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ORIGINAL ARTICLE

Phototherapy with combination of super-pulsed laser and light-emitting diodes is beneficial in improvement of muscular performance (strength and muscular endurance), dyspnea, and fatigue sensation in patients with chronic obstructive pulmonary disease

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Abstract Phototherapy is an electrophysical intervention being considered for the retardation of peripheral muscular fatigue usually observed in chronic obstructive pulmonary disease (COPD). The objective of this study was to evaluate the acute effects of combination of super-pulsed laser and light-emitting diodes phototherapy on isokinetic performance in patients with COPD. Thirteen patients performed muscular endurance tests in an isokinetic dynamometer. The maximum voluntary isometric contraction (MVIC), peak torque (PT), and total work (TW) of the non-dominant lower limb were measured in two visits. The application of phototherapy or placebo (PL) was conducted randomly in six locations of femoral quadriceps muscle by using a cluster of 12 diodes (4 of 905 nm super-pulsed lasers, 0.3125 mW each; 4 of 875 nm LEDs, 17.5 mW each; and 4 of 640 nm LEDs, 15 mW each, manufactured by Multi Radiance Medical™). We found statistically significant increases for PT (174.7±35.7 N·m vs. 155.8±23.3 N·m, $p=0.003$) and TW after application of phototherapy when compared to placebo (778.0±221.1 J vs. 696.3±146.8 J, $p=0.005$). Significant differences were also found for MVIC (104.8±26.0 N·m vs. 87.2±24.0 N·m, $p=0.000$), sensation of dyspnea (1 [0–4] vs. 3 [0–6], $p=0.003$), and fatigue in the lower limbs (2 [0–5] vs. 5 [0.5–9], $p=0.002$) in favor of phototherapy. We conclude that the combination of super-pulsed lasers and LEDs administered to the femoral quadriceps muscle of patients with COPD increased the PT by 20.2 % and the TW by 12 %. Phototherapy with a combination of super-pulsed lasers and LEDs prior to exercise also led to decreased sensation of dyspnea and fatigue in the lower limbs in patients with COPD.

Keywords Chronic obstructive pulmonary disease · Phototherapy · Fatigue

Introduction

Chronic obstructive pulmonary disease (COPD) is a pulmonary pathological disorder that evolves with systemic manifestations including significant adverse effects on peripheral muscle function and changes to the structure and metabolism of the peripheral muscles, leading to decreased muscle strength and endurance [1]. Factors that may be responsible for premature muscle fatigue in this population include the reduction of muscle strength, decrease in aerobic capacity, dependence on glycolytic metabolism, and the fast buildup of lactate during exercise [2]. Therefore, eletrophysical interventions such as phototherapy with lasers, light-emitting diodes (LEDs), or the combination of both are being studied to minimize or delay muscle fatigue.

Several studies have used phototherapy as a non-invasive therapeutic modality to increase muscle vasodilation [3], improve collateral circulation, increase the level of oxygen in the

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tissue, and increase adenosine triphosphate (ATP) in peripheral muscle mitochondria [4–7]. Many studies have used phototherapy in the treatment of muscular disorders such as fatigue in postmenopausal women during endurance training [8] and for neck pain [9, 10]. In addition, the ability of phototherapy to reduce inflammatory processes and decrease oxidative stress is also beneficial in muscular and sports-related injuries [11, 12]. The physiological changes caused by phototherapy therefore have an important role in the prevention and recovery of muscular fatigue.

In a previous study, Miranda et al. [13] were the first to study the effect of phototherapy with LEDs in patients with COPD. The authors found a decrease in the median frequency of electromyographic outcome for evaluation of muscle fatigue after isometric endurance testing and an increase in a muscular endurance time test in ten patients with COPD after application of LED phototherapy in the femoral quadriceps muscle.

As previous studies have shown beneficial effects by using different wavelengths for enhancing muscle performance in animal experiments [7, 14, 15], we hypothesized that a combination of super-pulsed lasers and LEDs could be a promising alternative in preventing muscular fatigue induced by exercise in patients with COPD. Furthermore, this is an innovative, non-invasive, and non-pharmacological therapy. The purpose of this study was to evaluate the acute effects of combined super-pulsed laser and LED phototherapy on the isokinetic performance (strength and muscular endurance) of patients with COPD.

