Research Paper

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Photobiomodulation therapy is not better than placebo in patients with chronic nonspecific low back pain: a randomised placebo-controlled trial

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Abstract

Photobiomodulation therapy (PBMT) has been used in several musculoskeletal disorders to reduce pain, inflammation, and promoting tissue regeneration. The current evidence about the effects of PBMT on low back pain (LBP) is still conflicting. We aimed to evaluate the effects of PBMT against placebo on pain intensity and disability in patients with chronic nonspecific LBP. This was a prospectively registered, randomised placebo-controlled trial, with blinded patients, therapists, and assessors. The study was conducted on an outpatient physical therapy clinic in Brazil, between April 2017 and May 2019. A total of 148 patients with chronic nonspecific LBP were randomised to either active PBMT (n = 74) or placebo (n = 74). Patients from both groups received 12 treatment sessions, 3 times a week, for 4 weeks. Patients from both groups also received an educational booklet based on "The Back Book." Clinical outcomes were measured at baseline and at follow-up appointments at 4 weeks, 3, 6, and 12 months after randomization. The primary outcomes were pain intensity and disability measured at 4 weeks. We estimated the treatment effects using linear mixed models following the principles of intention-to-treat. There was no clinical important between-group differences in terms of pain intensity (mean difference = 0.01 point; 95% confidence interval = −0.94 to 0.96) and disability (mean difference = −0.63 points; 95% confidence interval = −2.23 to 0.97) at 4 weeks. Patients did not report any adverse events. Photobiomodulation therapy was not better than placebo to reduce pain and disability in patients with chronic nonspecific LBP.

Keywords: Photobiomodulation therapy, Low back pain, Clinical trial

1. Introduction

Low back pain (LBP) is one of the most common health conditions worldwide.[24,37] Low back pain leads the ranking of years lived with disability[20] and is associated with frequent use of health services.[37] The main clinical practice guidelines for chronic LBP recommend nonpharmacological interventions and endorse the use of education, advice, and exercise to improve pain and function.[42,45,50] However, these interventions provide, at best, modest effects.[37] Although some guidelines do not recommend passive therapies,[45,50] other guidelines consider these therapies as an additional option to active treatments.[42,51] Among passive therapies, photobiomodulation therapy (PBMT) is recommended for the treatment of chronic LBP by the American College of Physicians guidelines.[42] By contrast, although the National Institute for Health and Care Excellence (NICE) guidelines currently do not recommend the use of PBMT because of conflicting evidence, these guidelines state that evidence of the clinical benefits of PBMT cannot be ruled out.[50]

Photobiomodulation therapy consists of applying a nonionizing form of light, which includes lasers (light amplification by stimulated emission of radiation), light-emitting diodes (LEDs), and/or other light sources with a broader spectrum ranging, varying from visible to infrared.[2] Photobiomodulation therapy is a nonthermal intervention, and the mechanism of action is through the interaction between irradiated light and photoreceptors present in mitochondria in different biological tissues.[2] This interaction can trigger either stimulation or inhibition of cellular metabolism.[28,29] Photobiomodulation therapy has a biphasic dose-response pattern in which optimal doses are responsible for triggering therapeutic effects.[28] The World Association of Photo-biomoduLation Therapy (WALT) provides recommendations for the appropriate minimum dose for treatment of various musculoskeletal disorders.[52] For LBP, the recommended dose is at least 4 J per treatment point (4-8 points or cm^2) using 780 to 860 nm laser and at least 1 J per treatment point (4 points or cm^2) using 904 nm.[52]

Photobiomodulation therapy is an intervention often used in clinical practice for the treatment of musculoskeletal disorders and have been tested with positive results in a number of clinical trials and systematic reviews.[7,8,18,21,53] For LBP, however, the latest systematic review in this field included 12 randomised controlled trials and found no convincing evidence to support the

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use of PBMT in chronic LBP.[46] The trials included in this review had important methodological flaws and small samples.[46] Furthermore, the quality of evidence was low, and future trials are likely to change the estimates of effect. Nevertheless, to date, we are unaware of high quality trials investigating the use of PBMT to treat chronic back pain with an adequate sample size and followed the WALT recommendations for choosing PBMT parameters.[34,52]

We hypothesized that the use of PBMT following the WALT recommendations would provide benefits over and above placebo effects. Therefore, we aimed to evaluate the effects of PBMT vs placebo on pain intensity, general and specific disability, and global perceived effects (GPEs) in patients with nonspecific chronic LBP.

2. Methods

2.1. Study design

This is a superiority, prospectively registered (NCT03089424), randomised placebo-controlled, triple-blind trial (patients, therapists, and assessors). The detailed protocol of this trial was published elsewhere.[47] There were no changes to the original protocol while conducting the study. This study was approved by the Research Ethics Committee of the Universidade Cidade de São Paulo (#1.964.094).

2.2. Participants and recruitment

This trial was conducted at the Center for Excellence in Clinical Research in Physical Therapy at Universidade Cidade de São Paulo, between April 2017 and May 2019. We included patients seeking care for chronic nonspecific LBP with symptoms present for at least 3 months,[1] with a pain intensity of at least 3 points (measured by a 0-10 pain numerical rating scale),[9] aged between 18 and 65 years, of any gender, and be able to read and speak Portuguese. Patients were excluded if they presented nerve root compromise (tested by clinical examination of dermatomes, myotomes, and reflexes),[14,36] serious spinal pathology (such as fractures, tumors, inflammatory, and infectious diseases), serious cardiorespiratory and decompensated metabolic syndrome, severe skin diseases (eg, skin cancer, erysipelas, severe eczema, severe dermatitis, severe psoriasis, lupus, and urticaria), previous spinal surgery, or pregnancy.

