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Plasma Levels of Peptide YY in Obese Adolescents Throughout A Year of Treatment for Weight Loss

Simone Pereira Fernandes[1,2], Janine Alessi[1,2], Mirian Benites Machado[2], Zilda Elisabeth de Albuquerque Santos[1,2], Carlos Alberto Nogueira-de-Almeida[3] and Elza Daniel de Mello[1,2]

[1]Hospital de Clínicas de Porto Alegre; Porto Alegre, Rio Grande do Sul, Brasil.

[2]Universidade Federal do Rio Grande do Sul; Porto Alegre, Rio Grande do Sul, Brasil.

[3]Universidade Federal de São Carlos, São Carlos, São Paulo, Brasil.

***Correspondence:**
Simone Pereira Fernandes, Av nonoai 1458 m211, CEP 91720000, Bairro Nonoai, Porto Alegre, Rio Grande do Sul, Brasil, Tel: (051) 92126133.

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ABSTRACT

Objective: *To evaluate serum PYY levels in obese adolescents treated in an outpatient obesity treatment program at a public hospital in southern Brazil.*

Methods: *Fifty-one adolescents with obesity were included and followed up for 12 months. They attended 12 consultations with weight loss recommendations based on quantitative and qualitative food goals and reduction of sedentary behavior. Fasting serum levels of PYY, total cholesterol, HDL-cholesterol, triglycerides (TG), LDL-cholesterol (LDL-C), insulin and glycemia were collected in T0 (before the first consultation), T1 (after 24 weeks) and T2 (after 48 weeks). Besides blood samples, abdominal circumference (AC) was measured, and the homeostasis model assessment (HOMA-IR) was calculated. By electrical bioimpedance analysis, fat mass and basal metabolic rate were measured.*

Results: *Between T0 and T2, there was weight loss with a significant reduction of body mass index (BMI) Z-scores ($p<0.001$). There were also a significat reduction of PYY ($p=0.026$), TRIG ($p=0.016$), LDL-C ($p=0.016$), HOMA-IR ($p=0.004$), AC ($p<0.001$) and BMI ($p=0.002$). In T2, there was a reduction in the baseline weight and in the proportion of severe obesity, and there was an increase in PYY levels ($r=-0.421$; $p=0.002$).*

Conclusion: *Obese adolescents who changed their sedentary behavior and adopted a balanced diet showed weight loss and increse in PYY levels.*

Keywords

Adolescent, Peptide YY, Lifestyle interventions, Obesity, Weight loss.

Introduction

Obesity is the cause of many comorbidities and is currently the most common chronic disease among children and adolescents, affecting 20 to 25% of children under 19 years of age in Latin America [1]. In the southern region of Brazil, the evolution of overweight in the last 6 years among adolescents increased from 4.7 to 27.2% among boys and from 9.7 to 22.0% among girls [2]. It is an important public health problem, as it not only impairs a person's quality of life but also considerably increases the national health budget. That is why it is one of the major public health challenges of the 21st century.

Obesity results from an imbalance between energy intake and expenditure and appears to be associated with changes in the concentrations of peptide hormones derived from the intestine, such as peptide YY (PYY), involved in decreased satiety and

increased energy intake [3,4]. One of the ways to measure satiety is by measuring the production of PYY after a particular food intake. PYY is a hormone produced in the walls of the distal portion of the ileum, colon and rectum, and secreted when ingested nutrients begin to reach this location [3]. Its best known physiological function is to signal to the central nervous system that food intake occurred, causing the sensation of satiety [3]. The administration of PYY to human volunteers demonstrated a relevant ability to reduce food intake regardless of nutritional status [5,37]. Current data indicate that PYY influences energy homeostasis through different mechanisms, but resistance to PYY action in obese individuals has never been demonstrated [6]. In the short term it has been suggested its association with lower dietary intake and reduction of body weight [7]; in the long term, there is association with increased thermogenesis and lipolysis [8].

The objective of this study was to evaluate the evolution of serum PYY levels in obese adolescents treated at an outpatient clinic for the management of childhood and juvenile obesity in a public hospital in southern Brazil.

Methods

An intervention study with clinical follow-up was carried out over a year with adolescents ages 10 to 19 years with evaluation of Tanner pubertal staging [9] above 2, BMI percentile ≥ 97 and BMI Z-score ≥ +2 at baseline at an outpatient clinic for obesity at a university hospital in Porto Alegre, Brazil. Those taking continuous medication were excluded. Obesity was defined as z-score of BMI greater than or equal to +2 and severe obesity greater than +3 for sex and age [10].

