

Topical therapies for pressure wound healing: identifying the effectiveness in research of the last five years

Terapias tópicas para cicatrização de lesão por pressão: identificando a efetividade em pesquisas dos últimos cinco anos

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Vasconcelos AF, Nascimento TSV, Dias RS, Nunes MPV, Leardini GM, Araújo GSS, Rodrigues DAS, Macedo ABT. Topical therapies for pressure wound healing: identifying the effectiveness in research of the last five years / *Terapias tópicas para cicatrização de lesão por pressão: identificando a efetividade em pesquisas dos últimos cinco anos*. Rev Med (São Paulo). 2023 Nov-Dec;102(6):e-209828.

ABSTRACT: Objective: to identify in the scientific literature the evolution of topical therapies for healing pressure injuries in adults. **Method:** This is an integrative review built in six stages, carried out in the BVS, SciELO, PUBMED and Google Scholar databases. The descriptors were “Pressure injury” and “Healing” separated by the Boolean AND operator. Clinical trials published from 2018 to February 2023 were included, and duplicate articles or those that are not available in full were excluded. For screening, a synoptic table was constructed and the data were analyzed descriptively. **Results:** The identification evolved in 424 articles and the final sample in 17 scientific productions, 16 (94.1%) in English. Therapies tested in the last five years were topical natural medications and extracts, blood derivatives, electrical stimulation, gelatin and low-intensity laser therapy. Identified himself competed in 16 (94.1%) of the standard treatments in selected publications. **Conclusion:** It is identified that combined therapies, in addition to the conventional dressing, accelerate the healing process of PI, contribute to the reduction of chronic injuries and bring about improvements in the quality of life of affected patients.

DESCRIPTORS: Pressure Ulcer; Wound Healing; Therapeutic; Review.

RESUMO: Objetivo: identificar na literatura científica a efetividade de terapias tópicas para a cicatrização lesão por pressão em adultos. **Método:** Trata-se de uma revisão integrativa construída em seis etapas, realizada nas bases de dados BVS, SCIELO, PUBMED e Google Acadêmico. Os descritores foram “Lesão por pressão” e “Cicatrização” separados pelo operador booleano AND. Foram incluídos ensaios clínicos publicados de 2018 a fevereiro de 2023, e excluídos artigos duplicados ou que não estivessem disponíveis na íntegra. Para a extração foi construído um quadro sinóptico e os dados foram analisados de forma descritiva. **Resultados:** A identificação resultou em 424 artigos e a amostra final em 17 produções científicas, sendo 16(94,1%) em inglês. As terapias testadas nos últimos cinco anos foram medicações e extratos naturais tópicos, derivados sanguíneos, estímulo elétrico, gelatina e terapia a laser de baixa intensidade. Identificou-se efetividade em 16 (94,1%) dos tratamentos propostos nas publicações selecionadas. **Conclusão:** Identifica-se que terapias combinadas, além do curativo convencional, aceleram o processo de cicatrização das LP, podendo contribuir para redução de lesões crônicas e trazer melhorias na qualidade de vida dos pacientes acometidos.

DESCRIPTORES: Lesão por pressão; Cicatrização; Terapêutica; Revisão.

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INTRODUCTION

Pressure injury (PI) is caused by damage to the skin and underlying tissues mainly due to pressure, shear or other factors that lead to disruption of integrity. The incidence of PI is a global problem, at all levels of health care, resulting in significant financial burdens for health systems, with increased investment in materials, equipment, medicines, surgical procedures and hospitalization time. Promoting skin health and preventing PI are still the best way¹.

The prevalence of PI in health institutions varies from 0 to 72.5%, with wide differences depending on geographic location and the scenarios researched². In Brazil, studies on this issue are still in the early stages, but between 2020 and 2021, PIs were the most reported adverse events, totaling approximately 50,000 cases³. In the United States of America (USA), it is estimated that around 2.5 million individuals are affected annually⁴.

The wound healing process involves a complex interaction between various types of cells, cytokines, mediators and the vascular system, and in some cases it can be slow and painful⁵. Dressings are used in the treatment of PI in order to promote healing, and there are currently many primary coverage options on the market. Some topical agents have also been used as an alternative to promote healing. To properly use this range of options, health professionals need a basis in scientific evidence to facilitate decision-making in the ideal choice for the treatment of LP⁶.

