

Treating bacterial burden in chronic lower leg ulcers

A Randomised Controlled Trial Comparing
Two Antimicrobial Dressings
- Cadexomer Iodine and Nanocrystalline Silver

EXECUTIVE SUMMARY

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Charne Miller¹, Nelly Newall^{2,3}, Suzanne Kapp¹,
Gill Lewin^{2,3}, Leila Karimi¹, Keryln Carville^{2,3},
Terry Gliddon¹, Nick Santamaria³

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Address for Correspondence:

**Royal District Nursing Service
Helen Macpherson Smith Institute of Community Health
31 Alma Rd
St Kilda Victoria 3182
Australia**

Library:
Email: getinfo@rdns.com.au
Telephone: 61 3 9536 5249
Fax: 61 3 9537 0271

RDNS Helen Macpherson Smith Institute of Community Health:
Telephone: 61 3 9536 5251
Fax: 61 3 9537 5300

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Executive Summary

The impact of chronic leg ulcers on the physical and emotional wellbeing of those affected is significant. The high incidence and recurrence of ulceration and the protracted healing time of these wounds translates into considerable and costly demands on health care resources. Any advancement that can be achieved by identifying and disseminating best practice clinical care and circumventing barriers to the application of best practice care can make sizable inroads to improving the quality of life of many and optimising the use of community health care services.

Two of Australia's largest community nursing services, Royal District Nursing Service (RDNS) in Victoria and Silver Chain Nursing Association (Silver Chain) in Western Australia, obtained funding to undertake an initiative aimed at improving the care provided to and outcomes for all people living with a lower leg ulcer who, at these services, represent a large proportion of clients attended and between 35-48 per cent of all wounds seen (Carville & Lewin, 1998; Kapp & Nunn, 2005). Consisting of three components, this initiative included a best practice education programme (Kapp, Flowers, Karimi, & Gliddon, 2008), a study to investigate the enablers and barriers to implementing best practice compression therapy (Annells, O'Neill, & Flowers, 2006), and a Randomised Controlled Trial (RCT) comparing two commonly used antimicrobial dressings for wounds showing signs of critical colonisation or infection. The results of this report reflect the latter RCT outcomes.

Antimicrobial treatment is clinically indicated when a wound appears critically colonised or infected (*Principles of best practice: Wound infection in clinical practice. An international consensus*, 2008). Nanocrystalline Silver (Silver) and Cadexomer Iodine (Iodine) are two of the most commonly used antimicrobials but these have never been the focus of any direct comparison in clinical studies. An RCT was conducted between March 2006 and February 2007 at RDNS and Silver Chain with clients randomised to one of these treatments. The RCT aim was stated as: *To refine existing knowledge and protocols for lower leg ulcer management and develop an evidence based solution to the problem of bacterial colonisation and wound infection.*

The specific objectives of the RCT were:

1. To evaluate and compare the clinical effectiveness of two antimicrobial treatments (Iodine and Silver dressings) in the control of bacterial colonisation and infection in wounds, and to demonstrate the subsequent effect on wound healing.
2. To compare the cost effectiveness, acceptability, ease of use and utility of Iodine and Silver dressings in controlling critical colonisation and infection in wounds.
3. To develop an evidence-based protocol for the management of critically colonised and infected wounds.

Data were gathered from 281 clients, 266 (95%) of whom were able to be included in an intention-to-treat analysis. Primary outcome measures included wound healing rate assessed fortnightly and quantified by the Medseed AMWIST™ wound imaging software (Santamaria, Austin, & Clayton, 2002; Santamaria, Carville, Ellis, & Prentice, 2004; Santamaria & Clayton, 2000) and wound healing within a 12 week monitoring period. Data were collected on potential covariates while costs associated with wound product usage and nursing care were monitored. Wound swabs were attended at baseline, when ceasing or recommencing an antimicrobial treatment, and at six and 12 weeks if treatment with an antimicrobial continued.

Results are reported for the sample overall and for several segmentations (sub-groups) including comparisons of the treatment groups for the segment of clients who healed during the observation period and those that did not, for segments with short and long wound duration (defined as more or less than 12 weeks of duration) and those with small and large wound size (defined as more or less than 3.6cm² in size).

This trial found both antimicrobial dressings had a positive effect on healing lower leg ulcers that were complicated with signs of critical colonisation and infection; 64% of ulcers healed in the 12 week observation period. Both antimicrobials had a comparable performance with respect to the number of wounds healed, healing rate, and in the resolution of pain. There were two circumstances in which Silver was associated with quicker healing times. This occurred in the first fortnight though overall healing rates were comparable after 12 weeks of study observation. Secondly, Silver was found to be more clinically effective for wounds unlikely to heal in a 12 week period. In this sample these wounds were characterised as being larger (an average size of 10cm²), more enduring (a median of 24 weeks duration or almost six months), and with moderate to high levels of wound exudate (a quarter of the sample) as compared to the wounds which did heal in the 12 week observation period.

Research may also consider the area of wound inflammation to examine the hypothesis that the effectiveness of Silver in the first fortnight reflects Silver's anti-inflammatory mechanism (Sibbald et al., 2007) as contrasted to Iodine's inflammatory action (Moore, Thomas, & Harding, 1997). Examination of wound inflammation may also identify situations in which one antimicrobial, based on the level of inflammation present, would be preferred over the other.

