ResearchGate

See discussions, stats, and author profiles for this publication at: https://www.researchgate.net/publication/282134637

Can Low level laser therapy (LLLT) associated with an aerobic plus resistance training change the cardiometabolic risk in obese women? A placebo-controlled clinical trial

Article *in* Journal of photochemistry and photobiology. B, Biology · September 2015

DOI: 10.1016/j.jphotobiol.2015.08.026

CITATIONS
7

READS
346

10 authors, including:



Fernanda O Duarte
University of São Paulo
30 PUBLICATIONS **223** CITATIONS
SEE PROFILE



Marcela Sene-Fiorese
University of São Paulo
37 PUBLICATIONS **182** CITATIONS
SEE PROFILE



Antonio Eduardo De Aquino Junior
University of São Paulo
26 PUBLICATIONS **87** CITATIONS
SEE PROFILE



Raquel M S Campos
Universidade Federal de São Paulo
62 PUBLICATIONS **691** CITATIONS
SEE PROFILE

Some of the authors of this publication are also working on these related projects:

Sodium BEC @USP View project

Regenerative Medicine and Tissue Engineering for Musculoskeletal and Tegumentar Tissues View project

All content following this page was uploaded by Fernanda O Duarte on 27 June 2018.

The user has requested enhancement of the downloaded file.

Journal of Photochemistry & Photobiology, B: Biology 153 (2015) 103–110

Contents lists available at ScienceDirect

Journal of Photochemistry & Photobiology, B: Biology

journal homepage: www.elsevier.com/locate/jpb

Can low-level laser therapy (LLLT) associated with an aerobic plus resistance training change the cardiometabolic risk in obese women? A placebo-controlled clinical trial

Fernanda Oliveira Duarte [a,*], Marcela Sene-Fiorese [b], Antonio Eduardo de Aquino Junior [a,c], Raquel Munhoz da Silveira Campos [d], Deborah Cristina Landi Masquio [d], Lian Tock [e], Ana Claudia Garcia de Oliveira Duarte [f], Ana Raimunda Dâmaso [d], Vanderlei Salvador Bagnato [b,c], Nivaldo Antonio Parizotto [a,c]

[a] Therapeutic Resources Laboratory, Department of Physiotherapy, Federal University of São Carlos (UFSCar), Rodovia Washington Luis, Km 235, 13565-905 São Carlos, São Paulo, Brazil
[b] São Carlos Institute of Physics, University of São Paulo (USP), Avenida Trabalhador Sãocarlense, 400, PO Box 369, 13560-970 São Carlos, São Paulo, Brazil
[c] Post-Graduated Program of Biotechnology, Federal University of São Carlos (UFSCar), Rodovia Washington Luis, Km 235, 13565-905 São Carlos, São Paulo, Brazil
[d] Post-Graduated Program of Nutrition, Federal University of São Paulo (UNIFESP), Rua Marselhesa, 650, 04021-001 São Paulo, São Paulo, Brazil
[e] Weight Science, rua Teodoro Sampaio, 744, Cj. 98, 05406-000 São Paulo, São Paulo, Brazil
[f] Nutrition and Metabolism Applied to Exercise Laboratory, Department of Physical Education, Federal University of São Carlos (UFSCar), Rodovia Washington Luis, Km 235, 13565-905 São Carlos, São Paulo, Brazil

ARTICLE INFO

Article history:
Received 12 May 2015
Received in revised form 28 August 2015
Accepted 31 August 2015
Available online 2 September 2015

Keywords:
Obesity
Low-level laser therapy (LLLT)
Aerobic exercise
Resistance exercise
Inflammation
Cardiometabolic risk

ABSTRACT

Introduction: Obesity is one of the most important link factors to coronary artery disease development mainly due to the pro-inflammatory and pro-thrombotic states favoring atherosclerosis progression. The LLLT acts in the cellular metabolism and it is highly effective to improve inflammation. The same occur in response to different kinds of exercise. However, we have not known the associate effects using LLLT therapies with aerobic plus resistance training as strategy specifically with target at human obesity control and its comorbidities.
Objective: Investigate the effects of the LLLT associated with aerobic plus resistance training on cardiometabolic risk factors in obese women.
Methodology: Women aged 20–40 years (BMI ≥ 30 kg/m^2), were divided into 2 groups: Phototherapy (PHOTO) and Placebo. They were trained aerobic plus resistance exercises (in a concurrent mode), 1 h, 3 times/week during 16 weeks. Phototherapy was applied after each exercise session for 16 min, with infrared laser, wavelength 808 nm, continuous output, power 100 mW, and energy delivery 50 J. The body composition was measured with bioimpedance. Inflammatory mark concentrations were measured using a commercially available multiplex.
Results: LLLT associated with aerobic plus resistance training was effective in decrease neck ($P = 0.0003$) and waist circumferences ($P = 0.02$); percentual of fat ($P = 0.04$); visceral fat area ($P = 0.02$); HOMA-IR ($P = 0.0009$); Leptin ($P = 0.03$) and ICAM ($P = 0.03$). Also, the reduction in leptin ($P = 0.008$) and ICAM-1 (0, 05) was much more expressive in the phototherapy group in comparison to placebo group when analyzed by delta values.
Conclusion: LLLT associated with concurrent exercise (aerobic plus resistance training) potentiates the exercise effects of decreasing the cardiometabolic risk factors in obese woman. These results suggest the LLLT associated with exercises as a new therapeutic tool in the control of obesity and its comorbidities for obese people, targeting to optimize the strategies to control the cardiometabolic risk factors in these populations.
© 2015 Elsevier B.V. All rights reserved.

1. Introduction

Obesity is a complex disease and its pathogenesis is multifactorial, resulting mainly from sedentary behaviors coupled with inadequate eating habits [1,2]. It is strongly associated with subclinical inflammation, metabolic syndrome, type 2 diabetes and an elevated risk of cardiovascular diseases [3]. Some cytokines with higher concentrations in obesity promote the development of cardiovascular disease, mainly pro-inflammatory proteins such as leptin, plasminogen activator inhibitor (PAI-1), interleukin-6 (IL-6), tumor necrosis factors alpha (TNF-α), intracellular adhesion molecule 1 (ICAM-1) and vascular cell adhesion molecule 1 (VCAM-1), among others [4,5].

* Corresponding author at: Therapeutic Resourses Laboratory, Department of Physiotherapy, Federal University of São Carlos (UFSCar), Rodovia Washington Luis, Km 235, 13565-905 São Carlos, São Paulo, Brazil. Tel.: +55 16 3351 8985.
E-mail address: fefa.duarte74@gmail.com (F.O. Duarte).

http://dx.doi.org/10.1016/j.jphotobiol.2015.08.026
1011-1344/© 2015 Elsevier B.V. All rights reserved.

In this context, the obesity, mainly the visceral fat, is directly associated with major risk for cardiovascular and metabolic diseases and is a feature of systemic inflammation [6]. The hyperleptinemia and hyperinsulinemia configure the profile of most obese individuals and appear to be the key factors of the metabolic abnormalities, providing inadequate response to weight loss therapy [7]. Furthermore, the PAI-1 increase in plasma of the obese individuals leads to a hyperthrombotic state by hypofibrinolysis, hypercoagulability and platelets activation that leads to the development of atherosclerotic plaques formation, main predictor for myocardial infarction [8,9].