Methods

Thirteen patients were consecutively recruited from the outpatient chronic pulmonary diseases clinic at the Nove de Julho University. All patients had a diagnosis of COPD according to the global initiative for chronic obstructive lung disease (GOLD) criteria [16]. The patients were at a stable phase of the disease indicated by no change in the medical therapy (including oral steroids) or exacerbation of symptoms in the preceding 4 weeks. Patients with other known severe chronic diseases, including cardiac, neuromuscular, or orthopedic disorders, were excluded. The study was approved by the institutional ethics committee (process 632.222), and written informed consent was obtained from all patients.

Randomization and blinding procedures

Randomization was performed by simple drawing of lots, which was used to determine whether the active combination of super-pulsed laser and LEDs phototherapy or placebo would be given at the first session. Participants were crossed over to receive whichever treatment was not given at the first session. Randomization labels were created by using a randomization table at a central office where a series of sealed, opaque, and numbered envelopes were used to ensure confidentiality. A participating researcher who had the function of programming the phototherapy device based on the randomization results conducted randomization. This researcher was instructed not to inform the participants or other researchers regarding the phototherapy dose. Thus, the researcher in charge of the administration of the phototherapy was blinded to the dose applied to the volunteers. Blinding was further maintained by the use of opaque goggles by the participants.

Study design and protocol

A crossover, double-blinded, placebo-controlled, and randomized clinical trial was carried out. The study was conducted in the Laboratory of Phototherapy in Sport and Exercise at the Nove de Julho University, São Paulo, Brazil. Patients were administered either phototherapy or placebo treatments on two visits, 1 week apart. Immediately after the application, the maximum voluntary isometric contraction (MVIC) was determined and the endurance test—total work (TW). A summary of the protocol is presented in Fig. 1.

Procedures

Spirometry

Spirometry (Koko Spirometer, AL, USA) was performed as per the American Thoracic Society/European Respiratory Society criteria [17]; FVC, FEV_1, and FEV_1/FVC are expressed as absolute values and percent of predicted [18].

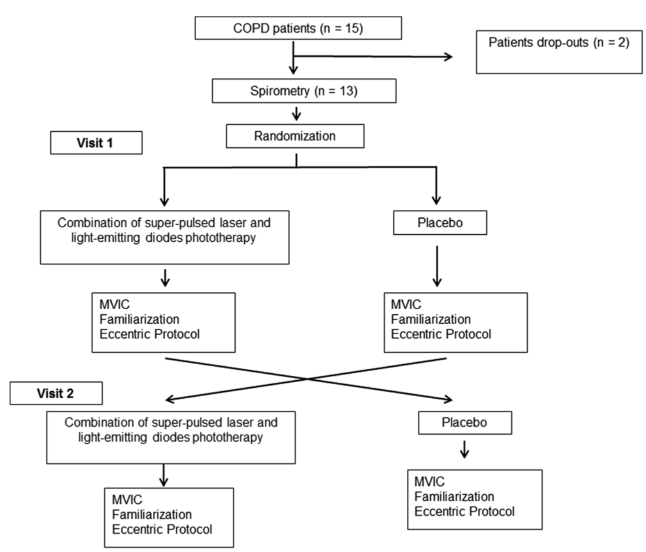

Fig. 1 CONSORT flow chart

Isokinetic protocol

An isokinetic dynamometer (System 4, Biodex®, USA) was used for the evaluation of muscle function and the execution of the exercise protocol. This is currently considered the method with the greatest reliability for the measure of musculoskeletal performance. For the MVIC test, the volunteers sat at an angle of 100° between the trunk and hips with the non-dominant leg positioned with the knee at 60° of flexion (0° corresponds to complete knee extension) and were strapped to the dynamometer seat. The dominant leg was positioned at 100° of hip flexion and was strapped to the seat. The volunteers were fastened to the seat of the dynamometer by using two additional straps crossing the trunk. The volunteers were instructed to cross their arms over their trunk, and the axis of the dynamometer was positioned parallel to the center of the knee.

