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Treatment of Localized Infections in Hard-to-Heal Wounds: An Integrative Review

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ABSTRACT

Objective: To identify the knowledge production on the treatment of localized infections in hard-to-heal wounds. **Method:** An integrative literature review was conducted in the Virtual Health Library, Nursing Database, Scientific Electronic Library Online, Web of Science, Cochrane Library, Catalog of Theses and Dissertations of the Coordination for the Improvement of Higher Education Personnel, and PubMed. The selected articles had no time limit. The studies were exported to the Rayyan application and subjected to double-blind evaluation through title and abstract reading, based on inclusion and exclusion criteria. The information was analyzed and synthesized according to the level of evidence. **Results:** A total of 19 publications were fully analyzed. The evidence obtained on the topic includes wound hygiene, cleaning with 1% acetic acid, identification and treatment of biofilms, the use of dressings, and solutions with antimicrobial action. **Conclusion:** Localized wound infections have been the subject of various research studies, and the recommended practices refer to topical treatments.

DESCRIPTORS: Ulcer. Skin ulcer. Wound healing. Wounds and injuries. Infections.

Tratamento de infecções localizadas em feridas de difícil cicatrização: uma revisão integrativa

RESUMO

Objetivo: Identificar a produção de conhecimento sobre o tratamento de infecções localizadas em feridas de difícil cicatrização. **Método:** Revisão integrativa da literatura realizada na Biblioteca Virtual em Saúde, Base de Dados de Enfermagem, *Scientific Electronic Library Online*, *Web of Science*, Biblioteca *Cochrane*, Catálogo de Teses e Dissertações da Coordenação de Aperfeiçoamento de Pessoal de Nível Superior e *Public Medline*. Os artigos selecionados não possuem limite temporal. Os estudos foram exportados para o aplicativo *Rayyan* e submetidos à avaliação duplo-cega por meio da leitura do título e do resumo, com base nos critérios de inclusão e exclusão. As informações foram analisadas e sintetizadas de acordo com o nível de evidência. **Resultados:** Foram analisadas 19 publicações em sua totalidade. Obteve-se como evidências acerca do tema a higienização da ferida, a limpeza com ácido acético 1%, a identificação e o tratamento de biofilmes, o uso de coberturas e as soluções com ação antimicrobiana. **Conclusão:** A infecção localizada de feridas tem sido objeto de várias pesquisas e as práticas recomendadas referem-se a tratamentos tópicos.

DESCRITORES: Úlcera. Úlcera cutânea. Cicatrização. Ferimentos e lesões. Infecção.

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Tratamiento de infecciones localizadas en heridas de difícil cicatrización: una revisión integrativa

RESUMEN

Objetivo: Identificar la producción de conocimiento sobre el tratamiento de infecciones localizadas en heridas de difícil cicatrización. **Método:** Revisión integrativa de la literatura realizada en la Biblioteca Virtual en Salud; Base de datos de enfermería; *Scientific Electronic Library*; *Web of Science*; Biblioteca Cochrane; Catálogo de Tesis y Disertaciones de la Coordinación para el Perfeccionamiento del Personal de Educación Superior; y PubMed. Los artículos seleccionados no tienen límite de tiempo. Los estudios fueron exportados a la aplicación Rayyan y sometidos a evaluación doble ciego mediante la lectura del título y el resumen, según los criterios de inclusión y exclusión. La información fue analizada y sintetizada según el nivel de evidencia. **Resultados:** 19 estudios fueron incluidos para lectura completa. Se encontró como evidencia la higiene de la herida; la limpieza con ácido acético al 1%; la identificación y el tratamiento de biopelículas; el uso de cobertores y soluciones con acción antimicrobiana. **Conclusión:** La infección localizada de la herida ha sido objeto de varias investigaciones y las prácticas recomendadas se refieren a tratamientos tópicos.

DESCRIPTORES: Úlcera. Úlcera cutánea. Cicatrización de heridas. Heridas y lesiones. Infecciones.

INTRODUCTION

The term "hard-to-heal wound" is used for wounds that do not respond to standard evidence-based care for their etiology1. Wounds that show an increase or worsening in exudate characteristics, the presence of slough in the wound bed, and an increase in size after three days can be defined as hard-to-heal and are considered to have biofilm presence[1,2].

An infection occurs when there is an invasion and proliferation of microorganisms at levels capable of triggering a local, disseminated, and/or systemic response related to the wound1. The microorganisms multiply, and depending on the virulence factors and/or host immunity, they can cause infections with local tissue damage, interfering with the normal healing process[3]. Assessing the patient's risk factors, clinical conditions, wound characteristics, and surrounding tissues is crucial to identify signs and symptoms of localized infection, spread to adjacent tissues, or systemic infection[4].

