OBJN
ONLINE BRAZILIAN JOURNAL OF NURSING
ISSN: 1676-4285

ORIGINAL

The use of low-level laser therapy in the treatment of cutaneous leishmaniasis: a quasi-experimental study

Uso da laserterapia de baixa potência no tratamento cutâneo da leishmaniose: um estudo quase-experimental

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Submission: 08/31/2023
Approved: 12/04/2023

ABSTRACT

Objective: To analyze the effects of low-level laser therapy in treating lesions resulting from cutaneous leishmaniasis. **Methods:** This is a double-blind, randomized, quasi-experimental study conducted at a reference center in the northern region of Minas Gerais. Seven patients were randomly assigned to receive intravenous and local wound care for cutaneous leishmaniasis. Specifically, three patients were assigned to the control group and received conventional treatment, while four patients were assigned to the experimental group and received low-level laser therapy plus standard therapeutic measures. The primary outcome measure was the reduction in lesion size as assessed by the adapted Pressure Ulcer Scale for Healing. Paired comparison statistics using the t-test were used for data analysis. **Results:** No significant difference was observed between the control and experimental groups. **Conclusio**n: Low-level laser therapy does not appear to improve the healing of cutaneous leishmaniasis lesions.
Descriptors: Leishmaniasis, Cutaneous; Laser Therapy; Wounds and Injuries.

RESUMO

Objetivo: Analisar os efeitos do laser de baixa potência na intervenção às lesões decorrentes da Leishmaniose Cutânea. **Método:** Trata-se de um estudo quase-experimental, duplo-cego e randomizado realizado em um centro de referência do Norte de Minas Gerais. Foram alocados aleatoriamente 07 pacientes que foram submetidos ao tratamento endovenoso e curativos locais da leishmaniose cutânea, a saber: 03 no grupo controle, onde fizeram uso do tratamento convencional, e 04 no grupo experimental, que foram submetidos a aplicação da laserterapia de baixa potência, além da terapêutica habitual. Foi avaliado como desfecho primário a redução do tamanho das lesões, por meio da adaptação da ferramenta *Pressure Ulcer Scale for Healing*. A análise dos dados foi conduzida por meio de uma estatística comparativa pareada com teste T. **Resultados:** Não houve diferença significativa entre os grupos controle e experimental. **Conclusão:** A laserterapia de baixa potência não parece favorecer a cicatrização das lesões por leishmaniose cutânea.
Descritores: Leishmaniose Cutânea; Terapia a Laser; Ferimentos e Lesões.

INTRODUCTION

Leishmaniases are a group of diseases considered endemic in Brazil, manifesting as visceral leishmaniasis and cutaneous leishmaniasis (CL). They represent a significant public health challenge due to their magnitude and geographic distribution, potentially causing mortality, disability, and disfigurement[1].

Globally, the epidemiology of leishmaniasis remains a concern, with approximately 1.5 million new cases reported annually and an estimated 20,000 to 40,000 of these cases resulting in death[2]. This reality is no different in Brazil: in 2019, the country ranked first in the Americas for disease incidence, with 15,484 reported cases. Of these, 14,659 ca-

How to cite: Scarcella MFS, Silva CS de O e, Barbosa AX, Ribeiro VES. The use of low-level laser therapy in the treatment of cutaneous leishmaniasis: a quasi-experimental study. Online Braz J Nurs. 2024;22 Suppl. 2:e20246681. https://doi.org/10.17665/1676-4285.20246681

ses were cutaneous (94.7%), representing an incidence rate of 14.4 cases per 100,000 inhabitants[3].

Cutaneous Leishmaniasis (CL) is a noncontagious infectious disease endemic to over 98 countries. It is transmitted vectorially to humans by the bite of an infected female sandfly, which carries protozoa of the genus Leishmania. It is, therefore, classified as a zoonotic disease[4].

