Topical silver-impregnated dressings and the importance of the dressing technology

Keith Cutting, Richard White, Hans Hoekstra

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ABSTRACT

A wide variety of silver-impregnated wound dressings has become available in recent years. This has given the practitioner choice but little evidence by which an appropriate dressing may be selected. In many instances, the ancillary function(s) of the dressing will become differentiating factors that influence choice. For example, the dressing capacity to manage exudate, maintain an optimum moist environment, reduce or avoid maceration, maintain an intimate contact with the wound bed, promote autolytic debridement, sequester bacteria and bind matrix metallo proteases (MMPs) are some of those functions that are of clinical significance and may dictate choice. In this article we present the evidence for these functions, thereby enabling practitioners to evaluate comparative dressing attributes, and so make an informed choice of which silver dressing best suits the needs of the wound under differing circumstances.

Key words: silver impregnated dressings • dressing technology • dressing characteristics • maceration • intimate contact with wound bed • autolytic debridement • bacterial sequestration • binding of MMPs

Key Points

- the incorporation of silver into wound dressings is a contemporary development that has initiated a revolution in the management of local wound infection
- modern silver dressings run the risk of being viewed by the uninformed as no more than a combination of two technologies–the dressing with added silver

INTRODUCTION

The use of silver in medicine has an extensive history (1) but the incorporation of silver into wound dressings is a contemporary development that has initiated a revolution in the management of local wound infection. It is interesting to note that the use of topical antiseptics came under severe criticism in 1980s and 1990s (2) with the main target being those antiseptics that were identified as cytotoxic in vitro not only to micro-organisms but to the host's own cells (3). However, history has taught us that caution should always be exercised when translating in vitro findings to the in vivo situation. More recently, clinical concerns associated with the use of silver dressings in wound care have been explored and discussed (4).

Authors: K Cutting, MN, RN, Buckinghamshire New University, Buckinghamshire, UK; R White, M.I. Biol, C. Biol, PhD, University of Worcester, Worcestershire, England WR2 6AJ, UK; H Hoekstra, MD, Burns Research Institute, Beverwijk, the Netherlands
Address for correspondence: K Cutting, Buckinghamshire New University, Buckinghamshire, UK
E-mail: keith.cutting@bucks.ac.uk

Modern silver dressings run the risk of being viewed by the uninformed as no more than a combination of two technologies – the dressing with added silver. This sometimes leads to a misdirected emphasis being placed on issues such as bacterial time to kill and kill rate thereby implying that there is an enhancement of dressing performance in terms of clinical safety and antimicrobial efficacy. Such issues are of dubious clinical significance and run the risk of appearing no more than marketing exercises, intended to influence choice. This approach, in turn, ignores the intrinsic value of the *carrier* dressing suggesting that it is no more than a passive delivery vehicle for silver and disregards the contribution that the dressing itself can make to a successful clinical outcome.

One of the most significant statements focussing on silver dressings has been made recently by Mooney et al. (5). Their opinion can be summarised as follows:

- Silver broad spectrum antimicrobial efficacy is not in dispute.

- Choice of dressing rests on
  - characteristics of the carrier dressing;
  - delivery kinetics of silver to the wound;
  - the needs of the wound at any given time.

Viewing all silver dressings from the sole perspective that they are no more than *dressings with added silver* relegates the dressing component to that of a simple vehicle for the delivery of silver. It is, therefore, now necessary to look beyond the mere delivery of the topical agent and its antimicrobial impact and examine the contribution that the *carrier* dressing has to make to the progress of the wound. That is, what does the dressing do that impacts on the factors that inhibit healing?

