REVIEW ARTICLE

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Effects of low-level laser therapy on the healing of foot ulcers in people with diabetes mellitus

Efeitos da laserterapia de baixa intensidade na cicatrização de úlceras nos pés em pessoas com diabetes mellitus

Efectos de la terapia con láser de bajo nivel sobre la curación de las úlceras del pie en personas con diabetes mellitus

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ABSTRACT

Objective: Identify the effects of low-level laser therapy on the healing of diabetic foot. **Method:** Systematic review of the PubMed, LILACS, SciELO, CINAHL, Cochrane, Web of Science and Scopus databases, in which 92 articles were identified and six were included in the final sample after the eligibility criteria. **Results:** The articles pointed out as effects of laser therapy the effectiveness in the progression of the tissue repair process of the diabetic foot, pain relief, anti-inflammatory action, increased tissue perfusion of the lesion and improvement of the vascular response and the nervous system. **Conclusion:** Laser is an adjuvant therapy that can accelerate the wound healing process, relieve pain, improve neovascularization, and thus minimize the risk of complications, such as lower limb amputation and improvement of quality of life for people with diabetes and impaired skin integrity.

DESCRIPTORS: Laser therapy; Wound healing; Diabetic foot; Stomatherapy.

RESUMO

Objetivo: Identificar os efeitos da laserterapia de baixa intensidade na cicatrização do pé diabético. **Método:** Revisão sistemática nas bases de dados PubMed, LILACS, SciELO, CINAHL, Cochrane, *Web of Science* e Scopus, em que foram identificados 73 artigos, dos quais seis foram incluídos na amostra final, após verificação dos critérios de elegibilidade. **Resultados:** Os artigos apontaram como efeitos da laserterapia a efetividade na progressão do processo de reparo tecidual do pé diabético, alívio da dor, ação anti-inflamatória, aumento da perfusão tecidual da lesão e melhora da resposta vascular e do sistema nervoso. **Conclusão:** O laser é uma terapia adjuvante que pode acelerar o processo de cicatrização da lesão, diminuir a dor, melhorar a neovascularização e, assim,

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minimizar o risco de complicações, como amputação do membro inferior e melhora da qualidade de vida de pessoas com diabetes e integridade da pele prejudicada.

DESCRITORES: Terapia a laser; Cicatrização de feridas; Pé diabético; Estomaterapia.

RESUMEN

Objetivo: Identificar los efectos de la terapia con láser de bajo nivel en la curación del pie diabético. **Método:** Revisión sistemática en las bases de datos PubMed, LILACS, SciELO, CINAHL, Cochrane, Web of Science y Scopus, en las que se identificaron 73 artículos, de los cuales seis se incluyeron en la muestra final, después de verificar los criterios de elegibilidad. **Resultados:** Los artículos señalaron como efectos de la terapia con láser la efectividad en la progresión del proceso de reparación de tejidos del pie diabético, alivio del dolor, acción antiinflamatoria, aumento de la perfusión tisular de la lesión y mejora de la respuesta vascular y el sistema nervioso. **Conclusión:** El láser es una terapia adyuvante que puede acelerar el proceso de curación de la lesión, disminuir el dolor, mejorar la neovascularización y, por lo tanto, minimizar el riesgo de complicaciones, como la amputación de miembros inferiores y la mejora de la calidad de vida de las personas con diabetes e integridad de la piel deteriorada.

DESCRIPTORES: Terapia con láser; Curación de heridas; Pie diabético; Estomaterapia.

INTRODUCTION

Diabetes mellitus (DM) is one of the most prevalent chronic diseases in the world and one of the most significant public health challenges of the 21st century[1]. Among the most frequent complications of DM are diabetic foot ulcers[2].

Diabetic foot is caused mainly by peripheral neuropathy and arterial disease, which lead to foot ulceration. This ulceration can progress with infection and/or soft tissue destruction, which results in walking deficits and considerable impact on the quality of life, in addition to resources spent on prolonged hospitalization, rehabilitation, home care and direct and indirect costs to the patient, their families and society, due to loss of productivity[3,4].

Approximately 15% of people with DM will suffer from foot ulcers in their lifetime, where conventional treatments such as daily cleansing and dressing with 0.9% saline solution, essential fatty acids, hydrogel and betadine solution have shown little success in progressing tissue repair, with a higher rate of complications[5–7].

