J. Health Biol Sci. 2015; 3(1):10-17 doi:10.12622/2317-3076jhbs.v3i1.115p.10.2015

ORIGINAL ARTICLE

One year of interdisciplinary therapy decreases predictors and prevalence of sleep-breathing disorder in obese adolescents

Um ano de terapia interdisciplinar diminui preditores e a prevalência de distúrbios respiratórios do sono em adolescentes obesos

Flávia Campos Corgosinho*[1a], Ana Raimunda Dâmaso[1a], Sérgio Tufik[1b], Aline de Piano[1a], Priscila de Lima Sanches[1a], Raquel Munhoz da Silveira Campos[1a], Patrícia Leão Silva[1a], June Carnier[1a], Lian Tock[c], Monica Levy Andersen[1b], Gustavo Antônio Moreira[1b], Marcia Pradella-Hallinan[1b], Lila Missae Oyama[1a], Marco Túlio de Mello[1b]

1. Universidade Federal de São Paulo – Escola Paulista de Medicina – Rua Professor Francisco de Castro, no 93, Vila Clementino – São Paulo/SP, Postal CEP: 04020-050, Brasil. a. Department of Nutrition. b. Department of Psychobiology. c. Weight Science.

Abstract

Introducion: Obesity is considered a chronic sub-inflammatory disease, being a risk factor for many diseases such as Sleep-Breathing Disorder (SBD). Although, the interaction between obesity and sleep has been explored lately, not much is known in the adolescent population. **Objective:** Thus the aims of this study were threefold: first, to determine the prevalence of SBD in a sample of Brazilians' obese adolescents; second, to assess the effect of weight loss therapy on sleep, metabolic and inflammatory parameters; third, to compare sex-differences between the adolescents. **Methods:** A total of 55 obese adolescents were submitted to one year of interdisciplinary weight loss therapy. Sleep, anthropometric, metabolic and inflammatory profiles were evaluated at baseline and after one year of therapy. **Results:** At the beginning of the treatment, 21.9% of the obese adolescents presented SBD, whereas only 8.9% did so after intervention. The weight loss therapy was able to improve significantly the metabolic, inflammatory markers, and sleep pattern in both genders. Negative correlation was found between leptin and REM sleep, but only in boys. Positive correlations were found between body fat (kg) with respiratory events (r=0.48) and the respiratory disturbance index (r=0.49). Boys presented significant higher prevalence of sleep-breathing disorders. **Conclusion:** Our results support the importance of an early intervention as a strategy to prevent and control obesity and its comorbities, showing a decrease in SBD, visceral adiposity and other parameters.

Keywords: Obesity. Sleep-Breathing Disorders. Adolescents; Inflammation.

Resumo

Introdução: A obesidade é considerada uma doença crônica inflamatória de baixo grau, sendo um fator de risco para diversas doenças, como o Distúrbio Respiratório do Sono (DRS). Embora a interação entre obesidade e sono tem sido muito estudada, poucos dados se tem na população adolescente. **Objetivos:** Assim, os objetivos do atual estudo foram três: primeiro, determinar a prevalência de DRS em uma amostra de adolescentes obesos; segundo, avaliar o efeito da terapia de perda de peso nos parâmetros de sono, metabolismo e inflamação; e por último comparar a diferença entre os gêneros. **Resultados:** Um total de 55 adolescentes obesos foram submetidos a um ano de terapia interdisciplinar. Parâmetros de sono, antropométricos, metabólicos e inflamatórios foram avaliados no início e após 1 ano de terapia. **Resultados:** No início do tratamento , 21,9% dos adolescentes obesos apresentavam DRS, e apenas 8,9% mantiveram o distúrbio após a intervenção. A terapia de perda de peso melhorou significativamente o perfi metabólico, inflamatório assim como o padrão de sono em ambos os gêneros. Houve correlação negativa entre a leptina e a sono REM no grupo dos meninos. Também foram encontradas correlações positivas entre gordura corpora (Kg) com eventos respiratórios (r=0,48) e com o índice de distúrbios respiratórios (r=0,49). Os meninos apresentaram significativamente maior prevalência de DRS que meninas. **Conclusão:** Nossos resultados reforçam a importância de uma intervenção precoce como estratégia de prevenção e controle da obesidade e suas comorbidades, mostrando uma redução na prevalencia de DRS, da adiposidade visceral assim como outros parâmetros metabólicos e inflamatórios.

Palavras-chave: Obesidade. Distúrbios respiratórios do sono. Adolescentes. Inflamação.

INTRODUCTION

Obesity is a chronic sub-inflammatory disease and its prevalence has increased worldwide, especially among children and adolescents[1]. One of the obesity-related complications is Sleep-Breathing Disorders (SBD), a well-documented health complication which includes primary snoring, upper airway resistance syndrome, and obstructive sleep apnea syndrome (OSAS)[2]. Furthermore, SBD in overweight children and adolescents is independently associated with the metabolic syndrome and Non-alcoholic fat liver disease (NAFLD), becoming a potential additional risk factor for the development of cardiovascular diseases[3,4]. Although it is well established that the prevalence of SBD are higher in men, it is unclear in adolescent population[5].

Leptin, in high concentrations, plays an important role in inflammatory process in obesity, being an important marker. Recent data have shown that most of the obese patients present hyperleptinemia while adiponectin is reduced[6]. Many studies have focused on the interaction between sleep restriction and neuro-endocrine hormones, showing the role of sleep on the regulation of energy balance[7-9]. However, the role of inflammatory markers, such as leptin and adiponectin

Correspondência: Flávia Campos Corgosinho. Departamento de Nutrição da Universidade Federal de São Paulo. Rua Professor Francisco de Castro, nº 93, Vila Clementino – São Paulo/SP, CEP: 04020-050, Brasil.e-mail: flaviacorgosinho@hotmail.com
Conflito de interesse: Não há conflito de interesse por parte de qualquer um dos autores.
Recebido em: 24 Set 2014; Revisado em: 09 Dez 2014; Aceito em: 28 Jan 2015.

has not been well explored yet. Thus, the aims of this study in obese adolescents were: first, to determine the prevalence of SBD in a sample of Brazilians' obese adolescents; second, to assess the effect of weight loss therapy on sleep, metabolic and inflammatory parameters; third, to compare sex differences among the adolescents.

