USE OF PHOTOBIOMODULATION IN THE HEALING OF DIFFICULT-TO-HEAL LEG ULCERS: A RANDOMIZED CLINICAL TRIAL

https://doi.org/10.56238/sevened2025.011-069

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ABSTRACT

Introduction: Leg ulcers are characterized by a prolonged course, delayed healing and high recurrence rates, bringing a great challenge to clinical treatment and care of people. Its prevalence increases with age, which also affects its recurrence and adherence to treatment. Objective: to compare the effect of adjuvant photobiomodulation versus conventional treatment alone on the healing of leg ulcers. Method: single-center, randomized clinical trial with 17 people treated at a referral service. The outcome of interest was wound healing. People with leg ulcers who had the lesion for six weeks were included. Data collection was done through a sociodemographic questionnaire, a form with aspects of life and clinical data, and the Pressure Ulcer Scale for Healing/adapted version for ulcer evaluation. Analyses were performed using the Statistical Package for the Social Sciences (SPSS), version 20.0, and descriptive and bivariate analyses were conducted. Results: the clinical indicators Amount of exudation and Lesion area showed a statistically significant difference in the intervention group. Conclusions: adjuvant photobiomodulation compared to conventional treatment returned better results in the healing process of ischemic leg ulcers.

Keywords: Leg ulcer. Injuries and injuries. Low-intensity light therapy. Cicatrization.

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INTRODUCTION

The prevalence and incidence of chronic ulcers have increased with the aging of the population and the increase in the prevalence of associated chronic conditions, such as systemic arterial hypertension and diabetes mellitus[1]. According to a recent meta-analysis, chronic ulcers in the lower limbs occur in 1.5 out of every 1,000 people in the general population[2]. In Brazil, epidemiological records of the incidence and prevalence of ulcers are scarce, and some authors estimate that approximately 3% of the Brazilian population has leg ulcers[3].

About 75% of leg ulcers (PU) worldwide are venous ulcers, which can affect 80% to 90% of cases. Some risk factors favor this number, such as: advanced age, female gender, family history of venous leg ulcers, diabetes, hypertension, obesity, sedentary lifestyle, smoking and prolonged position[4].

Despite the diversity of treatments available, the healing process of PU is difficult and prolonged. In view of this, photobiomodulation (FBM), specifically, Low Level Laser Therapy (TLBP), has been used as an adjuvant to conventional treatment to assist in wound tissue repair, due to its biomodulatory effects[5,6].

TLBP activates or inhibits physiological, biochemical, and metabolic processes through photophysical or photochemical effects. These biomodulatory phenomena promote the therapeutic effects of cell morphodifferentiation and proliferation, tissue neoformation, revascularization, reduction of edema, greater cell regeneration, increase in local microcirculation and vascular permeability[7].

In this context, some randomized studies show, based on clinical indicators, tissue regeneration and reduction in the size of skin lesions when this modality of adjuvant therapy is used in traditional therapy[8-10].

However, there is still a gap in knowledge about the specific protocols and late effects of this assistive technology on the healing process of difficult-to-heal ulcers. In this sense, the evaluation of the healing process of these wounds through indicators validated in clinical practice is essential for evidence-based care and has been little recorded in the literature through studies[11].

Thus, it is necessary to conduct studies to evaluate the efficacy and applicability of these health innovations, especially in the context of the public health care network. The search for treatments that enable the healing of chronic wounds or wounds that are difficult to heal must consider, in addition to their potential for cure, the costs for the health institution that offers these services. This study aimed to compare the effect of adjuvant photobiomodulation versus conventional treatment alone on the healing of leg ulcers.

METHODS

This was a randomized, single-center clinical study developed with two groups: intervention (IG), in which TLBP was used as an adjuvant to conventional treatment, and control (CG), in which conventional treatment was performed with the use of topical products and dressings and compression therapy. The study did not show blinding in the application of the intervention, due to the irradiation emitted by the laser light used in the IG. It was carried out at the Dr. Alpheu Gonçalves de Quadros Health Complex/Wound Outpatient Clinic, a reference in wounds in the city of Montes Claros – Minas Gerais, Brazil. This service provides care to people with wounds, of all etiologies, serves six people in the morning shift and six in the afternoon shift, from Monday to Friday. People with active leg ulcers treated by the Outpatient Clinic in 2022 and 2023 participated in this study. People who had had venous, arterial or mixed ulcers for at least six weeks of injury, aged ≥ 18 years, and who were regularly attending treatment, with the ability to respond to the research instruments, were included. People with infected wounds or coagulation necrosis in the wound bed were excluded.

Before data collection, the researchers were calibrated using the *kappa test,* obtaining an index of 1.

