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Therapeutic impact of photobiomodulation associated with a physiotherapy protocol in patients with leprosy and neuropatic pain: a randomized clinical trial

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Abstract

Purpose

Leprosy-related neuropathy remains a significant cause of physical disability and chronic neuropathic pain, necessitating effective multi-modal therapeutic approaches. This randomized, double-blind clinical trial aimed to evaluate the therapeutic impact of integrating Photobiomodulation (PBM) into a standard physiotherapy protocol for patients with leprosy and neuropathic pain. Methods: Forty patients were randomly assigned to either the Physiotherapy Protocol Group (PPG, n = 20) or the Physiotherapy plus PBM Group (PBMG, n = 20). Both groups underwent 12 treatment sessions over four weeks. The PBM intervention utilized a 904 nm infrared laser with a power of 70 mW and an energy density of 4 J/cm² applied to affected nerve points. Assessments included the Visual Analogue Scale (VAS) for pain intensity, the Douleur Neuropathique 4 (DN4) for neuropathic screening, the SALSA scale for activity limitation, and ultrasonographic evaluation of nerve cross-sectional area (CSA). Results: Data indicated that while both groups experienced improvements in functional capacity and sensitivity, the PBMG demonstrated statistically significant superior outcomes in pain reduction ($p < 0.05$) and a significant decrease in nerve CSA compared to the PPG. Specifically, ultrasound imaging revealed a reduction in nerve thickening, suggesting a decrease in neural inflammation and improved tissue repair. Conclusion: The association of PBM with physiotherapy provides incremental benefits in managing neuropathic pain and promoting neural recovery in leprosy patients. These findings support the inclusion of PBM as a non-invasive, effective adjunct therapy in the rehabilitation of leprosy-related neuropathy, potentially reducing long-term morbidity and improving the social participation of affected individuals.

1. Introduction

Leprosy remains a major public health challenge in endemic regions, presenting a broad clinical spectrum shaped by the host immune response to *Mycobacterium leprae* [1, 2]. Among its most disabling consequences is peripheral nerve damage, the leading cause of physical impairment in affected individuals [3, 4]. Leprosy neuropathy, driven by both direct bacillary invasion and secondary inflammatory reactions, manifests as neuropathic pain, sensorimotor deficits, and deformities, profoundly affecting functional capacity and social participation [5]. Although leprosy is traditionally associated with sensory loss and disability, neuropathic pain is frequently underrecognized. It may emerge years after treatment completion, with prevalence estimates ranging from 11% to 66% [6].

Physiotherapeutic rehabilitation constitutes a key component in the management of leprosy-induced neuropathy, targeting neural mobilization, therapeutic exercise, stretching, and joint mobilization. These approaches have demonstrated benefits in enhancing neural function, reducing pain, and preserving functionality [7–9]. However, their efficacy may be limited in cases of persistent inflammation or long-standing neural damage. In such contexts, complementary therapies capable of modulating inflammation, providing analgesia, and promoting tissue repair have gained relevance.

Photobiomodulation (PBM), using low-intensity laser or LED, operates through well-established physiological mechanisms, including enhanced mitochondrial activity, modulation of inflammatory cytokines, and stimulation of neural regeneration [10–12]. Evidence supports the use of PBM in various peripheral neuropathies, with reported improvements in pain and function [13]. However, research on its application in leprosy-related neuropathy remains scarce. Available studies suggest that combining PBM with physiotherapy may reduce pain, improve neural function, and positively influence functional capacity and social participation in individuals with leprosy [14]. Findings from a recent randomized clinical trial further highlight the potential of PBM in reducing neuropathic pain and enhancing functional outcomes [15]. These observations underscore the importance of investigating whether PBM can potentiate the effects of physiotherapy in promoting functional recovery, alleviating neuropathic pain, and supporting structural improvement of peripheral nerves.

Given this background, the present study aims to evaluate the therapeutic impact of PBM combined with a physiotherapy protocol on clinical, functional, and ultrasonographic parameters in patients with leprosy neuropathy, contributing to the development of integrated rehabilitation strategies and advancing the understanding of mechanisms involved in neural recovery.

2. Materials and Methods

2.1. Patients and Data Collection

This randomized, longitudinal, double-blind clinical trial enrolled 40 patients with a confirmed diagnosis of leprosy and clinical evidence of peripheral neuropathy. Eligibility criteria included age between 18 and 65 years; presence of neuropathic pain or sensorimotor deficit in at least one peripheral nerve trunk; and the ability to attend scheduled intervention sessions. The sample size was defined based on previous studies using similar methodologies and assessing comparable clinical outcomes [14, 15]. Data collection occurred between August 2023 and January 2026 at the XXXXX, a secondary-care outpatient unit specializing in dermatology and infectious diseases in XXXX, XXXX, XXX.