A cohort of 1055 people with DM in 19 specialized centers in Brazil showed that 24.2% had previous foot ulcer and 13.7% prior amputation, and out of these, 5.3% had more than one amputation[8].

Thus, in recent years, adjuvant therapies have been tested to stimulate the wound healing process in people with DM[5]. Among the new therapies, low-level laser therapy (LLLT) is considered a noninvasive, painless, low-cost and effective method of wound treatment, as it acts on the physiological and biochemical events of the healing process[9–11].

Studies available on the application of laser therapy for the treatment of foot ulcers in people with DM are still scarce. Although there are favorable reports for its use, further research should be carried out to obtain the effects of laser in the treatment of such lesions, as well as to identify the number of applications, dose and wavelength required for tissue repair, which reinforces the relevance of the study.

The high occurrence of DM justifies the research in the population in recent years and the increase in cases of nontraumatic amputations in the lower limbs, which highlights the need for not only treatment of the underlying disease, but also prevention of injuries and monitoring of diabetic foot with other adjuvant therapies that can promote healing progress.

This study aims to identify the effects of low-level laser therapy on diabetic foot healing.

METHODS

It is a systematic review of the literature, which aimed to identify, select and analyze the scientific production on the effects of laser therapy on the healing of diabetic foot. Systematic reviews use systematic and explicit methods to choose and critically evaluate relevant research[12].

The bibliographic survey was conducted between January and June 2019. To collect the data, the PICO strategy was used, whose acronym means: P – Population, points to the population in focus, I – Intervention, determines the type of intervention, C – Comparison, identifies which control

group will be tested with the response, and, O – Outcome, the outcomes that will be evaluated. This strategy helps to formulate the research question and enables the identification of keywords that assist in locating relevant primary studies in databases[13].

Given the above, the guiding question of this study, based on the PICO strategy, illustrated in Table 1, is: "what are the effects of low-level laser therapy on the healing of diabetic foot?"

Given the peculiar theme and the small number of scientific articles in the literature on the subject, the search was timeless in the following databases: National Library of Medicine (PubMed), Latin American and Caribbean Literature in Health Sciences (LILACS), Scientific Electronic Library Online (SciELO), Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane Library, Web of Science and Scopus, directly available on their websites or through the Capes Portal, performed by two independent researchers.

Table 1. Illustrative diagram of the process of elaboration of the guiding question based on the PICO acronym.

Population	People with diabetic foot
Intervention	Laser therapy
Compararison	Conventional therapy
Outcome	Wound healing

The search strategy adopted was the use of Boolean descriptors and operator "AND". The descriptors were also selected according to the PICO strategy and identified through the Descriptors in Health Sciences (DECS): Low light therapy and Wound healing and Diabetic foot; and using Medical Subject Headings (MeSH): Low-level light therapy and Wound Healing and Diabetic Foot.

Experimental studies were considered as inclusion criteria, electronically available in English, Portuguese and Spanish, which performed the treatment of diabetic foot with LLLT. Experiments performed with lesions of other etiologies or with animals, review articles with humans or other animal species and studies *in vitro* were excluded.

Ninety-two articles were identified in the seven databases consulted. After the survey of publications, duplicate articles were excluded (n = 38). Then, the titles were analyzed and the abstracts were read and categorized according to pre-established inclusion and exclusion criteria, making a final sample of six articles, after the analysis of two researchers, as shown in Fig. 1.

To certify the methodological quality of the articles included, the PRISMA recommendation was used, which consists of a checklist with 27 items of systematic analysis and metanalysis[14]. All scientific productions used were duly cited and referenced concerning research copyrights.