2.3. Randomisation

The randomisation schedule was generated using Excel Office 2010 and performed by a researcher (S.S.T.) not involved in patient assessment and treatment. Other researcher (E.C.P.L.) was responsible for programming the PBMT device into active therapy or placebo therapy and coding the treatments according to the randomisation schedule. We generated a simple randomisation schedule with an allocation ratio of 1:1. Allocation concealment was obtained using sequentially numbered, sealed, and opaque envelopes. Before initiation of treatment, eligible patients were allocated to their respective intervention groups (active PBMT or placebo PBMT) by one of the therapists who opened the next available numbered envelope (A.C.A., D.P.N., F.C.M., and M.A.A.).

2.4. Blinding

Study outcomes were collected by an assessor (L.d.S.G.) who was unaware of patient's allocation. The PBMT device used was previously programmed in active or placebo mode. The device used has no thermal effects,[22] and during irradiation, it produced the same sounds, lights, and information on the display, regardless of the mode used, ensuring the blindness of the therapist and patients. At the end of the study, the assessor was asked to guess the patients' group allocation to measure blinding success.

2.5. Interventions

For ethical reasons, on the first day of treatment, all patients received a version of *The Back Book* translated into Brazilian Portuguese.[38] *The Back Book* is a guide on LBP management based on previous clinical practice guidelines.[42] In addition, patients from both groups received treatment for 4 weeks, 3 times a week (every other day), totaling 12 treatment sessions. The choice of treatment frequency was based on the study by Basford et al.[4] that found positive effects using this frequency. Patients were preferably positioned in prone;[4] however, in specific cases, in which the patient did not tolerate that position due to pain, patient preference was respected. The treatment was performed individually by 6 independent physiotherapists using the same treatment protocol. All physiotherapists had from 3 to 13 years of experience with patients with chronic LBP. In all treatment sessions, information on pain intensity, adverse effects, and the use of The Back Book[38] were collected. After the completion of the trial, we audited all treatment notes. We counted the number of visits of each patient and calculated the mean number of completed sessions in each of the groups, as well as adverse events and crossovers during the course of the trial.

For the treatment of both groups, the Multi Radiance Medical Super Pulsed Laser MR4 console (Solon, OH) was used with the LaserShower and SE25 cluster probes as emitters. Specification of interventions is described below:

2.5.1. Active photobiomodulation therapy group

Nine sites were irradiated in the patients' lumbar region: 3 central sites (above the spinous processes between T11 and T12, L2 and L3, L5 and S1) using the SE25 emitter (4 cm^2 area, 3000 Hz frequency, 3 minutes of irradiation, and 24.75 J per site, totaling 74.25 J irradiated from SE25); in the same direction, but laterally, 3 sites on the left and 3 sites on the right (under the paravertebral muscles) were irradiated, using the LaserShower emitter (20 cm^2 area, 1000 Hz frequency, for 3 minutes, and 24.3 J per site, totaling 145.8 J irradiated from LaserShower). **Figure 1** shows the PBMT irradiation sites. At each treatment session, patients received a total dose of 220.05 J. The total treatment time per session per patient was 27 minutes. At the end of the 12 treatment sessions, patients received a total dose of 2640.6 J. The optical power of the device was checked before the beginning of the trial and after the trial was completed. For such, a Thorlabs thermal power meter (Model S322C; Thorlabs, Newton, NJ) was used. **Table 1** details the parameters used. The choice of PBMT frequency of treatments, positioning of the patients, and irradiation sites was based on previous studies that found positive effects with the use of PBMT on chronic LBP[4,23] and aimed to cover the largest possible area of the lumbar region.[33] The parameters used for the PBMT (**Table 1**) were based on WALT-recommended parameters for LBP regarding dosage.[52]

2.5.2. Placebo photobiomodulation therapy group

The placebo PBMT treatment was similar to the active PBMT treatment, that is, the same sites and time of irradiation were

Table 1

Parameters for SE25 and LaserShower cluster probe.

No. of lasers	**SE25**	**LaserShower**
	1 super-pulsed infrared	**4 super-pulsed infrared**
Wavelength (nm)	905 (±1)	905 (±1)
Frequency (Hz)	3000	1000
Peak power (W)—each	25	12.5
Average mean optical output (mW)—each	7.50	1.25
Power density (mW/cm^2)—each	17.05	2.84
Energy density (J/cm^2)—each	3.07	0.51
Dose (J)—each	1.35	0.23
Spot size of laser (cm^2)—each	0.44	0.44
No. of red LEDs	**SE25**	**LaserShower**
	4 red	**4 red**
Wavelength of red LEDs (nm)	640 (±10)	640 (±10)
Frequency (Hz)	2	2
Average mean optical output (mW)—each	15	15
Power density (mW/cm^2)—each	16.67	16.67
Energy density (J/cm^2)—each	3	3
Dose (J)—each	2.7	2.7
Spot size of red LED (cm^2)—each	0.9	0.9
No. of infrared LEDs	**SE25**	**LaserShower**
	4 infrared	**4 infrared**
Wavelength of infrared LEDs (nm)	875 (±10)	875 (±10)
Frequency (Hz)	16	16
Average mean optical output (mW)—each	17.5	17.5
Power density (mW/cm^2)—each	19.44	19.44
Energy density (J/cm^2)—each	3.5	3.5
Dose (J)—each	3.15	3.15
Spot size of LED (cm^2)—each	0.9	0.9
Magnetic field (mT)	35	35
Irradiation time per site (s)	180	180
Total dose per site (J)	24.75	24.30
Aperture of device (cm^2)	4	20
Application mode	Cluster probe held stationary in skin contact with a 90-degree angle and slight pressure	Cluster probe held stationary in skin contact with a 90-degree angle and slight pressure