It is estimated that 2 to 6% of the global population has lesions related to aging, and people aged 65 and older are at higher risk for hard-to-heal wounds[5]. Impaired healing is multifactorial, and non-healing wounds share similar characteristics such as high protease levels, elevated inflammatory markers, low growth factor activity, and reduced cell proliferation[6].

Biofilm, in turn, is defined as a complex community of various species of microorganisms, such as bacteria and fungi, capable of rapid formation and maturation (48 to 72 hours), adhering to the wound surface and enveloping themselves in an extracellular matrix that protects against antimicrobial agents[4,6]. The hygiene of hard-to-heal wounds includes cleaning the wound bed and perilesional skin, debridement, edge reconstruction, and the use of dressings, and is recommended as an early anti-biofilm intervention[1].

The treatment of infections in people with wounds should be individualized and based on the etiology and risk factors, comprising regular assessment and monitoring of localized infection signs and symptoms based on tissue characteristics in the wound bed and edges, exudate characteristics and quantity, pain, and odor, with systematic observation for signs and symptoms of spread to adjacent tissues or systemic infection1. Microbiological examinations should be guided by clinical indication to minimize unnecessary use of systemic antibiotics[1-7].

The treatment of localized infections in hard-to-heal wounds represents a significant challenge in clinical practice, as it requires specialized and individualized approaches to prevent aggravation, promote healing, and minimize waste from using therapeutics without proven evidence.

The availability of scientific evidence on effective strategies for treating these infections may be limited. Therefore, the objective of this research is to identify the knowledge production on the treatment of localized infections in hard-to-heal wounds.

METHODS

This is an integrative literature review aimed at synthesizing results obtained from research on a specific topic or question in a systematic, orderly, and comprehensive manner.

Considering the integrative review methodology, the steps evaluated in this study were:

1. Selection of the guiding question;
2. Definition of inclusion and exclusion criteria and sample selection;
3. Representation of the selected studies in chart format;
4. Analysis and evaluation of the studies included in the integrative literature review;
5. Interpretation of results; and
6. Presentation of the review.

For step 1, the identification of the topic and selection of the guiding research question to conduct the integrative review was considered, using the PICO strategy, which takes into account the patient, intervention, comparison, and expected outcomes. To formulate the research question, the PICO acronym was used: "P" for patient (adults or elderly), "I" for intervention (medical or nursing care for hard-to-heal wounds), "C" for comparison (none), and "O" for outcomes (recommended practices).

Based on the PICO description, the following guiding question was obtained: What are the treatments for localized infections in hard-to-heal wounds in adults or elderly individuals?

The literature search was conducted without a time limit and in the following databases: Virtual Health Library (VHL), which includes the Latin American and Caribbean Health Sciences Literature (LILACS) and Nursing Database (BDENF); Scientific Electronic Library Online (SciELO); Web of Science; Cochrane Library; Catalog of Theses and Dissertations of the Coordination for the Improvement of Higher Education Personnel (CAPES); and PubMed, which includes the Medical Literature Analysis and Retrieval System Online (MEDLINE). The descriptors were selected from DeCS/MeSH (Health Sciences Descriptors/Medical Subject Headings), using Boolean operators (AND, OR, NOT) for their combinations.

The search terms were obtained from MeSH through the following strategies: "Wounds" [Mesh] AND "Injuries" [Mesh] AND "Ulcer" [Mesh] AND "Skin Ulcer" [Mesh] AND "Wound Healing" [Mesh] OR "Chronic" [Mesh] OR "Occlusive Dressing" [Mesh] AND "Wound Closure Techniques" [Mesh] OR "Therapeutic" [Mesh] AND "Treatment". The search strategy was adapted according to the specifics of each database while maintaining a similar combination of descriptors. In chart 1, the adopted descriptors and search keys created in PubMed are listed.

The data obtained from the search were imported into the free Rayyan® application, available on the web (https://rayyan.qcri.org/), for organization and screening of the articles. Subsequently, two researchers read the titles and abstracts of all available publications, selecting those potentially eligible for the study. Any selection doubts were resolved in plenary sessions with the participation of a third researcher. After reaching a consensus on the selection of publications, they were read in full.

Articles published in Portuguese, English, and Spanish, available in full in the selected databases and related to the guiding question, with a publication time limit of 20 years (from 2002 to 2022), were included in the sample. Articles that did not address the guiding question, such as pediatric, neoplastic, acute, and dental lesions; animal studies; articles not available in full; those written in languages other than those defined; gray literature; comments; and editorials were excluded.

