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Aerobic exercise program performed on a stationary bicycle associated to a photobiomodulation for knee osteoarthritis treatment: A placebo-controlled, double-blind, randomized, clinical trial and pilot study

Programa de exercícios aeróbicos realizado em uma bicicleta estacionária associado à fotobiomodulação para o tratamento da osteoartrite de joelho: Um estudo clínico e piloto randomizado, duplo-cego e controlado por placebo

Programa de ejercicios aeróbicos realizados en una bicicleta estática asociados a la fotobiomodulación para el tratamiento de la osteoartritis de rodilla: Un estudio clínico y piloto aleatorizado, doble ciego y controlado por placebo

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Abstract
Objective: Investigate the effects of photobiomodulation (PBMT) and an exercise program aerobic on pain, range of motion, mobility, functionality and quality of life of women with knee osteoarthritis (OA). 24 volunteers were included and randomized into 2 groups: Exercise and Placebo PBMT Group (EPPG) (n=12) and Exercise and Active PBMT Group (EAPG) (n=12). The aerobic exercise program was performed on a stationary bicycle, 2 times a week and PBMT was applied in the most affected lower limb. Visual Analogue Scale (VAS) of pain, Knee Injury and Osteoarthritis Outcome Score (KOOS), and Medical Outcomes Study 36-item Short Form Health Survey (SF-36) were used. In addition, Knee Flexion Range of Motion (ROM), 40m Fast-Paced Walk Test (40mFPWT), 9-Stair Climb Test (9-step SCT) and, 30s Chair Stand Test (30sCST). Results: The level of pain was significantly reduced for both groups after the intervention (EAPG p= 0.01; EPPG p= 0.01). Also, a significant increase in the variables measured by KOOS evaluation for both groups were seen after the treatment. An increase in functional capacity of SF-36 was observed only in the EAPG group (p= 0.004) in the revaluation compared to evaluation. For the evaluations of active flexion ROM, 40m Fast-Paced Walk, 9-Stair Climb and 30s Chair Stand Tests no differences were seen for both groups in the reevaluation. Conclusions: After 8 weeks, the aerobic exercise program (with or without PBM) was effective pain, symptoms, activities of daily living, function in sport and recreation, quality of life and general KOOS score in women with knee osteoarthritis (KOA).
Keywords: Exercise; Photobiomodulation; Chronic pain; Osteoarthritis.

Resumo
Objetivo: Investigar os efeitos da fotobiomodulação (PBMT) e de um programa de exercícios aeróbicos na dor, amplitude de movimento, funcionalidade e qualidade de vida de mulheres com osteoartrite (OA) no joelho. 24 voluntárias foram incluídas e randomizadas em 2 grupos: Grupo de Exercício e PBMT Placebo (EPPG) (n=12) e Grupo de Exercício e PBMT Ativo (EAPG) (n=12). O programa de exercícios aeróbicos foi realizado em uma bicicleta estacionária, 2 vezes por semana, e a PBMT foi aplicada no membro inferior mais afetado. Foram utilizadas a Escala Visual Analógica (VAS) de dor, Questionário Knee Injury and Osteoarthritis Outcome Score (KOOS) e o SF-36. Além disso, foram realizados testes de Amplitude de Movimento de Flexão do Joelho, Teste de Caminhada Rápida de 40m (40mFPWT), Teste de Subida de 9 Degraus (9-step SCT) e Teste de Levantar da Cadeira em 30s (30sCST). Resultados: O nível de dor foi significativamente reduzido para ambos os grupos após a intervenção (EAPG p= 0,01; EPPG p= 0,01). Além disso, um aumento significativo nas variáveis medidas pela avaliação do KOOS foi observado para ambos os grupos após o tratamento. Um aumento na capacidade funcional do SF-36 foi observado apenas no grupo EAPG (p= 0,004) na reavaliação em comparação com a avaliação inicial. Para as avaliações da Amplitude de Movimento ativa de flexão do joelho, Teste de Caminhada Rápida de 40m, Teste de Subida de 9 Degraus e Teste de Levantar da Cadeira em 30s, não foram observadas diferenças para ambos os grupos na reavaliação. Conclusões: Após 8 semanas, o programa de exercícios aeróbicos (com ou sem PBM) foi eficaz na dor, sintomas, atividades da vida diária, função no esporte e recreação, qualidade de vida e pontuação geral do KOOS em mulheres com OA de joelho.
Palavras-chave: Exercício físico; Fotobiomodulação; Dor crônica; Osteoartrite.

Resumen
Objetivo: Investigar los efectos de la fotobiomodulación (PBMT) y de un programa de ejercicios aeróbicos en el dolor, rango de movimiento, funcionalidad y calidad de vida de mujeres con osteoartritis (OA) en la rodilla. Se incluyeron y se asignaron al azar 24 voluntarias en 2 grupos: Grupo de Ejercicio y PBMT Placebo (EPPG) (n=12) y Grupo de Ejercicio y PBMT Activo (EAPG) (n=12). El programa de ejercicios aeróbicos se realizó en una bicicleta estacionaria, 2 veces por semana, y se aplicó PBMT en el miembro inferior más afectado. Se utilizaron la Escala Visual Analógica (VAS) para el dolor, el Cuestionario Knee Injury and Osteoarthritis Outcome Score (KOOS) y el SF-36. Además, se realizaron pruebas de Rango de Movimiento de Flexión de Rodilla, Test de Caminata Rápida de 40m (40mFPWT), Test de Subida de 9 Escalones (9-step SCT) y Test de Levantarse de la Silla en 30s (30sCST). Resultados: El nivel de dolor disminuyó significativamente para ambos grupos después de la intervención (EAPG p= 0,01; EPPG p= 0,01). Además, se observó un aumento significativo en las variables medidas por la evaluación del KOOS para ambos grupos después del tratamiento. Se observó un aumento en la capacidad funcional del SF-36 solo en el grupo EAPG (p= 0,004) en la reevaluación en comparación con la evaluación inicial. Para las pruebas de Rango de Movimiento activo de flexión de rodilla, Test de Caminata Rápida de 40m, Test de Subida de 9 Escalones y Test de Levantarse de la Silla en 30s, no se observaron diferencias entre ambos grupos en la reevaluación. Conclusiones: Después de 8 semanas, el programa de ejercicios aeróbicos (con o sin PBMT) fue efectivo en el dolor, síntomas, actividades de la vida diaria, función deportiva y recreativa, calidad de vida y puntaje general del KOOS en mujeres con OA.
Palabras clave: Ejercicio físico; Fotobiomodulación; Dolor crónico; Osteoartritis.

