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Clinical Research

The Effect of Peptide YY3-36 in Body Mass Regulation in Patients with Exogenous Constitutional Obesity

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Abstract

The article deals with PYY3-36 level in the blood serum of patients suffering from exogenous constitutional obesity and overweight, as well as its role in the process of the body mass growth. Among the 327 patients diagnosed with obesity and overweight, particularly those with Class I and II degrees of obesity ($p<0.05$) showed a significantly increased level of PYY 3 -36. The highest PYY3-36 level was observed in those with the Class II or second degree of obesity ($p<0.05$). Exogenous Constitutional Obesity is accompanied by a significant increase in PYY3-36 in patients with Class I and II degrees of obesity.
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Introduction

At present, it has been proved that the mechanism of lipid metabolic disorder is polyetiologic. Scientific research and experimental studies conducted recently show that the increase in the body mass is caused by abnormalities in the synthesis as well as production of biologically active substrata, which participate in the regulation of food consumption [1].

Eating behavior is known to be controlled by the ventromedial (VMN) and lateral hypothalamic nuclei. The hypothalamus is a multifunctional system. In 1954, E. Stellar described the functional capacity of the different parts of the hypothalamus. Currently, the theories of hunger and saturation control have undergone some changes. The lateral hypothalamic nucleus shows tonic activity which is being periodically inhibited by the impulses from the saturation center which are sent out after food intake [2]. There are several subcortical types of hypothalamic nuclei that form the feeling of hunger. These include the paraventricular nucleus (PVN), arcuate nucleus (AN), lateral hypothalamic area and solitary nucleus (SN). These brain areas host the synthesis and reception of orexigenic and anorexigenic peripheral and central factors. They also interact with the hypothalamic VMN which plays the role of the saturation center. Appetite is controlled by the satiety center (ventromedial hypothalamic area) and the hunger center (lateral hypothalamic area) [3].

At present, the causes of Exogenous Constitutional Obesity (ECO) progression are being widely debated. Peptide YY 3-36 (PYY3-36) is considered to play the main role in the regulation of eating behavior. PYY 3-36 is synthesized by the L-cells in the distal portions of the small and large intestines. An anorexigenic hormone, it enters the circulation after food intake. Although it was discovered in 1980, it was only recently that researchers noted its appetite-regulating function [4, 5]. PYY3-36 penetrates the blood-brain barrier and becomes active at the level of AN in the hypothalamus, stimulating the feeling of satiety and reducing food intake. According to international research data, a low level of PYY3-36 is observed in obese people [6, 7] and it has been assumed to participate in the pathogenesis of obesity. Scientists have

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proved that in obese patients PYY3-36 synthesis is 30% less compared with the norm [8]. It is therefore necessary to point out that the peptide level increases post prandially and its basal rate should not be regarded as the only marker of its secretion. Recent research data reveals that increased fat and protein intake can lead to the long-term increase in PYY3-36 postprandial concentration [9]. Scientists' desire that the data collected will promote the development of new methods of treating obesity.

However, the PYY3-36 level of in ECO patients in Russia has never been diagnosed. No research related to the excess of body mass and hormonal-metabolic dysfunctions is available. Therefore, investigating the PYY 3-36 secretion has become a matter of great necessity. A good understanding of the interaction between PYY 3-36 circulation and the risk of endocrine dysfunction occurring becomes crucial in the selection of the correct treatment method of body mass stabilization in obese patients.

The ***purpose*** of the following research was to investigate the features of lipid exchange and to determine the PYY 3-36 level in the blood serum of ECO patients and those who were overweight, to analyze the features of the ECO course and to scrutinize the influence of PYY 3-36 on body mass changes.

Material and Methods

In all, 327 people (228 women and 99 men, residents of Moscow and Kirov) participated in the study. Annually, they gained 5 kg or more in their body mass. All the patients work in large companies, where medical check -ups are held on a regular basis. The choice of large enterprises is explained by the examination of more employees in different age groups.

