



## Trabajo Original

## Obesidad y síndrome metabólico

### Interdisciplinary therapy had positive effects on inflammatory state, mediated by leptin, adiponectin, and quality of diet in obese women

*La terapia interdisciplinaria tuvo efectos positivos en el estado inflamatorio, mediado por la leptina, la adiponectina y la calidad de la dieta en mujeres obesas*

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### Abstract

**Background:** obesity is a chronic disease associated with inadequate eating habits and reduced levels of physical activity. Because of obesity, the risk for comorbidities is increased, especially for cardiovascular diseases, insulin resistance, and increased pro-inflammatory factors. The aim of the present investigation was to analyze potential correlations between pro/anti-inflammatory adipokines, glycemic index, and other markers of diet quality using a metabolic profile in women undergoing interdisciplinary weight loss therapy.

**Methods:** thirty-two women with obesity were enrolled in a 12-week program of interdisciplinary therapy combining a clinical, nutritional, and physical exercise approach. Body composition, quality of diet, metabolic profile, and pro/anti-inflammatory adipokines were analyzed.

**Results:** the therapy showed to be effective in reducing body weight (from  $93.16 \pm 16.96$  to  $88.36 \pm 16.23$ ;  $p = 0.0000001$ ), body mass index (from  $34.01 \pm 4.00$  to  $32.29 \pm 3.96$ ;  $p = 0.0000001$ ), and body fat (from  $38.25 \pm 5.05$  to  $36.13 \pm 5$ ;  $p = 0.0000001$ ). There was also an improvement in lipid profile, including total cholesterol (from  $196.16 \pm 34.78$  to  $183.53 \pm 43.15$ ;  $p = 0.001$ ), non-HDL-cholesterol (from  $142 \pm 30.05$  to  $133.69 \pm 35.41$ ;  $p = 0.01$ ), VLDL-cholesterol (from  $27.13 \pm 12.4$  to  $22.06 \pm 8.55$ ;  $p = 0.002$ ), triglycerides (from  $135.88 \pm 61.21$  to  $110.75 \pm 43.09$ ;  $p = 0.002$ ) and glucose metabolism, including glucose (from  $97.13 \pm 10.43$  to  $92.6 \pm 6.6$ ;  $p = 0.004$ ), and insulin (from  $13.05 \pm 5.54$  to  $11.29 \pm 4.85$ ;  $p = 0.03$ ). As for food intake, there was a decrease in calorie consumption (from  $1991.45 \pm 677.78$  to  $1468.88 \pm 390.56$ ;  $p = 0.002$ ), carbohydrates (from  $50.37 \pm 6$  to  $47.04 \pm 8.67$ ;  $p = 0.04$ ), lipids (from  $31.83 \pm 5.53$  to  $30.37 \pm 7.04$ ;  $p = 0.3$ ), and glycemic load (from  $80.53 \pm 39.88$  to  $54.79 \pm 23.69$ ;  $p = 0.02$ ), and an increased consumption of proteins (from  $18.3 \pm 2.39$  to  $22.89 \pm 4.9$ ;  $p = 0.002$ ). Positive correlations were demonstrated between insulin concentration and waist circumference ( $r = 0.82$ ;  $p = 0.003$ ); leptin and body fat and abdominal circumference ( $r = 0.74$ ;  $p = 0.01$ ); and LDL-cholesterol fraction and total cholesterol consumption ( $r = 0.69$ ;  $p = 0.027$ ). Negative correlations were demonstrated between leptin and monosaturated fat consumption ( $r = -0.71$ ;  $p = 0.02$ ); and adiponectin and liver enzyme GGT levels ( $r = -0.65$ ;  $p = 0.04$ ).

**Conclusions:** interdisciplinary therapy had positive effects on inflammatory state, mediated by leptin, adiponectin, and quality of diet. Our findings suggest the effectiveness and clinical relevance of the interdisciplinary clinical therapy applied for obesity.

### Keywords:

Obesity. Inflammation. Interdisciplinary intervention. Food intake. Physical exercise.

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## Resumen

**Introducción:** la obesidad es una enfermedad crónica asociada con hábitos alimentarios inadecuados y niveles reducidos de actividad física. Debido a la obesidad, el riesgo de comorbilidad aumenta, especialmente el de las enfermedades cardiovasculares, la resistencia a la insulina y el aumento de los factores proinflamatorios. El objetivo de la presente investigación fue analizar las posibles correlaciones entre las adipocinas pro/antiinflamatorias, el índice glucémico y otros marcadores de calidad de la dieta con el perfil metabólico en mujeres sometidas a terapia interdisciplinaria para perder peso.

**Métodos:** treinta y dos mujeres con obesidad participaron en 12 semanas de terapia interdisciplinaria en la que se combinaron los enfoques clínico, nutricional y de ejercicio físico. Se analizaron la composición corporal, la calidad de la dieta, el perfil metabólico y las adipocinas pro/antiinflamatorias.