Five factors were identified as predictive of time to healing. Adherence to compression bandaging made a positive contribution to healing times. The presence of slough and exudate was associated with slower healing. Wounds that were large and of long duration prior to treatment were also slower to resolve. These findings add weight to existing evidence regarding the clinical effectiveness of compression therapy (Moffatt, 2002; O'Meara, Cullum, & Nelson, 2009), and swifter healing when wounds are smaller and younger (Margolis, Allen-Taylor, Hoffstad, & Berlin, 2004; Phillips et al., 2000; Tennvall & Hjelmgren, 2005). They also reaffirm the need to adopt appropriate dressings or treatments to reduce wound exudate and slough to optimise healing times.

A comparison of microbiology data gathered using wound swabs and clinician assessed signs of critical colonisation and infection from a list of 10 markers derived from the literature, revealed no association between the two diagnostic approaches. As such, the finding from wound culture data that Silver was more effective when there was a low level of bacterial growth has been treated with caution. Additional studies can confirm the reliability of this result and further explore the disparity between wound swab and clinician assessment. The role of the biofilm in obstructing the wound swab from reliably sampling the bacteria on the surface of the wound is tendered as a possible reason for this lack of comparability.

The antimicrobials were generally equivalent with respect to the cost associated with products for the study period. Nurse time, the cost of products used, and a combination of these were used as an overall costing for this analysis. However, there are two instances where, in the absence of a clinical rationale indicating the use of one particular antimicrobial, one product might be favoured over the other. Firstly, if considering the cost to the client, Iodine might be a preferred product if the client's wound is a young wound (less than 12 weeks old) given that product costs were cheaper for this group than Silver. However, from a Health Service perspective adding the nursing care costs to the product cost does not show the same benefit for young wounds, indicating that the delivery of Iodine in terms of treatment time and frequency outweighs the initial product cost saving. If treating a large wound (greater than 3.6cm²) there are cost savings possible for both client and health care service with a Silver antimicrobial. There is also merit in changing from Acticoat® Absorbant as soon as clinically indicated, and in selecting Acticoat® 7 to minimise the cost associated with home visits.

This trial offers the first data, gained from a large multi-site RCT, directly comparing two commonly used antimicrobial treatments. The following recommendations emerge directly from the results of this trial.

1. That clinical guidelines be revised to reflect the results of this trial as indicating:
 - a) Both Silver and Iodine treatments achieved comparable *clinical effectiveness* with the exception of two instances in which Silver had a quicker healing rate than Iodine including:
 - i. the first fortnight of treatment.
 - ii. wounds that did not heal in a 12 week period. In the study these wounds, in comparison to wounds that did heal, were larger (an average size of 10cm²) and of longer duration (a median of 24 weeks duration), and more likely (a quarter of this sample) to have moderate to high levels of exudate.
 - b) Both Silver and Iodine treatments are comparable from a *cost perspective* with the exception of:
 - i. young wounds (less than 12 weeks old) which have cheaper product costs when treated with Iodine, though this difference was not extended to the costs of nursing related to its application nor to the combined product-nursing cost.

- ii. large wounds (bigger than 3.6cm²) which, though comparable for product costs, had cheaper nursing costs and combined product-nursing cost when treated with Silver.
 - c) Wound healing was expedited by the use of multi-layer compression bandaging therapy, resolving wound slough, managing wound exudate, and by intervening when the wound is young and small.
- 2. That emphasis in Australian Venous Leg Ulcer Management Guidelines would be warranted with respect to:
 - a) enhancing access to multi-layer compression bandaging therapy when clinically indicated and optimising adherence to its use.
 - b) dressings and treatments to resolve wound exudate and slough.
 - c) early intervention before wounds become large and chronic.
- 3. That further research is required to compare:
 - a) Silver and Iodine in managing moderate to high levels of wound exudate generally.
 - b) Silver and Iodine in managing wound exudate in the absence of compression bandaging therapy.
- 4. That research undertaken to compare these two antimicrobials in the future incorporate measures of wound inflammation to help understand the mechanism through which Silver and Iodine act and to explore whether the antimicrobials would be better suited to particular wounds based on the presence or risk of inflammation.
- 5. That the role of biofilms in wounds is the focus of additional research to identify:
 - a) how microbiology measures can reliably sample wound bacteria in the presence of a biofilm.
 - b) effective antimicrobial and other treatments to resolve critical colonisation and infection in a wound with a biofilm.
- 6. That to inform the disparity observed for clinician assessment and wound culture results:
 - a) the inter and intra rater reliability and validity of clinician assessment of signs of critical colonisation and infection is investigated.
 - b) future trials explore the use of multiple measures of critical colonisation and infection as well as other markers of wound status including inflammation to assist with the optimisation of therapies to match healing.

7. That future investigations contrast healing outcomes of antimicrobial treatment:
 - a) with a comparison, no antimicrobial treatment group given the presence of recommended multi-layer compression therapy and best practice wound bed preparation for both groups.
 - b) for individuals living with Diabetes Mellitus, arterial leg ulcers, and wounds other than lower leg ulcers.

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