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LED phototherapy in tissue repair of chronic wounds in people with diabetes: a systematic review

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Fototerapia com LED no reparo tecidual de feridas crônicas em pessoas com diabetes: revisão sistemática

Fototerapia LED en la reparación de tejidos de heridas crónicas en personas con diabetes: una revisión sistemática

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ABSTRACT

Objective: To identify scientific evidence of LED photobiomodulation in the treatment and tissue repair of chronic wounds in people with Diabetes Mellitus, types I and II.
Method: Systematic review conducted from September/2021 to April/2022 in PubMed, LILACS, SCIELO, COHRANE, EMBASE and Web of Science. Randomized and observational clinical trials using LED in wound healing in diabetics, published between 2015 and 2022 were included. Data were descriptively analyzed with title/abstract screening, full text articles reading and definitive selection after meeting the predefined inclusion and exclusion criteria.
Results: Fromthe total of 840 references, eight articles were selected, that evaluated the effectiveness of LED phototherapy in wounds of diabetic patients.
Conclusion: LED light proved to be beneficial in tissue repair, with increased production in collagen and fibroblasts, angiogenesis, reduction of inflammation and, consequently, a decrease in lesion size.
Keywords: Phototherapy. Wound healing. Diabetes Mellitus. Diabetic foot. Foot ulcer.

RESUMO

Objetivo: Identificar evidências científicas da fotobiomodulação com LED no tratamento e reparo tecidual em feridas crônicas de pessoas com Diabetes Mellitus, tipo I e II.
Método: Revisão sistemática realizada de setembro/2021 a abril/2022 na PubMed, LILACS, SCIELO, COHRANE, EMBASE e Web of Science. Incluídos ensaios clínicos randomizados e observacionais utilizando LED na cicatrização de feridas em diabéticos, publicados entre 2015 a 2022. Os dados foram analisados descritivamente com triagem de título/resumo, leitura dos artigos em texto completo e seleção definitiva após atender aos critérios de inclusão e exclusão pré-definidos.
Resultados: Do total de 840 referências encontradas, foram selecionados oito artigos que avaliaram a eficácia da fototerapia LED em feridas de pacientes diabéticos.
Conclusão: A luz LED mostrou-se benéfica no reparo tecidual, com aumento na produção de colágeno e fibroblastos, angiogênese, redução da inflamação e consequentemente, diminuição no tamanho da lesão.
Palavras-chave: Fototerapia. Cicatrização. Diabetes Mellitus. Pé diabético. Úlcera do pé.

RESUMEN

Objetivo: Identificar evidencias científicas de fotobiomodulación con LED en el tratamiento y reparación de tejidos de heridas crónicas en personas con Diabetes Mellitus, tipos I y II.
Método: Revisión sistemática realizada de septiembre/2021 a abril/2022 en PubMed, LILACS, SCIELO, COHRANE, EMBASE y Web of Science. Se incluyeron ensayos clínicos aleatorizados y observacionales con uso de LED en la cicatrización de heridas en diabéticos, publicados entre 2015 y 2022. Los datos fueron analizados descriptivamente con selección de título/resumen, lectura de artículos a texto completo y selección definitiva después de cumplir con la inclusión e inclusiones ex – predefinidas.
Resultados: Del total de 840 referencias encontradas, se seleccionaron ocho artículos que evaluaron la efectividad de la fototerapia LED en heridas de pacientes diabéticos.
Conclusión: La luz LED demostró ser beneficiosa en la reparación de tejidos, con aumento de la producción de colágeno y fibroblastos, angiogénesis, reducción de la inflamación y, en consecuencia, disminución del tamaño de la lesión.
Palabras clave: Fototerapia. Cicatrización de heridas. Diabetes Mellitus. Pie diabético. Úlcera del pie.

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INTRODUCTION

Diabetes Mellitus (DM) is a chronic metabolic disease that compromises the metabolism of glucose and other energy substrates, and it is associated with complications in organs essential to life[1]. It is considered one of the chronic diseases with the greatest impact on health expenses, with high morbidity and mortality and increasing incidence due to the increase in life expectancy of the population[2]. In 2017, around 56.9% of deaths in Brazil in the age group of 30 to 69 years were due to chronic non-communicable diseases (CND), including DM[3]. It is estimated that by 2045, if current trends persist, the number of people with the disease will exceed 628.6 million[1].