**Resultados:** la terapia demostró ser efectiva para reducir el peso corporal (de  $93,16 \pm 16,96$  a  $88,36 \pm 16,23$ ;  $p = 0,0000001$ ), el índice de masa corporal (de  $34,01 \pm 4,00$  a  $32,29 \pm 3,96$ ;  $p = 0,0000001$ ) y la grasa corporal (de  $38,25 \pm 5,05$  a  $36,13 \pm 5,00$ ;  $p = 0,0000001$ ). También hubo una mejora del perfil lipídico, incluidos el colesterol total (de  $196,16 \pm 34,78$  a  $183,53 \pm 43,15$ ;  $p = 0,001$ ), el colesterol no HDL (de  $142,00 \pm 30,05$  a  $133,69 \pm 35,41$ ;  $p = 0,01$ ), el VLDL-colesterol (de  $27,13 \pm 12,4$  a  $22,06 \pm 8,55$ ;  $p = 0,002$ ), y el metabolismo de la glucosa, incluyendo la glucosa (de  $97,13 \pm 10,43$  a  $92,6 \pm 6,6$ ;  $p = 0,004$ ) y la insulina (de  $13,05 \pm 5,54$  a  $11,29 \pm 4,85$ ;  $p = 0,03$ ). En cuanto a la ingesta de alimentos, hubo disminución en el consumo de calorías (de  $1991,45 \pm 677,78$  a  $1468,88 \pm 390,56$ ;  $p = 0,002$ ), carbohidratos (de  $50,37 \pm 6,00$  a  $47,04 \pm 8,67$ ;  $p = 0,04$ ), lípidos (de  $31,83 \pm 5,53$  a  $30,37 \pm 7,04$ ;  $p = 0,3$ ) y carga glucémica (de  $80,53 \pm 39,88$  a  $54,79 \pm 23,69$ ;  $p = 0,02$ ), y aumento del consumo de proteínas (de  $18,3 \pm 2,39$  a  $22,89 \pm 4,90$ ;  $p = 0,002$ ). Se demostraron correlaciones positivas entre la concentración de insulina y la circunferencia de la cintura ( $r = 0,82$ ;  $p = 0,003$ ); la leptina, la grasa corporal y la circunferencia abdominal ( $r = 0,74$ ;  $p = 0,01$ ), y la fracción de colesterol LDL y el consumo total de colesterol ( $r = 0,69$ ;  $p = 0,027$ ). Se demostraron correlaciones negativas entre la leptina y el consumo de grasa monosaturada ( $r = -0,71$ ;  $p = 0,02$ ), y la adiponectina y la enzima hepática GGT ( $r = -0,65$ ;  $p = 0,04$ ).

**Conclusiones:** la terapia interdisciplinaria tuvo efectos positivos sobre el estado inflamatorio, mediado por la leptina, la adiponectina, y la calidad de la dieta. Nuestros hallazgos sugieren la efectividad y la relevancia clínica de la terapia clínica interdisciplinaria aplicada a la obesidad.

### Palabras clave:

Obesidad.  
Inflamación.  
Intervención interdisciplinaria.  
Ingesta de alimentos.  
Ejercicio físico.

## INTRODUCTION

Obesity has been increasing in the last decades across the world and presents a major challenge to chronic disease prevention and health. Improper eating habits with high-carbohydrate and high-fat diets and sedentary lifestyle are two main reasons for the increase in the prevalence of the disease (1-3).

It was well known that severe obesity was characterized by a state of chronic low-grade inflammation that increased the development of other chronic diseases, including cardiovascular disease, diabetes mellitus, non-alcoholic fatty liver disease, chronic kidney disease, many cancers, and an array of musculoskeletal disorders (1,3-7).

The inflammatory process present in obesity may induce a state of hyperleptinemia and low adiponectin concentration. It means that both altered hormonal conditions may be an important contributor to increased risk for metabolic diseases, including atherosclerosis, in adolescent and adult populations (8,9).

Moreover, the nutritional profile plays a determinant role in obesity-related inflammatory processes (10). In fact, it was previously shown that an increase in saturated fat intake and a diet with a high glycemic index may induce the expression of inflammatory molecules, and may also accentuate inflammatory status in obesity (11).

Additionally, it is currently known that the hypothalamus is affected during the early stages of obesity (12). The variation in energy depot size acts on the hypothalamus through circulating signals that regulate food intake (13). Excessive consumption of saturated fat may increase hypothalamic inflammation, which may alter orexigenic/anorexigenic pathway function as well as food intake regulation and energy expenditure. Consequently, lesions in this brain area have a rather unremarkable impact on these parameters, leading to a vicious cycle between food consumption and obesity (13).

Therefore, we aimed to analyze potential correlations between pro-/anti-inflammatory adipokines, leptin, and adiponectin with glycemic index and other markers of diet quality with the metabolic profile in women undergoing interdisciplinary weight loss therapy.

## MATERIAL AND METHODS

This study consisted of a 12-week interdisciplinary weight loss therapy, with a clinical approach including a nutritionist and an exercise physiologist, and was approved by the Ethics and Research Committee at the Federal University of São Paulo (CEP nº 1013/2019). All volunteers signed an informed consent form.

