TECHNOLOGY UPDATE:

Understanding the role of PHMB: a topical approach to wound infection

The practice of wound cleansing has become a basic principle in modern wound management, where it forms part of the process of wound bed preparation. Cleansing, debridement and disinfection help to reduce bacterial load in the wound and gently remove debris and exudate to prepare the wound bed for closure. This article focuses on the use of polyhexamethylene biguanide (polihexanide, PHMB) in combination with advanced wound dressings as a topical approach to wound cleansing and disinfection.

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Page points

1. *Wound bed preparation is aimed at preparing the wound bed to promote healing using various tools such as debridement, cleansing and wound disinfection*
2. *PHMB can be used as a topical approach to wound cleansing and disinfection*

INTRODUCTION

The number of patients with chronic wounds is increasing rapidly due to an ageing population. This has a considerable impact on diagnostic, therapeutic and socio-economic resources. To support wound healing in these secondary healing wounds, both systemic and local factors need to be addressed[1-3]. Antiseptics can provide a useful alternative to antibiotics, are easy to use and widely available. Topical antiseptic agents in common use in wound dressings include silver, iodine and honey. In addition, PHMB has been widely used in Europe and in the US, although is a relative newcomer to the UK market

TOPICAL ANTISEPTICS FOR WOUND INFECTION

Most open chronic wounds will be heavily colonised with bacterial or fungal organisms[3]. Infection can cause a delay or failure in wound closure if not treated promptly using good hygiene, debridement and wound cleansing. When the problems caused by bacteria remain localised to a wound (critical colonisation), treatment with topical antiseptics may be indicated and is usually sufficient[4].

When providing a topical approach to treatment, it is important to differentiate between inflammation, increased bacterial burden, and superficial and deep infection[1,2]. Microbiological management is aimed at achieving an optimal organism loading within the wound that does not only focus on infected wounds, but also on critically colonised (locally infected) and non-healing wounds[1-3].

The presence of bacteria in a wound does not necessarily impede wound healing. This is dependent on the quantity and pathogenicity as well as patient immunity (host response)[1]. Bacteria may stimulate a persisting inflammation, which can lead to the production of inflammatory mediators and proteolytic enzymes, extracellular matrix (ECM) degradation and inhibition of re-epithelialisation[2]. Controlling the bacterial burden will therefore facilitate wound healing.

Contaminated trauma wounds as well as stagnating wounds and those that show general signs and symptoms of clinically manifest infection can be treated using topical antiseptics for the following reasons:

- **Colonised wounds have the potential to develop infection, which can cause a delay or a failure in wound closure**
- **Infection may spread and, in some cases, leads to sepsis**
- **Colonisation or infection caused by multi-resistant pathogens (for example, Methicillin-resistant *Staphylococcus aureus*; MRSA) should be treated to prevent spreading of the infection.**

STRATEGIES FOR MICROBIAL MANAGEMENT

Topical agents are used primarily when there are local signs of infection and when a wound is not healing[4]. Systemic agents such as antibiotics are used when clinical signs of infection are present such as spreading cellulitis. A further distinction is made between

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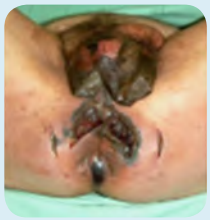
CLASSIFICATION	DESCRIPTION	TREATMENT
Primary wound Infection 	Trauma wounds (bites, traffic injuries, stab wounds) surface micro-organisms can migrate into the deeper tissues	Antiseptic prophylaxis
Secondary wound Infection 	▪ Infection developing in an existing wound: ▪ Localised infection ▪ Systemic infection ▪ Life-threatening infections, such as streptococci in acute necrotising fasciitis	▪ Antiseptics ▪ Antibiotics ▪ Surgical intervention

Figure 1 – Primary and secondary wound infection

primary and secondary infection[1,5] *(Fig 1)*. When a wound infection is detected, the following principles apply:

- **Localised infections should be treated with antiseptics**
- **Wound infections that exhibit signs of spreading or systemic infection as well as sepsis should be treated with systemic antibiotics in combination with an appropriate antiseptic agent.**

Exceptions to these principles include specific cases where a rapid life-threatening systemic infection is suspected, for example, *Staphylococci* infections of the drainage area of central veins and lymph vessels leading to the central nervous system; or *Streptococci* infections resulting in acute necrotising fasciitis. Such infections must always be treated early with high doses of systemic antibiotics and topical antiseptics. In all cases, surgical intervention, eg radical debridement, is likely to be the primary treatment[5].