METHODS

Subjects

A total of 55 obese adolescents (21 boys and 34 girls) who entered the Interdisciplinary Obesity Program of the Universidade Federal de São Paulo were divided by gender. The evaluations were performed at baseline and after one year of an interdisciplinary approach. The ages of the participants ranged from 15 to 19 years and all of them presented obesity (Body Mass Index - BMI>95th percentile). The inclusion criteria for the post-pubertal stage were based on the Tanner scale stage 5, for both boys and girls[10]. Non-inclusion criteria were as follows: other metabolic or endocrine diseases, such as hypothyroidism and Cushing syndrome; chronic alcohol consumption; previous use of drugs, such as anabolic-androgenic steroids or psychotropics which may affect appetite regulation; and pregnancy. The study was carried out in accordance with the principles of the declaration of Helsinki and was approved by the Ethical Committee of Universidade Federal de São Paulo (#0135/04). All subjects and/or their parents signed an Informed Consent. Clinical trial registration numbers: NCT01358773.

Polysomnography

All subjects underwent to polysomnography (PSG) before and after one year of the interdisciplinary weight loss therapy. A full-night PSG was performed using a digital system (EMBLA® S7000, Embla Systems, Inc., Broomfield, CO., USA) at the sleep laboratory during the subjects' habitual sleep time. The following physiological variables were monitored simultaneously and continuously: 4 channels for the electroencephalogram (EEG), 2 channels for the electro-oculogram, 2 channels for the surface electromyogram (submental, anterior tibialis muscle), one channel for an electrocardiogram; oronasal airflow detection through a thermocouple and nasal pressure transducer (nasal cannula), respiratory effort of the thorax and abdomen using inductance plethysmography, neck microphone, body position, and oxygen saturation (SpO2). Trained technicians visually scored all PSG according to standard criteria. The PSG was further reviewed by an experienced Sleep Medicine specialist.

The sleep staging was performed as proposed by the new America Academy of Sleep Medicine (AASM) manual[11]. Apnea was defined as the cessation of airflow lasting ≥2 breaths. Obstructive apneas were defined as the presence of chest and/or abdominal motion in the absence of airflow. Central apnea was scored as cessations in airflow without respiratory effort lasting 20 seconds, or less, if associated with oxygen desaturation. Mixed apneas were defined as having central and obstructive components. Hypopnea was defined as ≥50% decrease in the amplitude of the airflow signal lasting ≥2 breaths with a concurrent oxygen desaturation of >3% or an arousal. The apnea hypopnea index (AHI) was calculated as the sum of obstructive apneas, mixed apneas, and hypopneas divided by total sleep time[12,13].

Arousals were defined as recommended by the American Sleep Disorders Association. Briefly, an arousal was defined as an abrupt shift in EEG to alpha frequencies (8-13 Hz) or frequencies > 16 Hz for a minimum of 3 seconds. During rapid eye movement (REM) sleep, arousals were scored if the change in EEG were accompanied by a concomitant increase in the amplitude of the sub-mental EMG signal[14].

Sleep-breathing disorder was considered when AHI was ≥ 5 events/hour. Snoring was rated as mild, moderate, or severe according to the PSG technician opinion. Periodic leg movements were scored according to the international recommendations. Briefly, Periodic limb movements (PLM) were defined as a sequence of 4 or more limb movements of 0.5 to 5.0 seconds in duration that were separated by more than 5 seconds and less than 90 seconds, and the amplitude of which were greater than 8 μV from de baseline[15]. The PLM index was cal¬culated by dividing the number of PLM by the total sleep time. Leg movements associated with respiratory events were not scored.

It is important to mention that polysomnography was used to verified sleep disorders and not total sleep time, considering that they were awakened early in the morning due to school schedule. At baseline, there were performed 2 PSGs, in order to avoid the first-night effect, being the first night data disregarded (data not shown).

Serum analysis

Blood samples were collected in the outpatient clinic around 8 a.m., after an overnight fast. Insulin resistance was assessed by the homeostasis model assessment-insulin resistance (HOMA-IR) index and it was calculated using the fasting blood glucose (FBG) and immuno-reactive insulin (I): [FBG (mg/dL)×I (mU/L)]/405. Total cholesterol, Triglycerides (TG) and HDL were analyzed using a commercial kit (CELM, Barueri, Brazil). The HOMA-IR data were analyzed according to reference values reported by Schwimmer et al[16]. Total adiponectin and leptin concentrations were measured using a commercially available enzyme-linked immuno-sorbent assay (ELISA) kit from R&D Systems (Minneapolis, USA) according to the manufacturer's instructions.

Anthropometric variables and body composition

Subjects were weighed while wearing light clothing and no shoes on a scale to the nearest 0.1 kg. Height was measured to the nearest 0.5 cm with a wall-mounted stadiometer (Sanny, model ES 2030). Waist circumference was measured by non-stretch-able tape measure, and recorded to the nearest 0.1cm. BMI was calculated as body weight divided by height squared. Body composition was measured by plethysmography in a BOD POD body composition system (version 1.69; Life Measurement Instruments, Concord, CA, USA).

Visceral and subcutaneous adiposity measurements

All abdominal ultrasonographic procedures and measurements of visceral and subcutaneous fat tissue were performed by a specialist in imaging diagnostics. A 3.5-MHz multi-frequency transducer (broad band) was used to reduce the risk of misclassification. The intra-examination coefficient of variation for ultrasound (US) was 0.8%. US measurements of intra-abdominal (visceral) and subcutaneous fat were obtained.

Clinical therapy

Medical follow-up included initial medical history and physical examination following to regular clinical surveillance (once each month). The doctor monitored and evaluated all biochemical exams and treated health problems developed during therapy. It was also evaluated the weight loss process of each adolescent, helping them to reach the goals and counselling the parents on how to proceed to enhance the therapy.

Psychological therapy

The adolescents were submitted to weekly psychological orientation group sessions, guided by a trained psychologist, based on the psychodynamic approach in which family problems, body image, low self-esteem and eating disorders were discussed. Individual psychological therapy was recommended when behavioural alterations were found. Data not shown.