Data supports that the interdisciplinary intervention model associated to aerobic plus resistance training was more effective in improving the visceral adiposity, inflammatory markers and metabolic profile in obese adolescents [10,11]. In addition, Jackson and colleagues [12] find changes in the body composition as in circumferential measurements across waist, hips, and thighs compared to placebo subjects after LLLT treatment, with a total of six treatments across 2-weeks. The authors suggest that change in the adipose tissue occurs due to adaptations in the membrane permeability of adipocytes, releasing fatty acids in blood circulation, but their removal and metabolism mechanisms still remain unclear [12].

Actually the advance in studies involved low-level laser therapy (LLLT) or light-emitting diode (LED) therapy has allowed a better understanding of their mechanisms in the biologic tissues. Therefore, the use of light in different applications like LLLT as ancillary non-invasive treatment has been disseminated in recent years, mainly in controlling pain, inflammation, mucositis, tissue repairs besides the muscle performance and also in the aesthetic treatments [13–16].

Although, recently a pioneer study of our research group demonstrated that phototherapy when associated with swimming training was efficient to potentiate the weight loss, as well as ameliorate the lipid profile in exogenous obese rats [17]. Nonetheless, we did not find studies using the association between LLLT therapies with aerobic plus resistance training as strategy specifically with target at human obesity control and its comorbidities.

This way, we hypothesized that the LLLT associated with aerobic plus resistance training may promote a reduction in pro-inflammatory and prothrombotic markers, contributing to reduce cardiometabolic risk factors in obese women in a placebo-controlled clinical trial.

2. Material and Methods

The details about experimental design are shown in Fig. 1.

2.1. Subjects

For this study, a total of 64 adult obese women, with the age of 20–40 years were involved in this randomized double blind controlled clinical trial. The volunteers were recruited by impress and electronic media, TV and radio. The inclusion criteria were: 1) primary obesity, body mass index (BMI) between 30 and 40 kg/m^2 and 2) age between 20 and 40 years old. Exclusion criteria were: 1) the use of cortisone, anti-epileptic drugs; 2) history of renal disease; 3) alcohol intake; 4) smoking and 5) secondary obesity due to endocrine disorders.

The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the ethics committee on human research at Universidade Federal de São Carlos — UFSCar (#237.050) and registered at Clinical Trial: 231.286. All procedures were made clear to the volunteers and consent for research was agreed. The evaluations were performed at different times: in the beginning and the end of therapy; and in the middle (4 months) of interdisciplinary intervention. The main reasons for dropping out (n = 12) in our study were pregnancy, family problems and job opportunities.

The volunteers were randomly assigned between two groups through the sample randomization program (www.randomization.com): placebo group and phototherapy group (PHOTO). The treatment consisted in physical exercise intervention – moderate aerobic plus resistance training – and the individually application of phototherapy immediately after the end of the training. The same interventions of phototherapy group were applied for placebo group voluntaries however, during the application of phototherapy the placebo group did not received the incidence of laser light, characterizing the study as a placebo-controlled clinical trial. This one is the blind analyzer and the other is the person that analyzed the data, without the knowledge of the treated group. The voluntaries do not know which group they belonged. During the experimental

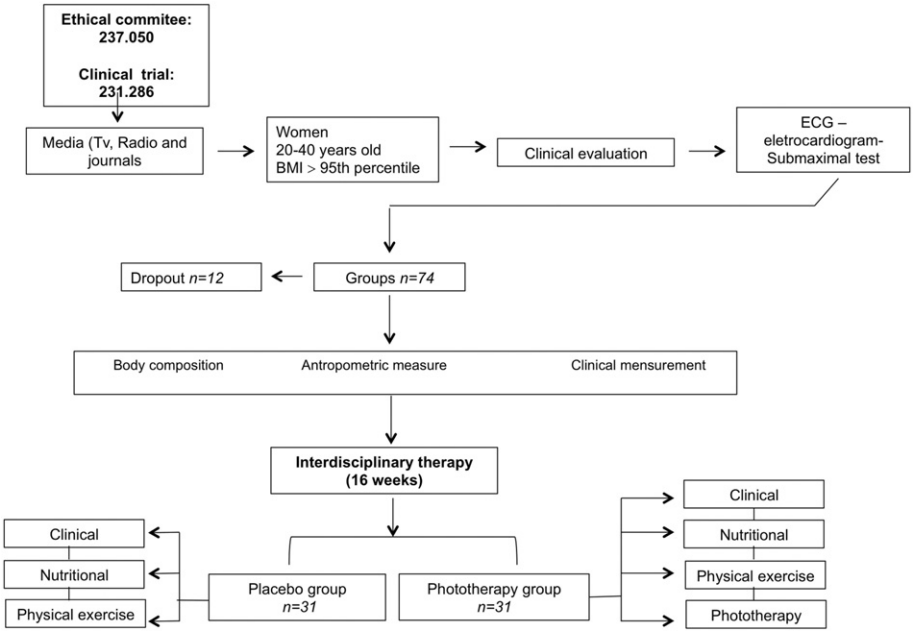


Fig. 1. Methodological description.

protocol, all volunteers received nutritional counseling. The only one that differs among groups was the presence of the light.

2.2. Anthropometric and Body Composition Measurements

Volunteers were measured for weight and height using light clothes and no shoes using an electronic scale. The parameters used in this study were: body mass (kg); total body fat (kg and %) and visceral body fat (cm^2). We used the bioelectrical impedance analysis (BIA) devices to measure the change in impedance in body tissues by sending detectable electrical signals through the body. The BIA device used in this study was the InBody® 720 (Biospace Co. Ltd.; Seol, Korea), which uses 6 frequencies (1, 5, 50, 250, 500, and 1000 kHz). The body mass index (BMI) was calculated as body mass (kg) dividing stature $(m)^2$.

Neck circumference (NC) was measured at the base of the neck, below the cricothyroid cartilage with the volunteer's head positioned in the Frankfurt horizontal plane, keeping in inspiratory apnea with an inelastic tape. Values above 34 cm for women and 37 cm for men indicate an increased risk for the occurrence of cardiovascular risk [18].

Waist circumference (WC) was determined at the end of normal expiration at the midpoint between the iliac crest and the last rib using a flexible and inelastic tape without compressing the skin. Values above 80 cm for women and above 94 cm for men indicate a risk for cardiovascular disease [19].

Hip circumference (HC) was measured at the most salient point between the waist and the thigh, using an inelastic tape. The waist–hip ratio was calculated [19].

2.3. Serum Analysis

Blood samples were collected after 12 h of overnight fast at approximately 8:00 am in the outpatient clinic.

Insulin sensitivity was assessed using the homeostasis model assessment IR (insulin resistance) index (HOMA-IR). HOMA-IR was calculated using the following formula:

$$\text{HOMA-IR}\left[\text{fasting blood glucose}\left(\frac{\text{mg}}{\text{dL}}\right)\times\text{fasting insulin}\left(\frac{\mu\text{U}}{\text{mL}}\right)\div 405\right].$$

The cut-off value determined for Brazilian population is HOMA-IR ≤ 2.71 for classified the subjects with IR [20].