1. Introduction

Osteoarthritis (OA) is a common chronic degenerative disease directly associated with the aging process, affecting mainly middle-aged and older women (Huang et al., 2020; Soleimanpour et al., 2014). It is characterized by cartilage degenerative lesions, culminating in articular pain and in a decrease of functional capacity, range of motion, muscular strength, and balance, culminating in a deterioration of the quality of life of the affected subjects (Huang et al. 2015; Martel-Pelletier et al., 2016).

It can be cited as risk factors for the development of knee osteoarthritis (KOA) the gender (female), previous joint injuries, obesity, genetic predisposition, lower limb muscle weakness, abnormal joint alignment, and age above 55 years old (Mandl LA 2019). In addition, the initiation and progression of KOA occurs by an imbalance in the catabolic and anabolic mediators and an overproduction of matrix degrading enzymes (Chen & Yu 2020).

OA treatment is based mainly on the use of analgesics, non-steroidal anti-inflammatory drugs, and surgical procedures (Chen & Yu 2020). Additionally, physical exercise programs (especially aerobic exercises) (Fallah et al., 2013). Aerobic exercises, through mechanical stimulus, are able of modulating the synthesis of proteolytic enzymes, reducing the synthesis of pro-inflammatory mediators and chondrocyte death, attenuating the signs of joint cartilage degradation and, consequently OA progression (Fallah et al., 2013; Brosseauet al., 2017).

Furthermore, additional strategies to optimize the beneficial effects of physical exercises have been used to offer an improved treatment for patients with OA, highlighting the positive effects of photobiomodulation therapy (PBMT) (Huang, et al. 2015; de Matos et al., 2018). Its effects occur from the absorption of infrared light by cytochrome c oxidase in mitochondria that causes an increase in cellular oxygenation, ATP production, and enzyme activity, leading to release of anti-inflammatory mediators (Sommer 2019; de Matos et al., 2018). Also, several studies have demonstrated, using experimental models of OA in rats, that PBM is able of decreasing the expression of inflammatory cytokines and increases antioxidant enzyme levels, attenuating the articular degenerative process (Thompson et al., 2020; Brosseau, et al., 2017). Moreover, in clinical trials, Sommer (2019) demonstrated that patients with OA treated with PBM presented lower level of pain and improved articular function. Moreover, the association of PBM and physical exercises has been demonstrating positive effects for treating the symptoms of OA, both in experimental and clinical studies (Assis, et al. 2018; de Paula Gomes et al., 2018). In an experimental study, Assis et al., (2018) observed that PBM associated with an exercise program (treadmill; 16 m/min; 50 min/day) prevented cartilage degeneration and modulated joint inflammatory process. De Paula Gomes et al., (2018) observed that PBM (using a cluster device with 905-nm super-pulsed diode laser, 875- nm LED, and 640-nm LED) associated with a physical exercise program had positive effects on reducing pain intensity among individuals with knee osteoarthritis.

Although all the positive effects of physical exercise programs and PBMT, there is a lack of studies investigating the use of aerobic activity in association with the PBMT on the managing of KOA symptoms. In this context and based on the need of investigating the effects of innovative treatments for OA, the aim of this present pilot study was to determine the effects of an aerobic exercise program performed on a stationary bicycle in association with PBMT (cluster device) on the level of pain, range of motion, mobility, functionality, dynamic balance, and quality of life of this population.

2. Methodology

This pilot study was a prospective, randomized, double-blind placebo-controlled study. This project was approved by the Human Research Ethics Committee of the Federal University of São Paulo (UNIFESP) nº 2,686,003 and registered on the Brazilian Clinical Trials Registry (https://ensaiosclinicos.gov.br/rg/RBR-4g256m). Participants were informed about the procedures to be performed and signed a Consent and Clarification Term. All the evaluations and interventions were performed at the Laboratory of Manual and Physical Resources of the Federal University of Sao Paulo.