## POPULATION

Thirty-two women ( $31 \pm 4$  years) were recruited from ads served in the media (newspapers, magazines, radio, television, and social media: Instagram®). Enrollment was performed for women who lived in the city of São Paulo or nearby, so they could attend meetings. The volunteers underwent clinical, nutritional, and physical exercise evaluations and educational sessions every month, supporting adherence.

Besides that, the volunteers followed weekly the instructions found in the platform #12Semanas® to complete the Education Behaviors Program. The volunteers must be women aged 20 to 45 years, with a body mass index (BMI) above  $30 \text{ kg/m}^2$ , classified as obesity according to the World Health Organization (WHO). They could not present any pathology that could influence or compromise the results of the research (heart disease, musculoskeletal deformities, diseases related to the immune system, genetic, metabolic or endocrine diseases, as identified by the physician).

## INTERDISCIPLINARY THERAPY

Once included in the study, the volunteers were evaluated at baseline and at the end of the intervention (week 12) by a health team including an endocrinologist, a nutritionist, and an exercise physiologist. The target weight loss was 5 % to 10 % with changes in eating habits and physical exercise that were taught during treatment. In the baseline and final periods, weight, height, and waist, hip and neck circumferences were evaluated. Body composition, nutritional assessment, physical activity level, and blood pressure at rest evaluations were performed. Blood samples were collected for biochemical testing. During treatment, the study volunteers received support including doubt solving and orientation, either in groups or individually, when necessary as part of the interdisciplinary clinical approach (1<sup>st</sup> and 12<sup>th</sup> weeks). They received electronic support and educational videos about eating, exercising, and healthy habits every week.

## ANTHROPOMETRIC MEASURES AND BODY COMPOSITION

Body mass was measured with the patients using light clothes and barefoot on a Filizola® (São Paulo, Brazil) mechanical anthropometric scale with a maximum capacity of 150 kg and a sensitivity of 100 g. Height was measured with a Sanny® brand stadiometer (São Paulo, Brazil) with a precision scale of 0.1 cm. Subsequently, body mass index (BMI) was calculated using the formula: body mass (kg) times height (m) squared.

Neck, waist, abdominal, and hip circumferences were measured with a flexible and inelastic tape. Body composition was measured with a bio-impedance meter (BIA) and a basal metabolic rate estimation was provided by a BIODYNAMICS 310e device (TBW®, Shoreline, USA).

## SERUM ANALYSIS

Blood samples were collected after a 12-hour overnight fast. The serum was separated, and glucose, insulin, triglycerides (TG), total cholesterol (TC), high-density lipoprotein-cholesterol (HDL-c), low-density lipoprotein-cholesterol (LDL-c), very low-density lipoprotein-cholesterol (VLDL-c), and hepatic transaminases such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), and gamma-glutamyltransferase (GGT) levels were determined by enzymatic colorimetric methods (CELM) immediately after blood collection. Serum samples were stored at -80 °C for subsequent adipokine testing. An enzyme-linked immuno-sorbent assay (ELISA) measured leptin concentration (RD191001100, Bio Vendor) and adiponectin concentration (RD195023100, Bio Vendor, Melbourne, Australia).

Insulin resistance was determined using the homeostasis model of assessment for insulin resistance (HOMA-IR), and was calculated with the following formula: [fasting glucose (mmol/L) x fasting insulin (μU/L)] / 22.5 (14). According to the cutoff point determined for the Brazilian population, HOMA-IR values above

2.71 were considered markers of insulin resistance (IR) (15). The homeostasis model of assessment-adiponectin (HOMA-AD) was calculated as follows: [fasting glucose (mmol/L) x fasting insulin (μU/L)] / [22.5 x fasting adiponectin (μg/mL)] (16).

## INTERDISCIPLINARY INTERVENTION

### Clinical therapy

Medical follow-up involved the initial clinical history, physical examination with blood pressure, heart rate, and body composition, and checking for adherence to all the interdisciplinary therapies administered. Volunteers underwent two in-clinic medical monitoring sessions, at baseline and at the end of the interdisciplinary therapy.

### Nutritional therapy

Volunteers participated in group and individual interventions conducted by nutritionists. Monthly, all patients received individual nutritional counseling and relevant healthy nutrition topics were discussed, including principles of healthy eating, differences between hunger and satiety, importance of understanding these sensations for body weight control, phases of weight loss with their characteristics and fundamentals, food behavior and nutrition, and guidelines for achieving continuous weight loss and weight maintenance.

Furthermore, according to the basal metabolic rate (BMR) obtained by the bioimpedance test, volunteers were allocated to 4 groups for calorie consumption guidelines according to energy needs: group 1 (BMR between 1400 and 1600; they received a 1400-kcal menu); group 2 (BMR between 1600 and 1800; a 1600-kcal menu); group 3 (BMR between 1800 and 2000; 1800-kcal menu); group 4 (BMR > 2000; 2000-kcal menu). These menus were planned with suggestions of food groups and contemplated daily intake following the energy distribution recommended by the FAO/WHO, 2003 for proteins (10-15 %), lipids (15-30 %), and carbohydrates (55-75 %).

