Using antimicrobial dressings to treat infected wounds

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Article points

1. Reduction of bacterial colonisation and the management of infection should be a key aspect of wound care.
2. Guidelines from the National Institute of Clinical Excellence must be considered when selecting dressings and managing infection.
3. Holistic wound assessment is essential with a minimum of a two weekly review when antimicrobials are in use.

Key words

- Antimicrobial
- Infection
- Resistance

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Infection and appropriate management remains a high priority for diabetic foot ulcers. Clinicians are increasingly seeking alternative and adjunctive options for treatment, one of these being antimicrobial dressings. Like antibiotics, some of these have a risk of toxicity and bacterial resistance. Understanding the composition of such dressings and the guidelines on their use is essential to providing safe and effective care for patients. Holistic wound assessment is key to selecting the dressing and this should take account of the patient's experience and personal preference, as well as clinical evaluation.

Diabetic foot ulcers (DFUs) are generally colonised with bacteria. Due to the poor immune response in people with diabetes, their ulcers often become infected and remain so unless there is intervention, capable of spreading rapidly and increasing the risk of amputation (Dhatariya et al, 2016). Treatment of infection and the reduction of bacterial colonisation should be a key aspect of care (Falanga, 2005). This has led to antibiotic prescription becoming relatively routine for infected DFUs. However, with increasing problems associated with antibiotic resistance and biofilms, clinicians are looking to alternative and adjunctive options for treating and preventing wound infection. One of these options is the use of antimicrobial dressings.

Although already used for centuries in some cases, their availability and use has become more widespread in recent decades, and they are now viewed as an essential part of good wound care for DFUs (Richmond et al, 2013). Barrett et al (2010) highlighted concern over the widespread use of such dressings, particularly prophylactically, as this has led to worries about associated microbial resistance and the significant cost to health care. There are a variety to choose from, including those impregnated with iodine, silver and honey. More recently, there has been the development of bacterial binding dressings, designed to reduce bacterial load rather than destroy bacteria. Understanding when to consider which dressings and their mechanism of action is essential if optimum care and the best outcome for the patient are to be achieved.

A Cochrane review on dressings for DFUs in 2015 (Wu et al, 2015) concluded there is no robust evidence that any advanced wound dressing type (including antimicrobials) is more effective than basic dressings. This conclusion was mainly due to the paucity of evidence available and small-scale studies of poor quality. However, a later review specifically on topical antimicrobials for DFUs found some evidence, although low certainty, that use of an antimicrobial dressing may increase the numbers of wounds healing over the medium term (Dumville et al, 2017).

Iodine

There are two types of iodine impregnated into

ointments or dressings for wound use; cadexomer and povidone. Both release free iodine when exposed to wound fluid affecting multiple sites in the cells of microbes, resulting in cell death (Cooper, 2007) and have a broad spectrum of activity (Dumville et al, 2017).

Cadexomer dressings and ointments, such as Iodoflex® (Smith & Nephew) and Iodosorb® (Smith & Nephew), have been shown to significantly reduce bacterial load in DFUs (Schwartz et al, 2013) and, according to a recent Cochrane review, are indicated for use in cleaning wet ulcers and reducing microbial load (Dumville et al, 2017), rather than prevention of infection. They are contraindicated in patients receiving lithium (National Institute for Health and Care Excellence [NICE], 2018) and may cause stinging when initially applied.

Povidone iodine is available as a solution, ointment, gel and aerosol, as well as impregnated onto dressings such as wound contact layers. The most common example is inadine. Povidone is less potent than iodine and it requires at least 2 minutes of contact to stimulate its antibacterial action (Dumville et al, 2017). As with cadexomer preparations, povidone iodine may cause stinging upon initial application. A Cochrane review on antimicrobial dressings for DFUs suggested this preparation is indicated for cleansing and prevention of infection in superficial burns, incisions, and other superficial wounds (Dumville et al, 2017). Povidone iodine is contraindicated in patients with severe renal impairment (NICE, 2018).