In recent years, the insertion of new technologies aimed at PI healing has optimized the wound healing process and provided patients with better recovery. It is known that the use of combined treatments accelerates healing, depending on the stage and degree of tissue destruction. However, the use of the wide variety and availability of materials that enable better adaptation and management of different types of wounds requires specialized knowledge in the area⁷.

Low-power laser therapy (TLBP), negative pressure therapy (NPT), use of blood derivatives, ozone therapy, in addition to coverage with a combination of compounds has been gaining visibility. However, some of these therapies are not easily accessible to the population and health professionals do not know their effects. TPN, for example, is a treatment that promotes healing in a humid environment through controlled and locally applied subatmospheric pressure, composed of an interface material (foam or gauze), removing excessive exudate. It is a treatment with many benefits, but with high costs².

The advancement of strategies for the prevention and treatment of PI is emphasized, covering the use of prophylactic dressings, such as silicone dressings, and therapeutic dressings such as creams, ointments and gels. In recent studies, these dressings demonstrated clinical

effectiveness in the prevention and treatment of PI in specific populations, taking into account the context in which the studied patients found themselves⁸. Thus, this study is justified by the need to produce scientific knowledge and identify in the literature the effectiveness of therapies tested in the last five years, providing a basis for professionals and filling possible gaps on the topic.

In view of the above, the study aims to identify in the scientific literature the effectiveness of topical therapies for healing pressure injuries in adults.

METHOD

This is an integrative literature review (IR), organized in the following stages: formulation of the research question, bibliographic search, data extraction, critical evaluation, analysis and summary of studies and synthesis of knowledge⁹.

The formulation of the guiding question took place with the support of the PICO strategy (acronym for P - population, I - intervention/area of interest, C - comparison and O - result/outcome)¹⁰. Where the population was adults with LP; intervention sought therapies for PI treatment; comparison at the author's discretion, which may be placebo or another therapy; and results/outcomes of interest were effectiveness in PI healing. Therefore, the guiding question was defined as follows: "What evidence is available in the scientific literature over the last 5 years on the effectiveness of topical therapies for PI healing in adults?"

The search for studies took place in February 2023 in the databases that make up the Virtual Health Library (VHL), the Scientific Electronic Library Online (SCIELO), Medline via PUBMED and Google Scholar. The choice of databases considered the scope and affinity with the topic. The data search in Medline via VHL versus PUBMED presented divergent results. For this reason, we decided to analyze the results of both search engines.

Aiming at a broad search in the literature, the strategies combined the controlled descriptors "pressure injury" and "scarring", in English, Spanish and Portuguese, which were selected through research in the Descriptors in Health Sciences (DECS), combined through of the Boolean operator AND. The terms were searched in the title and summary of publications in the databases that allowed this selection.

Original articles from randomized or non-randomized clinical trials, in English/Spanish/Portuguese, published between 2018 and 2023, that dealt with the research topic were included. Publications presented in the form of thesis, dissertation, editorials, review articles, manuals, protocols, book chapters, reflections, opinions or comments from experts, case reports, as well as duplicate publications in the databases, which were not included, were excluded. referred to the research topic or

population or did not answer the guiding question. Studies that evaluated multiple types of injury without separately presenting the result on LP, as well as animal studies, were also excluded.

There were three moments of exclusion: first of duplicate publications by evaluating the titles, in a second stage by reading the title and abstract and finally, after reading the texts in full. For mapping, publications were exported to Excel® software and organized and summarized in a form created by the authors. The data summary will be presented in a flowchart constructed with the support of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)¹¹ protocol and the reporting of the results of the articles in tables with descriptive analysis.

In analyzing the level of evidence of the studies, the

classification according to Melnyk, Fineout-Overholt¹² was used. Regarding clinical trials, the design included in this study, level II indicates a randomized controlled clinical trial and III non-randomized. Ethical aspects were respected, with reliable citation of the authors' sources and definitions.

