

Effectiveness of polyhexamethylene biguanide on microbial load in patients with wounds: a systematic review

*Eficacia de la polihexametileno biguanida sobre la carga microbiana en pacientes con heridas:
una revisión sistemática*

Efetividade de polihexametileno-biguanida na carga microbiana em pacientes com feridas: revisão sistemática

**Bruna Maiara Barreto Ferreira
Pires^{1*}**

ORCID: 0000-0002-5584-8194

**Beatriz Guitton Renaud Baptista
de Oliveira¹**

ORCID: 0000-0001-7494-7457

Fernanda Soares Pessanha¹

ORCID: 0000-0002-8082-5242

**Priscila Gleice Mariano Garcia
Bayao¹**

ORCID: 0000-0002-3297-7575

¹Universidade Federal
Fluminense. Rio de Janeiro,
Brazil.

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***Corresponding author:**

bruna_barreto@id.uff.br

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Abstract

The aim was to analyze the effectiveness of polyhexamethylene biguanide regarding microbial load and infection incidence in patients with wounds. A systematic review was conducted following the recommendations of the Joanna Briggs Institute and the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist. Studies involving acute or chronic wounds treated with polyhexamethylene biguanide at concentrations between 0.04% and 0.5% were included. Risk-of-bias assessment tools and the GRADE (Grading of Recommendations Assessment, Development and Evaluation) system were used to evaluate the quality of the evidence. Seven studies (three cohort studies, three randomized clinical trials, and one before-and-after study) were included. The risk of bias was low in the clinical trials and moderate in the cohort studies. The quality of evidence was moderate for microbial load and very low for infection. Polyhexamethylene biguanide was effective in reducing microbial load ($p < 0.001$) and infection incidence ($p < 0.001$) in acute wounds. The use of polyhexamethylene biguanide is recommended to reduce microbial load and infections in acute wounds. The heterogeneity of interventions and measurement methods highlights the need for further studies. The use of polyhexamethylene biguanide is an effective strategy for controlling microbial load in acute wounds, supporting clinical decision-making.

Descriptors: Wound Healing; Nursing; Wounds and Injuries; Wound Infection; Systematic Review.

Resumen

El objetivo fue analizar la efectividad de la polihexametileno biguanida en la carga microbiana y la incidencia de infección en pacientes con heridas. Se realizó una revisión sistemática de acuerdo con las recomendaciones del Instituto Joanna Briggs y la lista de verificación PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses). Se incluyeron estudios realizados en heridas agudas o crónicas que utilizaron polihexametileno biguanida entre 0,04% y 0,5%. Se utilizaron herramientas de análisis de riesgo de sesgo y el sistema GRADE (Grading of Recommendations Assessment, Development and Evaluation) para medir la calidad de la evidencia. Se incluyeron siete estudios (tres cohortes, tres ensayos clínicos aleatorizados y un ensayo antes y después). El riesgo de sesgo fue bajo en los ensayos clínicos y moderado en las cohortes. La calidad de la evidencia fue moderada para la carga microbiana y muy baja para la infección. La polihexametileno biguanida fue efectiva para reducir la carga microbiana ($p < 0,001$) y la incidencia de infección ($p < 0,001$) en heridas agudas. Se recomienda el uso de polihexametileno biguanida para reducir la carga microbiana y las infecciones en heridas agudas. La heterogeneidad de las intervenciones y los métodos de medición subraya la necesidad de realizar más estudios. El uso de polihexametileno biguanida constituye una estrategia eficaz para controlar la carga microbiana en heridas agudas, lo que respalda la toma de decisiones clínicas.

Descriptores: Cicatrización de Heridas; Enfermería; Heridas y Lesiones; Infección de Heridas; Revisión Sistemática.

