

EFFECTS OF LASER THERAPY ON THE TISSUE HEALING PROCESS IN THE DIABETIC FOOT

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Abstract: Chronic non-communicable diseases (NCDs) constitute a global health challenge, being the main cause of morbidity and mortality and causing substantial economic and social impacts. In Brazil, in 2015, NCDs were responsible for 75% of deaths, and projections indicate an increase to 19.2 million cases by 2035. Additionally, approximately 15% of individuals with NCDs will develop diabetic foot ulcers during their lives. The main objective of the present study is to conduct a systematic review to evaluate the effectiveness of the clinical use of Low Intensity Laser Therapy (LLLT) in the process of repairing chronic wounds in patients with diabetic foot. The results to date have demonstrated that the application of laser therapy to chronic wounds associated with the diabetic foot is effective in accelerating the tissue repair process in a short period of time. The formation of epithelial tissue and a significant reduction in the area of the wounds were noted, with an approximate decrease of 30 to 50%, in around 15 days in patients undergoing laser therapy compared to those who did not receive this treatment. These results indicate that LLLT may be a promising therapeutic option for the treatment of chronic wounds in patients with diabetic foot. It is important to highlight that treatment with LLLT did not present significant side effects and promoted recovery from pain and sensitivity. However, we emphasize the need to conduct more clinical studies to consolidate these findings and establish effective therapeutic protocols that can benefit this growing population.

Key words: Diabetes. Diabetic foot. Lasertherapy. Photobiomodulation.

INTRODUCTION

Chronic non-communicable diseases (NCDs) are the main cause of global morbidity and mortality, imposing substantial social and economic burdens. In Brazil, they represented 75% of deaths in 2015, with an estimated 19.2 million cases by 2035. A serious complication related to NCDs is diabetic foot, which results from neurological, pathological or ischemic complications, which can lead to complications biomechanics, especially in the areas of interdigital compression. In cases of loss of sensation, these injuries can progress to infections and amputations.

Wound healing is a complex process regulated by molecular and cellular mechanisms. Low-level laser therapy (LLLT) has emerged as a promising approach to improving wound healing, with reports of benefits since 1971. LLLT has the potential to modulate biological processes related to wound healing, reducing inflammation, edema, and oxidative stress.

Studies in animal models have explored the efficacy of LLLT in cutaneous wounds. Recent results indicate that LLLT can regulate the expression of inflammatory mediators, contributing to the reduction of edema and leukocyte influx, in addition to reducing oxidative stress. Furthermore, LLLT stimulates the formation of epithelial tissue and significantly reduces the wound area in a short period, compared to the absence of this therapy.

However, NCDs represent a significant concern for global health, with diabetic foot being a serious and disabling complication. Low-level laser therapy (LLLT) has shown promise in promoting wound healing, with studies demonstrating benefits in animal models. However, it is important to highlight the need for more clinical research to validate these results and establish effective treatment protocols to benefit patients with diabetic foot.

THEORETICAL DEVELOPMENT

LASERTHERAPY AND PHOTOBIMODULATION

Photobiomodulation therapy, which involves the application of low-power monochromatic light to wounds, has been shown to be effective in promoting healing, repairing complex wounds, and increasing local vascularization, as indicated by several studies (Brassolatti et al., 2018; Hawkins et al., 2006; Martignago et al., 2018; Otterço et al., 2018).

This therapy has demonstrated the ability to optimize healing in the early stages of the process, mainly due to the antioxidants and other effects it provides, such as the ability to modulate the intensity of inflammation, stimulate the production of macrophages and collagen synthesis (Avci et al. al., 2013; Brassolatti et al., 2016).

Furthermore, studies have confirmed that photobiomodulation stimulates the subsequent steps of the repair process, promoting the formation of granulation tissue through the stimulation of fibroblast synthesis, neovascularization and maturation of type III and type I collagen (Fiório et al., 2014; Martignago et al., 2018; Otterço et al., 2018).