RESULTS

424 publications were identified. Figure 1 shows the stages of study selection. After selecting 26 articles for full reading, 5 were still excluded for not being available in full and 4 for not answering the research question during evaluation by the reviewers. The sample consisted of 17 clinical trials.

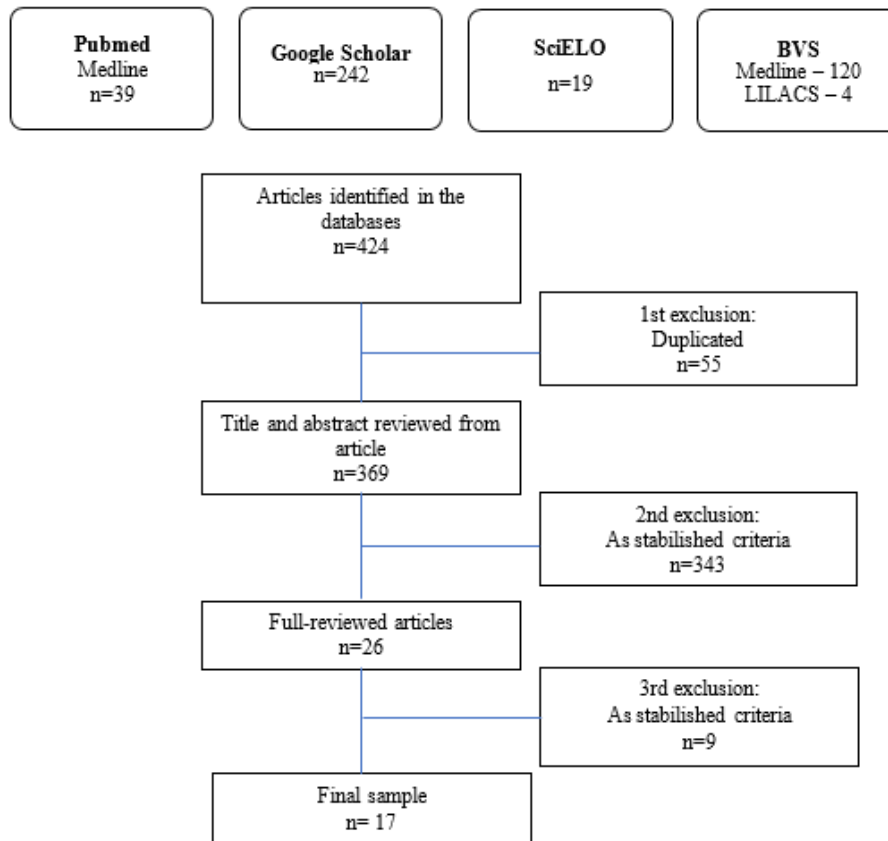


Figure 1 - Flowchart of selection of primary studies, according to the PRISMA recommendation. Teresina – PI, Brazil, 2023

Table 1 presents the characterization of the selected studies regarding authorship, year, country and journal of publication, language and objective of the study. There were 6 (35.3%) publications from the year 2022, two

(11.8%) from 2021, three (17.6%) from 2020, two (11.8%) from 2019 and 4 (23.5%) in 2018, 16 (94.1%) in English. Table 2 presents study data, such as number of participants, therapy tested and results found.

Table 1 - Characterization of studies according to authorship, year and country of publication, periodical, language and objective. Teresina – PI, Brazil, 2023

