New approaches to combating antibiotic resistance

KEY WORDS
- Antimicrobial resistance
- Wound bed preparation
- Wound infection

Antimicrobial resistance (AMR) threatens the effective prevention and treatment of an ever-increasing range of infections and poses a serious threat to global public health (World Health Organization [WHO], 2014). As well as sustaining effectiveness of existing antibiotics through better prescribing practices, it is important that other options are explored to combat infection. Topical antimicrobials can be used for locally infected wounds to inhibit or kill microorganisms within a wound. These have broad-spectrum activity and can be used to prevent progression from localised colonisation to more invasive infection states, thereby reducing antibiotic usage.

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Infection is the most common cause of delayed wound healing (Gottrup et al, 2013). Modern clinical practice relies on the widespread availability of effective antimicrobials to prevent and treat infections. However, inappropriate use of antibiotics has led to the mutation and spread of bacteria that are resistant to multiple antibiotics (Odonkor and Addo, 2011). Resistance to all antimicrobials, including antivirals and antifungals, is increasing, but of greatest concern is the rapid development of bacteria resistance to antibiotics. This has led to an increasing number of infections that are difficult to treat or no longer can be treated using conventional antibiotics (Department of Health [DH], 2013). Treatment failure contributes to increasing costs of care and patient wellbeing. To address the challenges of antibiotic or antimicrobial resistance (AMR), the government has set out a five-year plan, which has identified seven key areas for future action (*Box 1*).

Despite this, Public Health England recently reported a 6% increase in prescriptions for antibiotics between 2010 and 2013. The chief medical officer, Professor Dame Sallie Davies, warned that, during the next 50 years, drug resistance of microorganisms will increase, and new strains with resistance to a wide variety of agents will emerge, rendering antimicrobial drugs ineffective. In addition, poor incentive to develop new antibiotics, leaves fewer options for treating infections, potentially giving rise to apocalyptic scenarios including routine infections becoming fatal once again (Davies, 2013).

It is, therefore, essential that clinicians identify wound infections correctly and, when appropriate, choose products that do not influence the development of AMR in wound management (Wounds UK, 2014). This has led to the importance of finding alternatives to systemic antibiotics for the prevention and management of wound infection.

Box 1: Seven key areas for future action (Department of Health [DH], 2013).

- Improve infection prevention and control practices
- Optimise prescribing practice
- Improve professional education, training and public engagement
- Develop new drugs, treatments and diagnostics
- Facilitate greater consistency and standardisation of data collected and encourage improved data linkage
- Identify and prioritise research needs to focus activity and inform understanding of antimicrobial resistance
- Strengthen international collaboration to influence opinion, galvanise support and mobilise action.

WOUND CLEANSING AND PREVENTION OF INFECTION

The concepts of wound bed preparation and TIME were created in 2003 to help clinicians identify the key barriers to healing in individual patient's wounds and to implement a plan of care to remove these barriers and promote healing (Dowsett and Newton, 2005).

Taking steps to manage infection is one of the key principles of wound bed preparation. This involves removing devitalised tissue (T), reducing the bacterial burden (I), maintaining adequate moisture (M), and managing the

wound edge to encourage epithelialisation (E) for optimal wound healing (Schultz et al, 2003).

Wound cleansing can help to achieve the goals of wound bed preparation by assisting in the removal of loosely attached cellular debris and surface pathogens contained in wound exudate or residue from topically applied products (Wolcott and Fletcher, 2014). The choice of wound cleansing solution should be one that will prevent infection while doing no harm. Although the most recent Cochrane review shows no evidence that saline or tap water are harmful to wounds (Fernandez et al, 2012), these solutions may not actively promote healing (Cutting, 2010). While tap water has been found to be as effective as saline, variations in water purity make it difficult to support the widespread use of tap water for irrigation (Jefferies et al, 2012). For example, Gram-negative *Pseudomonas* bacteria is a well-reported issue in tap water (Trautmann et al, 2005).

In addition, since both tap water and saline solution do not exhibit antimicrobial activity they cannot be viewed as the most effective solutions for the irrigation of chronic wounds (Rowley and Clare, 2014). Commercial antiseptic wound cleansing solutions with broad-spectrum activity and rapid antimicrobial kill rate offer an alternative and can be used to enhance the efficacy of wound cleansing. They may also have a role in biofilm-based wound care (Leaper et al, 2012).

Antiseptic agents are not routinely recommended for use in all wounds (Cutting, 2010). However, for wounds progressing from simple colonisation to the pre-infection stage of critical colonisation or local infection, it is important to intervene with the use of a topical antimicrobial agent (Wolcott and Fletcher, 2014). Selection criteria should be based on the ability of the solution to reach killing concentrations at the wound's surface to eradicate bacteria, reducing the risk of bacteria developing resistance. Non-toxic agents that are effective at low concentrations should be considered where possible to aid wound bed preparation.

Hypochlorous acid is produced by the body's immune cells in response to invading pathogens (Eryilmaz and Palabruyik, 2013) and is now available as a commercially prepared wound cleansing solution (Woundox® Irrigation Solution, Martindale Pharma) (Wang et al, 2007; Crew et al, 2012). Woundox Irrigation Solution is effective against a broad range of microorganisms, is non-toxic, and has a rapid kill rate (Eryilmaz and Palabruyik, 2012). It has also been shown to improve wound healing outcomes in a range of wound types (Robson et al, 2007; Crew et al, 2012).

