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ORIGINAL ARTICLE

Comparative study on laser and LED influence on tissue repair and improvement of neuropathic symptoms during the treatment of diabetic ulcers

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Abstract

To compare the influence of laser and LED on tissue repair and neuropathic symptoms during treatment of diabetic foot. An intervention survey conducted in a health center located in Brazil, contemplating ten sessions, twice a week, with randomization in two groups. In one group, the wounds were treated with GaAlAs laser, with a wavelength of 830 nm, 30 mW, and power density 0.84 W/cm^2, the other group by LED 850 nm, 48 mW, and power density 1.05 W/cm^2. For the analysis of wound size, photographic records analyzed by the ImageJ® software were used, and the neuropathy evaluation card examined. With regard to the laser group, a reduction in wound extension of 79.43% was observed at the end of the 10th session; the patients in the LED group had a 55.84% decrease in the healing process; comparing the two therapies was observed a better healing in the participants of the laser group, with 81.17%, in relation to the LED after the end of the sessions; regarding the evaluation of the neuropathic condition, there was a significant improvement in both therapies. There was improvement of the neuropathic signs and symptoms, also improvement of the tissue repair in the two therapeutic modalities; however, the laser presented a higher rate of speed in relation to the LED.

Keywords Diabetes mellitus · Ulcers · Phototherapy · Lasers

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Introduction

According to the International Diabetes Association [1], there are about 285 million diabetics in the world, which could rise to approximately 440 million by 2030.

After 5 to 10 years of onset of the disease, the chronic complications of DM may appear to be among these complications, ulceration and amputation, some of the most serious and of greater socioeconomic impact [2]. In addition to the formation of ulcers and amputation, diabetic neuropathy (ND) represents another chronic complication that is very prevalent among individuals with DM, affecting more than 50% of patients [3].

Individuals with DM have endothelial dysfunction, which promotes modifications in cellular performance, such as proliferation, migration, and angiogenesis. This dysregulation could predispose appearance of ulcers [4]. The application of phototherapy using different light sources has been proposed as a possible alternative for the activation of the enzymatic action and progression of the cell cycle during the healing process [5].

The light-emitting diode (LED) is a light source generated from a p-n junction diode that generates light when applying a current to the electrodes [6]; electrons are able to recombine within the device, generating energy in the form of photons. The light color depends on the crystal and the doping impurity with which the component is manufactured [7]. On the other hand, the mechanism of generation of lasers is conditioned by the pumping of electrons from one layer of valence to another making it excited having light, chemical reactions, or electricity as a source of energy. By the excitation of most electrons (population inversion), an input photon will lead to the emission of a large number of new photons (coherent and polarized) and the light will be magnified. Mirrors at each end of the laser cavity are positioned so that light jumps from one side to the other leading to a significant amplification [8].

There are two important differences between a light laser and a LED. One is bandwidth. Lasers usually have a very small bandwidth (fraction of a nano meter), whereas in LED, a band width is generally 1 to 2 nm. Another design asserts that a collimated laser is more likely to be scattered in front of the fabric than a divergent LED beam [9]. Although LEDs have higher emission spectrum than lasers, they have some advantages, such as they do not need lenses, they can be applied directly to the surface of the body, and they have the ability to irradiate a large area of tissue at once, possibility of wearable devices [8]. In addition, they do not attack the eyes, which is an important advantage in a clinical environment [10].

We can also point out as another property of photobiomodulation, its probable benefits in the reduction of neuropathic symptoms through the mechanisms of cytokine stimulation and release, an increase of circulation growth factors, ATP production by mitochondria of cellular oxygen consumption, corroborating for a greater vasodilation and nerve regeneration [11].

Based on these possible effects of phototherapy resources on the healing process and neuropathic pain, this study aimed to compare the influence of laser and LED on tissue repair and neuropathic symptoms during the treatment of diabetic foot.

Materials and methods

This study is a comparative, quantitative approach study in patients with diabetic ulcers who were followed-up at a health clinic located in the city of Fortaleza-CE, Brazil. The intervention period occurred between June and November 2017, after approval of the research ethics committee under the opinion of No. 1.817.533 which continued to comply with the norms of Resolution No. 466/12 of the National Health Council [12].