Energy intake was set at the levels recommended by the dietary reference intake for subjects using dietary reference intake equations according to low levels of physical activity based on age and patient gender. Each participant filled in a three-day dietary record at baseline and at the end of therapy. These dietary data were transferred to a computer by the nutritionist, and the nutrient composition was analyzed by the computer program Diet Smart (Diet Smart Copyright®, 2012-2018), based on western and local food tables. No pharmacotherapy, antioxidants, or supplements were recommended.

### Physical activity

During the twelve weeks of interdisciplinary therapy the volunteers received weekly physical exercise orientation via a website,

with demonstrative videos for exercises and educational text to improve lifestyle changes (> 150 min/week). Moreover, the exercise physiologist provided information regarding the frequency, duration, and type of physical exercise, and recommended the monitoring of heart rate. The exercise program included endurance, resistance, flexibility, and balance. The Borg Scale was used to monitor training intensity (17). Body composition variables and basal metabolic rate were used by the physiologist to recommend exercise training and promote adherence, and to facilitate the choice of the modality to be practiced by volunteers. The program followed the recommendations given by the American College of Sports Medicine (18,19).

- 4) learn to choose physical exercise according to your identity;
- 5) make the right choice and learn to eat healthy;
- 6) use the food pyramid in your favor;
- 7) the importance of dietary fractionation;
- 8) learn how to assemble your dish by combining foods efficiently;
- 9) slow chewing is one of the steps to weight loss success; and
- 10) learn to drink water.

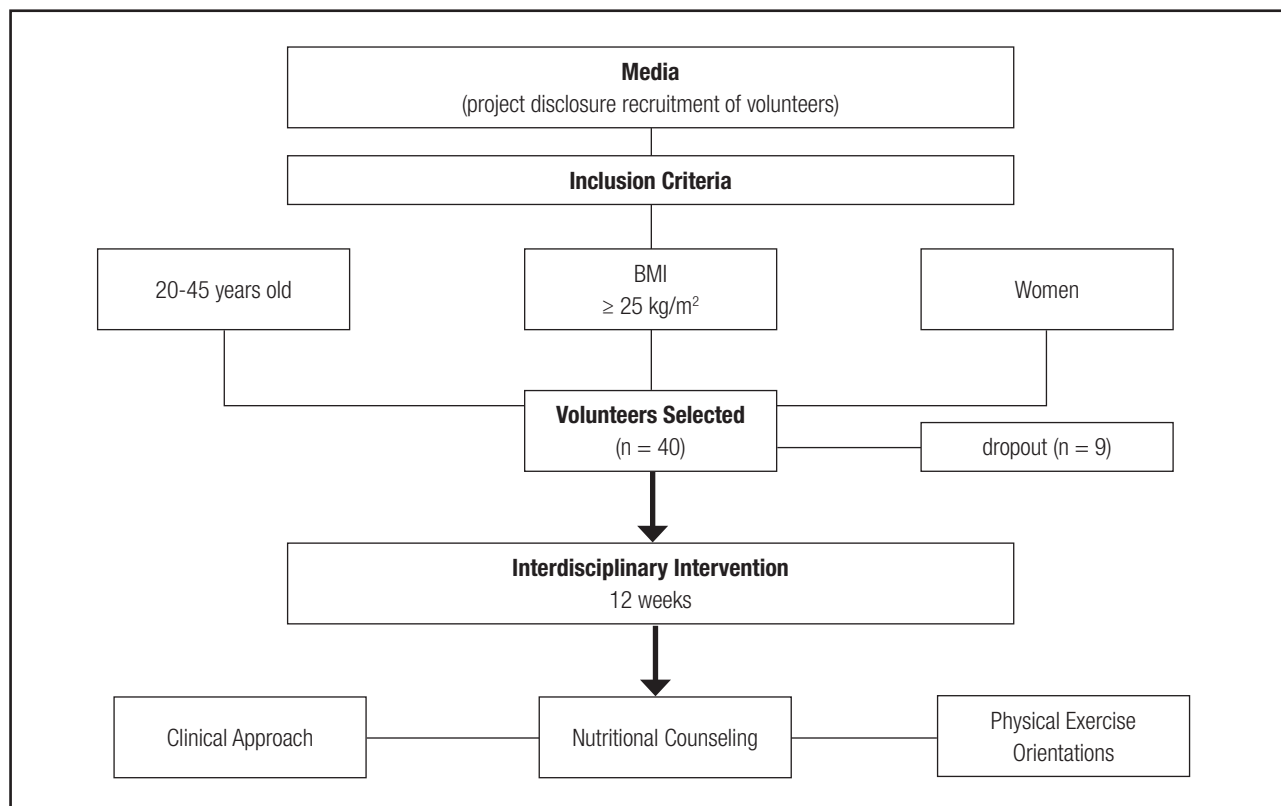
In addition, the volunteers needed to fill out the session form weekly for the professionals to observe how they were involved and to allow interactions with the other volunteers as motivational strategies (Fig. 1).

