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CelluDress-PHMB made easy

PRODUCTS FOR PRACTICE

Introduction

Polyhexamethylene biguanide (PHMB) is a synthetic compound with a broad-spectrum antimicrobial action. PHMB works by disrupting microbial cell membranes and metabolism, interfering with function and, ultimately, destroying the microbial cell. Due to its mechanism of action, development of resistance is unlikely. PHMB has been used in wound care products for some time and has demonstrated reductions in wound pain, odour and slough. This Made Easy looks at the role of PHMB as a topical antiseptic and focuses on a new absorbent dressing, CelluDress-PHMB, for the management of infected wounds or those at risk of infection.

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WHAT IS PHMB?

Polyhexamethylene biguanide (PHMB) is a synthetic antiseptic agent that has been used for over 60 years in a wide range of applications. PHMB is chemically stable, has very low toxicity and has been found to be safe. It is one of a group of cationic (positively-charged) biocides known as biguanides. The other notable member of this group is chlorhexidine.

PHMB is a linear polymer with a hydrophobic backbone and multiple cationic groupings separated by hexamethylene chains (Gilbert and Moore, 2005). This chemical structure, consisting of three chemical groupings (an ammonium end group, a central biguanide group and a cyanoguanide end group), creates the antimicrobial activity. The biguanide group is the active part and PHMB has a high efficacy over a wide range of microorganisms.

PHMB has been incorporated into a range of wound care products in a variety of formats. It has been available as a wound irrigation solution in Europe and international markets for some time. More recently, it has been used successfully within wound dressing materials that are capable of donating PHMB to the wound surface (Wounds UK, 2010).

BOX 1: PHMB is also known as:

- Polyhexamethylene biguanide hydrochloride
- Polyhexamethylene guanide
- Polymeric biguanide hydrochloride
- Polyhexanide

HOW DOES PHMB WORK?

The outer surface of a bacterial cell carries an overall negative charge. This helps the positively-charged PHMB molecules to bind to the surface molecules of the bacterial cells. PHMB also attaches to negatively-charged acidic phospholipids in the bacterial cytoplasmic membrane. Neutral membranes in human cells are only marginally affected (Ikeda et al, 1983). PHMB interacts with the acidic membrane lipids to cause areas of disruption, resulting in loss of function, leakage of potassium and cellular components and rapid lysis of the cell (Broxton et al, 1984; Ikeda et al, 1984).

Attachment of PHMB tends to become concentrated around points of increased density of negative charge within the membrane (Ikeda et al, 1984). It is known that integrated proteins can create such areas within the membrane and therefore the initial interactions of PHMB and the membrane will be concentrated around such proteins. This leads to a loss of their function through changes in the boundary phospholipid (Gilbert and Moore, 2005). Therefore, differences within the cell membrane of different bacteria could account for differences in susceptibility to PHMB.

The basic molecular chain of PHMB can be repeated 2–30 times, with increasing polymer chain length correlating with increasing antimicrobial efficacy (Wounds UK, 2010).

RANGE OF ACTIVITY OF PHMB

PHMB is fast acting at high concentrations. It has a broad spectrum of activity against both Gram-positive and Gram-negative bacteria (Gilbert and Moore, 2005), viruses (Valluri et al, 1997) and some reported activity against parasites, especially *Acanthamoeba* (Kim et al, 1999). It retains activity in hard water and is stable over a wide pH range. It is not effective against spores.

PHMB is bacteriostatic (prevents bacteria from growing or reproducing) at low concentrations (1–32mg/l), but bactericidal (kills bacteria) at higher concentrations (8–208mg/l) depending upon the microorganism tested (Moore et al, 2008). Laboratory studies have demonstrated that PHMB is effective against wound-colonising bacteria including methicillin-resistant *Staphylococcus aureus* (MRSA) (Kirker et al, 2009).

There are no documented reports of acquired resistance to PHMB and this is unlikely to develop because of its mode of action (Gilbert and McBain, 2001).

EVIDENCE OF EFFICACY

The efficacy of PHMB has been studied in randomised control trials (Fabry et al, 2006; Sibbald et al, 2011) and case studies (Mueller and Krebsbach, 2008). PHMB has eradicated pathogens, including MRSA, from skin and wounds and has also been shown to reduce persistent pain and pain experienced during dressing change (Galitz et al, 2009; Sibbald et al, 2011).

In the laboratory, efficacy can depend on test conditions and the strains tested, especially with respect to viruses. For example, PHMB has been shown to be active against herpes virus *in vitro* but not *in vivo* (Valluri et al, 1997). Such results can be explained in part by soiling (fluid) rather than lack of virus activity.

Temperature might also play a key role in enhancing the efficacy of PHMB, because it helps disperse virus particles, as shown by light scattering, and possibly increasing virus susceptibility because of structural changes (Pinto et al, 2010). The length of the alkyl chain might affect efficacy although the reasons are unclear (Kim et al 1999).

PHMB has demonstrated reductions in wound pain (Galitz et al, 2009; Sibbald et al, 2011), odour (Daeschlein et al, 2007) and slough (Mueller and Krebsbach, 2008).