Among the chronic complications, people with DM have a great potential for foot ulceration, approximately 40 to 70% of non-traumatic lower limb amputations result from this disease[4,5]. This results in high costs related to hospitalization, treatment and rehabilitation, in addition to causing physical, mental and social effects on the individual, such as: suffering, anguish, change of their self-image, loss of function, among others[6].

The World Health Organization (WHO) estimates that the number of adults with DM will reach 629 million in 2045[7]. This number will affect, above all, low- and middle-income countries, which often have a high annual expenditure on the health of diabetics[7].

A person with DM has a 25% risk of having a foot ulcer, and this lesion is responsible for 20% of hospitalizations of diabetics[6,8]. More than half of all foot ulcers require hospitalization due to infections and 20% of lower limb infections result in amputation[6,8]. In view of the socioeconomic impact of wounds on diabetic people in modern society, greater involvement and better treatments are needed to avoid complications.

Such disease is related to deficient healing, due to vascular lesions (hypoxia) and changes in phagocytic cells, which favor the occurrence of infections; narrowed blood perfusion (vasculopathy); to neuropathy, due to the reduction of inflammation stimuli released by nerve endings[9,10]. The wounds that affect people with DM, also called diabetic foot, often result from repetitive trauma, bone deformity, limitation of movement, pressure on an extremity or bone prominence whose sensitivity is already deficient or absent[11,12].

Despite the variety of therapeutic methods available for wound treatment, there are still chronic wounds that are difficult to heal, and a large number (more than 70%) of them do not heal even with appropriate topical therapy[10]. In addition, the recurrence is very common and represents a challenge for both health care professionals and patients, causing long and complex treatments[10]. Thus, given the chronicity and the possibility of recurrence of these lesions, it is necessary to search for innovative therapeutic approaches as a way to accelerate the tissue regeneration process and provide better quality of life for affected individuals[13].

Over the years, several technologies have been used as a therapeutic resource for these lesions, and one of them is photobiomodulation therapy with LED (Light-Emitting Diode), based on the interaction of light with the human body tissues[14]. LED is a phototherapeutic resource widely used in cutaneous alterations and it has been shown to be applicable in wounds, with beneficial results in different lesions, mainly due to its action in the inflammatory and proliferative phases of wound healing[9,15,16]. This type of light source has been showing advantages over LASER, it is more economically viable, can radiate a larger surface area in a shorter time, is easy to handle, does not cause pain or burns and requires less energy[17].

It is believed that these therapies promote the proliferation of fibroblasts, osteoblasts and epithelial cells, local circulation, as well as collagen synthesis, being essential for accelerating the tissue restoration process, improving tissue regeneration and healing, in addition to have an analgesic and anti-inflammatory effect[18–21].

In recent years, research conducted with the use of photobiomodulation by LASER and LED (Light-Emitting Diode) at different wavelengths, application doses and different energy densities has been frequent in the clinical practice of wound care, due to its biostimulator nature for tissue repair. Researchers have obtained excellent results with regard to neovascularization, improvement in microcirculation and in the healing process, greater retraction of the ulceration area, acceleration of the healing process by stimulating the production of granulation tissue and collagen synthesis[14,22–25].

Studies have showed relevant results regarding the use of light emitting diodes (LEDs) in tissue regeneration, however the effects of LED phototherapy are still poorly understood[11,16,26]. These devices are low cost, are easier to handle, work with relatively low electrical currents compared to LASER with highly safe and non-invasive irradiation power, and a great option as an alternative therapy to traditional treatments or even to be used with other coverings to optimize results, thus helping the healing process, reducing costs and the final treatment time[18,27].

People with DM can develop chronic ulcers that affect the lower limbs and are characterized by a slow and costly healing process, responsible for frequent hospitalizations, infections and amputations, leading to disability and impairment of the individual's quality of life[28]. Thus, the appropriate treatment of chronic wounds in this population represents a continuous challenge for health care workers and patients.

Due to the high incidence rates, diversity of parameters, socioeconomic impacts generated on family members and health services, and the difficulty in establishing protocols for the treatment of chronic wounds in people with DM, the objective of this review is to identify scientific evidence of the use of LED photobiomodulation in the treatment and tissue repair of chronic wounds in people with DM types I and II.

METHOD

This study is a systematic review with a framework based on The Joanna Briggs Institute (JBI)[29] recommendations. The model allowed a rigorous and structured analysis to achieve a reliable selection of the following items from the analyzed articles: 1) title; 2) objective and guiding question; 3) introduction; 4) inclusion criteria; 5) methods; 6) results and discussion; 7) conclusion.