The mechanism underlying this process involves the absorption of light by a photoreceptor called a chromophore, located in cells, especially in the mitochondria, where it acts on the electron transport chain known as cytochrome c oxidase. Light absorption leads to the modulation of cellular biochemical reactions and stimulates mitochondrial respiration, resulting in the production of molecules such as adenosine triphosphate (ATP) (Pinto et al., 2013).

It is important to note that the wavelengths of light used, mainly in the range of 600 to 700 nm, are the most effective in absorption

by cytochrome c oxidase, triggering a cascade of events that optimize cellular energy production and vasodilation through release of nitric oxide (Mosca et al., 2019).

Furthermore, light absorption also modulates key ions, such as sodium, potassium and calcium, influencing responses that regulate inflammation and analgesia. Another relevant effect is the activation of TGF, which induces changes in its conformations (Mosca et al., 2019).

In vitro and animal studies have demonstrated that LLLT amplifies mitochondrial activity, DNA and RNA, accelerating the fracture repair process and increasing bone mineral density (Liu, 2007; Pinto, 2013).

In summary, low-intensity laser therapy is a promising approach for tissue regeneration, acting at the cellular level with analgesic, anti-inflammatory and reparative effects, providing significant benefits in several therapeutic applications.

DIABETIC FOOT

Diabetes Mellitus (DM) is a set of metabolic disorders that result in hyperglycemia, related to problems in the action or secretion of insulin. The duration and severity of hyperglycemia play an important role in the progressive development of microvascular complications, negatively affecting the healing process, especially in the lower limbs.

DM and foot ulcers are significant risk factors for amputations, accounting for a high rate of amputations worldwide, with two amputations occurring every minute. These places these patients in a vulnerable social and economic situation and reduces life expectancy.

Pressure ulcers are classified into five stages, ranging from intact skin with signs of impending ulceration to complete loss of skin integrity with extensive destruction of

underlying tissue, including muscles, bones or supporting structures. These classifications help determine the severity of ulcers and guide appropriate treatment.



Figure 1 - Mechanism of ulcer formation caused by repetitive or excessive mechanical stress

Source: Available at: https://www.endocrino.org.br/media/finalissimo_1o_dez_iwgdf_guidelines_v11_atfh_1.pdf. Acesso em: 10 de outubro de 2021

Neuropathy and mild trauma, such as inappropriate shoes or acute injuries, can trigger foot ulcers, especially in cases of loss of protective sensation, foot deformities and limited joint mobility. This results in abnormal biomechanical loads, leading to callus formation. Calluses, in turn, increase pressure on the foot, causing subcutaneous hemorrhage and, eventually, skin ulcers.

Diabetes mellitus (DM) is associated with several health complications, including lower limb amputations. The World Health Organization (WHO) predicts that by 2030, DM will be the seventh leading cause of global mortality, contributing to problems such as stroke and heart disease.

In a recent review published by Monteiro-Soares (2020), several classifications and scoring systems were found to aid in the diagnosis and recognition of DFUs.

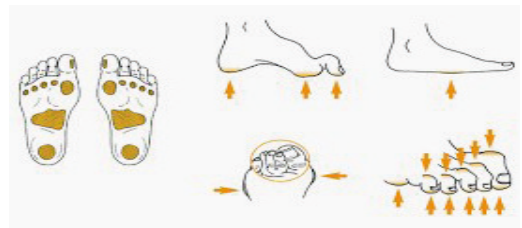


Figure 2 - Áreas do pé com maior risco de ulceração.

Source: Available at: https://www.endocrino.org.br/media/finalissimo_1o_dez_iwgdf_guidelines_v11_atfh_1.pdf. Acesso em: 10 de outubro de 2021

However, these different instruments can confuse the clinician and make communication between different health professionals difficult. A more homogeneous language and a more assertive classification could help communication between different professionals around the world.

GOALS

MAIN GOAL

Conduct a systematic review in order to critically analyze whether the clinical use of LLLT is effective in the process of repairing chronic wounds in patients with diabetic feet.