The leptin, PAI-1, VCAM and ICAM-1 concentrations were measured using a commercially available multiplex assay (EMD Millipore; HMHMAG-34 K). Manufacture-supplied controls were included to measure assay variation and all samples were analyzed on the same day to minimize day-to-day variation. A minimum of 100 beads were collected for each analyzed using a Luminex MagPix System (Austin, Texas), which was calibrated and verified prior to sample analysis. Unknown sample values were calculated offline using Milliplex Analyst Software (EMD Millipore) [21].

2.4. Therapy

Three times during the intervention period (4 months) at Unidade de Saúde Escola (USE)/Universidade Federal de São Carlos — UFSCar, all voluntaries were monitored and evaluated by clinical tests. These evaluations were done by the team of health professionals including endocrinologist, nutritionist and physical educator. The medical follow-up included the initial medical history and a physical examination of blood pressure, cardiac frequency and body composition were checked (Fig. 1).

2.5. Physical Exercise Intervention — Moderate Aerobic Plus Resistance Training (M-Rt)

During the 4 months period, the voluntaries followed a combined exercise training therapy. The protocol was performed three times per week and included 30 min of aerobic training and 30 min of resistance training per session. The aerobic training consisted of running on a motor-driven treadmill (Movement®) between 70–85% of a maximal cardiac frequency (FC) intensity, which was previously determined by treadmill submaximal test. The physical exercise intervention was based on the guidelines from the American College of Sports Medicine (ACSM) [22]. Resistance training was also designed based on ACSM recommendations [23] (Fig. 1).

2.6. Phototherapy Intervention

The device prototype used was composed of 4 plates with 16 infrared laser emitters. The characteristics of phototherapy equipment are described below (Table 1).

The phototherapy equipment (Table 1 and Fig. 2) was developed by the Laboratory Technology Support-LAT, Center for Research in Optics and Photonics Institute of Physics in São Carlos city at Universidade de São Paulo — USP. For phototherapy intervention, the plates were placed in abdominal, gluteal and lower limbs in the quadriceps and biceps femoral region. The positioning of the plates in each region is demonstrated in Fig. 2. The emitters are disposed perpendicularly (90°) to the skin. The total application time was 16 min (8 min per side) and the application was performed after each exercise session, in accordance with the previous study of our research group [24,25] (Fig. 2).

2.7. Statistical Analysis

Statistical analysis was performed using the program STATISTICA version 7.0 for Windows (StatSoft Inc., Tulsa, OK, USA). The significance level

Table 1
Device information, irradiation and treatment parameters.

Type	Ga-Al-As semiconductor diode laser
Wavelength	808 nm
Operating mode	Continuous wave
Number of Emitters	16 (per plate)
Number of Plate	4
Number of electronic control box	2
	Per emitter
Spot diameter (elliptical shape)	Horizontal 0.3692/vertical 0.0582 cm
Spot area	0.0169 cm^2
Output power	100 mW
Irradiance	6.0 W/cm^2
Radiant energy	96 J
	Characteristic of the application
Application technique	Plates over the following perpendicularly to the skin in the regions: anterior region: abdominal and quadriceps simultaneously during 8 min. Change the position to irradiate the posterior region: gluteus and biceps femoral during 8 min totalizing 16 min
Number of points irradiated	64 (per position)/128 (total)
Total radiant energy delivered	Per session (16 min): 6,144 J/all sessions (48): 294,912 J
Number and frequency of treatment sessions	Three times per week after physical exercise, totalizing 48 sessions of treatment



Fig. 2. Illustrative places of phototherapy application. Volunteer receiving phototherapy after physical exercise — A. In ventral decubitus — 8 min of phototherapy application per session; B. In dorsal decubitus — 8 min of phototherapy application per session; C. Prototype phototherapy equipment.

was set up at $p < 0.05$. The Kolmogorov–Smirnov test was applied to assess the assumption of normality for the data. Parametric data were expressed as mean ± standard deviation (SD). To analyze the effects intervention and difference between the groups, a two-way ANOVA was applied followed by Tukey post hoc test. Comparing the delta values was performed by t test independent by groups.

Table 2
Effect of LLLT associated aerobic plus resistance training on body composition and anthropometric measurements.

Placebo group				Phototherapy group		
Variables	Baseline	End	Δ value (%)	Baseline	End	Δ value (%)Δ
Age	33.954 ± 4.805	__ ± __	__ ± __	32.20 ± 4.969	__ ± __	__ ± __
Height (m)	1.63 ± 0.04	__ ± __	__ ± __	1.65 ± 0.06	__ ± __	__ ± __
Body mass (Kg)	97.212 ± 13.002*	94.487 ± 12.795 P = 0.0000001**	−4.743 ± 2.180	94.487 ± 12.79	89.293 ± 12.834 P = 0.000001**	−5.546 ± 2.051 P = 0.3916
Body mass index (Kg/m^2)	36.083 ± 4.137	33.886 ± 4.278 P = 0.0000001**	−6.181 ± 2.722	34.396 ± 4.036	32.629 ± 3.921 P = 0.000001**	−5.480 ± 2.589 P = 0.4520
Waist circumference (cm)	113.225 ± 13.825	110.562 ± 13.02 P = 0.000006**	−2.309 ± 1.139	107.687 ± 10.024	103.812 ± 9.07 P = 0.00001**	−3.554 ± 0.708 P = 0.02***
Neck circumference (cm)	36.983 ± 2.109	36.583 ± 1.942 P = 0.0361**	−1.044 ± 1.939	38.093 ± 2.265	36.266 ± 1.869 P = 0.00009**	−4.711 ± 3.202 P = 0.00031***
Fat mass %	40.886 ± 3.159	39.113 ± 3.0507 P = 0.0000001**	−4.332 ± 1.504	40.950 ± 2.467	38.833 ± 2.4473 P = 0.000007**	−5.608 ± 1.599 P = 0.048***
Visceral fat (cm^2)	160.891 ± 21.449	154.400 ± 22.228 P = 0.00004**	−4.425 ± 2.824	150.480 ± 19.938	140.710 ± 19.982 P = 0.0000001**	−7.094 ± 2.001 P = 0.0209***
Hip (cm)	119.8 ± 6.2	118.2 ± 5.6	1.28 ± 1.9	118.2 ± 7.7	112.8 ± 7.7	4.56 ± 3.3 P = 0.0073***

Values expressed by mean ± SD. References values: body mass index: ≤24.9 Kg/m^2; waist circumference: ≤80 cm for women and ≤94 cm for men; neck circumference: ≤34 for women and ≤37 for men; fat mass%: 18 to 28% for females; visceral fat: ≤100 cm^2. Kg: kilogram, m^2: square meter, %: percentage, cm: centimeter, cm^2: square centimeter.

* Statistical difference between baseline values.

** Statistical difference between baseline vs after therapy values.

*** Statistical difference between delta values.

The delta values were obtained from the formula: $\Delta = \frac{\text{final value} - \text{initial value}}{\text{initial value}} \times 100$.

