

BACTERIAL MANAGEMENT: IN MODERN WOUND CARE

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Successful management of bacteria in the wound is a complex issue. The role of bacterial management is therefore of great importance, particularly for those with a compromised immune response. Dressings with PHMB offer the clinician a new wound care modality with a proven track record of clinical efficacy, cost effectiveness, and most importantly patient safety.

The influence of bacteria on wound healing is complex; all wounds are colonised with bacteria at, or soon after inception, and yet most wounds, even chronic wounds, can heal. Wound infection is the result of the interaction between the patient's immune system, the wound conditions and the numbers and virulence of the bacteria present (Dowsett et al, 2004).

Chronic wounds are often heavily colonised with bacteria or fungal organisms, due in part to being open for prolonged time periods, but also because of underlying medical problems such as poor blood supply, lack of oxygen and metabolic disorders like diabetes (Hunt and Hopf, 1997).

Bacteria normally live in multi-species communities; single species communities of bacteria being rare in nature (Cooper and Okhria, 2008). In certain circumstances, these communities exist within a protective three-dimensional extracellular polysaccharide (EPS) matrix and are known as biofilms. Polymicrobial colonies of bacteria

are known to exist in most chronic wounds and are thought to negatively influence wound healing (Gethin, 2009), however understanding of biofilms and their effect on wound healing is limited, although they seem to be a key component in resistant bacterial colonisation (Serralta et al, 2001). It is known they are dynamic; constantly changing and adapting to their environment.

This constant adaptation results in colonies that are uniquely able to survive, resisting the effects of antibiotics and host defence mechanisms. Many biofilms may be 50–1,000 times more resistant to antibiotics than 'planktonic' or free-floating bacterial cells (Ceri, et al, 1999).

The presence of bacteria in chronic wounds in itself does not necessarily indicate that infection has occurred or that impaired wound healing will occur (Kerstein, 1997; Dow et al, 1999). Generally it has been believed that if the wound does not display the classic signs of infection, (redness, pain, swelling and localised heat) clinical

intervention is not required. However, as new information is presented, many now believe that high levels of bacteria may inhibit healing in the absence of traditional signs of infection (Edwards and Harding, 2004; Warriner and Burrell, 2005). This state is frequently called 'critical colonisation' (Kingsley, 2001).

For some individuals, bacterial numbers in the wound increase and the wound progresses from contamination through colonisation to critical colonisation and infection (termed the 'infection continuum') (Kingsley, 2001; White et al, 2001).

The classic signs of infection may only become obvious when the numbers of bacterium and the virulence factors the bacteria produce are greater than the host's immune defences, resulting in harm to the host. In 1994, Cutting and Harding added discharge, delayed healing, wound breakdown, pocketing at the base of the wound, epithelial bridging, unexpected pain or tenderness, the presence of friable granulation tissue,

discolouration of the wound bed, abscess formation and malodour as potential signs of infection.

Once colonisation and infection occurs it can prolong the inflammatory phase of healing, cause pain and discomfort for the patient and, unless correctly treated, can lead to serious and potentially fatal systemic sepsis. Wound infection is not just costly to the patient; financial costs increase with prolonged treatment and on occasions, hospital admission is required. Therefore, the effective management of wound bioburden has been identified as a central tenet when undertaking wound bed preparation (WBP).

When the balance in the wound is tipped in favour of the bacteria and wound healing is interrupted, active measures are needed to control them (EWMA, 2006; Gethin, 2009). The presence of spreading infection has potentially serious implications for patient well-being and appropriate systemic antibiotic therapy should be commenced (EWMA, 2006). The use of topical antibiotics is linked to the development of bacterial resistance, therefore these should be avoided. However, systemic antibiotics are not recommended for wounds that only show signs of local infection and/or critical colonisation (Bowler et al, 2001) and other interventions are indicated. Topical antimicrobials have been shown to have a significant role to play in reducing bacterial load (EWMA, 2006) and represent first-line treatment in the management of bacterial burden as they provide a high antimicrobial concentration at

the site of infection (White et al, 2001; Cooper, 2004), do not interfere with the remainder of the protective bacterial flora in other parts of the body, and are less likely to produce an allergic reaction. Some also have bactericidal effects against multiresistant organisms such as methicillin resistant *Staphylococcus aureus* (MRSA) (Lawrence, 1998; Sibbald et al, 2001) and biofilms.