An antiseptic wound care regimen should only be commenced after careful assessment and identification of the infecting organism. In addition, clinicians need to have a clear rationale for choosing a particular antiseptic agent[3,5]. In cases of contamination, colonisation or infection, the aim is to reduce or eliminate pathogens from the wound to support rapid wound healing[4]. When choosing an antimicrobial agent, the clinician should consider various criteria, including the agent's safety and antimicrobial efficacy based on objective (*in vivo*) and subjective (*in vitro*) tissue tolerance and lack of systemic side effects[3,5,6]. Other factors include availability, ease of use, cost and familiarity with the product[4].

POLYHEXANIDE (PHMB): MODE OF ACTION

PHMB is a positively charged (cationic) polymer, which works against negatively charged micro-organisms and can be used for the treatment of local infections. It contains a surface-active substance (surfactant – a wetting agent that lowers the surface tension of a liquid), which can penetrate difficult coatings (slough, biofilms, etc) to stimulate wound healing[5-6]. Surface tension is the property of a liquid surface that acts like a stretched elastic membrane. The proposed mechanism of action of PHMB is based on its low surface tension, which supports the physical removal of debris and bacteria from the wound bed[6,8]. In addition, its antimicrobial properties facilitate a reduction in microbial loads[9]. These properties mean that PHMB is ideal for use in the treatment of wounds[9-12].

PHMB has a broad spectrum of activity against Gram-positive and Gram-negative bacteria, fungi and biofilms[6-8] and can be applied over a long period of time due to its low toxicity[9]. PHMB has good tissue compatibility based on its activity against the acid lipids contained within the bacterial cell membranes

Page points

1. *The basic therapeutic principle for contaminated or infected wounds is to use local treatments for local infections and adequate systemic treatment for systemic infections*
2. *Systemic treatment may be combined with local measures using appropriate antimicrobial substances*

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and minor effect on the neutral lipids of human cell membranes. This helps to prevent damage to the surrounding healthy tissue[6,8].

PHMB has demonstrated efficacy in the management of non-healing chronic and/or refractory wounds (eg second degree burns), as well as for lavages[9-12]. Povidone (PVP)-iodine and octenidine-based antiseptics (the later is currently being used increasingly in continental Europe) have been shown to be comparable to one another[5,13]. Different antiseptic agents have individual properties, strengths and weaknesses. For example, PVP-iodine is effective against bacteria, fungi, viruses, mycoplasms and spores. Octenidine has a slower onset than PVP-iodine and is not effective against viruses and spores[5]. The microbiocidal activity of PHMB, depending on the pathogen and concentration of the agent, is slower in comparison to, for instance, iodophores[6,10,11].

Antiseptic agents with a microbiocidal effect such as iodophors, octenidine and PHMB are reported to be more effective than topical antibiotics[5,13]. In addition, antiseptics are less likely to cause allergic reactions, sensitisation or resistance[4]. In contrast to iodophors, PHMB provides an effective concentration in the wound with a low risk of systemic side effects[5,6].

WOUND CLEANSING AND DISINFECTION USING PHMB

A wide variety of pharmaceuticals and medical devices containing PHMB are available in various formulations, each with different characteristics and applications.

Local antiseptic treatment is usually for a period of 2-5 days and should not exceed 14-21 days. If the signs of infection do not improve or resolve during this time, the efficiency of the approach should be investigated. In colonised wounds with fibrin layers, the use of wound antiseptics such as PHMB should be complemented with other treatment approaches such as debridement[9]. For wound disinfection and antisepsis, PHMB solutions are commonly used at concentrations of 0.01%, 0.02% or 0.04%. The solution should be used only for local applications, eg for rinsing (lavage), rinse/suction drainage, as a liquid combination with ultrasound or combined with moist wound dressings.

As PHMB has a slow onset of action and the individual microorganisms respond to the agent with different levels of sensitivity over time, it is important to allow a minimum exposure time of 10–15 minutes after the wound bed has been well moistened[3,5]. For therapeutic antisepsis in acute, contaminated, severely purulent and clinically infected chronic wounds, PHMB is used as a 0.04% solution. For application in suction/rinse drainage or in combination with the application of medical devices such as ultrasound, a 0.02% solution is used and for intra-operative wound contamination a 0.01% PHMB solution is applied[5].