Resumo

Objetivou-se analisar a efetividade de polihexametileno-biguanida na carga microbiana e na incidência de infecção em pacientes com feridas. Revisão sistemática conforme recomendações do *Joanna Briggs Institute* e do *checklist Preferred Reporting Items for Systematic Reviews and Meta-Analyses*. Incluíram-se estudos realizados em feridas agudas ou crônicas que utilizaram polihexametileno-biguanida entre 0,04% e 0,5%. Utilizaram-se ferramentas de análise do risco de viés e sistema *Grading of Recommendations Assessment, Development and Evaluation* para mensurar qualidade da evidência. Sete estudos (três coortes, três ensaios clínicos randomizados e um ensaio antes e depois) foram incluídos. O risco de viés foi baixo nos ensaios clínicos e moderado nas coortes. A qualidade da evidência foi moderada para carga microbiana e muito baixa para infecção. Polihexametileno-biguanida foi efetivo na redução da carga microbiana ($p < 0,001$) e na incidência de infecção ($p < 0,001$) em feridas agudas. Recomenda-se o uso de polihexametileno-biguanida para reduzir carga microbiana e infecções em feridas agudas. A heterogeneidade das intervenções e dos métodos de mensuração reforça a necessidade de novos estudos. O uso de polihexametileno-biguanida é uma estratégia efetiva para controle da carga microbiana em feridas agudas, o que respalda a tomada de decisão clínica.

Descritores: Cicatrização; Enfermagem; Ferimentos e Lesões; Infecção da Ferida; Revisão Sistemática.



Introduction

Wounds are damage to the skin surface¹ and can be classified as acute or chronic². That is, acute wounds are those that pass through the healing stages promptly, while chronic wounds are considered to be lesions that take more than twelve weeks to heal²⁻³.

One of the main factors responsible for the chronification of a lesion is the occurrence of infection²⁻⁴, which leads to a prolongation of the inflammatory phase of healing and is commonly related to the presence of biofilms in wounds, defined as complex polymicrobial communities associated with a polysaccharide matrix that protects microorganisms against the host's immune response and against antimicrobial and antiseptic molecules¹⁻². Therefore, evaluating and treating infections is one of the principles for improving health outcomes in patients with wounds⁴. Different active principles and treatments have been used, such as dressings with antimicrobial and antiseptic compounds, such as silver, iodine, chlorhexidine, methylene blue, and polyhexamethylene biguanide (PHMB)⁴.

PHMB is an antiseptic that was first synthesized in the 1950s and binds to negatively charged phospholipid groups in the bacterial cell wall, affecting the proximity and functioning of different components of this structure (lipids, proteins, enzymes, receptors, etc.), leading to increased permeability and rupture of the cell wall and, consequently, to the death of the exposed microorganisms⁵. Commercially, it is available in liquid form, in gel or sheets, in preparations combined with different solutions and vehicles and concentrations that vary between 0.02% and 0.5%⁵⁻⁶. Despite the efficacy of PHMB reported in *in vitro* and *in vivo* research with microorganisms prevalent in wounds⁵⁻⁸, preliminary searches in the International Prospective Register of Ongoing Systematic Reviews (PROSPERO), the Cochrane Database of Systematic Reviews, and the Joanna Briggs Institute (JBI) Evidence Synthesis did not retrieve current or ongoing systematic reviews on the effect of PHMB on microbial load or on the incidence of infections in wounds, which justifies conducting investigations on this theme. Thus, this study aimed to analyze the effectiveness of polyhexamethylene biguanide (PHMB) on microbial load and on the incidence of infection in patients with wounds.

Methodology

Type of Study

This is a systematic literature review, conducted in accordance with the JBI methodology⁹ and for the construction of the report, the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses PRISMA Checklist¹⁰ were followed. Registration on the PROSPERO platform was carried out under number CRD42022226093.

Search Strategies

The research question was: "What is the effectiveness of polyhexamethylene biguanide (PHMB) when compared to solutions in reducing the microbial load of wounds?". For its elaboration, the acronym PICO⁹ (Population - Intervention - Comparator - Outcome) was

used, in which: the population was composed of individuals with wounds; the intervention was the use of PHMB; the comparator was the use of solutions; and the outcome was the evaluation of microbial load.

The construction of the search strategies was performed by a librarian, a specialist in scientific and technological information in health. Controlled terms were used, based on the Health Sciences Descriptors (DeCS) and the Medical Subject Headings (MeSH), as well as non-controlled terms. The search process was carried out in two stages.

Initially, a pilot test was conducted that included a limited search in the databases: Latin American and Caribbean Literature in Health Sciences (LILACS) via the Virtual Health Library Portal (VHL); Nursing Databases (BDENF) via the Virtual Health Library Portal (VHL); Medical Literature Analysis and Retrieval System Online (MEDLINE) via the US National Library of Medicine (PubMed); and Excerpta Medica dataBASE (Embase) via the Journal Portal of the Coordination for the Improvement of Higher Education Personnel (CAPES) on September 21, 2020. These searches used the following thesauri: wounds and injuries; ulcer; lesion; polyhexamethylenebiguanide; PHMB; wound healing; microbial load; infection load; bacterial load.