The MVIC test consisted of three 5-s isometric contractions of the knee extensors of the non-dominant leg. The highest torque value of the three contractions (peak torque [PT]) was used for the statistical analysis. This parameter was chosen because it reflects the maximum generation of force by the muscle. Instructions on how to execute the test were given prior to testing, and the volunteers received verbal encouragement during the execution of the test.

A resting period of 60 s was allowed, followed the MVIC test after which volunteers performed a familiarization isokinetic protocol. The familiarization consisted of five submaximal voluntary repetitions of knee flexion-extension in an eccentric contraction protocol, followed by a resting period of 60 s. The eccentric contraction protocol consisted of 20 eccentric, isokinetic contractions of the knee extensor musculature in the non-dominant leg (two sets of ten repetitions, 30 s rest intervals between sets) at a velocity of 60° seg^{-1} in both the eccentric and concentric movements with a 60° range of motion (between 90° and 30° of knee flexion). At each contraction, the dynamometer automatically (passively) positioned the knee at 30°; the dynamometer then flexed the knee until reaching 90°. The volunteers were instructed to resist against knee flexion movement imposed by the dynamometer with maximum force. Despite the diversity of protocols proposed for the execution of eccentric exercises on isokinetic dynamometers, we used a modified protocol based on a previous study carried out by our research group [19] in which this method proved effective and reproducible for the exercise-induced muscle damage. The researcher in charge of the eccentric contractions protocol was blinded to randomization and allocation of volunteers to experimental groups.

Before and after the endurance test, the perceived effort (dyspnea and leg fatigue) was assessed by using the modified Borg scale [20].

Phototherapy

Patients received a single application of combined super-pulsed laser and LED phototherapy or placebo 1 week apart. The phototherapy combining super-pulsed laser and LEDs or placebo was administered immediately before the testing of lower limb isokinetic dynamometry. A 12-diode cluster of super-pulsed laser and LEDs was used. Each cluster consisted of four diodes of super-pulsed laser (905 nm, 0.3125 mW average power and 12.5 W peak power for each diode), four diodes of infrared LEDs (875 nm, 17.5 mW average power for each diode), and four diodes of red LEDs (640 nm, 15 mW average power for each diode); they were manufactured by Multi Radiance Medical™ (Solon, OH, USA). In view of the extensive area of radiation employed in this project, the use of clusters becomes fundamental to the application of the therapy. The application of phototherapy was held with the cluster in direct contact with the skin, at six sites of the quadriceps femoris (two centrally, rectus femoris and vastus intermedius; two laterally, vastus lateralis; and two medially, vastus medialis). For placebo, the same procedures were performed, but without irradiation. During the application of combined super-pulsed laser and LEDs phototherapy or placebo, the patient wore protective goggles to prevent them from seeing whether or not there was light being radiated.

Since the cluster has 12 diodes that were used to irradiate six different locations of the extensor muscles of the knee (as illustrated in Fig. 2), a total of 72 points in the musculature were irradiated. Phototherapy parameters were chosen based on a previous study performed by our research group [15]. Table 1 provides a full description of the phototherapy parameters.

Statistical analysis

The intention-to-treat analysis was followed. The Kolmogorov–Smirnov test was used to verify the normal distribution of data. Parametric data were expressed as mean and standard deviation. Non-parametric data were expressed as median and interquartile intervals. Differences in the variables of muscle function between combined phototherapy and placebo treatments were compared by using paired, two-sided Student's *t* tests, and the differences of Borg scale were compared by using the Wilcoxon test. The level of statistical significance was set at $p<0.05$.