Anthropometric indicators were measured: height, body mass, body mass index (BMI), and waist circumference (WC). BMI is a result of body mass (kg) divided by the squared height (m). Electronic scales were used to record body weight, waist circumference was determined with a measuring tape and height with an auxanometer. The BMI was calculated according to the WHO classification of 1997. For instance, if the IMT was 25-29 kg/m^2, excessive body mass was diagnosed; if it equaled 30.0-34.9 kg/m^2, Class I degree of obesity was recorded; if it were 35.0-39.9 kg/m^2 Class II degree and if 40 kg/m^2 and above, Class III degree of obesity. The patients were included in the study based on the following criteria: BMI≥25 kg/m^2 and a dysfunction of 5 years' duration or more. Patients with the following criteria were not included in the study: those with endocrinal genesis of obesity, serious course of concurrent pathology, decompensation of hemodynamics and carbohydrate metabolism, substitutive therapy with thyroid medicines, glucocorticosteroids and hormonal therapy in climacteric.

The PYY3-36 level was determined in the blood serum using the Enzyme-linked immunosorbent assay (ELISA) DSL-10-33600 kit. Laboratory indicators were recorded in the laboratory of clinical immunology along with the radio-immunological analysis group in the Russian Cardiology Scientific and Production Complex RosMed Technology (Head – Prof. V. P. Mosenko). Rates of 29-125 pg/ml on an empty stomach were considered normal.

The Dual Energy X-ray Absoptiometry method was used to examine the patients' body composition in the radionuclide diagnostics laboratory of N.A. Semashko Railway Clinical Hospital (Head – S. A. Sovtsova, PhD).

Statistical analysis of the data collected was performed with the software Statistic SPSS 12.0 for Windows. Method χ^2 and the Kruskal-Wallis analysis were applied to evaluate the differences among the groups. When testing the hypotheses, the critical value level p was found to be equal to 0.05. To evaluate the interaction of quantitative attributes, Spearman's rank correlation coefficient was applied. Data was presented in the form of a median, the 25th and 75th percentiles.

Results and Discussion

The vast majority of patients included in the study were obese. Overweight patients constituted the 1st group, Class I degree of obesity patients formed the 2nd group, Class II degree comprised the 3rd group, and Class III degree comprised the 4th group. It was shown that 38 patients (11.6%) had excess body mass and 289 patients (88.4%) were diagnosed with different degrees of obesity (Table 1.) Abdominal type of obesity was observed among 73.7% females and 37.5% males.

Based on the inclusion criteria, all the patients had excessive body mass or a certain degree of obesity. Figure 1 presents the general tendency of body mass increase among the ECO and overweight patients. The most significant body weight increase was observed in the Group 3 patients. Therefore, it becomes necessary to emphasize the fact that this group shows higher PYY3-36 rates (p<0.05).

Table 1.
Patients' anthropometric data.

Indicator	Group 1 (N=38)	Group 2 (N=97)	Group 3 (N=78)	Group 4 (N=114)
Age (years)	39 (35, 43)	35 (29, 47)	46 (40, 49)	45 (38, 50)
BMI, kg/m^2	28 (25, 29)	32 (32, 34)*	37 (37, 39)*	44 (42, 48)*
Body mass, kg	76 (72, 87)	94 (89, 105)*	102 (93, 112)*	121 (113, 131)*
WC, cm	97 (85, 100)	106 (100, 110)*	114 (107, 120)*	127 (114, 136)*

Notes: *median 25th and 75th percentile is shown;*
**p<0.05 compared to the 1st group (Mann-Whitney criterion).*

