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Short- and long-term beneficial effects of a multidisciplinary therapy for the control of metabolic syndrome in obese adolescents

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Abstract

Visceral fat is highly correlated with metabolic syndrome in obese adolescents. The aims of this study were to determine the prevalence of metabolic syndrome and to assess the effect of a long-term (1 year) intervention with multidisciplinary therapy in predicting metabolic syndrome among obese adolescents, as well as to compare short- with long-term therapy. Eighty-three postpuberty obese adolescents were recruited, including 37 boys (body mass index [BMI], 36.19 ± 3.85 kg/m^2) and 46 girls (BMI, 35.73 ± 4.42 kg/m^2). Body composition was measured by plethysmography using the BOD POD body composition system (version 1.69, Life Measurement Instruments, Concord, CA), and visceral fat was analyzed by ultrasound. Metabolic syndrome was determined according to the World Health Organization criteria. Patients were assigned to a weight loss multidisciplinary intervention consisting of nutritional, exercise, psychological, and clinical therapy. At the beginning of therapy, we found that 27.16% of the obese adolescents presented metabolic syndrome, whereas only 8.3% did so after intervention. Indeed, in boys, BMI (36.19 ± 3.85 to 32.06 ± 5.85 kg/m^2), visceral fat (4.88 ± 1.35 to 3.63 ± 1.71 cm), homeostasis model assessment of insulin resistance (4.77 ± 3.41 to 3.18 ± 2.33), and percentage of body fat (38.24% ± 6.54% to 30.02% ± 13.43%) presented a statistically significant reduction; and their fat-free mass percentage increased (62.14% ± 5.78% to 69.17% ± 12.37%). In girls, after long-term therapy, BMI (35.73 ± 4.42 to 33.62 ± 3.78 kg/m^2), visceral fat (3.70 ± 1.40 to 2.75 ± 1.01 cm), and percentage of body fat (46.10% ± 5.66% to 39.91% ± 5.59%) showed a statistically significant reduction; and their fat-free mass increased (53.61% ± 5.65% to 59.82% ± 5.78%). In conclusion, long-term multidisciplinary therapy was effective in promoting beneficial changes in some predictors and decreasing the prevalence of metabolic syndrome in obese adolescents.

1. Introduction

Obesity has emerged as a major health problem worldwide [1]. The prevalence of overweight in youths has increased dramatically in recent years, especially among children in minority ethnic groups. Recent data suggest that the prevalence of overweight (body mass index [BMI] >95th percentile for age and sex) among Latino children has approximately doubled in the past 10 years, in such a way that 23.4% of Latino youths aged 12 to 19 years are overweight [2].

Adolescence, the transitional period that begins with puberty, is marked by physiological, dynamic, and psychological changes in boys and girls. Mediated in part by hormonal influences, patterns of fat distribution during this developmental period also demonstrate sex differences. Pronounced centralization of fat stores with increase in subcutaneous and visceral fat in the abdominal region occurs in boys. In addition, fat tends to be deposited peripherally in breasts, hips, and buttocks in girls during this period. Adolescence has also been emphasized as a critical period

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for the development and expression of obesity-related comorbidities in both sexes, especially the metabolic syndrome [3].

Arguably, the major pathogenic factor in the metabolic syndrome is the central obesity. Whereas abdominal obesity is determined by accumulation of both subcutaneous and visceral adipose tissues, the excessive accumulation of visceral adipose tissue seems to play a more significant pathogenic role [4].

The metabolic syndrome is a constellation of interrelated risk factors of metabolic origin—*metabolic risk factors*—that seem to directly promote the development of atherosclerotic cardiovascular disease [5].

Clinical findings most commonly associated with metabolic syndrome include insulin resistance, dyslipidemia (specifically high triglycerides [TG], low levels of high-density lipoprotein [HDL], small dense low-density lipoprotein [LDL]), central obesity, hypertension, impaired glucose tolerance or diabetes mellitus, and high rates of atherosclerotic disease [6]. Several definitions and criteria have been proposed for the metabolic syndrome diagnosis; the 2 most widely used definitions come from the World Health Organization (WHO) [7] and the US National Cholesterol Education Program [8].

However, cutoff points for visceral fat that develops into metabolic syndrome have not been established yet. Currently, there is no consensus on the diagnosis of metabolic syndrome in children and adolescents, with the prevalence of metabolic syndrome varying from 4.2% to 23% in several populations. The highest rates were found in adolescents with Latino or African backgrounds [9-12], showing consequently that the metabolic syndrome in a group of Brazilian adolescents is similar to those found in several studies conducted in the United States and Europe, although there are differences in the metabolic syndrome characteristics among all groups.

Health consequences associated with early obesity have been repeatedly assessed and have justified prevention and research in childhood obesity [13-15]. Thus, the aims of this study were to determine the prevalence of metabolic syndrome, to evaluate the effect of a lifestyle intervention with multidisciplinary therapy in predicting the metabolic syndrome among obese adolescents, as well as to compare short- with long-term therapy.

