Obese adolescents with eating disorders: Analysis of metabolic and inflammatory states

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Abstract

Objective: The purpose of the present investigation was to compare the effect of interdisciplinary therapy on the physical and metabolic profiles, including body composition, insulin resistance and sensitivity as well as adiponectin and leptin concentrations, of obese adolescents with and without eating disorder symptoms.

Methods: A total of 83 obese adolescents (28 with and 55 without eating disorder symptoms) were enrolled for 1 year of interdisciplinary weight-loss therapy (clinical, nutritional, exercise, physiotherapy and psychological). Bulimic and binge eating symptoms were measured by the Bulimic Investigatory Test, Edinburgh, and the Binge Eating Scale, respectively. Leptin and adiponectin concentrations were measured with enzyme-linked immunosorbent assay kits. Visceral and subcutaneous fat were assessed by ultrasonography.

Results: Both groups demonstrated improved body mass, body mass index, body fat (%), lean mass, visceral fat, subcutaneous fat, homeostasis model assessment insulin-resistance index (HOMA-IR), quantitative insulin sensitivity check index, total cholesterol, LDL-cholesterol, VLDL, triglycerides, adiponectin and leptin concentrations after therapy. We found a positive correlation between leptin concentrations and subcutaneous fat in the control group and a negative correlation between adiponectin concentrations and HOMA-IR and fat mass (%). The prevalence of obese adolescents with eating disorders was reduced by 89% after 1 year of interdisciplinary therapy.

Conclusion: The eating disorder symptoms did not impair the metabolic state during weight loss therapy of obese adolescents. Additionally, long-term interdisciplinary therapy was effective in reducing the chances of developing several co-morbidities in both groups.

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disorders can present different concentrations of leptin from other individuals. Serum leptin concentrations are higher in obese patients with binge eating disorders than in those without binge eating disorders [7]. Because of the effects of leptin, this hormone may contribute to the development of diabetes mellitus and hypertension, increasing the chances of individuals to develop atherosclerosis [6].

Adiponectin is an anti-inflammatory protein that is secreted by adipose tissue. It increases insulin sensitivity and the oxidation of free fatty acids. Adiponectin concentrations inversely correlate with body fat and are reduced in obese subjects. These low concentrations of adiponectin are related to cardiovascular disease and metabolic syndrome [8]. Study suggests that abnormal eating behavior in patients with eating disorders may reduce circulating levels of adiponectin [9].

Multidisciplinary programs for weight loss usually display good results in obese children and adolescents, bringing beneficial changes to body composition, aerobic fitness and hormone concentrations [10–13]. Nevertheless, the literature demonstrates a relationship between binge eating, body image, depression and self-efficacy [14,15]. Negative emotional states are highly prevalent in obese individuals and predict poor outcomes in the treatment for weight loss [14]. Additionally, low levels of psychological distress may promote weight stability [16].

Levine et al. [17] shows that treatment for weight loss in children is not disrupted by the presence of eating disorders [17]. However, concerns with body shape is associated with less weight loss. In contrast, Goossens et al. (2009) demonstrates that pathological eating behavior can affect the outcome of obesity treatment in children and adolescents [18].

Considering the greater difficulty of individuals with eating disorders to control their behavior and who therefore present a worse metabolic state, as well as the small number of scientific studies evaluating obese adolescents with eating disorders, the purpose of the present investigation was to compare the effects of interdisciplinary therapy on the physical and metabolic profiles (including body composition, insulin resistance, insulin sensitivity and adiponectin and leptin concentrations) of obese adolescents with and without eating disorder symptoms.

2. Methods

2.1. Study population

For the present study, we selected adolescents who participated in the GEO (Interdisciplinary Obesity Program) of the Federal University of São Paulo in recent years. Therefore, our initial sample was 128 adolescents. Of these 128 participants, we excluded those who did not complete therapy for reasons such as having found work, changes in school hours, lack of motivation and lack of money for transportation, as well as patients who did not perform all necessary examinations for this study in three stages of evaluation. Ultimately, a total of 83 obese adolescents (28 with eating disorder symptoms and 55 without eating disorder symptoms) were evaluated in this study. There were 21 boys and 34 girls without eating disorder symptoms and 7 boys and 21 girls with eating disorder symptoms.