All participants had monthly consultations that each consisted of: anthropometric evaluation (weight, height, waist circumference), nutritional guidance and food anamnesis. All information was discussed in an interdisciplinary team and a plan of action was defined, with nutritional recommendations and stimulus to the reduction of sedentary behaviors, as suggested by Barlow [11], Beghetto et al. [12], Fernandes et al. [13], de Mello et al. [14] and by Ministry of Health of Brazil [15]. The following are the nutritional recommendations provided to the participants: reduction and / or withdrawal of sugary drinks (artificial juices and soft drinks) and unhealthy foods (cookies, savory snacks, pastries and chocolates); intake of 3 units of fruit / day; ingestion of dairy products (milk or yogurt or 2 slices of cheese) at least once a day; reduction of the portion size of the usually consumed foods; ingestion of breakfast; eating at the table; chewing the food thoroughly; and setting time for each meal. As a stimulus to the reduction of sedentary behavior, the adolescents were advised to: limit screen time (television, tablet, telephone, computer) to two hours a day and to practice physical activity (volleyball, soccer, handball, dancing, walking, playing with friends).

After 8-hours fasting, blood samples were collected at T0 (baseline), T1 (24 weeks) and T2 (48 weeks) in order to evaluate: total cholesterol; (c-HDL), (c-LDL), TG, insulin, blood glucose and PYY_{3-36}. Besides those data, an electrical impedance test (BioDynamics450) was carried out in order to evaluate the percentage of fat mass (%FM) and basal metabolic rate (BMR). HOMA-IR was calculated using blood glucose and insulin results. PYY_{3-36} was determined by Elisa (*Enzyme-Linked Immunosorbent Assay*), through commercial kits of *Phoenix*.

The outcomes evaluated were: the evolution of BMI Z-score and abdominal circumference, body composition, basal metabolic rate, laboratory markers and PYY. To compare the three time points (T0, T1, T2), variance analysis (ANOVA) tests were applied for repeated measures, complemented by Bonferroni, or Friedman test, in conjunction with Wilcoxon's test. The associations between the variables were evaluated by the Pearson or Spearman correlation coefficients. The statistical analysis was performed in the SPSS program V21.0, and the level of significance considered was of $p < 0.05$. All the study procedures were evaluated and approved by the ethics committee of the Hospital de Clínicas of Porto Alegre, under protocol 130190.

Results

The mean age of the 51 adolescents involved in the study was 12.02 ± 0.9, of which 29 (56.9%) were female; 50.5% had at least 1 obese parent, with a prevalence of maternal and paternal obesity of 33.3% and 37.2%, respectively. Of these adolescents, 21 (41.2%) were obese and 58.8% were severely obese. Table 1 presents the biochemical, anthropometric, %FM and BMR results, in the three time points that were evaluated. We observe that PYY significantly increased over time ($p = 0.026$). The other parameters evaluated did not present significantly statistic changes.

The intervention provided a significant improvement in BMI Z-score and AC. Table 2 shows that there was a significant reduction in the number of patients who started the study with severe obesity and, over the course of 12 months, this number dropped to 15 ($p < 0.001$).

In relation to PYY, a negative and significant variation was observed with BMI Z-score (Table 3).

Discussion

During childhood and adolescence, a number of factors including age, puberty, gender, and body composition may contribute to differences in satiety, food intake, and appetite-related peptide levels [16]. Other authors examined the effect of weight loss on PYY release in obese children and found a significant increase in fasting hormone after weight reduction [17]. The present study showed that the increase in plasma concentrations of PYY and the reduction of BMI occurred after 12 months of intervention. Weight reduction resulted in changes in the adiposity status represented by the decrease in AC and the reduction of the following biochemical values: insulin, LDL-C, TC and TRIG. Considering that the plasma concentration of PYY does not change within the age group [18], the changes observed are due to the proposed interventions.

Table 1: Results of the biochemical parameters, anthropometric measurements, body fat percentage and basal metabolic rate in the three time points evaluated.