The disease is characterized by the appearance of skin lesions that progress from papules and nodules to plaques and ulcers, often with prolonged healing over months and years, resulting in physical and emotional damage. Although it is characterized as a low-mortality disease, there is usually a delay in the healing process, resulting in scarring that interferes with a person's self-image and negatively impacts the quality of life[5-6].

There needs to be more studies in the literature that address local therapy in the treatment of cutaneous lesions resulting from leishmaniasis, with more emphasis placed on systemic treatment. No clinical studies were found that tested nursing interventions in the cutaneous treatment of the disease to achieve better results in lesion management, thereby accelerating the healing process and promoting favorable outcomes in scar formation.

In this context, the advanced practice of laser therapy in nursing emerges as an innovative intervention for patients with cutaneous leishmaniasis lesions. Laser therapy is a therapeutic tool that amplifies light through stimulated emission of radiation. The result of this process enhances the biological response of organisms, such as anti-inflammatory, analgesic, cicatrizing, anti-edematous, nerve/muscle repair responses as well as antibacterial and antifungal effects, promoting cellular proliferation and protein synthesis[7].

Nurses have recently been using laser therapy to treat cutaneous lesions, with positive results. However, the available studies have a methodological approach with a low level of evidence, consisting mainly of case reports, case series, and observational studies[8-10].

Advanced practice nursing in combination with laser therapy represents a promising approach to improving health care[11]. The ability of nurses to assess, prescribe, and administer laser therapy treatments can lead to positive outcomes for a wide range of clinical conditions[12-13]. Therefore, this study is a tool to generate knowledge and substantiate advanced nursing interventions. The results provide a basis for discussing current practice, planning, and implementation to improve care.

The study question arises from observing the high prevalence and the negative impact these lesions have on individuals. In addition, there is a lack of nursing interventions for the non-pharmacological treatment of this condition. This shortage can hurt the lives of these patients and health services. Therefore, the question arises: "What is the best nursing intervention for treating cutaneous lesions in people with leishmaniasis?"

Hypotheses have been raised that low-level laser therapy may have anti-protozoal effects in addition to its bactericidal and antifungal effects. Furthermore, the beneficial effects of laser therapy, well documented in the literature for promoting the healing process, are likely to have a therapeutic impact superior to commonly used treatments in conventional therapy of cutaneous lesions caused by leishmaniasis.

To this end, the present study aims to analyze the effects of low-level laser therapy in treating lesions resulting from CL.

MÉTODO

This study was conducted according to the adapted recommendations of the Consolidated Standards of Reporting Trials (CONSORT).

This is a quasi-experimental, randomized, double-blind study consisting of two groups: the control group (CG), composed of participants who received standard care for CL, including intravenous drug administration and conventional dressings; and the experimental group (EG), composed of participants who received laser therapy sessions in addition to conventional intravenous and topical CL treatment. The study was conducted from January 2022 to February 2023 at a reference center for outpatient CL and wound care in Montes Claros, MG, Brazil. This place is considered an endemic region for CL in the state, identified by the Pan American Health Organization as an area of moderate transmission. Epidemiologic data indicate a 5.3% increase in the incidence of cutaneous leishmaniasis from 2019 to 2020, with 264 cases reported in 2019 and 278 cases in 2020[3,14-15].

The population for this study included all patients admitted to the study site during the period above (n = 18). The study sample consisted of 7 participants, of whom 4 were in the experimental group (EG) and 3 in the control group (CG). Figure 1 illustrates the flow chart of the study.

The following inclusion criteria were adopted: age 18 or older and at least one cutaneous lesion healing by secondary intention. Exclusion criteria included pregnant patients, patients with current or previous neoplasms, and patients with healed or mucosal lesions.

The evaluated intervention used low-level laser therapy with the GaA1As (gallium aluminum arsenide, 808nm/infrared) & InGaAlP (indium gallium aluminum phosphide, 660 nm/red) dual diode LASER, LASER duo - MMOptics device. The protocol developed by the research team based on the literature[16-17] included four sessions of low-level laser therapy with a wavelength in the visible light range (red light) using a dose of 4 J/cm^2. Standard outpatient care was maintained concurrently with the intervention.

