

Low-level laser therapy (LLLT) associated with aerobic plus resistance training to improve inflammatory biomarkers in obese adults

Raquel Munhoz da Silveira Campos¹ · Ana Raimunda Dâmaso¹ · Deborah Cristina Landi Masquio¹ · Antonio Eduardo Aquino Jr.^{2,3} · Marcela Sene-Fiorese² · Fernanda Oliveira Duarte⁴ · Lian Tock⁵ · Nivaldo Antonio Parizotto^{3,4} · Vanderlei Salvador Bagnato^{2,3}

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Abstract Recently, investigations suggest the benefits of low-level laser (light) therapy (LLLT) in noninvasive treatment of cellulite, improvement of body countering, and control of lipid profile. However, the underlying key mechanism for such potential effects associated to aerobic plus resistance training to reduce body fat and inflammatory process, related to obesity in women still unclear. The purpose of the present investigation was to evaluate the effects of combined therapy of LLLT and aerobic plus resistance training in inflammatory profile and body composition of obese women. For this study, it involved 40 obese women with age of 20–40 years. Inclusion criteria were primary obesity and body mass index (BMI) greater than 30 kg/m² and less than 40 kg/m². The voluntaries

were allocated in two different groups: phototherapy group and SHAM group. The interventions consisted on physical exercise training and application of phototherapy (808 nm), immediately after the physical exercise, with special designed device. Proinflammatory/anti-inflammatory adipokines were measured. It was showed that LLLT associated to physical exercise is more effective than physical exercise alone to increase adiponectin concentration, an anti-inflammatory adipokine. Also, it showed reduced values of neck circumference (cm), insulin concentration (μU/ml), and interleukin-6 (pg/ml) in LLLT group. In conclusion, phototherapy can be an important tool in the obesity, mostly considering its potential effects associated to exercise training in attenuating inflammation in women, being these results applicable in the clinical practices to control related risk associated to obesity.

✉ Raquel Munhoz da Silveira Campos
raquelmunhoz@hotmail.com

✉ Ana Raimunda Dâmaso
ana.damaso@unifesp.br

¹ Paulista Medicine School—Universidade Federal de São Paulo, Rua Marselhesa, 650—Vila Clementino, São Paulo, SP 04020-050, Brazil

² São Carlos Institute of Physics, University of São Paulo (USP), PO Box 369, São Carlos 13560-970, Brazil

³ Post Graduated Program of Biotechnology, Federal University of São Carlos (UFSCar), São Carlos, SP 13565-905, Brazil

⁴ Department of Physiotherapy, Therapeutic Resouces Laboratory, Federal University of São Carlos (UFSCar), São Carlos, SP 13565-905, Brazil

⁵ Weight Science, São Paulo, SP, Brazil

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Introduction

Nowadays, strong evidence has been found that LLLT is an important tool in widely clinical applications, including esthetic treatments, chronic kidney disease, cancer, and different branches of regenerative medicine and dentistry [1]. Supporting this, it was recently demonstrated in experimental conditions that LLLT promoted improvement in some metabolic syndrome parameters in rats [2], although its effects in human obesity are unknown in the literature.

Metabolic syndrome is a constellation of metabolic alterations leading to cardiovascular diseases. In this way, obesity, mostly considering central and visceral fat and insulin resistance, has been strongly associated with the development of metabolic syndrome and cardiovascular diseases [3, 4]. In addition, the prevalence of metabolic syndrome in obese people ranges between 30 and 70 % [5, 6] in adolescents and adults, respectively, showing the necessity for new techniques to optimize the treatment of metabolic comorbidities. Moreover, the related inflammatory process involved in obesity promotes an increase in the proinflammatory adipokines and a reduction in the anti-inflammatory adipokines which are associated with several metabolic disorders such as type 2 diabetes, obesity, and cardiovascular disease [7, 8].

The key inflammatory mediators in obesity are adiponectin, interleukin-6 (IL-6), and TNF- α . Adiponectin is a 244-amino acid-long protein that is secreted from adipocytes and has anti-inflammatory and insulin-sensitizing properties [9]. However, reduced levels of this adipokine are linked to increased carotid intima-media thickness (cIMT), visceral adiposity, insulin resistance, diabetes, dyslipidemia, hypertension, hyperleptinemia, cardiovascular disease, metabolic syndrome, and systemic inflammation [10].

On the other hand, the members of proinflammatory cytokines, IL-6 and TNF- α , are known to be elevated in obesity and its comorbidities [11, 12] and have been accepted as clinical markers. Additionally, in metabolic syndrome patients, it is known that both are strong inhibitors of adiponectin. Nonetheless, weight loss therapies including physical exercise promote an improvement in the inflammatory biomarkers, showing that an increase in the adiponectin concentration and a reduction in the interleukin-6 and TNF- α occur [13, 14].

Interestingly, an initial proof-of-concept was previously shown suggesting that LLLT can be used in some inflammatory diseases to provide a noninvasive and clinical therapeutic strategy due to photochemical effects that change cellular functions in irradiated cells; thus, the therapeutic effect is not thermal [15, 16].