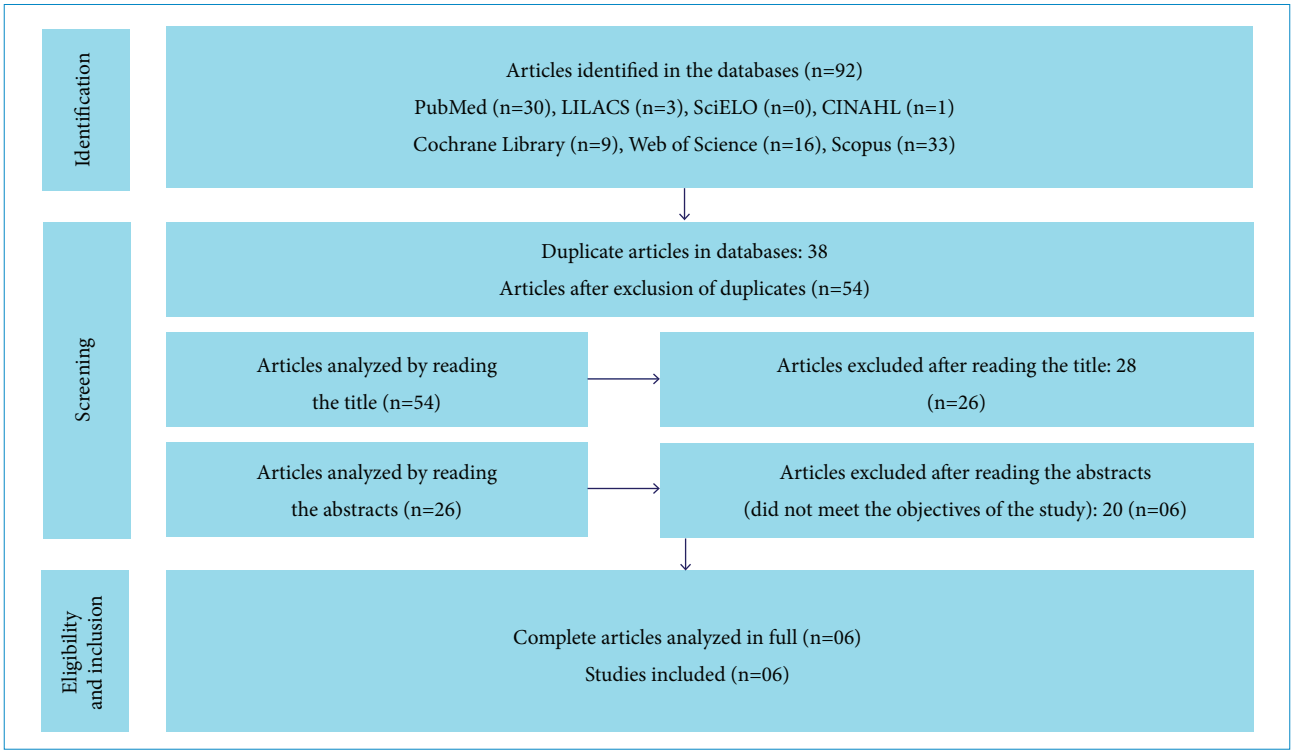

Figure 1. Illustrative flowchart of the study selection process according to the PRISMA recommendation.

RESULTS

Profile of publications

The six articles included in this review are presented in Table 2, which aimed to analyze the effects of laser therapy on the healing process of diabetic foot.

Regarding the year of publication, there is one article dated 2018, two from 2017, one from 2016, one from 2015 and one from 2011. As for the language, all publications are in English.

The selected studies were conducted in the following countries: Brazil (n = 3), India (n = 1), Italy (n = 1) and Iran (n = 1). Regarding the category of the main author of the publications, two belong to physiotherapy, two to medicine, one to nursery and one to biomedicine.

Treatment protocol

The number of participants in the studies varied from 16 to 56 patients. Patients in five studies were randomly allocated to different groups: the control group and intervention group.

In the research of Santos et al. (2018)[6], the injuries in the control group were treated with 0.9% saline solution and hydrogel. In the study of Carvalho et al. (2016)[15], participants were randomly assigned to four groups: control (simple cleaning and dressing), low-level laser therapy, essential fatty acids (EFA) from *Calendula officinalis* and laser associated with EFA. In the study of Feitosa et al. (2015)[16], the participants of the control group performed a simple dressing with physiological solution 0.9%; Mathur et al. (2017)[17] used betadine solution. The other studies did not report the treatment used in the control group.

The wavelength in nanometers (nm) used for laser applications ranged from 632.8 to 830 nm. The doses in joules (J) were from three to 20 J/cm^2. In the study of Salvi et al. (2018)[18], the amount of wound laser applications and follow-up time was not specified. In four studies, 12 laser therapy sessions were performed for the treatment of diabetic foot[6,7,15,16].

The study of Santos et al. (2018)[6] showed the laser sessions of 48/48 h in four weeks. In the study of Mathur et al. (2017)[17], the wounds were exposed to laser light daily for 15 days. In Carvalho et al. (2016)[15] and Feitosa et al. (2015)[16], 12 sessions were performed, comprising three weekly services on alternate days. In the research conducted by Kaviani et al. (2011)[7], patients received radiation with laser over the wounds six times a week, for at least two consecutive weeks and then every other day until healing was completed.