A total of 209 articles were retrieved, whose titles and abstracts were evaluated by two independent reviewers, both nurses with experience or specialization in the wound area. This analysis was performed aiming at verifying adequacy to the inclusion criteria of the review and led to the identification of 72 potentially relevant articles, which were read in full and had their reference lists evaluated, allowing the inclusion of new thesauri, as well as the expansion of search strategies.

A second, broader search using all the thesauri identified from the pilot test was performed on June 10, 2024, in the same databases cited previously, by the same librarian. The search strategies used specifically in each database are presented in Figure 1.

Selection Criteria

The inclusion criteria for study selection were: people of both sexes, of any age group, with acute or chronic wounds; treatments with PHMB in concentrations between 0.04% and 0.5%, in the following topical application presentations: PHMB solution in irrigation; compress or gauze soaked with PHMB solution; dressing impregnated with PHMB; collagen dressing with PHMB; foam dressing with PHMB; dressing with PHMB solution in sponge associated with negative pressure; which evaluated as a primary outcome the microbial load of wounds or as a secondary outcome the incidence of clinical infections in the lesions.

For the evaluation of microbial load, studies that performed cultures of swabs from the lesions, with subsequent counting of colony-forming units (CFU), calculation of prevalence of microbial species alone or by spectrophotometry, as well as those in which biopsies of the wounds were performed (electron microscopy of tissue fragments), were considered.



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[illegible]

\$MEDLINE = Medical Literature Analysis and Retrieval System Online; || PubMed = US National Library of Medicine; ¶Embase = Excerpta Medica dataBASE;

****CAPES = Journal Portal of the Coordination for the Improvement of Higher Education Personnel.**

Regarding the measurement of infection incidence, studies that classified as infected wounds that presented: erythema; local heat; edema; purulent exudate; increase in wound size; increase in the level of pain reported by the patient from baseline; fetid odor¹¹ were considered. For surgical site infections, the criteria established by the Centers for Disease Prevention and Control (CDC) were considered, which classify infections as:

- Superficial incisional: less than 30 days since surgery; and involvement of only skin and subcutaneous tissue; and one of the following findings: purulent drainage from the incision; or isolation of microorganism from culture of material obtained aseptically from the incision; or opening of the incision by the surgeon upon the occurrence of inflammatory signs; or diagnosis of superficial incisional surgical site infection by a physician¹².
- Deep incisional: less than 90 days since surgery; and involvement of deep soft tissues (such as fascial and muscle layers), in addition to skin and subcutaneous tissue; and one of the following findings: a) purulent drainage from the incision; or b) opening of the incision by the surgeon or spontaneous suture dehiscence; and isolation of microorganism from culture of material obtained aseptically from deep soft tissues; and presence of any of the following signs or symptoms: fever (>38°C); localized pain or tenderness; c) abscess

or other evidence of infection involving the deep incision detected on macroscopic anatomical examination, histopathological examination, or imaging examination¹².

- Organ/space: less than 90 days since surgery; and involvement of any part of the body deeper than the fascial/muscle layers (organs or cavities); and one of the following findings: a) purulent drainage from a drain placed in the organ/space; b) isolation of microorganism from culture of material obtained aseptically from tissues in the organ/space; c) an abscess or other evidence of infection involving the organ/space detected on macroscopic anatomical examination or histopathological examination, or on equivocal imaging examination of infection¹².

This review considered analytical observational studies (cohorts) and experimental studies (randomized controlled trials, non-randomized controlled trials, before-and-after studies). No restrictions were established regarding language or year of publication. Ongoing studies and research protocols were excluded, as well as preclinical studies (in animals or in vitro), expert opinions, letters to the editor, or case studies.

Article Selection and Data Extraction

The results of each database were electronically imported into the online application Rayyan



(<https://rayyan.ai/>) for removal of duplicates. The titles and abstracts of the publications were examined by two researchers independently. Then, the two reviewers evaluated the full texts of the potentially eligible studies regarding compliance with the eligibility criteria, also independently. Divergences that arose were resolved by discussion between the reviewers or with the participation of a third reviewer.