2. Methods

2.1. Recruitment of subjects

Youths were recruited between January and February 2005 and 2006 by television, newspapers, and radio. A total of 83 postpuberty obese adolescents including 37 boys and 46 girls with primary obesity were included in this study. Ages ranged from 15 to 19 years. The inclusion criterion was pubertal stage assessed using the Tanner classification. The adolescents must be in the Tanner pubertal stage 3 or higher. Girls were questioned about the menstrual cycle, and only those with a menarche were included. Adolescents had primary obesity according to the revised Centers for Disease Control and Prevention growth charts (BMI >95th percentile of the reference growth charts) [16]. The adolescents and their families agreed to participate, on a voluntary basis, in a weight loss multidisciplinary therapy. All subjects performed an electrocardiogram before starting the program with the approval of a physician. Exclusion criteria were (*a*) identified genetic disease; (*b*) metabolic or endocrine disease; (*c*) long-term alcohol consumption; (*d*) previous drug use such as glucocorticoids, insulin sensitizers, or psychotropics, which may affect appetite regulation; (*e*) other causes of orthopedic limitations; (*f*) pregnancy; and (*g*) less than 75% compliance in all exercise, nutritional, psychological, and clinical sessions. Informal telephone surveys were done by calling the adolescents and their families to ask them about the reasons for dropping out of the program.

The study was conducted in accordance with the guidelines in the Declaration of Helsinki and was formally approved by the Ethical Committee of the Federal University of São Paulo-Paulista Medicine School (0135/04). All patients and their families received information about the protocol. The adolescents and their parents also signed a consent form.

2.2. Intervention design

Adolescents were invited to participate in a 1-year multidisciplinary therapy to promote changes in their sedentary lifestyle and nutritional habits. The basic requirements for the adolescents to participate were motivation and high attendance to the sessions.

The multidisciplinary intervention consisted of aerobic exercise and nutritional, psychological, and clinical therapy for the management of obesity and metabolic syndrome. The personnel who were involved in the program included 2 physicians, 1 nutritionist, 2 physiologists, and 1 psychologist. All measurements were performed before the treatment, after the short-term therapy, and finally, at the end of the long-term therapy. This criterion of multidisciplinary therapy was suggested by WHO.

2.3. Anthropometric measurements

Standing height and weight were measured in the same day. Weight was measured on a Filizola scale (Filizola, São Paulo, Brazil) to the nearest 0.1 kg with the volunteers wearing light clothing and no shoes. Height was measured to the nearest 0.5 cm by using a wall-mounted stadiometer (model ES 2030, Sanny, São Paulo, Brazil). Body mass index was calculated as the weight in kilograms divided by the square of height in meters. Body composition was measured by plethysmography using the BOD POD body composition system (version 1.69, Life Measurement Instruments, Concord, CA) [17].

2.4. Metabolic syndrome diagnosis

According to the adapted WHO criteria, metabolic syndrome is a disturbance of the glucose/insulin metabolism—type 2 diabetes mellitus, impaired glucose tolerance, or normal glucose tolerance with insulin resistance (defined as the highest quartile of the homeostasis model assessment of insulin resistance [HOMA-IR]). In addition, the diagnosis of metabolic syndrome requires at least 2 of the following 4 components:

1. Hypertension, either treatment by medication or ≥140/90 mm Hg untreated.
2. Dyslipidemia with elevated plasma TG (≥1.7 mmol/L or >150 mg/dL) and/or low HDL (<0.9 mmol/L or <35 mg/dL in men, <1.0 mmol/L or <39 mg/dL in women).
3. Obesity with BMI >30 kg/m^2 or central adiposity (waist-hip ratio >0.90 in men or >0.85 in women).
4. Microalbuminuria (urinary average excretion rate ≥20 μg/min or albumin-creatinine ratio ≥20 mg/g) [3,5,7,18].

Participants having impaired glucose tolerance or insulin resistance by HOMA-IR and meeting 2 or more of the previous criteria were defined as having the metabolic syndrome.

2.5. Visceral and subcutaneous adipose tissue

Abdominal ultrasound procedures before and after intervention were performed by the same examiner double-blinded to the medical history using a 3.5-MHz multifrequency transducer (broadband) located 1 cm from the umbilicus.

The ultrasound measurements of intraabdominal ("visceral") and subcutaneous fat were taken. Ultrasound-determined *subcutaneous fat* was defined as the distance between the skin and external face of the rectoabdominal muscle, and *visceral fat* was defined as the distance between the internal face of the same muscle and the anterior wall of the aorta. Cutoff points to define visceral obesity by ultrasonographic parameters were based on a previous methodological description by Ribeiro-Filho et al [19].