This systematic review was conducted according to the "PICOS" strategy, which means "Patient, Intervention, Comparator, Outcomes and Study design", that is, participant, intervention, comparator, outcome, and study design (Chart 1).

From this strategy, the research question was elaborated to contemplate the expected objective: what is the scientific evidence of LED photobiomodulation in the treatment and tissue repair in chronic wounds of people with DM types I and II?

Protocol and Registration

The systematic review protocol was previously registered in the International Prospective Register of Systematic Reviews (PROSPERO) in June 2022 under number CRD42022339365.

Literature research

A systematic review of the literature was performed in PubMed (National Library of Medicine), LILACS (Latin American and Caribbean Literature in Health Sciences), SCIELO (Scientific Electronic Library Online), COHRANE, CINAHL, EMBASE and Web of Science from September 9, 2021 to April 5, 2022. The methodological rigor followed the PRISMA (Preferred Reporting of Systematic Reviews) checklist used to support the construction of systematic reviews and the Cochrane recommendations[30].

Since it is a new treatment method for wound healing in people with DM, no old studies were found involving the theme, which justifies the time being less than 10 years, as shown in the search flowchart.

The search was carried out by title, abstract and descriptors, when not possible, the full-text of document was read. There were no restrictions on language, date of publication or place of study. Original articles published in the pre-defined period and full-text available in the database were validated. The descriptors used for the search were related to the condition of interest and the clinical outcome to be analyzed.

For the selection of terms and retrieval of publications of interest in the databases, the strategy of terms MeSH (Medical Subject Headings) and DECS (Descriptors in Health Sciences) was used. Boolean operators AND and OR were

Participant	People with chronic wounds caused by DM I and II
Intervention	LED Photobiomodulation Intervention followed by conventional treatment
Comparator	Conventional treatment or placebo
Outcome	Reduction of wound area and healing
Study Design	Randomized and observational clinical trial

Chart 1 – Elements of the PICOS strategy. Diamantina, Minas Gerais, Brazil, 2022
Source: Authors, 2022.

adopted to detect simultaneous or individual occurrences of the research theme. The MeSH and DECS terms were: Phototherapy OR diabetic foot AND Wound Healing OR Low-Level Light Therapy. Phototherapy AND foot ulcers, Group 2: Diabetic Foot AND Diabetes Mellitus AND phoyotherapy. Wound Healing AND Diabetic Foot AND Phototherapy.

As for the study selection for the present research, the following inclusion criteria were used: randomized clinical trials (RCT) and observational that described the use of LED phototherapy in wound healing and/or improvement of tissue regeneration in people with DM, published from 2015 to 2022. Studies were also included that evaluated the effect of LED phototherapy on wounds healing in people with DM in which the comparison groups received standard treatment, placebo or another type of phototherapy such as LASER.

The outcomes of the clinical studies included in this study were not limited to the presentation of a complete healing, but also to the effects of phototherapy in reducing the wound area, accelerating the tissue repair process, pain relief, among others.

Ineligible articles published as editorials, systematic reviews, studies with animals, letters, interviews, guidelines, erratum, reflection articles and articles that studied LED for purposes other than wound healing in people with DM, such as for example, in the areas of aesthetics, dentistry, management of neonatal jaundice, among others were excluded. For duplicate or identical articles, only the first edition was included.

Screening process

In the second phase, the study selection was made by two independent reviewers (C.A.F.C, N.C.S) through analysis and verification of eligibility criteria in order to minimize the risk of bias and ensure that relevant studies were not excluded. The data search was performed using Rayyan QCR to enhance the screening of clinical trials found, which guarantees authenticity of the selection[31].

A descriptive analysis was carried out with screening of title and abstract, then comprehensive reading of the full-text articles and ending the definitive selection of studies that meet the predefined inclusion and exclusion criteria, exchanging publications between them. Any differences were resolved through mutual agreement between the researchers and consensus in meetings. Disagreements between researchers were solved with a third reviewer (V.S.B), who defined the inclusion or exclusion of the article.

The level of evidence of each study was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE)[32]. The quality of evidence was classified into four levels (high, moderate, low and very low). Randomized clinical trials started with high scores and observational studies with low scores. However, researchers were aware of methodological limitations and the presence of biases that could change the score.