DOES PHMB HAVE A ROLE IN BIOFILM MANAGEMENT?

Biofilms are complex polymicrobial communities embedded in an extracellular matrix made of excreted sugars and proteins (Phillips et al, 2010). This matrix acts as a barrier, protecting microorganisms from the external environment and immune defences. Biofilms are not visible to the naked eye but can be visualised by microscopy and have been demonstrated in wound biopsies from chronic wounds (James et al, 2008). They can delay wound healing (Phillips et al, 2010).

Many biofilm-associated infections do not respond to antibiotic treatment. Comparison of planktonic (free floating) and sessile strains of *S. aureus* has found that *S. aureus* biofilms can be up to 1000 times more resistant than planktonic cells (Das et al, 1998; Ceri et al, 1999).

Disruption by debridement (Bowling et al, 2009) followed by application of topical antiseptics has been shown to be effective in the laboratory (Wolcott et al, 2009; Wolcott et al, 2010). However, multiple strategies are required to continually suppress biofilm reformation (Wolcott et al, 2009). To persist as a biofilm, the organisms need to communicate with each other. They do this by secreting molecules known as quorum-sensing molecules; these molecules are involved in cell-to-cell signalling, allowing the biofilm to respond and adapt to changes in the environment (McClean et al, 1997; Phillips et al, 2010).

ROLE OF ANTIMICROBIAL DRESSINGS

In recent years, topical antimicrobial agents have become the first line of treatment in managing wound bioburden, particularly in chronic wounds (Cooper, 2004). Once the need for topical antimicrobial dressings has been identified, it is important to select a product that provides optimum conditions to support healing. Choose specific products to reflect the overall treatment requirements of the wound following comprehensive wound assessment. Current opinion suggests that the ideal properties of an antimicrobial dressing include:

- Clinical evidence of broad range of antimicrobial efficacy, including resistant strains
- Low cytotoxicity
- Rapid, but sustained, activity
- Assists in wound bed preparation (eg exudate management)
- Conforms to site and shape of the wound
- Reduces malodour/pain
- Easy to use
- Cost-effective (Vowden et al, 2011).

WHAT IS CELLUDRESS-PHMB?

CelluDress-PHMB is a sterile moist wound dressing impregnated with a PHMB Antimicrobial Complex. The dressing has a three-layer structure. The outer layer (on either side) is non-adherent to prevent adherence to the wound and aid patient comfort. The middle layer of the dressing structure is designed to function as a 'reservoir' for the antimicrobial solution as well as an 'absorption layer' for the bacterial and fungal pathogens in the wound.

HOW DOES CELLUDRESS-PHMB WORK?

The dressing acts as a carrier for antimicrobial activity. It protects against the development of wound infection by absorbing and binding to the negatively-charged microorganisms, decreasing the bacterial load in the dressing and preventing bacterial growth in the wound bed.

WHEN IS CELLUDRESS-PHMB INDICATED?

CelluDress-PHMB can be considered for the treatment of acute and chronic wounds at risk of infection, with low to moderate exudate. It can be used on wounds at different stages of healing to promote granulation, while providing antimicrobial protection and effective exudate management. It can be also be used under compression. Wound types include:

- Postoperative wounds
- First- and second-degree burns
- Chronic leg ulcers (venous, arterial and mixed)
- Diabetic foot ulcers
- Pressure ulcers (Category I and II).

Contraindications and precautions:

- CelluDress-PHMB can only be used on skin wounds or mucosal membranes
- CelluDress-PHMB should not be used where there is known hypersensitivity to one of the ingredients or where bone

tissue is exposed or where there is cartilage damage
- CelluDress-PHMB should be used only on babies and pregnant women after consultation with the lead clinician.

HOW TO APPLY CELLUDRESS-PHMB

CelluDress-PHMB is easy to use and can be applied to superficial or deep wounds as follows:

1. Clean and prepare the wound according to local protocols.
2. Tear the aluminium sachet to remove the CelluDress-PHMB dressing. The dressing can be cut to the size of the wound using sterile scissors.
3. Place the dressing on the wound and press down gently to ensure the best possible contact with the wound bed. For deep wounds loosely pack a piece of dressing into the wound.
4. CelluDress-PHMB is suitable for use on both sides. It is not self-adhesive and must be fixed in place using adhesive tape or retention bandage. A non-adherent absorbent secondary dressing can be used to manage wounds with higher levels of exudate. A superabsorbent dressing, which can lead to faster drying of the dressing, is not recommended.
5. The dressing can be changed as required but should not remain on the wound for longer than three days. Daily changing is recommended for infected wounds.
6. For dry wounds, applying a hydrogel as a secondary dressing is recommended to rehydrate the wound.

WHEN TO DISCONTINUE CELLUDRESS-PHMB?

The safety, due to low toxicity and the excellent tissue compatibility of PHMB, allows application over a long period of time providing the required number of dressing changes are applied. It is important to reassess the suitability of the dressing at each dressing change, with continuation of the dressing decided on an individual basis. Where there is suspicion of deep or spreading infection, initiate systemic antibiotic therapy.