The GEO project has occurred every year since 2004 in São Paulo, Brazil. At the beginning of each year, the project is published in newspapers and magazines from São Paulo to recruit adolescents. The inclusion criteria for participating in this program for weight loss were as follows: post-pubertal adolescents presenting obesity who are healthy enough to perform physical activity and to want and to be available to participate in the program for 1 year. The exclusion criteria were limitations such as an identified genetic disease, metabolic or endocrine diseases, chronic alcohol consumption and previous use of drugs, such as glucocorticoids and psychotropics, or pregnancy.

All adolescents were aged from 15 to 19 years, presented obesity (BMI ≥95th percentile, according to the Center for Disease Control and Prevention) and were considered post-pubertal (Tanner Stage = 5). The endocrinologist assessed the Tanner stage, appointing the figure that best identified the stage of sexual maturation for each adolescent [19]. Before performing any examination for inclusion in the project, all adolescents completed the effort electrocardiogram test to verify whether they could safely perform exercise.

We considered patients with eating disorders who presented severe or moderate symptoms of bulimia nervosa (score 10–19: unusual eating behavior or score ≥20: presence of binge eating behavior with a high chance of diagnosing bulimia nervosa) according to the Bulimic Investigatory Test, Edinburgh (BITE) and/or who presented severe or moderate symptoms of binge eating (score 18–26: moderate or score ≥27: severe) according to the Binge Eating Scale (BES).

This study was performed in accordance with the principles of the declaration of Helsinki and was formally approved by the Ethical Committee of the Federal University of São Paulo, Paulista Medicine School (#0135/04). Informed consent was obtained from all subjects and/or their parents.

2.2. Research design

During the first month the adolescents were submitted to all evaluations. Thereafter, they started the interdisciplinary weight loss program described below. The same evaluation procedures were performed after short- (6 months) and long-term (1 year) therapy [20]. All interventions and evaluations were conducted in a location suitable for performing research projects of the CEPE (Centro de Estudos em Psicobiologia e Exercício) from Unifesp. This site has a gym, rooms for individual assistance, an amphitheater and apparatuses to perform the evaluations (Fig. 1).

2.2.1. Measurements

Subjects were weighed to the nearest 0.1 kg on the Filizola scale wearing light clothing and no shoes. Height was measured to the nearest 0.5 cm using a wall-mounted stadiometer (Sanny, model ES 2030). Body mass index (BMI) was calculated as the body weight (wt) divided by height (ht) squared (wt/ht²). Body composition was measured by air-displacement in a BOD POD body composition system (version 1.69, Life Measurement Instruments, Concord, CA) [21].

Visceral and subcutaneous fat were assessed by ultrasonography (US). US-determined subcutaneous fat was defined as the distance between the skin and external face of the recto abdominis muscle while visceral fat was defined as the distance between the internal face of the same muscle and the anterior wall of the aorta. The methodological descriptions of Ribeiro-Filho et al. [22] were used to define the cutoff points of visceral obesity by ultrasonographic parameters. All abdominal ultrasonographic procedures, in the three periods of evaluation, were performed by the same physician who was blinded to the subjects’ assignment group. This physician was a specialist in imaging diagnostics using a 3.5-MHz multi-frequency transducer (broad band), which reduces the risk of misclassification [22].

Blood samples were collected in the outpatient clinic around 8:00 a.m. after an overnight fast. Glucose, insulin, total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), very low density lipoprotein (VLDL) and triglyceride (TG) concentrations were analyzed using a commercial kit (CELMA, Barueri, Brazil). Leptin and adiponectin concentrations were measured in serum using a biochemical assay kit from Phoenix Pharmaceuticals (Belmont, CA) according to the manufacturer’s instructions. Insulin resistance was assessed by the homeostasis model assessment insulin-resistance index (HOMA-IR). HOMA-IR was calculated by fasting blood glucose (FBG) and immunoreactive insulin (I): [FBG (in mg/dL)] × 1 (in milliunits/L)]/405 [23]. The quantitative insulin sensitivity check index (QUICKI) was calculated as 1/(log I + log FBG).
The symptoms of binge eating and bulimia nervosa were assessed using the BES [24] and BITE [25], respectively. These tests were based on DSM-IV criteria and were translated into Portuguese and validated for obese individuals, including obese adolescents, submitted to weight loss treatment [24–28]. It is relevant to note that the tests were only applied to identify the symptoms and severity of these disorders and not with the purpose of offering a diagnosis because clinical interviews are necessary for confirmation.