Variables	T0	T1	T2	p
PYY (Pg/mL)	55.9 ± 17.4[a]	58.2 ± 16.6[ab]	61.2 ± 17.7[b]	**0.026**
***Insulin (mg/dL)**	19.3 (15.2 – 27.9)	18.7 (14.1 – 26.3)	17.3 (12.9 – 24.3)	**0.052**
Glucose (mg/dL)	90,84 ± 7.78	88.76 ± 5.44	87.98 ± 6.87	0.071
TC (mg/dL)	163.6 ± 29.4[b]	156.9 ± 24.4[ab]	151.0 ± 22.5[a]	**0.003**
LDLc (mg/dL)	100.04 ± 22.02	96.34 ± 19.95	93.30 ± 18.28	**0.058**
TG (mg/dL)	99.7 ± 46.1[ab]	101.9 ± 43.5[b]	88.6 ± 32.8[a]	**0.022**
HDLc (mg/dL)	42.12 ± 9.22	41.04 ± 8.17	41.90 ± 7.49	0.533
BMI (kg/m²)	29.6 ± 4.4b	28.8 ± 4.5ab	28.6 ± 5.3a	**0.002**
BMI Z-score	3.4 ± 0.9c	3.0 ± 0.8b	2.8 ± 0.9a	**<0.001**
AC (cm)	93.0 ± 11.3b	90.8 ± 10.4a	90.2 ± 12.1a	**0.003**
Body fat percentage (%)	32.9 ± 6.0	31.9 ± 5.9	32.3 ± 6.2	0.340
BMR (Kcal/day)	1382 ± 388	1430 ± 333	1447 ± 334	0.110

Variables described as mean ± SD or * median (percentiles 25-75)

[a,b] Equivalent letters do not differ by the Bonferroni test at 5% significance

Lable: peptide tyrosine tyrosine (PYY), Total Cholesterol (TC), HDLcholesterol (HDLc), triglycerides (TG), LDLcholesterol (LDLc), abdominal circumference (AC), percentage (%), basal metabolic rate (BMR), body mass index (BMI), body mass index Z score (BMI Z-score), low density lipoprotein (LDL), high density lipoprotein (HDL).

Table 2: Number of individuals, with undesired biochemical results, in the three time points evaluated.

Variables	T0 n=51	T2 n=51	T2 n=51	p
HOMA IR >3,6	40	40	34	0,105
Glucose > 100 mg/dL	4	2	2	0,368
Total Cholesterol > 170 mg/dL	19	18	15	0,234
LDLc> 130 mg/dL	6	2	1	**0,016**
TG > 130 mg/dL	8	10	4	**0,016**
HDLc < 45mg/dL	34	36	37	0,494

Lable: Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), LDL cholesterol (LDLc), triglycerides (TG), HDL cholesterol (HDLc), low density lipoprotein (LDL), high density lipoprotein (HDL).

Table 3: Association of PYY levels with other variables through the Pearson (r) or Spearman (rs) correlation coefficients.

PYY vs variables	T0 correlation coefficients	T1 correlation coefficients	T2 correlation coefficients	Time variation 0 -2 (Δ) correlation coefficients
BMR (Kcal/day)	0.006	0.072	-0.011	0.002
% FM	-0.087	-0.104	-0.042	0.139
Lean mass	0.105	0.165	0.010	-0.182
BMI (Kg/m²)	0.041	0.129	0.018	-0.421
HDL c	0.137	-0.068	0.226	-0.185
BMI Z-score	0.105	0.144	-0.037	**-0.340***
TG	-0.094	-0.272	-0.082	-0.107
TC	0.129	-0.050	0.065	0.041
LDLc	-0.070	0.051	-0.128	-0.079
Glucose	0.176	0.086	0.308*	0.165
Insulin	-0.116	-0.120	-0.077	0.109
AC	0.011	0.102	0.030	-0.186

** p<0,01 - significant inverse association: the lower the BMI, the higher the levels of the PYY hormone.

*p<0,05- significant inverse association: the lower the z-score BMI, the higher the levels of the PYY hormone.

Lable: percentage (%), body mass index (BMI), body mass index Z score (BMI Z-score), HDL cholesterol (HDLc), Total Cholesterol (TC), triglycerides (TG), LDL cholesterol (LDLc), abdominal circumference (AC), basal metabolic rate (BMR), low density lipoprotein (LDL), high density lipoprotein (HDL), T0 (baseline), T1 (24 weeks) and T2 (48 weeks).

Insulin concentrations change physiologically during puberty [19] and the reasons for these changes are not well understood, which makes it difficult to interpret them in adolescents [20]. However, it is agreed upon that central obesity is the main aspect related to insulin resistance [21,22] and that the changes refer to the physiological insulin resistance of adolescence, which is a mechanism used by the body to make the necessary anabolism to the adolescent's rapid growth. [23,24]. The findings presented here showed that individuals with higher BMI and AC had the highest levels of insulin, glycemia and HOMA-IR at the beginning of the study, which is in agreement with other recent studies [25,26]. Taking into account the effect of puberty, longitudinal studies report that insulin resistance increases more during puberty in obese children than in children with healthy weight [27,28].

