Effectiveness of polyhexamethylene biguanide impregnated dressing in wound healing: a systematic review protocol

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Review question/objective: The objective of this review is to review and synthesize evidence on the effectiveness of polyhexamethylene biguanide (PHMB) impregnated dressing in wound treatment for patients with chronic or acute wounds, compared with standard dressings or any other antimicrobial dressings. Specifically the questions for this review are:

- Does PHMB impregnated dressing improve healing in chronic and acute wounds?
- Does PHMB impregnated dressing or the comparator reduce infection rates in chronic and acute wounds?
- Does PHMB impregnated dressing or the comparator reduce the production of exudate in chronic and acute wounds?

Keywords Heal; iodine; polyhexamethylene; silver; wounds

Background

Wounds occur on any part of the body that is exposed to trauma or surgery. Acute wounds are wounds that heal according to a normal healing process within a specific time frame. From acute wounds, it may become chronic when the wound healing process prolongs. When the skin and underlying tissues are injured, the natural response of the body is to initiate the healing mechanism. Inflammation is the first stage of the healing process.

During this stage, the permeability of the blood vessels increase, allowing fluid and white blood cells (leucocytes, neutrophils, monocytes and macrophages) to migrate into the surrounding tissues. Then, the excess extracellular fluid will be absorbed into the blood and lymphatic system as the inflammation subsides, and the wound healing progresses. However, in a wound with delayed healing, the increased permeability of the capillaries allows more fluid and white blood cells to transit into the wound. 

A favorable condition for wound healing is a moist wound bed, but an excess or over production of the exudate could pose a good medium for bacteria growth and hinder wound healing. The excess exudate has components of dead tissues, cells, bacteria and macrophages. Macrophages engulf bacteria, dead cells and tissues as the wounds heal. If the function of the macrophages is inhibited by colonies of bacteria, the wound may take a longer time to heal. These wounds would then be continuously exposed to bacteria that may cause wounds to further break down with infection, and the healing process is impeded. Acute wounds that are not healed within one month would become chronic wounds. Chronic wounds may produce excessive exudate and biofilm, and require appropriate antibacterial impregnated or gel dressing to reduce and remove biofilm for wound healing.

Chronic wound has a biofilm that may contain multi-strains of bacteria colonies. James et al. found that 60% of 50 chronic wounds and 6% of 17 acute wounds contained biofilm structures. The biofilm protects the bacteria by building a matrix that prevents bacteria from being destroyed. A barrier is formed for preventing tissue from generating new cells to promote wound healing. Therefore, it may be necessary to remove the biofilm to improve wound healing. Topical bactericide agents have been recommended to stop the bacteria from multiplying and to reduce infection of the wounds.
Infected chronic wounds may produce exudate with offensive odor. Friends and relatives may feel that the odor is unbearable when they are near the patients. Because of this, the patients may develop low self-esteem because of the odor, which can affect their quality of life. The patients may go into seclusion, avoiding friends and relatives, and cascade to depression. To reduce the odor and alleviate patients’ suffering, and improve their quality of life, these wounds have to be managed with appropriate dressings and cleansing solutions.

There are several types of wound dressings for wound management. These wound dressings may be impregnated with antimicrobial agents or in the form of donating antimicrobial agents. Silver, silver with charcoal, iodine and honey are common topical agents used for wound dressing. Silver with charcoal seems to have effect on reducing malodor and improve healing at the periwound area. However, an accumulation of silver in the body system may cause patients to have argyria, which turns skin grayish.

Povidone iodine and cadexomer iodine have antimicrobial properties. Cadexomer iodine was found to be effective in promoting epithelialization and reducing exudate in wounds. However, patients experience pain when using cadexomer iodine. Honey has been used as wound dressing for chronic wounds. Shukrimi et al. studied honey and povidone dressings on patients who had Wagner type II leg ulcers and found that honey was able to retain moisture, reduce swellings, decrease exudate and odor, and during the changing of povidone dressing patients expressed increased pain than with honey dressing. Iodine being absorbed in the body system is excreted by the kidney, and patients who have thyroid or kidney problems may have to be monitored, when using iodine product.

Polyhexamethylene biguanide (PHMB) is a synthetic compound that has a similar structure of a broad-spectrum antimicrobial agent. It kills bacteria by binding antimicrobial peptides to the cell membrane causing lysis of the cells. Polyhexamethylene biguanide activity acts on the lipopolysaccharide layer of the bacteria to destroy the cell wall, thereby killing the bacteria. There are different types of PHMB impregnated dressings such as non-adherent gauzes, sponges and biocellulose foam wound dressings. These dressings may have PHMB that are manufactured in various strengths of 0.2, 0.3 and 0.5%. When PHMB dressing was used on chronic and acute wounds, patients experienced reduced pain and increased wound healing rates. It may be attributed to the effectiveness of PHMB in reducing the bacteria colonies by destroying multi-strain bacteria, biofilm and curb infection.

Use of PHMB appears to have low risk of causing allergy and toxicity. PHMB has been used to preserve cosmetics, to clean contact lenses, as mouth wash for oral care, and cleansing solution and dressing for acute and chronic wounds. As there are many studies conducted on various strengths of PHMB-impregnated dressings for chronic and acute wounds, this systematic review aims to determine the effectiveness of different strengths of PHMB to promote wound healing and reduce infection rates. The evidence will be used to inform practice.

Inclusion criteria

Types of participants
The current review will consider studies that include all adult participants who are aged 18 years and above, with chronic or acute wounds. Perineum wounds will be excluded.

Intervention(s)/phenomena of interest
The current review will consider studies that evaluate the application of PHMB-impregnated dressings in various strengths of 0.2, 0.3 and 0.5%, compared with standard dressings or any other antimicrobial dressings.