3. Results

3.1. Effects of Phototherapy Associated With Aerobic Plus Resistance Training on Anthropometric Measures and Body Composition

In initial treatment, there are no differences between the group placebo and phototherapy for all anthropometric and body composition parameters — body weight (Kg), height (cm), BMI (Kg/m2), hip, waist and neck circumferences (cm), percentage of total fat mass (%), visceral fat (cm^2), and waist–hip ratio.

At the end of treatment in relation to initial treatment, placebo and phototherapy groups had decrease in body mass, BMI, waist and neck circumferences, percentage of total fat mass, visceral fat, hip and waist–hip ratio. Furthermore, those decreases were greater in the phototherapy group than in the placebo group with exception for body mass and BMI that had no differences between groups (Table 2).

3.2. Effects of Phototherapy Intervention Associated With Aerobic Plus Resistance Training on Metabolic Profile

In initial of treatment, there are no differences between the group placebo and phototherapy for glucose (mg/dl), insulin (uU/ml), HOMA-IR and platelets plasma concentration (K/uL). After interdisciplinary intervention, an improvement was observed on the metabolic profile with reduction in the insulin, HOMA-IR and platelets in plasma concentration in both groups. Interestingly, once again the phototherapy intervention potentiated the effects on those parameters when compared to placebo group. Glucose concentration didn't change with treatment (Table 3).

3.3. Effects of Phototherapy Intervention Associated With Aerobic Plus Resistance Training on Inflammatory Markers

In this study, it didn't have any differences in PAI-1 (ng/ml), leptin (ng/ml), SCAM-1 (pg/ml) and ICAM-1 (pg/ml) concentrations in initial of treatment in both groups. Significant reduction in the PAI-1, leptin and ICAM-1 was shown only in the phototherapy group. The reduction in leptin, PAI-1 and ICAM-1 was much more expressive in the phototherapy group in comparison with the placebo group when analyzed by delta values (Table 4, Fig. 3). The VCAM-1 delta showed no statistical difference between the groups.

4. Discussion

The aim of the present investigation is to analyze the possible mechanism linking the effects of the LLLT associated with aerobic plus resistance training on cardiometabolic risk in obese women. Therefore, the most important finding in this clinical approach was to know that the LLLT associated with physical exercise was effective in reducing some cardiometabolic risk factors in the analyzed population, including a reduction on hyperleptinemia state, PAI-1, HOMA-IR, ICAM and visceral adiposity. LLLT is highly effective to relieve pain, inflammation and edema as well as to prevent death tissue and stimulate tissue regeneration, treating different pathologies even in cellulite treatment [26–28]. But we do not found in the literature clinical studies that could relate to phototherapy with aerobic plus resistance training specifically targeting the treatment of obesity and obesity-correlated disease.

Interdisciplinary intervention (nutrition, psychology, physical exercise and clinical therapy) has been used with success for obesity treatment, without the use of the agent pharmacological or surgery [10,11]. In fact, in our study, the application of lifestyle intervention was effective in reducing all parameters of body composition, metabolic profile and inflammatory marks in obese women confirming to be necessary in the union of different professionals working together to treat obesity.

However, interestingly, the highlight findings of our study demonstrated that when we associated the phototherapy with aerobic plus resistance training intervention in obese women, all the beneficial effects promoted by lifestyle intervention were potentiated, mainly the improvement in inflammatory markers, platelets and HOMA, and besides it promote greater reduction in the visceral fat and in the percentage of body fat.

We know that the adipose tissue produces and releases different hormones, peptides, and cytokines. Thus, this tissue participates in food intake regulation, in the metabolism of glucose and lipid, inflammation, coagulation, and blood pressure control, may affect cardiovascular function through the mechanism endocrine, paracrine and autocrine [29]. The increase in size of adipocytes leads to a dysfunction of adipose tissue that pass to release increased amounts of free fat acids (FFAs) that inhibit insulin's antilipolytic action and exert pro-atherogenic effects, contributing to the development of atherosclerosis. Besides that, these excess of released FFAs establish a paracrine continuous cycle that leads to the development of chronic low-grade inflammatory state of the adipose tissue due to the increase in the TNF-α production and secretion by adipose tissue and macrophages [30,31]. Indeed, enlarged adipose tissue also increases vascular endothelial cell damage with increase in VCAM-1 and ICAM-1 by endothelium, contributing for release in pro-inflammatory cytokines [5]. So, obesity is accompanied by many adverse health effects for instance hypertension, insulin resistance, diabetes, dyslipidemia and subclinical inflammation, all factors leading to atherosclerosis [3,32].

In accordance with recent studies, the phototherapy promotes photobiomodulation characterized by a change in physiological processes inside the tissues triggered by specific wavelengths of light. Some body systems like circulatory, musculoskeletal and adipose tissue

Table 3
Effect of LLLT associated aerobic plus resistance training on metabolic profile.

	Placebo group			Phototherapy group		
Variables	Initial	End	Δ value (%)	Initial	End	Δ value (%)
Glucose (mg/dl)	91.000 ± 5.621	91.750 ± 6.255 P = 0.573	0.943 ± 5.633	93.866 ± 7.586	93.133 ± 7.954 P = 0.476	−0.725 ± 4.099 P = 0.355
Insulin (μU/ml)	18.212 ± 7.148*	14.156 ± 4.737 P = 0.002**	−19.915 ± 13.718	20.192 ± 13.651	12.476 ± 7.644 P = 0.0008**	−36.151 ± 9.277 P = 0.0011***
HOMA-IR	4.219 ± 1.797	3.273 ± 1.419 P = 0.002**	−20.913 ± 14.421	4.683 ± 2.887	2.836 ± 1.701 P = 0.0002**	−38.080 ± 9.230 P = 0.00094***

Values expressed by mean ± SD. References values: baseline glycaemia: 70 to 100 mg/dl; baseline insulin: ≤29.1 uU/ml; HOMA-IR ≤ 2.71. mg/dl: milligram/deciliter, μU/ml: microunits/milliliter.

* Statistical difference between baseline values.

** Statistical difference between baseline vs after therapy values.

*** Statistical difference between delta values.

Table 4
Effect of LLLT associated aerobic plus resistance training on inflammatory marks.