The sample used was of the convenience and not probabilistic, with 12 patients with diabetic ulcers chosen through randomization in 2 blocks that corresponded to group A "Laser" and group "LED".

Included were (1) diabetic patients with uninfected neuropathic ulcers and (2) authorization to participate by signing the informed consent form and clarified consent. The following were excluded: (1) patients presenting with ulcers due to venous alterations, (2) presence of peripheral vascular disease with a requirement for immediate surgery, (3) use of topical medication in the injured region for therapeutic purposes, and (4) that was absent for more than 3 days following treatment.

Evaluation

The patients were evaluated concerning the neuropathic condition by applying a scale for the diagnosis of diabetic neuropathy [13], and the neuropathic symptom scores and neuropathic signal scores were determined to obtain results that varied according to intensity (standard, mild, moderate, and severe) [14].

In the examination of the neuropathic signs, the Achilles reflex and the vibratory, painful, and thermal sensitivities are tested. In the evaluation of the signs, the patient is questioned about the existence of neuropathic symptoms in relation to the type of sensation (burning, numbness and tingling, and/or fatigue, cramp, and pain), location, period of the day in which there is greater exacerbation of symptoms, severity, and relief of symptoms [13, 14].

The wound classification instrument of the University of Texas was used due to its high applicability and wide reproducibility. According to this classification, the lesion is divided into stages A, B, C, and D. In this study, due to the exclusion of infected diabetic wounds, only stage A was considered for absence of infection or ischemia. When the lesion is analyzed in degree zero (0) pre- or post-ulcerative lesion

Table 1 Phototherapy parameters

Parameters	Laser	LED
Wavelength	830 nm	850 nm
Average radiant power	30 Mw	48 mW
Pulse structure	Continuous wave	Continuous wave
Radiant exposure	15.48 J/cm^2	14.64 J/cm^2
Irradiance at target (mW/cm^2)	0.25 W/cm^2	0.24 W/cm^2
Time delivery (per point)	28 s (per point)	22 s (per point)
Energy	0.25 J	0.20 J
Spot size (cm^2)	0.116 cm^2	0.196 cm^2
Application technique	Contact	Contact
Average number of points irradiated	3.3	6.15
Frequency of treatment	2×/weeks for 10 days alternate	2×/weeks for 10 days alternate

completely epithelialized; degree I referring to superficial wound not involving tendon, capsule, or bone; grade II referring to the wound with tendon or capsule exposure; and grade III referring to the wound with bone or joint exposure [2].

Treatment

The proposed treatment occurred twice a week, in an individualized way, totaling ten consultations until the end of the research. The diode laser gallium-aluminum-arsenide (GaAIAs) device (Saphire Line, IBRAMED, Amparo, Brazil) was used with the following parameters: wavelength 830 nm, output power of 30 mW, continuous wave mode, and the power density 0.25 W/cm^2. Contact technique was used. Each session was performed delivering a fluence of 7 J/cm^2 per point. Energy was delivered on the treatment site, producing a resulting spot size on the tissue surface of 0.116 cm^2 (irradiance 0.25 W/cm^2). Each entrance or exit of the needle puncture was irradiated in a contact mode of 28-s per point (0.84 J at7 J/cm^2). The LED device was a prototype and the following parameters were used: wavelength 850 nm, output power of 48 mW, continuous wave mode, and the power density 0.20 W/cm^2. Contact technique was used. Each session was performed delivering a fluence of 4.49. Energy was delivered on the treatment site, producing a resulting spot size on the tissue surface of 0.196 cm^2 (irradiance 0.24 W/cm^2). Each entrance or exit of the needle puncture was irradiated in a contact mode of 22-s per point (1.0 J at5.28 J/cm^2). The time of delivery per point of application was calculated using the formula (time) = D (dose-fluence)Å~A (area of the spot)/P (output power).