Data extraction from each study included the recording of the following information: authors' names; title; country of origin; year and journal of publication; study design; population; clinical characteristics of the patients and the wounds evaluated; characteristics of the interventions performed in the intervention and control groups; primary and secondary outcomes evaluated; existence of conflict of interest and funding of the research.

Data Synthesis, Risk of Bias Assessment, and Quality of Evidence

Some of the included studies evaluated the microbial load outcome exclusively, while another part also evaluated the secondary outcome of the presence of clinical infection in the wounds. Thus, it was decided to synthesize the data through narrative summaries, presented in the form of figures.

The risk of bias of the studies was evaluated based on the recommendations of the Joanna Briggs Institute critical appraisal tools⁹ for quasi-experimental studies (before and after), randomized clinical trials, and cohort studies.

The tool for analysis of randomized clinical trials contains the following questions: 1 – Was true randomization used for assignment of participants to treatment groups?; 2 – Was allocation to groups concealed?; 3 – Were treatment groups similar at baseline?; 4 – Were participants blind to treatment assignment?; 5 – Were those delivering treatment blind to treatment assignment?; 6 – Were outcome assessors blind to treatment assignment?; 7 – Were treatment groups treated identically other than the intervention of interest?; 8 – Was follow-up complete and, if not, were differences between groups in terms of follow-up adequately described and analyzed?; 9 – Were participants analyzed in the groups to which they were randomized?; 10 – Were outcomes measured in the same way for treatment groups?; 11 – Were outcomes measured in a reliable way?; 12 – Was appropriate statistical analysis used?; 13 – Was the trial design appropriate for the topic and were any deviations from the standard randomized clinical trial design accounted for in the conduct and analysis?.

The tool for before-and-after clinical trials (quasi-experimental studies) contains the following questions: 1 – Is it clear in the study what is the "cause" and what is the "effect" (i.e., there is no confusion about which variable comes first)?; 2 – Was there a control group?; 3 – Were participants included in any similar comparison?; 4 – Were participants included in any comparison that received similar treatment/care, in addition to the exposure or intervention of interest?; 5 – Were there multiple measurements of the

outcome, both before and after the intervention/exposure?; 6 – Were the outcomes of participants included in any comparison measured in the same way?; 7 – Were outcomes measured in a reliable way?; 8 – Was follow-up complete and, if not, were differences between groups in terms of follow-up adequately described and analyzed?; 9 – Was appropriate statistical analysis performed?.

The instrument recommended for evaluating the risk of bias of cohort studies is composed of the following questions: 1 – Were the two groups similar and recruited from the same population?; 2 – Were the exposures measured similarly to assign people to exposed and non-exposed groups?; 3 – Was the exposure measured in a valid and reliable way?; 4 – Were confounding factors identified?; 5 – Were strategies to deal with confounding factors stated?; 6 – Were the groups/participants free of the outcome at the beginning of the study (or at the time of exposure)?; 7 – Were the outcomes measured in a valid and reliable way?; 8 – Was the follow-up time reported and sufficient to be long enough for the outcomes to occur?; 9 – Was follow-up complete and, if not, were the reasons for loss to follow-up described and explored?; 10 – Were strategies to address incomplete follow-up utilized?; 11 – Was appropriate statistical analysis used?.

In the three tools, the evaluation parameters of the studies are based on the answers to each question of the evaluation tools. That is, there was: high risk of bias when a study obtained up to 49% of "yes" answers; moderate risk of bias when it obtained 50 to 69% of "yes" answers; and low risk of bias when it received 70% or more of "yes" answers.

The evaluation of the quality of evidence was performed according to the Grading of Recommendations Assessment, Development and Evaluation Working Group (GRADE)^{13,14}, considering five main factors: risk of bias; inconsistency; indirect evidence; imprecision; publication bias, through GRADEpro software¹⁵.