Chart 1. Adopted Descriptors. Divinópolis (MG), Brazil, 2023.

Wounds and Injuries	Chronic	Dressing	Treatment
Wounds and Injuries Injuries and Wounds Wounds and Injury Injury and Wounds Wounds, Injury Injuries, Wounds Injuries Injury Wounds Wound Ulcer Ulcers Skin Ulcer Skin Ulcers Ulcer, Skin Ulcers, Skin Wound Healing Healing, Wound Healings, Wound Wound Healings	Chronic Chronics	Dressing, Occlusive Occlusive Dressing Dressings Dressing Closure Techniques, Wound Technique, Wound Closure Techniques, Wound Closure Wound Closure Technique	Therapeutic Therapeutics Therapy Therapies Treatment Treatments

Source: Prepared by the authors, 2023.

The levels of evidence were analyzed according to the following stratification:

Level I: Evidence resulting from meta-analyses of multiple controlled and randomized clinical studies;

Level II: Evidence obtained from individual studies with experimental design;

Level III: Evidence from quasi-experimental studies, such as non-randomized studies with a single group pre and post-test, time series, or case-control;

Level IV: Evidence from descriptive (non-experimental) studies or those with a qualitative approach;

Level V: Evidence from case reports or experience reports; and

Level VI: Evidence based on expert opinions[8].

RESULTS

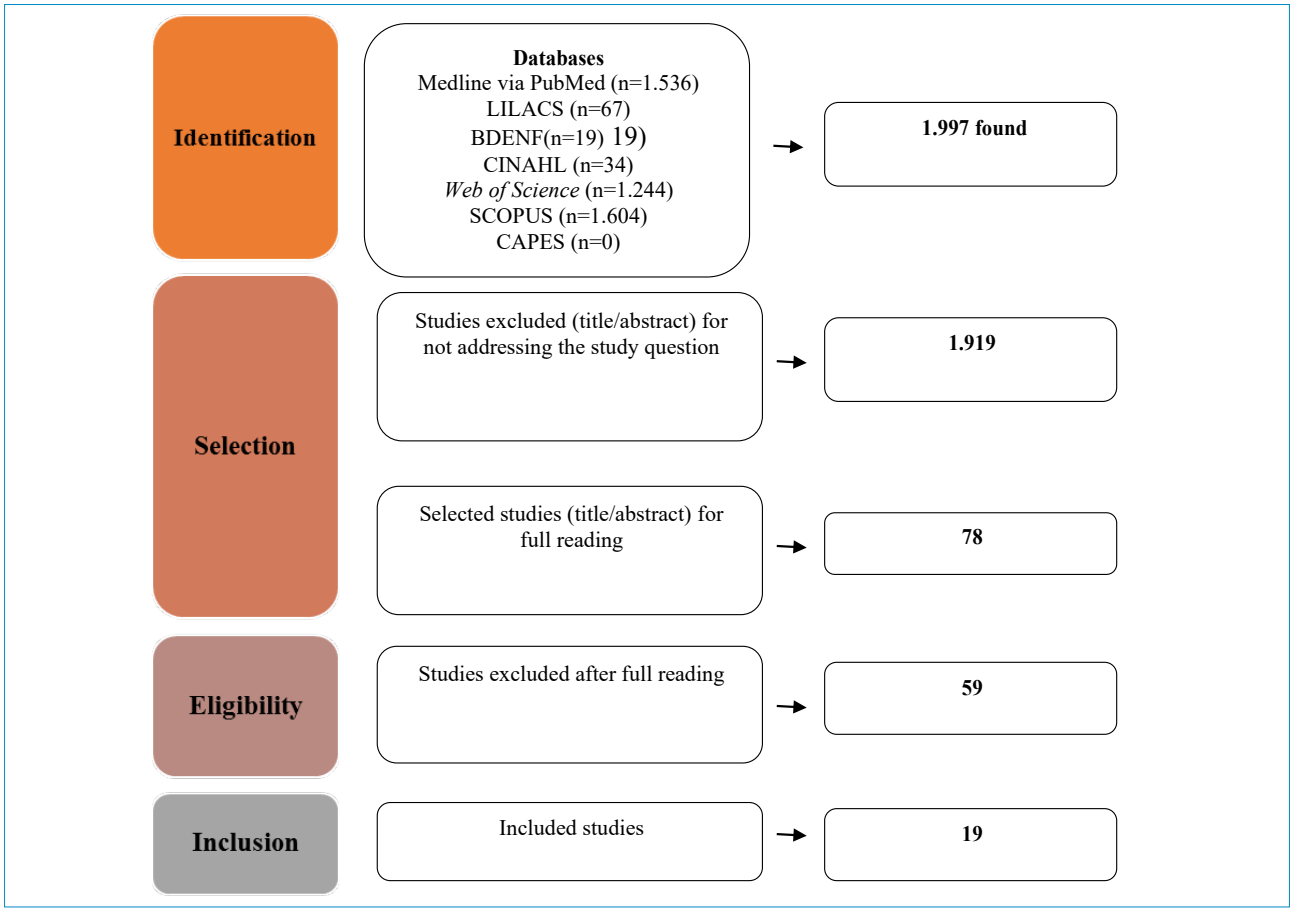
A total of 1,997 studies were found, distributed as follows: MEDLINE via PubMed (n=1,536), LILACS (n=67), BDENF (n=19), CINAHL (n=34), Web of Science (n=1,244), Scopus (n=1,604), and CAPES (n=0). Of these, 1,919 articles were excluded for not addressing the guiding question, leaving 78 eligible studies.