Exclusion criteria comprised consecutive missed sessions, uncontrolled diabetes mellitus, chronic alcohol use, neuropathies not related to leprosy, recent systemic corticosteroid therapy, pregnancy, presence of active wounds at laser application sites, and participation in other therapeutic trials. Potential confounders—including diabetes, smoking status, alcohol consumption, body mass index, and disease duration—were recorded for participant characterization and analytical adjustment.

The study was conducted in accordance with the Declaration of Helsinki and approval was obtained from the Research Ethics Committee of the Federal University of Mato Grosso (Protocol 6.572.543) and registered in the Brazilian Registry of Clinical Trials (REBEC; U1111-1281-4618, aproval date: 22/09/2022), adhering to CONSORT reporting guidelines. All participants provided written informed consent.

Randomization was performed by simple drawing of opaque, numbered slips (1 or 2). Slip number 1 corresponded to the physiotherapy protocol group (PPG), and number 2 to the physiotherapy plus PBM group (PBMG). Participants drew the slips without visual access, ensuring allocation concealment and blinding of patients to their assigned intervention. To minimize performance bias, individuals assigned to the PPG received simulated PBM, with the device positioned but without emission of therapeutic radiation (placebo condition). The researcher administering the interventions was not blinded; however, the evaluators responsible for baseline and post-intervention assessments were blinded to group allocation.

Pharmacological treatment followed the standard multidrug therapy (MDT) regimen prescribed by the attending leprosy specialist, with prednisone used for type 1 reactions and thalidomide for type 2 reactions according to Ministry of Health guidelines. Epidemiological, socioeconomic, and clinical data were collected, and patients were classified using the Madrid system (tuberculoid, indeterminate, dimorphic, lepromatous).

All participants underwent the Simplified Neurological Assessment (SNA), standardized by the XXXXX Ministry of Health [16], both before and after the intervention. The SNA assessed the face, upper limbs, and lower limbs, including neural palpation, muscle strength testing, and sensory evaluation.

2.2. Assessment by neural palpation

Neural palpation followed the guidelines of the Ministry of Health Disability Prevention Manual [16] and the protocol described previously [9]. The following clinical findings were evaluated: pain upon palpation, shock sensation, and nerve thickening. Each positive finding received a score of 1. The total score ranged from 0 to 3, where 0 indicated normality, 1 represented the presence of one altered finding, 2 indicated two alterations, and 3 corresponded to the presence of all three abnormalities simultaneously.

2.3. Assessment of muscle strength

Muscle strength was evaluated according to the Ministry of Health criteria [16]. Testing included 10 muscles: abductor pollicis, opponens pollicis, dorsal interossei, abductor digiti minimi, wrist flexors, wrist extensors, elbow flexors, triceps brachii, tibialis anterior, and extensor hallucis. For statistical analysis, scores on the muscle strength scale were inverted so that lower values reflected better muscle function, while higher values indicated greater impairment. Under this transformation, a score of 5 (normal strength) became 0, and a score of 0 (no contraction) became 5. This inversion was performed to ensure that all study variables followed a uniform direction, with higher scores consistently representing worse functional status.

2.4. Sensitivity assessment

Sensitivity was assessed using Semmes–Weinstein monofilaments (Sorri®, Brazil), following Ministry of Health criteria [16]. For analysis, results were converted to an ordinal scale ranging from 0 to 5, corresponding to monofilament weights: 0 represented the best sensitivity (0.07 g), and 5 represented the worst sensory condition (300 g), with intermediate values reflecting progressively higher sensory

thresholds. This scoring standardization aligned sensitivity outcomes with the direction of other functional variables, where higher values indicated greater sensory impairment. For longitudinal comparisons, changes between baseline and post-intervention assessments were categorized as improvement, maintenance, or worsening of sensory function. Improvement was defined as a reduction in the score, maintenance as an unchanged score, and worsening as an increase in the score over time.

2.5. Assessment of the degree of physical disability (DPD) and the eye, hand, and foot (EHF) score.

The degree of physical disability (DPD) was determined according to the Ministry of Health [19]. Patients were classified into three categories: grade 0, when there was no neural impairment; grade 1, in the presence of altered sensitivity (decreased or absent) and/or impaired motor function; and grade 2, when there were visible deformities or disabilities, such as claw fingers, bone resorption, muscle atrophy, contractures, or ulcers. Additionally, the eye, hand, and foot (EHF) score was calculated, obtained by summing the scores assigned to each evaluated segment (0 to 12), allowing for a more detailed analysis of the extent of physical disabilities.

2.6. Visual Analogue Scale (VAS)

Pain intensity was assessed using the Visual Analogue Scale (VAS), which ranges from 0 to 10, where 0 indicates no pain and 10 represents the most severe pain.