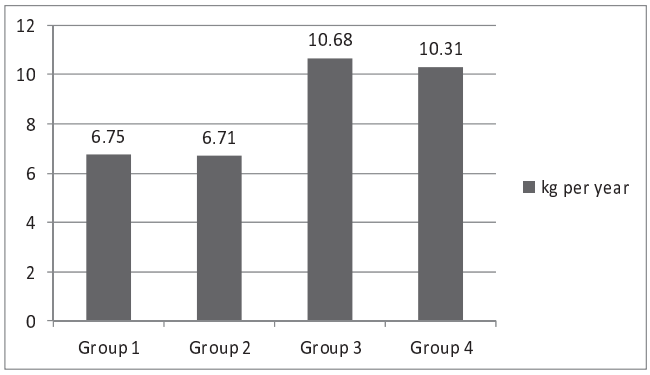
Dysfunction of the processes which maintain stable body mass can be the cause or the result of regulatory system disorders at all levels (mainly ensuring nutrition and the associated processes). The following differences were marked in the study of the PYY3-36 level in the patients studied (Table 2).

Table 2.
General PYY3-36 level in patients with exogenous constitutional obesity and excessive body mass in relation to the obesity degree.

Indicator	Group 1	Group 2	Group 3	Group 4
YY3-36, pg/ml	80 (44, 122)	94 (58, 186)*	174 (75, 306)*	86 (56, 135)
% fat	35 (29, 37)	41 (34, 46)*	44 (43, 50)*	51 (47, 51)*

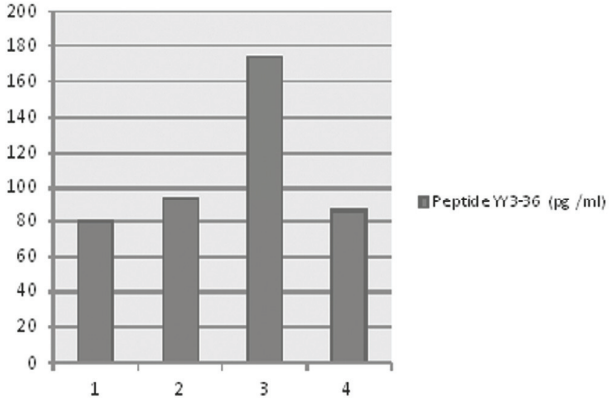
Notes: *median 25th and 75th percentile is shown;*
**p<0.05 compared to the 1st group (Mann-Whitney criterion).*

Figure 1.
Average annual body mass increase among patients with obesity and overweight according to the questionnaire.



The concentration of PYY3-36 in the blood serum considerably increased on an empty stomach. Typically, the PYY3-36 content (compared with overweight patients) is 1.17 times higher in patients with Class I degree of obesity (p<0.05) and 2.1 times higher in patients with Class II degree (p<0.01). As the body mass indicator grows, the same is seen occurring in the PYY3-36 secretion (p<0.05) (Fig. 2).

Figure 2.
PYY3-36 level among ECO and overweight patients.

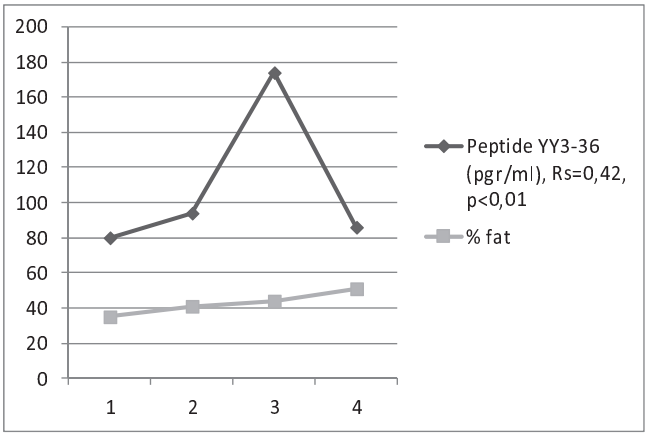


The characteristic feature of the body composition in ECO patients is the increase in the total fat compared with overweight persons. It was found to be 1.17 times higher for the patients having Class I degree of obesity (p<0.05), 1.25 times for the Class II degree (p<0.05) and 1.45 times for the Class III degree (p<0.01). The PYY3-36 level was observed to have risen along with body mass.