Table 2 Clinical data of patients with diabetic foot ulcers who underwent low-level laser therapy technique versus LED therapy

Patients	Gender	Number of punctures (mean)	Treatment
1	F	2.6	LED
2	M	1.8	Laser
3	F	2.3	Laser
4	F	1.8	Laser
5	F	3.4	Laser
6	M	7.4	LED
7	F	3.3	LED
8	M	3.7	Laser
9	M	6.9	Laser
10	M	7.2	LED
11	F	4.5	LED
12	F	11.9	LED

Researchers choose this wavelength by recent evidences with this wavelength in pathologic conditions. Bastos (2009) used 880 nm laser in burns and other researchers used LED 850 nm in patients with diabetic conditions; both correlated inflammatory response and wound healing, and both were effective in improving the organization of collagen fiber [15, 16].

Before the start of the intervention, the laser and LED emission area was wrapped in a plastic PVC film to avoid contamination of the patients, and the wound was sanitized with 0.9% saline solution. For protection during phototherapy, both the patient and the therapist used appropriate glasses.

The technique of debridement was used to extract necrotic tissues with excessive bacterial load and the presence of non-viable dead cells by means of a mechanical instrument [2]. This was performed by a team nurse and applied to all patients involved in the research depending on the condition of the wound. After performing the procedures, the lesion was covered by sterile gauzes, bandage, and surgical tape. The patient was instructed to replace it daily and clean it with saline solution, without making use of other coverages (Tables 1 and 2).

Data analysis

The evolution of the lesion was recorded from a digital camera (Sony Cyber-Shot DSC-W190 brand) at a distance of 10 cm

Table 3 Characterization of the studied population with laser and LED interventions

		Laser	LED
Variable		Mean ± standard deviation	Mean ± standard deviation
Age (years)		59 ± 6.2	64 ± 17.3
Time of diabetes (years)		19 ± 8.4	17 ± 9.0
Neuropathic Symptoms Score (Pre)		3.1 ± 0.4	3.0 ± 1.3
Neuropathic Signal Score (Pre)		2.0 ± 0.6	3.0 ± 0.4
Variable		Percentage (population)	Percentage (population)
Sex	Male	50% (6)	33% (2)
	Female	50% (6)	67% (4)
Previous ulcers	Yes	17% (1)	67% (4)
	No	83% (5)	33% (2)
Proper footwear	Yes	83% (5)	33% (2)
	No	17% (1)	67% (4)

from the camera lens to the injured region, and these were analyzed using ImageJ® software. This software allows the measurement in square centimeters (cm^2), concerning the circumscription of the edges of the wound, thus calculating the total area of the lesion [17].

After data collection, the results were attributed and analyzed with the help of the *Statistical Package for the Social Sciences*—SPSS (version 22.0 for *Windows*). Data are described as mean ± standard deviation (SD) or absolute and percentage numbers. Regarding the numerical parameters, these were analyzed by parametric and non-parametric tests. For the correlations, the Pearson correlation coefficient was used. It was considered statistically different when the level of significance was equal to or less than 5% ($p \leq 0.05$).

Results

Twelve diabetic patients with foot injuries were treated, and their characteristics are presented in Table 3.

Regarding the participants belonging to the laser group, a statistically significant difference was observed in the reduction of wound size when compared with the beginning of therapy. This same characteristic was observed in the LED group (Tables 4 and 5).

In addition to these results, we can observe an evolution, according to the University of Texas Diabetes Injury Classification [2], in classification of grade I (superficial wound) for grade zero (completely epithelialized lesion) in 8 of the 12 patients followed-up. The remaining 4 presented an improvement in the cicatricial process; however, they maintained the same classification (grade I) until the end of the 10th session.

Regarding the results of the comparative analysis between the performance of the laser and the LED in the healing improvement of the diabetic wounds, we can see a more significant reduction of the lesion in the laser group when compared to the LED group at the end of the therapy (Table 6, Graphic 1 and Graphic 2).

Discussion

In this study, we can demonstrate that the photobiomodulation effects of laser and LED not only accelerated the process of tissue repair of diabetic ulcers but also influenced the diabetic neuropathy positively by significantly reducing the score of signs and symptoms.