2.1 Experimental procedures

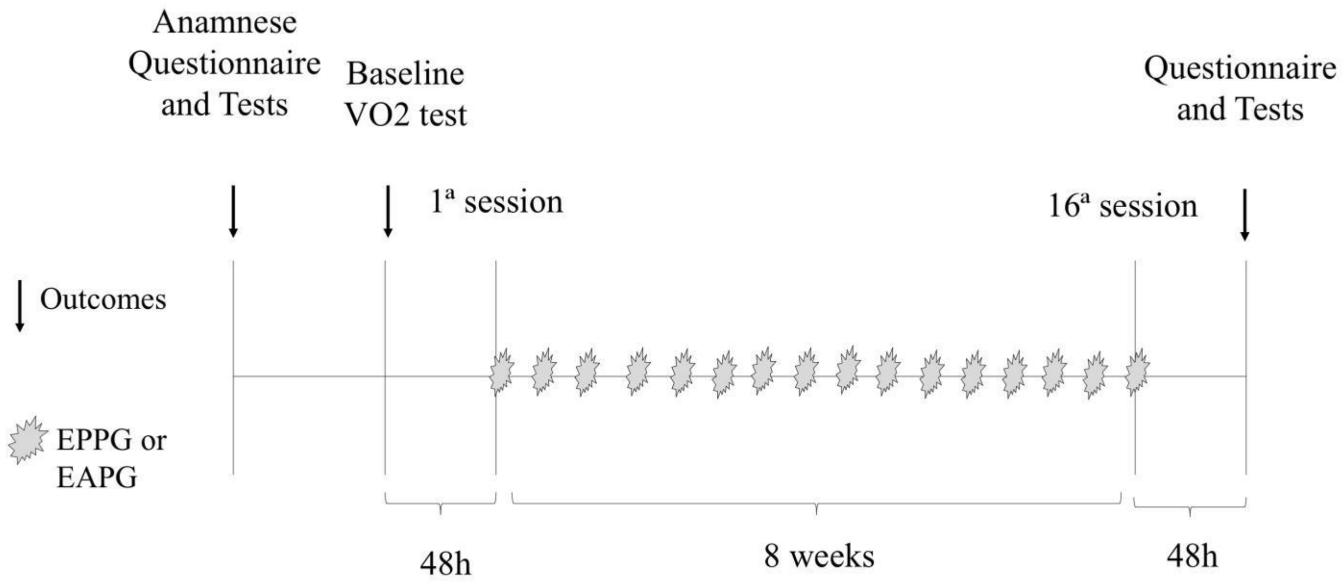
The experimental design of the present pilot study was constituted by the baseline assessments of the volunteers through data collections (anamnesis), evaluation of the radiological image exam by a rheumatologist and application of the questionnaires and tests (Figure 1). The questionnaires and tests used were: the Visual Analogue Scale (VAS) of pain, 40m Fast-Paced Walk Test (40mFPWT), 9-Stair Climb Test (9-step SCT), 30s Chair Stand Test (30sCST), Knee Injury and Osteoarthritis Outcome Score (KOOS) and Medical Outcomes Study 36-item Short Form Health Survey (SF-36). The goniometer was used to assess the most affect knee joint range of motion (ROM).

After the first assessments, all volunteers were submitted to a maximum oxygen consumption (VO_{2max}) test using a gas analyzer (Quark PFT, COSMED, Pavona di Albano, Italy), calibrated before every test following the manufacturer's recommendations. The test was performed on a stationary bicycle (Lode Corrival, Lode BV, Groningen, The Netherlands) by using a ramp protocol, in which the applied power progressively increased to the maximum VO2 estimated according to the characteristics of each volunteer (Neder & Nery, 2002). All tests were performed at the same altitude, atmospheric pressure and temperature (22°C) and were supervised by a certified cardiologist. Heart rate (HR) and heart rhythm were continuously observed through 12-lead electrocardiography (ECG) (C12x; COSMED, Pavona di Albano, Italy). Arterial blood pressure was measured at rest, every 2 min during the test and after test completion.

It was considered as a maximum test when the maximum HR was equal to or greater than 85% of that estimated by age (220 - age) and/or the gas exchange rate (R) was greater than or equal to 1.00 and/or there was a plateau in oxygen consumption (Wasserman et al., 2004). The peak VO2 was considered as the average of the values during the last 15 seconds of the incremental phase of the test. The VO_{2max} test for the entire sample occurred over a 48-hour before the 1st session of treatment period. This test was essential to estimate each volunteer's individual HR, based on the maximum HR achieved during the VO2max test.

At the end of the experimental period, the volunteers were re-evaluated using the following questionnaires and tests: Visual Analogue Scale (VAS) of pain, 40m Fast-Paced Walk Test (40mFPWT), 9-Stair Climb Test (9-step SCT), 30s Chair Stand Test (30sCST), Knee Injury and Osteoarthritis Outcome Score (KOOS) and Medical Outcomes Study 36-item Short Form Health Survey (SF-36) and goniometry of the most affected knee (ROM).

Figure 1 - Experimental design of stud.



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2.1.1 Inclusion criteria

Inclusion criteria comprised women with the age between 55 and 70 years old, unilateral or bilateral KOA with grade II or III according to radiographic confirmation and Kellgren-Lawrence scale and body mass index (BMI) between 22 and 35 kg/m2 (criteria established by Pan American Health Organization), > 2 points on the Numeric Rating Pain Scale, and classified as low and irregularly active, who performed physical activity with a frequency of at least 3 times a week or totaling a minimum of 150 min per week, according to Criteria established by American College of Sports Medicine measures by the International Physical Activity Questionnaire–Short Version (IPAQ).

2.1.2 Exclusion criteria

Those with any kind of previous musculoskeletal injury in the quadriceps femoris and/or hamstring muscles, orthopedic or rheumatic diseases, fibromyalgia, or pain that may prevent the physical exercise, and volunteers with diagnoses of lung diseases, cardiologic alterations, uncontrolled hypertension, or diabetes were excluded from the study; volunteers had received an intra-articular injection in the last 3 months. During the study, volunteers who developed any musculoskeletal injury, did not perform the tests of the experimental procedures, did not perform at least 80% of training sessions, or missed two consecutive training sessions were excluded. In addition, we excluded individuals who had malnutrition (BMI <22) or morbid obesity (BMI ≥35), and who had unavailability to participate of the treatment.

