WHAM evidence summary: Polyhexamethylene biguanide for chronic wounds

Emily Haesler, PhD, P Grad Dip Adv Nurs (Gerontics), BN, Fellow Wounds Australia

1. Adjunct Professor, Curtin Health Innovation Research Institute, Wound Healing and Management (WHAM) Collaborative, Curtin University, Perth, Australia
2. Adjunct Associate Professor, Australian Centre for Evidence Based Aged Care, La Trobe University, Melbourne, Australia
3. Honorary Senior Lecturer, Australian National University Medical School, Australian National University, Canberra, Australia

CLINICAL QUESTION

What is the best available evidence for using polyhexamethylene biguanide (PHMB) to reduce infection and promote healing in chronic wounds in all populations?

SUMMARY

Polyhexamethylene biguanide is an antiseptic available as solution, gel or impregnated in wound dressings. Level 5 bench research indicates that PHMB products have broad-spectrum antimicrobial activity against gram positive and negative bacteria (including biofilms), methicillin-resistant Staphylococcus aureus (MRSA), fungus and viruses. Level 1 and 2 evidence reports mixed findings on the effectiveness of PHMB in delivering significant reduction in bacterial load in chronic wounds, with some studies reporting superiority compared to control cleansers and others finding no statistically significant differences. However, this evidence is generally of low quality. Level 5 expert opinion supports the use of PHMB in combination with debridement for managing infection, particularly biofilm. Level 1, Level 3 and Level 4 evidence indicates PHMB is associated with improvements in wound healing outcomes, reduction in wound pain, and management of wound odour.

CLINICAL PRACTICE RECOMMENDATIONS

All recommendations should be applied with consideration to the wound, the person, the health professional and the clinical context.

Polyhexamethylene biguanide (PHMB) can be used to reduce local infection and promote healing in chronic wounds (Grade B).

SOURCES OF EVIDENCE

This summary was conducted using methods published by the Joanna Briggs Institute. The summary is based on a literature search combining search terms related to PHMB and wounds. Only studies that reported on the use of PHMB for a chronic wound were included in the clinical evidence summary. Searches were conducted in CINAHL, Medline, the Cochrane Library and Google Scholar for evidence published up to December 2019 in English. Levels of evidence for intervention studies are reported in Table 1.

Table 1: Sources of evidence and the level

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<thead>
<tr>
<th>Level 1 Evidence</th>
<th>Level 2 Evidence</th>
<th>Level 3 Evidence</th>
<th>Level 4 Evidence</th>
<th>Level 5 Evidence</th>
</tr>
</thead>
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<tr>
<td>1.a Systematic review of RCTs</td>
<td>Level 2.c Quasi-experimental prospectively controlled study</td>
<td>Level 3.e Observational study without a control group</td>
<td>4.c Case series</td>
<td>5.c Bench research</td>
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<td>1.b Systematic review of RCTs and other study designs</td>
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<td>4.d Case studies</td>
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<td>1.c RCT</td>
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<td>5.a Systematic review of expert opinion</td>
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<td>5.b Expert consensus</td>
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<td>5.c Bench research and single expert opinion</td>
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BACKGROUND
Polyhexamethylene biguanide is an antiseptic, that has a chemical structure similar to naturally occurring antimicrobial peptides (AMPs).26, 27

A systematic review (SR) 1 of bench research included nine in vitro studies that reported on the antibacterial qualities of PHMB. This review found PHMB is effective in reducing non-specified strains of biofilm, with an average performance superior to silver but inferior to iodine1 (Level 5). Additional studies have demonstrated that PHMB-impregnated wound dressings and PHMB solutions are effective against gram positive and gram negative bacteria (including MRSA), fungus and viruses in laboratory settings.2-5, 8 (Level 5). Effect against confirmed biofilm has also been demonstrated in vitro6 (Level 5).

CLINICAL EVIDENCE

Reduction in local infection
In a SR10 that included six (primarily low quality) randomised controlled trials (RCTs),26-33 treatment of chronic wounds with PHMB dressings was associated with more substantial reduction in bacterial count (two studies), reduction in types of bacteria in the wound (two studies) and reduction in specific strains of bacteria (two studies), including Pseudomonas aeruginosa, Enterobacter cloacae and Staphylococcus aureus.10 The comparators included non-antimicrobial gauze, sponge and foam dressings, polihexadine impregnated cotton swab and a silver dressing10 (Level 1).

In an RCT conducted in venous leg ulcers (VLUs, n= 27 analysed) that had biofilm presence confirmed by microscopy, cleansing with a PHMB-iodine solution statistically significantly reduced overall bacterial count compared to baseline, but this was not significantly different from saline cleansing (p > 0.05). There was a statistically significantly greater reduction in bacterial count in relation to wound size in the PHMB-iodine group (p = 0.07)11 (Level 1).

