Low-level laser dosimetry for venous ulcer healing: a protocol for systematic review

RESUMO

Objetivo: Analisar a dosimetria do laser de baixa intensidade no processo de cicatrização de úlcera venosa. Método: Trata-se de um protocolo de revisão sistemática registrado no International Prospective Register of Systematic Reviews (PROSPERO) sob código de registro CRD420211256286. Serão realizadas buscas por evidências científicas em 11 bases de dados, utilizando os idiomas português, inglês e espanhol. A exportação das publicações seguirá as etapas de identificação e seleção dos estudos, e extração dos dados. As divergências serão resolvidas por consenso dos dois revisores, e caso persistam, um terceiro revisor será consultado para decidir sobre a inclusão do material. A ferramenta Risk of Bias 2 (RoB 2) será utilizada para avaliar o risco de viés dos ensaios clínicosrandomizados, ao passo que a ferramenta Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) será utilizada para avaliar o risco de viés dos ensaios clínicos não randomizados. A análise crítica dos materiais selecionados quanto à dosimetria do laser de baixa intensidade para cicatrização de úlcera venosa resultará em uma síntese narrativa, sem metanálise.

Descritores: Terapia com Luz de Baixa Intensidade; Úlcera Varicose; Revisão Sistemática.

INTRODUÇÃO

The increase in longevity, the chronicity of diseases, and the incidence and prevalence of skin problems make venous ulcers (VUs) one of the most relevant public health issues worldwide(1). They are characterized by circumscribed or irregular loss of epidermis and dermis, potentially extending into the subcutaneous tissue, and account for 70% to 90% of lower extremity ulcers, with a lifetime prevalence of 0.1% to 2% in the global population. However, this number may be underreported(2). The gold standard for treating VU is elastic or inelastic com-
pression\(^3\). However, treatment can last more than 12 months, negatively impacting patients’ quality of life and high healthcare costs\(^4\). Therefore, there is interest in using lasers to treat VUs. Low-level laser therapy (LLLT) shows promising results in patients with ulcers\(^2\). Its use is safe and valuable in wound treatment due to its wound-healing, anti-inflammatory, analgesic, and edema-reducing effects, reducing the recurrence rate of deep ulcers\(^5\-6\). In addition, a systematic review of the effects of LLLT on ulcers due to diabetic vasculopathy suggests that adjuvant therapy may improve neovascularization and minimize the risk of complications\(^7\).

Light Amplification by Stimulated Emission of Radiation (LASER) uses electromagnetic radiation, which differs from normal light due to its specific physical properties. It comprises a collimated, monochromatic, coherent light beam\(^8\). Dosimetry is used for therapeutic purposes and is directly related to the interaction of light with tissue. It corresponds to the energy required to be deposited in a specific area to produce the desired effect. The safety of dosimetry is established based on criteria such as irradiance or power density, beam area, fluence or energy density, radiation exposure, radiant energy or radiant power, and time. These parameters vary depending on the equipment used, the technique used (pulsed or continuous, scanning or spot), and the size of the irradiated area\(^9\).

Patients with VUs require topical, systemic treatments and adjunctive technologies such as LLLT to optimize clinical conditions, tissue regeneration, and quality of life. Health technology assessment should be part of the routine of professionals seeking clinical, psychosocial, and financial answers and developing and disseminating technologies in the health care system and services\(^10\). The relevance of studies evaluating LLLT dosimetry in VU treatment is fundamental to supporting strategies and actions to improve the quality of care.

A preliminary search for similar protocols and studies was conducted in the International Prospective Register of Systematic Reviews (PROSPERO) platform and the Cochrane Database of Systematic Reviews (CDSR) and Joanna Briggs Institute (JBI) Evidence Synthesis databases. No related studies or protocols were identified. This systematic review is crucial as it will employ systematic methods to select and synthesize data from auxiliary studies for decision-making, therapeutic technique development, and protocol formulation based on evidence synthesis for safer clinical practice\(^11\). It is expected that this study can contribute to LLLT dosimetry as an adjuvant therapy in wound healing, aiming to strengthen individualized care for people with VUs. Additionally, it enables the development of a randomized clinical trial on the use of LLLT in individuals with VUs. This systematic review aims to analyze LLLT dosimetry for VU healing.

**METHOD**

A systematic review will be conducted according to the guidelines of the JBI\(^12\-13\) and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)\(^14\). A protocol has been registered in PROSPERO with registration code CRD42021256286. We will use a narrative synthesis, without meta-analysis, to systematize the results of LLLT dosimetry in healing venous ulcers. No specific treatment protocol will be proposed.