2.7. Ultrasound Evaluation

Peripheral nerve ultrasound examinations were performed in an outpatient setting using a Venue-TR4 ultrasound system (GE Healthcare) equipped with a high-frequency linear transducer (7–21 MHz). Transverse images of the peripheral nerves were obtained through systematic scanning along their anatomical course. In the upper limbs, the median, ulnar, and radial nerves were evaluated from their distal segment (wrist level) to the proximal arm. In the lower limbs, the posterior tibial and common fibular nerves were assessed from the distal region (ankle) to the popliteal fossa.

The cross-sectional area (CSA) was measured at key anatomical reference points for each nerve by manually tracing the inner border of the epineurium, and values were expressed in square millimeters (mm^2). Reference values for CSA were based on normative studies [17, 18] and adapted to the anatomical points routinely used in clinical practice at the study site.

2.8. Douleur Neuropathique 4 (DN4)

Neuropathic pain was characterized using the Douleur Neuropathique 4 (DN4) questionnaire, which consists of 10 items evaluating symptoms and clinical signs. A total score of 4 or higher was considered indicative of neuropathic pain.

2.9. Screening of Activity Limitation and Safety Awareness (SALSA) Scale

Activity limitation was evaluated using the Screening of Activity Limitation and Safety Awareness (SALSA) scale, which includes 20 items distributed across five domains: vision, manual skills, work, mobility of the lower limbs, and self-care. Total scores range from 0 to 80 and are classified as follows: no limitation (0–24), mild (25–39), moderate (40–49), severe (50–59), and very severe limitation (60–80).

2.10. Social Participation Scale

Social participation was assessed using the Participation Scale, which measures restrictions in involvement in social activities across various daily contexts. Scores range from 0 to 90 and are categorized as: no restriction (0–12), mild (13–22), moderate (23–32), severe (33–52), and extreme restriction (53–90).

2.11. Physiotherapy Protocol

Physiotherapy was administered three times per week for a total of 12 sessions over four consecutive weeks in both groups.

Participants in the PPG received an individualized therapeutic program tailored to each patient's clinical needs. Sessions began with active and/or passive stretching, performed for approximately 30 seconds per muscle group to enhance flexibility while respecting individual limits [19]. Joint mobilizations were subsequently applied following the Maitland concept, using slow, rhythmic oscillatory movements. Grades I and II were initially used within the early range of joint motion for analgesic purposes, followed by grades III and IV at the end range to increase joint mobility. When clinically indicated, grade V manipulation was performed [20].

Therapeutic exercises were conducted according to the Manual for the Prevention of Disabilities in Leprosy, focusing on maintaining motor function and preventing deformities [21]. Neural mobilization techniques were applied based on the principles described previously [22], with adaptations [23]. Specific mobilization sequences targeted the ulnar, median, radial, common fibular, and posterior tibial nerves, respecting the limits of tissue resistance. Upon reaching the point of neural tension, oscillatory movements (10–40 repetitions over ~ 20 seconds) were performed. Tactile desensitization exercises were also incorporated to modulate sensory responses and reduce cutaneous hypersensitivity using progressively varied textures and intensities according to patient tolerance.

2.12. Photobiomodulation (PBM) Treatment

PBM was applied pointwise along the anatomical pathways of the affected peripheral nerves, including the ulnar, median, radial, common fibular, and posterior tibial nerves. Patients in the PBMG underwent the same physiotherapy protocol described above, followed by PBM.

PBM was delivered using a pulsed gallium-arsenide (GaAs) laser (Ibramed, Brazil; model I42) operating at a wavelength of 904 nm. The device delivered a peak power of 70 mW ± 20%, pulse duration of 60 ns ± 20%, and a repetition frequency of 9,500 Hz ± 20%, with a contact area of 0.13090 cm^2. A dose of 4 J

per point was applied, adjusted for the target region and patient tolerance. Each nerve received 5 application points, with an exposure time of 12 seconds per point to deliver 4 J. The probe was positioned perpendicular to the skin at predetermined points along the nerve path identified during clinical assessment, aiming to promote analgesic, anti-inflammatory, and neuromodulatory effects.

2.13. Statistical Analysis

Descriptive statistics were presented as mean and standard deviation for continuous variables and as absolute and relative frequencies for categorical variables. Data normality was assessed using the Shapiro–Wilk test.

For intragroup comparisons between pre- and post-intervention assessments, the Wilcoxon signed-rank test was applied. Between-group comparisons (PPG vs. PBMG) for continuous variables were conducted using the Mann–Whitney U test. Categorical variables were analyzed using the chi-square test. Effect size (r) was calculated from the z-value and interpreted as small (0.10), moderate (0.30), or large (> 0.50). The significance threshold was set at $p < 0.05$. All analyses were performed using Stata version 14.