It is well settled in the literature that physical exercise favors the control of obesity and related inflammatory processes, since this kind of strategy leads to a reduction in body weight, visceral fat, and insulin resistance through an increase in the lipolysis [17, 18]. However, the association of LLLT with aerobic plus resistance training in obese women is scarce in the literature. Therefore, in the present study, it was hypothesized that in obese women, changes in proinflammatory markers should be compensated by altered anti-inflammatory markers after treatment with LLLT combined with aerobic plus resistance training.

Material and methods

Population

For this study, it involved 40 obese women with age of 20–40 years. Inclusion criteria were primary obesity and body mass index (BMI) greater than 30 kg/m² and less than 40 kg/m². Noninclusion criteria were the use of cortisone, antiepileptic drugs, history of renal disease, alcohol intake, smoking, and secondary obesity due to endocrine disorders.

The main reasons for dropout ($n=4$) in our study were financial and family problems, followed by job opportunities. The study was conducted with the principles of the Declaration of Helsinki and was approved by the ethics committee on research at the Universidade Federal de São Carlos-UFSCar with the number (237.050), Clinical Trial: 231.286. All procedures were clear to the volunteers, and it obtained consent for research. All evaluations were performed at two different times (baseline and at the end of therapy: after 4 months of interdisciplinary intervention).

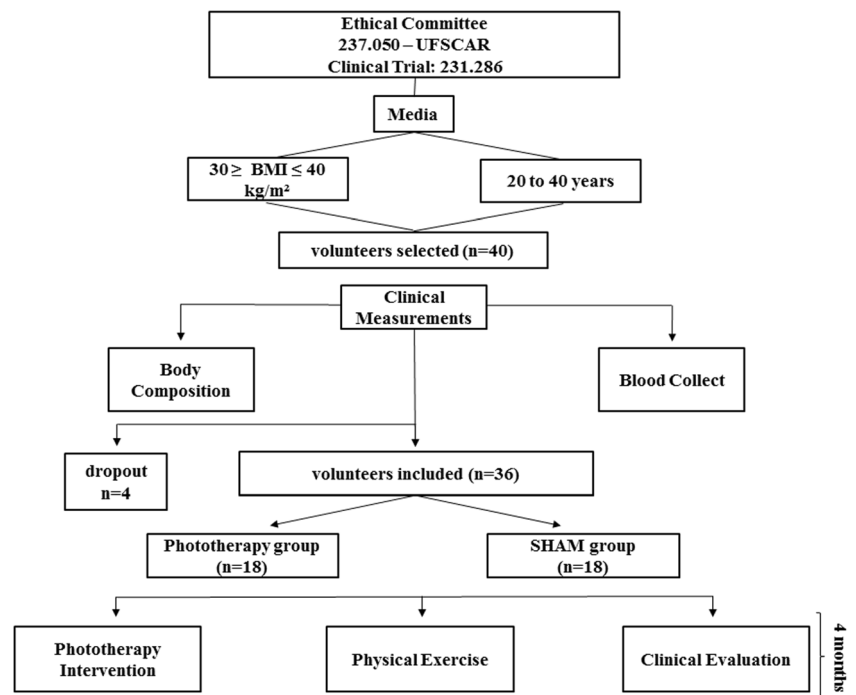
The voluntaries were allocated in two different groups: phototherapy group and SHAM group. The interventions consisted in to participate of physical exercise intervention, and immediately after physical exercises, the voluntaries received, individually, the application of phototherapy. The SHAM group participated the same interventions of phototherapy group, although, during the application of phototherapy, this group did not receive the incidence of laser light. It is important to note that the voluntaries do not know which group they belonged (Fig. 1).

Anthropometric measurements

Weight and height were measured for all patients who wore minimum clothing. After obtaining, the data was calculated using the BMI by dividing the weight by height squared (kg/m²). Fat mass (% and kg) and lean mass (% and kg) were obtained through the Bioelectrical Impedance InBody[®].

Serum analysis

Blood samples were collected at the outpatient clinic at approximately 8:00 A.M. after an overnight fast (12 h). Insulin resistance was assessed using the homeostasis model assessment-insulin resistance (HOMA-IR) calculated by the fasting blood glucose (FBG) and the immunoreactive insulin (I): $[FBG \text{ (in milligrams per deciliter)} \times I \text{ (in milliunits per liter)}] / 405$. The cutoff value determined for Brazilian population is $HOMA-IR > 2.71$ for classifying the subjects with insulin resistance [19]. The normal range for insulin is 2.60–24.90 $\mu\text{U/ml}$ [20]. The adipokines adiponectin (ng/l) and interleukin-6 (pg/ml) concentrations were measured using a commercially available multiplex assay (EMD Millipore;

Fig. 1 Diagram of methodology study

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].

Descriptive methodology of weight loss therapy

All voluntaries visited the team of health professionals (endocrinologist, nutritionist, and physical educator) three times during the intervention period: (1) baseline (before the participation in the physical exercise and LLLT interventions); (2) after 2 months of participation in the interventions; and (3) after therapy (in the end of 4 months of interventions). They monitored and evaluated all clinical exams of voluntaries and treated health problems during intervention. The medical follow-up included the initial medical history, and a physical examination of blood pressure, cardiac frequency, and body composition were checked.