N	Author/ Year of publication	Periodical	Language country	Main objective of the study
01	Yoshikawa Y et al., 2022 ¹³	Prog Rehabil Med	English Japan	Verify the effect of electrical stimulation therapy on LP.
02	Avendaño-Coy J et al., 2022 ¹⁴	Int J Environ Res Public Health	English Spain	To evaluate the effectiveness of microcurrent therapy for PI healing.
03	Verdú-Soriano J et al., 2022 ¹⁵	J Clin Med	English Spain	Test the effect of the gel with <i>Olea europaea</i> leaf extract (EHO-85).
04	Yang J et al., 2022 ¹⁶	Comput Math Methods Med	English China	To explore the effectiveness of computed tomography to evaluate the effect of PRP combined with TPN in the treatment of LP.
05	Ghanadian M et al., 2022 ¹⁷	Int J Low Extrem Wounds	English Iran	To evaluate the clinical efficacy of <i>Plantago</i> hydroalcoholic extract. major in the healing of diabetic foot ulcers and LP.
06	Oliveira ER et al., 2022 ¹⁸	BJD	Portuguese Brazil	To evaluate results of TLBI in LP healing.
07	Liu Q et al., 2021 ¹⁹	Clinics	English Brazil	To analyze the results of PRP gel on LP healing time and quality of life.
08	Zolfagharneshad H et al., 2021 ²⁰	Am J Ther	English Iran	To investigate the effect of topical application of 3% nifedipine on LP healing.
09	Huang S et al., 2020 ²¹	Medicine	English China	To investigate the effectiveness of gelatin sponge combined with nursing intervention in LP healing.
10	Baek W et al., 2020 ²²	Pharmaceutics	English Switzerland	Evaluate the effectiveness of TPN with polyester mesh versus conventional TPN
11	Uçar Ö; Çelik S. 2020 ²³	Int Wound J	English Turkey	Compare the effects of PRP gel in relation to saline dressing in LP.
12	Polak A et al., 2019 ²⁴	Wound Manag Prev	English Poland	To determine the effect of high-voltage anodal and cathodal electrical stimulation on the serum concentration of cytokines and growth factors in patients with LP.
13	Mari W et al., 2019 ²⁵	Wounds	English England	To evaluate healing with the use of a natural porcine extracellular matrix with TPN in stage 4 LP.
14	Ala S et al., 2018 ²⁶	Am J Ther	English USA	To evaluate the effectiveness of topical sucralfate in the management of LP.
15	Najafi E et al., 2018 ²⁷	J Wound Care	English UK	Observe the effects of topical Pentoxifylline in critical patients and with LP
16	Tarada J et al., 2018 ²⁸	Int J Med Sci	Inglês EUA	To analyze the results of different wavelengths of laser therapy on growth factors related to LP healing.
17	Polak A et al., 2018 ²⁹	Physical Therapy	English England	To evaluate the effects of cathodic and anodic high voltage single-phase pulsed current on reducing LP size.

LP: pressure injury; PRP: Platelet-rich plasma; TPN: Negative pressure therapy; USA: United States of America; TLBI: low intensity laser
Source: survey data, 2023

Table 2 – Effect of therapies in the treatment of pressure injuries. Teresina – PI, Brazil, 2023