Of the 78 studies pre-selected for full-text reading, 59 were excluded due to incomplete texts, in vitro studies, or case studies. In the end, the sample consisted of 19 studies. Figure 1 illustrates the process of identification, selection, eligibility, and inclusion of the studies.

Regarding the year of publication, the selected articles were distributed as follows: 2015 (n=3; 15.8%), 2016 (n=4; 21%), 2019 (n=1; 5.3%), 2020 (n=2; 10.5%), and 2022 (n=2; 10.5%). The remaining articles were published between 2004 and 2014 (n=7; 36.8%) (Chart 2)4,9-26.

In terms of nationality, Europe had the highest number of articles (n=7; 36.8%). There was a notable lack of publications on the treatment of localized infections in hard-to-heal wounds from Brazil, as no national articles met the proposed criteria of this research (Chart 2).

Regarding the types of studies, most were clinical trials (n=11; 57.8%), literature reviews (n=4; 21%), methodological studies (n=2; 10.5%), observational studies (n=1; 5.2%), and prospective studies (n=1; 5.2%) (Chart 2). Concerning the levels of evidence, most were level I studies (n=8; 42.1%), followed by levels IV (n=6; 31.5%), III (n=4; 21%), and II (n=1; 5.2%). Level V was not identified in the results (Chart 2).



Note: MEDLINE/PubMed: National Library of Medicine and National Institutes of Health; CINAHL: Cumulative Index to Nursing and Allied Health Literature; LILACS: Latin American and Caribbean Health Sciences Literature; and BDENF: Nursing Database.
Source: Prepared by the authors, 2022.
Figure 1. Selection Flow of Studies for the Integrative Review. Divinópolis (MG), Brazil, 2022.

Given the number of approaches in the articles included in this review, the articles were stratified into thematic categories, with their major areas and subcategories, as presented in Chart 3, which describes the findings of each major area.

The 19 included articles were divided into three major areas and subdivided into categories defined as the recommended practices. The articles used in Chart 3 presented statements related to subcategories in the conclusions, which were shown to be effective for treating localized infections in hard-to-heal wounds.

Chart 3 was constructed by reading the 19 articles and separating them into distinct themes related to recommended practices. It is important to note that complementary literature searches, including international consensuses and guidelines, were necessary.

DISCUSSION

Regarding the nationality of the studies, it is worth noting that each continent develops practices according to local and cultural realities, which are determining and qualifying factors for the efficiency of interventions and actions in treating localized infections in hard-to-heal wounds. However, it was observed that there is a lack of research in this area in Brazil.

We highlight the quality of the studies included in this research as a requirement for the selection of studies with a high level of evidence. In vitro and case studies did not meet the article selection standards.

To discuss the practices evidenced in this research, we highlight the following items: wound hygiene, identification and treatment of biofilms, and the use of dressings and solutions with antimicrobial action..

Chart 2. Characterization of the Studies Included in the Literature Review Regarding Title, Year, Country of Origin, Objective, Population, Location, Type of Study, Level of Evidence, and Result. Divinópolis (MG), Brazil, 2023.