It is currently unknown if the relationships between glucose and / or insulin affect PYY. In the present study there was no association between PYY and insulin, HOMA-IR or fasting glucose. King et al. [7] suggest that signs of anorectic hormones, such as PYY, may have a likely mediation in insulin sensitivity (HOMA-IR) due to central nervous system activity and muscle metabolism. Data from the present study show that TG and TC levels showed a significant reduction after 48 weeks of follow-up. According to Chagas et al. [29], high TG values in adolescents may be due to obesity and insulin resistance and it has been shown that the degree of obesity is directly proportional to the increase in TG [26]. Bell et al. [30] showed that lifestyle intervention results in an improvement in plasma lipid concentrations and insulin sensitivity in obese children, even in the absence of weight loss and changes in body composition. Ho et al. [18] showed that lifestyle interventions resulted in better levels of TC and TG up to 2 years from baseline and, of insulin and HOMA-IR within 1 year, but found no association with weight loss or body fat reduction.

The present study also showed no association between BMI reduction and the evaluated metabolic indexes. The weight loss and change of some variables obtained in this study are consistent with interventions based on lifestyle changes in adolescents, as found in the review of Oude Luttikhuis et al. [31]. A meta-analysis of 18 studies by Ho et al. indicated that lifestyle interventions that incorporated dietary modifications lead to significant weight loss when compared to no treatment and that weight loss is greater when the duration of treatment is longer than 6 months.

The results in the improvement of some biochemical and anthropometric patterns and the reduction of the number of individuals with undesired biochemical results may reflect the adherence to weight loss recommendations, which included dietary goals and stimulus to reduce sedentary behavior. The standardized technique in the service was an approach that aimed at changing eating habits and lifestyle gradually, focusing first on the quantitative changes in food and, later, on qualitative changes in food, without the traditional prescription of restrictive diets. Thus, it was postulated that, along the nutritional recommendation, this sample modified the caloric content of the meals, corroborating with the findings of Murphy et al. [32] which showed that the increase in PYY secretion was positively correlated with the caloric content of meals. One of the agreed tasks of nutritional recommendations was the increased intake of complex carbohydrates and the reduction in the amount of saturated fats stimulating the polyunsaturated fats. Troke et al. [33] showed that a diet rich in carbohydrates and low in fat is associated with higher levels of PYY in humans. Ludwig [34] has shown in a clinical trial evidence of the benefit of a diet focused on food quality instead of fat restriction as a strategy for altering energy balance.

In prepubertal adolescents who are obese, balanced macronutrient diets have been proposed as a more adequate dietary strategy in weight loss [11]. Considering the potential adverse effects of low-calorie diets in individuals who did not complete their pubertal growth, the recommendations did not include food exclusion / restriction in the nutritional management of pubescent obese adolescents according to Figueroa-Colon et al. [35]. In the Center where the present study was conducted, a multidisciplinary approach was used and the results corroborate with other clinical programs of childhood and juvenile obesity that are based on simple dietary changes and modifications of lifestyle to improve the body composition of obese children and adolescents [15,36]. Overall, PYY levels in obesity are low, but it is unclear whether these low levels of PYY determine the development of obesity or whether fasting PYY levels are reduced because of obesity. Thus, it is unclear whether the positive effects of the findings were attributable to the increase in PYY and subsequent to weight reduction or if weight reduction caused PYY levels to rise.

Although more studies are needed, the present study suggests that lifestyle interventions based on quantitative food changes such as reducing the current portion size and / or withdrawing sugary drinks, cookies, salted foods, chocolates; qualitative changes in diet such as ingestion of 3 units of fruit / day, intake of dairy at least once a day, thoroughly chewing of foods, setting the time for each meal, reducing sedentary behavior by limiting screen time to up to 2 hours per day and practicing physical activity may be a therapeutic strategy for increasing PYY levels in obese adolescents. By analyzing the number of individuals who are no longer severely obese and improving the undesirable biochemical values from baseline to the end of the study, the results were relevant and provide important information on the underlying mechanism of this effect. The data suggest some components for future interventions in weight management of children and adolescents. More comprehensive investigations of serum regulation of hormone-derived gut signals with behavioral and clinical outcomes are needed to understand the consequences on appetite deregulation in obese adolescents.

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