2.6. Metabolic variables

Blood samples were collected in the outpatient clinic at around 8:00 AM after an overnight fast. Lipids (total, HDL cholesterol, LDL cholesterol, and TG), fasting blood glucose, and immunoreactive insulin were measured. Insulin resistance was assessed by the HOMA-IR index [20].

The HOMA-IR was calculated as (fasting blood glucose [mg/dL] × insulin [mU/L]) / 405 [15]. Total cholesterol, HDL cholesterol, and triacylglycerol were analyzed using a commercial kit (CELM, Barueri, Brazil).

2.7. Blood pressure

Blood pressure (BP) was measured on the right arm using a mercury-gravity manometer with proper cuff size, with the volunteers in the seated position. The first appearance of sound (phase 1 Korotkoff sound) was used to define systolic BP, and the disappearance of sound (phase 5 Korotkoff sound) was used to define diastolic BP [21]. According to the adapted WHO criteria for children, hypertension (high BP) values were considered as ≥140/90 mm Hg untreated [5].

2.8. Lifestyle orientation

2.8.1. Nutritional therapy

The adolescents received nutritional training once a week (1 hour) during the short- and long-term therapy. Topics included food pyramid, recordatory inquiry, how to reduce total and saturated fat and cholesterol intake, portion control, weight loss diets and strategies for eating out, diet vs light, fat and cholesterol, nutrition facts, food preparation, cooking habits, regular meals, and controlling healthy lifestyle behavior. The aim of this therapy was to provide changes in the poor habits of nutrition during the weight loss phase. In addition, the parents were encouraged by a nutritionist to call if they needed further information. Nutritional education concerns changing nutritional behavior as well as providing information about the qualitative and quantitative aspects of food requirement.

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 sex [22]. However, no fixed caloric intake was prescribed; they were only encouraged to reduce their food intake and follow a balanced diet. No drugs and antioxidants were suggested. All dietary consumption data were analyzed using the Nutwin software, version 1.5 (UNIFESP, São Paulo, Brazil, 2003). The baseline and postintervention food intake was assessed by 3-day recordatory inquiry.

To minimize possible errors, the nutritionist trained them on how to fill out the 3-day recordatory inquiry and the importance of this instrument. Although this is a limited instrument to the interpretation of our findings, because of the lack of consistency and/or unrealistic reporting of the dietary intake by obese adolescents, it was applied broadly in several studies [23].

2.8.2. Exercise therapy

The subjects were initially diagnosed as sedentary-lifestyle individuals. The duration of exercise was about 60 minutes (180 min/wk) every session. All adolescents had 3 training sessions per week. The initial duration of the short-term intervention was 6 months, but progressed to 12 months. The mode of exercise included walking and stationary cycling (Life Fitness 9500HR, Franklin Park, IL). The exercises were made in the cardiac frequency intensity of the ventilatory threshold I, determined in the ergospirometric test (American College of Sports Medicine); the moderate intensity was determined in the aerobic evaluation (ventilatory threshold I), and the maximal oxygen consumption was measured.

Subjects performed an exercise test before the program, after 6 weeks, and at the end of short-term therapy with the same protocol for us to assess improvement in their cardiovascular function. The same procedure was performed in the long-term therapy. A physiologist supervised the cardiac frequency during all the sessions. The physiologists who worked in the program (members of the multidisciplinary therapy) participated regularly in the training sessions to encourage changes in lifestyle.

2.8.3. Clinical therapy

Medical follow-up included initial medical history, physical examination, and appropriate tests followed by a regular clinical surveillance by an endocrinologist every month. Pubertal stage was assessed; to be included in the therapy, adolescents must be in the Tanner pubertal stage 3 or higher for both sexes [24]. All patients were submitted to a multidisciplinary therapy.

2.8.4. Psychological therapy

Psychological therapy was established by validated questionnaires considering some psychological problems caused by the obesity as described in the literature, including depression, eating disorders, anxiety, decreased self-esteem, and dissatisfaction of body image. This modality of therapy took place once a week [25].

During the psychological sessions, the adolescents received orientation in a weekly group therapy. The psychologist discussed body image and eating disorders such as bulimia, anorexia nervosa, and binge eating; their signals, symptoms, and consequences for health; the relation between feelings and food; familiar problems such as alcoholism; and other topics. An individual psychological therapy was recommended when we found problems in weight or in dietary habits.

2.8.5. Statistical analysis

All statistical analyses were performed using STATISTIC 6.0 program for Windows (Statsoft, Tulsa, OK). The Kolmogorov-Smirnov test was used to assess all variables for normality of distribution. All data are shown as means ± SD. Repeated measures were compared, followed by a Scheffe post hoc test. Results were considered statistically significant at the level of $P < .05$.

3. Results

3.1. Participant retention on the multidisciplinary therapy to metabolic syndrome control in obese adolescents

At the beginning of therapy, 81 obese adolescents were enrolled in the program; 62 patients completed short-term therapy, and 37 (15 boys and 22 girls) completed long-term therapy with more than 75% of treatment sessions.

