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ORIGINAL RESEARCH

Effect of photobiomodulation associated with exercise on pain and functionality of patients with knee osteoarthritis: a pilot study

Efeito da fotobiomodulação associada a exercícios na dor e na funcionalidade de pacientes com osteoartrite de joelho: estudo-piloto

Efecto de la fotobiomodulación asociada a ejercicios sobre el dolor y la funcionalidad en pacientes con osteoartritis de rodilla: un estudio piloto

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ABSTRACT | Our study evaluated the effect of photobiomodulation associated with exercise on pain and functionality of patients with knee osteoarthritis. Twenty patients with unilateral or bilateral knee osteoarthritis were selected and divided into two groups: Control group (CG), which underwent photobiomodulation (PBM) placebo and exercise protocol; and the photobiomodulation group (PG), which performed an active application of the PBM and the exercise protocol – performed twice a week for eight weeks and consisting of passive stretching of the lower extremity muscles, straight leg raise, proprioceptive training and exercises for gait control. PBM was applied through a cluster apparatus containing four diodes of 670 nm and five diodes of 850 nm, with an output power of 540 mW and with a dose of 4J / cm^2. The groups were evaluated before and after treatment with the SF-36, Lequesne and Tinetti questionnaires as well as the Visual Analog Pain Scale. Data were analyzed using the Anova method, followed by the post-hoc Bonferroni test. The data indicated significant improvements in the PG at the end of treatment for Visual Analog Pain Scale (2±1.25 vs. 0.7±0.82, p=0.009). Although both groups achieved significant improvements throughout the treatment, we could not observe significant differences between them for the rest of the evaluations at the end of the treatment. Therefore, the use of PBM associated with exercises showed pain improvement in patients with knee osteoarthritis, although it was not possible to observe significant differences in patients' functionality.

Keywords | Osteoarthritis, Knee; Exercise Therapy; Low-Level Light Therapy.

RESUMO | O objetivo do estudo foi avaliar o efeito da fotobiomodulação associada a exercícios na dor e na funcionalidade de pacientes com osteoartrite de joelho. Para isso foram recrutados 20 pacientes com osteoartrite do joelho uni ou bilateral, que foram distribuídos em dois grupos: grupo-controle (GC), que realizou aplicação de fotobiomodulação (FBM) placebo e um protocolo de exercício; e grupo fotobiomodulação (GF), que realizou aplicação ativa da FBM e o protocolo de exercício, sendo esse realizado duas vezes por semana durante oito semanas e consistindo de alongamentos passivos dos músculos de membros inferiores, straight leg raise, treinamento proprioceptivo e exercícios para o controle da marcha. A FBM foi aplicada com o aparelho *cluster* contendo quatro diodos de 670 nm e cinco diodos de 850 nm, com uma potência de saída de 540 mW, sendo a dose utilizada de 4 J/cm^2. Os grupos foram avaliados pré e pós-tratamento com os questionários SF-36, Lequesne, Tinetti, e por meio da Escala Visual Analógica de dor (EVA). Os dados foram analisados com o método Anova, seguido do Bonferroni. Os dados indicaram melhoras significativas para o GF ao fim do tratamento para as avaliações da EVA (2±1,25 vs. 0,7±0,82; *p*=0,009). Embora ambos os grupos tenham obtido melhoras significativas ao longo do tratamento, não foi possível observar diferenças significativas entre eles para o restante das avaliações ao final do tratamento. Portanto, conclui-se que o uso da FBM associada a exercícios apresentou melhora da dor nos

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pacientes com osteoartrite de joelho, embora não tenha sido possível observar diferenças significativas no que diz respeito à funcionalidade.
Descritores | Osteoartrite do Joelho; Terapia por Exercício; Terapia com Luz de Baixa Intensidade.