### TOPICS COVERED VIA THE WEBSITE

In the web support weekly interval-modified exercises were suggested for a better way to improve results. The motivation of the volunteers was built up through conversations with the exercise physiologist and nutrition professionals via chat, WhatsApp® groups, and also videos and explanatory texts on various themes including: 1) nutrition, physical exercise and motivation; 2) esthetics is the consequence of the search for health; 3) sedentary lifestyle can increase expression of a gene responsible for obesity;

### STATISTICAL ANALYSIS

The statistical analysis was performed using the program STATISTICA version 7.0 for Windows. The adopted significance value was  $\alpha \leq 5\%$ . Sample size was obtained considering the variable glycemic index, and was performed using the program G\*Power 3.1.9.2; significance level was 0.05, test power was 0.80, and effect size was 0.35. Data normality was verified with the Shapiro-Wilk test. Parametric data were expressed as mean  $\pm$  SD, and non-parametric were assessed for normality using Z-score values. To analyze the effects of the intervention a t-test was used; for dependent samples Pearson's correlation analysis test was applied. For sample size the



**Figure 1.**

Methodological design of the interdisciplinary clinical approach to improve health habits in women with obesity.

G\*Power v. 3.0.10 program was used and the t-test was adopted. Significance level was 5 %, test power was 85 %, and effect was 0.5. The sample size obtained was of 31 volunteers submitted to the interdisciplinary intervention for 12 weeks.

**RESULTS**

**EFFECTS OF THE INTERDISCIPLINARY THERAPY ON BODY COMPOSITION**

The therapy model used was shown to be effective in reducing body weight, body mass index, body circumferences, and body fat. Moreover, lean body mass was maintained (Table I).

**EFFECTS OF THE INTERDISCIPLINARY THERAPY ON LIPID PROFILE**

In relation to metabolic variables the therapy achieved significantly decreased values of total cholesterol, high-density lipo-

protein cholesterol (HDL-cholesterol), non-high-density lipoprotein cholesterol (non-HDL-cholesterol), low-density lipoprotein cholesterol (LDL-cholesterol), very low-density lipoprotein cholesterol (VLDL-cholesterol), and triglycerides (TG) (Table II).

**EFFECTS OF THE INTERDISCIPLINARY THERAPY ON GLUCOSE METABOLISM, INSULIN, INFLAMMATORY PROFILE, AND HEPATIC ENZYMES**

Interestingly, in the present investigation were found significantly decreased values of metabolic, hormonal, and inflammatory biomarkers, including insulin, leptin concentration, homeostatic model of assessment-insulin resistance (HOMA-IR), and homeostasis model of assessment-adiponectin (HOMA-AD). However, no changes in hepatic enzymes were observed. However, it is important to note that these had normal values at baseline and after therapy. Adiponectin and leptin/adiponectin ratio remained unchanged (Table III).

**Table I. Body composition of obese women submitted to interdisciplinary therapy**

	Baseline			After therapy			
	media	±	SD	media	±	SD	p-value
Body weight (kg)	93.16	±	16.96	88.36	±	16.23	0.0000001
Body mass index (kg/m <sup>2</sup> )	34.01	±	4	32.29	±	3.96	0.0000001
Neck circumference (cm)	36.41	±	1.97	35.32	±	1.77	0.00
Waist circumference (cm)	95.47	±	8.91	90.22	±	8.16	0.00
Abdominal circumference (cm)	107.13	±	8.84	102.13	±	8.81	0.00
Hip circumference (cm)	120.05	±	9.73	115.73	±	9.04	0.00
Waist/hip ratio	0.79	±	0.07	0.78	±	0.06	0.02
Fat body mass (%)	38.25	±	5.05	36.13	±	5	0.0000001
Lean body mass (kg)	57.40	±	7.46	56.67	±	9.17	0.36

Values expressed as mean ± SD. Statistical significance: p ≤ 0.05; p-values refer to comparison of baseline vs post-therapy values in the same group. Reference values: body mass index, 18.5-24.9 kg/m<sup>2</sup> (20); waist/hip ratio, < 0.85; abdominal circumference, < 88 cm (21).

**Table II. Biochemical profile of obese women submitted to interdisciplinary therapy**

	Baseline			After intervention			
	media	±	SD	media	±	SD	p-value
Total cholesterol (mg/dL)	196.16	±	34.78	183.53	±	43.15	0.001
HDL-cholesterol (mg/dL)	52.55	±	13.3	51.32	±	11.37	0.25
Non-HDL-cholesterol (mg/dL)	142	±	30.05	133.69	±	35.41	0.01
LDL-cholesterol (mg/dL)	114.91	±	26.98	111.63	±	31.81	0.3
VLDL-cholesterol (mg/dL)	27.13	±	12.4	22.06	±	8.55	0.002
Triglycerides (mg/dL)	135.88	±	61.21	110.75	±	43.09	0.002

Values expressed as mean ± SD. Statistical significance: p ≤ 0.05; p-values refer to comparison of baseline vs post-therapy values in the same group. Reference values: total cholesterol, < 190 mg/dL; high-density lipoprotein (HDL)-cholesterol, > 40 mg/dL; low-density lipoprotein (LDL)-cholesterol, < 100-130 mg/dL; very low-density lipoprotein (VLDL)-cholesterol, 10-50 mg/dL; triglycerides (TG), < 150 mg/dL (22,23).