It is important to note that there are no differences for all variables in completers and the last known information about noncompleters. The main reasons for dropping out in our study are financial and family problems, followed by school and job opportunities. No sex differences were observed in adherence rates.

3.2. Effects of the multidisciplinary therapy on anthropometric variables, body composition, and visceral and subcutaneous fat in obese adolescents

The means and SDs in the anthropometric variables, body composition, and visceral and subcutaneous fat are summarized in Table 1. Body mass, BMI, body fat percentage, and visceral fat were significantly reduced in boys after 6 months of intervention ($P < .05$). Comparing values at baseline conditions with those after 12 months, the boys presented a significant reduction in body mass, BMI, body fat percentage, and visceral fat. On the other hand, fat-free mass percentage presented an increase ($P < .05$). For girls, a significant reduction after long-term therapy was observed in BMI, body mass, body fat percentage, and visceral fat; and they showed an increase in fat-free mass percentage ($P < .05$). In overall variables, there were significant differences in body mass, body fat percentage, visceral fat, and fat-free mass between boys and girls when we compared both sexes at baseline. However, these differences were observed after long-term therapy in both body fat and fat-free mass.

Table 1
Anthropometric variables, body composition, and visceral and subcutaneous fat measured at baseline and after multidisciplinary therapy in obese adolescents

Variables	Boys			Girls		
	Baseline	6 mo	1 y	Baseline	6 mo	1 y
Body mass (kg)	102.84 ± 8.98	95.92 ± 10.53 [a]	92.29 ± 13.37 [b]	92.45 ± 15.13 [d]	89.50 ± 13.73	87.55 ± 12.60 [b]
BMI (kg/m^2)	36.19 ± 3.85	33.29 ± 4.62 [a]	32.06 ± 5.85 [b]	35.73 ± 4.42	34.55 ± 4.07	33.62 ± 3.78 [b]
Body fat %	38.24 ± 6.54	33.361 ± 8.13 [a]	30.02 ± 13.43 [b]	46.10 ± 5.66 [d]	44.57 ± 4.77	39.91 ± 5.59 [b, c, d]
Fat-free mass %	62.14 ± 5.78	65.63 ± 8.23	69.17 ± 12.37 [b]	53.61 ± 5.65 [d]	55.41 ± 4.78	59.82 ± 5.78 [b,c,d]
Visceral fat (cm)	4.88 ± 1.35	3.76 ± 1.2 [a]	3.63 ± 1.71 [b]	3.70 ± 1.40 [d]	2.80 ± 1.02	2.75 ± 1.01 [b]
Sub fat (cm)	3.01 ± 0.46	2.59 ± 0.61	2.58 ± 1.08	3.42 ± 0.86	3.22 ± 0.92	3.36 ± 1.05

Sub indicates subcutaneous.

[a] Basal vs 6 months; $P \leq .05$.

[b] Basal vs 1 year; $P \leq .05$.

[c] Six months vs 1 year; $P \leq .05$.

[d] Boys vs girls at same time; $P \leq .05$.

Table 2
Metabolic variables measured at baseline and after multidisciplinary therapy in obese adolescents

Variables	Boys			Girls		
	Baseline	6 mo	1 y	Baseline	6 mo	1 y
SBP (mm Hg)	127.09 ± 7.81	118.18 ± 4.05[a]	118.63 ± 7.75[b]	140.63 ± 9.7[c]	112.89 ± 7.69	117.36 ± 7.33
DBP (mm Hg)	80.00 ± 7.74	77.27 ± 5.17	75.45 ± 5.22	74.73 ± 6.69	71.57 ± 3.74	74.73 ± 5.12
Glucose (mg/dL)	91.13 ± 7.30	92.33 ± 9.20	93.33 ± 8.92	90.78 ± 5.59	88.89 ± 6.44	89.73 ± 7.36
TG (mg/dL)	158.6 ± 81.67	122.60 ± 50.22[a]	122.73 ± 61.70[b]	87.73 ± 35.49[c]	85.00 ± 33.25	82.26 ± 20.67[c]
HDL-C (mg/dL)	43.86 ± 6.94	42.66 ± 6.00	44.66 ± 9.35	52.05 ± 11.83[c]	50.68 ± 10.16	50.21 ± 10.58
TC (mg/dL)	127.20 ± 31.18	155.00 ± 32.26	150.93 ± 28.46[b]	156.05 ± 29.21	154.94 ± 26.54	146.00 ± 22.04
LDL-C (mg/dL)	91.66 ± 26.66	87.86 ± 28.38	81.73 ± 26.32	86.52 ± 25.33	87.31 ± 25.10	79.26 ± 21.95
Insulin (μIU/mL)	20.74 ± 13.55	16.00 ± 10.86[a]	13.42 ± 9.19[b]	15.76 ± 5.80	13.31 ± 5.92	13.68 ± 7.26
HOMA-IR	4.77 ± 3.41	3.80 ± 2.86[a]	3.18 ± 2.33[b]	3.60 ± 1.35	2.98 ± 1.42	3.11 ± 1.56

SBP indicates systolic BP; DBP, diastolic BP; HDL-C, HDL-cholesterol; TC, total cholesterol; LDL-C, LDL-cholesterol.
[a] Basal vs 6 months; $P \leq .05$.
[b] Basal vs 1 year; $P \leq .05$.
[c] Boys vs girls at same time; $P \leq .05$.