RESUMEN | El presente estudio tuvo como objetivo evaluar el efecto de la fotobiomodulación asociada a ejercicios sobre el dolor y la funcionalidad de pacientes con osteoartritis de rodilla. Para ello, se reclutaron a 20 pacientes con osteoartritis de rodilla unilateral o bilateral, que se dividieron en dos grupos: el grupo control (GC), que recibió placebo de fotobiomodulación (FBM) y un protocolo de ejercicio; y el grupo de fotobiomodulación (GF), que recibió la aplicación activa de FBM y el protocolo de ejercicio, el cual se realizó dos veces por semana, durante ocho semanas, y consistió en estiramientos pasivos de los músculos de las extremidades inferiores, *straight leg raise*, entrenamiento propioceptivo y ejercicios para el control de la marcha. La FBM se aplicó con el dispositivo *cluster* que contenía cuatro diodos de 670 nm y cinco diodos de 850 nm, con una potencia de salida de 540 mW, y la dosis utilizada fue de 4 J/cm^2. Los grupos se evaluaron antes y después del tratamiento por medio de los cuestionarios SF-36, Lequesne, Tinetti y de la Escala Visual Analógica de Dolor (EVA). Los datos se analizaron utilizando el método Anova, seguido del Bonferroni. Los datos apuntaron una mejora significativa en el GF al final del tratamiento mediante las evaluaciones de la EVA (2±1,25 vs. 0,7±0,82; p=0,009). A pesar de que ambos grupos lograron obtener mejoras significativas durante el curso del tratamiento, no fue posible observar diferencias significativas entre ellos en las evaluaciones al final del tratamiento. Por lo tanto, se concluye que el uso de la FBM asociada a ejercicios ocasionó una mejora del dolor en pacientes con osteoartritis de rodilla, aunque no fue posible observar diferencias significativas con respecto a la funcionalidad.
Palabras clave| Osteoartritis de la Rodilla; Terapia por Ejercicio; Terapia por Luz de Baja Intensidad.

INTRODUCTION

Osteoarthritis (OA) is a common disorder defined by the American College of Rheumatology as a heterogeneous group of conditions, which begins in the joints and is associated with symptoms and defects in the integrity of the articular cartilage, joint lining and ligaments. OA is also related to changes in cortical bone and joint margin[1,2]. It is one of the most prevalent rheumatic diseases in developing countries, with a global incidence of 9.6% in men and 18% in women over 60 years of age, according to the World Health Organization[3].

Of these individuals, 80% have movement limitations and 25% have difficulties in performing activities of daily living[3], which may be related to loss of muscle strength and consequent gait disorders, thus resulting in a high risk of falls. Therefore, previous studies have proposed treatments related to proprioception and muscle strengthening exercises[4-7]. Given the OA chronic nature, exercise-based rehabilitation may not be sufficient to reduce pain[2].

Thus, photobiomodulation (PBM) has been studied as a therapeutic resource capable of controlling or reducing pain[8], as well as other physical agents such as TENS[9] and therapeutic ultrasound[10,11].

PBM can be applied with different parameters, especially at different wavelengths, power and energy. It can also be applied with different equipment, such as clusters or single, with different advantages and disadvantages. The cluster allows the coverage of a larger treatment area and reduces the application time to achieve the same energy in a region, besides enabling the application of different wavelengths and allowing a greater number of photoreceptor cells to be irradiated[12].

However, the association of physical agents with rehabilitation protocols still requires studies on the efficacy in pain control and functional improvement of patients with knee OA. Therefore, we evaluated the effect of photobiomodulation associated with physical exercises in pain and functionality of patients with knee osteoarthritis.

METHODOLOGY

This is a longitudinal, prospective and simple blind study with preliminary results. Our study included 20 individuals clinically diagnosed with knee OA and that presented characteristic symptoms after knee X-ray evaluation, considering the criteria of the Osteoarthritis Research Society International (OARSI)[13].

All participants signed an informed consent form with guidance on the study, which was approved by the Ethics and Research Committee of the *Universidade Federal de São Paulo* under protocol no. 215,142.

Patients had to be older than 50 years, with osteoarthritis only in the knee joint for at least two years, X-ray with a classification of at least grade II (Kellgren-Lawrence)[14], pain in the knee joint with at least three points in the Visual Analog Pain Scale (VAS) and who have not undergone therapy in the prior three months. Individuals were not included if they presented uncontrolled diabetes mellitus, untreated hypertension, neurological deficits and peripheral neuropathies.