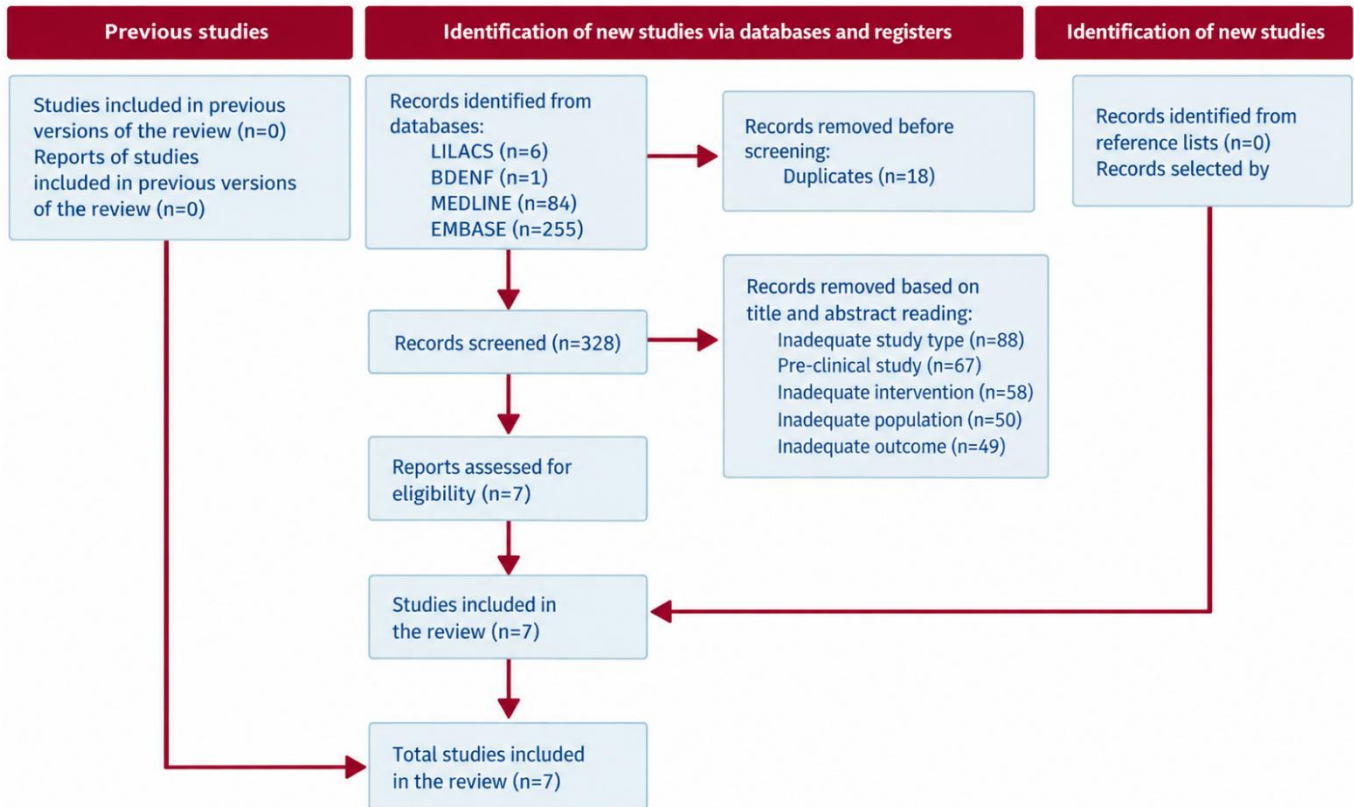
Results

The search strategies employed allowed the retrieval of 346 studies. After applying the eligibility criteria, 7 articles were included in the final sample (Figure 2).

Most of the articles included in this study came from Switzerland and were published between the years 2015 and 2023. The seven studies evaluated 7,553 participants, with 7,594 wounds. The majority were acute traumatic lesions (n=7,197, 95%). The chronic lesions were primarily venous ulcers (n=124, 2%). The descriptive synthesis about the samples, methodological designs, and active agents used in the intervention/exposed groups and in the control/non-exposed groups is presented in Figure 3.

Regarding the evaluations of the primary and secondary outcomes of the present review, great heterogeneity was evidenced in the methods used for analysis in the included studies, as observed in Figure 4, which describes the evaluations aimed at "microbial load" and "infection in wounds".