In chronic wounds with clinical signs of local infection (n = 31), one group received 0.5% PHMB for cleansing and as a gauze-soaked dressing, and a comparator group received the same regimen using Ringer’s solution. After daily treatment for three weeks, there was no statistically significant between-group difference in percent of wound tissue cultures that were negative (47.4% PHMB versus 52.6% Ringer’s solution, p=0.886). However, individuals receiving the PHMB regimen had statistically significant superior reductions in C-reactive protein (CRP) and white blood cell count (WBC)12 (Level 2).

Improvement in wound healing outcomes
In a SR10 that included six RCTs,28-33 treatment of chronic wounds with PHMB dressings was superior to comparator for complete wound healing in only one study. One of the RCTs also noted PHMB to be associated with improved granulation.10 Comparators are reported above (Level 1).

In chronic wounds with clinical signs of local infection (n = 31), treatment with 0.5% PHMB solution daily for three weeks showed no statistically significant between-group difference in percent of wounds reaching full closure compared with Ringer’s solution (66.7% PHMB versus 43.8% Ringer’s solution, p=0.181)12 (Level 2).

In non-healing wounds (n=16), treatment with a biocellulose dressing impregnated with 0.3% PHMB solution for 2-3 weeks (length determined by visual condition of the wound) was associated with improved condition. At 24 weeks, granulation tissue had significantly increased (38.2 ± 34.6% versus 77.4 ± 36.0%, p < 0.04), slough had significantly decreased, and 75% of wounds had completely healed15 (Level 3).

Improved wound healing with PHMB products has been reported in case studies. Case studies reporting use of 0.5% PHMB impregnated dressings demonstrated decrease in wound size for VLUs (n = 5) treated for up to seven weeks,16 complete wound healing within six weeks for diabetic ulcers (n = 5)17 and reduction in wound size for lower leg ulcers (n = 5) treated for three weeks.17 Improvements were also reported for lower leg ulcers receiving (n = 4) receiving PHMB solution in combination with ultrasonic debridement.18 (all Level 4).

CONSIDERATIONS FOR USE
The following points could be considered when using PHMB:

- A PHMB topical solution alone is unlikely to eradicate biofilm in a chronic wound.7 Although bench research has established the effectiveness of PHMB in vitro,6 it has been demonstrated that in vitro biofilm modelling fails to account for clinical realities (e.g. time the solution spends in contact with the tissue).7 Combining topical antimicrobials with debridement is recommended for biofilm management in chronic wounds13 (Level 5) and has been demonstrated in a
small case series combining use of topical PHMB with ultrasonic debridement\(^8\) (Level 4).

- A PHMB product might help manage wound pain. In a SR,\(^9\) treatment with PHMB dressings was associated with statistically significantly greater reductions in patient-reported pain (two studies), compared with a non-antimicrobial foam and a silver dressing\(^10\) (Level 1). However, an additional RCT (\(n = 24\)) found the pain reduction associated with 0.2% PHMB solution was not significantly different from that achieved with 0.8% metronidazole solution\(^14\) (Level 1).

- A PHMB solution might reduce wound odour. An RCT (\(n = 24\)) found that wound odour statistically significantly reduced after four days of treatment with 0.2% PHMB solution. This was not significantly different from 0.8% metronidazole solution\(^14\) (Level 1). A case series conducted in wounds with clinical signs of local infection (\(n = 25\)) also reported reduction in odour in 100% of wounds treated with 0.5% PHMB solution\(^19\) (Level 4).

- Three of the RCTs,\(^28, 30, 32\) included in a SR,\(^10\) reported no adverse effects associated with PHMB (Level 1). A safety review concurred that studies have reported minor or no adverse events; however, the review noted the lack of good quality, sufficiently large trials\(^23\) (Level 1). Caution has been recommended for use in wounds with exposed bone and cartilage due to PHMB's cytotoxicity on cartilage and suppression of PHMB action by joint/nasal cavity fluid\(^9, 25\) (Level 5).

CONFLICTS OF INTEREST

The author declares no conflicts of interest in accordance with International Committee of Medical Journal Editors (ICMJE) standards.

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ABOUT WHAM EVIDENCE SUMMARIES

WHAM evidence summaries are consistent with methodology published in


Methods are provided in detail in resources published by the Joanna Briggs Institute as cited in this evidence summary. WHAM evidence summaries undergo peer-review by an international review panel. More information on the website: [http://WHAMwounds.com](http://WHAMwounds.com).

WHAM evidence summaries provide a summary of the best available evidence on specific topics and make suggestions that can be used to inform clinical practice. Evidence contained within this summary should be evaluated by appropriately trained professionals with expertise in wound prevention and management, and the evidence should be considered in the context of the individual, the professional, the clinical setting and other relevant clinical information.

**PUBLICATION**

This evidence summary has been published in Wound Practice and Research:


**REFERENCES**


24. Bowen G, Spruce P. An evaluation of a foam dressing impregnated with 0.5% polyhexamethylene biguadine (PHMB) within the care pathway of the diabetic foot ulcer. UK: Wounds UK; 2009.


34. Bowen G, Spruce P. An evaluation of a foam dressing impregnated with 0.5% polyhexamethylene biguadine (PHMB) within the care pathway of the diabetic foot ulcer. UK: Wounds UK; 2009.