The twenty individuals selected were randomly divided into two groups using a computerized randomization table, with confidentiality of allocation in sealed and opaque envelopes. The control group (CG) was subjected to the application of placebo PBM and the exercise protocol. The photobiomodulation group (PG) was subjected to the active application of the PBM and the exercise protocol.

For the pre- and post-treatment evaluations, the questionnaires SF-36, Lequesne and Tinetti were used, besides the VAS.

Treatment protocol

The treatment protocol lasted eight weeks and was applied for one hour twice a week.

Initially, the individuals performed static passive stretching of the hamstring, femoral quadriceps and sural triceps muscles, bilaterally (3 sets of 30 seconds).

After stretching, straight leg raise (SLR) strengthening exercises of the hamstrings, femoral quadriceps, adductors and abductors were performed, with three series of twelve repetitions. The progression of isometric to isotonic strengthening exercises was acquired with the individual evolution of each patient.

After these exercises, a sensory-motor training was performed, with unstable bipodal balance exercises on the board with open eyes, progressing to closed eyes. Then bilateral unipodal balance exercises were performed in stable soil, with evolution to balance board and open eyes, progressing to closed eyes. Finally, a balance and gait training was performed with limb elevation. All these exercises were performed in the same format: 3 sets of 1 minute of maintenance.

Photobiomodulation

At the end of the exercise protocol, in all sessions, photobiomodulation (Table 1) was applied in two points (Figure 1) in the joint anterior line of the two knees. For the placebo application, the device was covered, so participants could not know which group they belonged to.

Table 1. Parameters of photobiomodulation (cluster)

Application	Stationary in contact with skin
Wavelength (nm)	850 and 670
Output power 850 nm (mW)	100
Output power 670 nm (mW)	10
Total output power (mW)	540
Energy per point (Joules)	30
Energy density (J/cm²)	4
Number of points applied	2

Figure 1. Photobiomodulation application points

Statistical Analysis

To study the behavior of the CG and PG groups, the Anova variance analysis model was used with repeated measures, in addition to the multiple Bonferroni comparison method, adopting a significance level of $p<0.05$.