2.2.2. Clinical therapy

All obese adolescents visited the endocrinologist with their parents once each month. In all of these visits, the entire GEO team was also present. The doctor monitored and evaluated all clinical exams of adolescents and treated health problems during therapy. The medical follow-up included the initial medical history and a physical examination of blood pressure, cardiac frequency and body weight, and the patients were checked for their adherence to all interdisciplinary therapies. The team discussed with the patients and their parents some possible changes in lifestyle to promote their health.

2.2.3. Psychological therapy

All adolescents had weekly psychological orientation group sessions (15 people per session) based on the psychodynamic approach with one trained psychologist, where they discussed family problems, body image, low self-esteem and eating disorders such as bulimia, anorexia nervosa, and binge eating, their signals, symptoms and consequences for health, in addition to other topics. Individual psychological therapy was recommended when behavioral alterations were found. During psychological therapy, all adolescents completed the Portuguese versions of the BES [26] to verify the symptoms of binge eating and BITE to verify bulimia symptoms, including the purgative subtype [27], respectively. Behavioral changes were identified by the psychologist who attended the volunteers, as well as through others questionnaires validated for each specific type of behavior, such as the Body Shape Questionnaire (BSQ), Depression Inventory (BECK), Profile of Mood States (POMS) and SF-36—Health Research.

2.2.4. Physical therapy

During the year of therapy, the adolescents followed a personalized aerobic training program (30 min) plus resistance training (30 min) three times a week, under the supervision of a sports physiologist. The aerobic exercises were performed at the cardiac frequency intensity of the ventilatory threshold I (±4 bpm), and the mode was running performed on a motor-driven treadmill (Life Fitness—Model TR 9700HR). After every 6 months of training, aerobic tests were performed to assess physical capacity and to individually adjust physical training intensity. Additionally, the adolescents worked each of the main muscle groups with resistance training. All adolescents had 2 weeks for adaptation to training to learn the movement (three sets of 15–20 Maximum Repetition). After this adaptation period, the training load was adjusted, and every eight weeks, volume and intensity were adjusted inversely, decreasing the number of repetitions from 15–20 to 10–12 and 6–8, respectively, for three sets. All exercises were rigorously performed by both groups, and all sessions were individually supervised by an experienced sports physiologist. During the exercises sessions, the adolescents’ heart rates were continuously monitored by cardiometer at intervals of 5 min during all training sessions (Polar—Model FS1 dark blue). The exercise program was based on the American College of Sports Medicine [29].

2.2.5. Nutritional therapy

Energy intake was set at the levels recommended by the dietary reference intake for subjects with low levels of physical activity of the same age and gender [30]. Once a week, adolescents had nutritional lessons (e.g., food pyramid, recordatory inquiry, weight loss diets, diet and light concepts, fat and cholesterol and eating disorders) by trained nutritionists to encourage the adolescents to follow healthy eating habits. Furthermore, all adolescents were seen individually twice a month.

2.2.6. Physiotherapy

The adolescents participated in an intervention with two physical therapists once a week. The themes of these interventions were global postural reeducation, isostretching, diaphragmatic breathing, hydrotherapy, balance and stretching. Individual consultations were also
performed if the patient had any injuries. The interventions were conducted in a room next to the gym, suitable for this type of intervention.

2.3. Statistical analyses

Distributional analyses were verified by the Kolmogorov–Smirnov test. An analysis of variance for repeated measures (ANOVA) was used to compare: 1) changes in time for each treatment (intra-effect); 2) differences between treatments during all time periods (inter-effect); and 3) differences in time between treatments (effect of interaction treatment x time). The Wilcoxon test was used to compare the data from the three time points, and the Mann–Whitney test was used to verify statistical differences between groups at the same time as non-parametric variables. Possible correlations were verified by the Spearman correlation test. The chi-square test was used to assess statistical differences in the prevalence of eating disorders before and after interdisciplinary therapy. Delta values were calculated as \( X (\text{after 1 year}) - Y (\text{at baseline}) \). The data were analyzed by means of STATISTICA version 7.0 for Windows, with significance set at \( p < 0.05 \) and expressed as the mean \( \pm \) S.D.