The care at the outpatient clinic is carried out through a waiting list, and the people are referred by the Primary Care (PA) services, and the treatment obeys the longer registration time of people with injuries on this list and the operational capacity of the outpatient clinic (number of consultations, physical structure, available professionals and products for treatment). After being approached by the researchers, people answered a sociodemographic questionnaire and a form with aspects of life, the clinical data were collected from the medical records. They were randomized into two groups: IG, who received the laser intervention associated with the conventional treatment used by the service, and CG, who received only the conventional treatment already used by the service.

The Pressure Ulcer Scale for Healing *was used to evaluate the lesions.* Participants were followed for four weeks. For the GI group, photobiomodulation with a wavelength within the visible light range was used, three times a week at a dosage of 4 J/cm2 of lesion, and the conventional treatment standardized daily was used. In the CG, only conventional treatment was performed daily. The wounds were photographed and measured on the first, fifteenth and thirtieth days of follow-up.

The variables investigated were: sociodemographic characteristics (gender, age, skin color, marital status, years of schooling, professional activity, family income, and household), behavioral characteristics (performed physical exercise in the last three

months, participated in religious activity, drank alcohol, and smoked), clinical conditions (BMI, associated diseases, and type of treatment), and characteristics of the lesion (region, time, area, border, epithelialization, amount of exudate, type of exudate, and necrotic tissue).

Initially, descriptive analyses of all the variables investigated were performed using simple, relative, mean and standard deviation frequencies. Normality tests were then performed for the characteristic variables of the lesion. The variables were categorized to compare day one of collection with day thirty, for each type of treatment (conventional treatment, laser treatment). For this, the Wilcoxon test was used. To compare the means of the variable lesion area on day one with day 30, in each treatment, Student's t-test was used. Considering a significance level of 5%. All analyses were performed using the Statistical *Package for the Social Sciences* (SPSS), version 20.0.

This study was approved by the Research Ethics Committee of the Institution, in accordance with Resolution No. 466/2012 of the National Health Council.

RESULTS

A total of 17 people participated in the study, (10, 58.8%) allocated to the IG and (7, 41.2%) to the CG. Most were female (7.42%), elderly (9.52.9%), with a family income ≤ 2 minimum wages (16.94.1%) and without schooling or only with elementary education (11.73.3%), non-white (13.76.5%)

Regarding behavioral habits, the majority (14, 82.4%) did not perform physical activity or ingested alcoholic beverages. Only (1.5.9%) reported being a smoker. Regarding clinical conditions, the presence of Arterial Hypertension (88.2%) was found in a higher percentage of people, and less frequently, Diabetes Mellitus (11.8%).

The largest number of wounds was located on the leg (14, 82.4%). When characterizing the groups according to the time of the injury, and investigating the presence of adverse factors to healing, such as comorbidities and the presence of non-viable tissue, it was found that in the group with wound >= 1 year (13, 76.5%) were overweight or obese, and in the wound there was the presence of sloughing (15, 88.2%) on day 1 and (9, 69.2%) on the 300th day of treatment. At the beginning of follow-up, the wounds did not show epithelialization, and after 30 days of treatment, the wounds had < 25% of the epithelialized area (7.43.8%), between 25 and 50% (5.31.3%) and between 50 and 100% epithelialized (4.25%) (Table 1).

Table 1- Sociodemographic, behavioral, clinical and laboratory conditions of people with venous, mixed and other insufficiency, Montes Claros, MG, 2022 to 2023.

Variables	n	%
Sociodemographic		
Sex		
Male	7	41,2
Female	10	58,8
Age		
< 60 years	8	47,1
≥60 years old	9	52,9
Skin color		
White	4	23,5
Non-white	13	76,5
Marital status		
With partner	11	64,7
No companion	6	35,3
Years of study		
Higher/Secondary/Technical Education	4	26,7
Elementary school/no study	11	73,3
Professional activity		
Retiree/pensioner	12	80,0
Formal/informal remuneration	3	20,0
Household income		
>2 minimum wages	1	5,9
≤ 2 minimum wages	16	94,1
Domicile		
Own	13	76,5
Rented/Leased	4	23,5
Behavioral		
Has exercised in the last 3 months		
Yes	3	17,6
No	14	82,4
Participate in religious activity		
Yes	9	52,9
No	8	47,1
Drink alcohol		
No	14	82,4
Yes	3	17,6
Smoke		
No	16	94,1
Yes	1	5,9
Clinical conditions		
BMI		
Eutrophic/Low Weight	4	23,5
Overweight/obesity	13	76,5
Associated diseases		
Hypertension/Other	15	88,2
Hypertension/diabetes	2	11,8
Type of treatment		
Laser plus conventional treatment	10	58,8
Conventional treatment	7	41,2

Source: study data, 2024.