Study Identification	Study/Country of Origin	Objective	Population	Location	Type of Study	Level of Evidence	Result
A1	Chang et al.[9] Australia	Review the application of bacteriophages for wound infections.	Studies on infected wounds	International literature	Literature review	Level IV	Bacteriophages are buffered topical solutions that have been studied as an alternative to the topical use of other antimicrobial products. Phage therapy in liquid, semi-solid formulations, liposome-encapsulated, and phage-immobilized dressings has been used safely and effectively in clinical studies, primarily in acute and chronic wounds infected by multi-resistant microorganisms.
A2	Dissemond et al.[10] German	Describe wounds treated with a polyabsorbent silver dressing and evaluate the short-term clinical impact of the dressing on the wound healing process under real conditions.	2,270 patients	81 centers in Germany	Multicenter prospective observational study	Level III	The average duration of dressing application was 13 to 22 days. In chronic wounds, there was an improvement in the healing process in 90.6% of cases, stabilization in 6.1%, and aggravation in 3.2%.
A3	Wei et al.[11] China	Review the diagnosis of biofilms in chronic wounds and discuss current treatment approaches.	Studies involving patients with chronic wounds and biofilm	International literature	Literature review	Level IV	Effective diagnostic techniques for biofilms were electron microscopy and laser scanning confocal microscopy. Therapeutic strategies include debridement, negative pressure, ultrasound, topical antimicrobials, silver dressings, and hyperbaric oxygen therapy.
A4	Adis Medical Writers[12] New Zealand	Review literature on the treatment of infected venous ulcers.	Studies involving patients with infected venous ulcers	International literature	Literature review	Level IV	Antimicrobial treatment is not routinely indicated and should be reserved for cases with clinical evidence of infection. Therapeutic options include systemic antibiotics, topical antibiotics and antiseptics combined with standard wound hygiene treatment, the use of dressings, and compression therapy.

Continue...

Chart 2. Continuation.

Study Identification	Study/Country of Origin	Objective	Population	Location	Type of Study	Level of Evidence	Result
A5	Madhusudhan[13] India	Analyze the use of 1% acetic acid as the sole antimicrobial agent for treating wound infections caused by Pseudomonas aeruginosa.	32 patients with chronic wounds infected by Pseudomonas aeruginosa.	Department of Plastic Surgery, Christian Medical College, Vellore, India	Prospective randomized controlled clinical trial	Level I	A six-month study compared wound cleaning with acetic acid to saline solution. In the group that used 1% acetic acid for cleaning, P. aeruginosa was eliminated in 4 to 5 days, while in the saline solution group, the average was 11.5 days. Topical 1% acetic acid was more effective than saline solution in eliminating P. aeruginosa in infected wounds.
A6	Jeong et al.[14] South Korea	Evaluate the combined use of negative pressure therapy and acetic acid irrigation in the treatment of chronic infected wounds.	Three patients, all with treatment-refractory wounds (>3 weeks)	Department of Plastic and Reconstructive Surgery, Kangnam Sacred Heart Hospital, Hallym Medical Center	Randomized controlled clinical trial	Level I	By combining acetic acid irrigation with negative pressure therapy, both the pH and size of chronic wounds can be reduced and infections controlled, improving angiogenesis and collagen synthesis.
A7	Lenselink e Andriessen[15] Netherlands	Assess the clinical efficacy of a medication containing biocellulose dressing with polyhexanide for eradicating biofilms in non-healing wounds.	16 patients with non-healing wounds	Medical Center Haaglanden	Cohort	Level III	In 24 weeks, 12 wounds (75%) healed. Of those that did not progress to healing, the average wound area was reduced by 61% at week 24. Ten patients (63%) experienced a reduction in biofilm. The continuous application of PHMB, using a biocellulose dressing, reduced biofilm in stagnant wounds, promoting healing.
A8	Cwajda-Białasik et al.[16] Poland	Analyze, evaluate, and systematize the available scientific evidence on the efficacy and safety of antiseptic preparations intended for the treatment of chronic wounds.	Literature review of clinical trials	International literature	Systematic review of clinical trials	Level I	The new generations of antiseptics and antimicrobials are effective in both the prevention and treatment of infections. These products should not be used on clean or colonized wounds. Antiseptics are recommended for wounds showing clinical symptoms of infection, at risk of infection, and in patients with immune system disorders or concomitant chronic diseases. Octenidine solution (OCT/PE, 0.1%) is recommended for the treatment of chronic wounds and ulcers. For cleaning, we recommend irrigation fluids based on OCT, PHMB, or hypochlorite. Maintaining the antimicrobial effect during therapy should be ensured by a compatible dressing that sequesters microorganisms and/or contains an antibacterial substance.
A9	Walker et al.[17] England	Evaluate the efficacy of a new-generation antimicrobial hydrofiber dressing with silver.	113 patients	33 healthcare units in 15 countries, between May and October 2013	Multicenter, international non-randomized clinical trial	Level III	The hydrofiber dressing with silver showed efficacy in the healing of the studied wounds, achieving partial or total healing. The dressing helps to eliminate the biofilm barrier.