Physical exercise intervention

Aerobic plus resistance training

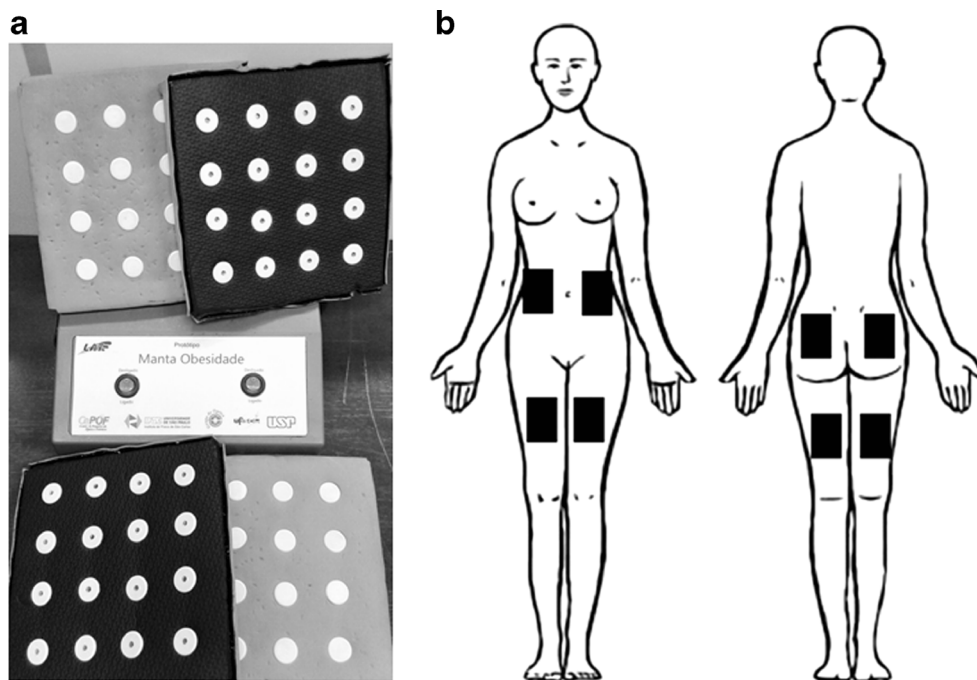
During the 4-month period, the voluntaries followed a combined exercise training therapy. The protocol was performed three times per week and included 30 min of aerobic training

and 30 min of resistance training per session. At each training session, subjects were instructed to invert the order of the physical exercises, that is, in one session, the individual started the training session with resistance training, and in the subsequent session, the same individual started with aerobic training. The aerobic training consisted of running on a motor-driven treadmill (Movement®) at a 50–75 % of cardiac frequency maximum intensity established by Bruce test adapted. The resistance training was made recruiting the muscle groups: pectoralis major, quadriceps, back, hamstrings, calf, deltoid, biceps, triceps, abdomen, and extensor muscles by performing the following exercises: chest press, leg press, lat pulldown, hamstring curls, calf raises, military press, arm curls, bench press, sit ups, and lower back. The first 2 weeks were used for training adaptation and to learn the movements (3 sets of 15–20 maximal repetitions [MRs]). The protocol consisted of weekly changes of the load, divided into weeks of high loads (6–8 MR), weeks of moderate loads (10–12 MR), and weeks of light loads (15–20 MR). The volunteers performed 18 sets per session, divided into 3 sets of each exercise, followed by rest intervals between the series and exercises: 15–20 MR=45 s, 10–12 MR=1 min, and 6–8 MR=1.5 min of rest. The physical exercise intervention was based on the guidelines from the American College of Sports Medicine (ACSM) [22, 23].

Device description

The phototherapy equipment was developed by the Laboratory Technology Support-LAT, Center for Research in Optics

Fig. 2 **a** Illustrative of phototherapy design, **b** illustrative regions of phototherapy application



and Photonics Institute of Physics in São Carlos city at University of São Paulo-USP. The device is composed of four plates made of rubberized material measuring 20 by 20 cm each. Each two plates are connected to an electronic control box. The emitters of Ga-Al-As diode Lasers are distributed in the plate every 2.5 cm, totaling 16 emitters per plate and 64 emitters in total. The device is illustrated in Fig. 2a, and irradiation parameters are in Table 1 [24].

Phototherapy intervention

The application of phototherapy by continuous wave lasers (808 nm) occurs always at the final of training session. Thus, in each week, the patients received 3 sessions of phototherapy. The emitters were arranged perpendicularly to the skin and were allocated in the anterior region: abdominal and quadriceps simultaneously during 8 min. After this, change the position to irradiate the posterior region: gluteus and biceps femoral during 8 min, totalizing 16 min of its application (Fig. 2b).

According with the disposition of the emitters, the irradiance per emitter was 6.0 W/cm². The energy delivered per session, per point, was 96 J. The diameters of elliptical spot were 0.3692 cm for horizontal and 0.0582 cm for vertical. The value of spot area was 0.0169 cm². The emission and device parameters are described in Table 1 to become reproducible conditions.