3.3. Effects of the multidisciplinary therapy on metabolic variables in obese adolescents

In Table 2, we can verify the mean and SD in the metabolic variables. Systolic BP, TG, and HOMA-IR values were significantly reduced only in boys after 6 months ($P < .05$). A significant reduction in systolic BP, TG, total cholesterol, fasting insulin, and HOMA-IR was found after 12 months of intervention when those values were compared with the baseline conditions ($P < .05$). However, we did not observe reduction in the variables when comparing short- and long-term therapy.

3.4. Effects of the multidisciplinary therapy on metabolic syndrome prevalence in obese adolescents

At baseline conditions, the prevalence of metabolic syndrome in all obese adolescents was 27.16%, whereas it was only 8.3% after intervention (Fig. 1). For boys, the prevalence of metabolic syndrome decreased from baseline to short-term therapy (35.13% to 20.0%), and finally to 13.3% after long-term therapy. For girls, the prevalence of metabolic syndrome decreased from baseline to both short- and long-term therapy (19.46% to 10.81% and 4.54%, respectively).

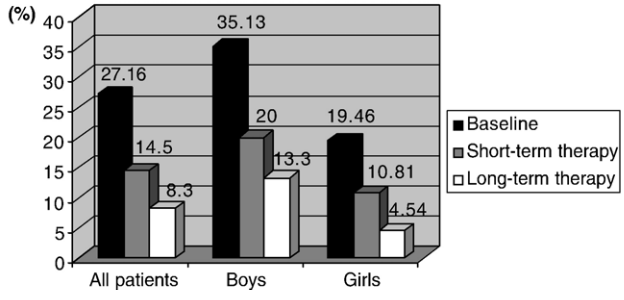

Fig. 1. Prevalence of metabolic syndrome at baseline and after multidisciplinary therapy in obese adolescents.

3.5. Effects of the multidisciplinary therapy on each component of the metabolic syndrome in obese adolescents

The frequency of each component of metabolic syndrome from baseline to long-term therapy was changed as follows: for boys—BMI, 100% to 64.28%; TG, 40.54% to 28.57%; HOMA-IR, 51.35% to 35.71%; glucose, 18.91% to 21.42%; and HDL, 5.4% to 4.28%; for girls—BMI, 100% to 90.9%; TG, 15.21% to 0%; HOMA-IR, 45.65% to 27.27%; glucose, 10.86% to 0%; HDL, 13.04% to 9.09%; and high BP, 2.46% to 0% (Table 3).

4. Discussion

The aims of this study were to determine the prevalence of metabolic syndrome and assess the effects of a long-term multidisciplinary therapy in predicting metabolic syndrome among obese adolescents, as well as to compare short- with long-term therapy.

Short-term therapy results showed significant reduction in body mass, BMI, body fat percentage, and visceral fat only in boys. A recent prospective analysis demonstrated that BMI was the central feature of the metabolic syndrome over time [21,26]. The reductions in the BMI observed in boys after

Table 3
Prevalence of metabolic syndrome predictors at baseline and after multidisciplinary therapy in obese adolescents

Predictors of MS (WHO)	Boys			Girls		
	Baseline (%)	6 mo (%)	1 y (%)	Baseline (%)	6 mo (%)	1 y (%)
BMI (kg/m^2)	100	84	64.28	100	91.89	90.90
Glucose intolerance (mg/dL)	18.91	12	21.42	10.86	10.81	0
HDL (mg/dL)	5.4	4.28	4.28	13.04	8.1	9.09
TG (mg/dL)	40.54	32	28.57	15.21	13.51	0
BP (mm Hg)	2.46	–	–	–	–	–
HOMA-IR	51.35	36	35.71	45.65	27.02	27.27

short- and long-term therapy may play an essential role in the prevention and management of such metabolic syndrome.

The major finding of the present study is that the long-term multidisciplinary therapy promotes an effective control to metabolic syndrome in both boys and girls. However, short-term therapy in boys was sufficient to promote significant reduction in body fat percentage and visceral fat; there was a further improvement in these parameters after long-term therapy. Several studies highlight the importance of preventing and controlling other chronic diseases by undertaking both short- and long-term strategies for metabolic syndrome control. A recent investigation by Balagopal et al [27] reported a decrease in weight gain and an improvement of inflammatory markers in obese youth who participated in a 3-month exercise program (short-term therapy). Furthermore, another recent study developed by our research group demonstrated a decrease in the prevalence of nonalcoholic fatty liver disease in obese adolescents subjected to a similar intervention for weight control [28]. Therefore, our results are in agreement with those by Monzavi et al [23], Balagopal et al [27], and Chen et al [29], who suggest that an intensive lifestyle intervention that combines nutrition education, exercise, and psychological and clinical intervention improved metabolic outcomes, body composition, and visceral fat in as little as 6 months, with the short-term intervention resulting in a significant effect on obesity and other comorbidities such as inflammatory markers and nonalcoholic fatty liver disease.