Quality assessment

The studies were assessed based on their purposes, on the operationalization of the outcome measures and then underwent a peer review process to ensure the reliability of the research, two independent judges (T.C.L, M.F.D.P) participated in this stage. It is considered the most relevant stage because it allows to guarantee the validation or not of the selected articles by the researchers regarding the inclusion criteria. The final decision on publications was made by consensus. Additional searches through the references of the original articles were made to identify other publications that were not retrieved in the previous stages. The selected publications were validated by the researchers.

The results of the included studies were coded and analyzed by content categorization. All publications were retrieved in PDF. Data tabulation was performed from a spreadsheet in Microsoft Excel, consisting of the variables: authorship, year, study location, title, methodology, sample, frequency, intervention, wavelengths/application dose and outcome. The results were subdivided into groups, and a descriptive and comparative analysis of the studies found was performed.

Ethical issues

As it is a literature systematic review, submission to the Research Ethics Committee was not necessary.

RESULTS

From the database search with the terms MeSH and DECS, 840 articles were initially identified in PubMed, LILACS, Scielo and Web of Science, five were manually selected. The manual search was performed by reading the annals and abstracts of congresses in the area of interest, lists of references of published studies and other relevant references.

The results of the literature research and the strategy used to design this study are described in the flowchart (Figure 1) according to Prisma recommendations. By applying the filters and reading the titles and abstracts 626 articles

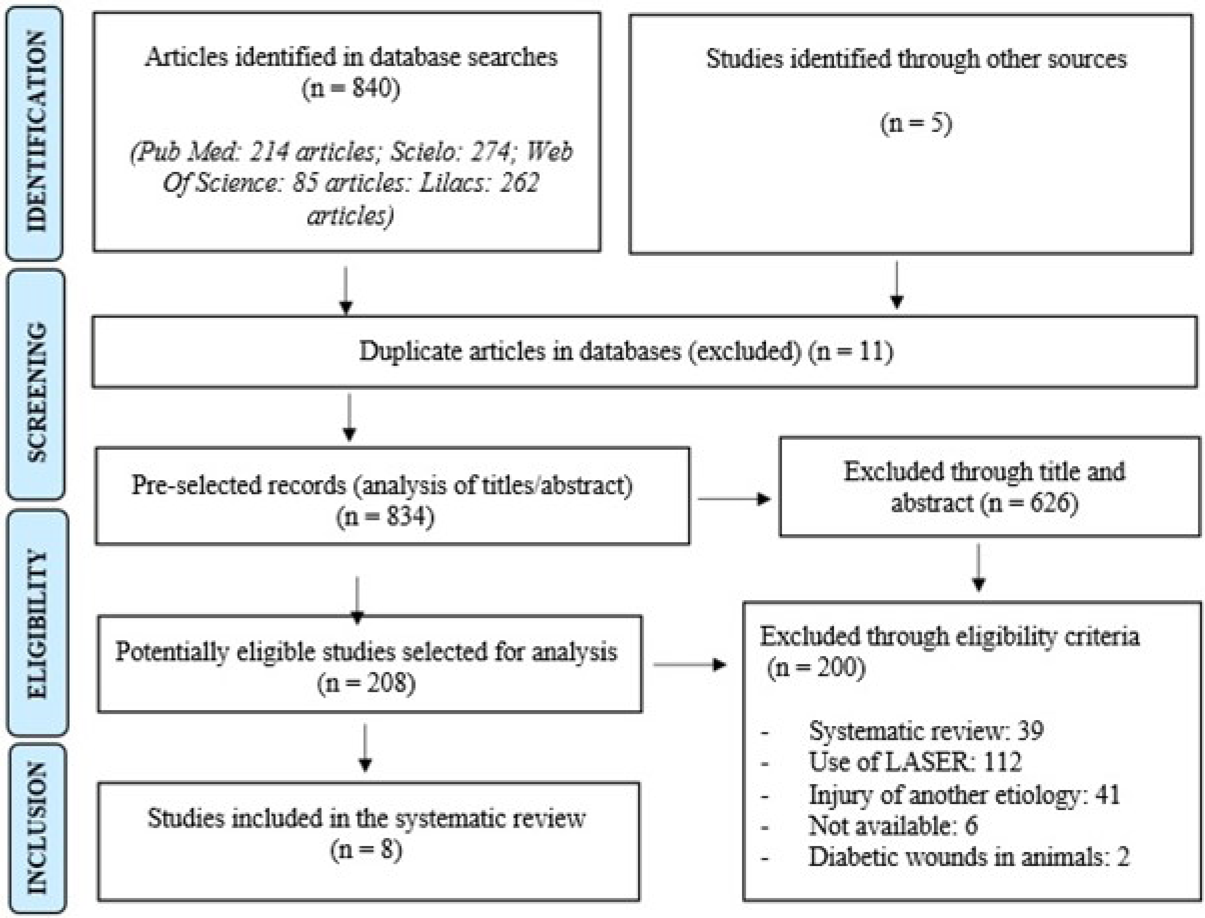

Figure 1 – Flowchart of study selection according to Prisma. Diamantina, Minas Gerais, Brazil, 2022
Source: Authors, 2022.