One of the researchers developed the intervention with a wound care specialist and tested it in a pilot study with five patients not included in the final sample. The researcher remained blinded to participant allocation, and the intervention was delivered by the specialist nurse in charge of the outpatient clinic, who was trained in this technique.

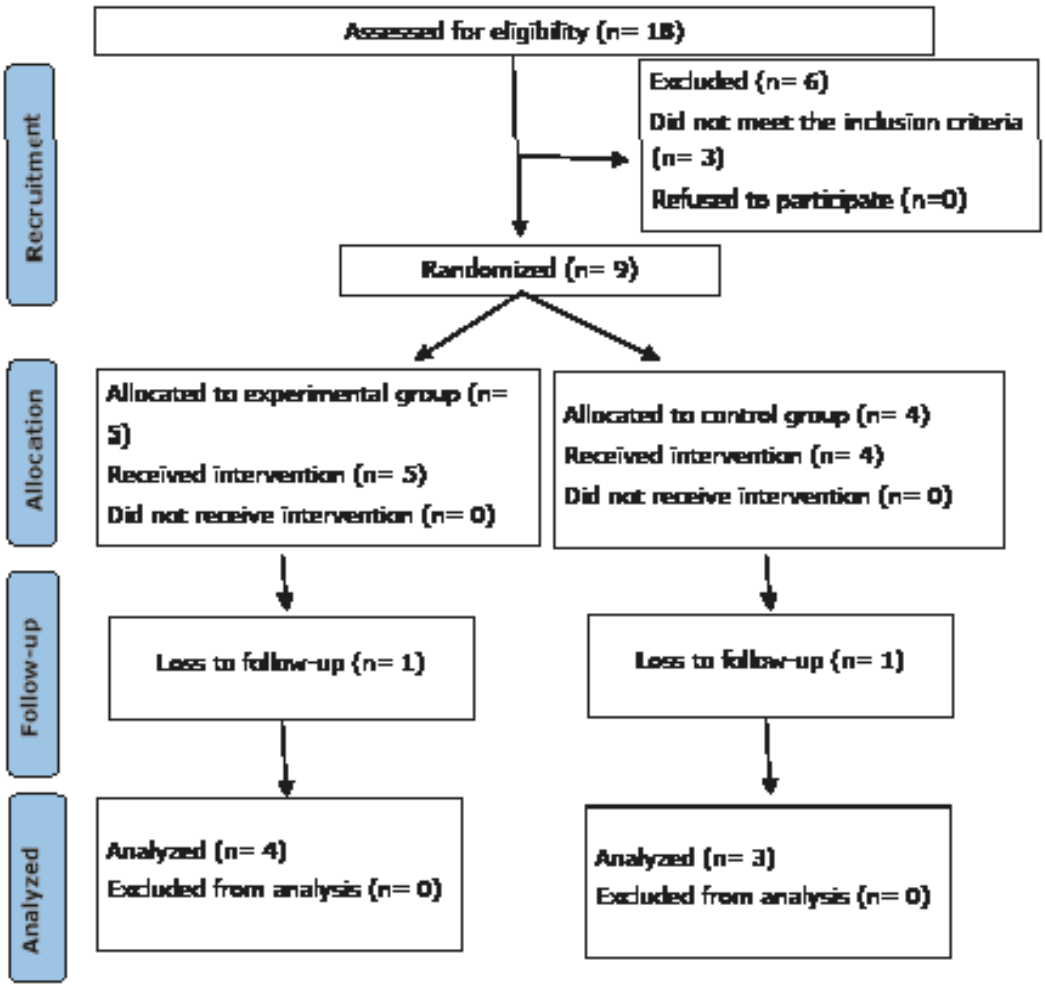
Participants in the control group (CG) received standard care during the treatment period. Standard care included the use of conventional dressings according to the routine of the outpatient clinic and intravenous therapy prescribed by a specialist.