Continue...

Chart 2. Continuation.

Study Identification	Study/Country of Origin	Objective	Population	Location	Type of Study	Level of Evidence	Result
A10	Percival et al.[18] Manchester and Oxford (United Kingdom), Rome (Italy), and Geneva (Switzerland)	Support clinical practice by developing an algorithm to demonstrate evidence of biofilm presence in a wound to aid in its treatment.	Literature review	International literature	Literature review	Level IV	The algorithm was created to assist in identifying biofilms in stagnant or non-healing chronic wounds and to guide treatment. The items in the algorithm refer to clinical procedures, the presence of necrotic tissue, signs of infection and inflammation, and response to topical antimicrobial interventions. Biofilm elimination measures include debridement and antimicrobial therapy. The topical antimicrobials considered effective are: polyhexamethylene biguanide hydrochloride, benzalkonium chloride, silver, iodine, and chlorhexidine.
A11	Dalac et al.[19] France	Evaluate the efficacy, safety, and acceptability of a new polyabsorbent silver dressing in managing chronic exudative wounds at risk of infection and with inflammatory signs suggestive of a high bacterial load.	37 patients with chronic wounds	General Hospital (Argenteuil)	Prospective, multicenter, non-comparative clinical trial	Level I	The study demonstrated that the dressing contributed to the healing process by reducing the wound surface area, rapidly decreasing inflammatory signs and slough tissue, and providing real clinical benefit for chronic wounds at risk of infection.
A12	Hurlow et al.[20] Estados United States	Analyze wound biofilm from a clinical perspective.	Debridement samples from human wounds were collected from adult patients with chronic wounds	Memphis, Tennessee	Descriptive study	Level IV	Some visual signs that may suggest the existence of biofilm include a yellowish, whitish, or grayish layer on the wound surface, unpleasant odor, and stagnation in the healing process despite appropriate treatment.
A13	Lipsky et al.[21] United States	Treatment of infection in the feet of people with diabetes.	Literature review	International literature	Literature review	Level IV	Infections in the feet of patients with diabetes cause high morbidity, require frequent visits to healthcare professionals, and can lead to the amputation of a lower limb. These infections require local (foot) and systemic (metabolic) care, coordinated by a multidisciplinary foot care team, considering proper wound cleaning, debridement of any callus and necrotic tissue, and especially pressure reduction. Most of these infections require the use of systemic antibiotics.

Continue...

Chart 2. Continuation.

Study Identification	Study/Country of Origin	Objective	Population	Location	Type of Study	Level of Evidence	Result
A14	Jørgensen et al.[22] Denmark	Investigate the clinical performance and safety of a new wound contact layer containing silver and hydrocolloid particles and petrolatum in the treatment of chronic venous leg ulcers with delayed healing and signs of critical colonization.	30 patients	Wound Healing Center of Copenhagen	Multicenter, prospective, non-comparative, open clinical study	Level I	The silver-impregnated dressing has been shown to be safe and easy to use in chronic venous leg ulcers with difficult healing and signs of localized infection.
A15	Banu et al.[23] United States	Determine if the topical use of Aloe vera gel has antibacterial activity in leg wounds infected with multi-resistant bacteria.	30 patients	Tertiary hospital affiliated with a medical school	Prospective interventional study	Level II	Out of 30 cases, 28 showed no microbial growth at the end of 11 days, while 2 cases did not show a decrease in bacterial count. The gel has a 100% inhibitory effect on P. aeruginosa and Staphylococcus aureus. Aloe vera proved to be effective, low-cost, and easily available compared to modern dressings.
A16	Moore[4] United States	Compare calcium alginate dressing with hydrofiber silver ulcer dressing.	19 patients	USA	Randomized, prospective, multicenter, open study	Level I	Both dressings demonstrated ease of use, absorption, and adherence to the wound bed. They were effective for treatments incorporating debridement and compression therapy. Ulcer closure rates were consistent.
A17	Jørgensen et al.[24] Denmark	Investigate the effect of sustained-release silver foam dressing compared to foam dressing without added silver in venous leg ulcers.	129 patients	Wound Healing Center of Copenhagen	Multicenter, open, randomized, controlled study with a duration of four weeks	Level I	The present study provided evidence of the superior performance of the silver-releasing dressing compared to traditional moist foam dressing in healing wounds in the treatment of chronic venous ulcers with localized infection.
A18	Lipsky e Hoey[25] United States	Review pertinent concepts regarding the consideration of topical antimicrobial therapy, describe currently available agents, and offer suggestions on when they may be useful.	Literature review	International literature	Literature review	Level IV	Topical antimicrobial therapy, although currently not advisable for most clinically non-infected chronic wounds, has its role in specific circumstances. Evidence supports its use in burns and malodorous wounds. There is no consensus on how to treat hard-to-heal wounds with signs of infection. Cadexomer iodine or silver dressings are preferable to topical antibiotics, especially those available for systemic use.
A19	Amirrah et al.[26] Malaysia	Analyze the efficacy of collagen-based antibacterial dressing for treating diabetic foot ulcers in a clinical setting.	Literature review	International literature	Literature review	Level IV	The evidence was not robust enough for a conclusive statement due to the small sample size, although most studies reported positive results for the use of collagen dressings loaded with antibacterial properties for healing diabetic foot wounds.