N	Level of evidence; sample and study location	Treatment protocol	Results
01 ¹³	NII; GI 6, GC 6 patients; Hosp. from Japan	Electrical stimulation therapy once a day for 60 min, six times a week for 2 weeks.	There was a difference in healing rates $p = 0.002$ and contraction rates $p =$ in GI versus CG
02 ¹⁴	NII; GI 15, CG 15 patients; Nursing homes in Spain	TIME protocol and 10 h/day of microcurrents for 25 consecutive days or until healing	the reduction in wound area was 28.6% greater in GI
03 ¹⁵	NII; GI 103, CG 92 patients; Spanish health center	Application of hydrogel with Olea europaea leaf extract (EHO-85) 3 times a week, up to 8 weeks	The GI doubled the reduction in wound area versus the CG ($p < 0.001$).
04 ¹⁶	NII; 21 patients per group; China Hospital	A group; GC GB: PRP every 3 days, GC: weekly TPN GD: weekly PRP+TPN	Healing time in DG was shorter than in groups A, B and C ($p < 0.05$).
05 ¹⁷	NII; GI 50, CG 44 patients; Hosp. from Iran	Plantago major hydroalcoholic extract applied once a day for two weeks.	GI showed a greater reduction in wound size in the first ($p < 0.001$) and second week ($p < 0.001$).
06 ¹⁸	NIII; CG 6 and GI 6 injuries; Hosp. de Belo Horizonte	TLBI twice a week for three months	There was a difference in healing in TLBI versus GC ($p < 0.001$).
07 ¹⁹	NII; GI 51, CG 51 patients; Hosp. from China	PRP(GC) gel versus PRP with TPN(GI) every 7 days, three times	The total efficacy rate in the GI was higher than in the CG ($p < 0.050$)
08 ²⁰	NII; GI 83, CG 83 patients; Hosp. from Iran	3% nifedipine ointment twice a day for 14 days	The decrease in the LP stage in the GI was greater than in the CG ($p < 0.001$)
09 ²¹	NII; GI 40, CG 40 patients; Hosp. from China	Daily gelatin sponge change	The intervention increased the healing efficiency.
10 ²²	NII; GI 19, CG 19 patients; Hosp. from Korea	TPN with and without non-adherent lipidocolloid dressing (Urgotul)	there was a reduction in wound size in the TPN group with dressing ($p = 0.001$)
11 ²³	NII; GI 30, CG 30 patients; Hosp. from Türkiye	PRP gel changed every 3 days for 2 months	area, exudate and tissue type scores decreased ($p < 0.001$).
12 ²⁴	NII; GA: anode 15, CG: cathodal 13 and GP (placebo) 15 patients; Hosp. from Poland	50 min. of high voltage single-phase pulsed currents on 5 days a week, for 8 weeks.	There was a difference between GA and CG ($p = 0.009$) and GA and GP ($p = 0.0054$).
13 ²⁵	NII; GI: 8 and CG 8 patients Does not indicate location	GI: dressing with porcine extracellular matrix (2/2 weeks and TPN (twice a week) versus CG: TPN, for 12 weeks	The mean cure rate in GI was higher than in CG $p < 0.01$
14 ²⁶	NII; GI 19 GC and 19 patients; Hosp. from Iran	Daily topical sucralfate for 14 days.	There was no significant difference in healing time ($p = 0.070$) and injury reduction ($p = 0.420$)
15 ²⁷	NII; GI 60 GC 62 patients; ICU in Iran	Topical pentoxifylline twice daily for 14 days	There was a difference between GI and CG in relation to healing ($p < 0.001$).
16 ²⁸	NII; GA: 17 GB Group: 18 GC Group: 16 GP (placebo): 17 patients; Medical centers, no country specified	Laser therapy with different wavelengths	The GA wavelength showed a difference in relation to the others, in all measurements ($p < 0.001$).
17 ²⁹	NII; GP (placebo) 20; GC: cathode 21, GA: anode 20; Hosp. from Poland	50 min. of high voltage single-phase pulsed currents 5 days a week, for 8 weeks.	reduction in wound area for GA ($p = 0.0391$) and CG ($p = 0.0024$) in relation to GP.

Legend: N: level; GI: Intervention group; CG: Control group; GP: Placebo group;
Source: Survey data, 2023

The therapies tested were derived from electrical current, medicinal and non-medicinal topical products, application of blood derivatives to the lesion, laser therapy, treatments combined with TPN and animal coverage. There was effectiveness in 16 (94.1%) tested therapies, when compared to the control group.

DISCUSSION

This study identified research with topical natural medications and extracts, blood derivatives, electrical stimulation, gelatin-based dressings and low-intensity laser therapy, with effectiveness in 16 (94.1%) of the treatments proposed in the selected publications. This result may support health professionals in the development of clinical protocols, as there are new technologies on the market for the treatment of PI, making it necessary, therefore, to have an understanding for an ideal therapeutic choice^{30,31}.

In two studies, natural medicine showed positive results^{15,17}. Plants have enormous potential for wound healing, having been used by indigenous peoples in many countries for thousands of years. Herbal products are considered more economical, more accessible and safe, and their therapeutic potential is due to the existence of active ingredients with pharmacological effects^{15,17}.

Among the biologically active substances in the different parts of the plant, there are alkaloids, saponins, tannins, glycosides, flavonoids and essential oils, the latter being widely used in the prevention and treatment of LP. In this sense, research is important because medicinal plants may contain active ingredients that cause allergic reactions or toxicity, showing that these substances, despite being natural, are likely to harm health, therefore, the correct preparation method must be indicated³¹. Topical medications have also been tested for PI healing^{20,26,27} with effective results for nifedipine and pentoxifylline. Nifedipine has a vasodilatory and antioxidant effect, improving circulation in the skin around the lesion and the LP²⁰. Used in the treatment of intermittent claudication, pentoxifylline is a xanthine derivative with several pharmacological characteristics. Its vasodilatory effect, improves peripheral blood flow and oxygenation, and due to its antithrombotic, fibrinolytic, anti-inflammatory effect, immunomodulatory and antioxidant properties, it is indicated for various pathologies, which makes pentoxifylline a drug with potential for the treatment of wounds²⁶.