All iodine dressings may discolour the wound and can stain skin and clothing. Although there have been concerns regarding the use of povidone-iodine dressings in chronic wounds and thyroid disorder, the risk is thought to be small (Teot, 2004). These dressings are a popular choice of antimicrobial for DFUs as they are readily available at relatively low cost, can be used for a variety of wound types, including cavities and superficial wounds, and have a long history of clinical use compared to other antimicrobials.

Silver

Originally used for its antimicrobial properties in other fields, such as food and water sanitisation (Leaper, 2006), a variety of standard dressings have more recently been impregnated with silver, including foams, wound contact layers, hydrogels, alginates and hydrofibers, as well as creams. Silver in dressings reduces bioburden and has a detrimental effect on a wide range of microbes (Jude and Unsworth, 2004). There have been concerns about toxicity from overuse of silver and potential bacterial resistance, however, if used appropriately these risks should remain low.

Dressings and creams for wound use are usually impregnated with nanocrystalline, such as Acticoat® (Smith & Nephew), or silver sulphadiazine (SSD), including Aquacel Ag+ EXTRA (ConvaTec), Mepilex® Transfer Ag (Mölnlycke Health Care) and Flamazine® (Smith & Nephew). With both types, silver ions are released when exposed to moisture, such as wound fluid. The ions have a variety of effects on bacterial cells by binding to the cell protein eventually leading to their death (Moore, 2013).

David Leaper (2006) provided a comprehensive explanation of the mechanism of action of silver, explaining that rapid or sustained release gives a wide spectrum of activity with strong evidence to suggest that silver is effective against *Staphylococcus aureus* and *Pseudomonas spp,* as well as on other bacteria, fungi and viruses. It has been suggested that nanocrystalline silver is less painful than SSD (Munteanu et al, 2016), although this is less of a concern in the neuropathic foot.

It is believed that repeated use of low levels of silver in a wound may make resistance more likely (Warriner and Burrell, 2005). Therefore, appropriate use and adherence to manufacturer's instructions is crucial. The International Consensus Group (2012) recommended that application of silver dressings should initially be for 2 weeks. At this point, an alternative dressing can then be selected. However, if review of the wound suggests improvement, but signs of infection remain, it may be reasonable to continue the use of silver with regular reassessment (International Consensus Group, 2012).

Staining of the wound tissue and surrounding skin can occur with silver dressings. This is generally a temporary effect. Patients should be warned of this to avoid concern at dressing changes.

Honey

It is widely acknowledged that honey has been

Page points

1. Choices available for managing bacteria in wounds include dressings impregnated with iodine, silver and honey.
2. All these impregnated dressings are appropriate for use in people with diabetes. Patients should be monitored for changes in blood glucose levels while honey is in use.
3. Other dressing applications are available to manage bacterial bioburden and avoid bacterial resistance.

used in wound care since ancient times. It is now impregnated into a variety of preparations, including gels and wound contact layers, as well as being available for application in its pure form. Honey releases low concentrations of hydrogen peroxide, which gives it an antimicrobial effect and promotes wound debridement without harming granular tissue (Kateel et al, 2016). It also controls malodour.

Manuka honey, however, is now the primary honey used for dressings as it does not rely on peroxide release for its antibacterial effect. The actual substance responsible for this is not yet understood, but manuka honey releases Unique Manuka Factor (UMF), which has a non-peroxide antibacterial action (Jull et al, 2015).

Examples of manuka honey dressings are Actilite® (Advancis Medical), Activon® (Advancis Medical), Medihoney® (Derma Sciences) and L-Mesitran® (Aspen Medical). Few studies have investigated honey dressings on DFUs (Kateel et al, 2016) and the evidence for most wound types is of low quality (Jull et al, 2015). Majtan (2011) raised concerns about the high levels of methylglyoxal in manuka honey and the potential for this to delay healing in diabetic wounds. However, there is no further work to support or reject this speculation. Although honey applications are acceptable for use in people with diabetes, NICE (2018) recommends patients are monitored for changes in blood glucose levels while the dressing or honey preparation is in use. It is contraindicated in patients with extreme sensitivity to honey, bee stings or bee products (NICE, 2018).