Statistical analysis

Statistical analysis was performed using the program STATISTICA version 7.0 for Windows. The adopted

significant value was $\alpha < 5\%$. Data normality was verified with the Kolmogorov-Smirnov test. Parametric data were expressed as mean \pm SD, and nonparametric data were expressed as median, minimum, and maximum values. To analyze the effects of intervention and difference between the groups, it applied ANOVA for repeated measures (ANOVA two-way) followed by Tukey post hoc test. The delta values (Δ) were used for the statistical analysis obtained from the difference between the after therapy and baseline values for each variable: Δ variable = after therapy value – baseline value. Comparing the delta values between the groups was performed by *t* test independent by groups to parametric variables and Mann-Whitney test to nonparametric variables.

Results

In the beginning of interdisciplinary intervention, no statistical differences were observed between the groups for the variables: age (years), height (m), weight (kg), BMI (kg/m²), fat mass (% and kg), lean mass (% and kg), neck circumference (cm), glucose (mg/dl), insulin (μ U/ml), HOMA-IR, adiponectin (ng/l), IL-6 (pg/ml), adiponectin/IL-6 ratio, adiponectin/fat mass (kg and %) ratio, and lean mass/fat mass (kg and %) ratio. These data are important to show that the groups present in the investigation were paired at the beginning of the study and future alterations could result by the possible influence of the purpose interdisciplinary therapy in the study (Table 2).

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
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

These are the characteristics of equipment and wavelength used during the study. All applications were realized by the same person

Effects of weight loss therapy in the phototherapy group

After 4 months of interdisciplinary intervention associated with the phototherapy sessions, a reduction was observed in the phototherapy group in the body mass (kg), BMI (kg/m²), fat mass (kg and %), neck circumference (cm), insulin (μU/ml), interleukin-6 (pg/ml) [from 1.11 (0.56–6.8) to 0.56 (0.28–3.62) $p=0.01$] and an increase in the lean mass (%), adiponectin concentration (ng/l) [from 7.01 (2.44–15.14) to 8.44 (5.42–17.14) $p=0.00$], adiponectin/interleukin-6 ratio, lean mass/fat mass (kg and %) ratio, and adiponectin/fat mass (kg and %) ratio. No statistical differences were observed for the variables lean mass (kg), glucose (mg/dl), and HOMA-IR (Table 2 and Fig. 3a, b).

Effects of weight loss therapy in the SHAM group

After 4 months of interdisciplinary intervention, a reduction was observed in the SHAM group in the body mass (kg), BMI (kg/m²), fat mass (kg and %), neck circumference (cm), increase in the lean mass (% and kg), and lean mass/fat mass (kg

and %) ratio. No statistical differences were observed for the variables glucose (mg/dl), insulin (uU/ml), HOMA-IR, adiponectin (ng/l) [from 6.20 (2.38–16.53) to 5.76 (3.14–9.22) $p=0,86$], IL-6 (pg/ml) [from 0.91 (0.28–2.79) to 0.56 (0.28–3.34) $p=0.13$], and adiponectin/fat mass (kg/%) ratio (Table 2 and Fig. 3a, b).

Effects of weight loss therapy between the groups

Comparing the delta values between the groups, it was observed that the phototherapy group showed a statistical reduction in the values of neck circumference (cm) [-2.08 ± 1.49 to -0.88 ± 1.08 ; $p=0.01$], insulin concentration (μU/ml) [-5.72 ± 3.68 to -1.60 ± 4.05 ; $p=0.00$], interleukin-6 (pg/ml) [-0.97 (-4.29 – 0.76) to -0.20 (-0.81 – 1.8); $p=0.00$] compared to SHAM group. Also, an increase in the adiponectin concentration (ng/ml) [1.08 (0.04–3.62) to -0.42 (-3.15 – 2.26); $p=0.03$] and adiponectin/fat mass (%) ratio [0.09 ± 0.13 to 0.003 ± 0.04 ; $p=0.05$] was shown compared with SHAM group (Table 3; Figs. 4 and 5a–d).

Discussion

The most important finding in the present investigation is that we were able to show an increase in adiponectin concentration associated with a reduction in IL-6 after 20 weeks of treatment with LLLT associated with aerobic plus resistance training (Fig. 3a, b). There is strong evidence that demonstrates that LLLT was effective as a supporting noninvasive tool in the treatment for the reduction of body measurements and cellulite and improvement of lipid profile [20, 21]. However, the underlying key mechanism of actions for such potential effects to reduce body fat and the inflammatory process related to obesity in women is still unclear.

As we know, adiponectin has a great anti-inflammatory effect, mediated by an increase in the insulin sensitivity and improvement of glucose metabolism, providing an antiatherogenic effect in humans [22, 25]. This is supported by the present investigation where a significant reduction in the insulin concentration was only shown in the phototherapy group, suggesting a possible improvement in insulin sensitivity. However, no changes were observed in the glucose concentration and HOMA-IR, probably because the volunteers showed glucose concentration and insulin levels according to reference values [26]. Nevertheless, this needs to be confirmed in a long-term therapy using LLLT.