Note: BVS: Virtual Health Library; LILACS: Latin American and Caribbean Health Sciences Literature; MEDLINE/PubMed: National Library of Medicine and National Institutes of Health; CINAHL: Cumulative Index to Nursing and Allied Health Literature; SciELO: Scientific Electronic Library Online; IBECS: Spanish Bibliographic Index of Health Sciences.
Source: Prepared by the authors, 2023.

Chart 3. Categorization of Topics Addressed in the Articles Included in the Study.

Recommended Practices		
Topics	Major Area	Subcategories
A5, A6, A13	Wound Hygiene	Cleaning is one of the components of hygiene and is fundamental for bed preparation. It involves the active removal of surface contaminants, loose debris, non-adherent non-viable tissue, microorganisms, and/or remnants of previous dressings from the bed and perilesional skin. Debridement of the bed, reconstruction of the edges, and use of anti-biofilm dressings complete the hygiene process.
A3, A10, A12	Identification and Treatment of Biofilms	Identify biofilm signs through local indicators, electron microscopy, or laser scanning, and establish early treatment.
A1, A2, A4, A7, A8, A9, A11, A14, A15, A16, A17, A18 e A19	Use of Antimicrobial Dressings and Solutions	Solutions and dressings with antimicrobial and anti-biofilm action contribute to the treatment of localized infections in hard-to-heal wounds. The highlighted solutions in this review were: 1% acetic acid solution for cleaning, irrigation with OCT, PHMB, or hypochlorite, polyabsorbent silver dressings, bacteriophages, products and solutions with polyhexamethylene biguanide (PHMB) hydrochloride, benzalkonium chloride, silver, cadexomer iodine or chlorhexidine (biocellulose dressings with PHMB, hydrofiber dressings with silver), and Aloe vera gel.

Wound Hygiene

Wound hygiene aims to remove factors detrimental to the healing process. The concept of wound hygiene involves four stages: cleaning, debridement, edge reconstruction, and dressing application[1,27].

Cleaning is a crucial element in wound treatment as it removes contaminants and necrotic tissue from the wound surface and surrounding skin, preparing the wound for natural healing processes, helping to prevent infections, and regenerating tissues[1].

The debridement method to be used depends on the evaluation of the wound bed, perilesional skin, pain, and patient tolerance[1]. This stage is essential in the wound hygiene process and should be performed on all hard-to-heal wounds1.

The reconstruction of wound edges plays an essential role in complete hygiene1. In deep wounds, primary cells essential for epithelialization tend to concentrate at the edges and hair follicles. The biofilm is also more active in these regions, which can hinder the formation of new and healthy tissue[1].

The use of antimicrobial dressings should be reevaluated at least every two weeks to determine their clinical use. However, it is necessary to implement an anti-biofilm strategy to clean the wound throughout the healing process1.

Identification and treatment of biofilms

Biofilm poses a serious threat to wound healing and can reform in less than 24 hours. It consists of a conglomerate of multiple species of microorganisms. The increase in the number and complexity of microorganisms in the wound heightens the risk of infection[7,10].

Biofilm is primarily located in the wound bed and can be found in deeper tissues and edges. To confirm its presence, as it is not visible to the naked eye, advanced microscopy and molecular biology techniques are necessary[2,27].

However, due to the impracticality of accessing these technologies in many healthcare institutions, it is proposed to assume the presence of biofilm in hard-to-heal wounds; it is necessary to remove it to promote healing[7,10].

Clinical signs of biofilm presence include exudate, visible necrosis or necrotic tissue, and wounds with slough, which can also increase the risk of biofilm proliferation and contribute to resistance to antimicrobial treatments1. According to the literature, microbiological staining techniques and wound biopsy sampling are currently available to assist in diagnosis[19].