LED, light-emitting diode; nm, nanometers; Hz, hertz; W, watt; mW, milliwatt; cm^2, square centimetres; J, joules; mT, magnetic field; s, seconds.

used, however, without any emission of therapeutic dose. In the PBMT device used, the only visible diode is the red one. For the placebo treatment, 905 nm laser diodes and the 875 nm LED diodes were deactivated (turned off), and the power of the 640-nm LED diodes were turned down to 1 mW (mean power for each diode) to keep the visual aspect of red light, but not to deliver an effective therapeutic or considerable dose according the current available evidence.[52] It is important to mention that this placebo method has been used in previous trials using the same PBMT device.[11,13,31,32]

2.6. Outcomes

Initially, the participants were screened to confirm the eligibility criteria. After confirming the inclusion criteria, the participants were invited to participate and signed the consent form. Subsequently, demographic, clinical characteristics (eg, marital status, educational status, medication, smoking, and physical activity), patient's expectancy for improvement, and primary and secondary outcomes were collected before randomisation. Clinical outcomes were collected at baseline, at the end of treatment (4 weeks after randomisation), and at follow-up appointments at 3, 6, and 12 months after randomisation. Primary outcomes were pain intensity[9] and general disability[10,39] obtained 4 weeks after randomisation. Secondary outcomes were pain intensity[9] and general disability,[10,39] measured at 3, 6, and 12 months after randomisation. In addition, we also measured specific disability[6,9,41] and GPE in all time points.[9]

Pain intensity was measured using the Numeric Pain Rating Scale, which assesses the patient's perceived pain levels over the past 7 days and ranges from 0 (no pain) to 10 (worst possible

Figure 1. Photobiomodulation therapy irradiation sites. Source: Tomazoni et al. (2017).

pain).[9] General disability was measured using the Roland–Morris Disability Questionnaire, which measures disability associated with back pain ranging from 0 (no disability) to 24 (high disability).[10,39] Specific disability was measured using the Patient-Specific Functional Scale, based on the average score of 3 specific activities that the patient has difficulty to perform. The Patient-Specific Functional Scale ranges from 0 (unable to perform) to 10 (able to perform at the same level as before injury).[6,9,41] Global perceived effect was measured using the GPE Scale, which compares the patient's current state with when the symptoms started, and ranges from −5 (much worse) to +5 (fully recovered).[9] Patient expectancy for treatment was collected at baseline using the Expectancy of Improvement Scale, which ranges from 0 (no expectancy of improvement) to 10 (expectancy for the greatest possible improvement).[15] All measures were previously cross-culturally adapted into Brazilian–Portuguese and tested for their measurement properties.[9,10] All measures have good levels of reliability, validity, and responsiveness.[9,10] The assessments at 3, 6, and 12 months after randomisation were conducted over the telephone.

2.7. Statistical analysis

A sample of 148 patients (74 per group) provided 80% statistical power to detect an 1-point difference for pain intensity (with an estimated standard deviation of 1.84 points)[9] and a 4-point difference for disability (with an estimated standard deviation of 4.9),[10,39] considering a level of significance of 5% and a possible lost to follow-up of up to 15%. Despite the clinical important changes are estimated as 2 points for pain intensity and 5 points for disability, we performed the sample size calculation with lower values to generate a larger statistical precision.[40] Statistical analysis was conducted following intention-to-treat principles.[17,25,26] Data normality was tested by visual inspection of histograms, and participant characteristics were calculated using descriptive statistical tests.

Between-group differences (treatment effects) and their 95% confidence intervals (CIs) were calculated by using mixed linear models[49] using group vs time interaction terms. The follow-up data are highly dependent on baseline values; therefore, the estimates of differences between groups were adjusted for baseline data.[49] Linear mixed models automatically adjust the between-group differences taking baseline data differences into account, even if these differences are very small.[49] Chi-square tests were used to test for possible differences in cointerventions between the groups. Analyses were performed using the software program SPSS V.19.0. All data were double-entered and audited before analysis. All analyses were calculated by one of the authors (L.O.P.C.) who was blinded to group allocation and performed the entire analysis using the randomisation codes. The codes were only revealed after the analyses were completed.

3. Results

3.1. Recruitment and baseline data

From a total of 362 patients seeking care for LBP, 148 were considered eligible and were included in the study between April 2017 and May 2018. A total of 214 (59.1%) were considered ineligible to participate. First, patients were screened over the phone, and then, we booked an appointment for the baseline assessment. A total of 111 patients were excluded in the screened phase by phone. The reasons for exclusion were as follows: did not meet the inclusion criteria (n = 46), declined to participate (n = 10), time constrains (n = 33), and could not be contacted by telephone (n = 22). A total of 251 patients booked an appointment for the baseline assessment; however, 103 were excluded. The reasons for exclusions were as follows: did not meet the inclusion criteria (n = 49), declined to participate (n = 17), time constrains (n = 2), and patients did not attend baseline assessment (n = 35) (**Fig. 2**). Demographic and clinical characteristics of patients at baseline were similar in both groups and are described in **Table 2**.

Most participants were women (73.6%), married (48%), sedentary (65.5%), overweight (66.9%), and had a mean age of 43 years. Almost half of the patients were taking medication for LBP. Patients in both groups began treatment with moderate levels of pain intensity (mean score 6.7 points) and general disability (mean score 11.2 points). At the beginning of the study, patients had a high expectancy that LBP would improve with the treatment (mean score 8.9). All patients received treatment according to the treatment allocation. We audited all clinical notes after the trial completion, and the adherence to treatment was similar in both groups. Of the 12 proposed treatment sessions, patients in the active PBMT group attended an average of 10.7 (SD = 3.0) sessions, whereas patients allocated to the placebo PBMT group attended on average 11.4 (SD = 1.8) sessions.