Furthermore, there is a consensus that a state of hypo adiponectinemia was present in the metabolic syndrome and obesity population exacerbating the inflammatory process and increasing cardiovascular risk [22]. It has also been shown that hypo adiponectinemia was inversely correlated with

Table 2 Effects of aerobic plus resistance training associate with phototherapy in body composition and inflammatory biomarkers in obese adults

	Phototherapy group			SHAM group			<i>p</i> [*]
	Baseline	After therapy	<i>p</i> [#]	Baseline	After therapy	<i>p</i> [#]	
Age (years)	33.06±4.72	—	—	34.33±4.95	—	—	—
Height (m)	1.66±0.07	1.66±0.07	—	1.62±0.05	1.62±0.04	—	—
Body mass (kg)	96.60±11.36	91.86±13.20	0.00	90.73±11.25	86.74±11.05	0.00	0.80
BMI (kg/m ²)	34.35 (29.13–42.18)	31.67 (27.47–38.28)	0.00	34.19 (29.76–40.31)	33.03 (0–40.23)	0.00	0.99
Fat mass (%)	40.12±3.14	37.77±3.44	0.00	40.42±2.97	38.07±3.37	0.00	0.97
Fat mass (kg)	38.92±6.92	36.30±6.90	0.00	36.44±7.40	33.88±7.41	0.00	0.78
Lean mass (%)	59.88±3.14	63.70±6.90	0.01	59.57±2.97	66.11±7.42	0.00	0.87
Lean mass (kg)	57.52±5.42	56.44±5.31	0.08	54.03±4.44	53.35±4.29	0.02	0.56
Neck circumference (cm)	37.51±2.97	36.21±2.01	0.00	36.92±2.08	36.22±2.04	0.04	1.00
Glucose (mg/dl)	91.47±8.69	93.06±6.63	0.77	92.67±7.89	93.89±10.89	0.87	0.99
Insulin (μU/ml)	16.90±5.61	11.34±4.17	0.01	16.69±6.26	14.3±6.89	0.39	0.97
HOMA-IR	3.72±1.77	2.99±1.67	0.42	3.87±1.62	3.04±1.54	0.31	0.99
Adiponectin/IL-6 ratio	6.08±5.28	16.47±12.29	0.01	9.15±7.83	11.41±6.88	0.65	0.95
Adiponectin/fat mass (kg) ratio	0.19±0.09	0.31±0.15	0.00	0.19±0.10	0.16±0.05	0.99	0.16
Adiponectin/fat mass (%) ratio	0.19±0.08	0.27±0.13	0.00	0.16±0.08	0.14±0.04	0.99	0.92
Lean mass/fat mass (kg) ratio	1.5±0.19	1.61±0.24	0.00	1.52±0.21	1.65±0.23	0.00	0.98
lean mass/fat mass (%) ratio	1.5±0.19	1.71±0.31	0.00	1.48±0.18	1.76±0.34	0.00	0.95

HOMA-IR homeostasis model assessment-insulin resistance, IL-6 interleukin-6

Statistical significance *p*<0.05

[#] Statistical differences are related to comparison of baseline vs after therapy values in the same group

^{*} Statistical differences are related to comparison of after therapy values between the groups

cIMT, an important subclinical surrogate of inflammation, confirming its key role in atherogenesis [27]. This is substantiated by our results which may support the evidence that LLLT is an important tool in the inflammatory process related to obesity since we were able to show a significant increase in adiponectin concentration in the LLLT group alone; it is

important to note that in the SHAM group, this adipokine concentration was not changed.

In corroboration, Wu and colleagues [28] recently showed that human adipose-derived stem cells (hADSCs) expressed toll-like receptors (TLR) and that lipopolysaccharide (LPS) increased the production of proinflammatory interleukin-6