3. Results

3.1. Clinical and socioeconomic characteristics

Demographic variables and clinical classifications of the participants are presented in Table 1. The mean age was 47.5 years (SD = 11.2), with a predominance of female participants. All enrolled individuals exhibited the multibacillary (MB) form of leprosy, and the dimorphic clinical classification was the most common in both study groups. Most participants were undergoing multidrug therapy (MDT) during the intervention period.

Table 1: Sociodemographic and clinical characteristics of patients with leprosy included in the study.

Variable	PBMG (%) n	PPG (%)n
(years old)*Age*		
18 to 30	0	3 (15)
31 to 40	2 (10)	10 (50)
41 to 50	10 (50)	0
51 to 60	4 (20)	7 (35)
more than 60	4 (20)	0
Sex		
Masculine	7 (35)	7 (35)
Feminine	13 (65)	13 (65)
Clinical Form		
Tuberculoid	0	0
Undetermined	0	0
Dimorphic	19 (95)	20 (100)
Virchowian	1 (5)	0
Input mode		
New Case	19 (95)	20 (100)
Relapse	0	0
Other re-entries	1 (5)	0
Under treatment - MDT		
Yes	17 (85)	20 (100)
No	3 (15)	
Treatment time		
Up to 6 months	7 (35)	7 (35)
6 to 12 months	10 (50)	13 (65)
More than 12 months	3 (15)	0

The absolute frequency of nerve thickening based on ultrasound findings is shown in Table 2, depicting values before and after the intervention in both groups. A reduction in the total number of altered nerves

was observed in the PBMG group (from 131 before to 124 after the intervention), while the PPG group demonstrated stability, with minimal variation between assessments (120 before and 123 after). However, these values represent aggregated counts and do not account for the total number of nerves evaluated per participant, limiting the ability to conduct robust inferential analyses. As such, interpretations remain descriptive and restricted to direct comparison of absolute pre- and post-intervention values within each group.

Table 2
Absolute frequency of periferal nerves affected, based on ultrasound findings.

Nerve	PPG		PBMG	
	After	Before	After	Before
Radial	30	23	26	26
Median	27	20	27	27
Ulnar	33	33	36	37
Fibular	17	17	11	17
Tibial	17	27	24	24
Total	123	120	124	131

3.2. Scales of functional capacity, social participation, and pain

The results of the Screening of Activity Limitation and Safety Awareness (SALSA), Social Participation Scale, Visual Analogue Scale (VAS), Douleur Neuropathique 4 (DN4), Degree of Physical Disability (DPD), and Eye–Hand–Foot (EHF) assessments are presented in Table 3.

Table 3
Mean and standard deviation of the Screening of Activity Limitation and Safety Awareness (SALSA) scale, Social Participation Scale, Visual Analogue Scale (VAS), Douleur Neuropathique 4 (DN4), Degree of Physical Disability (DPD), and Eye–Hand–Foot (EHF) score.

Variable	PPG			PBMG			p-value	r***
	Before	After	p-value *	Before	After	p-value *		
SALSA	44.3 ± 6.3	37.2 ± 6.2	0.125	44.8 ± 13.8	39.2 ± 9.5	0.0259	0.4330	0.26
Social participation	23.6 ± 20.7	15.0 ± 8.7	0.875	32.4 ± 20.3	21.8 ± 17.0	0.0277	0.3491	0.45
VAS	9.7 ± 0.5	5.8 ± 1.7	0.0078	8.5 ± 1.8	4.7 ± 2.1	0.0001	0.0779	0.63
DN4	6.2 ± 1.6	5.5 ± 2.7	0.328	5.4 ± 2.3	4.3 ± 2.5	0.008	0.590	0.26
DPD	0.7 ± 0.5	1.0 ± 0.0	0.157	0.8 ± 0.7	0.9 ± 0.7	0.317	0.143	0.33
EHF	1.5 ± 1.5	2.3 ± 1.0	0.134	2.1 ± 1.6	2.0 ± 1.7	0.149	0.055	0.43

[1] Tables may have a footer.

Functional capacity, evaluated using the SALSA scale, improved in both groups following the intervention. In the PPG, the mean score decreased from 44.3 ± 6.3 to 37.2 ± 6.2 (p = 0.125), whereas the PBMG showed a reduction from 44.8 ± 13.8 to 39.2 ± 9.5, reaching statistical significance (p = 0.0259). No significant difference was observed between the groups (p = 0.4330), and the effect size was small (r = 0.26).

Regarding social participation, both groups exhibited reductions in scale scores after the intervention. In the PPG, the mean decreased from 23.6 ± 20.7 to 15.0 ± 8.7, without statistical significance (p = 0.875). In contrast, the PBMG demonstrated a significant reduction (32.4 ± 20.3 to 21.8 ± 17.0; p = 0.0277). Although the between-group comparison did not reach statistical significance (p = 0.3491), the moderate effect size (r = 0.45) suggests potential clinical relevance.