Antimicrobial wound cleansing solutions such as Woundox Irrigation Solution can be used across the spectrum of chronic wounds without the risk of bacterial resistance as they are antiseptic rather than antibiotic (*Box 2*). When used as part of wound bed preparation, Wolcott and Fletcher (2014) suggested that lightly irrigating the wound prior to debridement can aid inspection and assessment. Then the wound can be re-irrigated with a wound cleansing agent before applying a suitable wound dressing.

Topical therapy is often adequate in wounds that present with local signs of infection. For wounds with spreading or deep tissue infection, systemic antibiotics are indicated. These may be used in combination with topical agents to provide antimicrobial treatment directly to the wound dressing interface. This may be pertinent in patients with poor vascular supply (Chadwick, 2013) as systemic antibiotics may not be well delivered to extremity wounds.

CAN DRESSINGS REDUCE RELIANCE ON ANTIBIOTICS?

Although infection is one of the most important barriers to wound healing, there is often more than one factor present and these factors may be interlinked (Bullough and Spruce, 2013). For example, excessive exudate could be the result of increased bacterial burden related to local wound infection. Managing these different barriers can be challenging for clinicians in terms of selecting the most appropriate wound care product to address the different problems identified in the non-healing wound.

Debridement is an essential component of effective wound management and is primarily aimed at reducing the risk of infection and achieving wound healing (Vowden and Vowden,

Box 2: Benefits of Woundox® Irrigation Solution.

- Non-cytotoxic, non-irritating and non-sensitising
- Effective against a broad spectrum of microbes
- Rapid bactericidal action
- Safe in a variety of wounds
- Does not result in development of resistance (attacks bacteria at multiple sites).

Box 3: Three modes of action of Drawtex® Hydroconductive Debridement.

1. Draws fluid and devitalised tissue from the wound into the dressing
2. Controls bacteria levels in the wound by trapping microorganisms in the dressing fibres
3. Absorbs exudate vertically and horizontally into the dressing to achieve a moist but not macerated wound bed. The dressing can be layered to manage exudate volume.

2011). There are a number of methods to choose from, although these demand different levels of competency, knowledge and skills. Wound dressings can be used to achieve simple autolysis but this is normally a relatively slow process, which may increase the risk of infection and delay wound healing (Wounds UK, 2013). Achieving the correct moisture level also relies on good clinical judgement and appropriate dressing selection.

Hydroconductive debridement differs from autolytic or mechanical debridement in that it absorbs rather than donates fluid, selectively removes non-viable tissue, and maintains a moist wound environment by absorbing excess exudate containing harmful substances, leaving the wound bed clean and facilitating the formation of healthy granulation tissue (Bullough, 2014).

Drawtex® Hydroconductive Debridement Wound Dressing (Martindale Pharma) incorporates LevaFiber™ technology, which combines hydroconductive, capillary and electrostatic activities in order to debride, manage exudate and reduce bioburden (*Box 3*).

When in contact with the wound bed, the dressing draws exudate through the tissue, breaking down the non-viable tissue, which is then pulled into the dressing (Ortiz et al, 2012). The dressing is able to hold large volumes of exudate, sequestering bacteria and trapping harmful substances such as microorganisms, cytokines and proteases (e.g. MMP2 and MM9) (Edwards-Jones et al, 2014) contained in the exudate, which can help to control bacteria levels in the wound (Couch, 2012; Ortiz et al, 2012; Ochs et al, 2012) and suppress biofilm activity (Wolcott, 2012). These actions can facilitate wound bed preparation, reducing the risk of infection and the need for topical antimicrobials (e.g. silver)and/or systemic antibiotics. Where appropriate, wound cleansing with a non-cytotoxic solution (e.g. Woundox Irrigation Solution) can be used as a first step in conjunction with Drawtex to further inhibit an increase in bacterial bioburden (Wolcott and Fletcher, 2014).

Drawtex helps to simplify the dressing selection process in wounds where more than one barrier to healing has been identified (Bullough and Spruce, 2013). In addition to reduction in wound area (Ochs et al, 2012) and faster healing rates (Wendelken et al, 2012), a 10-patient evaluation has also shown potential cost-savings with a reduction in expenditure on wound care products (Bullough and Spruce, 2013).

CONCLUSION

Judicious prescribing will slow down the emergence of AMR (DH, 2013). Antibiotics should be reserved for situations where there is good evidence to support their use and/or the consequences of infection are serious. Where antibiotics are prescribed, a drug should be chosen that will limit the development of bacterial resistance based on available evidence and local protocols (Lipsky et al, 2012). Antibiotics should be used for infection and not colonisation (Wounds UK, 2013).

For wounds at risk of infection or where local infection is suspected, alternative treatments to prevent and manage infection should be sought to decrease reliance on antibiotics. Wound cleansing using a broad-spectrum, rapidly-acting, non-cytoxic antimicrobial solution should be considered as an integral part of wound bed preparation along with a dressing that can address different elements of TIME. Incorporating innovative and effective topical antimicrobial products within a structured wound infection protocol allows clinicians to control AMR, while maximising the potential for wounds to heal. WUK

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