A multicenter study on the prevalence of diabetes in Brazil evidenced the influence of age on people with diabetes and observed an increase of 2.7% in the age range from 30 to 59 years to 17.4% in the age group of 60 to 69 years, an increase of 6.4 times [18]. Diabetic foot ulcers are usually caused by high pressures and repetitive stresses in patients diagnosed with diabetic neuropathy and microvascular changes [19]. According to Armstrong et al. [19], studies on ulcer recurrence rates, even after complete wound healing, can be estimated at 40% in patients with recurrence within 1 year, almost 60% at 3 years, and 65% at 5 years.

Table 4 Analysis of wound size in the laser and LED group

	Wound area 1st session	Wound area 5th session	Wound area 10th session	*p*
Laser group	1.76 ± 1.69*	1.01 ± 0.95	0.36 ± 0.50*	* = 0.002
LED group	1.45 ± 1.52#	0.90 ± 1.22	0.64 ± 0.81#	# = 0.006

Table 5 Analysis of wound size in the laser and LED group (percentage)

	Wound area 1st session	Wound area 5th session	Wound area 10th session	*p*
Laser group	–	42.61%*	79.55%*	* = 0.002
LED group	–	37.93%#	55.86%#	# = 0.006

Laser therapy has become a treatment option for diabetic ulcers due to the presence of anti-inflammatory effects, increased proliferation of myofibroblasts and stimulation of collagen fibers [20]. The decision to use phototherapy is due to the works like Beckmann et al. [21]. These authors related that chronic state of hyperglycemia promotes a degradation of the extracellular matrix. It leads a tensile strength of the skin and delay in the process of wound healing. A case study using low-intensity laser showed similar results to our research during the treatment of two diabetic ulcers in the calcaneus and the hallux region through 10 sessions, with a frequency of 1 to 2 times a week, with a significant reduction of the lesion and decrease of local pain. Therefore, the laser irradiation, even with few repetitions, can minimize the enzymatic expression and contribute to the control of the inflammatory response [4].

LED therapy has been the object of studies on its effect in wound healing and pain reduction and is promising in tissue injury [22]. A survey involving 36 Wistar rats, divided into diabetic, non-diabetic, and control groups, compared the action of the laser versus LED after a dorsal surgical lesion [23]. Similarly in our results, the benefits of phototherapy in reducing the diameter of the wounds in this paper were observed both in the groups treated with laser or LED. However, this reduction was more evident in the group of diabetic mice treated with LEDs, demonstrating their efficacy and ability to stimulate multiple chromophores and triggering various biochemical reactions.

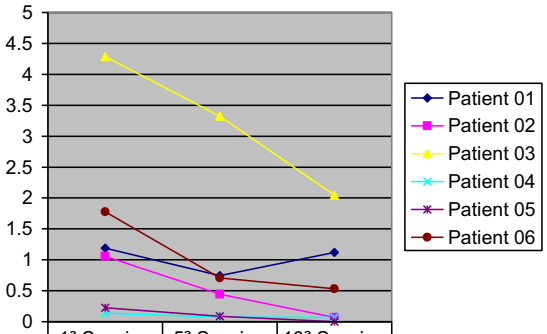
Diabetic neuropathy, considered a complication due to neurological changes, may also be related to vascular changes, very common in patients with diabetic ulcers [11]. Evidence presented by Shashi et al. [11], as in our results, pointed out the benefits of laser therapy in diabetic patients with neuropathic pain and changes in vibratory signals after evaluation of the signs and symptoms, as well as the application of visual analogic scale of pain and infrared thermal imaging.

From the data analyzed, it was possible to infer that the group of patients who underwent laser presented a reduction of the lesion size of 81.17% when compared to the LED group, with a reduction of 62.26%. For Chaves et al. [24], the probable difference between the action of the laser and the LED is due to a characteristic known as coherence, present in the laser, that plays a more efficient mechanism due to the presence of waves with the same frequency and the same direction, unlike the LED (not coherent) that would be less efficient in therapeutics.