3.2. Primary and secondary outcomes

There was no clinically important difference between groups for pain intensity (mean difference—MD = 0.01 point; 95% CI = −

Table 2

Demographic and clinical characteristics of the patients at baseline (n = 148).

Variables	PBMT (n = 74)	Placebo (n = 74)
Duration of symptoms (mo)	47.2 (61.4)	51.3 (81.3)
Age (y)	43.4 (10)	44.2 (13)
Sex (%)		
Female	51.0 (68.9)	58.0 (78.4)
Male	23.0 (31.1)	16.0 (21.6)
Marital status (%)		
Single	20.0 (27.0)	27.0 (36.5)
Married	41.0 (55.4)	30.0 (40.5)
Divorced	6.0 (8.1)	10.0 (13.5)
Others	7.0 (9.5)	7.0 (9.5)
Weight (kg)	75.0 (17.2)	77.3 (17.8)
Height (m)	1.6 (0.10)	1.6 (0.08)
Body mass index (kg/m^2)	27.3 (5.4)	28.4 (6.1)
Education status (%)		
Primary education	8.0 (10.8)	13.0 (17.6)
Secondary education	43.0 (58.1)	36.0 (48.6)
University degree	23.0 (31.1)	25.0 (33.8)
Use of medication (%)	37.0 (50.0)	34.0 (45.9)
Recent low back pain episode (%)	39.0 (52.7)	47.0 (63.5)
Other treatments (%)	7.0 (9.5)	8.0 (10.8)
Physically active (%)	21.0 (28.4)	30.0 (40.5)
Smoker (%)	8.0 (10.8)	3.0 (4.1)
Pain intensity (0-10)	6.8 (1.86)	6.6 (1.68)
Disability (0-24)	12.0 (5.18)	10.7 (4.73)
Specific disability (0-10)	4.4 (1.77)	4.6 (1.59)
Global perceived effect scale (−5 to +5)	−1.7 (2.69)	−0.8 (2.69)
Expectancy of improvement	8.8 (1.74)	8.9 (1.50)

Categorical variables are expressed as number (%). Continuous variables are expressed as mean (SD).
PBMT, photobiomodulation therapy.

0.94-0.96) and general disability (MD = −0.63 point; 95% CI = −2.23-0.97) at the end of treatment (4 weeks) (**Table 3**). Similarly, there was no clinically important difference between groups for pain intensity and general disability at 3, 6, and 12 months after randomisation (**Table 3**). Patients allocated to the active PBMT group had improved in terms of GPE (MD = 1.31; 95% CI = 0.38-2.25) at the end of treatment compared with patients allocated to the placebo PBMT group (**Table 3**). Finally, there were no statistically significant differences between the groups for any other secondary outcomes at any time point.

3.3. Other measurements

In all follow-up assessments, patients were asked about cointerventions (**Table 4**). The most frequently observed cointerventions were use of pain medication (47.9%), followed by conventional physiotherapy (14.8%), acupuncture (14.2%), and Pilates (9.5%). There was no clinically important difference between the groups at any time point regarding cointerventions. We asked on every session if patients have read the Back Book. A total of 122 (82.4%) patients read it, being 64 patients from the PBMT group and 58 from the placebo group.

To measure assessor blinding, immediately after the last assessment (12 months), the assessor was asked about the allocation of patients to treatment groups. The assessor correctly guessed the allocation for 68 (45.9%) patients, suggesting that the assessor was blinded during the study.

Patients reported no major adverse effects. However, during the sessions, 27 (18.2%) patients reported discomfort with the prone position, and 23 (15.5%) patients reported some discomfort during the application of PBMT, being 15 (10.1%) from the PBMT group and 9 (5.5%) from the placebo group. None of the patients withdrew from the study because of these minor reactions.

4. Discussion

This is the first triple-blinded randomised controlled trial that investigated the efficacy of PBMT using WALT recommended doses[52] compared with placebo in patients with chronic LBP.[47] We observed reductions in pain intensity and disability in both groups, but there was no clinically important difference between the PBMT and placebo groups in pain and disability reduction at short term. For the secondary outcomes, we observed a moderate effect for GPE in favor of PBMT at short term.

4.1. Strengths and limitations of the study

One of the strengths of this clinical trial was the blinding of assessor, therapists, and patients. By contrast, one of the