**Table III.** Glucose metabolism, insulin, inflammation, and hepatic enzyme profiles of obese women submitted to interdisciplinary therapy

	Baseline			After intervention			p-value
	media	±	SD	media	±	SD	
AST enzyme (U/L)	16.03	±	5.26	15.71	±	5.03	0.76
ALT enzyme (U/L)	16.83	±	9.50	17.77	±	10.32	0.53
GGT enzyme (U/L)	23.53	±	15.02	21.19	±	11.26	0.25
Glucose (mg/dL)	97.13	±	10.43	92.58	±	6.6	0.004
Insulin (uIU/mL)	13.05	±	5.54	11.29	±	4.85	0.03
Adiponectin (µg/mL)	4.76	±	2.66	4.02	±	2.17	0.15
Leptin (ng/mL)	68.51	±	22.38	58.16	±	30.53	0.02
Lep/adipo ratio	20.47	±	14.23	18.02	±	12.02	0.35
HOMA - IR	3.09	±	1.59	2.51	±	1.19	0.01
HOMA-AD	13.35	±	10.60	10.32	±	9.36	0.02

Values expressed as mean ± SD. Statistical significance:  $p \leq 0.05$ ; p-values refer to comparison of baseline vs post-therapy values in the same group. Reference values: alanine aminotransferase (ALT), < 40 U/L; aspartate aminotransferase (AST), < 40 U/L; gamma-glutamyltransferase (GGT), > 38 U/L; insulin, 2.5-30.0 µIU/mL; HOMA-IR, < 2.7 (15,24).

### EFFECTS OF THE INTERDISCIPLINARY THERAPY ON FOOD INTAKE

The interdisciplinary therapy was effective to promote a reduction in food intake of carbohydrates, lipids, saturated and monosaturated fat. Additionally, protein intake was increased and dietary glycemic load was significantly reduced (Table IV).

### CORRELATION ANALYSES

In the present study positive correlations were demonstrated between insulin concentration and waist circumference ( $r = 0.82$ ;  $p = 0.003$ ); leptin concentration and abdominal circumference ( $r = 0.74$ ;  $p = 0.01$ ), and LDL-cholesterol and total cholesterol consumption ( $r = 0.69$ ;  $p = 0.027$ ). Negative correlations were demonstrated between leptin concentration and monosaturated fat consumption ( $r = -0.71$ ;  $p = 0.02$ ). Additionally, a negative correlation was also found between adiponectin concentration and GGT ( $r = -0.65$ ;  $p = 0.04$ ) (Fig. 2).

### DISCUSSION

The aim of the present investigation was to analyze potential correlations between pro/anti-inflammatory adipokines, glycemic index, and other dietary markers using the metabolic profile in women undergoing an interdisciplinary therapy for weight loss. Therefore, the most important finding was that the interdisciplinary therapy administered had positive effects on the inflammatory state, mediated by leptin, adiponectin, and improved diet quality.

Interestingly, in the present study we were able to obtain a reduction in both HOMA-IR and HOMA-AD; and importantly, evidence strongly suggests that improving this biomarker of inflammation plays a key role in the prevention of many chronic diseases, including obesity and diabetes (25,26). Moreover, previous research by our team showed that insulin resistance is the most commonly altered parameter in obesity, thus increasing the chances of developing dyslipidemia, atherosclerosis, non-alcoholic fatty liver disease, respiratory disease, metabolic disorders, cardiovascular disease, and type-2 diabetes (25-28).

These issues occur in association with low adiponectin concentration. In fact, the present study found a negative correlation between adiponectin concentration and hepatic GGT. Together, these results reinforce the importance that improving these risk factors has in obesity and its related comorbidities.

Additionally, we were able to show a decrease in carbohydrate consumption associated with an increase in protein intake. These improvements in food consumption are important as nutritional strategies in the prevention not only of obesity, but also of many other chronic diseases, including diabetes (29). Interestingly, glycemic load was reduced thus favoring insulin and glucose homeostasis. These results may partially explain the reduction in HOMA-IR and HOMA-AD observed in the present investigation, which contributed to controlling the pro-inflammatory state present in obesity.

Moreover, it is important to note that in the present study women reduced their lipid intake, including saturated and monosaturated fatty acids. Excessive saturated fat intake is related to increases in the inflammatory state associated with obesity and many chronic diseases, including cardiovascular diseases. In addition, associations have been reported between high glycemic index diet and raised inflammatory status in people with obesity (30).