were excluded. The articles that were excluded evaluated wounds in animals or for other purposes than healing, such as aesthetics, dentistry, management of jaundice in newborns, among others.

From the potentially eligible studies (n= 208), eight met the inclusion criteria and were selected to the review, since they referred to the use of LED phototherapy in wound healing in people with DM (Chart 2). Among the eight selected studies, all were published in English, with publications between the years 2015 and 2019. No articles related to this topic were found between the years 2020 and 2022. Chart 2 shows the results of the studies that were included in this systematic review.

DISCUSSION

It was found with the results of this review that conventional treatments associated with LED phototherapy were more effective when compared to a control group that had not been treated with LED[33,34]. In the control groups, none of the wounds were completely healed considering the time and method evaluated in the studies.

The healing time, however, varied with the total area irradiated, duration of the wound and etiology[33]. Another factor that influences healing rates are the parameters of the LED used, with the time of application in the wound, wavelength, application dosage, usually is in the range of 630 ± 20 nm and 940 ± 20 nm, density energy, spot size and number of LEDs[34–36,38].

The parameters showed in the studies, however, are in line with reports in the literature that LED phototherapy with wavelengths between 600 and 1000 nm promotes greater speed in tissue repair[14,24,25,40]. Moreover, studies have suggested that phototherapy with wavelengths of light ranging from the red to the near infrared spectrum (600 to 980 nm) can speed wound healing[14,41,42].

No.	Author/ Year Country/	Participants	Study Design/ Level of evidence	Intervention group (IG)	Control group (CG)	Frequency	Method for wound assessment	Treatment outcome
01	Nteleki B, Abrahamse H, Houreld NN. (2015) South Africa[33]	Seven adult patients with 15 lower limbs ulcers diagnosed with type II diabetes	Prospective single-blind experimental pilot study.	Group 2: LED phototherapy and standard treatment. Group 3: LED phototherapy of the ulcer and lymph nodes and standard treatment (cleaning with 0.9% SS, Iruxol mono if slough, cured with Silbecor 1% with bandage and Primapore).	Group 1: Placebo LED phototherapy and standard podiatric treatment (cleansing with 0.9% SS, Iruxol mono if slough, Silbecor 1% together with bandage and Primapore.	Twice a week until healing or a maximum period of 90 days	The ulcers were examined visually and by digital photography. Photographs were taken before and after each treatment session. A tripod was used for standardization.	The combination of standard podiatric treatment and LED phototherapy has the potential to stimulate and increase ulcer healing rates. There was an increase in the healing rate in all three groups. Of the 67% ulcers treated with LED phototherapy, 40% healed within eight weeks and only 10% of placebo-treated ulcers healed.
02	Nunes GAMA, Reis MC, RosaMFF, PeixotoL-RT, Rocha AF, Rosa SSRF. (2016) Brazil[34]	Five patients who had ten chronic ulcers associated with diabetic foot	Randomized clinical trial	Eight ulcers treated with a natural latex insole and an LED phototherapy matrix	Five ulcers treated with a standard dressing. Before applying the silver foam dressing, debridement and cleaning with 0.9% saline solution and gauze	Weekly – minimum of 28 days	The ulcers were photographed with a digital camera. The patient sat on chair, with the camera on a tripod parallel to the wounds, with a focal length of 15 cm.	After four weeks the conventional treatment achieved a healing of 51.8% while the treatment with LED phototherapy achieved 78.4%.