	Placebo group			Phototherapy group		
Variable	Initial	End	Δ value (%)	Initial	End	Δ value (%)
PAI-1 (ng/ml)	16.77 ± 6.51*	15.24 ± 13.23	−2.148 ± 18.21	24.24 ± 13.24	20.28 ± 10.77 P = 0.05**	−14.79 ± 6.48
sICAM-1 (pg/ml)	243.57 ± 47.65	243.28 ± 47.88	−1.7209 ± 8.929	230.0 ± 57.11	206.2 ± 75.57 P = 0.03**	−11.911 ± 12.862 P = 0.05***
sVCAM-1 (pg/ml)	347.42 ± 103.54	336.0 ± 89.99	2.270 ± 17.513	344.40 ± 38.42	319.0 ± 76.84	−4.040 ± 16.125
Leptina (ng/ml)	36.949 ± 12.058	35.650 ± 15.657	−4.493 ± 17.905	27.682 ± 8.370	19.767 ± 7.786 P = 0.0039**	−28.958 ± 14.722 P = 0.008***
Platelet (K/uL)	292.78 ± 52.99	287.0 ± 50,08 P = 0.01**	−1.89 ± 1.66	270.0 ± 22.24	249.80 ± 23.77 P = 0.05**	−7.53 ± 2.89 P = 0.00008***

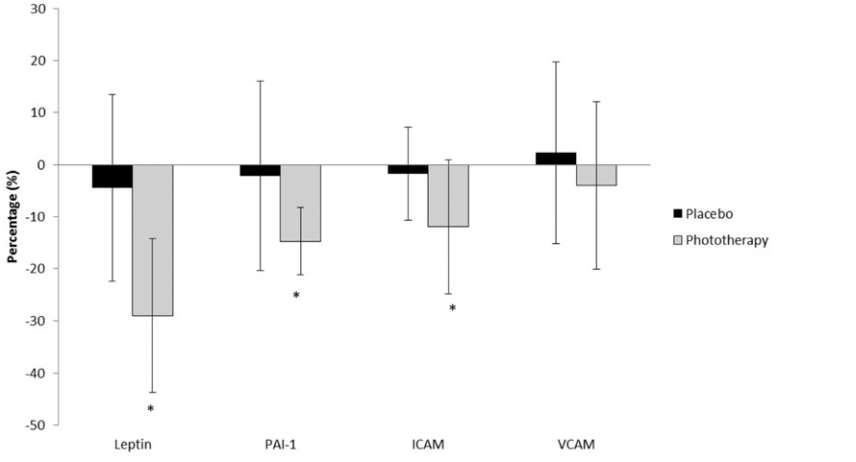
Values expressed by mean ± SD. Leptin values: between 4.9 and 24 ng/ml for females. PAI-1: plasminogen activator inhibitor, ICAM-1: intracellular adhesion molecule 1, VCAM-1: vascular cell adhesion molecule 1, pg/ml: picogram/milliliter and ng/ml: nanogram/milliliter, K/uL:thousands/microliter.
* Statistical difference between baseline values.
** Statistical difference between baseline vs after therapy values.
*** Statistical difference between delta values.

have chromophores (light-absorbing molecules) that are capable of absorbing photons, for example hemoglobin, myoglobin, cell membranes and mitochondria [27,33]. In fact, we observed in the current study that the LLLT treatment associated with aerobic plus resistance training promoted improvement in cardiometabolic risk factors in obese women, first due to the decrease of visceral fat then for the decrease of inflammatory markers. It is well established in the literature that chromophores, present in the respiratory chain of the cellular mitochondria, including in adipocytes, absorb red and near-infrared photons, increase of membrane potential, oxygen consumption and ATP (adenosine triphosphate), a transient rise in ROS (reactive oxygen species), and release of NO (nitric oxide) leading to an up regulation's cAMP (cyclic protein adenosine monophosphate). The cAMP increased, in turn activates PKA (protein kinase) and phosphorylates HSL (hormone sensitive lipase) that cause degradation of TG (triacylglycerol) and diglycerides to monoglycerides that are further degraded to fatty acid (FA) and glycerol [27,34–36]. It also occurs an increase in the catecholamine that binds to adrenergic β3 receptors presents in the adipocytes membranes, triggering a cascade reaction to the degradation of TG into FFA and glycerol ensuring the supply of lipids as an energy source during physical exercise [37].

In this context, other researchers examined benefits of LLLT associated with physical resistance exercise in lean humans. The authors demonstrating that phototherapy reduces lactate levels in the circulation due to increased local microcirculation and consequently increased in oxygen supply. As a consequence, there is an improvement in muscle fatigue, faster recovery of muscle damage and improved performance, both in humans and animals [34–36,38]. In this context, our research group demonstrated in exogenous obese rats that the association of low-level laser therapy (LLLT) plus moderate swimming training promoted decrease in adipocyte area and increase in the energetic demand and in the mitochondrial oxidative capacity besides greater workload (data not published).

Thus, we can suggest that aerobic plus resistance training associated with LLLT had synergistic effects for degradation on TG in adipocytes, what may explain the great decrease in percentage of fat, mainly in the visceral fat in our study. These results show us an important finding. The LLLT associated with aerobic plus resistance training promotes biomodulation even in the deep fat, in this case represents for visceral fat, which can diminish the risk to development of cardiovascular disease in obese women.

In fact, the visceral fat predisposes to atherosclerosis development since it is a prevalent source of inflammatory cytokine secretion and a possible reservoir for pro-inflammatory molecules [5]. In these sense, leptin (an adipose tissue-derived hormone) levels rise with obesity and correlate strongly with percent body fat. Central obesity (mainly



Values expressed by mean ± SD
* Statistical difference between delta values
PAI-1: plasminogen activator inhibitor, ICAM-1: intracellular adhesion molecule 1, VCAM-1: vascular cell adhesion molecule 1

Fig. 3. Effects of LLLT on inflammatory marks. Differences between delta.

the visceral fat), as well as waist and more recently neck circumferences, all of them are associated to high risk of insulin resistance and metabolic complications [42–46].

Besides that, both hyperleptinemia and insulin resistance are considered risk factors for cardiometabolic disease. Due to the leptin role in regulating blood pressure and activating the sympathetic nervous system, insulin resistance, platelet aggregation, arterial thrombosis, angiogenesis, and inflammatory vascular responses, the leptin has a close relationship with the development of coronary heart disease, when in hyperleptinemia state, as our volunteers at the beginning of treatment [39,47]. Thereby, in this current study, the LLLT associated with aerobic plus resistance training can auxiliary decrease the cardiometabolic risk observed in obesity, since this treatment reduce hyperleptinemia state and insulin resistance measured by HOMA-IR, beyond greater decrease in waist and neck circumferences compared to a placebo group.

In a recent study, the authors observed that LLLT can modulate the balance between pro and anti-inflammatory cytokines, both systemically and peripherally in lean rats [40]. Other study shows that laser irradiation with wavelength of 808 nm, similar with our study, in coronary artery, results in increase of anti-inflammatory and decrease in the pro-inflammatory interleukins levels [41]. In fact, we observed in the current study evidence that LLLT in wavelength of 808 nm promoted, beyond the effect on the reduction of adipose tissue, a systemic effect in the modulation of inflammatory process. The LLLT associated with aerobic plus resistance training decreased PAI-1, ICAM-1, VCAM-1 besides reducing circulating concentrations of leptin and insulin as discussed above.

These findings are important since in most cases of obesity, individuals have vascular endothelial cell damage that in turn expresses cell adhesion molecules 1 (CAMs), including ICAM-1 and VCAM-1. Circulating leukocytes are selective attracting and monocytes chemotactic protein 1 (MCP-1) are released by endothelial cells that stimulate to recruit mononuclear cell circulating differentiated into macrophages in the vessel wall. This development in the local inflammatory responses stimulates other cell types to produce pro-inflammatory cytokines, resulting in an inflammatory response that magnified beyond the original local area of endothelial dysfunction [32].