HOW THE DRESSING TECHNOLOGY CAN ASSIST IN MANAGING PAIN

Pain is a known impediment to healing that produces physiological stress (6). The changing of a wound dressing is recognised as a time when pain is most likely to occur (7). Preventing wound trauma and pain were identified as the two main considerations at dressing change highlighted via a survey of nearly 4000 clinicians using a multiple choice questionnaire (7). It is therefore important to use tactics that avoid/minimise trauma to the wound/peri-wound skin and the occurrence of what Krasner (8) has called cyclic acute wound pain. Wound dressing technology has an important role to play if it can avoid those factors that are considered as contributing to pain at dressing change. The three most important factors identified by Moffatt et al. (7) are dried out dressings, products that adhere and adhesive dressings. There are limited clinical studies that focus on the relationship of wound pain and the dressing material.

Pain occurring at dressing change, that is operational pain, has received increasing attention in recent years. Two influential publications have focussed on pain associated with dressing related procedures: the World Union of Wound Healing Societies' Principles of best practice (9) and European Wound Management Association's Position document (10). These publications propose broad strategies to assist in minimising pain at dressing change [reviewed by White and Harding (11)]. A third publication by Thomas (12) proposed that the term 'atraumatic dressing' could be used to describe those products that are proven to avoid causing trauma to the wound bed or peri-wound skin on removal, and included a review of the literature focussing on soft silicone dressings. Soft silicone dressings until very recently have not been available in topical antimicrobial form, nevertheless the atraumatic dressing performance characteristic is important (13).

In a randomised study comparing a silver polyethylene mesh dressing with 0.5% silver nitrate solution, Tredget et al. (14) found that on dressing removal, patients reported wound pain was lower with the silver polyethylene mesh than on removal of the silver nitrate solution. However, patients also reported that the pain was comparable during application and 2 hours following application of either dressing. Therefore, in the short term there appears to be little merit in using this dressing approach.

In an open, prospective, randomised, controlled, multicentre study, a total of 131 leg ulcer patients were recruited and randomised to hydrofibre or to alginate dressing groups (15). Ease of application was rated 'excellent' by 76% in the hydrofibre group compared with 55% in the alginate group ($P = 0.03$). More importantly, ease of removal was rated as excellent by 51% of the hydrofibre group compared with 24% of the alginate group ($P = 0.006$). No pain at dressing removal was experienced by 82% of the hydrofibre group compared with 62% in the alginate group ($P < 0.001$). Less adhesion ($P < 0.001$) and less residue ($P < 0.001$) were also reported in the hydrofibre group thus minimising trauma to the wound bed. Moffatt et al. (7) stated that products such as hydrofibres, alginates amongst others are least likely to cause pain. In the above study it can be seen that hydrofibre outperformed alginate according to the identified parameters.

In a randomised acute/surgical wound study in 100 patients, hydrofibre performance was compared with that of alginate (16). Ninety-two per cent of patients randomised to the hydrofibre dressing were found to experience less pain (mild or none) compared with those who received alginate dressings 80%. Similarly, those patients who were pain free at week one postoperatively were hydrofibre

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- it is, therefore, necessary to look beyond the mere delivery of the topical agent and its antimicrobial impact and examine the contribution that the *carrier* dressing has to make to the progress of the wound
- the changing of a wound dressing is recognised as a time when pain is most likely to occur
- preventing wound trauma and pain were identified as the two main considerations at dressing change highlighted via a survey of nearly 4000 clinicians using a multiple choice questionnaire
- wound dressing technology has an important role to play if it can avoid those factors that are considered as contributing to pain at dressing change
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84% compared with alginate 58%. Although statistical significance was not shown, the researchers concluded that the hydrofibre dressing consistently performed better than the alginate.

A multicentre prospective randomised controlled trial (RCT) (17) reported on the use of a carboxymethylcellulose dressing containing ionic silver (AgNaCMC) and 1% silver sulphadiazine (SSD) cream impregnated gauze in the management of partial-thickness burns ($n = 84$). The authors reported less pain during dressing change and less burning/stinging during wear time (up to 21 days) with the AgNaCMC together with a decreased demand for procedural and narcotic analgesia.