Nutritional therapy

Energy intake was set at the levels recommended by the dietary reference intake (DRI) for subjects with low levels of physical activity of the same age and gender[17]. Once a week, adolescents had nutritional lectures on (food pyramid, recordatory inquiry, weight loss diets, diet and light concepts, fat and cholesterol, etc.) by trained nutritionists. All patients received individual nutritional consultation during the intervention program.

At the beginning of the study and at the end of therapy, each adolescent filled in a 3-day dietary record with the help of his⁄her parents. Portions were measured in terms of familiar volume and size and by reference to an atlas of local food portions. These dietary data were transferred to a computer by a nutritionist, allowing for nutrient composition (data not shown) analysis by a PC program (data not shown), developed at the Universidade Federal de São Paulo (Nutwin software, for Windows, version 1.5, 2002).

Exercise training

The combined exercise-training program was performed three times a week for one year and included 30 minutes of aerobic training plus 30 minutes of resistance training per session. The subjects were instructed to reverse the order of the exercises (aerobic and resistance) at each training session. The aerobic training consisted of running on a motor-driven treadmill (Life Fitness–Model TR 9700HR) at a cardiac frequency intensity representing ventilatory threshold I (±4 bpm), according to the results of an initial oxygen uptake test for aerobic exercises. Every session was supervised individually by an experienced physiologist.

Statistical analysis

Statistical analyses were performed using STATISTICA (version 7.0 for Windows). The Gaussian distribution of variables (including Δ values) was verified with a Kolmogorov Smirnov test. Variables with normal distribution were expressed as mean ± standard deviation (SD) while variables without normal distribution were expressed as median [quartile range] in a descriptive table. Comparisons between measures at baseline and after weight-loss intervention were made using Student's t test for parametric variables and Wilcoxon's signed rank test for non-parametric variables. Comparisons between groups were performed using Student's t test or Mann–Whitney test (non-parametric variables). A correlation study of the delta's values was performed using the appropriated tests, Spearman and Pearson's. A p value < 0.05 was considered statistically significant.

RESULTS

Statistical analysis

Fifty five obese adolescents were enrolled in the interdisciplinary weight loss therapy. The patients were paired according to BMI and analyzed by gender: boys (n=21) and girls (n=24). The descriptions of the analysed variables are shown in Table 1. All anthropometric variables portray the pathogenic of obesity, including a high percentile of fat mass, reduction in the proportion of lean mass, waist circumference higher than recommended. The entire group presented high levels of leptin and reduced concentrations of adiponectin, suggesting an inflammatory process.

At baseline 21.9% of the obese adolescents presented SBD, 12.5 % presented SBD index higher than >5/hour and 75% of the teenagers presented snoring ranged between moderate to severe. It was also observed that the adolescents presented low percentage of REM sleep, and an increased percentage of stage 1 sleep. Sleep data are presented in table 2.

Impact of the therapy on sleep

Entire group

Long-term therapy promoted beneficial changes reducing prevalence of SBD and PLM by 60% and 42%, respectively. Indeed, the snoring frequency decreased from 75% to 31%.

The therapy was effective to increase statistically REM sleep =-2.44, p=0.01) (Figure 1), and baseline oxygen saturation (z=2.3; p=0.02) among 59.6% adolescents. It was also verified that after one year of weight loss therapy, there was a reduction on sleep stage N1, arousals, respiratory events, respiratory disturbance index, obstructive apnea index, hypopnea index, and arousal index. However, this decrease did not reach statistically significant values. Furthermore, it was observed statistically decrease in REM sleep latency (t=3.24; p=0.002) (figure 1) and desaturation index on NREM sleep (z=2.45; p=0.01). The descriptions of the analysed variables are shown in Table 2.

Table 1. Anthropometric and clinical data among obese adolescents before and after weight loss therapy.

VARIABLES/TIME	ENTIRE GROUP (N=55)		BOYS (N=21)		GIRLS N=34	
	BASELINE	AFTER THERAPY	BASELINE	AFTER THERAPY	BASELINE	AFTER THERAPY
BODY WEIGHT (KG)	107.1±17.65	97.47±18.9[A]	112.2±19.66	102.6±21.62[A]	104±15.87	94.46±16.71[A]
BMI (KG/M2)	37.6±5.3	33.75±5.91[A]	36.8±5.7	33±6.8[A]	38±5.2	34.16±5.3[A]
BODY FAT (%)	47.1±5.1	39.72 ±6.68[A]	44.66±5[B]	36.81±6.59[AB]	48.54±4.6	41.41±6.2[A]
BODY FAT (KG)	50.8±11.85	39.31±38[A]	50.71±13.31	38.62±13.83[A]	50.9±11.1	39.7±11.47[A]
FAT FREE MASS (%)	52.88±5.12	60.28±6.68[A]	55.33±5.05[B]	63.1±6.5[AB]	51.45±4.6	58.59±6.2[A]
FAT FREE MASS (KG)	56.25±8.5	58.1±9.5[A]	61.55±8.5[B]	63.86±9.5[AB]	53±6.85	54.75±7.9[A]
VISCERAL FAT (CM)	4.69±1.69	3.1±1.48[A]	5.38±2[B]	3.8±1.8[AB]	4.2±1.25	2.6±1[A]
SUBCUTANEOUS FAT (CM)	4.3±0.93	3.2±0.84[A]	3.9±0.66[B]	3.01±0.84[A]	4.5±1	3.4±0.8[A]
WAIST CIRCUNFERENCE	102.38±10.16	97.54±11.54[A]	105.8±10.72	100.8±11.42[A]	100.3±9.4	95.9±11.61[A]
GLUCOSE	90.73±7.5	91.8±7.3	94.42±8.4[B]	94.57±7.99[AB]	88.58±6.11	90±6.45[A]
HOMA-IR	3.59 (1.24-16)	2.67 (0.7-22)	3.57 (1.6-16)	2.3 (0.7-22)	3.1 (1.2-11.76)	2.7 (0.72-7.6)[A]
TOTAL CHOLESTEROL (MG/DL)	170±34	160.2±29.34[A]	178.9±40.19	165.9±36.19[A]	164.91 ± 29.2	156.7 ± 24.29[A]
TRIGLYCERIDES (MG/DL)	118.85±72.23	92.51±43.61[A]	143.2±104	101.8±51.29[A]	104.6±39.9	86.91±37.9[A]
HDL (MG/DL)	44.5±9.2	46.76±9.9[A]	40.52±8.27[B]	42.33±8.4[B]	46.8±9.1	49.4±9.8[A]
LDL (MG/DL)	102.33±28.57	94.9±24.8[A]	111.85±32.43	103±31.77[A]	97±25.13	89.9±18.28[A]
VLDL (MG/DL)	22.32±9.3	18.53±15.5[A]	24.75±11.16	20.47±10.25[A]	20.9±8	17.3±7.6[A]
ADIPONECTIN	3.38 (0.26-12.79)	4.3(2.4-21.6)[A]	3.6 (1.8-7.88)	4.2 (2.4-14)	4.17 (0.26-12.79)	4.9 (2.53-21.6)[A]
LEPTIN	54.1 ± 28.3	24.95 (1.8-99.2)[A]	43.9 ± 24.93[B]	17.8 (1.8-95.58)[A]	60.5 ± 28.7	28.6 (10.8-99.2)[A]