On the other hand, only after long-term therapy did the boys present significant increment in the fat-free mass (percentage), indicating that the sustained treatment for a long time can promote all the necessary changes in body composition. It may be partially explained by the dramatic changes in body composition that occur during adolescence and differ between boys and girls [3]. The different conditions in both sexes during the pubertal period suggest an increase in the metabolic rate and, finally, a good condition to regulate a negative energy balance. An observable change during puberty is in the amount and regional distribution of body fat. The total fat mass and fat stored in the visceral, subcutaneous, and muscle depots that increase with body size during puberty are all associated with insulin resistance. Increase in the visceral fat is thought to lead to a cascade of metabolic derangements resulting in insulin resistance [30].

In fact, we found no significant changes in body composition and in subcutaneous and visceral fat in the girls followed up in this investigation in the short-term therapy; but there were better initial values for body fat percentage, visceral fat, and body mass in girls when compared with boys. According to Dao et al [15], a low-calorie diet seems to be unnecessary to induce a negative energy balance when a multidisciplinary approach is used. However, our best results were obtained only in boys, and not in girls, with short-term therapy. Therefore, the results after long-term therapy showed a significant reduction in body mass, BMI, body fat percentage, and visceral fat in girls. Indeed, fat-free mass percentage increased.

This kind of multidisciplinary treatment can be effective in improving metabolic and hormonal profile, as well as in controlling the obesity and related comorbidities in obese adolescents [31].

Visceral fat accumulation is known to be associated with features of the insulin resistance syndrome in adults and obese adolescents, although the nature of this association and the relative importance of visceral and subcutaneous abdominal fat remain to be clarified [32]. According to Fu et al [33], pubertal insulin resistance occurs during a time of profound changes in body composition and hormone levels and might have an effect in the adolescent's metabolic syndrome development, although obesity beginning in childhood often precedes the hyperinsulinemic state.

A recent key finding was that insulin resistance as measured by the HOMA-IR was greater in the late-pubertal group than that in the prepubertal and midpubertal groups with normal weight [30]. The cause of pubertal insulin resistance is uncertain but, because of its universal nature, is likely due to pubertal alterations in adiposity, body fat distribution, and hormone release. It reinforces the notion that, in obesity, intervention should be started as early as possible [33].

In fact, our results showed a significant decrease in visceral fat that may contribute to improve insulin sensitivity and decrease HOMA-IR (4.77 to 3.18 for boys and 3.60 to 3.11 for girls) after long-term therapy. However, the insulin resistance value found by Roemmich et al [30] in normal-weight adolescents in puberty (2.54 for girls and 2.21 for boys) is lower when compared with the results observed at baseline in the present investigation with obese adolescents at the same pubertal stage.

Previous evidences have shown that modest insulin resistance occurs in both lean and obese youth. Moreover, normal pubertal increases in fat mass, intermuscle fat, and visceral fat may be responsible for the reduction in insulin sensitivity in puberty. Although our study is limited by the lack of a control group, our results observed at baseline and after intervention, when compared with previous researches, emphasize that the complete panel of features of the metabolic syndrome may already occur mostly in childhood obesity not only in consequence to late puberty [30,33].

An analysis of the metabolic parameters showed that the short-term therapy promoted a significant reduction in 4 parameters of the metabolic syndrome criteria by WHO for boys: BP, TG, insulin concentration, and HOMA-IR. One of the major findings of the present investigation is that these adaptations were accentuated after long-term therapy. Indeed, we observed a significant reduction in total cholesterol for boys after long-term therapy (Table 2). These adaptations were not similarly demonstrated in girls. However, this group presented a decrease in the prevalence of all metabolic syndrome parameters investigated in the present study (Table 3).

Although both sexes (boys and girls) participating in the multidisciplinary therapy had similar values in the major part of the variables, the girls presented lower values in the BP and TG concentrations. When HDL concentrations were compared, we observed higher values in girls than in boys at the beginning of this study. In addition, we were able to detect significant sex differences in visceral adipose tissue between groups. Similar results are not observed by Weiss et al [32], which may be partially explained by differences between sample sizes. Moreover, after long-term therapy, visceral fat in both sexes presented similar values in these parameters. According to Nishina et al [34], visceral accumulation, hyperinsulinemia, and hyperleptinemia compose a group of factors to be considered in the primary prevention of hypertension. Therefore, our results of decreasing HOMA-IR, visceral adiposity, and other parameters analyzed in this study support the importance of implementing such a strategy to prevent obesity and will contribute to future decrement in cases of metabolic syndrome, including those involving hypertension.