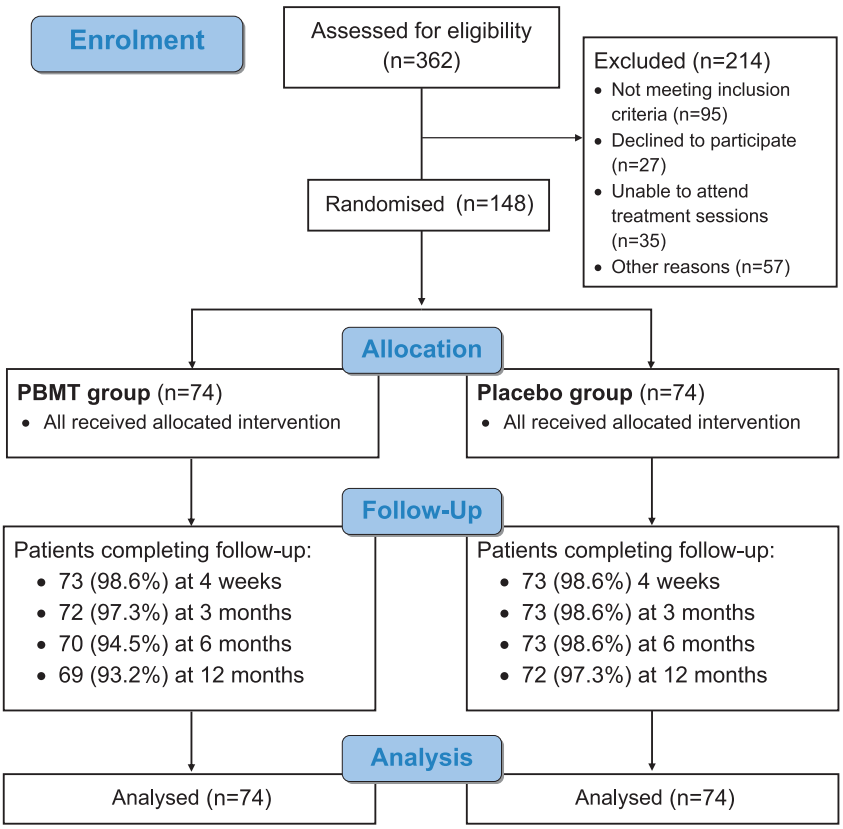

Figure 2. Flow diagram of the study. PBMT, photobiomodulation therapy.

Table 3

Unadjusted mean (SD) and adjusted mean difference and 95% CIs for the outcomes of the study (n = 148).

Outcomes	Unadjusted mean (SD)		PBMT vs placebo
	PBMT (n = 74)	Placebo (n = 74)	Adjusted mean between-group differences (95% CI)
Pain intensity (0-10)			
Baseline	6.76 (1.86)	6.56 (1.68)	
4 weeks	**3.35 (2.45)**	**3.35 (2.34)**	**0.01 (−0.94 to 0.96)**
3 months	3.88 (3.07)	3.93 (2.67)	−0.04 (−0.99 to 0.92)
6 months	4.56 (3.25)	4.28 (2.99)	0.13 (−0.83 to 1.09)
12 months	4.25 (3.07)	4.20 (2.77)	0.05 (−0.92 to 1.01)
Disability (0-24)			
Baseline	12.01 (5.18)	10.70 (4.73)	
4 weeks	**5.57 (5.19)**	**5.35 (4.59)**	**−0.63 (−2.23 to 0.97)**
3 months	5.96 (6.17)	5.14 (5.44)	0.16 (−1.44 to 1.76)
6 months	6.34 (6.63)	5.46 (5.63)	−0.07 (−1.68 to 1.54)
12 months	6.56 (6.64)	5.13 (5.32)	0.59 (−1.02 to 2.21)
Specific disability (0-10)			
Baseline	4.36 (1.77)	4.60 (1.59)	
4 weeks	6.89 (2.14)	6.82 (2.00)	0.08 (−0.65 to 0.82)
3 months	7.03 (2.31)	6.55 (2.20)	0.47 (−0.26 to 1.20)
6 months	6.44 (2.65)	6.96 (2.01)	−0.47 (−1.21 to 0.26)
12 months	6.75 (2.44)	6.66 (2.32)	0.09 (−0.65 to 0.83)
Global perceived effect (−5 to +5)			
Baseline	−1.69 (2.69)	−0.83 (2.69)	
4 weeks	3.09 (1.87)	2.62 (2.12)	1.31 (0.38 to 2.25)
3 months	2.62 (2.31)	2.45 (2.52)	0.91 (−0.03 to 1.85)
6 months	1.87 (3.03)	2.27 (2.67)	0.60 (−0.34 to 1.54)
12 months	2.21 (2.66)	2.61 (2.33)	0.45 (−0.49 to 1.39)

Primary outcomes are highlighted in bold. Pain intensity was measured using NPRS, with scores ranging from 0 ("no pain") to 10 ("worst pain possible"); disability by RMDQ, with scores ranging from 0 ("no disability") to 24 ("high disability"); specific disability by PSFS, with scores ranging from 0 ("unable to perform activity") to 10 ("able to perform activity at the preinjury level"); global perceived effect scale by GPE, with scores ranging −5 ("vastly worse") to 0 ("no change") to +5 ("completely recovered").

CI, confidence interval; GPE, global perceived effect; PBMT, photobiomodulation therapy; PSFS, Patient-Specific Functional Scale.

Table 4

Proportion of cointerventions in both treatment groups (n = 148).

Time points	Medication		*P*	Placebo		*P*
	Medication PBMT	Medication placebo		Other cointerventions PBMT	Other cointerventions placebo	
Baseline	37 (25.0%)	34 (23.0%)	0.6	7 (4.7%)	8 (5.4%)	0.8
4 weeks	5 (3.4%)	2 (1.3%)	0.2	7 (4.7%)	6 (4.0%)	0.8
3 months	1 (0.6%)	3 (2.0%)	0.3	7 (4.7%)	14 (9.5%)	0.1
6 months	5 (3.4%)	7 (4.7%)	0.6	14 (9.5%)	10 (6.7%)	0.3
12 months	3 (2.0%)	1 (0.6%)	0.3	23 (15.5%)	18 (12.2%)	0.3

Estimates are expressed as number (%). *P* values are based on χ^2 tests.
PBMT, photobiomodulation therapy.

limitations was that we did not measured fidelity of blinding of therapists and patients. The sample of this clinical trial was based on an appropriate sample size calculation to detect clinically important differences between the groups. This trial was prospectively registered; the protocol was previously published,[47] and it was followed without violations. True randomisation, allocation concealment, and intention-to-treat analysis were performed. We had a total lost to follow-up rate of only 2.9% and excellent adherence to proposed treatments. The use of a placebo group allowed to control possible confounding factors, such as regression to the mean, therapist bias, and placebo effects.[35] Finally, we have controlled for expectation and cointerventions in both groups.