RESULTS

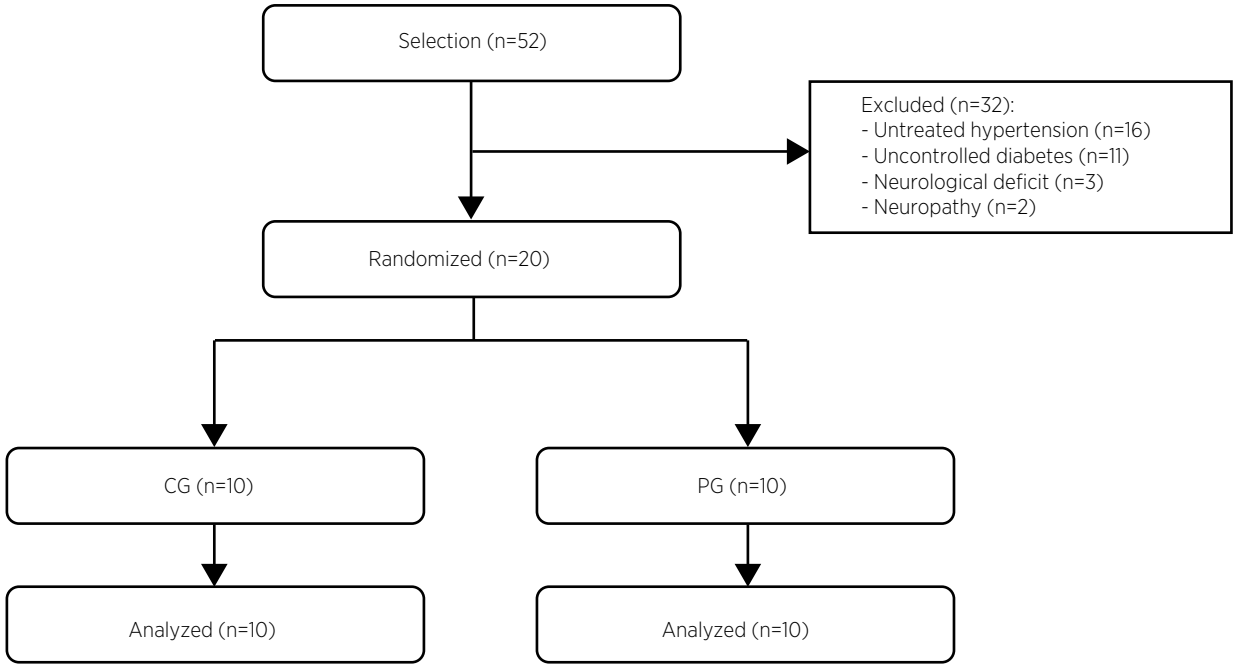

Figure 2. Study flowchart

Table 2. Sample characteristics

	CG	PG
Male	1	2
Female	9	8
Age (years)	65.7 (3.2)	65.1 (1.9)
Weight (kg)	72.8 (9.2)	74.9 (8.5)
Height (m)	1.67 (1.3)	1.66 (0.7)
BMI (kg/m^2)	23.5 (2.3)	24.3 (3.1)
Grade II	4	4
Grade III	6	6

The means for all variables of the SF-36 questionnaire were lower at the pre-treatment moment when compared with the post-treatment. However, no significant difference was found between the groups.

The Lequesne questionnaire showed an improvement in both groups, considering the initial and final evaluations, eight weeks after the beginning of treatment. However, significant difference was found in the evaluation between the groups at the end of treatment, as shown in Table 3.

In the evaluation with the Tinetti questionnaire, we could observe significant improvement in both groups, comparing the data from the beginning with those referring to the end of the treatment. Moreover, we observed a significant difference of the initial data in the comparison between the two groups, showing a heterogeneous sample for this evaluation at the beginning of treatment. However, a significant difference was observed at the end of the treatment in the comparison between the groups, according to Table 3.

In the evaluation of pain with the visual analog scale, observed significant improvement in both groups, when comparing the beginning and end of treatment. However, we also observed a significant difference at the end of treatment in the evaluation between the groups, as shown in Table 3.

Table 3. Data from the Lequesne, VAS and Tinetti questionnaire

		CG	PG	*p*
Lequesne	Beginning	12.65 (4.18)	15.35 (4.19)	0.209
	End	7.25 (3.97)	5.15 (2.11)	0.413
	p	0.002*	0.001*	
Tinetti	Beginning	26.2 (1.75)	21.5 (3.84)	0.001§
	End	23.9 (2.28)	25.4 (2.84)	0.048#
	p	0.047*	0.001*	
VAS	Beginning	4.1 (2.47)	5.3 (1.49)	0.999
	End	2 (1.25)	0.7 (0.82)	0.009#
	p	0.001*	0.001*	

Data expressed in mean and standard deviation.
p = post hoc test of Bonferroni.
* = significant intragroup difference in the comparison between the beginning and end of treatment.
# = significant intergroup difference at the end of treatment.
§ = significant intergroup difference at the beginning of treatment.

DISCUSSION

In our study, after eight weeks of treatment with exercises, we observed improvement in individuals' quality of life, functionality, pain and balance. Moreover, the

effect of adding PBM to the proposed protocol was also compared, showing significant results that lead us to improve the protocol for a future clinical trial, with a larger number of patients.

Strengthening exercises have been described by randomized clinical trials[15-18], correlating the increase in strength with consequent improvement in the clinical picture of individuals with OA, especially regarding pain reduction.

Considering the high risk of falls in this population, proprioceptive exercises are also recommended for individuals with knee OA, as they improve balance and functionality, decreasing the risk of secondary injuries, such as fractures due to falls[19], also being able to show better results regarding measures related to the sense of joint position[20]. Thus, our study corroborates the literature by presenting data that show the improvement of the clinical picture of participants throughout the treatment.