2.2 Randomization

The randomization procedure was performed through a computer program that created a random table of numbers in which each number corresponded to groups A or B (below). A researcher conducted the drawing procedures without informing the participants and evaluators which PBMT (placebo or active) would be applied. Thus, participants and researchers were blinded to the allocation of treatment.

A- Exercise and Placebo PBMT Group (EPPG): Exercise protocol associated with placebo irradiation;

B- Exercise and Active PBMT Group (EAPG): Exercise protocol associated with active irradiation.

It is also important to state that the researcher and the volunteers were blinded to the treatment during the period of sections. For blinding the volunteers, a modification of the laser device was made and for the placebo treatment the same sounds of the intervention treatment were made by the device.

2.3 Experimental procedures

After the initial evaluation, the following experimental procedures were made before and after treatment as described below:

2.3.1 Visual Analogue Scale (VAS) of pain

VAS was used to assess the level of pain. This scale is a valid and responsive measure of pain in OA and is widely used to determine treatment effectiveness. The VAS consists of a 10cm rule (without numbers). At the left side, 'no pain' is written, while on the right side, 'unbearable pain'. Patients were instructed to mark in the rule the level of pain felt in the previous week in their most affected knee (Begum & Hossain, 2019).

2.3.2 40m Fast-Paced Walk Test (40mFPWT)

According to the Osteoarthritis Research Society International (OARSI), the 40m FPWT test is recommended to assess physical function in people diagnosed with knee osteoarthritis, evaluate the capacity to walk quickly, the dynamic balance, and the ability to change directions whilst walking short distances (Bennell, Dobson, Hinman, 2011). It scores the maximal walking speed on walks around the marker and returns to the starting point to a marker 10m away, four times, excluding turns. The time was recorded and the result was calculated as speed in m/s (Tolk, Janssen, Prinsen, et al., 2019). During the test, patients had to walk at a self-chosen walking speed and try to cover as much distance as possible without running.

2.3.3 9-Stair Climb Test (9-step SCT)

The 9-step SCT, assesses the ability of the volunteers to climb and to descend some steps, as well as the strength of the lower limbs and dynamics balance, is highly recommended for evaluating knee performance and is recommended by OARSI, since patients with knee OA may end up showing slower speed when climbing stairs compared to healthy adults (Dobson, Hinman, Rooss, et al., 2013; Gonçalves et al., 2017). The volunteers go up and down 9 steps (around 16 to 20cm in height), and use the rail if necessary to realize a maximum achieve at a maximum achievable speed. The result corresponds to the time (s) it takes a person to complete an ascent and descent of the test (Dobson, Hinman, Rooss, et al., 2013). During the test, patients had to go up and then down stairs at a self-chosen speed, being able to use the handrail if necessary. The time during which the test was performed was recorded.

2.3.4 Knee joint range of motion (ROM) – Goniometer

Goniometer is instrument a reliability outcome to measure maximum active knee flexion in degrees (Cibere, Bellamy, Thorne, et al 2004). ROM is assessed for identifying restrictions in joint mobility and for gauging the patient's advancement within an intervention or rehabilitation regimen (Akizuki, Yamaguchi, Morita, Ohashi, 2016). During the evaluation, the axis of the goniometer was centered at the lateral condyle of the femur, the proximal arm in the line of the greater trochanter and long axis of the distal arm in the line of the fibula of the knee most affected (Mullaney, McHugh, Johnson, et al., 2010). During the test, patients were positioned in the ventral decubitus position and they were instructed to perform the knee flexion movement and the angle obtained was recorded.

2.3.5 Knee Injury and Osteoarthritis Outcome Score (KOOS)

The KOOS is a questionnaire that assesses a total knee health, and it has validity and ability for applied in patients who have KOA (Tolk, Janssen, Prinsen, et al., 2019). It is composed of 42 items with 5 subscales: perception of pain (frequency and intensity during movement), other symptoms, ability to take part in activities of daily living, function in sport and recreation, and quality of life) for each of the questions, the degree of difficulty that occurred in the last week due to the knee was indicated. Each item was assigned a score from 0 to 4 and normalized by a document, in which 100 indicated no symptoms and 0 indicated extreme symptoms (Ross, et al. 1998; Roos & Lohmander, 2003).

2.3.6 Medical Outcomes Study 36-item Short Form Health Survey (SF-36)

The SF-36 has been utilized used for describe quality of life of individuals experiencing various general health, post-operative, and musculoskeletal issues, is an important tool for the assessment of quality of life (Laguardia, Campos, Travassos, Najar, et al., 2013). The questions in the SF-36 are straightforward and applicable to the majority of individuals' daily lives, incluid individuals with OA. It has 36 items with 8 subscales (functional capacity, limitation due to physical aspects, pain globally and how much pain interfered with their work in the last four weeks, general health status, vitality, social aspects, emotional aspects, and mental health) resulting in a score between 0 and 100 (where a score of 0 is worst and 100 is better). This questionnaire is widely accepted as an outcome measure in chronic diseases, mainly KOA (Webster & Feller, 2016).

2.3.7 30s Chair Stand Test (30sCST)

The 30-sCST is a test that evaluates the dynamic balance, lower limb strength, and functionality, and the OARSI recommended for people with knee OA (Dobsonet al., 2013). A reliable test (Martín-Martínez et al., 2019) in which the patient starts seated in a chair and needs to do the maximum amount of complete stand movements, with feet flat on the ground and shoulder width apart, during 30 seconds (Dobson, Hinman, Rooss, et al., 2013). A chair with ˜43cm of high and without armrests was used (Tolk, Janssen, Prinsen, et al., 2019). During the test, patients were instructed to sit down and get up from a chair with their arms crossed and feet parallel, as many times as possible for 30 seconds.