The study's primary outcome was to assess lesion size reduction by comparing measurements at baseline and at the end of treatment. The Pressure Ulcer Scale for Healing (PUSH) 3.0 instrument was adapted to assess wounds and collect pre- and post-intervention data.

Randomization was performed using a block randomization scheme via http://www.randomization.com/. A statistician with no clinical involvement in the study generated a random sequence corresponding to two blocks (i.e., EG and CG) of four participants each for randomization. They were assigned after a sequentially numbered list was generated. The study is considered double-blind because both the researchers collecting the data and the data analyst must be made aware of the interventions offered.

To conduct the study, the team comprised a nurse/researcher (Ph.D. student), a specialized nurse in charge of the outpatient clinic, two undergraduate students, and a supervisor. Regarding the distribution of responsibilities, the supervisor randomly assigned patients already admitted to the reference center for treatment. The three undergraduate students collected the questionnaire related to sociodemographic profiles and initial data about the lesion before the intervention. The nurse then administered standard care and/or laser therapy. At the end of the treatment, the PUSH 3.0 was used again to evaluate the lesion. A comparative analysis of the "lesion size" variable was then performed using the paired t-test for normally distributed data.

All ethical principles regarding research involving human subjects were followed under Resolution No. 466/2012 of the Brazilian National Health Council (NHC). The research was approved by the Research Ethics Committee (RES) of the State University of Montes Claros (Unimontes) (opinion number 3037397, attached amendment number 4332499). Before the start of data collection, all participants were informed through a two-part informed consent form, ensuring their informed consent for using the information obtained.



Fonte: Flowchart PRISMA-ScR adapted from Page et al., 2021.
Figure 1 - Flowchart of the research. Montes Claros, MG, Brazil, 2023

RESULTS

The study sample consisted of 7 participants, of whom 3 were in the control group (CG) and 4 in the experimental group (EG). According to the sociodemographic characterization of the participants, the mean age was 34.4 years, with 2 females and 5 males. None of the participants had completed higher education. The homogeneity of the study sample in terms of initial and final lesion size was evaluated using the t-test. The test showed that the CG and EG were comparable considering these variables.

Table 1 shows the study participants and the respective treatments they received as well as the evolution of lesion size at baseline and at the end of the interventions.

The results of the within-group statistical analysis comparing pre- and post-intervention or standard care showed that there was no significant difference in lesion size reduction when comparing the type of therapy used, as shown in Table 2.

Table 1 – Description of lesions and treatments for patients with leishmaniasis (n= 07). Montes Claros, MG, Brasil, 2023

Patients	Types of treatment	Initial Length (cm) × Width (cm)	Final Length (cm) × Width (cm)
P1	Standard treatment	24cm²	22cm²
P2	Standard treatment	6,25cm²	0
P3	Standard treatment	8 cm²	0
P4	Laser plus Standard Treatment	15cm²	13,5cm²
P5	Laser plus Standard Treatment	54cm²	0
P6	Laser plus Standard Treatment	12,5cm²	0
P7	Laser plus Standard Treatment	77cm²	1,5cm²

Upon examination of the efficacy in reducing the size of the lesions, the use of laser therapy did not show a greater reduction in the size of the lesions compared to the use of standard care dressings. The analysis also showed that the standard care only group was actually closer to significance (p = 0.09) than the experimental group.

Table 2 – Within-group comparison of patients with Leishmaniasis (n=07). Montes Claros, MG, Brazil, 2023

Groups	Statistic	g/	p
GC	3.04	2.00	0.093
GE	2.06	3.00	0,131

DISCUSSÃO

Recent studies have consistently demonstrated the beneficial effects of low-level laser therapy in promoting wound healing and tissue regeneration. Low-level laser therapy induces fibroblast proliferation, collagen synthesis, and increased vascularization in the wound area. These processes contribute to the accelerated formation of granulation tissue, resulting in faster and more effective healing[18].