It is relevant to mention that at the beginning of the multidisciplinary therapy, the prevalence of the metabolic syndrome in all obese adolescents was 27.16%, whereas it was only 8.3% after the intervention (Table 3). In a recent study, Brazilian investigators found the prevalence of metabolic syndrome in obese adolescents to be 26.1% [12]. Similar metabolic syndrome prevalence has been shown in diverse populations and researches [9,10,12,35], despite limitations of comparison. Previous investigation developed by Monzavi et al [23] and Weiss et al [36] based on the criteria adapted from the National Cholesterol Education Program found that approximately 50% of the overweight pediatric population had multiple risk factors for the metabolic syndrome. These investigators found that 95% of the patients had a BMI ≥97th percentile. Nemet et al [37] demonstrated the short- and long-term beneficial effects of a combined dietary-behavioral-physical activity intervention among obese children. These results highlight the importance of a multidisciplinary program in the treatment of childhood obesity, promoting and encouraging long-term beneficial effects to the management of metabolic syndrome.

The attrition rate in our program was ≅45.6%, which is consistent with the rates seen in other pediatric weight management programs [23,38,39] In addition, we did not evaluate either socioeconomic status or health insurance status because the program was offered without charge to the family. Through our telephone surveys, we found the attrition rate to be related, at least in part, to the high cost of transportation, distance from the program center, and time to attend each multidisciplinary session. There is similar difficulty in the research by Monzavi et al [23]. Finally, these aspects reinforce the importance of an early metabolic syndrome multidisciplinary intervention for improving the lifestyle modifications.

The lack of a control group could be seen as a weak point of the present study. However, it should be mentioned that the original objective of the present study was to compare the effects of short- and long-term multidisciplinary therapy on metabolic syndrome control in obese adolescents. Further investigation including a control group and long-term follow-up are needed to improve our findings.

In conclusion, our study clearly demonstrates a “dose-response” effect of multidisciplinary therapy when comparing short- and long-term interventions, respectively. Long-term therapy was effective in reducing the prevalence of metabolic syndrome and decreasing some predictors of metabolic syndrome in obese adolescents.

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References

[1] Xiong MA, Zhiping LI. Pathogenesis of nonalcoholic steatohepatitis (NASH). Chin J Dig Dis 2006;7:7-11.
[2] Shaibi GQ, Cruz ML, Ball GDC, et al. Cardiovascular fitness and metabolic syndrome in overweight Latino youths. Med Sci Sports Exerc 2005;37:922-8.
[3] Daniels SR, Arnett DK, Eckel RH, et al. Overweight in children and adolescents. Circulation 2005;111:1999-2012.
[4] Freedland ES. Role of a critical visceral adipose tissue threshold (CVATT) in metabolic syndrome: implications for controlling dietary carbohydrates: a review. Nutr Metab 2004;1:12.
[5] Grundy SM, Cleeman IJ, Daniels SR, et al. Diagnosis and management of metabolic syndrome. An American Heart Association/National Heart Lung, and Blood Institute Scientific Statement. Circulation 2005; 112:2735-52.
[6] Miranda PJ, DeFronzo RA, Califf RM, et al. Metabolic syndrome: definition, pathophysiology, and mechanisms. Am Heart J 2005;149: 33-45.
[7] World Healthy Organization (WHO). Report of a WHO consultation. In: Alwan A, King H, editors. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus. Geneva: World Healthy Organization Department of Noncommunicable Disease Surveillance; 1999. p. 1-59.
[8] Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001;1285:2486-97.
[9] Cruz ML, Weignensberg MJ, Huang TT-K, et al. The metabolic syndrome in overweight Hispanic youth and the role of insulin sensitivity. J Clin Endocrinol Metab 2004;89:108-13.
[10] Cook S, Weitzman M, Auinger P, et al. Prevalence of metabolic syndrome phenotype in adolescents: findings from the Third National Health and Nutrition Examination Survey; 1988-1994. Arch Pediatr Adolesc Med 2003;157:821-7.
[11] Klein DJ, Friedman LA, Harlan WR, et al. Obesity and the development of insulin resistance and impaired fasting glucose in black and white adolescent girl: a longitudinal study. Diabetes Care 2004;27:378-83.