VALUES EXPRESSED BY MEAN ± SD, OR MEDIAN (QUARTILE RANGE)
[A] COMPARISON OF BASELINE VS AFTER ONE YEAR OF THERAPY , P ≤ 0.05
[B] COMPARISON BETWEEN GROUPS , P ≤ 0.05

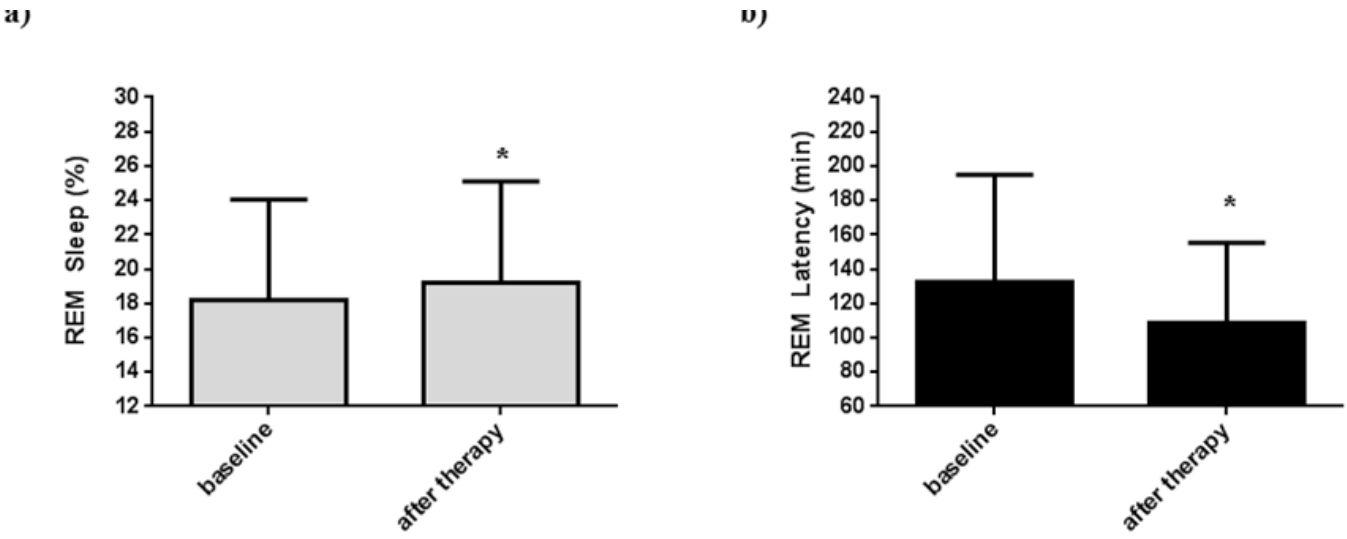
Table 2. Sleep data among obese adolescents before and after weight loss therapy.