While the use of laser therapy in wounds of various etiologies is well established in the literature, the same cannot be said for wounds resulting from CL. A review study examined the effects of low-level laser therapy in the treatment of pressure ulcers and concluded that photodynamic therapy can significantly accelerate healing. Stimulation of fibroblasts and promotion of collagen synthesis appear to be key factors in this process. In addition, increased neovascularization and improved local blood supply may contribute to faster granulation tissue formation[19].

Wounds resulting from leishmaniasis are often chronic, inflammatory, and have the potential for secondary infections. The exacerbated inflammatory response plays a role in the progression of the lesion and difficulty in healing, which can lead to complications such as deformity and functional disability[20].

In this context, that low-level laser therapy has anti-inflammatory and immunomodulatory properties. There is a reduction in the expression of pro-inflammatory cytokines and a greater regulation of the balance of immune responses. These modulations are essential to create an environment conducive to healing and to minimize the risk of infection[21].

In a study conducted on Leishmania-infected mice, the effects of low-level laser therapy on the wound healing process were investigated. The research focused on evaluating the therapeutic effects of laser therapy in the context of parasitic infection and tissue repair and demonstrated that low-level laser therapy promoted the formation of healthy granulation tissue, reduced edema, and increased vascularization in the wounds. These results suggest that low-level laser therapy may have a beneficial effect on accelerating healing and controlling inflammation in Leishmania-infected wounds,

indicating its potential as a therapeutic approach in the treatment of wounds associated with this parasitic infection[22].

In the literature, there are only a few human studies investigating laser therapy, and all of them are from graduate programs in Brazil.

A study conducted in Brazil suggests that low-level laser therapy may be an effective option for treating CL ulcers but does not appear to affect the ability of Leishmania parasites to cause infections. In fact, tests on these patients showed that the use of low-level laser therapy is a promising tool in the treatment of ulcers caused by leishmaniasis. In this study, the laser reduced swelling, stimulated the microbicidal activity of macrophages, and promoted proper collagen formation in the affected skin. However, tests with Leishmania parasites in a laboratory setting showed that low-level laser therapy had no significant effect on promoting programmed cell death of parasite cells and did not alter the composition of the parasite plasma membrane. This suggests that low-level laser therapy does not affect the ability of parasites to infect host cells[23].

This study is consistent with the results of the present research, as the laser-treated group did not show a statistically significant difference in lesion healing compared to the standard care group, which used only the usual topical dressings.

Recently, Camargo[24] studied the effects of photodynamic therapy with methylene blue on promastigotes and amastigotes of the major Leishmania species circulating in Brazil. The study concluded that laser therapy, especially at high concentrations of the photosensitizing agent, resulted in parasite inactivation, suggesting that the use of methylene blue during laser therapy may be an important factor in its efficacy[24].

This finding also provides a basis for the results of our study, as the effect of low-level laser therapy alone, without the photosensitizer, was also unsatisfactory for the control of leishmaniasis. However, studies with human lesions still need to be performed.

A limitation of the study is the small sample size, which was due to the low number of referrals for outpatient intravenous treatment of CL to the community reference center over one year.

CONCLUSION

This study did not statistically demonstrate an additional beneficial effect of using laser therapy in the treatment of lesions resulting from cutaneous leishmaniasis. Such results open the need and opportunity for experimental studies in humans on photodynamic therapy for ulcers of that etiology.

The literature is still in its early stages and inconclusive, making it essential to deepen it because of the prevalence of CL in Brazil. The present research meets this need and can contribute significantly to the implementation of preliminary evidence on the subject.

CONFLICT OF INTERESTS

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

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Writing and/or critical review of the intellectual content: Scarcella MFS, Silva CS de O e, Barbosa AX, Ribeiro VES
Final approval of the version to be published: Silva CS de O e
Responsibility for the text in ensuring the accuracy and completeness of any part of the paper: Scarcella MFS