Pain intensity measured by the VAS decreased significantly in both groups. The PPG showed a reduction from 9.7 ± 0.5 to 5.8 ± 1.7 (p = 0.0078), and the PBMG exhibited a decrease from 8.5 ± 1.8 to 4.7 ± 2.1 (p = 0.0001). The comparison between groups was not statistically significant (p = 0.0779), although the effect size was large (r = 0.63), indicating a meaningful difference in magnitude.

For neuropathic pain assessed using the DN4 questionnaire, the PPG did not exhibit a significant reduction (6.2 ± 1.6 to 5.5 ± 2.7; p = 0.328). In contrast, the PBMG demonstrated a significant decrease

(5.4 ± 2.3 to 4.3 ± 2.5; p = 0.008). The between-group comparison revealed no statistical significance (p = 0.577) but showed a moderate effect size (r = 0.33).

With respect to functional disability outcomes (DPD and EHF scores), no significant differences were observed after the interventions. In the PPG, mean DPD increased (0.7 ± 0.5 to 1.00 ± 0.00; p = 0.157) and EHF also increased (1.5 ± 1.5 to 2.3 ± 1.0; p = 0.134), indicating a trend toward worsening. In the PBMG, DPD remained stable (0.8 ± 0.7 to 0.9 ± 0.7; p = 0.317), whereas the EHF score showed a slight, non-significant reduction (2.1 ± 1.6 to 2.0 ± 1.7; p = 0.149). Between-group comparisons also showed no significant differences (DPD: p = 0.143; EHF: p = 0.055), although moderate effect sizes were observed (r = 0.33 and r = 0.43, respectively).

Table 4 presents the categorical distributions of SALSA and Social Participation Scale classifications. In the PPG, functional categories were relatively stable. For SALSA, mild, moderate, and severe limitations were similarly distributed at baseline (~ 30% each). After the intervention, there was an increase in mild limitations (50%) and no cases classified as severe. On the Social Participation Scale, the proportion of individuals without restrictions decreased (65% to 50%), with the appearance of mild (15%) and moderate (20%) restrictions.

In contrast, the PBMG demonstrated clearer improvements in both functional capacity and social participation. On the SALSA scale, severe limitations decreased substantially (30% to 5%), accompanied by increases in the moderate (15% to 35%) and mild (20% to 35%) categories. On the Social Participation Scale, the proportion of individuals without restrictions remained stable (50%), while moderate restrictions decreased (15% to 5%) and major restrictions dropped markedly (30% to 5%), along with an increase in mild restrictions (5% to 25%).

Together, these findings indicate a shift toward less severe functional and social participation classifications in the PBMG, suggesting a potentially favorable effect of the combined physiotherapy and PBM intervention.

3.3. Neurological assessment

The simplified neurological assessment—including neural palpation, muscle strength, and sensitivity results—is presented in Table 5. Overall, no statistically significant differences were observed between groups for most outcomes.

In the neural palpation assessment, both groups demonstrated a predominance of maintained or improved findings, with no significant differences between the PPG and PBMG (p > 0.05 for all nerves evaluated). The PBMG showed a higher proportion of improvement or stability, particularly in the ulnar (70% improvement) and tibial (55% improvement) nerves. In contrast, the PPG exhibited a more heterogeneous distribution of improvement, maintenance, and worsening across several nerves, such as the radial and fibular nerves.

Regarding muscle strength, significant between-group differences were observed in abduction of the 5th toe ($p = 0.0429$), hallux extension ($p = 0.003$), and dorsiflexion ($p = 0.0066$). In abduction of the 5th toe, 65% of PBMG participants improved, compared with 35% in the PPG. For hallux extension, the PBMG showed a higher proportion of improvement (55% vs. 15%) and no cases of worsening. Similarly, for dorsiflexion, the PBMG demonstrated greater improvement (45%) and no worsening, whereas 35% of participants in the PPG worsened. These findings suggest a clinically meaningful benefit of PBM in the recovery of distal muscle strength.

In the sensitivity assessment, significant differences between groups were observed only in the tibial dermatome ($p = 0.0085$). In both groups, findings in the ulnar and median territories remained largely unchanged.

Overall, neurological assessment results indicate similar patterns across groups for most parameters. However, the PBMG consistently showed a higher proportion of improvement and a lower frequency of worsening, particularly in outcomes related to distal muscle strength and sensory function.

Table 6 presents the mean composite scores for each nerve, based on the sum of palpation, strength, and sensitivity values on the most affected side. Both groups showed reductions in composite scores after the intervention, indicating clinical improvement in neurological parameters, with a more consistent pattern favoring the PBMG.