Wound evaluation

Various methods performed the evaluation of the healing process of diabetic foot treated with LLLT: application of the pressure ulcer scale for healing (PUSH)[6], measurement of the evolution of the wound using adhesive tape divided in centimeters[15] and evaluation of photographic records[7,16,17].

Benefits

The articles identified as the main result of laser therapy in the diabetic foot the effectiveness in the progression of the process of tissue repair in a shorter period, besides other effects such as pain relief, anti-inflammatory action, greater tissue perfusion of the lesion and improvement in the response of vascular and nervous systems.

DISCUSSION

Based on the analysis of the results, a consensus was reached regarding the use of LLLT to favor the progression of tissue repair of ulcers per diabetic foot. Moreover, it supports pain relief, higher tissue perfusion of the lesion, stimulation of neovascularization, and cell proliferation when compared to control groups that used essential fatty acids of *Calendula officinalis*, physiological solution 0.9%, hydrogel and betadine solution.

It is worth noting that there were no records of adverse events associated with the treatment in question and all studies showed positive results in the process of tissue repair with the use of LLLT compared to control groups.

The research conducted in Iran found that the size of wounds on the feet of people with diabetes significantly decreased in the fourth week of treatment with LLLT and was completely healed after 20 weeks[7].

Research conducted in India showed that foot ulcers in 75% of patients in the treatment group had a 30–50% reduction in the injured area and more granulation tissue in two weeks of LLLT[17]. Brazilian researchers identified

Tabke 2. Description of the studies included in the systematic review.

Title/Database	Authors/ Year	Objective	Method/ Sample	Wavelength (nm)	Dosage (j/cm²)	Number of applications	Summary of results
Effects of low-power light therapy on the tissue repair process of chronic wounds in diabetic feet. (PubMed)	Santos et al. 2018[6]	To analyze the effectiveness of low power laser therapy in tissue repair of diabetic foot.	Randomized clinical trial 18 patients	660	6	12 applications in 4 weeks	Pain relief and efficacy in the progression of the tissue repair process in a short period ($p < 0.013$).
Low-level laser therapy as an adjunct to conventional therapy in the treatment of diabetic foot ulcers. (PubMed)	Mathur et al. 2017[17]	To evaluate the effectiveness of the low-power laser in the treatment of the diabetic foot.	Randomized clinical trial 30 patients	660	3	15 applications in 2 weeks	Effectiveness in the progression of the tissue repair process in a short period ($p = 0.009$).
Effect of low-level light therapy on diabetic foot ulcers: a near-infrared spectroscopy study. (PubMed)	Salvi et al. 2017[18]	To evaluate the effectiveness of low power laser in modifying vascular and nervous systems in foot wounds.	Randomized clinical trial 56 patients	830	20	Not specified	Increased tissue perfusion of the lesion after application, improved response of vascular and nervous systems, effectiveness in the progression of the tissue repair process in a short period ($p = 0.017$).
Low-level laser therapy and calendula officinalis in repairing diabetic foot ulcers. (PubMed)	Carvalho et al. 2016[15]	To evaluate the effects of low-power laser on the repair of diabetic foot wounds.	Randomized clinical trial 32 patients	658	4	12 applications in 4 weeks	Pain relief ($p < 0.001$), anti-inflammatory action, reduction of the total area of ulcers ($p = 0.0032$), stimulation of neovascularization and cell proliferation.
Effects of the Low-Level Laser Therapy (LLLT) in the process of healing diabetic foot ulcers (PubMed)	Feitosa et al. 2015[16]	To evaluate the effects of low-level laser on tissue repair of diabetic foot.	Randomized clinical trial 16 patients	632,8	4	12 applications in 4 weeks	Tissue repair in diabetic foot ($p < 0.005$), biomodulation and analgesic effect ($p < 0.001$).
A randomized clinical trial on the effect of low-level laser therapy on chronic diabetic foot wound healing: a preliminary report. (Cochrane)	Kaviani et al. 2011[7]	To evaluate the effectiveness of low-power laser therapy in the treatment of the diabetic foot.	Randomized clinical trial 23 patients	685	10	12 applications in 2 weeks	Effectiveness in the progression of the tissue repair process in a short period ($p = 0.003$).

a statistically significant difference in the tissue repair rate of injuries in people with diabetes after treatment sessions with LLLT[6].