SPECIFIC OBJECTIVES

- Study the effects of laser therapy on the tissue healing process of the diabetic foot;
- Analyze methods and dosimetries that showed the most promising results for the healing of the diabetic foot.

METHODOLOGY

The present study followed the recommendations of PRISMA (LIBERATI et al., 2009; MOHER et al., 2009), and Cochrane Data base of Systematic Reviews (COCHRANE, 2017) for carrying out a systematic review of the literature.

In this study, the search for articles was

carried out in the MEDLINE, SciELO and PUBMED databases until September 2021, covering articles in Portuguese and English. Specific keywords were used, such as laser therapy, diabetic foot and tissue repair, as well as their equivalents in English: low level laser therapy, diabetic foot ulcer and tissue repair.

The article selection criteria were established based on the PICO concept (Person, Intervention, Comparison and Result), focusing on elderly people with diabetic foot aged 60 years or over, using low-power laser as an intervention, without a comparison specific, and measuring healing related to the time of laser application.

The selection of studies involved reading the abstracts to refine the sample, followed by a critical evaluation of the full articles and the creation of synoptic tables with the data collected from each research.

To assess the risk of bias, the Cochrane Collaboration tool was applied, considering domains such as random sequence generation, allocation concealment, blinding of participants and professionals, blinding of evaluators and outcome, incomplete outcomes, selective outcome reporting and other sources of bias.

Data analysis involved a descriptive and exploratory approach to the selected articles. The quality of evidence was assessed using the PEDro scale (Physiotherapy Evidence Data base Scoring Scale), which scores studies from 0 to 10, classifying them as low quality (below 3), fair quality (4 to 5) or high quality. quality (from 6 to 10).

RESULTS

The article search and selection process resulted in only three articles for analysis (Figure 3).

The relevant information from each article to answer the research objective was exported in table 1. For information, DM: Diabetes

mellitus; DFUs: Diabetic foot ulcers; LLLT: Low level laser therapy; LED: Light-emitting diode; n: number.

One study presented reasonable quality according to the PEDro scale (Table 2). This PEDro is based on the Delphi list, developed by Verhagen and colleagues from the Department of Epidemiology, Maastricht University. The objective of this scale is to help users of the PEDro databases to quickly identify which of the randomized controlled studies, or nearly so, may have internal validity (PEDro Database, 2020).

Regarding the analysis of the risk of bias of the selected articles, all presented a high risk of bias in the areas “allocation concealment” and “Random sequence generation” (Figure 4). This may compromise the completion of these surveys.

DISCUSSION

Literature review plays an essential role in the development of academic and scientific work, avoiding repetition of research and identifying gaps in existing knowledge. Furthermore, the review makes it possible to observe flaws in previous research, understand the resources needed to conduct specific research, and propose new topics and innovative research methods.

In the context of low-level laser therapy (LLLT) for the treatment of diabetic foot ulcers, the review highlights challenges in the search for research with significant samples and high methodological quality. This is due to factors such as psychosocial, biological and educational issues that affect patient participation in clinical trials.

The review also highlights the importance of establishing appropriate parameters for LLLT, considering the clinical particularities of patients with Diabetes Mellitus and pressure ulcers. The lack of description of reproducible parameters in the literature highlights the