Fig. 2 Illustration of irradiation areas of phototherapy

Table 1 Phototherapy parameters

Number of lasers	4 super-pulsed infrared
Wavelength (nm)	905
Frequency (Hz)	250
Peak power (W)—each	12.5
Average optical output (mW)—each	0.03125
Power density (mW/cm^2)—each	0.07
Dose (J)—each	0.07125
Spot size of laser (cm^2)—each	0.44
Number of red LEDs	4 red
Wavelength of red LEDs (nm)	640
Frequency (Hz)	2
Average optical output (mW)—each	15
Power density (mW/cm^2)—each	16.66
Dose (J)—each	3.42
Spot size of red LED (cm^2)—each	0.9
Number of infrared LEDs	4 infrared
Wavelength of infrared LEDs (nm)	875
Frequency (Hz)	16
Average optical output (mW)—each	17.5
Power density (mW/cm^2)—each	19.44
Dose (J)—each	3.99
Spot size of LED (cm^2)—each	0.9
Magnetic field (mT)	35
Irradiation time per site (sec)	228
Total dose per site (J)	30
Total dose applied in muscular group (J)	180
Aperture of device (cm^2)	20

Results

Our volunteer population was formed mostly by patients with moderate COPD according to the GOLD [16] criteria (GOLD 2, n=7), with the remaining patients classified as having mild (GOLD 1, n=1), severe (GOLD 3, n=4), and very severe (GOLD 4, n=1) COPD. Table 2 summarizes the characteristics of the patients.

A statistically significant difference was found for the increase of PT after the application of combined super-pulsed laser and LED phototherapy when compared with the placebo (174.7±35.7 N·m vs. 155.8±23.3 N·m, respectively; p=0.003). A similar finding was found for MVIC, with values of 104.8±26.0 N·m vs. 87.2±24.0 N·m for the phototherapy treatment and placebo, respectively (p=0.000). Fig. 3a, b summarizes the outcomes.

A greater value in the TW was observed during endurance testing with the combination of super-pulsed laser and LED phototherapy when compared to the placebo (778.0±221.1 J vs. 696.3±146.8 J, respectively; p=0.005—Fig. 4).

The dyspnea score after the combination of super-pulsed laser and LED phototherapy was lower in comparison with the placebo (1 [0–4] vs. 3 [0–6], p=0.003), and a similar result was seen in the fatigue score for the lower limbs (2 [0–5] vs. 5 [0.5–9], respectively; p=0.002). The findings are summarized in Fig. 5.

Discussion

To the best of our knowledge, this is the first study to analyze the acute effects of the combination of super-pulsed laser and LED phototherapy on isokinetic performance in patients with

Table 2 Volunteers' characteristics

Variables	Mean±SD
Age, years	61±6
BMI, kg/m^2	24.3±4.1
FVC, L (% predicted)	2.5±0.7 (74±15)
FEV_1, L (% predicted)	1.2±0.4 (53±16)
FEV_1/FVC ratio, %	60.3±12.2

BMI body mass index, *FVC* forced vital capacity, *FEV_1* forced expiratory volume in 1 s in liters and in percentage of predicted, *L (% predicted)* in liters and in percentage of predicted