An analysis of the correlation between the fat exchange dysfunction parameters (percentage of fat) and the PYY3-36 level in ECO patients revealed a relationship between the total fat and PYY3-36 concentration (r=0.42; p<0.01).

The study conducted reveals that the total PYY3-36 concentration changed with the increase in body mass in ECO patients and it can be considered the marker of lipid exchange (Fig. 3).

Figure 3.
PYY3-36 level and percentage of total fat in ECO and overweight patients.



The PYY 3-36 level was found to be markedly higher in the third group (Class II degree) rather than in the first (p<0.05), second (Class I degree, p<0.05) or fourth groups (Class III degree, p<0.05). An insignificant decrease in the PYY3-36 concentration in obese patients with Class III degree confirms the presence of other factors participating in the process of catabolism. Data collected shows the possible influence of PYY3-36 on a change in

the body mass in ECO patients. Regarding obesity in the light of the hypothalamic–pituitary–adrenal dysfunction concept (which explains the pathological reactions of the body through fat exchange dysfunctions) the PYY3-36 level can be considered the marker of dysfunctions in body mass regulation.

It is a known fact that neurons from the hypothalamic arcuate nucleus are involved in the regulation of nutritional behavior. These neurons are the first to respond to the satiety signals from the gastrointestinal tract (GIT). They transform the information into a neuronal response by the secretion of anorexigenic (appetite lowering) and orexigenic (appetite stimulating) neuropeptides and pass the signals on to the second-order neurons. They localize in the paraventricular and lateral hypothalamic nuclei.

However, a significant difference in the concentration of PYY3-36 was observed in ECO patients (compared with the group of patients with excess body mass), which reflects the features of secretion of this peptide for this category of patients examined. International research data proves that obese persons have low endogenous levels of PYY3-36 [11]. And the level of this peptide changes depending on the intake and content of the food, which is why it is advisable to measure its concentration first on an empty stomach and then after a meal. Our data corresponds to other research results. In the experiment the PYY3-36 level was found to increase considerably after food intake, as glucose-containing foods induce a significant increase in the PYY3-36 level, postprandially, in laboratory animals. The boost in the protein and fat concentration in food may cause a long-term increase in the PYY3-36 level, which gives a stronger feeling of satiety for a longer period of time [12].

At present, researchers know that a diet with less than 40% protein and less than 25% fat a day boosts the PYY3-36 concentration in the blood plasma rather than a diet with daily protein of less than 25% and less than 40% fat. This reveals the important role of proteins in the secretion of this peptide. However, it is not yet known how the proteins regulate the secretion of this hormone [13]. The results of our research show that obese persons develop an increased basal level of PYY3-36. Besides, ECO patients show resistance to this peptide, according to the experiments over recent years [12]. Thus, there could be a possible influence of PYY3-36 on the hypothalamus in the zones which are directly connected to the regulation of nutritional behavior and energy balance in ECO patients 14-18].

Peptide YY3-36 is normally produced by the GIT cells in obese patients and its quantity reflects energy metabolism dysfunctions. This prompts us to think of new possible controlling mechanisms which peptide YY3-36 possesses in the process of Exogenous Constitutional Obesity. This finding, regarding the role of neuropeptides in the regulation and control of the digestion processes plays an important part in the understanding of obesity as a biological problem, which in turn will assist in finding the adequate therapeutical cure for it. Finding a therapy for this condition is a global concern for Medical Science.

Conclusion

1. Body composition abnormalities are diagnosed in all ECO patients by the total fat increase in the body.
2. The Exogenous Constitutional Form of obesity is observed along with abnormality in the basal level of PYY 3-36; this can be the marker of energy balance dysfunction for this particular group of patients examined. Further investigation of the postprandial level of this peptide is warranted.

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