3. Results

Analyzing the adiposity of both groups according to the percentiles of the CDC (Center for Disease Control and Prevention) after 1 year of interdisciplinary weight loss therapy, we observed that 1.8% of the control group achieved a normal weight, that 23.6% were classified as overweight and that 74.5% were still obese. Analyzing the eating disorders group, 25% were classified as overweight, and 75% remained obese after 1 year of interdisciplinary weight loss therapy. In addition, we verified that the prevalence of obese adolescents with eating disorders decreased significantly by 89% after 1 year of interdisciplinary therapy (data not shown).

In Table 1, one can observe that both groups presented an improvement in body mass, BMI, body fat (%), lean mass, visceral fat, subcutaneous fat, HOMA-IR, total cholesterol, adiponectin and leptin concentrations after short- and long-term therapy. Quicki increased after long-term therapy in the control group and after short- and long-term in the eating disorder group. Participants without eating disorders displayed significantly reduced LDL-cholesterol, VLDL and triglycerides after short- and long-term therapy. The eating disorder group displayed significantly decreased VLDL and triglycerides after short-term therapy while LDL-cholesterol was reduced after long-term therapy. No statistical differences were found in HDL-cholesterol in either group. In addition, no significant differences were observed between the control group and the eating disorder group for all variables (Table 1).

In the control group, the preset study demonstrated a positive correlation between leptin concentrations and subcutaneous fat at baseline, as well as a correlation between the delta of leptin and subcutaneous fat. This group also displayed a negative correlation between the delta of adiponectin concentrations and the delta of HOMA-IR. A negative correlation between the delta of adiponectin and delta of fat mass (%) was also found in the control group. On the other hand, the eating disorder group did not show correlations between adipokines and fat mass or HOMA-IR (Table 2).

4. Discussion

One important finding in the present investigation is that we did not find significant differences in adiponectin levels between groups and no differences in variation of this adipokine during the therapy period comparing both groups. This result demonstrates that the abnormal eating behavior present in obese individuals with eating disorders (BN or BE) at baseline does not hinder the results obtained with the interdisciplinary treatment for weight loss. Conversely, the group with eating disorders displayed reduced symptoms, to 11%, at the end of the interdisciplinary therapy. Considering that this group did not maintain eating disorders during the entire therapy period, we can justify the improvement of adiponectin and leptin concentrations in this group.

In this study, we demonstrated that both groups presented an improvement in body composition, lipidemic and glycemic profiles after long-term therapy. Although the groups did not display an increase in HDL-cholesterol, this parameter was not altered during therapy according to reference values. These results demonstrate that both groups successfully performed the interdisciplinary therapy program.

Table 1

<table>
<thead>
<tr>
<th>Physical and metabolic characteristics of participants with eating disorders and without eating disorders at baseline, after 6 months and after 1 year of interdisciplinary therapy.</th>
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<tbody>
<tr>
<td><strong>Without eating disorders</strong></td>
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<td><strong>(Baseline (n = 55) 6 months (n = 55) 1 year (n = 55))</strong></td>
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<tr>
<td><strong>Body mass (kg)</strong></td>
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<td><strong>BMI (kg/m²)</strong></td>
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<td><strong>Body fat (%)</strong></td>
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<td><strong>Visceral fat (cm)</strong></td>
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<td><strong>Sub. fat (cm)</strong></td>
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<td><strong>Adipo (ng/ml)</strong></td>
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Reference values: HOMA-IR (~2.0), QUICKI (~0.33), total cholesterol (~170 mg/dL), HDL cholesterol (~38 mg/dL), LDL cholesterol (~130 mg/dL), TG (33–129 mg/dL); leptin: 1–24 (girls) and 1–20 (boys) ng/ml [31,32].

a Difference between baseline and short-term.

b Difference between baseline and long-term.

c Difference between short and long-term.

d Difference between groups in the 3 moments.
The levels of pro-inflammatory adipokines in individuals with eating disorders are still controversial in the literature. It is suggested that high levels of pro-inflammatory adipokines observed in these patients are due to low levels of anti-inflammatory adipokines [33]. Here, both groups were able to increase adiponectin levels after 1 year of therapy for weight loss. The increase in adiponectin suggests an increase of the protective effect of this adipokine against cardiovascular diseases, aside from better hypothalamic control of energy intake in both groups [34,35]. It is important to note that a reduction of psychological stress may be associated with the increase of adiponectin because this psychological stress may be involved in the increase of pro-inflammatory adipokines and consequently contribute to the decrease of anti-inflammatory adipokines [33].