2.4 Interventions

2.4.1 Aerobic exercise program

The aerobic exercise program was carried out in an ergometric stationary bicycle and supervised by a physiotherapist, with a duration of 20 minutes, twice a week, and it was divided into 3 phases: warm-up phase (light pedaling without increasing the load), stimulus phase (pedaling with high cadences, simulating the climb, but without getting up from the seat, in order not to overload the joint), and cooling phase (resume light and unloaded pedaling). The HR and the Borg scale were checked every 3 minutes throughout all the phases. The individuals increased the load in order to maintain the HRmax between 70% to 75% of the predicted, as previously checked through the VO2max test. After exercise, the subjects were submitted to quadriceps, flexor ankle, hamstrings and upper limbs stretching during 10 minutes. This protocol was based on a study developed by Salacinski et al. (2012).

2.4.2 PBMT

After the end of each session of the physical exercise, the placebo or active PBMT was applied on medial and lateral region, at the articular line, of the most affected knee. A cluster (DMC® São Carlos, SP, Brazil) with 7 infrared AsGaAl laser beams 808 nm was used. The radiation parameters are described in table 1 and followed recommendations of the World Association of Laser Therapy (WALT) (2006).

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Table 1 - PBMT parameters.

Parameters	Value
Wavelength	808nm
Operating mode	Continuous
Peak radiant power	100 Mw
Power density	2 W/cm^2
Energy	4 J per point/56 J per knee
Energy density	91 J/cm^2
Spot size	0.05 cm^2
Irradiation time	40s each application
Anatomical location	Perpendicular contact to the skin
Number of treatments	16 sessions

PBMT: Photobiomodulation therapy; Nm: nanometers; mW: miliWatts; W/cm$^{2:}$ Watts per centimeters square; j/cm^2: Joules per centimeter square; cm^2: centimeter square; s: seconds. Source: Authors.

2.5 Statistical Analysis

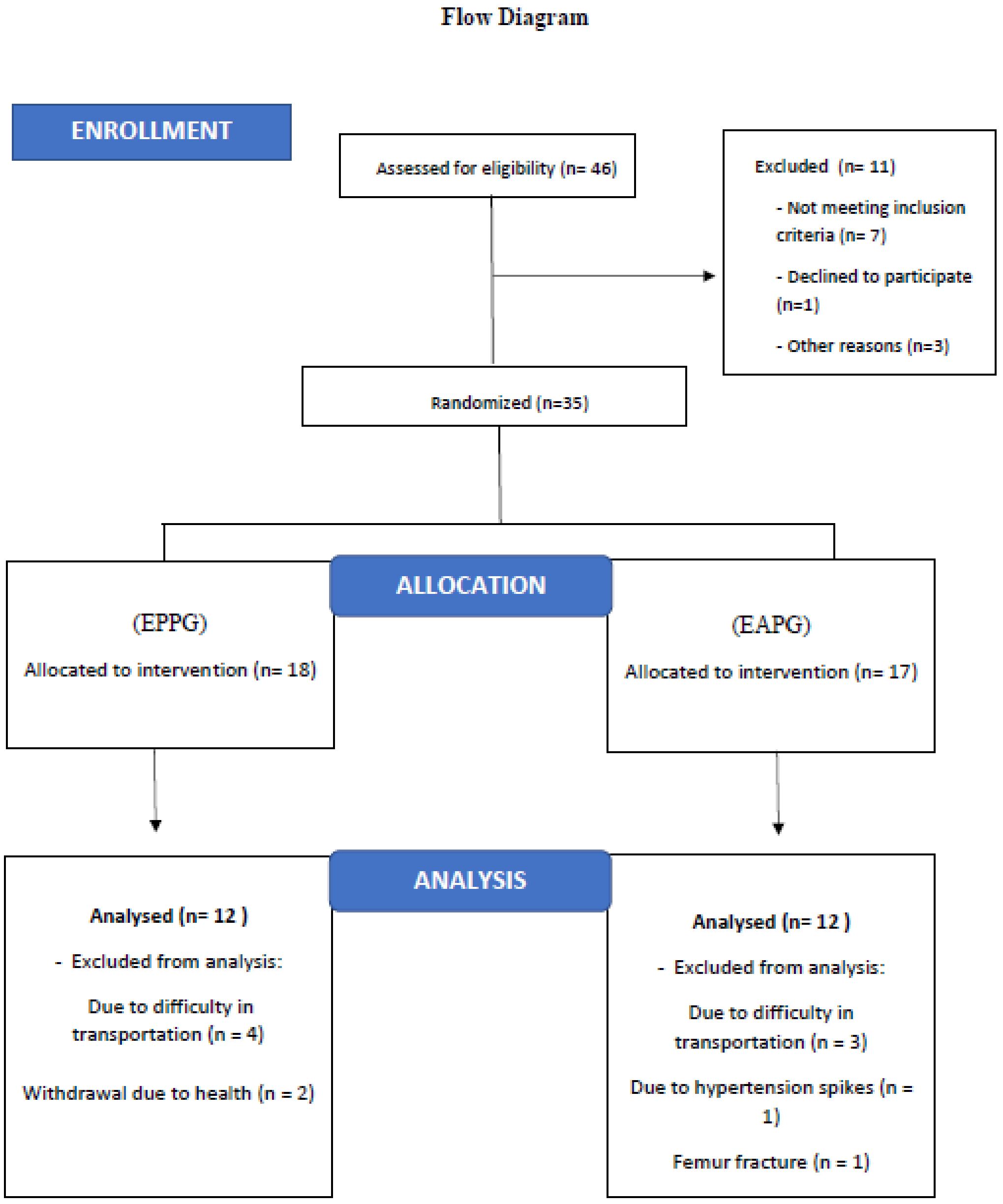
The sample size calculation was performed using the GPower 3.0.10 program with parameters: effects size of 0.25, power observed of 0.80 and α=5%, considering ANOVA model for two groups and based on previous studies [14]. The required sample would be 17 patients for each treatment group EPPG or EAPG with a total of 34 patients. To the analysis of the data, after confirming the normality in the data distribution and homogeneity of variances, the parametric statistic was chosen. For this reason, descriptive statistics were used with measures of central tendency and dispersion (means and standard deviations), and ANOVAs was used to compare groups and treatment effect. One-way ANOVAs were used to ensure no significant difference to anthropometric data between groups. Three ANOVAs were used to verify possible differences between the dependent variables for all analysis used and two factors: between groups (EPPG and EAPG) and treatment^ (before and after). The Bonferroni post hoc test was used for inter-group adjustments of multiple comparisons, and the Tukey HSD post hoc test was used for possible interaction effects. The level of significance was set at 5% (α = 0.05).