	ENTIRE GROUP (N =55)		BOYS N=21		GIRLS N=34	
VARIABLES/TIME	BASELINE	AFTER THERAPY	BASELINE	AFTER THERAPY	BASELINE	AFTER THERAPY
SLEEP LATENCY (MINUTES)	11.7 (0-167.6)	12 (0-63.3)	11.7 (0.3-79.2)	9.3 (0-148.2)	11.7 (0-167.6)	12.05 (0-63.3)
REM SLEEP LATENCY (MINUTES)	132.58 ± 62.25	108.07 ± 46.69[A]	148.94 ± 87.41	101.58±59.53[A]	132.58 ± 62.25	108.07 ± 46.69[A]
SLEEP TOTAL TIME (MINUTES)	401.8 ± 70.1	404.1 ± 70.16	377 ± 64.41	406.84±67.71[A]	401 ± 70.16	404.11 ± 40.11
SLEEP EFFICIENCY (%)	90.4(31.2-97.2)	87.1 ± 8.84	89.9 (50.6- 95.2)	85.54±11.7	85.89 (31.2 – 97.2)	88.1 ± 5.4
SLEEP STAGE N1 (%)	6.69± 4.07	5.98±2.78	7.57±4.33	7.03±3.2B	6 ± 4	5.3 ± 2.31
SLEEP STAGE N2 (%)	49.17±8.2	47.10±8.3	46.34±14.17	45.39±7.44	48.26 ±11.6	48.16 ± 8.7
SLEEP STAGE N3 (%)	25.88 ± 7.66	26.92±8.09	24.88±10.62	26.77±8.05	24.9 ± 8.3	27 ± 8.23
REM SLEEP (%)	18.2 ± 5.83	19.2±5.9[A]	16.41±7.3	20.79±7.5[A]	17.81 ± 6.24	19.21 ± 4.87
AROUSALS (N)	54.41±20.5	47.2± 19.39	71.15±42.53	70.54±29.4[B]	54.41 ± 20.5	47.2 ± 19.39
AROUSAL INDEX (N/HR)	9.5 ± 5.4	8.4 ± 3.95	11.8 ± 7.8[B]	10.66 ± 4.55[B]	8.2 ± 2.9	7.05 ± 2.8
PLM (N)	0 (0- 10.4)	0 (0-12.4)	0 (0- 9.3)	0 (0-11.7)	0 (0-10.4)	0 (0-12.4)
RESPIRATORY EVENTS (N)	2.5 (0-104)	1.5 (0-122)	9 (0-150)[B]	10 (0-92)[B]	2.5 (0-104)	1.5 (0-122)
RESPIRATORY DISTURBANCE INDEX (N/HR)	0.35 (0-16.5)	0.15(0-17.5)	1.5 (0-24)[B]	1.5 (0-13.8)[B]	0.35 (0-16.5)	0.15 (0-17.5)
APNEA/ HYPOPNEA INDEX (N/HR)	0.30(0-16.5)	0.15(0-17.5)	1.5 (0-22.6)[B]	1 (0-13.8)[B]	0.3 (0-16.5)	0 (0-17.5)
APNEA INDEX (N/HR)	0 (0-3.3)	0 (0-0.4)	0.3 (0-5.7)[B]	0.3 (0-1.2)[B]	0 (0-3.3)	0 (0-0.4)
HYPOPNEA INDEX (N/HR)	0.3 (0-13.8)	0.15 (0-17.5)	1.2 (0-20.3)	0.8 (0-13.5)	0.3 (0-13.8)	0.15 (0-17.5)
OBSTRUCTIVE APNEA INDEX (N/HR)	0 (0-22)	0 (0-1)	0 (0-20)	0 (0-9)[B]	0 (0-22)	0 (0-1)
CENTRAL APNEA	0 (0-18)	0 (0-2)	1 (0-14)[B]	0 (0-4)	1 (0-14)	0 (0-4)
MIXED APNEA	0 (0-2)	0	0 (0-2)	0 (0-4)[B]	0 (0-2)	0(0-4)

	ENTIRE GROUP (N =55)		BOYS N=21		GIRLS N=34	
VARIABLES/TIME	BASELINE	AFTER THERAPY	BASELINE	AFTER THERAPY	BASELINE	AFTER THERAPY
HYPOPNEAS	2 (0-82)	1 (0-122)	15 (0-127)[B]	6 (0-90)[B]	2 (0-87)	1 (0-122)
RESPIRATORY EFFORT–RELATED AROUSALS (RERAS)	0 (0-1)	0 (0-13)	0 (0-14)	0 (0-0)	0 (0-14)	0 (0-0)
BASELINE OXYGEN SATURATION	97.1 (95.6-98.3)	97.4 (95-98.6)[A]	96.6 (95.8-98.2)[B]	96.6 (95.6-98.6)[B]	97.2 (95.6-98.3)	97.5 (95-98.6)
MEAN OXYGEN SATURATION	96.4 (93.8-98)	96.33 ± 1.07	96.1 (93.8-97.6)	90.47 ± 4.47	96.55 (94.9- 98)	96.49 ±1.14
MINIMUM OXYGEN SATURATION	91 (80-96)	92 (77-96)[A]	90 (80-94)[B]	92 (77-94)[B]	92 (80-96)	93 (79-96)
REM DESATURATION ÍNDEX	2.2 (0- 93)	1.1 (0-48.4)	4.1 (0-25)	2.7 (0-37)	1.5 (0-93)	0.8 (0-48.4)
NREM DESATURATION INDEX	0.8 (0-25.5)	0.7 (0-10.7)[A]	2.7 (0-25.5)[B]	1.7 (0-10.7)[B]	0.3 (0-13)	0.1 (0-8.2)

VALUES EXPRESSED BY MEAN ± SD, OR MEDIAN (QUARTILE RANGE)
A COMPARISON OF BASELINE VS AFTER ONE YEAR OF THERAPY , P ≤ 0.05 B COMPARISON BETWEEN GROUPS , P ≤ 0.05

Figure 1. Effects of the weight loss in the percentage of REM sleep (a) and on REM sleep latency (b) among obese adolescents.



Difference between boys vs. girls group

After one year of therapy, boys presented statistically improvement in REM sleep latency (t=2.56; p=0.01), and REM sleep (t=-2.5; p=0.02). Girls presented statistically improvement in REM sleep latency (t=2.05; p=0.04).

Comparing the two groups, boys presented statistically higher arousal index, respiratory events, hypopnea, respiratory disturbance index, apnea/hypopnea index, and obstructive apnea index, in both baseline and after the therapy. Furthermore, boys also presented significant higher values of baseline and minimum oxygen saturation and NREM desaturation index, when compared with girls.

Impact of the therapy on anthropometric, metabolic and inflammatory parameters

Entire group

The interdisciplinary therapy was able to improve statistically body weight (t=8.7; p=0.00), BMI (t=9.6; p=0.00), body fat (%)(t=12.63; p=0.00), body fat (kg) (t=12.3; p=0.00), fat free mass (%)(t=8.9; p=0.00), fat free mass (kg) (t=-3.43; p=0.00), visceral (t=8.2; p=0.00) and subcutaneous fat (t=8.05; p=0.00), waist circumference (t=4.5; p=0.00), total cholesterol (t=17.24; p=0.00), triglycerides (t=3.4; p=0.00), HDL (t=-2.89; p=0.00), LDL (t=3.4; p=0.00) and VLDL cholesterol (t=3.6; p=0.00).

Difference between boys vs. girls group

At baseline, boys presented higher values of fat free mass (%) (t=-2.94; p=0.00), fat free mass (kg) (t=-4.05; p=0.00) and visceral fat (t=-2.46; p=0.01) compared with girls. On the other hand, girls presented higher values of fat mass (%) (t=2.93; p=0.00), subcutaneous fat (t=2.17; p=0.03) and HDL cholesterol (t=2.6; p=0.00). The therapy was effective to improve all anthropometric measurements in both groups. Girls reached recommended values of visceral fat, however the same was not observed for boys.