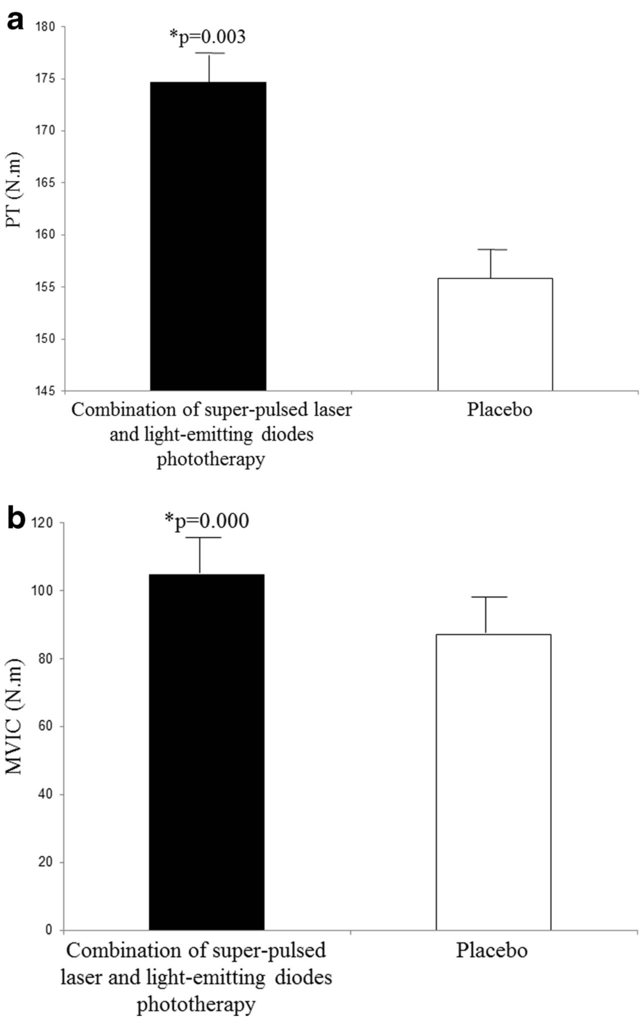

Fig. 3 **a**, **b** Comparison values of isokinetic protocol (PT and MVIC)

COPD. Briefly, we found that combining lasers and LEDs significantly increased the PT, TW, and MVIC, and decreased dyspnea and lower limb fatigue in patients with COPD.

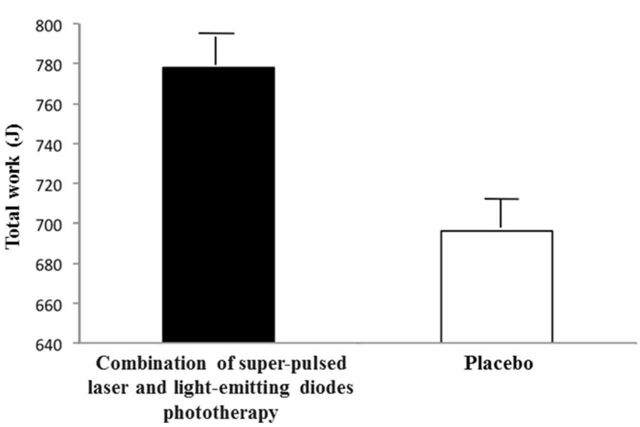

Fig. 4 Total work (TW) with combination of super-pulsed laser and light-emitting diodes phototherapy compared to placebo

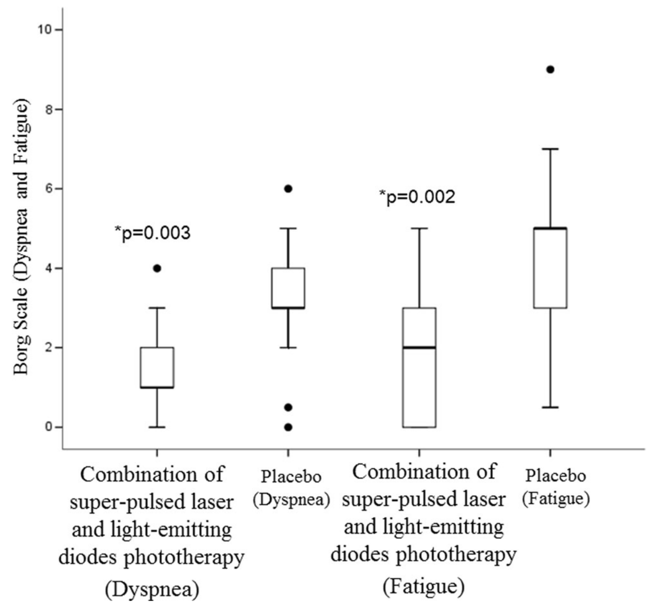

Fig. 5 Comparison of the Borg scale after phototherapy or placebo

The beneficial use of phototherapy with a combination of lasers and LEDs has been described recently in the literature. Antonialli et al. [15] used phototherapy with a combination of lasers and LEDs to test muscle performance and recovery after exercise. The authors found an increased MVIC, decreased biochemical levels of CK, and a decrease in the pain assessment scale, when compared to placebo after an eccentric protocol in an isokinetic dynamometer. In our study, we did not evaluate biochemical markers and muscle pain. However, we found a decreased sensation of dyspnea and fatigue in the lower limbs assessed by using the Borg scale, suggesting that the phototherapy with the combination of lasers and LEDs was able to improve these parameters after isokinetic exercise.