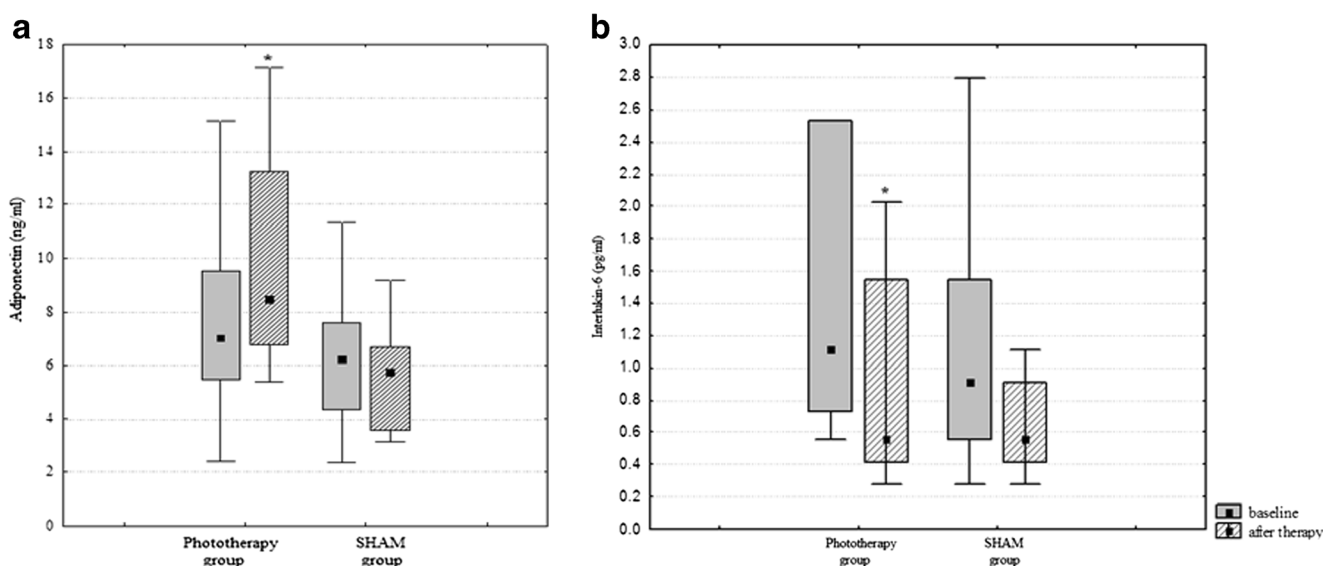


Fig. 3 Effects of interdisciplinary weight loss therapy in both groups. **a** Adiponectin, **b** Interleukin-6. *Statistical difference

Table 3 Comparison of magnitude effects of therapy between groups

	Phototherapy group	SHAM group	<i>p</i> [#]
Body mass (kg)	-4.60±3.083	-5.72±2.43	0.27
BMI (kg/m ²)	-1.9±1.02	-1.99±1.05	0.81
Fat mass (%)	-2.1±1.51	-2.26±1.22	0.73
Fat mass (kg)	-3.52±2.18	-3.94±1.97	0.57
Lean mass (%)	3.94±4.65	6.16±5.04	0.21
Lean mass (kg)	-0.92±1.75	-1.21±1.21	0.58
Glucose (mg/dl)	1.59±5.75	1.22±7.63	0.87
HOMA-IR	-0.73±2.43	-0.82±1.26	0.29
Adiponectin/IL-6 ratio	12.69±12.51	2.96±8.37	0.07
Adiponectin/fat mass (kg) ratio	0.04±0.10	0.004±0.04	0.22
Lean mass/fat mass (kg) ratio	0.13±0.11	0.14±0.10	0.67
Lean mass/fat mass (%) ratio	0.20±0.18	0.25±0.19	0.46

HOMA-IR homeostasis model assessment-insulin resistance, IL-6 interleukin-6

Statistical significance *p*<0.05

[#] Statistical differences are related to comparison between the groups

(IL-6). On the other hand, it was proposed that LLLT markedly inhibited LPS induction, corroborating the reduction in the expression of proinflammatory cytokines. In fact, LLLT promoted a reduction in IL-1 β , IL-6, and TNF- α in experimental studies [29, 30]. Some mechanisms are proposed to explain the LLLT action; one is based on the production of transient pores in adipocytes which stimulates lipolysis. Furthermore, it has been suggested that LLLT activates a cascade of activities, which could cause the induction of adipocyte apoptosis leading to a release of lipids [31].

Interestingly, it has been shown that the application of phototherapy can promote biochemical adaptation of the mitochondria with changes in the redox state, leading to a

conversion of electromagnetic to biochemical energy and consequently increasing the oxygen binding, production of ATP, respiration rate, and formation of giant mitochondria [32, 33]. Also, LLLT may activate enzymatic processes in cells to improve metabolism and lipid profile [16, 34]. Recent evidence in experimental investigations suggests that LLLT promotes skeletal muscle regeneration by reducing the duration of acute inflammation and accelerating tissue repair. This would happen through modulated cytokine expression during short-term muscle remodeling, inducing a decrease in TNF- α , TGF- β , and IL-1 β without cytotoxic effects [29, 30].

Our results support these findings since the significant reduction in IL-6 was only observed in the phototherapy group compared with the SHAM group. These results confirm our hypothesis that LLLT can modulate a cascade of reactions to change body homeostasis leading to better association between proinflammatory/anti-inflammatory adipokines, improving health in obese women. LLLT also acts on the markers of oxidative stress, such as protein carbonyls and superoxide dismutase [35, 36], in addition to yielding clinical signs of improvement, delayed muscle fatigue, and improved physical performance [36–39]. Corroborating this, it is known that IL-6 is an important interleukin produced by myocytes to improve muscle repair, and its production is stimulated by resistance training [36]. In fact, it was recently suggested that LLLT in conjunction with aerobic training may provide a therapeutic approach to intensely reduce proinflammatory markers in an experimental study, including a reduction in IL-6 and TNF-alpha. However, LLLT without exercise was not able to improve physical performance in elderly animals [36].