Figure 2. Flowchart of the selection process of randomized controlled trials included in the systematic review, adapted from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Niterói, RJ, Brazil, 2024**Figure 3.** Samples, methodological designs, and active agents used in the studies. Niterói, RJ, Brazil, 2024

Authors, year and location	Sample of patients and outcomes	Study design	Intervention group/ exposure group	Control group/ non-exposed group
Ceviker et al., 2015 ⁵ Turquia	31 participants 31 chronic wounds (LPP* and IC ⁴)	Prospective cohort	Aqueous solution of PHMB* at 0.5%	Ringer lactate solution
Borges et al., 2018 ²⁴ Brazil	27 participants 27 chronic wounds (UV ⁶)	Double-blind RCT	Aqueous solution of PHMB* at 0.1% and undecenamidopropyl betaine	Saline solution 0.9%
Assadian et al., 2018 ²⁶ Switzerland	260 participants 299 chronic wounds (UA ⁷ , LPP*, UV ⁶ , UPD**)	Prospective cohort	Aqueous solution of PHMB* at 0.1% and undecenamidopropyl betaine solution Cocamidopropyl betaine and PHMB*	Saline solution 0.9%
Payne et al., 2018 ²⁷ Switzerland	61 participants 61 acute wounds (cuts, bruises)	Double-blind RCT	Aqueous solution of PHMB* at 0.04%	Sterile isotonic Ringer solution
Saleh et al., 2016 ²⁸ Sweden	40 participants 40 acute wounds (surgical lesions)	Double-blind RCT	Foam dressing impregnated with PHMB* at 0.1% and undecenamidopropyl betaine	Curative silicone with sterile water
Roth et al., 2017 ¹⁹ Switzerland	7104 participants 7104 acute wounds (lacerations, abrasions, contusions)	Prospective cohort	Aqueous solution of PHMB* at 0.04%	Iodopovidone 1% Hydrogen peroxide 4% Ringer lactate
Raditya et al., 2023 ²⁰ Indonesia	30 participants 30 burns (traumatic lesions)	Experimental study before and after	Aqueous solution of PHMB* at 0.1% Betaine at 0.1%	Saline solution 0.9%

Note: *PI = Pressure injuries; †SSI = Surgical site infections; ‡PHMB = Polyhexamethylene biguanide; §VU = Venous ulcers; || RCT = Randomized controlled trial; ¶AU = Arterial ulcers; **DFU = Diabetic foot ulcers.

Figure 4. Methods of measuring the outcomes and main results of the studies included in the review. Niterói, RJ, Brazil, 2024

Authors and year	Evaluated outcome	Main results
 Ceviker et al., 2015 ⁵	Infection in wounds: Occurrence of bacterial cultures negative at the end of 21 days.	Difference between groups (PHMB® 0.5% and rinse with lactate): <i>p</i> value = 0.173 .
 Borges et al., 2018 ²⁴	Microbial load: Quantification of microorganisms per gram of tissue (homogenate of UFC/g) evaluated before and after irrigation of the wound.	Difference between groups (PHMB® 0.1% + undecylenamidopropyl betaine and saline solution 0.9%): <i>p</i> value = 0.5146 .
 Assadian et al., 2018 ²⁶	Microbial load: Quantification of microorganisms in 1 cm ² of the wound surface (fluid [UFC/cm ²] evaluated before and after one hour of irrigation, with a circular, closed dressing).	Difference between intra-group PHMB® 0.1% and undecylenamidopropyl betaine: <i>p</i> value = 0.051 . Difference between intra-group PHMB® + cocamidopropyl betaine: <i>p</i> value = 0.005 . The authors did not present the results between groups.
 Payne et al., 2018 ²⁷	Microbial load: Quantification of microorganisms in 1 cm ² of the wound surface (fluid [UFC/cm ²] evaluated seven days after the start of treatment).	Microbial load: Difference between groups of the curative dressing with PHMB® 0.1% and curative dressing with silicone with water after seven days of surgery: <i>p</i> value = 0.752 . Infection in wounds: Difference between groups of the curative dressing with PHMB® 0.1% and curative dressing with silicone with water after seven days of surgery: <i>p</i> value = 0.028 (higher incidence of infection in the PHMB group).
 Roth et al., 2017 ¹⁹	Infection in wounds: Incidence of superficial or incisional SCLs (%)	Difference between groups PHMB® 0.04% and povidone-iodine 1%: <i>p</i> value = 0.056 for the incidence of ISC* in superficial wounds and <i>p</i> value = 0.002 for deep wounds. Difference between groups PHMB® 0.04% and Ringer: <i>p</i> value = 0.631 for the incidence of ISC** in superficial wounds and <i>p</i> value < 0.001 for deep wounds. Difference between groups PHMB® 0.04% and hydrogen peroxide 4%: <i>p</i> value = 0.003 for the incidence of ISC** in superficial wounds and <i>p</i> value < 0.001 for deep wounds.
 Raditya et al., 2023 ²⁰	Microbial load: Quantification of microorganisms on the wound surface (UFC/cm ²)	There was a significant decrease in the levels of bacterial load (contagem de Log ₁₀ UFC/cm ²) after irrigation with saline solution, with a reduction in the levels of NaCl + PHMB® (<i>p</i> < 0.001). The reduction in bacterial levels was more significant with NaCl + PHMB® compared to saline solution, after irrigation (<i>p</i> =0.001).