[12] Silva CQR, Miranda MSC, Chacra AR, et al. Metabolic syndrome and insulin resistance in normal glucose tolerant Brazilian adolescents with family history of type 2 diabetes. Diabetes Care 2005;28:716-8.
[13] Dietz WH. Health consequences of obesity in youth: childhood predictors of adult disease. Pediatrics 1998;101:518-25.
[14] Must A, Jacques PF, Dallai GE, et al. Long-term morbidity and mortality of overweight adolescents follow-up of the Harvard Growth Study of 1922 to 1935. N Engl J Med 1992;327:1350-5.
[15] Dao HH, Frelut ML, Oberlin F, et al. Effects a multidisciplinary weight loss intervention on body composition in adolescents. Int J Obes 2004; 28:290-9.
[16] Centers for Disease Control and Prevention (1999-2000) prevalence of overweight among children and adolescents: United States 2006. Accessed on linewww.cdc.gov/nchs/products/pubs/pubd/hestats/overwght99.htm.
[17] Fields DA, Goran ML. Body composition techniques and the four-compartment model in children. J Appl Physiol 2000;89:613-20.
[18] Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. Diabet Med 1998;15:539-53.
[19] Ribeiro-Filho FF, Faria AN, Ajzen S, et al. Methods of estimation of visceral fat: advantages of ultrasonography. Obes Res 2003;11: 1488-94.
[20] Matthews DR, Hosker JP, Rudenski AS, et al. Homeostasis model assessment: insulin resistance and β-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 1985;28: 412-9.
[21] Park HS, Sim SJ, Park JY. Effect of weight reduction on metabolic syndrome in Korean obese patients. J Korean Med Sci 2004;19:202-8.
[22] NRC (National Academic Press) Dietary Reference Intake: applications in dietary assessment. Washington (DC): National Academic Press; 2001. Available at: http://www.nap.edu/catalog/10609.html.
[23] Monzavi R, Dreimane D, Geffner ME, et al. Improvement in risk factors for metabolic syndrome and insulin resistance in overweight youth who are treated with lifestyle intervention. Pediatrics 2006;117: 1111-8.
[24] Invitti C, Maffeis C, Gilardini L, et al. Prevalence of metabolic syndrome in obese children: an analysis using children-specific criteria (abstract). Diabetes 2003;52(Suppl 1):A70.
[25] Stella SG, Villar AP, Lacroix C, et al. Effects of type of physical exercise and leisure activities on the depression scores of obese Brazilian adolescents girls. Braz J Med Biol Res 2005;38:1683-9.
[26] Maison P, Byrne CD, Hales CN, et al. Do different dimensions of the metabolic syndrome change together over time? Evidence supporting obesity as central the feature. Diabetes Care 2001;24:1758-63.
[27] Balagopal P, George D, Yarandi H, et al. Reversal of obesity-related hypoadiponectinemia by lifestyle intervention: a controlled randomized study in obese adolescents. J Clin Endocrinol Metab 2005;90:6192-7.
[28] Tock L, Prado W, Caranti DA, et al. Non-alcoholic fatty liver disease in obesity adolescents after multidisciplinary therapy. Eur J Gastroenterol Hepatol 2006;18:1241-5.
[29] Chen AK, Roberts CK, Barnard RJ. Effect of a short-term diet and exercise intervention on metabolic syndrome in overweight children. Metabolism 2006;55:871-8.
[30] Roemmich JN, Clark PA, Lusk M, et al. Pubertal alterations in growth and body composition. VI. Pubertal insulin resistance: relation to adiposity, body fat distribution and hormone release. Int J Obes 2002; 26:701-9.
[31] Dâmaso AR, Tock L, Tufik S, et al. Tratamento Multidisciplinar reduz o tecido adiposo visceral, leptina, grelina e a prevalência de esteatose hepática não alcoólica (NAFLD) em adolescentes obesos. Rev Bras Med Esporte 2006;12:263-7.
[32] Weiss R, Dufour S, Taksali SE, et al. Prediabetes in obese youth: a syndrome of impaired glucose tolerance, severe insulin resistance, and altered myocellular and abdominal fat partitioning. Lancet 2003;232: 951-7.
[33] Fu JF, Liang L, Zou CC, et al. Prevalence of the metabolic syndrome in Zhejiang Chinese obese children and adolescents and the effect of metformin combined with lifestyle intervention. Int J Obes 2007;31: 15-22.
[34] Nishina M, Kikuchi T, Yamazaki H, et al. Relationship among systolic blood pressure, serum insulin and leptin, and visceral fat accumulation in Obese Children. Hypertens Res 2003;26:281-8.
[35] Csábi G, Török K, Jeges S, et al. Presence of metabolic cardiovascular syndrome in obese children. Eur J Pediatr 2000;159:91-4.
[36] Weiss F, Dziura J, Burgert T, et al. Obesity and the metabolic syndrome in children and adolescents. N Engl J Med 2004;350:2362-74.
[37] Nemet D, Barkan S, Epstein Y, et al. Short- and long-term beneficial effects of a combined dietary-behavioral-physical activity for the treatment of childhood obesity. Pediatrics 2005;115:443-9.
[38] Tershakovec AM, Kuppler K. Ethnicity, insurance type, and follow-up in a pediatric weight management program. Obes Res 2003;11:17-20.
[39] Zeller M, Shelly K, Randal C, et al. Predictors of attrition from a pediatric weight management program. J Pediatr 2004;144:466-70.