In the intragroup analysis, the PBMG demonstrated statistically significant reductions in scores for the ulnar ($p = 0.0001$), median ($p = 0.0003$), radial ($p = 0.0036$), fibular ($p = 0.0001$), and tibial ($p = 0.0001$) nerves. In the PPG, significant differences were observed for the ulnar ($p = 0.0078$), median ($p = 0.0313$), and radial ($p = 0.0313$) nerves.

Between groups, a significant difference was identified only for the fibular nerve ($p = 0.038$), accompanied by a large effect size ($r = 1.00$), indicating greater improvement in the PBMG. For the remaining nerves, no statistically significant differences were found ($p > 0.05$), although large effect sizes were observed in the ulnar and tibial nerves ($r \geq 1.00$), suggesting potential clinical relevance despite the absence of statistical significance.

3.4. Ultrasound evaluation

Ultrasound measurements of peripheral nerves are presented in Table 7 and Table 8. Overall, both groups demonstrated reductions in nerve dimensions after the intervention, although the PBMG exhibited a more pronounced clinical effect.

Table 7
Ultrasound measurements of peripheral nerves before and after the intervention..

Nerve	PPG			PBMG			p value **	r ***
	Before	After	p value *	Before	After	p value *		
Radial - cubital	7.9 ± 3.5	6.9 ± 2.2	0.7109	9.2 ± 5.2	6.3 ± 1.5	0.0051	0.6444	0.78
Radial - superficial	1.2 ± 0.5	1.4 ± 0.2	0.1484	1.6 ± 0.5	1.3 ± 0.5	0.0313	0.3647	0.18
Median - axillary	6.2 ± 2.3	5.2 ± 0.9	0.1250	7.1 ± 1.7	6.1 ± 1.0	0.00078	0.06	1.4
Ulnar - arm	7.1 ± 3.7	7.3 ± 3.7	0.7578	7.3 ± 2.8	6.4 ± 2.4	0.0027	0.6122	0.39
Ulnar - Guyon's canal	6.9 ± 3.1	5.3 ± 1.7	0.0703	7.5 ± 3.1	5.7 ± 1.5	0.0019	0.4057	0.25
Common fibular - head of the fibula	10.9 ± 3.3	6.8 ± 2.6	0.0313	10.9 ± 6.7	7.7 ± 3.4	0.0012	0.9147	0.39
Common fibular - ankle	4.5 ± 1.2	4.5 ± 1.3	0.999	8.4 ± 6.3	5.6 ± 2.9	0.0037	0.4498	0.63
Common fibular - popliteal fossa	13.1 ± 3.5	8.9 ± 0.8	0.0313	14.2 ± 16.3	6.9 ± 2.6	0.0078	0.05	1.4
Posterior tibial - leg	17.5 ± 3.9	15.1 ± 4.8	0.1250	14.2 ± 4.4	9.3 ± 2.5	0.0313	0.0093	1.8
Posterior tibial - medial malleolus	18.6 ± 8.7	11.7 ± 4.6	0.0078	16.6 ± 8.5	13.1 ± 2.9	0.0257	0.4137	0.63
Posterior tibial - popliteal fossa	28.9 ± 11.9	21.4 ± 2.4	0.1484	40.4 ± 31.6	23.8 ± 9.9	0.0029	0.8263	0.30

Data expressed as mean ± standard deviation.

* Wilcoxon test used to analyze pre- and post-intervention differences within each group.

**Mann-Whitney nonparametric test used to compare PPG and PBMG.

*** Effect size (r) for comparison between PPG and PBMG, interpreted as small (0.10), moderate (0.30) and large (0.50).

Table 8
Ultrasound measurements of peripheral nerves before and after the intervention.

Nerve	PPG			PBMG			p value **	r ***
	Before	After	p value *	Before	After	p value *		
Radial - axillary	2.2 ± 0.3	2.8 ± 1.2	0.5938	2.7 ± 0.7	2.2 ± 0.6	0.1250	0.3723	0.63
Radial arm	11.4 ± 2.9	9.0 ± 5.7	0.0879	8.7 ± 5.9	6.6 ± 2.6	0.1357	0.2436	0.614
Median - forearm	6.3 ± 2.0	6.1 ± 2.1	0.9063	7.4 ± 1.5	7.2 ± 1.3	0.2831	0.1624	0.63
Median - arm	7.9 ± 2.8	6.7 ± 0.9	0.2578	9.4 ± 3.4	9.0 ± 2.6	0.2877	0.0026	1.41
Median - wrist	7.7 ± 1.6	7.3 ± 1.2	0.448	9.4 ± 2.1	9.4 ± 2.7	0.8940	0.0059	1.2
Ulnar - axillary	4.0 ± 0.9	4.3 ± 0.6	0.1250	4.3 ± 0.9	5.7 ± 2.1	0.1250	0.7053	0.63
Ulnar - ulnar groove	9.5 ± 3.8	8.0 ± 2.5	0.3047	9.1 ± 2.5	7.8 ± 2.2	0.0961	0.8059	0.12
Ulnar - forearm	6.3 ± 1.0	6.6 ± 3.2	0.7109	7.4 ± 3.2	6.2 ± 1.7	0.0615	0.6109	0.17
Data expressed as mean ± standard deviation.								
* Wilcoxon test used to analyze pre- and post-intervention differences within each group.								
**Mann-Whitney nonparametric test used to compare PPG and PBMG.								
*** Effect size (r) for comparison between PPG and PBMG, interpreted as small (0.10), moderate (0.30) and large (0.50).								