4.2. Strengths and weaknesses compared with other studies

Several clinical trials compared PBMT with placebo for patients with LBP.[3,4,16,27,30,43,48] Most trials had results similar to ours, that is, PBMT was not superior to placebo in reducing pain intensity.[3,16,27,30] Despite the similar result, many of these trials have issues such as lack of allocation concealment, blinding of patients and therapists, and statistical analysis without following the principles of intention-to-treat. In addition, only 2 trials used doses according to WALT recommendations.[3,16] The trials presented extremely varied parameters, being the energy doses ranged from 0.06 to 31.2 J/point and average power output ranged from 13 to 110 mW.[3,4,16,27,30,43,48] Finally, these studies presented small samples,[3,4,16,27,30,43,48] whereas our trial had a calculated sample size to provide the statistical power to detect differences in primary outcomes.

By contrast, 3 trials suggested that the effects of PBMT were greater than placebo for reducing pain intensity compared with placebo at short term.[4,43,48] Although these trials have low risk of bias, there are some issues such as lack of allocation concealment and statistical analysis without following the principles of intention-to-treat.[12] The lack of these features does not allow adequate comparison between the groups and may have influenced the results of the trials. In addition, 1 trial used a modified high-intensity laser device,[4] and 2 trials did not properly describe the parameters used.[43,48]

A systematic review found evidence of the effectiveness of PBMT for neck pain.[7] This review showed that, by pooling the data from clinical trials with positive results, the PBMT parameters used were similar and within a narrow and specific therapeutic window.[7] The same occurred with other health conditions such as knee osteoarthritis[44] and lateral epicondylitis,[5] suggesting that therapeutic effects occur when applying optimal doses of PBMT. Although we used a dose based on the latest WALT recommendations (from 2010),[52] we did not observe differences between PBMT and placebo in patients with chronic LBP. Similar results were observed in 2 other trials with similar characteristics to ours.[3,16]

4.3. Meaning of the study: possible explanations and implications

The results of this trial demonstrate that active PBMT was not clinically superior to placebo. This result can be explained by factors such as placebo effect,[35] the use of *The Back Book* by all patients,[19] or the favorable clinical course in patients with chronic LBP.[24] Thus, the results found in this trial do not support the use of PBMT to decrease pain intensity and disability in patients with chronic nonspecific LBP. Our results are generalisable only for patients with chronic LBP who received PBMT using the dose that adheres to the WALT recommendations.

4.4. Unanswered questions and needs for future research

Further studies with rigorous methodological quality and adequate sample size are needed to investigate the optimization of PBMT parameters in chronic LBP. In addition, it is important to test new dosages within the therapeutic window for this condition.

5. Conclusion

There was no advantage in the use of PBMT, using the dose recommended by the WALT, to reduce pain and disability in patients with chronic nonspecific LBP.

Conflict of interest statement

E.C.P. Leal-Junior receives research support from Multi Radiance Medical (Solon, OH), a laser device manufacturer. S.S. Tomazoni has a personal relationship with a researcher who receives research support from Multi Radiance Medical (Solon, OH), a PBMTdevice manufacturer. Multi Radiance Medical had no role in the planning, execution, and data analysis of this trial. The remaining authors have no conflicts of interests to declare.

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Author contributions: All authors contributed to the concept and design of the study. L.d.S. Guimarães was involved in setting the writing article assisted by S.S. Tomazoni, L.C.M. Costa, and L.O.P. Costa. L.O.P. Costa also contributed in data interpretation and statistical analysis strategy. L.d.S. Guimarães was the blind

assessor and had access to the data in the study. A.C. Araujo, D.P. Nascimento, F.C. Medeiros, M.A. Avanzi, L.d.S. Guimarães, and S.S. Tomazoni were the therapists for both groups. S.S. Tomazoni, E.C.P. Leal-Junior, L.d.C.M. Costa, and L.O.P. Costa performed critical revisions of the article. All authors read and approved the final version of the article.

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This study was approved by the Research Ethics Committee of the Universidade Cidade de São Paulo (no 1.964.094), and the patient consent was obtained before participating in the investigation. This study was also prospectively registered at ClinicalTrials.gov (NCT03089424).