Furthermore, the main inhibitor of fibrinolysis, the PAI-1 (plasminogen inhibitor of fibrinolysis) increase in plasma of the obese individuals leads to a hyperthrombotic state by hypofibrinolysis, hypercoagulability and platelets activation that leads to development of atherosclerotic plaques formation, the main predictor for myocardial infarction [8,9]. Besides that, oxidative stress transforms an anti-atherosclerotic NO-producing enzyme into pro-atherosclerotic superoxide producing one, in addition to stimulates the inducible nitric oxide synthase raising the oxidative stress. Therefore, oxidative stress has been linked to increased platelet activation, characteristics in many obese individuals [32]. In a recent review, the authors showed some studies, with rats and humans, about the effect of the exercise aerobic and/or resistance training on inflammation in adipose tissue and endothelial cells, decreasing pro-inflammatory cytokine expression and increasing anti-inflammatory protein expression in this tissue [5]. These authors also show that chronic exercise as well reduce the number of pro-inflammatory monocytes and increase circulating numbers of regulatory T cells, which release anti-inflammatory cytokines and reduce chronic inflammation.

In this manner, the biophotomodulation generated by LLLT can affect the application area, as well as the surrounding regions affect metabolic changes, generating systemic effects [48]. In accordance with Novoselova and colleagues [49], the tissue irradiated with low-power laser produces signaling factors that will circulate into the lymphatic system and blood vessels. This way, associated the exercise effects with the local and systemic effects promoted by LLLT on the inflammation decreases dramatically the cardiometabolic risk in obese individuals. Finally, despite this as being a new study that uses new technologies (laser) aiming to control cardiometabolic disease in obese women, we were able to show that associated effects of exercise with LLLT, include the local and systemic improvements, is corroborating with an improvement in inflammatory state and a substantially decrease in the cardiometabolic risk factors in these individuals.

In conclusion, the results observed in the present investigation suggest that LLLT associated with aerobic plus resistance training may be a new therapeutic tool in targeting to optimize the control of cardiometabolic risk factors in obese people.

Conflict of Interest

None disclosed.

Financial Support

We thank the financial support for all research agencies like: CNPq (150177/2014-3); CNPq 300654/2013-8; FAPESP (2013/19046-0); FAPESP (2013/04136-4).

Acknowledgments

We thank Ms Jorge Camargo Oishi for the assistance with statistical analyses, Ms Cynthia Aparecida Castro and Ms Karina Ana da Silva for technical support during the training protocol and data collection and Paulo Henrique Colturato Reame for opening his gym (Oxy) for development to the project.

References

[1] F.O. Duarte, M. Sene-Fiorese, N.C. Cheik, A.S. Maria, A.E. de Aquino Jr., J.C. Oishi, E.A. Rossi, A.C. Garcia de Oliveira Duarte, A.R. Dâmaso, Food restriction and refeeding induces changes in lipid pathways and fat deposition in the adipose and hepatic tissues in rats with diet-induced obesity, Exp. Physiol. 97 (7) (Jul 2012) 882–894, http://dx.doi.org/10.1113/expphysiol.2011.064121.

[2] F.C. Corgosinho, C. Ackel-D'Elia, S. Tufik, A.R. Dâmaso, A. de Piano, L. Sanches Pde, R.M. Campos, P.L. Silva, J. Carnier, L. Tock, M.L. Andersen, G.A. Moreira, M. Pradella-Hallinan, L.M. Oyama, M.T. de Mello, Beneficial effects of a multifaceted 1-year lifestyle intervention on metabolic abnormalities in obese adolescents with and without sleep-disordered breathing, Metab. Syndr. Relat. Disord. 13 (3) (Apr 2015) 110–118, http://dx.doi.org/10.1089/met.2014.0110.

[3] N. Alexopoulos, D. Katritsis, P. Raggi, Visceral adipose tissue as a source of inflammation and promoter of atherosclerosis, Atherosclerosis 233 (1) (Mar 2014) 104–112, http://dx.doi.org/10.1016/j.atherosclerosis.2013.12.023.

[4] L. Jamar, P. Pisani, L.M. Oyama, C. Belote, D.C.L. Masquio, V.A. Furuya, J.P. Carvalho-Ferreira, S.G. Andrade-Silva, A.R. Dâmaso, D.A. Caranti, Is the neck circumference an emergent predictor for inflammatory status in obese adults? Int. J. Clin. Pract. 67 (3) (Mar 2013) 217–224, http://dx.doi.org/10.1111/ijcp.12041.

[5] T. You, N.C. Arsenis, B.L. Disanzo, M.J. Lamonte, Effects of exercise training on chronic inflammation in obesity: current evidence and potential mechanisms, Sports Med. 43 (4) (Apr 2013) 243–256, http://dx.doi.org/10.1007/s40279-013-0023-3.

[6] Jing-ya Zhou, Hui Ge, Ming-fan Zhu, Li-jun Wang, Li Chen, Yao-zong Tan, Yu-ming Chen, Hui-lian Zhu, Neck circumference as an independent predictive contributor to cardio-metabolic syndrome, Cardiovasc. Diabetol. 16 (May 2013) 12–76, http://dx.doi.org/10.1186/1475-2840-12-76.

[7] R.B. Harris, Leptin: much more than a satiety signal, Annu. Rev. Nutr. 20 (2000 July) 45–75, http://dx.doi.org/10.1146/annurev.nutr.20.1.45.

[8] V.Z. Rocha, E.J. Folco, Inflammatory concepts of obesity, Int. J. Inflamm. 2011 (May 2011) 1–14, http://dx.doi.org/10.4061/2011/529061.

[9] J. Chudek, A. Wiecek, Adipose tissue, inflammation and endothelial dysfunction, Pharmacol. Rep. 58 (Suppl.) (2006) 81–810.

[10] A.R. Dâmaso, A. de Piano, R.M. Campos, F.C. Corgosinho, W. Siegfried, D.A. Caranti, D.C. Masquio, J. Carnier, P. Sanches de L, P. Leão da Silva, C.M. Nascimento, L.M. Oyama, A.D. Dantas, M.T. de Mello, S. Tufik, L. Tock, Multidisciplinary approach to the treatment of obese adolescents: effects on cardiovascular risk factors, inflammatory profile, and neuroendocrine regulation of energy balance, Int. J. Endocrinol. 2013 (2013) 541032, http://dx.doi.org/10.1155/2013/541032.

[11] A.R. Dâmaso, R.M. Campos, D.A. Caranti, A. de Piano, M. Fisberg, D. Foschini, P.D. Sanches, L. Tock, H.M. Lederman, S. Tufik, M.T. de Mello, Aerobic plus resistance training was more effective in improving the visceral adiposity, metabolic profile and inflammatory markers than aerobic training in obese adolescents, J. Sports Sci. 32 (15) (2014) 1435–1445, http://dx.doi.org/10.1080/02640414.2014.900692.

[12] R.F. Jackson, F.A. Stern, R. Neira, C.L. Ortiz-Neira, J. Maloney, Application of low-level laser therapy for noninvasive body contouring, Lasers Surg. Med. 44 (3) (2012 Mar) 211–217, http://dx.doi.org/10.1002/lsm.22007.