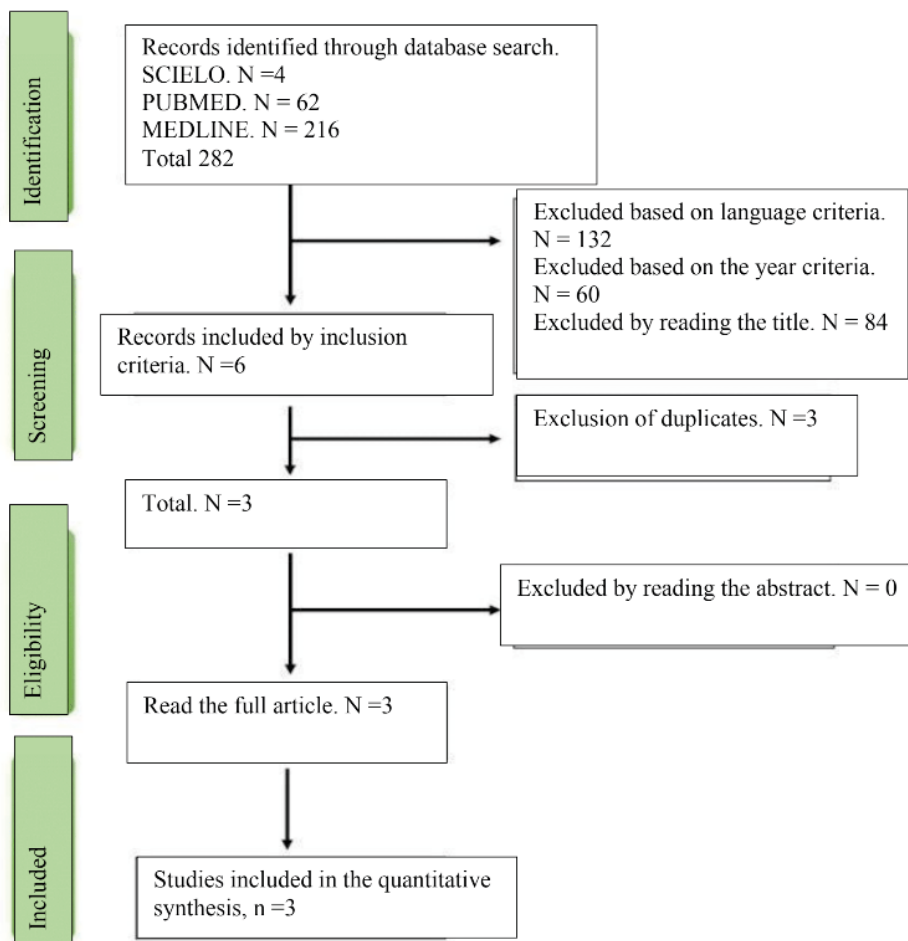


Figure 3 - Article selection process

Source: From the Author (2021)

AU-THOR/ YEAR	TITLE	POPULATION	STUDY METHODO- LOGY	RESULTS - CONCLUSION
Mathur <i>et al.</i> , 2017	Low Level Laser Therapy as an Adjunct to Conventional Therapy in the Treatment of Diabetic Foot Ulcers.	30 Type 2 DM patients with Meggitt Wagner grade I DFUs of at least 6 weeks were included.	Randomized controlled trial with placebo group.	OLLT was able to promote wound contraction more efficiently than the group without LLLT (37.2% LLLT group versus 15.12% control), and can be used as an adjunct in the treatment of diabetic foot wounds.
Santos <i>et al.</i> , 2018	Effects of low-power light therapy on tissue repair. Process of chronic wounds in diabetic feet.	18 patients between 30 and 59 years old presenting chronic foot wounds due to diabetes.	Randomized controlled trial with placebo group.	O uso de LLLT foi eficaz na redução de cicatrização de feridas em pé diabético e, como desfecho secundário houve retorno da sensibilidade.
Vitoriano <i>et al.</i> , 2019	Comparative study of the influence of laser and LED on tissue repair and improvement of neuropathic symptoms during the treatment of diabetic ulcers.	12 individuals distributed into 2 groups (Laser group/Led group) underwent 10 sessions twice a week.	Randomized quantitative comparative study in 2 groups.	Both laser and LED showed improvement in healing. However, wound reduction was greater in the laser group.