However, based on another study [25], it has been observed that the LED can be as effective as the laser, since both have positive biological effects. According to Karu et al. [25], the cellular response to photostimulation is not related to the properties such as consistency. For this, property is lost during the interaction of light with the biological tissue, thus not being a prerequisite for the process of photostimulation or photoinhibition. Due to this efficacy, the use of LED draws attention, as another significant fact, to its speed in the process of tissue repair. Between the participants of the LED group until the end of the 5th session, there was a reduction of 47.60% of the wound compared to 42.86% in the injuries treated with laser. With the hypothesis, the possibility of the wavelength and dispersion of the LED light were more significant compared to that of the laser [26]. However, with inaccuracies about the differences in the mechanisms of action between the laser and the LED, a greater understanding about the absorption of light should be considered, so that there is a better justification of these findings.

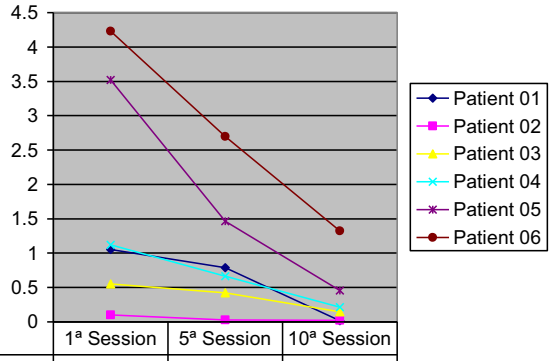
Table 6 Comparative analysis of wound reduction between the LED and laser groups

	Wound reduction percentage	
	1st and 5th session	1st and 10th session
LED	47.60% ($p = 0.028$)	62.26% ($p = 0.028$)
Laser	42.86% ($p = 0.028$)	81.17% ($p = 0.028$)



	1ª Session	5ª Session	10ª Session
Patient 01	1.188	0.742	1.118
Patient 02	1.059	0.444	0.069
Patient 03	4.288	3.323	2.049
Patient 04	0.139	0.074	0.067
Patient 05	0.228	0.09	0
Patient 06	1.778	0.708	0.53

Graphic 1 Evolution of wound treatment with LED intervention (1st to 10th session)



	1ª Session	5ª Session	10ª Session
Patient 01	1.054	0.789	0.019
Patient 02	0.101	0.027	0.022
Patient 03	0.554	0.424	0.145
Patient 04	1.122	0.667	0.214
Patient 05	3.521	1.462	0.455
Patient 06	4.231	2.697	1.322

Graphic 2 Evolution of wound treatment with Laser intervention (1st to 10th session)

We also emphasize that, in this research, we chose to compare only the action of the laser and the LED without the presence of the control group, based on studies [27–29] that showed the effectiveness of the phototherapy when compared to these groups.

In this way, we can point out that at the end of this study, despite the data presented, some limitations have probably hampered a better interpretation of the results regarding the healing process of diabetic ulcers, such as (a) the small number of participants that were included in the inclusion criteria of the research, (b) the presence of lesions with different sizes, and (c) the emergence of obstacles to the weekly implementation of therapy through financial deprivation and displacement of patients.

Consequently, we suggest as an alternative for future research the inclusion of a more substantial number of patients in the sample with standardization of lesion size and collection of oxidative markers for a better understanding of the mechanisms of action involved.

Conclusion

This study showed that phototherapy, whether with laser or LED, is a useful therapeutic modality to promote the healing of ulcers and to improve neuropathic signs and symptoms in patients with DM. A tissue repair with a higher speed rate was observed in the laser than in the LED. However, the mechanisms of action of laser and LED require further studies to better understand a probable superiority between the therapies involved, as well as more evidence of parameters more responsive to treatment.

Compliance with ethical standards

Ethical approval All procedures performed in this study, involving human participants, were in accordance with the ethical standards of the Ethics and Research Committee on Human Studies of the Federal University of Ceará (number 1.817.533).

Conflict of interest The authors declare that they have no conflict of interest.

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