In other studies, there was a statistically significant reduction of post-laser pain, through the evaluation of pain through the visual analog scale, which scores the levels of pain from 0 to 10, in which there was a reduction from an average of 9 on the scale to 5 after using the laser[15,16].

It is therefore perceived that, in addition to contributing to the decrease in treatment time, the laser is a supporting therapy that can provide relief in the Algic state and local discomfort. The reduction in pain can impact the quality of life and enable the patient to be more active in their daily life activities.

The application of laser also promoted increased neovascularization and proliferation of fibroblasts, with a decrease in the amount of inflammatory infiltrate in the lesions, which contributes to the modulation of tissue repair with faster and more organized healing[15,18]. Through this process, the laser can recruit cytokines and essential growth factors to stimulate wound healing[19].

There was no unanimity in the studies regarding the wavelength used during LLLT sessions in diabetic foot healing. However, five studies presented wavelengths between 632.8 and 685 nm[6,7,15,16,17].

South African researchers have shown that wounds in people with diabetes irradiated with a laser at wavelengths close to 632.8 nm had a higher degree of growth and cell migration as well as luminescence of adenosine triphosphate (ATP)[20]. A review study that integrated research on the efficacy of LLLT in DM ulcers identified that most studies used wavelengths of 632.8 nm during laser treatment sessions[21].

There was also no unanimity regarding the dosage in joules, but most studies applied dosimetry from 3 to 6 J/cm^2 in the area of tissue impairment[6,15–17]. A systematic European review of 20 studies on the parameters of laser application in diabetic wounds revealed that the use of 4 J/cm^2 was more effective in accelerating the rate of wound closure, reducing inflammatory action, increasing collagen deposition and more significant proliferation of myofibroblasts[22]. This data is relevant to develop and perfect an efficient LLLT technique for diabetic foot healing because it is essential to determine the exact mechanisms of action and interaction of the laser with the organism, with an adequate selection of dosimetry parameters and wavelength.

Studies in Latin America and Asia conducted 12 sessions of LLLT for diabetic foot treatment[6,7,15,16], sufficient amount to accelerate tissue repair of the wound and promote the expected results[23]. However, it is valid to infer the importance of health education with the client during the therapy, mainly on the maintenance of glycemic control, care with the feet and the use of appropriate footwear, besides the healthy lifestyle, to help with the success of the light source therapy.

Thus, LLLT can be seen as an effective therapeutic method in wound healing when certain factors such as dosage, potency, time and interval between sessions are adequately observed. Furthermore, laser therapy has the advantage of being easily administered. The benefits of using the laser help to promote the quality of life of the customer and can minimize possible complications, such as the risk of lower limb amputation[24].

Healthcare professionals, especially nurses, play an essential role in caring for people with wounds, so it is essential that they seek training to apply new therapies/technologies and thus achieve improvements in the quality of life of people with diabetes and the integrity of damaged skin.

CONCLUSION

The findings of this study indicate that the effects of laser therapy progress in the healing of diabetic foot, improvement in the Algic state, increase in tissue perfusion of the lesion, which favors greater blood supply and nutrition of the injured area, besides the stimulation of neovascularization and cell proliferation, when compared with the use of essential fatty acids of *Calendula officinalis*, physiological solution 0.9%, hydrogel and betadine solution.

There was no unanimity regarding the most indicated dosage and wavelength for the treatment of the diabetic foot. However, the evidence identified in the scientific productions used in this review indicates that the use of a laser with a wavelength close to 632.8 nm and a dosage of 4 J/cm^2 is the most efficient in the treatment under study.

The limitation in the number of published researches on diabetic foot and LLLT is stressed. It is, therefore, essential to conduct new studies that present increasingly promising results on the use of laser in wound treatment and that clarify the stages of healing, the scientific determination of the influential dosage parameters and wavelength, with strict study criteria to validate the efficacy and safety data demonstrated in this review.

AUTHOR'S CONTRIBUTION

Conceptualization, Brandão MGSA, Ximenes MAM, Ramalho AO, Veras VS, Barros LM and Araújo TM; Methodology, Brandão MGSA, Ximenes MAM and Barros LM; Investigation, Brandão MGSA and Ximenes MAM; Writing – Original Draft, Brandão MGSA, Ximenes MAM, Ramalho AO, Veras VS, Barros LM and Araújo TM; Writing – Review and Editing, Brandão MGSA, Ximenes MAM and Araújo TM; Supervision, Barros LM and Araújo TM.

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