**Table IV.** Food intake of women with obesity submitted to interdisciplinary therapy

	Baseline			After intervention			p-value
	media	±	SD	media	±	SD	
Calories (kcal)	1991.45	±	677.78	1468.88	±	90.56	0.002
Carbohydrate (g)	239.47	±	82.74	167.31	±	47.38	0.00
Carbohydrate (%)	50.37	±	6.01	47.05	±	8.66	0.04
Fiber (g)	20.29	±	10.66	15.49	±	5.56	0.03
Protein (g)	88.14	±	28.83	82.02	±	24.34	0.38
Protein (%)	18.3	±	2.39	22.89	±	4.9	0.002
Lipid (g)	72.02	±	30.03	51.64	±	22.83	0.00
Lipid (%)	31.83	±	5.53	30.37	±	7.04	0.3
Saturated (g)	21.77	±	10.67	16.38	±	8.24	0.05
Monosaturated (g)	19.93	±	10.48	14.41	±	8.13	0.04
Polysaturated (g)	21.79	±	48.24	7.73	±	3.72	0.20
Cholesterol (g)	365.46	±	158.11	378.48	±	196.34	0.82
Sodium (mg)	2146.38	±	1001.44	1657.93	±	486.51	0.06
Vitamin A (mcg)	1153.54	±	1692.14	1399.74	±	4472.82	0.82
Vitamin D (mcg)	125.88	±	321.66	46.85	±	151.56	0.35
Vitamin B6 (mg)	1.31	±	0.64	1.3	±	0.46	0.9
Vitamin B12 (mcg)	9.74	±	14.09	10.33	±	29.97	0.94
Folic acid (mcg)	164.59	±	99.42	149.83	±	73.39	0.53
Calcium (mg)	710.76	±	354.81	588.03	±	194.69	0.09
Iron (mg)	12.96	±	5.78	955	±	4.6	0.03
Zinc (mg)	9.02	±	5.49	7.95	±	3.16	0.45
Copper (mg)	1.25	±	1.08	0.99	±	0.84	0.42
Selenium (mcg)	40.52	±	27.87	40.42	±	31.41	0.99
Glycemic index	495.56	±	146.71	507.47	±	141.97	0.77
Glycemic load	80.53	±	39.88	54.79	±	23.69	0.02

Values expressed as mean ± SD. Statistical significance:  $p \leq 0.05$ ; p-values refer to comparison of baseline vs post-therapy values in the same group.

Conversely, a high consumption of saturated fat was found to increase serum cholesterol, hence cardiovascular risk, whereas polyunsaturated fat (PUFA) may reduce both. Thus, the reduction in saturated fat intake observed in the present investigation may protect this population by reducing the morbidity and mortality previously reported other researchers (31).

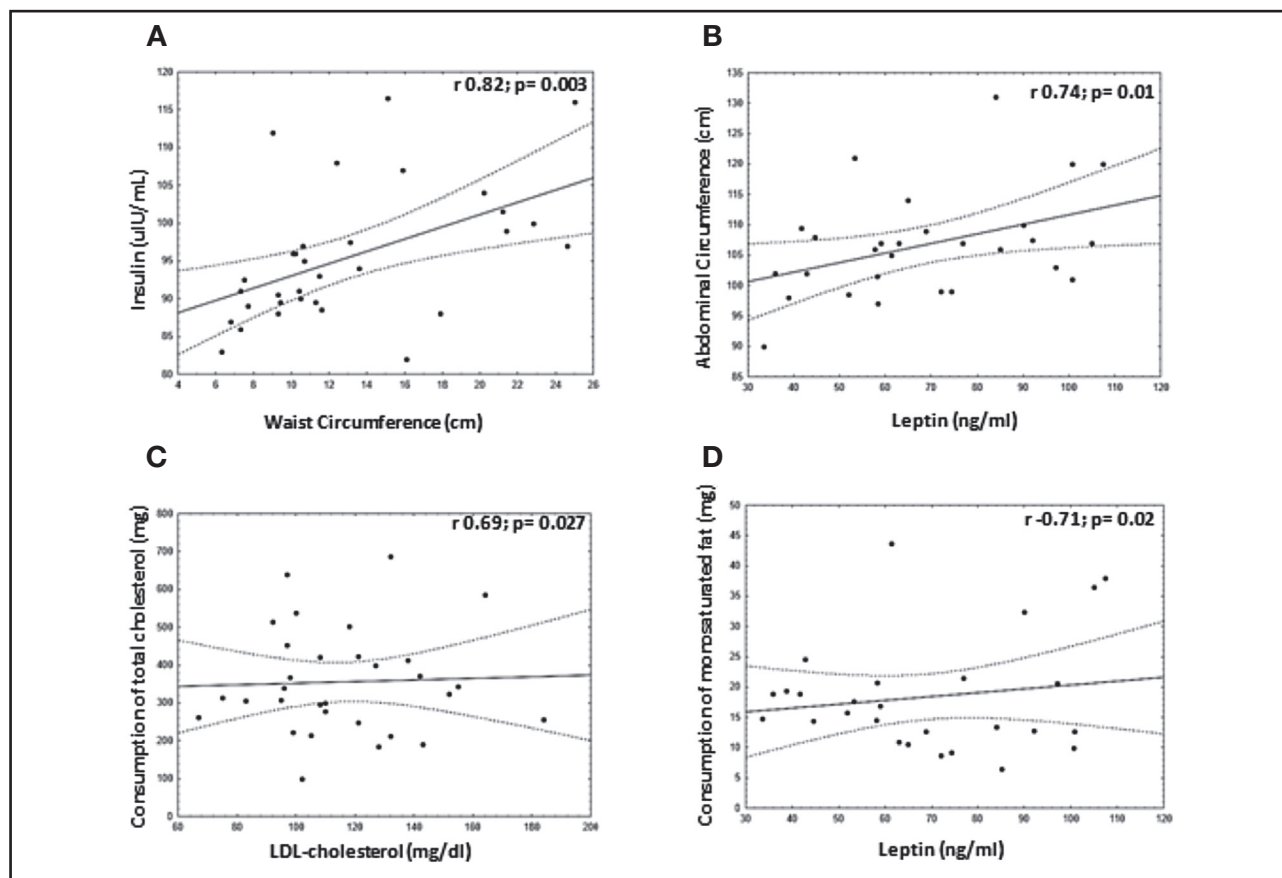
It is also known that diet-derived saturated fatty acids increase the expression of IL-6 and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), which are pro-inflammatory cytokines, whereas consumption of a diet rich in monounsaturated fatty acids results in a more anti-inflammatory profile. Moreover, acute n-3 PUFA dietary supplementation has been shown to improve fasting as well as postprandial lipid metabolism and components of the associated inflammatory response (32).