Interaction between sleep and anthropometric, metabolic and inflammatory markers

Regarding the entire group, we verified negative correlations between REM sleep atency with waist circumference (r=-0.70)

and HOMA-IR (r=-0.66). In addition, positive correlations were found between body fat (kg) with respiratory events (r=0.48) and respiratory disturbance index (r=0.49).

Considering only boys, positive correlation was found between fat mass (kg) with arousals (r=0.96), respiratory events (r=0.81), respiratory disturbance index (r=0.83), and apnea/hypopnea index (r=0.82). Moreover, it was found a positive correlation between visceral fat and arousals (r=0.9) and sleep stage N 1 (r=0.87)

For girls, positive correlations were found between visceral fat and sleep latency (r=0.61), and negative correlations between visceral fat with arousals (r=-0.66), respiratory events (r=-0.74), respiratory disturbance index (r=-0.74), and apnea/hypopnea index (r=-0.74). Correlations are show on table 3

Table 3. Interaction between the variables (Delta).

	Δ VARIABLES	R	P
ENTIRE GROUP	WAIST CIRCUMFERENCE AND REM SLEEP LATENCY	-0.70	0.002
	HOMA-IR AND REMM SLEEP LATENCY	-0.66	0.004
	BODY FAT (KG) AND RESPIRATORY EVENTS	0.48	0.046
	BODY FAT (KG) AND RDI	0.49	0.043
BOYS	FAT MASS (KG) AND RESPIRATORY EVENTS	0.81	0.047
	FAT MASS (KG) AND RDI	0.83	0.04
	FAT MASS (KG) AND APNEA/HIPOPNEIA INDEX	0.82	0.042
	FAT MASS (KG) AND AROUSALS	0.96	0.002
	VISCERAL FAT AND AROUSALS	0.9	0.014
	VISCERAL FAT AND SLEEP STAGE N1	0.87	0.02
	LEPTIN AND REM	-0.93	0.006
GIRLS	VISCERAL FAT AND SLEEP LATENCY	0.61	0.045
	VISCERAL FAT AND AROUSALS	-0.66	0.025
	VISCERAL FAT AND RESPIRATORY EVENTS	-0.74	0.008
	VISCERAL FAT AND RDI	-0.74	0.008

DISCUSSION

In this study, it was investigated simultaneously the impact of an interdisciplinary weight loss therapy on sleep quality and its correlation with metabolic and anthropometric markers of obese adolescents, and also the sex differences. We demonstrated that: 1) the interdisciplinary therapy was able to improve not only anthropometric parameters but also metabolic and sleep parameters; 2) an interaction between sleep, metabolic and anthropometric variables in the young population; 3) the male gender presents higher risk and percentages of SBD even in younger ages.

An interesting finding observed in the present study is related to sleep quality. It was observed that the entire group presented lower percentages of REM sleep and higher amount of sleep stage 1, when compared to literature[18], suggesting that these patients might have a poor quality of sleep. In fact, Vgonzas et al. showed that even obese adults without sleep apnea have a reduction in REM sleep[19]. However, the current therapy was able to improve sleep by increasing % of REM sleep and decreasing REM sleep latency (figure 1). REM sleep has therefore, considering the role of REM sleep in memory process and cognition this increase is remarkable, taken into account that this age is characterized by a wide learning development[20].

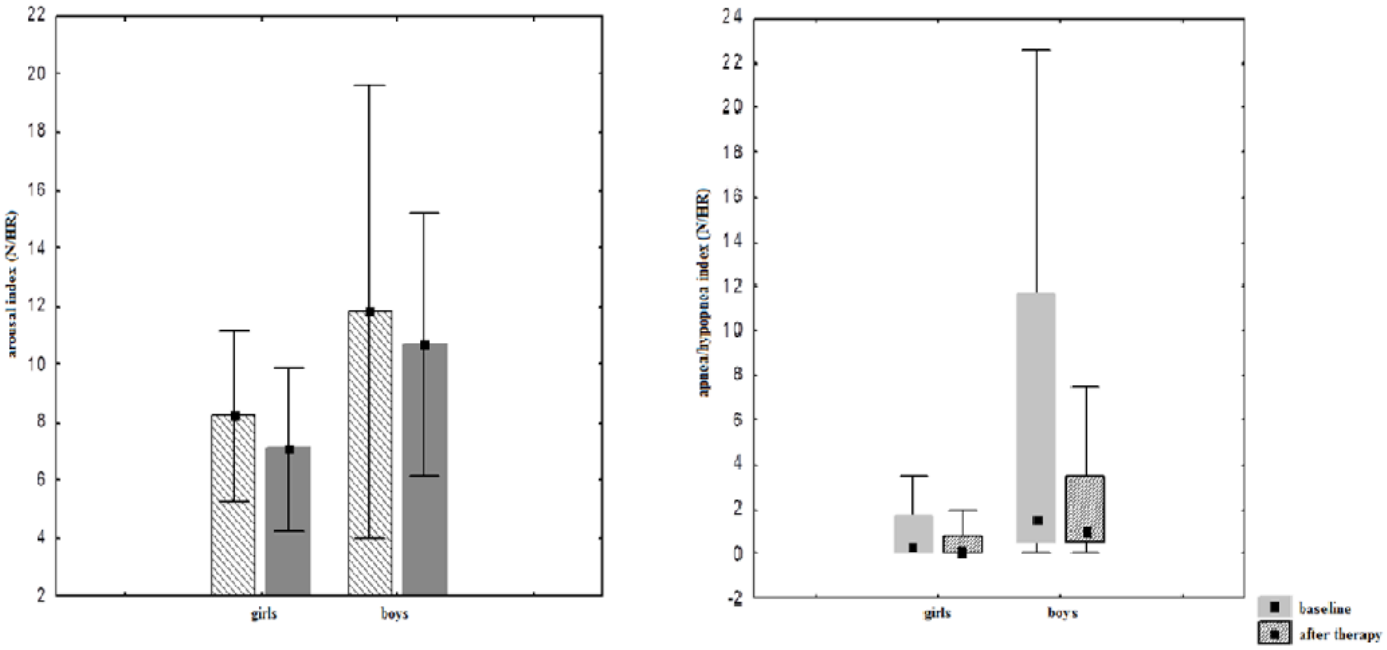
In addition, the weight loss program was effective to reduce in 60% the prevalence of SBD, confirming the importance of obesity in the pathogenesis of this disease. This result is in agreement with Siegfried et al. and Verhulst et al., which also had adolescents, as their studied population, submitted to a weight loss therapy[21,4]. Improvements in other sleep problems were also verified, in which snoring reduced from 75% to 31% and PLM from 12.5% to 8.9%. Although the teenagers remained obese after one year of treatment, it was demonstrated in the present study that a reduction of 10% in body weight is sufficient to improve sleep parameters as well sleep architecture (table 2), reinforcing the important role of an early lifestyle intervention to improve sleep pattern among obese adolescents.