However, their use has to be targeted and measured. Lack of a noticeable healing response within two weeks may necessitate the use of alternative topical or systemic agents (Bowler et al, 2001) and widespread, inappropriate use increases healthcare costs with no gain in outcome.

Recently, new concerns have arisen over the current topical antimicrobial products. A number of bacterial strains have been identified that demonstrate tolerance to products containing silver (Lansdown and Williams, 2007) and systemic absorption, the accumulation of chemicals within the body, and tissue toxicity to a number of commonly used antimicrobial elements has been described. This could be significant as it may severely restrict treatment options.

Unfortunately, dependence on these treatments is likely to increase as there appears to be no new antibiotics in development to take over the management of systemic infection (Sipahi, 2008). There are, therefore two actions which need to be undertaken:

- ▶▶ Control of the use of antimicrobials

- ▶▶ The development of new antimicrobial therapies.

Control of current antimicrobial usage is already being tackled by education, the development of treatment protocols and best practice statements, however the development of new antimicrobial technologies and products is something where cooperation between healthcare, research and industry is now a priority.

One possible solution is in the use of polyhexamethylene biguanide (PHMB), a product which has been available for many years in a number of formats, but which has not, until recently, made a significant impact on the UK wound care market.

What is PHMB?

The antiseptic PHMB (also known as polyhexanide) is a mixture of polymers, structurally similar to the naturally-occurring antimicrobial peptides, which support the innate immune response and naturally protect against infection.

PHMB appears to primarily target the outer and cytoplasmic membranes of bacterial cells. PHMB adheres to these membranes, causing them to leak potassium ions and other components within the cytoplasmic fluid resulting in cell death. There is also evidence that once inside the bacterial cell, PHMB binds to DNA and other nucleic acids damaging or inactivating them. Because PHMB changes the cell membrane, once it has gained entry it cannot be removed by the bacterium's defence system. PHMB is also effective

at controlling fungal infection but does not adhere to animal cell membranes, meaning it has no toxic effect on human cells.

Use of PHMB

PHMB has been in use as an antiseptic and disinfectant for approximately 60 years with proven effectiveness against a broad number of bacterial and fungal species with rapid and sustained action. It has been demonstrated to be effective at biofilm management with no evidence of bacterial resistance or systemic absorption. Tests have shown that PHMB has greater killing effect with less host toxicity than chlorhexidine, povidone-iodine, triclosan, silver and sulfadiazine. Studies have also shown that skin sensitivity to PHMB is very low even in high concentration.

Recently, PHMB has been introduced into a range of wound care products. In some cases, the PHMB molecule is chemically bound to the dressing material, providing it with antimicrobial properties when in contact with wound moisture. These products protect patients by decreasing the bacterial load in the dressing and preventing bacterial contamination. In other products the PHMB can be donated into the wound and periwound tissues; the dressing in this case being a carrier for a wider antimicrobial effect. Wound irrigation fluid containing PHMB is also available, however studies indicate that solution concentration should be between 0.01–0.04% (depending on clinical need) and contact between the bacteria and PHMB needs to be maintained for 10–15

minutes to ensure maximum effect. Continuous irrigation is possible, though this may not be suitable in community settings. The clinician must choose products that are suited to individual patient needs.

PHMB also has positive effects on wound healing. In the laboratory and in clinical use studies have shown that PHMB:

- ▶▶ Reduced wound pain rapidly and effectively
- ▶▶ Reduced wound odour
- ▶▶ Increases granulation tissue formation
- ▶▶ Increased keratinocyte and fibroblast activity
- ▶▶ Reduced slough within the wound
- ▶▶ Reduced protease-induced periwound breakdown
- ▶▶ Assisted in removing non-viable tissue (Cazzaniga et al, 2000; Daeschlein et al, 2007; Mueller and Krebsbach, 2008; Wiegand et al, 2008a,b; Galitz et al, 2009; Kaehn, 2009).

PHMB is, therefore used to control the bacterial burden within wounds; specifically, it is used to reduce bacteria in the critically colonised or infected wound and may be of benefit to prevent infection in individuals with a compromised immune response.

PHMB should also be considered for use in conjunction with systemic treatment when treating serious wound infections. As with all topical antimicrobial therapies, if the wound is unchanged after 10 days of use or deteriorates, alternative antimicrobial treatments should be considered (including systemic antibiotics).

In most cases, treatment should not extend beyond 14 days unless previously agreed by a local specialist.