Case reports: Using CelluDress-PHMB in patients with chronic wounds at risk of infection

Patient 1:

A 72-year-old-female had a seven-year history of recurrent venous ulceration. Her current wound had been present for 1.5 years and was located on the left leg gaiter area. She had osteoarthritis in both knees and had suffered back pain since 1970.

On presentation, the wound measured 5.6cm x 2.6cm. The wound did not show clinical signs of infection, although an increased bioburden was suspected. Due to a history of repeated infection, it was decided to treat the wound with CelluDress-PHMB with twice-weekly dressing changes. A non-adherent dressing was used as a secondary cover.

At review one week later, the wound showed signs of improvement, with increased granulation tissue and islands of epithelialisation present. CelluDress-PHMB was continued for a further week, with twice-weekly dressing changes.

At week 2, the wound had reduced in size to 4.8cm x 1.2cm and there were signs of healing, including 80% granulation tissue in the wound bed. The patient remained infection-free and she requested to continue with CelluDress-PHMB and twice-weekly dressing changes.

At week 3, there was 95% granulation in the wound bed and oedema had reduced. It was decided to continue the CelluDress-PHMB dressing as there was a history of recurrent infection when not using a topical antimicrobial. The clinical staff were satisfied with the overall performance of the dressing, which was easy to apply and could be cut to size.

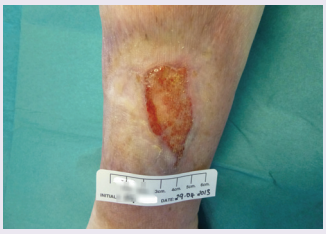

Figure 1: Wound prior to start of treatment with CelluDress-PHMB

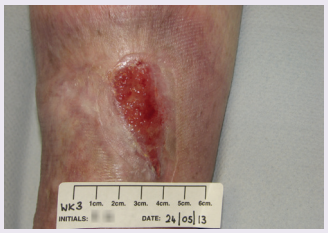

Figure 2: Week 3. CelluDress-PHMB was continued with twice-weekly changes.

Patient 2:

This was a 65-year-old female with a venous leg ulcer, which had occurred four years previously due to an initial traumatic injury. The wound measured 6.4cm x 4.9cm and was located on the left medial malleolus. She had a history of scleroderma and Raynaud's disease since 2004.

On presentation, the wound did not show clinical signs of infection, but was critically colonised. The patient had a pain score of 4 (on a visual analogue scale of 0–10). Due to recurrent infections, it was decided to treat the wound with CelluDress-PHMB and twice-weekly dressing changes. A non-adherent dressing was applied as a secondary dressing.

At review one week later, the patient reported a pain score of 8 on dressing removal. The exudate levels were slight and there was evidence of 25–50% granulation tissue in the wound bed with a reduction in the wound size (4.1cm x 5.5cm). CelluDress-PHMB was continued, but the dressing change frequency was increased to daily to prevent adherence of the dressing to the wound bed.

At week 2, the patient reported a pain score of 5 on dressing removal. The amount of granulation tissue had increased and exudate levels were moderate. It was decided to continue with CelluDress-PHMB and daily dressing changes.

At final review (week 7), the signs of infection were reduced with a decrease in exudate level. The patient did not report any pain at dressing changes. The wound bed consisted of 50–75% granulation tissue and looked healthier. As the dressing needed to be changed daily, the decision was made to change to a non-adherent dressing that did not contain an antiseptic agent. The patient was very experienced in looking after her wound and was happy to apply CelluDress-PHMB if required.

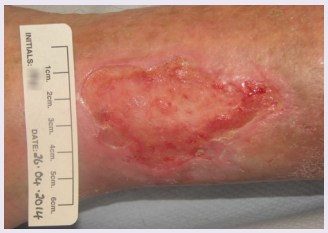

Figure 1: Week 3. Patient continued with daily dressing changes to prevent dressing adherence.

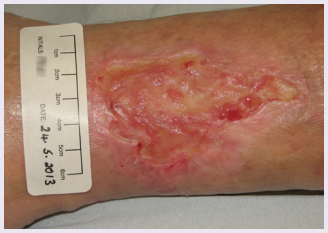

Figure 2: Week 7. Exudate had reduced and the wound bed appeared healthier.

BENEFITS OF USING PHMB-IMPREGNATED DRESSINGS

- Provides an alternative antiseptic agent to silver, honey or iodine (Vowden et al, 2011)
- Offers broad-spectrum antimicrobial activity in both acute and chronic wounds (Lee et al, 2004)
- Reduces wound pain/malodour (Daeschlein et al, 2007; Galitz et al, 2009)
- Increases formation of granulation tissue (Mueller and Krebsbach, 2008)
- Reduces slough in the wound bed (Mueller and Krebsbach, 2008).

The above benefits have led to the recommendation in many European countries that PHMB be used as the primary antimicrobial (Dissemond et al, 2010), and it appears to meet many of the criteria for an ideal antimicrobial agent. Research and testing have demonstrated that PHMB has a good safety record, has low toxicity to human tissue and is effective in reducing bacterial load. PHMB is now widely used in the UK and has been shown to be an effective option for managing wounds at risk of infection and infected wounds (Wounds UK, 2010).

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