The combination of lasers and LEDs has also been used to investigate the effects of phototherapy on non-specific knee pain. The outcomes evaluated in this study were pain (evaluated by using the visual analog scale) and quality of life (measured by using the quality of life questionnaire SF-36®). Phototherapy significantly decreased pain and improved quality of life when compared with the placebo in patients with knee pain [21]. In our study, the outcomes evaluated were the variables obtained during an isokinetic protocol and assessment of dyspnea and fatigue in the lower limbs by using the Borg scale. We believe that a low score on the Borg scale after application of phototherapy can be a good indicator of improvement in the physical capacity of individuals with COPD.

Miranda et al. [13] were the first to evaluate the acute effect of phototherapy on quadriceps femoris muscle function during isometric exercise in patients with COPD. Phototherapy treatment was found to increase endurance by 18 % and had a smaller decline on the median frequency of electromyographic outcome for the evaluation of muscle fatigue when contrasted with placebo. Corroborating our previous findings, we observed a 20.2 % increase in MVIC after application of phototherapy when compared with placebo.

Similar to our study, Paolillo et al. [22] reported an 8.5 % increase in TW assessed by using an isokinetic dynamometer in 20 postmenopausal women after application of phototherapy when compared with the control group. We found a 12 % increase in TW in our study that may be attributable to differences in the study populations and the isokinetic protocol used by Paolillo et al. [22].

Although the present study is the first to use the combination of lasers and LEDs in patients with COPD, our findings indicated that the magnitude of effect observed was higher than that observed in other studies [13, 15, 21, 22]. We believe the best results were obtained owing to the combination of different wavelengths (905, 875, and 640 nm) and different sources of light (super-pulsed-laser and LEDs) used in our study.

In animal studies, Albuquerque-Pontes et al. [7] radiated the tibialis anterior muscle of rats with different wavelengths (660, 830, and 905 nm). The authors found a significant increase of cytochrome c oxidase. This finding contributes to the understanding of how phototherapy can increase muscular performance and protect against the development of skeletal muscle fatigue and damage tissue [7].

The use of different wavelengths (660, 830, and 905 nm) was investigated by Santos et al. [14] to evaluate the effects of phototherapy immediately before tetanic contractions in the development of skeletal muscle fatigue and possible tissue damage in rats. The study showed that optimal doses of phototherapy could slow the development of muscle fatigue and protect against muscle tissue damage. The optimal doses were, in part, dependent on specific wavelengths, and therefore must be differentiated to obtain the optimal effects for tissue preservation and muscular fatigue.

The simultaneous use of different wavelengths may increase the effects of phototherapy on skeletal muscle performance and may represent a therapeutic advantage in clinical situations, which was observed in the present study and in previous studies [15, 21]. One of the possible explanations for the increase in isokinetic variables after applying the combination of lasers and LEDs is increased microcirculation around the irradiated area. According to some authors [23–26], increased local blood flow is able to reduce the buildup of blood lactate and increase the supply of oxygen to muscle tissues, thereby reducing muscle fatigue.

Based on these findings and previous studies, phototherapy with the combination of laser super-pulsed and LEDs can be considered as a new and non-invasive treatment to reduce fatigue and increase muscle strength in patients with COPD.

Conclusion

In this study, we demonstrate that a combination of super-pulsed laser and LED phototherapy on the femoral quadriceps muscle in patients with COPD was able to increase PT by 20.2 % and TW by 12 %. Furthermore, combined phototherapy prior to exercise still led to a decreased sensation of dyspnea and lower limb fatigue in patients with COPD.

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Conflict of interest Professor Ernesto Cesar Pinto Leal-Junior receives a research support from Multi Radiance Medical (Solon, OH, USA), a laser device manufacturer. The remaining authors declare that they have no conflict of interest.

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