3. Results

A total of 46 volunteers were recruited for the study. From those, 35 participants were selected for participating according to inclusion criteria and were randomized and included in the groups (EPPG n=18) and EAPG (n=17). At the end of the study, 11 volunteers were excluded because they have not finished the treatment sessions. Thus, the final sample size was 24 female volunteers (EPPG n=12 and EAPG n=12).

The flowchart with inclusion and exclusion of volunteers is shown in Figure 2

Figure 2 – Flowchart.



Source: Authors.

Table 2 demonstrates the anthropometric data of the EAPG and EPPG groups using the following variables. The mean values were 61.25 and 61.67 years, 1,62 and 1.58 m, 74.50 and 72.42 kgs and 28.50 and 28.83 kg/m^2 for EAPG and EPPG, respectively. No statistical difference was observed between groups.

Table 2 - Means and standard deviations of anthropometric characteristic values.

Variables	EAPG (n=12)			EPPG (n=12)			*p value*
	Mean		**SD**	**mean**		**SD**	
age (years)	61.25	±	4.20	61.67	±	5.73	0.841
height (m)	1.62	±	0.04	1.58	±	0.08	0.22
body mass (kg)	74.50	±	11.59	72.42	±	13.34	0.69
body mass index (kg/m²)	28.50	±	4.38	28.83	±	4.32	0.852

EAPG: exercise and active photobiomodulation group; EPPG: exercise and placebo photobiomodulation; SD: standard deviation. T-test, independent, by groups was applied. Source: Authors.

The evaluation of the level of pain through VAS scale demonstrated that in te evaluation the values were 3.85 and 6.45 for EAPG and EPPG, respectively. Moreover, in the reevaluation, the values were 1.7 and 2.9 for EAPG and EPPG, respectively. Both groups presented a significant reduction in the values found in the revaluation compared to evaluation (EAPG p= 0.01; EPPG p= 0.01). No differences between the groups were seen post-intervention.

For 40 m Fast paced walk, the means values of 29.43 and 26.78 was found in the evaluation, for EAPG and EPPG, respectively. In the evaluation, the values were 28.73 and 27.08 for EAPG and EPPG, respectively. No differences were observed between groups.

For 9-Stair Climb, in the evaluation it was observed a value of 14.25 and 11.98 for EAPG and EPPG. In the reevaluation, values of 13.69 and 11.51 was observed for EAPG and EPPG. No differences were observed between groups.

For 30s Chair Stand Test, 8.75 and 9.42 for EAPG and EPPG and in the reevaluation 9.58 for both groups. Similarly to the other analysis, no difference was observed. Moreover, for the variable active flexion, values of 111.83 and 112.82 were seen in the evaluation and 110.50 and 112.50 were found in the reevaluation. No difference was observed.

The KOOS evaluation indicated an improvement in total knee health in both groups in the revaluation compared to evaluation considering the subscales pain (EAPG p= 0.04; EPPG p= 0.02); symptoms (EAPG p= 0.007; EPPG p= 0.005); activities of daily living (EAPG p= 0.03; EPPG p= 0.02); function in sport and recreation EAPG p= 0.03; EPPG p= 0.009); quality of life (EAPG p= 0.04; EPPG p= 0.01) and total score KOOS (EAPG p= 0.008; EPPG p= 0.002). No intergroup differences were observed in the reevaluation. Significant difference between groups was observed for pain in baseline condition (p= 0.04) (Table 3).

An increase in functional capacity of SF-36 was observed only in the EAPG group (p= 0.004) in the revaluation compared to evaluation. No difference was showed in the others SF-36 domains comparisons between revaluation and evaluation values and post-intervention values (Table 3).

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Table 3 - Means and standard deviations of mobility, functionality, level of pain, range of motion and quality of life in baseline and after intervention protocol condition according groups.