Fifty patients with partial-thickness burns were randomised into two equal groups who received either 1% SSD or a silver-coated, high-density polyethylene mesh dressing (Ag polyethylene mesh) (18). Treatments consisted of either dry gauze dressing with 1% SSD changed twice daily or dry gauze moistened with sterile water and application of an Ag polyethylene mesh with the gauze being moistened twice daily and the outer Ag polyethylene mesh changed every 3 days. The conclusions drawn by the authors of this study were that the Ag polyethylene mesh provided a less painful alternative to wound care than 1% SSD because of longer wear time and ease of application/removal (average pain scores being 4 ± 0.6 for an Ag polyethylene mesh versus 5 ± 0.7 for 1% SSD).

In an open label, multicentre, non comparative study on 18 patients with chronic leg ulcers where the primary aim was to assess safety of an AgNaCMC dressing, Vanscheidt et al. (19) found that a significant reduction in the pain scores recorded by the patients was achieved. It needs to be borne in mind that 11 of the 18 subjects' wounds were infected at baseline. At each dressing change the patient was asked if the dressing had been comfortable since the last visit. All 129 responses were either very comfortable (13.18%) or comfortable (86.82%). For pain on dressing removal, no pain was recorded at 45.7% (59) of dressing changes with low levels of pain (score $\leqslant 2.5$) being recorded on 33.3% (43) occasions.

Jester et al. (20) recognises the fact that dressings differ in material characteristics and evaluated dressing performance and pain during dressing change of two silver dressings: a soft polyester with lipido-colloid coating impregnated with SSD (polyester LC SSD) and a non adhesive polyurethane foam dressing impregnated with silver (polyurethane foam Ag). This retrospective cohort study included two groups of 20 burns treated with polyester LC SSD and polyurethane foam Ag until the wounds healed or were grafted. There were 67 dressing changes in the polyester LC SSD group and 70 in the polyurethane foam Ag group. Both dressings were found to perform well when considering pain at dressing change and ease at dressing application. The polyurethane foam Ag dressing was found to have a greater absorptive capacity than the polyester LC SSD dressing.

In a prospective, randomised study, Glat et al. (21) assessed the clinical and microbiological characteristics of two silver-based topical agents in the management of paediatric partial-thickness burns. Twenty-four patients ranging in age from 2 months to 18 years with total body surface area (TBSA) burns ranging from 1% up to 40% were enrolled and completed the study. Patients were randomised to either a silver-containing gel or to a SSD cream for up to 21 days or to the point of full reepithelialisation of the wound. No statistically significant differences were found when assessing the rate of infection, time to reepithelialisation, or the number of dressings changes required during treatment. A reduction of pain and improved patient satisfaction with the use of the gel indicates an important role for it in the treatment of partial-thickness burns.

THE VALUE OF CLOSE ASSOCIATION OF DRESSING WITH THE WOUND BED

Snyder (22) has recorded that the presence of dead space may act as a nidus for infection and contribute to delayed healing. Robson et al. (1973) cited by Edberg (23) states that dead space lends itself to infection because it does not possess a defence mechanism.

These statements clearly indicate that there is a need to avoid the creation of dead space (void within a viscus or between dressing and wound bed) as there is an apparent association of dead space with risk of infection.

In order to circumvent this situation when applying a wound dressing, the clinician should ensure that the dressing has the capacity to maintain a close association with

the wound bed. It is also reasonable to assume that in those dressings with an absorptive capacity, a close association of the dressing with the wound bed will help promote absorption of exudate and the delivery of silver to the wound bed in silver-containing dressings. Vanscheidt et al. (19) made an empirical observation in their study on 18 patients with chronic leg ulcers that the gel matrix formed by the AgNaCMC dressing moulded itself over the wound surface and eliminated dead space. This observation was subsequently confirmed by Jones et al. (24) who investigated the conformability in vitro of two silver dressings to human wound tissue, dried dermal membrane and indented agar plates that had been seeded with MRSA or *Pseudomonas aeruginosa*. The results showed that there was excellent conformability of the AgNaCMC dressing to the dermal tissue (wound bed) but this was less evident with Ag polyethylene mesh dressing. Incidentally, the AgNaCMC dressing in this study was more effective at killing bacteria on the indented agar plates than the Ag polyethylene mesh dressing.