The current review will compare healing and infection rates, and amount of exudate in acute and chronic wounds that used the followings dressings (may include but not limited to):
- PHMB compared with silver
- PHMB compared with iodine
- PHMB compared with standard dressing
- PHMB compared with regular dressing, and
- PHMB compared with other antimicrobial dressings.

Outcomes
The current review will consider studies that include the following outcomes:
Primary outcome: healing rate
Secondary outcome: infection rate and amount of exudate
The analysis will be carried out according to:
- Nature of the wound (chronic, acute)
- Acute wounds
- Strength of PHMB

Types of studies
The quantitative component of the review will consider randomized controlled trials. In the absence of randomized controlled trials, other relevant study designs such as non-randomized controlled trials, quasi-experimental studies, before and after studies, case control studies and cohort studies will be included.

Search strategy
The search strategy aims at finding both published and unpublished studies. A three-step search strategy will be utilized in this review. An initial limited search of MEDLINE and CINAHL will be undertaken followed by an analysis of the text words contained in the title and abstract, and of the index terms used to describe the article. A second search using all identified keywords and index terms will then be undertaken across all included databases. Third, the reference list of all identified reports and articles will be searched for additional studies. Studies published in English will be considered for inclusion in this review. Studies published from 2006 will be considered for inclusion in this review.

The databases to be searched include
- Cochrane Central Register of Controlled (CENTRAL) Trials
- Scopus
- Web of Science
- MEDLINE
- CINAHL
- EMBASE

The search for unpublished studies will include MedNar. Initial keywords to be used will include wounds, heal, polyhexamethylene, silver and iodine.

Assessment of methodological quality
Papers selected for retrieval will be assessed by two independent reviewers for methodological validity prior to inclusion in the review using standardized critical appraisal instruments from the Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review Instrument (JBI-MAStARI) (Appendix I). Any disagreements that should arise between the reviewers will be resolved through discussion or with a third reviewer.

Data extraction
Quantitative data will be extracted from papers included in the review using the standardized data extraction tool from JBI-MAStARI (Appendix II). The data extracted will include specific details about the interventions, populations, study methods and outcomes of significance to the review question and specific objectives. The authors will contact the primary authors for any missing information or to clarify doubts in unclear data.

Data synthesis
Quantitative data will, where possible, be pooled in statistical meta-analysis using JBI-MAStARI. All results will be subjected to double data entry. Effect sizes expressed as an odds ratio (for categorical data) and weighted mean differences (for continuous data), and their 95% confidence intervals will be calculated for analysis. Heterogeneity will be assessed statistically using the standard chi-square and also explored using subgroup analyses based on chronic and acute wounds, and the different strengths of PHMB will be included in this review. Where statistical pooling is not possible, the findings will be presented in narrative form including tables and figures to aid in data presentation where appropriate.

Acknowledgements
The authors would like to thank Dr Emily Ang, the Director of Singapore National University Hospital JBI Collaborating Center and Evidence-Based Nursing Unit, National University Hospital, for her support, and National University Health System, Medical Publication Support Unit, for assisting us in our publications.

References
Appendix I: Appraisal instruments

**MAStARI appraisal instrument**

**JBI Critical Appraisal Checklist for Randomised Control / Pseudo-randomised Trial**

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<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
<th>Unclear</th>
<th>Not Applicable</th>
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<td>1. Was the assignment to treatment groups truly random?</td>
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<td>2. Were participants blinded to treatment allocation?</td>
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<td>3. Was allocation to treatment groups concealed from the allocator?</td>
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<td>4. Were the outcomes of people who withdrew described and included in the analysis?</td>
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<td>5. Were those assessing outcomes blind to the treatment allocation?</td>
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<td>6. Were the control and treatment groups comparable at entry?</td>
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<td>7. Were groups treated identically other than for the named interventions</td>
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<td>8. Were outcomes measured in the same way for all groups?</td>
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<td>9. Were outcomes measured in a reliable way?</td>
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<td>10. Was appropriate statistical analysis used?</td>
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Overall appraisal: Include ☐ Exclude ☐ Seek further info. ☐

Comments (Including reason for exclusion)

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# JBI Critical Appraisal Checklist for Comparable Cohort/ Case Control

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<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
<th>Unclear</th>
<th>Not Applicable</th>
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<tbody>
<tr>
<td>1. Is sample representative of patients in the population as a whole?</td>
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<td>2. Are the patients at a similar point in the course of their condition/illness?</td>
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<td>3. Has bias been minimised in relation to selection of cases and of controls?</td>
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<td>4. Are confounding factors identified and strategies to deal with them stated?</td>
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<td>5. Are outcomes assessed using objective criteria?</td>
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<td>6. Was follow up carried out over a sufficient time period?</td>
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<td>7. Were the outcomes of people who withdrew described and included in the analysis?</td>
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Overall appraisal: Include [ ] Exclude [ ] Seek further info. [ ]

Comments (Including reason for exclusion)

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Appendix II: Data extraction instruments

MAStARI data extraction instrument

**JBI Data Extraction Form for Experimental / Observational Studies**

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<th>Date</th>
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<tr>
<td>Author</td>
<td>Year</td>
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<tr>
<td>Journal</td>
<td>Record Number</td>
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**Study Method**

- RCT
- Quasi-RCT
- Longitudinal
- Retrospective
- Observational
- Other

**Participants**

<table>
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<tr>
<th>Setting</th>
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<tr>
<td>Population</td>
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**Sample size**

- Group A
- Group B

**Interventions**

- Intervention A
- Intervention B

**Authors Conclusions:**

- 

**Reviewers Conclusions:**

- 

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Study results

### Dichotomous data

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### Continuous data

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