Henriksen et al.[21] conducted a study to evaluate the effect of an exercise program directly on pain assessments, including strengthening and proprioception. For this purpose, they randomly divided 60 individuals into two groups, using the 12-week exercise protocol three times a week in one of the groups, totaling 36 sessions. At the end of the study, they observed a significant improvement in the pain of the individuals in the exercise group, similar to what we observed in our study. However, we obtained positive results in reducing pain in only eight weeks, with a frequency of twice a week, showing that these modalities of therapeutic exercises have a beneficial effect for individuals with knee OA even in the short term.

Another randomized clinical trial conducted by Bennell et al.[22] opted for 12 weeks of treatment, with 100 individuals, divided into two groups: one performing quadriceps strengthening training and the other performing proprioceptive training. The authors found no significant differences between the groups in pain and functionality assessments – the two groups obtained better results only after 12 weeks.

The results found in the literature and in our study show that both strengthening and proprioceptive exercise positively affects the treatment of individuals with knee OA. However, we consider important the fact that both groups were subjected to the exercise protocol, thus enabling comparisons regarding the real benefit of PBM.

In addition to treatment with therapeutic exercises, some studies have reported the benefit of the application of PBM in the joint of patients with knee OA[23-25]. Despite the focus on pain assessments, these studies lacked intervention with exercises of any sort. Hegedűs et al.[23] showed that PBM can change joint temperature, observed from thermographic evaluations, thus improving microcirculation in the irradiated area, besides the effects on pain modulation of individuals with knee OA.

Thus, the application of PBM should aim at reaching the largest possible area of injured tissue – in the case of knee OA, the joint line. We sought, then, to simplify the procedure, reducing the application to only two points in the anterior joint lines of the knee, resembling previous studies, due the the pilot nature of our research[24,25].

Covering these two therapeutic modalities – exercise and PBM – a study conducted by Al Rashoud et al.[26] randomly divided 49 patients into two groups: a group received PBM and another received placebo. Both groups performed straight leg raise exercises (SLR) after the PBM session, similar to those in our study. The authors found significant results in the improvement of pain and functionality when evaluating pain using VAS, corroborating our results.

Alghadir et al.[8] conducted a similar study, with 40 individuals, divided into two groups – placebo and PBM. However, SLR exercises were suggested to be done at home, four times a week. The authors observed a significant difference in pain and functionality at the end of treatment, favoring the PBM group. This result can be observed in our study, inferring that the reduction of pain can improve muscle strength and functionality.

The use of equipment "cluster" can justify our findings. Its use has been increasingly disseminated in scientific research in different situations[27-28] due to its size and the amount of diodes, which allows a shorter application time and offers higher doses of energy, besides allowing the application in larger areas.

Considering the pain data showed in our study, we could observe that PBM has a real positive effect even disregarding the placebo effect, considering that the same exercise protocol was performed in both groups: one group received placebo application and another group active application of PBM. Some studies in the literature show conflicting data on the improvement of pain in patients undergoing placebo PBM, and, in these cases, patients present the same improvement as the group receiving the active application of PBM[29-30]. In our study, with the use of the exercise protocol (the standard treatment in the rehabilitation process of patients with knee OA), the different results found for placebo and active application, evaluated by statistical analysis, can present robust and reliable data, showing that both groups have improved

their pain picture. However, the PG showed more significant gains when compared with the CG (placebo), considering that the sample was homogeneous for this variable at the beginning of treatment.

We used a dose of 30J of total energy per area of cluster, totaling 60J in each knee – compatible with the recommendation of the World Association of Laser Therapy (WALT)[31], which defines a minimum of 12J of energy per point (laser "single") for the treatment of knee osteoarthritis, possibly fitting into the window of opportunity, considering the significant results in the PG regarding pain reduction, when compared with the CG.

Therefore, our study could show the possibility of using both exercises and PBM in the treatment of individuals with knee OA. Moreover, we can affirm that the addition of PBM can reduce pain more significantly than exercises alone.

FINAL CONSIDERATIONS

The use of PBM associated with exercises showed improvement in pain in patients with knee osteoarthritis. This association, in turn, showed no significant differences regarding functionality.

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