The intimate association of a dressing with the irregular undulating topography of the wound bed would appear to offer advantages when considering the avoidance of the creation of dead space, absorption of exudate and bactericidal activity of ionic silver.

FLUID-HANDLING PROPERTIES ABSORPTION/RETENTION, LATERAL WICKING, SEQUESTRATION

Before the advent of products that incorporated antimicrobials, dressings were used principally from the perspective of material performance in situ. Up until the 1960s, dressings comprised mainly of woven textiles with a primarily covering/protective function and were not regarded as agents capable of enhancing healing. Following the work of Winter (25), dressing design took into account the contribution that the dressing material could make to the reparative process. However, traditional dressing materials such as gauze continue to be used despite recognition that it does not comply with optimal management requirements (26). Modern wound dressings have been developed primarily to afford a moist wound environment while at the same time providing an absorptive capacity. If problems associated with excess moisture at the dressing interface are not managed correctly, then optimal healing will be compromised. Where absorption of exudate is required, the dressing should also be capable of retaining the fluid ensuring at the same time that the peri-wound skin is not subjected to maceration. Parsons et al. (27) in an in vitro study investigated the clinical performance of seven proprietary silver-containing dressings including fluid-handling properties and dressing pH. The findings show that the best fluid retention under compression was achieved by AgNaCMC and a silver-containing alginate dressing (Ag alginate) with the lowest level of lateral wicking occurring with the AgNaCMC dressing. This paper also states, 'This study suggests that dressing selection should be based on the overall properties of the dressing clinically relevant to the wound type and condition'.

SEQUESTRATION

In addition to the ancillary attributes listed above, it has been claimed that the capacity of a dressing to absorb and retain (i.e. sequester) bacteria is an important function, particularly in chronic wounds (28). In vitro and animal in vivo microbiological studies have illustrated the extent of this effect in hydrofibre and alginate dressings (29–32). Whilst the clinical significance of this feature is yet to be shown, it is likely to be of value in reducing bioburden in colonised wounds where antimicrobials are not indicated, that is routine use in chronic wounds. This would not contribute to selection for resistance as the function is purely physical. A similar function has been described for the binding of bacterial toxins (33). In this context, a silver dressing containing activated charcoal has been shown to adsorb endotoxins from *Escherichia coli* and *P. aeruginosa* in a standard assay. Although this too has yet to be shown clinically, it is an important mechanism for neutralising an important virulence determinant.

The physical principle of hydrophobic interaction has been utilised to sequester bacteria through the addition of a hydrophobic coating containing a fatty acid derivative (dialkylcarbamoyl chloride) to the dressing fibres. Bacteria and other micro-organisms are 'bound' to the dressing when in contact with a

Key Points

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- traditional dressing materials such as gauze continue to be used despite recognition that it does not comply with optimal management requirements
- modern wound dressings have been developed primarily to afford a moist wound environment while at the same time providing an absorptive capacity
- if problems associated with excess moisture at the dressing interface are not managed correctly, then optimal healing will be compromised
- in addition to the ancillary attributes listed above, it has been claimed that the capacity of a dressing to absorb and retain (i.e. sequester) bacteria is an important function, particularly in chronic wounds

Key Points

- although inflammation is a necessary process, excessive or prolonged inflammation results in delayed healing and increased scarring
- solely considering antimicrobial activity as a measure of dressing performance views product efficacy from a too narrow perspective
- clinicians cannot afford to ignore the ancillary activity of the dressing if patients are to receive optimal and comprehensive care

moist environment. The micro-organisms are then removed when the dressing is changed. In a 116 patient multicentre study with a mean treatment period of 37 days, 81% of wounds showing signs of infection at the start of the treatment healed. Twenty-one per cent of patients' wounds healed with a further 72% showing improvement in wound healing (32). Hydrophobic interaction would appear to offer a 'natural' approach to wound healing. There are no chemically active agents and no known side effects or risk of bacterial/fungal resistance.