Table 2 shows the characteristics of the lesion on the 1st and 30th days. The largest number of wounds were located on the leg (14, 82.4%), which presented sloughing (15, 88.2%) on day one of treatment and nine (69.2%) on day 300 of treatment. At the beginning of follow-up, the wounds did not show epithelialization, and after 30 days of treatment, the wounds had < 25% of the epithelialized area (7.43.8%), between 25 and 50% (5.31.3%) and 50 to 100% epithelialized (4.25%) (Table 2).

Table 2 – Injury characteristics of people with venous, mixed, and other insufficiency, Montes Claros, MG, 2022 to 2023.

Variables	Day 1		Day 30	
	n	%	n	%
Region of the lesion				
Leg	14	82,4	14	82,4
Foot	3	17,6	3	17,6
Time of injury				
< 1 year	4	23,5	4	23,5
>= 1 year	13	76,5	13	76,5
Area (cm2)				
< 20	8	47,1	9	56,3
> 20	9	52,9	7	43,8
Edge				
Well defined and adhered to	13	76,5	11	84,6
Peeled/macerate/dry	4	23,5	2	15,4
Epithelialization				
50% to 100% covered	0	0	4	25,0
25% to 50%covered	0	0	5	31,3
<25% covered	0	0	7	43,8
Amount of exudate				
Absent/Small/Moderate	12	70,6	12	92,3
Big	5	29,4	1	7,7
Type of exudate				
Serosanguineous	1	5,9	0	0,0
Seroso	16	94,1	13	100,0
Fabric Type				
Missing/non-viable tissue/unadhered shedding	2	11,8	4	30,8
Yellow slough with little adhesion	15	88,2	9	69,2

Source: study data, 2024.

Table 3 shows the Wilcoxon test in the comparison of the characteristics of the lesion, according to the type of treatment. When comparing the characteristics of the IG and CG lesions, a significant difference between the groups was observed in the variable Amount of Exudation (p=0.046).

Table 3 - Wilcoxon test for lesion characteristics, according to type of treatment, of people with venous insufficiency, mixed and others, Montes Claros, MG, 2022 to 2023.

Conventional treatment				Laser treatment		
Injury Characteristics	**n**	**Average***	**p**	**n**	**Average***	**p**
Edge						
Day 1	7	1,0	0,317	10	1,0	0,655
Day 30	4	1,0		9	1,0	
Epithelialization						
Day 1	0	-	-	0	-	-
Day 30	6	1,0		10	1,0	
Amount of oozing						
Day 1	7	1,0	1,000	10	1,0	**0,046**
Day 30	4	1,0		9	1,0	
Oozing type						
Day 1	7	4,0	0,317	10	4,00	1,000
Day 30	4	4,0		9	4,00	
Fabric Type						
Day 1	7	2,0	0,317	10	1,80	0,564
Day 30	4	2,0		9	1,67	

Source: study data, 2024.

* Median of the positions

Table 4 presents the "t" test only for the variable area of the lesion, with a significant result when considering laser treatment (p=0.0.37).

Table 4 - "t" test for the lesion area variable, according to conventional treatment and laser treatment.

Conventional treatment				
Lesion area (cm2)	**n**	**Average**	**Standard deviation**	**p-value**
Day 1	6	36,38	39,4	0,335
Day 30	6	24,54	35,4	
Laser treatment				
Lesion area (cm2)	**n**	**Average**	**Standard deviation**	**p-value**
Day 1	10	45,55	47,1	0,037
Day 30	10	31,68	33,0	

Source: study data, 2024.

DISCUSSION

This study compared the effect of adjuvant photobiomodulation versus conventional treatment alone on the healing of leg ulcers at a thirty-day follow-up. It is worth noting that skin care has always been in the scope of nursing work, including the prevention and treatment of wounds[12].

Leg ulcers are frequent, with a particularly higher prevalence in the elderly population. The correct diagnosis of these conditions and the appropriate treatment, based on the best scientific evidence, are fundamental to reduce the negative impacts on people's lives[13].

The profile of the people in this study is compatible with the profile presented by the population with leg ulcers described in other studies carried out in different contexts and in different regions of Brazil. In addition to age and the underlying disease in the etiology of the ulcer, overweight and obesity were present in 76% of the people with ulcers[14].