Variables	EAPG (n=12)		EPPG (n=12)	
	Evaluation	**Revaluation**	**evaluation**	**Revaluation**
Visual Analogue Scale*	3.85 (1.3 - 7.5)	1.7 (0 - 9.1) A	6.45 (2 - 10)	2.9 (0 - 7.9) A
40m Fast-Paced Walk Test (m/s)*	29.43 (21.01 - 59.23)	26.78 (20.56 - 33.45)	28.73 (24 - 50.95)	27.08 (23.57 - 33.20)
9-Stair Climb Test (s)*	14.25 (10.01 - 24.40)	11.98 (8 - 26.73)	13.69 (8.93 - 19.02)	11.51 (9.49 - 19.19)
30s Chair Stand Test	8.75 ± 2.38	9.42 ± 2.15	9.58 ± 2.07	9.58 ± 1.73
Active Flexion	111.83 ± 7.84	112.82 ± 10.32	110.50 ± 9.42	112.50 ± 8.58
Knee Injury and Osteoarthritis Outcome Score (KOOS)				
pain*	70.5 (14 - 89)	79.5 (36 - 97) A	47.5 (3 - 64) B	70.5 (25 - 100) A
symptoms*	59 (11 - 79)	82 (32 - 89) A	50 (14 - 100)	71.5 (21 - 100) A
ADL	59.75 ± 16.63	76.08 ± 14.47 A	49.42 ± 25.62	66.75 ± 21.74 A
function in sport and recreation	26.67 ± 15.86	45.83 ± 19.17 A	20.42 ± 20.39	43.75 ± 30.90 A
quality of life	39.08 ± 20.88	53.75 ± 23.10 A	33.08 ± 23.82	51.08 ± 30.47 A
total score KOOS	48.08 ± 16.76	65.00 ± 16.06 A	39.67 ± 18.93	58.75 ± 22.55 A
Medical Outcomes Study 36-item Short Form Health Survey (SF-36)				
functional capacity	46.67 ± 19.81	65.42 ± 17.77 A	46.67 ± 19.81	54.58 ± 27.67
physical aspects*	100 (0 - 100)	100 (0 - 100)	50 (0 - 100)	100 (0 - 100)
Pain	55.42 ± 17.51	68.17 ± 19.09	51.67 ± 23.46	64.42 ± 25.63
vitality*	60 (40 - 85)	72.5 (25 - 90)	82.5 (0 - 100)	77.5 (25 - 100)
social aspects*	87.5 (50 - 100)	87.5 (25 - 100)	100 (25 - 100)	93.75 (62.5 - 100)
emotional aspects*	100 (33.3 - 100)	100 (0 - 100)	66.7 (0 - 100)	100 (0 - 100)
mental health*	76 (52 - 88)	84 (32 - 100)	78 (44 - 100)	80 (56 - 100)
general health status	68.33 ± 14.67	76.67 ± 14.67	67.50 ± 14.54	77.92 ± 12.15

EAPG: exercise and active photobiomodulation group; EPPG: exercise and placebo photobiomodulation; ADL: activities of daily living. *nonparametric data were expressed as median, minimum, and maximum values. Parametric data expressed as mean and standard deviation. [A]statistical difference between the evaluation and revaluation conditions in the same group; [B]statistical difference between groups in the same condition. Source: Authors.

Delta values did not show significant difference in intergroups comparisons (Table 4).

Table 4 - Delta values of study variables according groups.

	EAPG (n=12)						EPPG (n=12)					
	Mean		**SD**	**Median**	**Min**	**Max**	**Mean**		**SD**	**Median**	**Min**	**Max**
Visual Analogue Scale*	-2.02	±	2.56	-1.3	-7.4	1.6	-2.94	±	2.99	-2.25	-8.2	2.7
40m Fast-Paced Walk Test (m/s)*	-4.77	±	11.23	-2.78	-34.23	5.69	-2.28	±	7.56	-0.67	-24.86	5.37
9-Stair Climb Test (s)*	-1.09	±	2.50	-1.57	-4.86	3.97	-1.29	±	2.31	-0.54	-5	1.96
30s Chair Stand Test	0.67	±	1.83	1	-2	3	0.00	±	1.65	0	-4	3
active flexion	0.09	±	7.30	0	-12	15	2.00	±	6.66	3	-12	12
Knee Injury and Osteoarthritis Outcome Score (KOOS)												
pain*	15.00	±	26.80	9	-22	83	18.67	±	26.55	19	-14	83
symptoms*	20.42	±	20.34	21	-14	71	17.83	±	17.22	13	-7	53
ADL	16.33	±	14.38	16	-5	39	17.33	±	22.74	12	-15	58
function in sport and recreation	19.17	±	17.82	15	-5	55	23.33	±	26.83	25	-20	70
quality of life	14.67	±	19.43	19	-25	56	18.00	±	16.44	18	-6	50
total score KOOS	16.92	±	15.70	17	-3	61	19.08	±	17	15	-3	58
Medical Outcomes Study 36-item Short Form Health Survey (SF-36)												
functional capacity	18.75	±	13.67	15	0	45	7.92	±	19.24	5	-25	30
physical aspects*	10.42	±	49.38	0	-100	100	27.08	±	43.25	25	-50	100
Pain	12.75	±	21.06	5	-10	45	12.75	±	12.19	16.5	-15	25
vitality*	7.92	±	16.71	8	-15	40	5.83	±	24.20	0	-25	45
social aspects*	-1.04	±	29.42	0	-75	50	7.29	±	28.93	0	-37.5	50
emotional aspects*	-2.77	±	45.98	0	-100	67	30.56	±	45.97	0	0	100
mental health*	6.00	±	13.38	6	-20	32	5.33	±	16.48	2	-16	32
general health status	8.33	±	23.48	0	-30	55	10.42	±	18.64	12.5	-20	40

EAPG: exercise and active photobiomodulation group; EPPG: exercise and placebo photobiomodulation; ADL: activities of daily living. *nonparametric data. Source: Authors.