CONTROLLED SUSTAINED RELEASE

It is generally recognised that for any antimicrobial to be effective, it is important that the target organisms be exposed to a cidal concentration for sufficient time – without tissue toxicity (33). This applies to silver-containing wound dressings, the characteristics of the 'ideal' silver-containing dressing having been published (34). The antibacterial activity of silver emanates from the ionic form Ag^+; this has been studied extensively in vitro and reviewed (35). Whilst there is still very little published information on silver in controlling wound bioburden, it is possible to state that sustained exposure (over 24 hours or more) to very low levels (parts per million) will be effective against a wide range of bacterial species including those with known antibiotic resistance, for example MRSA and Vancomycin resistant enterococci (VRE) (12,24,35–37).

It is pertinent to emphasise at this point the fact that publications reporting on aqueous silver concentrations do not differentiate between active ionic silver (Ag^+) and inactive silver in solution (Ag^0); they only measure total silver content (26). Parsons et al.'s (26) in vitro findings also clearly inform us that the antimicrobial activity of *any* dressing is not necessarily dependant on the amount of silver released as 'there appears to be no correlation between total silver in solution and antimicrobial efficacy'.

This accentuates our earlier statement that the ancillary function of dressings containing silver should be taken into account and draws attention to the physical components of dressings and the role they have to play in promoting healing (38).

Silver has been used prophylactically and silver-coated metallic dressings have been found in vitro to be effective against fungi, bacteria and multiresistant bacteria (39–41). Atiyeh et al. (42) confirm that this form of silver dressing may be useful in preventing infection and also indicate that silver-coated metallic dressings provide a high concentration of silver (around 70 ppm) in the wound by releasing Ag^+ and Ag^0. What is not clear is the proportion of Ag^+ and Ag^0 present in the wound and the value of such a high concentration if silver is accepted as being bactericidal/bacteriostatic at oligodynamic concentrations. Although Ag^0 (metallic silver) may oxidise to Ag^+ in contact with the atmosphere, there is no evidence that it is antimicrobial in action. However, Atiyeh et al. (42) do suggest that the dissolution of silver may favour antimicrobial and anti-inflammatory activity.

MODULATION OF INFLAMMATION

Inflammation is an early and vital stage of the reparative process and is mediated by a number of cells (43). Although inflammation is a necessary process, excessive or prolonged inflammation results in delayed healing and increased scarring. In a study using a rat wound model, Hoekstra et al. (43) made a histological comparison of acute inflammatory responses in partial-thickness wounds when using a hydrofibre or tulle gauze dressing. The findings show that there was minimal inflammation in the hydrofibre dressed wounds when compared with the Tulle gauze dressed wounds. This difference was attributed to the formation of a thin fibrin polymerised layer between the hydrofibre dressing and the wound bed. This layer of fibrin clearly separated the Polymorphonucleocytes (PMNs) within the hydrofibre dressing from the macrophages that invaded the wound bed 3–4 days after wounding. Fewer macrophages were evident in the wound bed and none were detected in the dressing. Macrophages separated from granulocytes act in the repair mode and are not activated for defence purposes. This phenomenon of reduction of inflammation is termed 'quiet inflammation'. In the wounds dressed with Tulle gauze, material was found embedded in the wound bed which showed 'a disturbed pattern of epithelial outgrowth' and 'damage to the dermal matrix'.

CONCLUSIONS

It can be seen from the above discussion that solely considering antimicrobial activity as a measure of dressing performance views product efficacy from a too narrow perspective. Clinicians cannot afford to ignore the ancillary activity of the dressing if patients are to receive optimal and comprehensive care.

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