**Review question**

The research question was developed using the PICO mnemonic, where: P (population) refers to adults with VUs; I (intervention) refers to LLLT; C (comparison) refers to comparing treatments; and O (outcome) refers to improving the healing process. The research question is: “What is the appropriate dosimetry of LLLT for the healing process in patients with VUs?”

**Criteria for eligibility**

Two independent reviewers will select the studies. The studies must be published in Portuguese, English, and Spanish without temporal restrictions. They may include randomized and non-randomized clinical trials and should include people aged 18 years or older with venous ulcers in different care contexts. In addition, studies must evaluate venous ulcers in the healing process, and the full text must be available. Qualitative studies, observational studies, article abstracts, conference abstracts, literature reviews (narrative, integrative, and systematic), opinion articles, letters to the editor, proceedings, and abstracts will be excluded.

**Sources of information**

Searches will be conducted in the following databases: Cochrane Library, EMBASE, Medical Literature Analysis and Retrieval System Online (MEDLINE/PubMed) (via National Library of Medicine), Cumulative Index to Nursing and Allied Health Literature (CINAHL), SCOPUS, Web of Science, Scientific Electronic Library...
Online (ScIELO), *Literatura Latino-Americana e do Caribe em Ciências da Saúde/Base de Dados em Enfermagem* (LILACS/BDENF), ProQuest Dissertations & Theses Global (PQDT), Open Grey, and Google Scholar. The reference lists of all selected articles are also included in the search results.

**Search strategy**

Search strategies and descriptors were selected in collaboration with a librarian expert in bibliographic searching. Controlled vocabularies or synonyms from Medical Subject Headings (MeSH) and *Descritores em Ciências da Saúde* (DeCS) were consulted and extracted. These terms were combined using Boolean operators (OR/AND). Figure 1 shows the complete search strategies.

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**Figure 1** – Database search strategies. Florianópolis, SC, Brazil, 2023

**Data extraction**
The export of articles will be followed by three steps: identification, selection, and data extraction. In the first stage, two independent researchers will use defined search strategies to identify database articles. In the second stage, studies will be selected after reading the titles and abstracts of the identified material. Once eligibility has been determined, the full texts will be read, and the inclusion and exclusion criteria will be applied again. A PRISMA flowchart will represent the study selection and inclusion process. Data extraction will be performed using Excel (2016), including title, author, year, journal, database, objective, population, dosimetry, method, main results, and conclusions. All discrepancies will be resolved by consensus; if consensus cannot be reached, a third reviewer will decide on inclusion. Duplicate articles and other exclusions will be counted and justified according to the principles of transparency. In the case of insufficient data, authors will be contacted to obtain the necessary information.

**Assessment of risk of bias**
Two investigators will assess the risk of bias, and a third investigator will be consulted in case of disagreement. For the validation of randomized clinical trials, the Cochrane Risk of Bias 2 (RoB 2) tool will be used, which consists of five domains: (1) bias due to the randomization process; (2) bias due to deviations from the intended interventions; (3) bias due to missing outcome data; (4) bias in outcome measurement; (5) bias in the selection of the reported outcome. Each bias assessed will be rated as "low risk of bias", "some concerns", or "high risk of bias". For non-randomized clinical trials, the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool will be used, which assesses seven domains of bias: (1) bias due to confounding; (2) bias in the selection of study participants; (3) bias in the classification of interventions; (4) bias due to deviations from the intended interventions; (5) bias due to missing data; (6) bias in the measurement of outcomes; (7) bias in the selection of the reported outcome. The ratings for each domain include "low risk of bias", "moderate risk of bias", "serious risk of bias", "critical risk of bias", or "no information". Studies identified as having a high risk of bias will not be excluded.

**Data synthesis**
The narrative synthesis will follow the Synthesis Without Meta-analysis (SWiM) guidelines. Our primary outcome will be comparing the progression of VUs treated with LLLT and VUs treated with other conventional methods. A critical analysis will be performed using authoritative publications such as those from the World Health Organization (WHO), consensus guidelines on VU treatment, and other compatible sources. Study limitations are related to the lack of official guidelines for LLLT practice.

**Assessing certainty in conclusions**
After the review, it will be verified that the results obtained are entirely consistent with the
PICO strategy and that the study development is consistent with what was registered in this protocol without making any changes to the search strategies to avoid bias in the selection of articles.

*Paper extracted from the master’s thesis “Laser therapy combined with unna boot in the treatment of individuals with venous ulcers: a randomized clinical trial”, presented to the Universidade Federal de Santa Catarina, Florianópolis, SC, Brazil.

CONFLICT OF INTERESTS
The authors have declared that there is no conflict of interests.

REFERENCES


### AUTHORSHIP CONTRIBUTIONS

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<tr>
<td>Project design</td>
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