Moreover, in this study, the increase of adiponectin concentrations in the group without eating disorders was associated with the reduction of HOMA-IR and fat mass (%). The literature reports this effect of adiponectin on insulin sensitivity. The activation of MAP kinase by adiponectin appears to promote an improvement in insulin sensitivity and an increase of fatty acid oxidation [36]. Additionally, it has been demonstrated in scientific research that adiponectin concentrations inversely correlate with body fat. In fact, this group demonstrated a reduction of fat mass (%) after interdisciplinary therapy [9].

The present study is consistent with the data in the literature that show an increase in adiponectin levels in individuals undergoing treatment for weight loss [37]. However, no studies were found in the literature to evaluate changes in concentrations of adiponectin in obese individuals with eating disorders during interdisciplinary therapy for weight loss. One study has compared adiponectin levels between different types of individuals, including obese patients with eating disorders. This study reports that adiponectin levels are lower in obese people with eating disorders compared with individuals constitutionally lean and without eating disorders, suggesting an association between nutritional status and concentrations of adiponectin [38].

In contrast, another study suggests that abnormal eating behavior could influence adiponectin levels independently of nutritional status [9]. Additionally, it is known that adiponectin can modulate hunger by reducing food intake and activate hypothalamic signaling pathways that are classically involved in the signal transduction of leptin and insulin. However, mechanisms involving the feeding behavior of individuals with eating disorders and adiponectin levels are not well understood [35].

In addition, we observed that both groups significantly reduced leptin concentrations after long-term therapy, demonstrating that symptoms of eating disorders do not influence leptin concentrations during therapy for weight loss. The positive correlation of leptin concentrations with adiposity is clearly demonstrated in the literature [5]. In fact, both groups demonstrated a decrease of body fat (%) and BMI after short- and long-term therapy, explaining the reduction of leptin concentrations. However, in this study, only the control group was able to display a positive correlation between the variation of subcutaneous fat and leptin concentrations.

Tagami et al. [9] shows that adiponectin levels are negatively correlated with BMI and body fat mass among normal body weight controls, obese and constitutionally thin subjects [9]. In agreement, Housova et al. [39] demonstrates that adiponectin levels in patients with restrictive and binge/purge types of anorexia and bulimia nervosa were strongly related to nutritional status (BMI and fat mass) [39]. In fact, adiponectin is a protein, which is highly expressed in adipose tissue, its circulating is decreasing in obese patients and its serum levels increase with weight loss, suggesting an association between adiponectin and body composition [40]. However, as previously mentioned, we did not find correlation between fat mass and adiponectin in the group with eating disorder, contrasting the result observed in the control group. It is possible that the group with eating disorder has shown an insufficient number of volunteers to determine a possible statistically significant result, suggesting a limitation of this study. Conversely, Monteleone et al. [38], shows that circulating adiponectin is strongly correlated with the frequency of binge/purging episodes in patients with BN, demonstrating that an altered eating behavior may influence the concentrations of adiponectin [38].

In conclusion, long-term interdisciplinary therapy was effective in reducing the chances of developing several co-morbidities in both groups. Despite our expectation of finding greater difficulty in improving the metabolic profile in obese adolescents with eating disorders, this result was not observed in this study. Some studies in the literature report significant differences in adiponectin levels by comparing different types of individuals with eating disorders. However, no study has compared obese individuals with and without eating disorders. We should emphasize that this investigation examined adolescents who were identified with symptoms of eating disorders and not with an established diagnosis, so we encourage further studies to evaluate obese subjects with a diagnosis of eating disorders because the results may vary from those found here.

Viewed from a clinical perspective, understanding of this specific obese population may provide useful tools to more appropriately treat such individuals. Therefore, additional studies are necessary to increase the knowledge of health professionals about obese individuals with eating disorders.

**Conflicts of interest**

The authors have nothing to disclose.

**Acknowledgment**

AFIP, CAPES, CNPq, CEMSA, UNIFESP, FAPESP (CEPID/Sono no. 9814302-3) and FAPESP (2006/0084-3; 2008/53069-0; 2011/50356-0), that supported the CEPE-GEO Interdisciplinary Obesity Intervention Program. Special thanks to patients and their parents.

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