basis for this report were small and of poor quality (10). A 2007 literature review that focused specifically on assessing silver treatments for leg ulcers also concluded that the evidence base for the effects of silver dressings on leg ulcer healing was poor and therefore inconclusive, both in the quality of evidence available and the number of studies (11).

The nature of randomised controlled trials in this field is that they are always likely to be difficult to enact, and will have considerable associated costs. It is a pity therefore that the objectives of the VULCAN study were not more precise. A number of clinical and case studies have found that silver dressing use can promote wound healing (3,12,13). Miller *et al*. found that silver dressings were associated with a faster rate of healing in the early stages of treatment (first 2 weeks), and in wounds that were larger, older and with more exudate (14). Nanocrystalline silver dressings can provide a barrier against MRSA, and may also prevent wound cross-contamination (4). Clinical studies have also shown silver dressings to be effective against fungal infection (4,15), and they may reduce inflammatory events in wounds (13).

The VULCAN study is right to question whether the routine use of costly wound infection treatments is necessary, but the prevailing opinion appears to be that silver dressings are a valuable component of wound care, provided that they are used sensibly and according to the manufacturer's instructions. In general, they appear to be best used in wounds that are infected, to facilitate healing and prevent infection from spreading further. In his 2007 review on silver dressings (4), David Leaper comments that there seems to be little point in using silver dressings once infection has been reduced or abolished, or in managing an open wound in which there is no suggestion of infection. He suggests that silver dressings are best used for wound bed preparation, particularly in open wounds which have an increased bioburden, and recommends switching to maintenance dressings once this is reduced enough to promote healing – a suggestion not considered in the VULCAN study paper (1). He is also disappointed by the approach that the Cochrane Collaboration takes in that only evidence based level I data is clinically valid (16,17).

Many clinicians see silver dressings as a valuable component in the arsenal of wound care treatments, and concerns have been expressed that the findings of the VULCAN study may lead to their availability being limited (5). While the VULCAN study makes some valid points, it failed to study the main indicated use of silver dressings – which is to treat wounds that are infected. There are also flaws in the study design which limit its value as a comprehensive review of silver dressing viability.

As silver dressings are a relatively new treatment, their use is still being assessed, and further large-scale good-quality studies are needed to provide comprehensive information on silver dressing utility and best use. The complicated nature of this therapy area does not make this an easy task. An editorial published in *International Wound Journal* (18) argues that wound treatment is a multi-factorial issue, depending on the needs of the patient as well as the wound itself. They argue that this makes it difficult to expect a dressing to produce a consistent effect in a wound environment that is constantly changing and shows that, given the complex nature of wound treatment, collecting evidence using randomised controlled trials can be a challenge for wound care practitioners, as each wound, and each patient (and their needs), is different. It might therefore be preferable to pool the experience of individual clinicians who specialise in this type of wound healing, and to publish real data on wound healing (or infection control) from the treating clinician.

Given the complex nature of wound healing, the type of dressing required will depend on many variables, including the type and location of the wound, the patient demographics, and patient preference. Therefore it is not a 'one size fits all' situation as the VULCAN study implies. There is no value in applying silver dressings to all wounds, but equally no value in dismissing their evident benefits by only considering their use in one clinical area of wound care.

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