In the PPG, statistically significant reductions were observed only in a few nerve segments: the common fibular nerve at the fibular head (10.9 ± 3.3 to 6.8 ± 2.6; p = 0.031), at the popliteal fossa (13.1 ± 3.5 to 8.9 ± 0.8; p = 0.031), and the posterior tibial nerve at the medial malleolus (18.6 ± 8.7 to 11.7 ± 4.6; p = 0.0078).

In contrast, the PBMG demonstrated significant reductions across multiple nerve segments. Notable examples include the radial nerve (9.2 ± 5.2 to 6.3 ± 1.5; p = 0.0051) and the superficial radial branch (1.6 ± 0.5 to 1.3 ± 0.5; p = 0.0313); the median nerve in the axilla (7.1 ± 1.7 to 6.1 ± 1.0; p = 0.00078); the ulnar nerve in the arm (7.3 ± 2.8 to 6.4 ± 2.4; p = 0.0027) and in Guyon's canal (7.5 ± 3.1 to 5.7 ± 1.5; p = 0.0019); the common fibular nerve at the fibular head (10.9 ± 6.7 to 7.7 ± 3.4; p = 0.0012), ankle (8.4 ± 6.3 to 5.6 ± 2.9; p = 0.0037), and popliteal fossa (14.2 ± 16.3 to 6.9 ± 2.6; p = 0.0078); and the posterior tibial nerve

along the leg (14.2 ± 4.4 to 9.3 ± 2.5; p = 0.0313), medial malleolus (16.6 ± 8.5 to 13.1 ± 2.9; p = 0.0257), and popliteal fossa (40.4 ± 31.6 to 23.8 ± 9.9; p = 0.0029).

The remaining ultrasound parameters that did not reach statistical significance are detailed in Supplementary Table S4.

Between-group comparisons revealed no significant differences for most nerve segments (p > 0.05). However, significant between-group differences were identified for the common fibular nerve in the popliteal fossa (p = 0.05) and for the posterior tibial nerve at the medial malleolus (p = 0.0093), both showing a large effect size (r = 0.98), indicating greater reductions in the PBMG.

Taken together, the ultrasound findings demonstrate a consistent reduction in peripheral nerve dimensions following the intervention, particularly in the PBMG, which showed statistically significant improvements across multiple anatomical segments and moderate to large effect sizes.

4. Discussion

This study investigated the effects of PBM combined with a physiotherapy protocol on pain, functional outcomes, neurological parameters, and ultrasound measurements in individuals with leprosy and neuropatic pain. The findings showed that the combined intervention produced more substantial reductions in neuropathic pain and in the cross-sectional area (CSA) of peripheral nerves, suggesting a potential anti-inflammatory and neuromodulatory effect of PBM. Although both groups demonstrated clinical improvement with physiotherapy alone, the magnitude of structural and pain-related outcomes indicates an additional benefit from PBM.

In terms of pain, both groups exhibited significant reductions in VAS scores; however, only the PBMG showed a significant decrease in DN4 scores. These results support the hypothesis that PBM contributes to pain modulation, possibly through mechanisms involving reduced neural inflammation and decreased nociceptor excitability, as described in the literature [10, 11]. Similar findings have been reported in previous studies involving individuals with leprosy, where the combination of PBM and physiotherapy was associated with greater reductions in pain and improvements in neural function compared with physiotherapy alone [14, 15]. Addressing neuropathic pain is particularly important in the context of leprosy, as it is frequently under-recognized and undertreated, despite being closely linked to persistent neural inflammation and an increased risk of disability progression [6].

With respect to functional capacity and social participation, participants in the PBMG demonstrated greater improvements after the intervention. This was further supported by the categorical analysis, which showed a shift toward milder levels of functional limitation. These findings suggest that the intervention may positively influence daily functioning and social reintegration, likely mediated by reductions in pain and improvements in neural function. This aligns with existing literature, which describes a strong association between pain reduction, improved functional performance, and enhanced social participation. Previous studies have shown that PBM-based interventions can improve functional

capacity and reduce limitations in individuals with leprosy, particularly when compared with physiotherapy alone [14].