Chart 2 – Description of studies included in the systematic review. Diamantina, Minas Gerais, Brazil, 2022

No.	Author/ Year Country/	Participants	Study Design/ Level of evidence	Intervention group (IG)	Control group (CG)	Frequency	Method for wound assessment	Treatment outcome
03	Frangez I, Cankar K, Frangez HB, SmrkeDM. (2017) Slovenia/ Eastern Europe[35]	40 diabetic patients and 39 without diabetes with chronic wounds on the lower limbs	Randomized double-blind clinical trial	20 patients with LED phototherapy – (diabetics) 19 patients with LED-phototherapy (non-diabetics)	20 placebo therapy patients (diabetics, control). 20 placebo therapy patients (non-diabetic, control) The placebo was performed with light that simulated LED, but with no known biological effect.	Three times a week for eight weeks	Blood analysis and microcirculation that were assessed by Laser Doppler flowmetry before the first treatment and at the end. Assessment of the wound bed by the Falanga score.	Assessment of the wound bed showed faster healing in the LED-treated groups compared to the control group. Blood flow measured by Doppler revealed greater microcirculation in the groups treated with LED and no difference in the control groups.
04	Romanelli M, Piaggesi A, Scapagnini G, Dini V, Janowska A, Lacopi E, et al. (2018) Italy[36]	99 patients: 52 leg venous ulcers, 32 diabetic foot ulcers and 15 pressure ulcers	Multicenter, prospective, observational and uncontrolled study	Application of a layer of chromophore gel and light in the area with LED for 5 minutes. In combination with standard chronic wound care (debridement and cleaning with 0.9% SS).	-	Fortnightly	The assessment of the area and the healing time of the wound was performed with an imaging device called the Silhouette Imaging System.	Wound closure was achieved in 47 patients: 26 (50%) with venous ulcers (VU), 16 (50%) with diabetic foot and 5 (33.3%) with pressure ulcer (PU). The mean healing time was 41.3 days for diabetic foot, 82.3 days for VU and 81.2 days for PU. 18 wounds did not respond to treatment: 10 (19.2%) VU, 4 (12.5%) diabetic foot and 4 (26.6%) PU.

Chart 2 – Cont.

No.	Author/ Year Country/	Participants	Study Design/ Level of evidence	Intervention group (IG)	Control group (CG)	Frequency	Method for wound assessment	Treatment outcome
05	Frangezl, Nizic-Kos T, Frangez HB. (2018) Slovenia/ Eastern Europe[37]	30 patients with Diabetes Mellitus and chronic wound	Prospective dou-ble-blind and randomized study	Application of LED phototherapy in pa-tients with Diabetes Mellitus and chronic wound. There was no specification on the amount of each group.	30 patients treated with light simulating LED phototherapy	Three times/ week for eight weeks	The wound surface was measured using a photography im-age. The Pressure Ulcer Scale for healing instrument was used. The wound area was compared with the application of different wave-lengths:625,660 and 850 J/cm^{2}.	In patients who re-ceived LED, there was a reduction (56%) of the wound, and in the control group, it reduced by 65% ($p>0.05$). The rediction of did not vary with different wavelengths. Between the 4th and 8th week, there was a significant improvement ($p<0.05$) in the granulation tissue, with fibrin and exudate. There was no wound complete healing.
06	Ivanova YV, Klimo-va EM, Prasol VA, Mushenko EV, Ko-robov AM, Pogorielov MV, et al. (2018) Ukraine[38]	48 patients with ischemic and neu-roischemic forms of diabetic foot syndrome	Randomized clinical trial	24 patients with ischemic foot ne-crosis. Used violet, blue, green and red LED phototherapy. Debridement was associated with vacu-um therapy, autoder-moplasty, antiseptics, ointments, sorbent covers, etc.	24 patients with ischemic ischemic foot necrosis and wounds after debridement and daily dress-ings (antiseptics, ointments, sorbent covers, etc.). It also asso-ciated vacuum therapy and au-todermoplasty.	Three to five sessions	Clinical, laboratory, non-invasive, invasive tests of patients ate preoperative to determine the extent of disturbance in blood flow, collateral circulation, and microcirculation.	The treatment achieved complete healing in 91.7% of patients, partial healing (more than 50%) in 8.3% of patients, and prevented amputations. There was complete healing by 31 days after surgery. The combina-tion of dressings, LED and growth factor were effective in accelerating healing time.

Chart 2 – Cont.