[13] C. Ferraresi, O.T. de Brito, Z.L. de Oliveira, R.B. de Menezes Reiff, V. Baldissera, S.E. de Andrade Perez, E. Matheucci Junior, N.A. Parizotto, Effects of low level laser therapy (808 nm) on physical strength training in humans, Lasers Med. Sci. 26 (3) (2011 May) 349–358, http://dx.doi.org/10.1007/s10103-010-0855-0.

[14] F.R. Paolillo, J.C. Milan, I.V. Aniceto, S.G. Barreto, J.R. Rebelatto, A. Borghi-Silva, N.A. Parizotto, C. Kurachi, V.S. Bagnato, Effects of infrared-LED illumination applied during high intensity treadmill training in postmenopausal women, Photomed. Laser Surg. 29 (9) (2011 Sep) 639–645, http://dx.doi.org/10.1089/pho.2010.2961.
[15] T. Fujimura, A. Mitani, M. Fukuda, M. Mogi, K. Osawa, S. Takahashi, M. Aino, Y. Iwamura, S. Miyajima, H. Yamamoto, T. Noguchi, Irradiation with a low-level diode laser induces the developmental endothelial locus-1 gene and reduces proinflammatory cytokines in epithelial cells, Lasers Med Sci. 29 (3) (May 2014) 987–994, http://dx.doi.org/10.1007/s10103-013-1439-6.
[16] F.G. Basso, T.N. Pansani, D.G. Soares, D.L. Scheffel, V.S. Bagnato, C.A. Costa, J. Hebling, Biomodulation of inflammatory cytokines related to oral mucositis by low-level laser therapy, Photochem. Photobiol. 4 (2015 Mar), http://dx.doi.org/10.1111/php.12445.
[17] A.E. Aquino Jr., M. Sene-Fiorese, F.R. Paolillo, F.O. Duarte, J.C. Oishi, A.A. Pena Jr., A.C. Duarte, M.R. Hamblin, V.S. Bagnato, N.A. Parizotto, Low-level laser therapy (LLLT) combined with swimming training improved the lipid profile in rats fed with high-fat diet, Lasers Med. Sci. 28 (5) (2013 Sep) 1271–1280, http://dx.doi.org/10.1007/s10103-012-1223-z.
[18] S.R. Preis, J.M. Massaro, U. Hoffmann, R.B. D'Agostino Sr., D. Levy, S.J. Robins, J.B. Meigs, R.S. Vasan, C.J. O'Donnell, C.S. Fox, Neck circumference as a novel measure of cardiometabolic risk: the Framingham Heart study, J. Clin. Endocrinol. Metab. 95 (8) (2010 Aug) 3701–3710, http://dx.doi.org/10.1210/jc.2009-1779.
[19] C. Nishida, G.T. Ko, S. Kumanyika, Body fat distribution and noncommunicable diseases in populations: overview of the 2008 WHO Expert Consultation on Waist Circumference and Waist–Hip Ratio, Eur. J. Clin. Nutr. 64 (1) (2010 Jan) 2–5, http://dx.doi.org/10.1038/ejcn.2009.139.
[20] B. Geloneze, E.M. Repetto, S.R. Geloneze, M.A. Tambascia, M.N. Ermetice, The threshold value for insulin resistance (HOMA-IR) in an admixture population IR in the Brazilian Metabolic Syndrome Study, Diabetes Res. Clin. Pract. 72 (2) (2006 May) 219–220.
[21] L. Dossus, S. Becker, D. Achaintre, R. Kaaks, S. Rinaldi, Validity of multiplex-based assays for cytokine measurements in serum and plasma from "non-diseased" subjects: comparison with ELISA, J. Immunol. Methods 350 (1–2) (2009 Oct 31) 125–132, http://dx.doi.org/10.1016/j.jim.2009.09.001.
[22] J.E. Donnelly, S.N. Blair, J.M. Jakicic, M.M. Manore, J.W. Rankin, B.K. Smith, American College of Sports Medicine Position Stand. Appropriate physical activity intervention strategies for weight loss and prevention of weight regain for adults, Med. Sci. Sports Exerc. 41 (2) (2009 Feb) 459–471, http://dx.doi.org/10.1249/MSS.0b013e3181949333.
[23] W.J. Kraemer, N.A. Ratamess, D.N. French, Resistance training for health and performance, Curr. Sports Med. Rep. 1 (3) (2002 Jun) 165–171.
[24] M. Sene-Fiorese, F.O. Duarte, A.E. de Aquino Junior, R.M. Campos, D.C. Masquio, L. Tock, A.C. Duarte, A.R. Dâmaso, N.A. Parizotto, V.S. Bagnato, The potential of phototherapy to reduce body fat, insulin resistance and "metabolic inflexibility" related to obesity in women undergoing weight loss treatment, Lasers Surg. Med. 47 (6) (Jul 2015), http://dx.doi.org/10.1002/lsm.22395.
[25] R.M. da Silveira Campos, A.R. Dâmaso, D.C. Masquio, A.E. Aquino Jr., M. Sene-Fiorese, F.O. Duarte, L. Tock, N.A. Parizotto, V.S. Bagnato, Low-level laser therapy (LLLT) associated with aerobic plus resistance training to improve inflammatory biomarkers in obese adults, Lasers Med. Sci. 30 (5) (2015 Jul) 1553–1563, http://dx.doi.org/10.1007/s10103-015-1759-9.
[26] K.H. Beckmann, G. Meyer-Hamme, S. Schröder, Low level laser therapy for the treatment of diabetic foot ulcers: a critical survey, Evid. Based Complement. Alternat. Med. 2014 (2014) 626127, http://dx.doi.org/10.1155/2014/626127.
[27] P. Avci, T.T. Nyame, G.K. Gupta, M. Sadasivam, M.R. Hamblin, Low-level laser therapy for fat layer reduction: a comprehensive review, Lasers Surg. Med. 45 (6) (2013 Aug) 349–357, http://dx.doi.org/10.1002/lsm.22153.
[28] F.R. Paolillo, A. Borghi-Silva, N.A. Parizotto, C. Kurachi, V.S. Bagnato, New treatment of cellulite with infrared-LED illumination applied during high-intensity treadmill training, J. Cosmet. Laser Ther. 13 (4) (2011 Aug) 166–171, http://dx.doi.org/10.3109/14764172.2011.594065.
[29] L. Badimon, R. Hernández Vera, G. Vilahur, Atherothrombotic risk in obesity, Hamostaseologie 33 (4) (2013) 259–268, http://dx.doi.org/10.5482/HAMO-13-07-0034.
[30] B. Gustafson, A. Hammarstedt, C.X. Andersson, U. Smith, Inflamed adipose tissue: a culprit underlying the metabolic syndrome and atherosclerosis, Arterioscler. Thromb. Vasc. Biol. 27 (11) (2007 Nov) 2276–2283, http://dx.doi.org/10.1161/ATVBAHA.107.147835.
[31] S. De Ferranti, D. Mozaffarian, The perfect storm: obesity, adipocyte dysfunction, and metabolic consequences, Clin. Chem. 54 (6) (2008 Jun) 945–955, http://dx.doi.org/10.1373/clinchem.2007.100156.