Interestingly, in the present study we found an improvement in lipid profile, including a reduction in total cholesterol, VLDL cholesterol, triglycerides, and non-HDL cholesterol. In fact, the

reduction in cholesterol consumption presented a positive correlation with LDL cholesterol. Together, all these results reinforce the importance of diet quality for improving the inflammatory process related to obesity and its comorbidities.

Another important result observed in the present study was a positive correlation between insulin levels and both waist circumference and waist/hip ratio, which confirmed the role of this hormone as a trigger for central obesity. However, it is important to note that insulin concentration was significantly decreased in this analyzed population.

In fact, the reduction in insulin concentration may protect against the development of many chronic diseases mediated by adiponectin, including diabetes, atherosclerosis, and non-alcoholic fatty liver disease (NAFLD). In this way, negative correlations were demonstrated between adiponectin and hepatic GGT, thus confirming the importance of adiponectin as a key factor in the all-inflammatory process present in obesity.



**Figure 2.**

Correlations identified among studied variables: A. A positive correlation was demonstrated between insuline concentration and waist circumference:  $r = 0.82$ ,  $p = 0.003$ . B. A positive correlation was demonstrated between leptin concentration and abdominal circumference:  $r = 0.74$ ,  $p = 0.01$ . C. A positive correlation was demonstrated between the low-density lipoprotein (LDL) cholesterol fraction and total cholesterol consumption:  $r = 0.69$ ,  $p = 0.027$ . D. A negative correlation was demonstrated between leptin concentration and monosaturated fat consumption:  $r = -0.71$ ,  $p = 0.02$ .

Furthermore, it has been suggested that lipid accumulation in the liver may be a cause of insulin resistance via a local increase in lipogenesis and hepatic insulin resistance, leading to further compensatory hyperinsulinemia and hyperglycemia in adolescents with obesity (33).

We have previously showed that adolescents with obesity present a high prevalence of NAFLD that may reach 50 %, and this might be reduced following a long-term interdisciplinary approach (28,34). In the same investigation, insulin resistance and visceral fat were the independent risk factors.

Another interesting result from the present study was a significant reduction in leptin concentration. Moreover, leptin concentration in the present investigation was negatively correlated with monosaturated fat consumption. However, it is important to note that the analyzed population maintained a state of hyperleptinemia, which may partially explain the fact that adiponectin concentration was not increased.

A positive correlation between leptin, body fat, and abdominal circumference was found. In fact, we had previously shown that

hyperleptinemia and reduced levels of adiponectin may impair the increase in carotid intima-media thickness (cIMT), thus confirming the role of these hormones in the pro-inflammatory state related to obesity (35).

Limitations of the present study include a small sample size, short intervention period (only 12 weeks), lack of control group, and recording of physical activity. Moreover, the role of epigenetics was not explored. Secondly, the Brazilian database does not include all of the 45 food parameters that may be calculated. In conclusion, in the present investigation we showed that an interdisciplinary therapy had positive effects on the obesity-related inflammatory state mediated by leptin, adiponectin, and diet quality, including a decrease in glycemic load and saturated fat ingestion, and an increase in protein intake. Our findings suggest the effectiveness and clinical relevance of an interdisciplinary clinical therapy applied to obesity. However, it needs to be confirmed in the long term with a large cohort study to completely elucidate and understand the exact mechanisms involved in the role played by the glycemic index and glycemic load in the control of the inflammatory state related to obesity.



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