Note: *PHMB = Polyhexamethylene biguanide; †*p* value = Significance level; ‡CFU/g = Colony-forming units per gram of biopsied wound tissue; §CFU/ml = Colony-forming units per milliliter of saline processed in the laboratory from a swab collected from the wound; ||Log₁₀ CFU/ml = Colony-forming units per milliliter in serial dilutions of saline processed in the laboratory from a swab collected from the wound; ¶CFU/cm² = Colony-forming units per square centimeter from a swab collected from the wound; **SSI = Surgical site infection; ††NaCl = Sodium chloride.

Figure 5. Synthesis of the assessment of certainty of evidence, according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE). Niterói, RJ, Brazil, 2024

Evidence quality assessment								
 Number of studies	 Study type	 Risk of bias	 Inconsistency	 Indirect evidence	 Imprecision	 Other considerations	 Synthesis of evidence	 Quality of evidence
Microbial load								
5	3 RCTs ¹ , 1 clinical trial, and 1 study after and 1 cohort	Not serious ¹	Very serious ¹	Not serious	Not serious (418 individuals evaluated)	All the potential confounders were regularly reduced in the demonstrated effect	In an ECR ¹⁸ with chronic wounds, there were no significant differences between the products. Furthermore, ECR ¹⁸ with healing wounds did not describe statistically significant differences between groups. However, intra-groups, <i>P</i> <0.05, showed a significant reduction when comparing the baseline. Another ECR ¹⁸ with healed wounds did not show significant differences between the products evaluated (curative dressing and embedding in PHMB® 0.1% and silver). In the "cohort" study, chronic wounds did not show statistically significant differences between groups. However, intra-groups, there was greater reduction of the microbial load when using PHMB®. The clinical study before and after showed a significant decrease in the microbial load when using saline with PHMB® 0.1%.	⊕⊕⊕○ Moderate
Infection in healed wounds								
3	2 case reports and 1 ECR ¹⁸	Serious ¹	Very serious ¹	Not serious	Not serious (7,175 individuals evaluated)	All the potential confounders were regularly reduced in the demonstrated effect	In a case-control study with chronic wounds, there were no significant differences between the groups evaluated. In another study, with healed wounds, there were significant differences between the products, with greater effectiveness of PHMB®. In a third study, in groups with healed wounds, an increase in the incidence of surgical site infections was observed.	⊕○○○ Very low

Note: Figure elaborated and extracted from the GRADEpro software. *RCT = Randomized controlled trial; †Of the 5 studies considered, 4 were considered to have low risk of bias^{8,17-18,20} and 1 was considered to have moderate risk of bias¹⁶; ‡Significant variability was verified in the outcome measurement strategies and heterogeneity in the conduct of the research; §PHMB = Polyhexamethylene biguanide; ||Of the 3 studies considered, 2 were considered to have moderate risk of bias^{6,19}, and 1 was considered to have low risk of bias¹⁸.

In the risk of bias analysis of the three randomized clinical trials included, it was verified that two studies^{8,17} were characterized with 100% compliance regarding the methodological aspects considered in the assessment tool, and two studies^{18,20} were analyzed with 77% compliance.

Thus, globally, the clinical trials included in the review presented low risk of bias.

On the other hand, the cohort studies presented moderate risk of bias, since all three studies^{6,16,19} of this design presented 63% compliance with the methodological

aspects considered in the assessment tool. This is because there were inconsistencies in the similarity between the exposed and non-exposed groups at the beginning of the follow-up periods, as well as in the strategies for minimizing possible interferences generated by confounding variables and in the handling of loss to follow-up, so common in cohort studies.