Although the effectiveness of sucralfate was not identified in this study, it is known that it has antimicrobial and antioxidant effects, in addition to increasing blood flow and mucus formation. It has been used in wound healing in various ulcerative conditions, such as erythematous skin reactions caused by radiation, oral mucositis, diaper dermatitis, chronic venous ulcers, second and third degree burns, among others²⁶.

Blood derivatives were introduced as a therapy for LP with the aim of externally applying growth and healing factors, aiming for faster regeneration. PRP gel in PI care showed satisfactory results in the selected studies^{16,19,23}. This material is obtained from the patient's own blood, where cytokines, growth factors, chemokines and fibrin promote the production of collagen fibers, accelerating healing time. A study using PRP in LP showed a significant improvement in the type of tissue when compared to GC, in which a decrease in the amount of exudate and an increase in epithelialization was observed²³.

The gelatin sponge was also effective in healing LP, probably by maintaining a moist environment, conducive to healing. It is a water-insoluble, whitish, flexible material derived from leather or pig skin. It is an absorbable dressing used for hemostasis, which acts by promoting the breakdown of platelets, which releases clotting factors, resulting in blood clotting²¹.

Topical medications have also been tested for PI healing^{20,26,27} with effective results for nifedipine and pentoxifylline. Nifedipine has a vasodilatory and antioxidant effect, improving circulation in the skin around the lesion and the LP²⁰. Used in the treatment of intermittent claudication, pentoxifylline is a xanthine derivative with several pharmacological characteristics. Its vasodilatory effect, improves peripheral blood flow and oxygenation, and due to its antithrombotic, fibrinolytic, anti-inflammatory effect, immunomodulatory and antioxidant properties, it is indicated for various pathologies, which makes pentoxifylline a drug with potential for the treatment of wounds²⁶.

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LIMITATIONS OF THE STUDY

A limitation of this study is the diversity of methods for evaluating PI healing, some studies with small samples and some publications lacking important information, such as detailed statistical analysis, for example.

CONTRIBUTIONS TO PRACTICE

The availability of this material with the mapping and summary of therapies with effective results will contribute to increasing the knowledge of health professionals and, consequently, the quality of life of patients affected by PI. It will also serve to assist professionals when choosing

which treatment to use, providing support for care practice.

CONCLUSION

This review identified the effectiveness of therapies for PI healing in adults in the scientific literature of the last 5 years. Effective treatments allow optimizing the healing of chronic injuries, reducing damage. Few studies were identified in Brazil, which may be related to the high cost of current therapies, as many are imported.

The importance of investing in new research and testing the effectiveness of therapies at a reduced cost is highlighted, facilitating access for the population. It is also recommended that universities and public hospitals commit to organizing research that takes into account the situation of the Brazilian population.

Authorship contribution: Conception or design of the study: Vasconcelos, AF; Nascimento, TSV; Dias, RS; Nunes, MPV; Leardini, GM; Araújo, GSS; Rodrigues, DAS; Macedo, ABT. Coleta de dados: Vasconcelos, AF; Nascimento, TSV; Dias, RS; Nunes, MPV; Leardini, GM; Araújo, GSS; Rodrigues, DAS; Macedo, ABT. Análise e interpretação dos dados: Vasconcelos, AF; Nascimento, TSV; Dias, RS; Nunes, MPV; Leardini, GM; Araújo, GSS; Rodrigues, DAS; Macedo, ABT. Redação do artigo ou revisão crítica: Vasconcelos, AF; Nascimento, TSV; Dias, RS; Nunes, MPV; Leardini, GM; Araújo, GSS; Rodrigues, DAS; Macedo, ABT. Aprovação final da versão a ser publicada: Vasconcelos, AF; Nascimento, TSV; Dias, RS; Nunes, MPV; Leardini, GM; Araújo, GSS; Rodrigues, DAS; Macedo, ABT.

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Received: 2023, March 24

Accepted: 2023, November 21