No.	Author/ Year Country/	Participants	Study Design/ Level of evidence	Intervention group (IG)	Control group (CG)	Frequency	Method for wound assessment	Treatment outcome
07	López-Delis A, Rosa SSRF, Souza PEN, Carneiro MLB, Rosa MFF, Macedo YCL, et al. (2018) Brazil[23]	15 patients with lower limb ischemia and neuropathic ulcers.	Controlled and randomized study	Group I: Five participants, application of natural latex adhesive + LED phototherapy. Professional nurse made the dressing. Group III: Five participants, application of natural latex adhesive + LED phototherapy. The patient applied the dressing at home.	Group II: Five participants, standard care (use of silver alginate dressings) assisted by nurses	Fort-nightly	Two samples of the wound and venous blood were collected to assess the formation of free radicals. Collect tissue from the wound by scraping to assess the healing process. A spectrophoto-meter was used for measurements.	The association (latex + LED phototherapy) showed acceleration of wound healing with formation of granulation tissue, when compared to the control group. There was a high concentration of free radicals at the beginning and during the treatment and at the end its reduction, in the experimental group, being associated with the wound healing process. The wounds that nurses dressed healed faster and did not develop infection.
08	Vitoriano NAM, Mont' Alverne DGB, Martins MIS, Silva PS, Martins CA, Teixeira H.D, et al. (2019) Brazil[39]	12 patients with diabetic ulcer	Randomized clinical trial, comparative, with a quantitative approach.	Application of LED phototherapy	Wounds treated with GaAlAs Laser	Twice/ week with ten sessions	Photographic records and neuropathy assessment.	At the end of the 10th session, there was a reduction in the wound area of 79.5% in the LASER group and 55.86% in the LED group ($p<0.05$). As for the percentage, the Laser group showed a reduction of 81.7% and the LED group of 62.26%. As for the assessment of the neuropathic picture, there was a significant improvement ($p<0.05$) in both therapies.

Chart 2 – Cont.
Source: Authors, 2022.

The biological effects that LED causes in tissues depend on a set of factors that include individual characteristics, the clinical condition to be treated, tissue characteristics, in addition to overall parameters related to light dosimetry and wavelengths(14). Thus, if the physical and clinical characteristics of the ulcers and the LED parameters are not assessed in order to standardize a minimum healing time, the treatment may not be effective, mainly due to the hyperglycemia of diabetic patients that generate neuropathy and arterial periphery disease that can hinder an accelerated healing.

On the other hand, a study showed that LED phototherapy, regardless of the wavelength, was effective both for patients with diabetic ulcers and for those with chronic wounds(35). The effect on wound healing time was similar regardless of having DM.

Another study pointed out that the total wound healing time in diabetics was not longer when compared to patients who underwent the same treatment with LED phototherapy and who had venous ulcers and pressure ulcers(36). Pressure ulcers had approximately twice the time for total wound healing when compared to diabetic ulcers, even for this group of patients in which neuropathy and angiopathy could result in a low healing rate(36). This result showed the effectiveness of LED phototherapy regardless of the patient's underlying disease and heterogeneity of wound characteristics.

On the other hand, for some patients the treatment with LED was not effective(36). It was found that the reason for the ineffectiveness of the treatment was not investigated, such as associated comorbidities, the patient's clinical status and whether there was any specificity in the wounds such as infection or the presence of slough and necrotic tissue that could have interfered with treatment success.

Another study applied LED phototherapy for diabetic ulcers, however, it did not associate conventional treatment in patients(37). There was an improvement in the granulation tissue with an increase in microcirculation, but with little difference in area reduction between the placebo and experimental groups(37).

Despite the few clinical studies available in the literature, it can be assumed that LED phototherapy is more effective when associated with a certain standard treatment and that the healing rate, once again, was not dependent on the wavelength(37). More experimental studies, however, are needed for a standardized comparison of energy density doses and different LED wavelengths in the healing process, involving microscopic and histological analysis of different tissue layers, collagen production and punctual analysis of the total time to wound closure.

It was also found in this review that a study did not standardize the specific conventional treatment, but applied different invasive and non-invasive treatment techniques to accelerate the healing process and obtained successful results, when evidenced that, even with ischemic wounds, there was complete healing in a time of around one month when associated with LED phototherapy(38). It was concluded that, for wounds that will not close spontaneously after revascularization surgery in ischemic diabetic feet, LED phototherapy is indicated.

Another study indicated LED phototherapy to reduce the wound inflammatory process, when verifying the decrease of free radicals in the bed of ischemic wounds and neuropathic ulcers(23). During the inflammatory process, macrophages and neutrophils release free radical molecules, stimulating oxidative stress(43). High levels of this molecule prolong the inflammatory process, activate proteolytic pathways and lead to tissue damage(12,43). Thus, LED phototherapy contributed to reduce tissue injuries, especially granulation, promoting an acceleration of healing.