PHMB does have specific contraindications; it must not be used (Dissemond et al, 2010):

- ▶▶ For peritoneal lavage
- ▶▶ For antiseptic joint lavage (cartilage toxicity)
- ▶▶ In applications involving any part of the central nervous system (CNS), including the meninges, and intralumbar applications
- ▶▶ For applications involving the middle or inner ear, or for intraocular applications
- ▶▶ During the first four months of pregnancy (at any time thereafter, a strict benefit/risk assessment has to be performed)
- ▶▶ In patients allergic to PHMB.

As can be seen, apart from a very small minority of patients who fall within the last two groups, PHMB does not have any contraindications for application within the wound care population.

Cost-effectiveness

The targeted use of antimicrobial dressings has repeatedly been reported to reduce surgical site infection rates and so provides cost-savings. Gilliver (2009) identified three US-based studies which demonstrated that following introduction of PHMB:

- ▶▶ Overall surgical site infection (SSI) rate was reduced by 24% and MRSA SSI rate reduced by 47%, delivering a \$508,605 net saving during a one-year evaluation period (Mueller and Krebsbach, 2008)
- ▶▶ Hospital-wide introduction resulted in a reduction in

the incidence of infections from 23 to 11 (both reported in separate six-month observation periods) with a calculated net saving of \$171,537 (Beneke and Doner, 2005)

- ▶▶ Treatment of non-healing wounds was more cost-effective; calculations (based on material costs) averaging \$5.99–9.01 per patient per day and were as low as \$2.14 per day in one patient (Mulder et al, 2007).

PHMB offers a new method of bacterial control that has proven safe, efficient and cost-effective. This will provide benefits to patients and clinicians in providing alternative and additional tools to manage bacterial burden within the wound care environment.

Dressings

Moisture management and bacterial control are two of the fundamental issues in wound management. The new dressing Suprasorb® X+PHMB (Activa Healthcare) has been specifically designed to deal with these two issues simultaneously. The product is constructed of a unique structure composed of biosynthetic hydrobalance fibres. These are the products of a cellulose fermentation process using *Acetobacter xylinum*. The bacteria produce a mesh structure of cellulose fibrils, which are 200-times finer than cotton, giving the material an exceptionally high surface area with enhanced moisture handling capabilities and tensile strength. As a result, the dressing is able to regulate the absorption and donation of moisture at the wound-dressing interface.

Depending on the status of the wound, surplus exudate can be absorbed by the dressing, or moisture donated to provide an ideal moist environment. This ability to balance moisture levels can occur within one wound; the dressing removing exudate from one area and donating moisture to others. In addition, the dressing contains the potent antimicrobial polyhexamethylene biguanide (PHMB 0.3%). The PHMB component exerts its antimicrobial effects both within the dressing, but also at the wound surface.

As the PHMB is not bound to the fibre of the dressing, it is released into the surrounding fluid along a concentration gradient. The dressing is moist, meaning that antimicrobial activity is possible even on dry wounds (unlike silver-based antimicrobial dressings). Suprasorb X+PHMB dressings are indicated for use on lightly to moderately exuding, superficial and deep, critically colonised or infected wounds in all stages of wound healing (Kingsley et al, 2009).

Suprasorb X+PHMB in clinical practice

As well as anecdotal evidence from case studies, a number of trials have been undertaken to demonstrate the clinical effectiveness of Suprasorb X+PHMB in wound care. These provide strong evidence of the benefits of using the product to manage wound colonisation and infection.

An evaluation of Suprasorb X+PHMB in the treatment of four patients with wounds that had previously been treated

unsuccessfully with various silver-containing dressings was undertaken by Davis (2006). Although two wounds were locally infected, application of Suprasorb X+PHMB healed three of the four wounds, protected peri-wound tissue and resulted in a decrease in wound pain.

Similarly, a multicentre evaluation of Suprasorb X+PHMB in the treatment of 50 patients with 79 clinically infected or critically colonised wounds of varying wound types (including venous and arterial leg ulcers, diabetic wounds, pyoderma gangrenosum and vasculitic ulcers), revealed that healing or clinical improvement was achieved in more than 80% of the cases receiving treatment with Suprasorb X+PHMB (Cavorsi, 2006). In a subset of wounds that had not been responsive to prior treatment with silver dressings, a decrease in wound size of 33% was observed after three weeks. All wounds demonstrated continuous autolytic debridement and pain reduction.