In this study, 88.2% of the users had AH. A study that analyzed clinical trials of lower limb ulcers pointed out that in 4 studies (80%) there was a prevalence of venous ulcers and 1 (20%) ulcers due to ischemic complication resulting from peripheral arterial disease, this proportion is in line with the results pointed out here. There are different types of chronic ulcers of the lower limbs, which can be venous, arterial and mixed, but the most common etiology is chronic venous insufficiency, which accounts for approximately 80% of leg ulcer cases and occurs due to abnormal function of the venous system caused by valvular insufficiency, which may be related to obstruction of blood flow. Up to two-thirds of all leg

ulcers will be venous in origin, a prevalence of 1% to 3% of UV in the general population. (15)

The data showed that after thirty days of adjuvant FBM use, the wounds maintained better averages in the results Amount of Exudation and Lesion Area, with a statistically significant difference in relation to the group that used only conventional treatment. In line with this, a randomized study carried out in the city of Porto Alegre, Brazil, with 40 people presenting PU, which also compared the effect of adjuvant FBM versus conventional treatment alone in the healing of leg ulcers, showed a higher number of healed VU in less time, with better epithelial tissue when compared to the control group[16]. Other studies conducted in Poland, Austria, India and the United States with the use of FBM in the treatment of leg ulcers have shown results similar to those of the present study[17-20].

A systematic review on photobiomodulation demonstrated that it is an effective adjuvant therapy for the management of venous ulcers, as it is capable of stimulating cell growth and optimizing healing, so as to contribute to the clinical improvement of patients and, indirectly, improve their quality of life[21].

In vivo studies (animals and humans) have validated that low-level laser acts on the proliferation of fibroblasts and epithelial cells, the production of collagen and elastic fibers, increased vascularization, and antibacterial and immunological potential[19-20].

In a randomized clinical study conducted in Santa Catarina, Brazil, the use of laser associated with dressings was tested in six people with leg ulcers. People were randomly divided into two distinct groups: group 1: who was exposed to laser, a 660 nm 4J/cm² pen, associated with a dressing with fatty acid oil, for a period of ten days; and group 2, exposed to the same parameters as the laser, along with a papain dressing. The two protocols presented adequate results in relation to the healing process of the lesions, but the group that was exposed to the dressing with essential fatty acid oil and laser therapy presented better results in relation to the indicators, physical appearance of the skin and reduction of wound areas, indicating that the fatty acid associated with the laser led to better results[21].

A systematic review, with a search of articles published between 2004 and 2017, in the MEDLINE, LILACS and SciELO virtual library databases revealed that low-level laser therapy provides positive actions in oxygenation, growth and cell modulation due to irradiated light, which affects metabolic processes and produces cellular and vascular biostimulants essential to the tissue repair process, concluding that it is concluded that low-level laser therapy is an adjuvant treatment that accelerates the tissue repair process and promotes benefits to people's comfort(22).

In vivo research (animals and humans) corroborates that low-level laser acts on the uptake of fibroblasts and epithelial cells, the synthesis of collagen and elastic fibers, increased vascularization, and has an antibacterial and immunological effect (19).

A study shows that photobiomodulation has proven to be an effective adjuvant therapy for UV management, also contributing to the clinical improvement of the patient and, indirectly, improving the quality of life. It draws attention to the existence of few manuscripts on the use of photobiomodulation by nursing, while its use has been increased in other health areas, and it is necessary to develop more clinical studies aimed at the uniformity of the parameters of this therapeutic modality and that contribute to its wide use by the scientific community(23).

Considering the described benefits of TLBP adjuvant to conventional treatment for leg ulcers and other chronic wounds(24), it is essential that nursing seeks to update on the subject and can offer this technology to vulnerable people, in order to qualify care. Professionals qualified to apply laser therapy are more successful in the healing of leg ulcers(25).

A world free of leg ulcers is an ambitious goal, but it can be a challenge to achieve it with current knowledge of the pathophysiology and diagnostic and therapeutic protocols(26). It is reiterated that the improvement of wound care through new effective therapies is fundamental for the improvement of clinical practice.

When the focus of the evaluation is the treatment of complex lesions in institutions with reduced resources, that is, the reality of the great majority of Brazilian services, the implementation of a technology with low operational cost can serve as an adjuvant to cases that would previously only be solved with costly maintenance dressings, such as negative pressure dressings, and with a higher number of visits to the service, making laser therapy an option to be implemented by health managers(27-28). Finally, the limitations of the study are related to the small sample size and short follow-up period of the control and intervention groups.

CONCLUSION

The group that received application of photobiomodulation adjuvant to the conventional treatment used by the service presented leg ulcers with better control of exudate drainage and greater reduction in the area of the lesions when compared to the control group. It is indicated that future studies are needed, with larger samples, different dosimetry and randomized, blinded and placebo-controlled clinical trials, especially

multicenter, to clarify the techniques and operationalities with the objective of improving the care of these people.

REFERENCES