[32] K. Osawa, T. Miyoshi, Y. Koyama, S. Sato, N. Akagi, Y. Morimitsu, M. Kubo, H. Sugiyama, K. Nakamura, H. Morita, S. Kanazawa, H. Ito, Differential association of visceral adipose tissue with coronary plaque characteristics in patients with and without diabetes mellitus, Cardiovasc. Diabetol. 14 (Mar 2014) 13–61, http://dx.doi.org/10.1186/1475-2840-13-61.
[33] L.M. Nguyen, A.G. Malamo, K.A. Larkin-Kaiser, P.A. Borsa, P.J. Adhihetty, Effect of near-infrared light exposure on mitochondrial signaling in C2C12 muscle cells, Mitochondrion 14 (1) (2014 Jan) 42–48, http://dx.doi.org/10.1016/j.mito.2013.11.001.
[34] C. Ferraresi, B. Kaippert, P. Avci, Y.Y. Huang, M.V. de Sousa, V.S. Bagnato, N.A. Parizotto, M.R. Hamblin, Low-level laser (light) therapy increases mitochondrial membrane potential and ATP synthesis in C2C12 myotubes with a peak response at 3–6 h, Photochem. Photobiol. 91 (2) (2015 Mar) 411–416, http://dx.doi.org/10.1111/php.12397.
[35] W.H. de Brito Vieira, R.M. Bezerra, R.A. Queiroz, N.F. Maciel, N.A. Parizotto, C. Ferraresi, Use of low-level laser therapy (808 nm) to muscle fatigue resistance: a randomized double-blind crossover trial, Photomed. Laser Surg. 32 (12) (2014 Dec) 678–685, http://dx.doi.org/10.1089/pho.2014.3812.
[36] F.R. Paolillo, R. Arena, D.B. Dutra, R. de Cassia Marqueti Durigan, H.S. de Araujo, H.C. de Souza, N.A. Parizotto, G. Cipriano Jr., G. Chiappa, A. Borghi-Silva, Low-level laser therapy associated with high intensity resistance training on cardiac autonomic control of heart rate and skeletal muscle remodeling in wistar rats, Lasers Surg. Med. 46 (10) (2014 Dec) 796–803, http://dx.doi.org/10.1002/lsm.22298.
[37] Adriano Eduardo Lima-Silva, Fernando Adami, Fábio Yuzo Nakamura, Fernando Roberto de-Oliveira, Monique da Silva Gevaerd, Fat metabolism during exercise: mechanisms of regulation, Rev. Bras.Cineantropom. Desempenho Hum. 8 (4) (2006) 106–114 (ISSN 1980-0037. Article in Portuguese).
[38] C. Ferraresi, M.V. de Sousa, Y.Y. Huang, V.S. Bagnato, N.A. Parizotto, M.R. Hamblin, Time response of increases in ATP and muscle resistance to fatigue after low-level laser (light) therapy (LLLT) in mice, Lasers Med. Sci. 30 (4) (2015 May) 1259–1267, http://dx.doi.org/10.1007/s10103-015-1723-8.
[39] S.B. Chai, F. Sun, X.L. Nie, J. Wang, Leptin and coronary heart disease: a systematic review and meta-analysis, Atherosclerosis 233 (1) (Mar 2014) 3–10, http://dx.doi.org/10.1016/j.atherosclerosis.2013.11.069.
[40] V.S. Hentschke, R.B. Jaenisch, L.A. Schmeing, P.R. Cavinato, L.L. Xavier, P. Dal Lago, Low-level laser therapy improves the inflammatory profile of rats with heart failure, Lasers Med Sci. 28 (3) (Lasers Med Sci. 2013 May) 1007–1016, http://dx.doi.org/10.1007/s10103-012-1190-4.
[41] A. Derkacz, M. Protasiewicz, R. Poręba, A. Doroszko, R. Andrzejak, Effect of the intravascular low energy laser illumination during percutaneous coronary intervention on the inflammatory process in vascular wall, Lasers Med. Sci. 28 (3) (2013 May) 763–768, http://dx.doi.org/10.1007/s10103-012-1142-z.
[42] L.L. Ben-Noun, A. Laor, Relationship between changes in neck circumference and cardiovascular risk factors, Exp. Clin. Cardiol. 11 (1) (Spring 2006) 14–20.
[43] M. Sharda, P. Jain, A. Gupta, D. Nagar, A. Soni, Correlation and comparison of various anthropometric measurements of body fat distribution and sagittal abdominal diameter as a screening tool for cardio metabolic risk factors and ischaemic heart disease in elderly population, J. Assoc. Physicians India 63 (2015) 22–26.
[44] C. Stabe, A.C. Vasques, M.M. Lima, M.A. Tambascia, J.C. Pareja, A. Yamanaka, B. Geloneze, Neck circumference as a simple tool for identifying the metabolic syndrome and insulin resistance: results from the Brazilian Metabolic Syndrome Study, Clin. Endocrinol. (Oxf) 78 (6) (Jun 2013) 874–881, http://dx.doi.org/10.1111/j.1365-2265.2012.04487.x.
[45] C.J. Hsieh, P.W. Wang, T.Y. Chen, The relationship between regional abdominal fat distribution and both insulin resistance and subclinical chronic inflammation in non-diabetic adults, Diabetol. Metab. Syndr. 6 (1) (Apr 1 2014) 49, http://dx.doi.org/10.1186/1758-5996-6-49.
[46] L.S. Rallidis, K. Baroutsi, M. Zolindaki, M. Karagianni, C. Varounis, N. Dagres, J. Lekakis, M. Anastasiou-Nana, Visceral adipose tissue is a better predictor of subclinical carotid atherosclerosis compared with waist circumference, Ultrasound Med. Biol. 40 (6) (Jun 2014) 1083–1088, http://dx.doi.org/10.1016/j.ultrasmedbio.2013.12.017.
[47] P.L. Sanches, M.T. de Mello, N. Elias, F.A. Fonseca, R.M. Campos, J. Carnier, A. de Piano, D.C. Masquio, P.L. Silva, L.M. Oyama, F.C. Corgosinho, C.M. Nascimento, L. Tock, C.A. D'Elia, S. Tufik, A.R. Dâmaso, Hyperleptinemia: implications on the inflammatory state and vascular protection in obese adolescents submitted to an interdisciplinary therapy, Inflammation 37 (1) (Feb 2014) 35–43, http://dx.doi.org/10.1007/s10753-013-9709-9.
[48] T.Y. Fukuda, M.M. Tanji, S.R. Silva, M.N. Sato, H. Plapler, Infrared low-level diode laser on inflammatory process modulation in mice: pro- and anti-inflammatory cytokines, Lasers Med. Sci. 28 (5) (Sep 2013) 1305–1313, http://dx.doi.org/10.1007/s10103-012-1231-z.
[49] E.G. Novoselova, O.V. Glushkova, D.A. Cherenkov, V.M. Chudnovsky, E.E. Fesenko, Effects of low-power laser radiation on mice immunity, Photodermatol. Photoimmunol. Photomed. 22 (1) (Feb 2006) 33–38.

View publication stats