Other antimicrobial dressings

In the quest to address bacterial resistance and reduce the bioburden in wounds, other products are being developed. Dialkylcarbamoylchloride (DACC) is a fatty acid coating the Cutimed® Sorbact® (BSN Medical) range of dressings. It binds pathogens, including fungi, to its surface using a hydrophobic interaction, rather than destroying them (Cutting and McGuire, 2015). The microbes are then removed along with the dressing at dressing change. It is user friendly in the clinical environment and has demonstrated promising results (Cutting and McGuire, 2015) although further evidence, particularly in the diabetic foot, is needed.

Polyhexamethylene biguanide (also known as polyhexanide) (PHMB) is an antiseptic that has been used for decades for sanitising swimming pools and contact lens solution, among other things. It is made up of synthetic polymers similar to antimicrobial peptides produced by many cells within the wound and used to prevent the spread of infection (Butcher, 2012) particularly bacterial and fungal (namely *Candida albicans*) infections (Moore and Gray, 2007). It has been impregnated into many wound products including gels and solutions (for example, Prontosan®, B Braun), biocellulose dressings (for example, Suprasorb X®, L&R) and foams (such as Kendall™ AMD, H&R Healthcare).

It is suggested that PHMB products have numerous advantages, including reduction of pain levels, reduction of malodour, debridement of slough and other non-viable tissue, low risk of sensitivity and no evidence of microbial resistance (Moore and Gray, 2007; Barrett et al, 2010; Butcher, 2012).

More recently, octenidine dihydrochloride has been introduced to wound care. This is a surfactant active against Gram-positive and Gram-negative bacteria and is currently available in a solution and a gel, such as Octenilin® (Schülke). It has not yet been bound to or impregnated into dressings. Octenidine dihydrochloride removes non-viable tissue and debris from the wound bed and is effective at preventing and removing biofilm (Chadwick et al, 2016). Assessments have shown it to have a rapid effect on bacteria, reducing their numbers within 30 seconds (Assadian, 2016). Evaluation of its use in DFUs is promising (Chadwick et al, 2016; Haycocks, 2017) with results of case studies demonstrating a positive effect on pain, exudate and malodour, as well as reduction of infection (Haycocks, 2017), but further robust evidence is necessary.

A wound application that has been used for centuries to debride, larvae are now being recognised as effective against bacteria, including methicillin-resistant *Staphylococcus aureus*. Larvae used in wound care are *Lucilia sericata* (common green bottle fly) and their secretions contain antimicrobial peptides (AMPs). Jaklic et al (2008) investigated the effect of the Lucilia sericata larval secretions *in vitro* and *in vivo* and found it effective against Gram-positive bacteria. It was less effective against Gram-negative bacteria, especially *Proteus spp*. and *Pseudomonas spp*. strains (Jaklic et al, 2008).

Work is being done on synthesising AMPs similar to those excreted by the Lucilia sericata larvae and adding them to gels and dressings (Pöppel et al, 2015). This may provide a new generation of antimicrobial dressings in the future.

Conclusion

Antimicrobial dressings are generally accepted as an important part of routine care for the infected wound, particularly for DFUs where the risks of subsequent complications are high. Despite this, the availability and quality of evidence remains low. If clinicians are to ensure the best evidence-based care for their patients, this needs to be addressed.

When selecting any dressing, account must be taken of the outcome of holistic clinical wound assessment, as well as the patient's experience and personal preferences (Wu et al, 2015) and this process is ongoing. With antimicrobials, review should occur after 14 days when a decision can be made to change dressing type or continue with the same for up to another 2-week period.

Cost-effectiveness is essential as is selecting a dressing appropriate to the wound bed. Treating infection should not ignore the usual considerations, such as the requirement for absorbency, adherence, need for debridement and frequency of dressing changes. The patient must always remain the central focus and be on board with the plan of care. ■

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