Use of antimicrobial dressings and solutions

Bacteriophages are topical solutions that have been studied as alternatives to conventional antimicrobial products[9]. Phage therapy, available in liquid, semi-solid formulations, and encapsulated in liposomes, as well as phage-immobilized

dressings, has been used safely and effectively in clinical studies[9]. This approach has shown promising results, especially in treating acute and chronic wounds infected by multi-resistant microorganisms[9].

Solutions containing benzalkonium chloride applied to localized infections in hard-to-heal wounds can be toxic and interfere with the healing process. Therefore, they should be used cautiously and supervised by a qualified professional to maintain antimicrobial efficacy and result in proper skin healing[18].

Among the studies presented, silver-based solutions have powerful antimicrobial properties capable of combating numerous microorganisms, even in localized infections in hard-to-heal wounds, promoting an appropriate healing environment. It is important to note that all antimicrobials should be used appropriately, as they may cause adverse reactions impacting treatment[4,10,11,18,19,22,24,25].

Cadexomer iodine or chlorhexidine are effective agents due to their antimicrobial action, promoting a suitable environment for healing. Chlorhexidine, in particular, is also used for cleaning and disinfecting the skin around the wound[18].

Among the antiseptic preparations currently available on the market, octenidine (OCT/PE, 0.1%) stands out as an effective and safe option. Unlike PVP-I, this substance can be used in the treatment of hard-to-heal wounds with localized infection. For cleaning purposes, octenidine-based irrigation solutions, PHMB, or hypochlorite are recommended[17].

In a study involving 37 patients with hard-to-heal wounds, the efficacy of polyabsorbent silver dressings was observed, suggesting a clinical benefit for infected wounds due to the reduction in wound surface area, rapid decrease in inflammatory signs, and removal of necrotic tissue[19].

Irrigation with 1% acetic acid was effective for treating localized infection. According to laboratory results of immunostaining and polymerase chain reaction, the combined treatment of 1% acetic acid and negative pressure dressings increased CD31 and KI-67, procollagen, and vascular endothelial growth factor, leading to angiogenesis. The result was a reduction in the wound bed and pH, controlling the localized infection9.

In a multicenter, open, randomized study involving 129 participants over four weeks, the efficacy of prolonged-release silver foam dressings in treating infected venous ulcers was investigated compared to traditional foam dressings without additional silver. The results revealed that the group treated with prolonged-release silver foam dressings significantly reduced odor, exudate volume, and wound maceration. Thus, silver-impregnated foam proved to be an effective option in treating ulcers[24].

In this section, we present two studies. The first is a multicenter randomized study involving 60 patients followed for three months[23], which evaluated the efficacy of Aloe vera gel in treating infected venous ulcers and quantified the bacterial presence in the wound bed. The results demonstrated the efficacy of Aloe vera combined with antimicrobial agents, reducing bacterial colonization in about 90% of the participants in the group using Aloe vera oil[13].

The second study is a multicenter non-randomized study involving 121 patients followed for four weeks17, which evaluated the efficacy of a multilayer dressing in treating infected venous ulcers. The result was a 30% reduction in treatment costs with antimicrobial agents[14].

In another study using polyhexanide, 28 patients with localized infections in hard-to-heal wounds were evaluated over 24 weeks. Seventy-five percent of the wounds healed; of the 25% that did not heal, only 6% did not show a reduction in the wound bed[15]. Noteworthy results included a reduction in chronic pain, as reported by all participants[15]. Thus, we can conclude that the dressing is effective for wounds with light to moderate exudate. There were no reports on the dressing's permeability[15].

Furthermore, the articles presented in the literature describe recommended practices for treating localized infections in hard-to-heal wounds. However, the inclusion of this topic in Brazil is seldom addressed, highlighting the need to evaluate these practices within the context of Brazilian reality.

Study limitations

This integrative review presented limitations regarding the database search, as a high number of in vitro studies were found, which were not included in the research because they did not meet the quality level proposed in the review.

CONCLUSION

Localized infection in hard-to-heal wounds represents a risk factor for the healing process and is a common concern in healthcare. The main strategies for treatment involve the hygiene process, early identification and treatment of biofilm, and the topical use of antimicrobial solutions and dressings. The study identified evidence of these practices and products; however, it is worth noting that most were literature reviews, and these recommendations may have their efficacy related to the culture and conditions in which they were developed. Future research with a higher level of evidence and conducted on the Brazilian population is necessary.

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