Altogether, these results reinforce the potential effects of LLLT associated with combined training to promote some amelioration in the inflammatory process related to obesity in both animals and humans. Corroborating these findings,

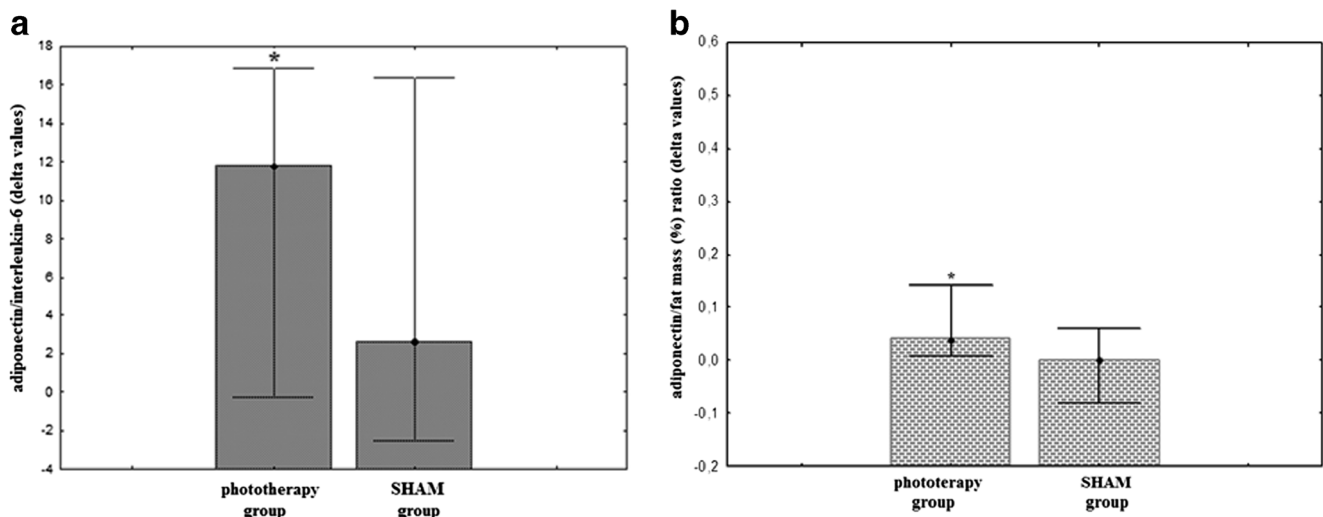


Fig. 4 Comparative effects of interdisciplinary weight loss therapy both groups. Adiponectin/fat mass (%) ratio. Delta value; *statistical difference