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References

[1] Airaksinen O, Brox JI, Cedraschi C, Hildebrandt J, Klaber-Moffett J, Kovacs F, Mannion AF, Reis S, Staal JB, Ursin H, Zanoli G. Chapter 4: European guidelines for the management of chronic nonspecific low back pain. Eur Spine J 2006;15:s192–300.
[2] Anders JJ, Lanzafame RJ, Arany PR. Low-level light/laser therapy versus photobiomodulation therapy. Photomed Laser Surg 2015;33:183–4.
[3] Ay S, Doğan SK, Evcik D. Is low-level laser therapy effective in acute or chronic low back pain? Clin Rheumatol 2010;29:905–10.
[4] Basford JR, Sheffield CG, Harmsen WS. Laser therapy: a randomized, controlled trial of the effects of low-intensity Nd:YAG laser irradiation on musculoskeletal back pain. Arch Phys Med Rehabil 1999;80:647–52.
[5] Bjordal JM, Lopes-Martins RA, Joensen J, Couppe C, Ljunggren AE, Stergioulas A, Johnson MI. A systematic review with procedural assessments and meta-analysis of low level laser therapy in lateral elbow tendinopathy (tennis elbow). BMC Musculoskelet Disord 2008;9:75.
[6] Chatman AB, Hyams SP, Neel JM, Binkley JM, Stratford PW, Schomberg A, Stabler M. The Patient-Specific Functional Scale: measurement properties in patients with knee dysfunction. Phys Ther 1997;77:820–9.
[7] Chow RT, Johnson MI, Lopes-Martins RA, Bjordal JM. Efficacy of low-level laser therapy in the management of neck pain: a systematic review and meta-analysis of randomised placebo or active-treatment controlled trials. Lancet 2009;374:1897–908.
[8] Clijsen R, Brunner A, Barbero M, Clarys P, Taeymans J. Effects of low-level laser therapy on pain in patients with musculoskeletal disorders: a systematic review and meta-analysis. Eur J Phys Rehabil Med 2017;53:603–10.
[9] Costa LO, Maher CG, Latimer J, Ferreira PH, Ferreira ML, Pozzi GC, Freitas LM. Clinimetric testing of three self-report outcome measures for low back pain patients in Brazil: which one is the best? Spine 2008;33:2459–63.
[10] Costa LO, Maher CG, Latimer J, Ferreira PH, Pozzi GC, Ribeiro RN. Psychometric characteristics of the Brazilian-Portuguese versions of the Functional Rating Index and the Roland Morris Disability Questionnaire. Spine (Phila Pa 1976) 2007;32:1902–7.
[11] da Silva MM, Albertini R, de Tarso Camillo de Carvalho P, Leal-Junior ECP, Bussadori SK, Vieira SS, Bocalini DS, de Oliveira LVF, Grandinetti V, Silva JA, Serra AJ. Randomized, blinded, controlled trial on effectiveness of photobiomodulation therapy and exercise training in the fibromyalgia treatment. Lasers Med Sci 2018;33:343–51.
[12] de Almeida MO, Saragiotto BT, Maher C, Costa LOP. Allocation concealment and intention-to-treat analysis do not influence the treatment effects of physical therapy interventions in low back pain trials: a meta-epidemiologic study. Arch Phys Med Rehabil 2019;100:1359–66.
[13] de Paula Gomes CAF, Leal-Junior ECP, Dibai-Filho AV, de Oliveira AR, Bley AS, Biasotto-Gonzalez DA, de Tarso Camillo de Carvalho P. Incorporation of photobiomodulation therapy into a therapeutic exercise program for knee osteoarthritis: a placebo-controlled, randomized, clinical trial. Lasers Surg Med 2018;50:819–28.
[14] Delitto A, George SZ, Van Dillen LR, Whitman JM, Sowa G, Shekelle P, Denninger TR, Godges JJ. Low back pain. J Orthop Sports Phys Ther 2012;42:A1–57.
[15] Devilly GJ, Borkovec TD. Psychometric properties of the credibility/expectancy questionnaire. J Behav Ther Exp Psychiatry 2000;31:73–86.
[16] Djavid GE, Mehrdad R, Ghasemi M, Hasan-Zadeh H, Sotoodeh-Manesh A, Pouryaghoub G. In chronic low back pain, low level laser therapy combined with exercise is more beneficial than exercise alone in the long term: a randomised trial. Aust J Physiother 2007;53:155–60.
[17] Elkins MR, Moseley AM. Intention-to-treat analysis. J Physiother 2015;61:165–7.
[18] Fulop AM, Dhimmer S, Deluca JR, Johanson DD, Lenz RV, Patel KB, Douris PC, Enwemeka CS. A meta-analysis of the efficacy of laser phototherapy on pain relief. Clin J Pain 2010;26:729–36.
[19] Garcia AN, Costa LDCM, Hancock MJ, Souza FS, Gomes GVFO, Almeida MO, Costa LOP. McKenzie Method of Mechanical Diagnosis and Therapy was slightly more effective than placebo for pain, but not for disability, in patients with chronic non-specific low back pain: a randomised placebo controlled trial with short and longer term follow-up. Br J Sports Med 2018;52:594–600.
[20] GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet 2017;390:1211–59.
[21] Glazov G, Yelland M, Emery J. Low-level laser therapy for chronic non-specific low back pain: a meta-analysis of randomised controlled trials. Acupunct Med 2016;34:328–41.
[22] Grandinétti VS, Miranda EF, Johnson DS, de Paiva PR, Tomazoni SS, Vanin AA, Albuquerque-Pontes GM, Frigo L, Marcos RL, de Carvalho PT, Leal-Junior EC. The thermal impact of phototherapy with concurrent super-pulsed lasers and red and infrared LEDs on human skin. Lasers Med Sci 2015;30:1575–81.
[23] Gur A, Karakoc M, Cevik R, Nas K, Sarac AJ. Efficacy of low power laser therapy and exercise on pain and functions in chronic low back pain. Lasers Surg Med 2003;32:233–8.
[24] Hartvigsen J, Hancock MJ, Kongsted A, Louw Q, Ferreira ML, Genevay S, Hoy D, Karppinen J, Pransky G, Sieper J, Smeets RJ, Underwood M. What low back pain is and why we need to pay attention. Lancet 2018;391:2356–67.
[25] Hicks GE, Fritz JM, Delitto A, McGill SM. Preliminary development of a clinical prediction rule for determining which patients with low back pain will respond to a stabilization exercise program. Arch Phys Med Rehabil 2005;86:1753–62.
[26] Hollis S, Campbell F. What is meant by intention to treat analysis? Survey of published randomised controlled trials. BMJ 1999;319:670–4.
[27] Hsieh RL, Lee WC. Short-term therapeutic effects of 890-nanometer light therapy for chronic low back pain: a double-blind randomized placebo-controlled study. Lasers Med Sci 2014;29:671–9.
[28] Huang YY, Chen AC, Carroll JD, Hamblin MR. Biphasic dose response in low level light therapy. Dose Response 2009;7:358–83.
[29] Karu T. Laser biostimulation: a photobiological phenomenon. J Photochem Photobiol B 1989;4:638–40.
[30] Klein RG, Eek BC. Low-energy laser treatment and exercise for chronic low back pain: double-blind controlled trial. Arch Phys Med Rehabil 1990;71:34–7.
[31] Langella LG, Casalechi HL, Tomazoni SS, Johnson DS, Albertini R, Pallotta RC, Marcos RL, de Carvalho PTC, Leal-Junior ECP. Photobiomodulation therapy (PBMT) on acute pain and inflammation in patients who underwent total hip arthroplasty-a randomized, triple-blind, placebo-controlled clinical trial. Lasers Med Sci 2018;33:1933–40.
[32] Leal-Junior EC, Johnson DS, Saltmarche A, Demchak T. Adjunctive use of combination of super-pulsed laser and light-emitting diodes phototherapy on nonspecific knee pain: double-blinded randomized placebo-controlled trial. Lasers Med Sci 2014;29:1839–47.
[33] Leal-Junior ECP, Lopes-Martins RB, Bjordal JM. Clinical and scientific recommendations for the use of photobiomodulation therapy in exercise performance enhancement and post-exercise recovery: current evidence and future directions. Braz J Phys Ther 2019;23:71–5.
[34] Lopes-Martins RAB, Marcos RL, Leal-Junior ECP, Bjordal JM. Low-level laser therapy and world association for laser therapy dosage recommendations in musculoskeletal disorders and injuries. Photomed Laser Surg 2018;36:457–9.