4. Discussion

This study investigated the effects of an aerobic exercise program on a stationary bicycle in association with PBM via cluster. It was hypothesized that PBM would promote an extra stimulus to the exercised volunteers, improving the parameters evaluated. In the reevaluation, it was observed that both groups presented a significant improvement in the level of pain and in the variables evaluated in the KOOS analysis such as pain, symptoms, activities of daily living, function in sport and recreation, quality of life and general KOOS score in both groups after 8 weeks of treatment. No other difference was observed.

One of the most remarkable findings of the present study is the significant decrease in the level of pain of all volunteers after the treatment. It is well known that chronic pain commonly affects patients with KOA and it is responsible by a severe reduction in function and quality of life. These results corroborated those of Goh et al., (2019) who observed the importance of an 8-week intervention with physical exercise in the reduction of pain, being considered one of the most effective interventions for people with KOA. In this context, the literature supports that physical exercise programs, mainly aerobic modalities, are able of modulating the synthesis of inflammatory biomarkers and decrease the death of chondrocytes, declining cartilage proteolysis process and consequence the level of knee pain (Alkatan, et al., 2016). However, the active PBM have not optimized the positive effects of physical exercises in this variable. In a recent systematic review, Vassão et al., (2021) showed that, until the moment, it can be found in the literature 7 randomized controlled trials, examining PBM in association with different types of exercise in pain and functional capacity of patients with KOA, and from them, only 2 (Huang, et al., 2015; Alfredo, et al., 2012) showed an extra effect of PBM. Possibly, the result may be related to the small sample size or the parameters of PBM used (which was not able of offering an extra stimulus for decreasing the level of pain).

There was no significant improvement in knee active flexion ROM in both groups comparing the revaluation and evaluation, and post intervention values. These findings did not corroborate with those of Nazari et al., (2019), who showed a significant improvement in the knee flexion ROM of patients with KOA after 12 sessions of treatment (high intensity light therapy plus PBM) when compared the conventional physical therapy protocol group and exercise therapy group. However, the study attributes these effects to the increase in local temperature by HILT considering a useful resource in improving knee flexion ROM more than others, as the PBM that is nonthermal and was used in our study.

The literature demonstrates that an aerobic exercise program on a stationary bicycle is effective to treat pain and consequence physical functioning in patients with KOA (I-III grades) compared to usual care (Rewald, et al., 2020). In these studies, the aerobic exercise program did not improve these functional capacity tests results after a treatment period. Perhaps, the exercises involving lower limbs muscle strength could be more effective on improve of this variable, since resistance exercise is capable of promoting an efficient gait (Mattos, et al., 2016).

KOOS evaluation demonstrated that, both groups had an improvement in the subscales after the period of treatment. Our findings are in agreement with previous published studies. Salacinski et al., (2012) observed that a stationary bicycle training (70-75% MHR) improved KOOS pain, function in sport and recreation, and quality of life subscales scores after 12 weeks of treatment, twice a week. However, PBM has not offered an extra improvement of symptoms after 8 weeks of treatment (one theory raised is that a higher number of sessions of PBM would be necessary). Interestingly, previous studies demonstrated that the association of both therapies (active PBM and exercise) was effective compared to placebo PBM and exercise for self-reported knee status (Alfredo, et al., 2012).

In this study, the aerobic exercise associated with active PBM improves the SF-36 functional capacity subscale. A recent systematic review and meta-analysis demonstrated that stationary cycling exercise offers physical benefits as relief of pain and improve of function individuals with KOA (Luan, et al., 2021). It is important to highlight that aerobic exercise on a stationary bicycle involves the use of large muscle groups of lower limbs Chen, Yu (2020), which consequently improved the functional capacity. Interestingly, active PBM with exercise had no influence in the pain, limitation due to physical aspects, general health status, vitality, social aspects, emotional aspects, and mental health SF-36 subscales.

Nowadays, the practice of integrating therapeutical approaches, which incorporate different and complementary treatments has been increasing significantly (Ghoreishi, et al., 2023). Thus, the association of aerobic exercise programs and PBM have been demonstrating positive effects on knee OA patients due to its analgesic and anti-inflammatory effects, decreasing pain and improving function (Ahmad, 2022). However, in the present study, combining PBM and exercise have not culminated in any significant extra effect on the variables evaluated. Perhaps, future studies with a higher sample size may produce positive results.

4.1 Limitation

The present study has some limitations that can be pointed and support future studies. The main limitation was the small simple size. Moreover, it did not perform follow-up after reevaluation to determine the long-term effects of the treatment. Second, the therapists that applied PBM could not be blinded to the emission mode (placebo or active). Finally, it was not possible to perform VO_{2max} test of the volunteers after the treatment as a form of monitoring the increase in the cardiorespiratory capacity of these volunteers. As this is pilot study, our results are underpowered, making it difficult to find a significant difference and whether a larger number of subjects could lead to a significant difference in the analysis. Therefore, researchers should be careful in the interpretation of the data of the present work, especially related to the optimization effects of PBM on exercised patients with KOA. Many evidences in the scientific literature show the promising stimulatory effects of PBM and further studies, with large samples should be performed for further investigated the effects of the integration of both treatments.

5. Conclusion

In this pilot study, after 8 weeks, an aerobic exercise program on a stationary bicycle in association with placebo or active PBM via cluster was effective pain, symptoms, activities of daily living, function in sport and recreation, quality of life and general KOOS score. A significant improvement was observed in SF-36 functional capacity in aerobic exercise program associate with active PBM group suggesting the positive effects of both therapies. However, these results need to be confirmed in future studies with a higher sample size. Future studies are need for further investigate the effects of the association of PBM and programs of physical exercises for patients with OA, using other parameters of irradiation and different protocols of physical exercises in this population in order of comparing other protocols of treatment.

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