The quality of the evidence varied according to the outcome (microbial load and infection in wounds), as shown in Figure 5. The data suggest moderate confidence for the microbial load outcome and very low for the infection in wounds outcome.

Discussion

In this study, the most used PHMB presentations were aqueous solutions with concentrations of 0.1%^{8,16,18}. However, in the study with the largest number of individuals evaluated¹⁹ PHMB was used in an aqueous solution concentrated at 0.04%. Only two studies were conducted with more than two evaluation arms^{16,19}, that is, they evaluated more than two products in the intervention or control groups. It is noteworthy that, in addition to solutions, there are also PHMB presentations in gels and impregnated dressings⁵.

The variability in the characteristics of the interventions may be related to differences between industries and products available in each region. In Brazil, the PHMB concentration of 0.1% is commercially available for access by patients and health professionals. On the other hand, for conducting review studies, it is known that variations in interventions can compromise the comparison between research results.

The products used as comparators also varied between studies, with emphasis on Ringer's solutions^{6,17,19}, preferentially used. In clinical practice, wound cleaning with 0.9% saline solution or potable water is often recommended, mainly due to economic issues and ease of use and access. However, their effects on the outcomes of infection incidence and healing were discussed in a recently published systematic review²¹, and all identified evidence was of low or very low certainty, which prevented recommendations.

Regarding the outcomes, the included studies presented different forms of measurement. For microbial load, swab-based biological material collection was prevalent^{16-18,20}, so only one study used lesion biopsies for microbiological analysis⁸. There are divergences in the literature regarding the preferred method for collecting wound samples; however, the use of swabs in clinical practice is frequent, as it is a simple, non-invasive, and relatively inexpensive procedure¹¹. It is noteworthy that the technique of choice is the one proposed by Levine²², in which the swab is firmly pressed on the granulation tissue present in the lesion and rotated over an area of 1 cm² to extract fluid from the tissue^{11,21}. In the present review, of the three studies that used swabs for collecting biological material, two used the Levine technique^{16,18}.

Likewise, there is no consensus in the literature on the techniques for calculating microbial load in microbiology

laboratories after collecting biological material. In this review, the measurement units for this quantity were basically based on the calculation of colony-forming units (CFU), but three studies considered CFU per area (cm²) of lesion^{16,18,20}, one study used CFU per gram (g) after biopsies⁸ and one study performed CFU counting based on serial dilutions¹⁷. Furthermore, it is known that molecular methods (such as real-time polymerase chain reaction microbial quantification) can also be used for this purpose²³⁻²⁴. Therefore, the need for methodological studies that validate the most reliable techniques for calculating microbial load is reiterated.

Similarly, regarding the measurement of infection incidence, the literature also presents different recommendations. In general, for chronic wounds, lesions that present signs and symptoms such as erythema; local heat; edema; purulent exudate; fetid odor¹¹ are considered infected. However, studies that develop and validate algorithms to guide decision-making regarding clinical signs of infection according to the etiologies of the multiple chronic lesions prevalent in clinical practice can collaborate to objectify the evaluations related to this topic. For surgical lesions, on the other hand, the consensus refers to the use of the Centers for Disease Prevention and Control (CDC) criteria¹², as observed in two studies included in the present review¹⁸⁻¹⁹.

The limitations of this research are based on the heterogeneity in the interventions and in the methods of measuring the outcomes of the included studies, which prevented the statistical summarization of the findings through meta-analysis.

As an impact factor in clinical practice, the findings of the present review regarding the impact of using PHMB in acute wounds significantly optimize therapeutic decision-making regarding the problem of the high microbial load commonly found in these conditions.

Conclusion

This study analyzed the effectiveness of polyhexamethylene biguanide (PHMB) on microbial load and on the incidence of infection in patients with wounds, and the results pointed to the promising use of PHMB in acute wounds aiming at reducing microbial load and infection incidence.

Although the final sample was composed of only seven studies, significant heterogeneity in the pharmaceutical presentations used in the intervention and control groups, as well as the different techniques for measuring outcomes, prevented the performance of meta-analysis, this being the limitation of the study. These aspects were also determinant in the quality of the evidence produced, considered moderate for the microbial load outcome and very low for the infection in wounds outcome. Therefore, research with methodological robustness and sample sizes that enable generalization and reproduction of findings is recommended to elucidate remaining knowledge gaps.

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