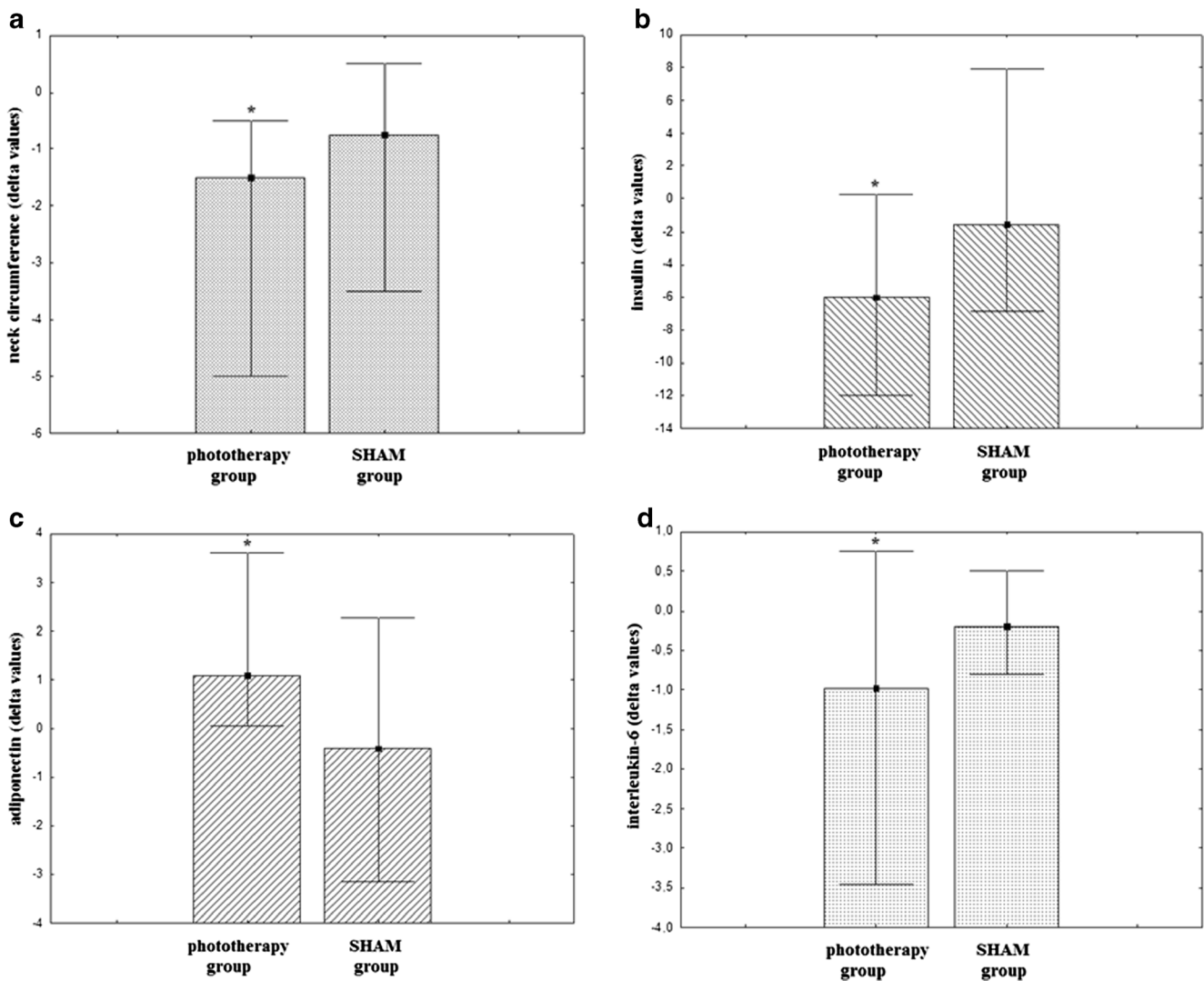


Fig. 5 Comparative effects of interdisciplinary weight loss therapy both groups. **a** Neck circumference, **b** insulin, **c** adiponectin, **d** interleukin-6. Delta values; *statistical difference

in the present study, we observed an increase in adiponectin concentration, a reduction in IL-6 and insulinemia, and a significant improvement in the adiponectin/interleukin-6 ratio, important markers of inflammatory state only in the phototherapy group.

Additionally, we were able to show an increase in the adiponectin/fat mass (kg and %) ratio in the phototherapy group. In fact, results published in the current year suggest that the use of LLLT may enhance cellular homeostasis, promoting an increase in the concentration of active mitochondria in irradiated cells through an upregulation of the genes involved in the mitochondrial complexes [40, 41]. In addition, physical exercise promotes biochemical and structural changes in the mitochondria [42]. Collectively, these results might suggest the hypothesis that phototherapy may help enhance the effects of physical exercise training proposed in the present investigation. The exact mechanisms of action following LLLT are not yet well understood; however, it has been

proposed that the chronic application of LLLT can activate or inhibit enzymes. In this context, it was previously suggested that LLLT intensifies the transfer of electrons within cytochrome-c oxidase by making more electrons available. Thus, it may accelerate oxidative metabolism leading to an increase in ATP synthesis [43].

There has been a recent discovery of irisin which is predominantly secreted by muscle tissue acting as an endocrine organ in response to physical exercise. During physical exercise, peroxisome proliferator-activated receptor coactivator 1 α (PGC1 α) is activated, inducing the release of fibronectin domain-containing protein 5 (FNDC5) which is then cleaved to irisin. This hormone may improve the transdifferentiation of white adipocyte to beige and brown, in both white and brown adipose tissues, by enhancing the lipid mobilization and activating the uncoupling protein 1 (UCP1) in mitochondria, resulting in the synthesis of adenosine triphosphate (ATP) and the dissipation of energy in the form of heat. This

process could promote reductions in body weight and improvements in metabolic profile, suggesting that irisin could be a possible novel treatment for diabetes and obesity [44]. Therefore, it is possible to hypothesize that the combination of LLLT associated with combined exercise in the present study may accentuate the response in the control of fat mass correspondent to a reduction in the inflammatory state, since we were able to show an increase in the adiponectin/fat mass (% and kg) in the phototherapy group. However, this needs to be confirmed in future research with a focus on investigations into the possible influences of LLLT intervention in the transdifferentiation process of white adipocyte to beige and brown associated with exercise training.

Our findings present some limitations, including the absence of experiments with different kinds of laser irradiation. The effects of laser irradiation are highly dependent on characteristics such as wavelength, power density, and fluency [40, 45–47].

However, to our knowledge, the current study is the first investigation to show that LLLT improves the inflammatory process related to obesity in obese women, particularly by promoting a reduction in the proinflammatory IL-6 and an increase in the anti-inflammatory adiponectin, adiponectin/interleukin-6, and adiponectin/fat mass ratio (kg and %). In addition, the LLLT showed higher changes in the control of neck circumference compared with the SHAM group. Interestingly, it was recently suggested that there is growing evidence that neck circumference is considered an interesting marker of inflammation and cardiovascular diseases [48, 49]. Nevertheless, it is important to note that in both analyzed groups, the BMI, body mass, and body fat presented similar changes, considering delta values after 20 weeks of LLLT associated with physical exercise training.

Finally, there are a limited number of clinical studies with the application of LLLT in obesity. However, a number of clinical applications have been found for the lasers in a variety of medical specialties [33]. Therefore, this needs to be confirmed in a large cohort study of the obesity population.

Conclusions

In the present investigation, we were able to show that the association of physical exercise training with low-level laser (light) therapy applied in obese women during a 4-month period promotes an improvement in the inflammatory framework and body composition. These are important results that suggest that phototherapy can be an important tool in the treatment of obesity, principally considering its potential effects associated with physical exercise training in attenuating inflammation in women, and as such, these results are applicable in the clinical practices to control the related risks associated with obesity.

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Conflict of interest The authors have nothing to disclose.

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