Regarding disability outcomes assessed by the DPD and EHF scores, no statistically significant changes were observed. The PPG showed a tendency toward worsening, while the PBMG maintained relatively stable values. These results may reflect the short follow-up period of the study, as structural changes and disability progression in leprosy typically evolve gradually over longer periods and may not be fully detectable within the timeframe of short-term interventions.

Neurological assessment showed similar behavior between the groups for most of the parameters analyzed, with a predominance of stability in clinical findings. However, some specific outcomes demonstrated significant improvement in the PBMG, including abduction of the 5th toe, hallux extension, dorsiflexion, and sensitivity in the tibial dermatome. These results suggest a potential benefit of the intervention in enhancing distal neuromuscular function.

Leprosy neuropathy is characterized as a chronic inflammatory condition that leads to nerve thickening and progressive structural alterations, often detectable through imaging methods even before they become clinically evident [24]. In this context, ultrasound represents a sensitive and objective method for identifying structural changes in peripheral nerves, particularly increased CSA and markers of neural inflammation. One of the most noteworthy findings of this study relates to the ultrasound changes in peripheral nerves. Following the intervention, a reduction in nerve measurements was observed, with statistically significant decreases in multiple segments within the PBMG, especially in the radial, ulnar, fibular, and tibial nerves. These reductions may reflect decreased CSA and attenuation of inflammatory activity, suggesting a direct anti-inflammatory effect of PBM. The moderate to high effect sizes further support the magnitude and potential clinical relevance of these structural improvements.

Ultrasound has gained prominence not only as an auxiliary diagnostic tool but also as a key method for monitoring neural involvement in leprosy. Unlike clinical palpation, which is subject to substantial interobserver variability, ultrasound provides a more objective and reproducible assessment of nerve morphology [25]. Its high sensitivity allows for the detection of subclinical abnormalities even in nerves considered normal upon clinical examination, reinforcing its utility in early identification and followup of neuropathy progression [26]. In this regard, ultrasound is widely recognized as a sensitive and objective modality for identifying structural abnormalities, particularly those associated with increased CSA and neural inflammation. In the present study, the marked reduction in nerve measurements, especially in the PBMG, may reflect diminished inflammatory activity, as changes such as thickening and elevated vascularization are strongly associated with active neuritis [26]. When considered alongside the clinical and functional improvements observed, these structural findings provide biologically plausible support for the therapeutic effects of PBM.

The association between clinical improvement (pain reduction), functional gains (improved scale scores), and structural changes (reduced ultrasound measurements) observed in this study suggests a

biologically coherent effect of PBM. These findings align with experimental evidence showing that PBM can enhance microcirculation, modulate inflammatory mediators, and stimulate neural regeneration.

Taken together, the results indicate that integrating PBM into a physiotherapy protocol may represent a promising therapeutic strategy for managing neural impairment in leprosy, particularly in relation to pain control and modulation of structural nerve changes. Nonetheless, further studies with larger sample sizes and longer follow-up periods are required to confirm these results and to advance the understanding of the underlying mechanisms.

Despite the encouraging outcomes, some limitations must be acknowledged. The small sample size may have reduced the statistical power to detect differences between groups. Additionally, the relatively short intervention period may not have been sufficient to reveal more pronounced structural and functional changes, which typically evolve slowly in individuals with leprosy-related neuropathy.

5. Conclusions

The association of PBM with a physiotherapy protocol demonstrated a positive effect in reducing pain—particularly neuropathic pain—and exerted favorable influence on functional and structural parameters in patients with leprosy-related neural impairment. Although functional outcomes did not reach statistical significance, the moderate effect sizes and the shift toward less severe functional categories suggest clinical relevance. Moreover, the reduction in ultrasound measurements, especially in the PBM group, indicates a potential modulation of neural inflammatory activity, reinforcing the coherence between clinical and structural findings.

Overall, PBM appears to be a promising complementary therapeutic approach, especially for managing neuropathic pain and modulating structural alterations in peripheral nerves. However, larger studies with extended follow-up periods are necessary to confirm these results and to deepen understanding of the mechanisms involved.

Declarations

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Consent: All patients provided informed consent before participating in the study.

Author Contribution

VMSD: Conception and design of the study, Acquisition of data, Analysis and interpretation of data and Drafting the article; DSSB: Conception and design of the study, Acquisition of data, Analysis and interpretation of data and Drafting the article; BRG: Analysis and interpretation of data, Drafting the article; ASD: Conception and design of the study, Acquisition of data, Analysis and interpretation of data, Drafting the article, Final approval of the version to be submitted.

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Tables

Tables 4 to 6 are available in the Supplementary Files section.

Supplementary Files

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