Table 1 - Characterization of selected studies

Source: From the author (2021)

Studies	Mathuret <i>et al.</i> , 2017	By Alencar Fonseca Santos <i>et al.</i> , 2018	Vitoriano <i>et al.</i> , 2019
PEDro Scale			
1. Eligibility criteria have been specified.	Yes	Yes	Yes
2. The subjects were randomly distributed into groups.	Yes	Yes	No
3. The allocation of subjects was secret.	No	No	No
4. Initially, the groups were alike with regard to the most important prognostic indicators.	Yes	Yes	Yes
5. All subjects participated blindly in the study.	Yes	Yes	Yes
6. All therapists who administered the therapy did so blindly.	No	No	No
7. All evaluators who measured at least one key outcome did so blindly.	No	No	No
8. Measurements of at least one key result were obtained in more than 85% of the subjects initially distributed among the groups.	Yes	Yes	Yes
9. All subjects from whom outcome measurements were presented received the treatment or control condition according to allocation or, when this was not the case, data analysis was carried out for at least one of the key outcomes by “intention of treatment”.	Yes	Yes	No
10. Results of intergroup statistical comparisons were described for at least one key outcome.	Yes	Yes	Yes
11. The study presents both precision measures and variability measures for at least one key result.	Yes	Yes	No
Total score	7/10	7/10	4/10

Table 2 - PEDro Scale.

Source: From the Author (2021)

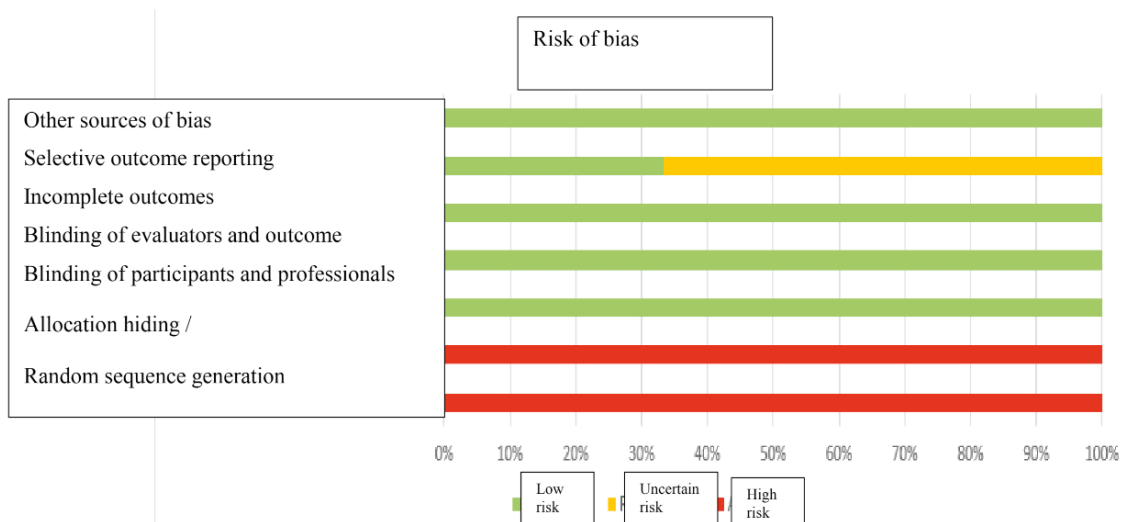


Figure 4 - Bias Risk Analysis Chart.

Source: From the Author (2021)

need for more research in this area.

Furthermore, the review highlights the lack of specific studies that evaluate the response to laser therapy in patients over 60 years of age who have Diabetes Mellitus and ulcers. This is relevant as diabetic ulcers are a chronic complication that can occur in patients with neuropathy.

However, all studies reviewed demonstrated effectiveness in healing ulcers, with some reports of return of sensitivity. The research also highlights the importance of more clinical

studies with greater scientific rigor in this area and the need to investigate how laser therapy specifically affects patients over 60 years of age.

CONCLUSION

Injuries in individuals treated with LLLT achieved tissue repair at a higher rate of speed compared to LED, with no collateral effects, in addition to the reintegration of pain and sensitivity.

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