For infection prophylaxis in critically colonised (locally infected) chronic wounds a 0.01–0.2% PHMB solution or wound dressings containing PHMB may be applied. Prophylaxis should follow clear indications and targets with specific timelines. Long-term routine use of antiseptics is not recommended[9,10].

PHMB is available as a pharmaceutical raw material for the manufacturing of pharmacy-prepared solutions for wound antisepsis[9,11,12]. It may be combined with a dry wound dressing to allow for continued wound cleansing during application[5,9]. Due to tissue compatibility and the absence of irritation, application under semi-occlusive and occlusive dressings is also possible[9]. When used in combination with an advanced biocellulose dressing, it has been shown to reduce microbial load and complications such as sepsis or systemic infection[14].

CONCLUSION

PHMB is an antimicrobial substance that is indicated for use in critically colonised (locally infected) or infected acute and chronic wounds. It has a broad antimicrobial spectrum and good cell and tissue compatibility. If combined with an advanced wound healing dressing, PHMB can also manage exudate to optimise the wound environment for healing.

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Conflict of interest: *Both authors conducted studies in wound healing that were supported with a scientific grant from Lohmann & Rauscher.*

Page points

1. *Different antiseptic agents have individual properties, strengths and weaknesses*
2. *A wide variety of pharmaceuticals and medical devices containing PHMB are available. PHMB solutions are used for local applications only*
3. *Advanced wound care dressings with PHMB can be used for locally infected or infected wounds for continued wound cleansing*

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Expert Commentary

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What are the advantages of PHMB?

The global threat of antibiotic resistance must be met – and probably by the more active use of antiseptic treatments for wounds. A more liberal attitude towards local antiseptics in wounds is reflected in the recent international consensus document regarding wound infections[1].

Polyhexamethylene biguanide (PHMB, polihexanide) is an antiseptic that is currently attracting interest from woundcare professionals, although it has a long history of being used in cosmetics, for example in contact lens cleaning solutions, wet wipes, and so on.

PHMB is available both as a cleansing solution (Prontosan®, B. Braun) and in biocellulose dressings such as Suprasorb® X+PHMB (Lohmann and Rauscher). In a concentration of 0.3% (for example in Suprasorb® X+PHMB) and of 0.1% (for example in Prontosan®), PHMB has proved to be non-cytotoxic and non-irritant, with a very low risk of sensitisation[2-4]*. Because of its high molecular weight, PHMB has a poor bioavailability*[2,3]*. PHMB has been found to be effective against a broad spectrum of bacteria, aerobic as well as anaerobic, and also against fungi, moulds and yeasts, and has a proven effect against methicillin-resistant* Staphylococcus aureus *(MRSA) and vancomycin-resistant enterococcus (VRE)*[2-6].

Tests have been performed on S. aureus *to investigate the potential risks of this bacterium developing resistance to PHMB; the risk was found to be very low. An additional positive influence on the inflammatory process of wound healing – especially in infected or critically colonised wounds – has been the binding of inflammatory parameters such as free radicals, showing its antioxidative potential*[7]*. The clinical effect of using PHMB in some non-healing wounds has been promising*[8].

When should a clinician consider using PHMB?
PHMB should be considered whenever there is a need for the safe and effective treatment of infected or critically colonised wounds and when chronic wounds have stopped healing or are enlarging. PHMB biocellulose dressings can be used in slightly or moderately exuding wounds, both in deep and superficial wounds.

Examples of wound types that can be considered for treatment with PHMB include:

- ***Second-degree burns***
- ***Post-surgical wounds***
- ***Traumatic wounds***
- ***Donor/recipient sites***
- ***Leg ulcers***
- ***Pressure ulcers***
- ***Epidermolysis bullosa and scleroderma wounds.***

Top tips for practitioners

- ***If used as a cleansing solution or gel, allow the solution to stay* in situ *for a few minutes to allow it to influence potential biofilm formation.***
- ***Use a biocellulose rope for small cavities.***
- ***Never let the dressing dry out when used on slightly exuding wounds. If a secondary dressing is used, this must allow moisture to be kept at the wound surface.***

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