[35] Machado LA, Kamper SJ, Herbert RD, Maher CG, McAuley JH. Imperfect placebos are common in low back pain trials: a systematic review of the literature. Eur Spine J 2008;17:889–904.
[36] Magee DJ. Orthopedic physical assessment. 6th ed. Alberta: Elsevier, 2014:550–620.
[37] Maher C, Underwood M, Buchbinder R. Non-specific low back pain. Lancet 2017;389:736–47.
[38] Manchester M, Glasgow G, York J. The Back Book. Clinical guidelines for the management of acute low back pain, 2002. p. 1–28.
[39] Nusbaum L, Natour J, Ferraz MB, Goldenberg J. Translation, adaptation and validation of the Roland-Morris questionnaire–Brazil Roland-Morris. Braz J Med Biol Res 2001;34:203–10.
[40] Ostelo RW, Deyo RA, Stratford P, Waddell G, Croft P, Von Korff M, Bouter LM, de Vet HC. Interpreting change scores for pain and functional status in low back pain: towards international consensus regarding minimal important change. Spine (Phila Pa 1976) 2008;33:90–4.
[41] Pengel LH, Refshauge KM, Maher CG. Responsiveness of pain, disability, and physical impairment outcomes in patients with low back pain. Spine (Phila Pa 1976) 2004;29:879–83.
[42] Qaseem A, Wilt TJ, McLean RM, Forciea MA. Noninvasive treatments for acute, subacute, and chronic low back pain: a clinical practice guideline from the American College of Physicians. Ann Intern Med 2017;166:514–30.
[43] Soriano F, Rios R. Gallium arsenide laser treatment of chronic low back pain: a prospective, randomized and double blind study. Laser Ther 1998;10:175–80.
[44] Stausholm MB, Naterstad IF, Joensen J, Lopes-Martins RB, Sæbø H, Lund H, Fersum KV, Bjordal JM. Efficacy of low-level laser therapy on pain and disability in knee osteoarthritis: systematic review and meta-analysis of randomised placebo-controlled trials. BMJ Open 2019;9:e031142.
[45] Stochkendahl MJ, Kjaer P, Hartvigsen J, Kongsted A, Aaboe J, Andersen M, Fournier G, Højgaard B, Jensen MB, Jensen LD, Karbo T, Kirkeskov L, Melbye M, Morsel-Carlsen L, Nordsteen J, Palsson TS, Rasti Z, Silbye PF, Steiness MZ, Tarp S, Vaagholt M. National Clinical Guidelines for non-surgical treatment of patients with recent onset low back pain or lumbar radiculopathy. Eur Spine J 2018;27:60–75.
[46] Tomazoni SS, Almeida MO, Bjordal JM, Stausholm MB, Machado CDSM, Leal-Junior ECP, Costa LOP. Photobiomodulation therapy does not decrease pain and disability in people with non-specific low back pain: a systematic review. J Physiother 2020;66:155–65.
[47] Tomazoni SS, Costa LDCM, Guimarães LS, Araujo AC, Nascimento DP, Medeiros FC, Avanzi MA, Costa LOP. Effects of photobiomodulation therapy in patients with chronic non-specific low back pain: protocol for a randomised placebo-controlled trial. BMJ Open 2017;7:e017202.
[48] Toya S, Motegi M, Inomata K, Ohshiro T, Maeda T. Report on a computer-randomized double blind clinical trial to determine the effectiveness of the GaAlAs (830 NM) diode laser for pain attenuation in selected pain groups. Laser Ther 1994;6:143–8.
[49] Twisk JWR. Applied longitudinal data analysis for epidemiology: a practical guide, 2003. ISBN: 0521819768.
[50] UK National Institute for Health and Care Excellence. Low back pain and sciatica in over 16s: assessment and management 2016. Available at: https://www.nice.org.uk/guidance/ng59.
[51] Wong JJ, Côté P, Sutton DA, Randhawa K, Yu H, Varatharajan S, Goldgrub R, Nordin M, Gross DP, Shearer HM, Carroll LJ, Stern PJ, Ameis A, Southerst D, Mior S, Stupar M, Varatharajan T, Taylor-Vaisey A. Clinical practice guidelines for the noninvasive management of low back pain: a systematic review by the Ontario Protocol for Traffic Injury Management (OPTIMa) Collaboration. Eur J Pain 2017;21:201–16.
[52] World Association for photobiomodulation (WALT). Recommended treatment doses for low level laser therapy. 2010. Available at: https://waltza.co.za/documentation-links/recommendations/dosage-recommendations/.
[53] Yousefi-Nooraie R, Schonstein E, Heidari K, Rashidian A, Pennick V, Akbari-Kamrani M, Irani S, Shakiba B, Mortaz Hejri SA, Mortaz Hejri SO, Jonaidi A. Low level laser therapy for nonspecific low-back pain Cochrane Database Syst Rev 2008;2:CD005107.