A clinical case series performed by Mulder (2007) to determine the antimicrobial effects of Suprasorb X+PHMB showed that it effectively reduced wound bioburden and had a positive effect on wound healing. Twelve patients with a total of 26 wounds were evaluated, 11 of whom had previously been unresponsive to silver or iodine-containing dressings. Wound swabs were taken before and after treatment with Suprasorb X+PHMB.

Before treatment, organisms were identified in the wounds of

eight patients, most commonly *Pseudomonas aeruginosa* and *Staphylococcus* (including MRSA). At the end of the evaluation, levels of bacteria had decreased in five of the eight patients (two patients were lost to follow up, and one patient experienced no change in bioburden). For the eight patients, there was a mean reduction in wound size from 6.79cm² to 4.57cm² in a mean of 25 days. Two wounds healed during the study and 13 showed improvement.

Galitz et al (2009) conducted a controlled randomised prospective multi-centre comparative study of the use of Suprasorb X+PHMB against the best local silver standard of care.

The 37 subjects were all assessed as having high wound pain and critically colonised or locally infected wounds and had similar demographic and wound-related presentations. Treatment was continued over 28 days.

The results of the study identified that both dressing regimes achieved a positive antimicrobial effect and pain reduction. However, in the case of the Suprasorb X+PHMB, pain reduction was consistently greater and more immediate with significant pain reduction occurring after the first day of treatment.

The authors concluded that the PHMB product provided an efficacious, patient-friendly option for the management of these types of wounds.

Mosti et al (2008a) evaluated the effect of Suprasorb X+PHMB on wound bed preparation in 18

patients with 30 painful, hard-to-heal wounds who were admitted for skin grafting.

A subgroup of eight patients with critically colonised or locally infected wounds and ulcer duration of between six months and four years received it as a primary dressing.

Results showed effective debridement and infection control. Time to wound bed preparation was 6.2 (± 1.3) days. In the subgroup, bioburden reduced significantly.

In another study, Mosti et al (2008b) evaluated the dressing's antimicrobial properties. They identified a subgroup of 11 outpatients with critically colonised or locally infected wounds among 60 patients with vascular leg ulcers being treated with Suprasorb X.

These 11 patients were given Suprasorb X+PHMB as a primary dressing plus a foam or absorbent secondary dressing. Three of the 11 patients underwent successful skin grafting as a result of good wound bed preparation. Seven healed in a little over 13 weeks. Bacterial bioburden decreased significantly after three dressing changes. This antimicrobial effect has been observed in a variety of wound aetiologies.

A prospective, randomised study was conducted to directly compare the efficacy of Suprasorb X+PHMB against another PHMB-containing product (Prontosan®; B. Braun) in the eradication of MRSA (Wild et al, 2009).

Thirty patients with MRSA-colonised pressure ulcers were randomly assigned to either treatment with a PHMB solution (Prontosan) and cotton dressings or Suprasorb X+PHMB. Wound assessments and microbiological swabs were taken before the start of the study and weekly for two weeks.

The results showed that in the PHMB solution group, six out of 15 patients (40%) were MRSA-free after one week of therapy, and 10 out of 15 were MRSA free by the end of week two.

In the Suprasorb X+PHMB dressing group, 13 out of 15 were MRSA negative at the end of week one ($p < 0.05$) and all were negative by the end of week two ($p < 0.05$). In addition to the antimicrobial activity of Suprasorb X+PHMB, wounds treated with the product demonstrated faster and more prolific production of granulation tissue.

Conclusion

Successful management of bacteria in a wound is a complex issue. The role of bacterial management is therefore of great importance, particularly for those with a compromised immune response.

Topical antimicrobial preparations provide the clinician with a method of reducing bacterial load and so reducing the burden on the individuals' immune system, greatly increasing the opportunity for positive wound healing outcomes.

However, the issue of silver-resistant bacterial strains and

the unknown effects of systemic absorption and accumulation of both silver and iodine have given rise to new concerns over their safety.

PHMB offers the clinician a new wound care modality with a proven track record of clinical efficacy, cost-effectiveness, and most importantly patient safety, which can fit within conceptual frameworks of wound care management such as Wound Bed Preparation and TIME to produce the clinical outcomes we all want for those in our care. Judicial use of this antimicrobial product can enhance care provision.

By carefully combining PHMB with Suprasorb X, a delivery vehicle that is easy to use, and is structured to manage moisture balance, a new approach to the prevention and treatment of infection has emerged. **WE**

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