Moreover, the negative correlation found between REM sleep and HOMA-IR suggests the link of sleep on glucose metabolism, in which poor quality of sleep could have an impact in the insulin resistance, linking obesity, sleep and inflammation. Previously we showed that insulin resistance is an independent predictor of atherosclerosis and NAFLD in obese adolescents[22,23]. In agreement, some studies have found associations among poor sleep quality/duration, and impairment in insulin efficiency; however it remains controversial in the literature[24-26].

The last objective of the present study was to compare genders. Thus, it is important to note that boys have worse sleep quality than girls, since they presented statistically higher breathing events and higher desaturation in NREM sleep (figure 2). Two possible hypotheses can be raised: the distinct body fat distribution; and the fact that the girls already present great levels of estrogen, since they are post-pubertal adolescents. In the adult population it is well known the correlation between central obesity and SBD[7,2] also shown by the correlations of the present study. In addition, some studies have shown that the estrogen can be a protector factor of sleep breathing disorders[28,29]. Corroborating with our findings, Fuentes-Pradera et al. reported that post-pubertal adolescents showed sex differences in clinical and polygraphic parameters that were not observed at earlier pubertal stages[30].

The lack of a lean control group is a limitation of the present study, however the results reinforce the importance of an early intervention in the weight control, and the strong link between obesity and sleep.

Figure 2. Difference between boys and girls among sleep-breathing disorders.



CONCLUSION

This proposed interdisciplinary therapy can be effective in improving not only metabolic and inflammatory profiles but also in controlling the obesity and related co-morbidities in adolescents. Our results suggest, for the first time in obese adolescents, an intrinsic role of inflammatory and neuroendocrine markers in sleep quality. Finally, boys had a worse quality of sleep than girls.

ACKNOWLEDGMENTS

We would like to thank the patients that participated in the study and the sources of funding: FAPESP (2008/53069-0, 2006/00684-3, 2011/50356-0 and 2011/50414-0), FAPESP (CEPID/Sleep #9814303-3 S.T), CAPES (AUX-PE-PNPD 2566/2011), AFIP, CNPq, CAPES, CENESP, UNIFESP-EPM, CENSA, and CEPE that supported GEO-CEPE.

REFERÊNCIAS

1. Liou YM, Liou TH, Chang LC. Obesity among adolescents: sedentary leisure time and sleeping as determinants. J Adv Nurs. 2010 Jun; 66(6):1246-56. doi: 10.1111/j.1365-2648.2010.05293.x. PubMed PMID: 20546358.

2. Verhulst SL, Schrauwen N, Haentjens D, Suys B, Rooman RP, Van Gaal L, , et al. Sleep disordered breathing in overweight and obese children and adolescents: prevalence, characteristics and the role of fat distribution. Arch Dis Child. 2007 Mar; 92(3):205-8. PubMed PMID: 17041010.

3. Redline S, Storfer-Isser A, Rosen CL, Johnson NL, Kirchner HL, Emancipator J, et al. Association between metabolic syndrome and sleep-disordered breathing in adolescents. Am J Respir Crit Care Med. 2007 Aug 15;176(4):401-8. doi: 10.1164/rccm.200703-375OC. PMCID: PMC1994215.

4. Verhulst SL, Jacobs S, Aerts L, Schrauwen N, Haentjens D, Rooman RP, et al. Sleep-disordered breathing: a new risk factor of suspected fatty liver disease in overweight children and adolescents? Sleep Breath. 2009 May;13(2):207-10. doi: 10.1007/s11325-008-0231-5. PubMed PMID: 19002513.

5. Tufik S1, Santos-Silva R, Taddei JA, Bittencourt LR. Obstructive sleep apnea syndrome in the Sao Paulo Epidemiologic Sleep Study. Sleep Med. 2010 May;11(5):441-6. doi: 10.1016/j.sleep.2009.10.005. PubMed PMID: 20362502.

6. Dâmaso AR, de Piano A, Sanches PL, Corgosinho F, Tock L, Oyama LM, et al. Hyperleptinemia in obese adolescents deregulates neuropeptides during weight loss. Peptides. 2011 Jul;32(7):1384-91. doi: 10.1016/j.peptides.2011.04.025. Epub 2011 May 6. PubMed PMID: 21641948.

7. Chaput JP, Després JP, Bouchard C, Tremblay A. Short sleep duration is associated with reduced leptin levels and increased adiposity: Results from the Quebec family study. Obesity (Silver Spring). 2007 Jan;15(1):253-61. PubMed PMID: 17228054.

8. Van Cauter E, Holmback U, Knutson K, Leproult R, Miller A, Nedeltcheva A, et al. Impact of sleep and sleep loss on neuroendocrine and metabolic function.

Horm Res. 2007;67 Suppl 1:2-9. PubMed PMID: 17308390.

9. Van Cauter E, Ehrmann DA. Sleep and metabolism. Preface. Best Pract Res Clin Endocrinol Metab. 2010 Oct;24(5):vii-viii. doi: 10.1016/j.beem.2010.09.009. PubMed PMID: 21112018.

10. Tanner JM, Whitehouse RH. Clinical longitudinal standards for height, weight, height velocity, weight velocity, and stages of puberty. Arch Dis Child. 1976 Mar;51(3):170-9. PubMed PMID: 952550.