Another type of phototherapy that accelerates healing is LASER, but even though it was not an inclusion criterion in this study, a study was included in this review that compared LED phototherapy with this method, which also promotes effective photobiomodulation(39). Despite the results indicate that LASER promoted better healing in wound area when compared to LED phototherapy, some limitations were identified in the study, such as lack of standardization of wound size, reduced number of participants and absence of other analyzes such as a histological study and microscopic and analysis of oxidative markers for a better understanding of the healing process involving these two methods. LASER however was effective in reducing the size of the wounds and can be used as support in the treatment of diabetic ulcers.

These studies showed that there is a limitation of studies related to LED phototherapy versus wound healing worldwide and, above all, the need for Brazil to develop more work involving this theme, due to the high number of people with diabetic wounds who need a better treatment and follow-up(23,34,39).

Regarding the treatment frequency, the studies revealed a lack of consensus for the use of phototherapy in the treatment of wounds in people with DM. Different periods of time were found, with studies that mentioned two to five daily sessions(38), fortnightly(23,36), weekly(34), twice a week(39,33)and three times a week(35,37), with the application time varying according to the size of the lesion and the method applied.

Even in the face of evidence from studies that indicated that LED phototherapy was an effective, safe, fast and low-cost therapeutic approach in the treatment of wounds[23,35–38,40,44], there is still a lack of robust data and more clinical research on its effect on the healing process in people with DM and comparison across different dosage schedules and wavelengths. Further studies are recommended to improve the technique and better standardize it with a view to creating protocols that help to reduce healing time, reducing inconvenience to patients and improving quality of life.

It is suggested the construction of a specific protocol on LED phototherapy, written by nurses, expert professionals in the treatment and clinical management of wounds, based on scientific evidence already published and analyzed for conducting the treatment of wounds in diabetic foot, since, it is still difficult to completely heal these wounds, which often appear in polyneuropathic, ischemic patients with uncontrolled DM. Last, a detailed analysis of the healing process from the inflammation, granulation, epithelialization and wound maturation phase with the application of LED phototherapy associated with the number of sessions and the time for complete healing will promote an effective and standardized treatment of this therapy.

One of the limitations of this review was the small number of studies related to the proposed theme, which was not sufficient to demonstrate a higher level of evidence. Most of the research available is related to the applicability of LED in different clinical situations or even related to the use of photobiomodulation with LASER. In this sense, further studies are needed for greater application in clinical practice of LED phototherapy in the treatment of wounds in patients with Diabetes Mellitus. It should be noted that the low cost of the equipment compared to those found on the market, and its quick and easy application may favor the use of this device in health services, aiming at promoting a better quality of life for patients with diabetes and reducing expenses with conventional treatment.

CONCLUSION

The care provided to the patient with injury, especially diabetic patients, is still a challenge, both for those who experience this problem and for caregivers and health care professionals. Greater engagement in care is needed since this injury directly interferes with the individual's quality of life, self-esteem and biopsychosocial aspects. The treatment of a chronic wound is hard, but it is important that it occurs globally, considering the patient's life history and the general conditions of the injury. In addition to conventional treatment, currently, low-intensity therapy using LED has brought good responses for wound repair/healing, acting as a biomodulator of cells and tissues and optimizing treatment time.

In view of the analyzed studies, there was a lack of standardization in the tests that prove the effectiveness of the association of standard treatment with LED light, which may hinder a faithfully comparison of the results of each research.

It was shown that LED light was beneficial for tissue repair of wounds in people with DM, especially in relation to collagen production, angiogenesis, reduction of inflammation and lesion size and stimulation of fibroblasts. However, studies related to the applicability of this resource in this population are still limited and bring little evidence of the benefit of LED. There was great heterogeneity regarding experimental designs, especially the energy density applied to the cells, wavelengths, application time and ideal number of sessions in the treatment, with no consensus or even standardization in the technique.

For teaching, this study may contribute to expand techniques with the aim of favoring wound healing in people with diabetes, which has been shown to be effective in clinical trials. Simulation strategies in nursing laboratories allow a greater approximation and active participation of the professional, integrating theory with practice, contributing to the teaching and learning process to reduce adverse events.

This study opens the prospect for greater expansion on the subject and the need for future studies to verify the acute and long-term effects of LED photobiomodulation in diabetic wounds for the prevention of injuries and complications.

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