11. Berry RB, Budhiraja R, Gottlieb DJ, Gozal D, Iber C, Kapur VK, et al. Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. J Clin Sleep Med. 2012 Oct 15;8(5):597-619. doi: 10.5664/jcsm.2172. PubMed PMID: 23066376.

12. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force. Sleep. 1999 Aug 1;22(5):667-89. PubMed PMID: 23066376.

13. Accardo JA, Shults J, Leonard MB, Traylor J, Marcus CL. Differences in overnight polysomnography scores using the adult and pediatric criteria for respiratory events in adolescents. Sleep. 2010 Oct;33(10):1333-9. PubMed PMID: 21061855.

14. M Bonnet, D Carley, M Carskadon, P Easton, Guilleminaut C, Harper R, et al. Sleep disorders atlas task force of ASDA. EEG arousals: scoring rules and examples. Sleep, 1992 Jan, 15(2): 173–184.

15. Zucconi M, Ferri R, Allen R, Baier PC, Bruni O, Chokroverty S, et al; International Restless Legs Syndrome Study Group (IRLSSG). The official World Association of Sleep Medicine (WASM) standards for recording and scoring periodic leg movements in sleep (PLMS) and wakefulness (PLMW) developed in collaboration with a task force from the International Restless Legs Syndrome Study Group (IRLSSG). Sleep Med. 2006 Mar;7(2):175-83. Epub 2006 Feb 3. PubMed PMID: 16459136.

16. Schwimmer JB, Deutsch R, Rauch JB, Behling C, Newbury R, Lavine JE. Obesity, insulin resistance, and other clinicopathological correlates of pediatric nonalcoholic fatty liver disease. J Pediatr. 2003 Oct;143(4):500-5. PubMed PMID: 14571229.

17. Institute of Medicine (US) Subcommittee on Interpretation and Uses of Dietary Reference Intakes; Institute of Medicine (US) Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. NRC. Dietary reference intake: applications in dietary assessment. Washington (DC): National Academies Press (US); 2000.

18. Nunes ML. Sleep disorders. J Pediatr (Rio J). 2002 Jul-Aug;78 Suppl 1:S63-72. doi: http://dx.doi.org/10.1590/S0021-75572002000700010

19. Vgontzas AN, Bixler EO, Tan TL, Kantner D, Martin LF, Kales A. Obesity without sleep apnea is associated with daytime sleepiness. Arch Intern Med. 1998 Jun 22;158(12):1333-7. PubMed PMID: 9645828.

20. Bawden FC, Oliveira CA, Caramelli P. Impact of obstructive sleep apnea on cognitive performance. Arq Neuropsiquiatr. 2011 Aug;69(4):585-9. PubMed PMID: 21877024.

21. Siegfried W, Siegfried A, Rabenbauer M, Hebebrand J. Snoring and sleep apnea in obese adolescents: effect of long-term weight loss-rehabilitation. Sleep Breath. 1999;3(3):83-88. PubMed PMID: 1189113.

22. de Piano A, Prado WL, Caranti DA, Siqueira KO, Stella SG, Lofrano M, et al. Metabolic and nutritional profile of obese adolescents with nonalcoholic fatty liver disease. J Pediatr Gastroenterol Nutr. 2007 Apr;44(4):446-52. PubMed PMID: 17414142.

23. de Lima Sanches P, de Mello MT, Elias N, Fonseca FA, de Piano A, Carnier J, Oyama LM, et al. Improvement in HOMA-IR is an independent predictor on reduction of carotid intima-media thickness in obese adolescents submitted to an interdisciplinary weight loss program. Hypertens Res. 2011 Feb;34(2):232-8. doi: 10.1038/hr.2010.225. Epub 2010 Dec 2. PubMed PMID: 21124323.

24. Sanders MH, Givelber R. Sleep disordered breathing may not be an independent risk factor for diabetes, but diabetes may contribute to the occurrence of periodic breathing in sleep. Sleep Med, 2003 Jul, 4(4): 349–50. PubMed PMID: 14592310.

25. Knutson KL, Van Cauter E, Zee P, Liu K, Lauderdale DS. Cross-sectional associations between measures of sleep and markers of glucose metabolism among subjects with and without diabetes: the Coronary Artery Risk Development in Young Adults (CARDIA) Sleep Study. Diabetes Care. 2011 May;34(5):1171-6. doi: 10.2337/dc10-1962. PubMed PMID: 21411507; PMCID: PMC3114508

26. Nena E, Steiropoulos P, Papanas N, Tsara V, Fitili C, Froudarakis ME, et al. Sleepiness as a marker of glucose deregulation in obstructive sleep apnea. Sleep Breath. 2012 Mar;16(1):181-6. doi: 10.1007/s11325-010-0472-y. PubMed PMID: 21207173.

27. Vgontzas AN. Does obesity play a major role in the pathogenesis of sleep apnoea and its associated manifestations via inflammation, visceral adiposity, and insulin resistance? Arch Physiol Biochem. 2008 Oct;114(4):211-23. doi: 10.1080/13813450802364627 . PubMed PMID: 18946782.

28. de Campos HH, Bittencourt LRA, Haidar MA, Tufik S, Baracat EC. Prevalência de distúrbios do sono na pós-menopausa. Rev Bras Ginecol Obstet. 2005, 27(2): 731–6.

29. Lin CM, Davidson TM, Ancoli-Israel S. Gender Differences in Obstructive Sleep Apnea and Treatment Implications. Sleep Med Rev. 2008 Dec;12(6):481-96. doi: 10.1016/j.smrv.2007.11.003. PMCID: PMC 2042982.

30. Fuentes-Pradera MA, Sánchez-Armengol A, Capote-Gil F, Quintana-Gallego E, Carmona-Bernal C, Polo J, et al. Effects of sex on sleep-disordered breathing in adolescents. Eur Respir J. 2004 Feb;23(2):250-4. PubMed PMID: 14979499.

Como citar este artigo/How to cite this article:
Corgosinho FC, Dâmaso AR, Tufik S, Piano A, Sanches PL, Campos RMS, et al. One year of interdisciplinary therapy decreases predictors and prevalence of sleep-breathing disorder in obese adolescents**.** J Health Biol Sci. 2015 Jan-Mar; 3(1): 10-17