

Levels Orexigenic and Anorexigenic Hormones in Adolescents with Obesity

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Abstract

Background: About 20 thousands of new cases of obesity (Ob) are first registered in children and adolescents in Ukraine annually (morbidity 2.72/1000, prevalence 13.50/1000 of the corresponding population on 01.01.2016). Adolescent Ob shows catastrophic rise (prevalence 8.9/ 1000 in 2001 vs 28.3/1000 in 2015). Completely unclear the role of Ghr in the etiopathogenesis of obesity in adolescents with HD.

Material and Methods: A total of 39 obese children with HD (14 boys, 15, 1 ± 1, 4 y) and 14 healthy control (mean age 14, 6 ± 1, 2 y) were included into the study. Among patients with HD- 16 patients (41, 03 %) had visceral abdominal obesity (VAOb), 23 patients (58, 97 %) had gluteofemoral obesity (GFOb). Serum Ghrelin, Insulin level, HOMA-IR were studied. Such studies are conducted in Ukraine for the first time.

Results: Overweight was revealed in 15 (38, 5 %) patients with HD, ObI – in 8 (20, 5 %) people, ObII – in 10 (25, 6 %) persons, ObIII – in 6 people (15, 4 %). The signs of insulin resistance (HOMA-IR > 2, 77; IRI > 20 µIU/mL) were noted in 60 % patients. Serum Ghr level was found significantly lower in obese adolescents compared to that of control group and was dependent on the degree of Ob. The level of Ghr was the lowest (582, 58 ± 59, 37 ng/mL) in patients with ObIII. The level of Ghr was significantly lower ($p < 0.05$) in patients with VAOb than with GFOb (656, 63 ± 113, 16 vs 1212, 13 ± 114, 6 ng/ml, respectively). The levels of hyperinsulinemia and insulin resistance were increased with an increase in the degree of obesity.

Conclusion: Hypothalamic dysfunction, associated with obesity in adolescents, is accompanied by a low serum Ghr level. A high degree of obesity is accompanied by a greater decrease in the Ghr level. A significantly lower Ghr level was registered in abdominal Ob comparing to gluteofemoral type of obesity. Further studies the relationship of Ghr level, insulin resistance and hyperinsulinemia in obese adolescents with hypothalamic dysfunction are required.

Keywords: Obesity, Hypothalamic Dysfunction, Children, Adolescents, Ghrelin, Leptin

Introduction

About 20 thousands of new cases of obesity (Ob) are first registered in children and adolescents in Ukraine annually (morbidity 2.72/1000, prevalence 13.50/1000 of the corresponding population on 01.01.2016). Adolescent Ob shows catastrophic rise (prevalence 8.9/ 1000 in 2001 vs 28.3/1000 in 2015) [1]. Obesity in Ukrainian children (age 0-14) per 1000 (2002 – 2015) (Figure 1).

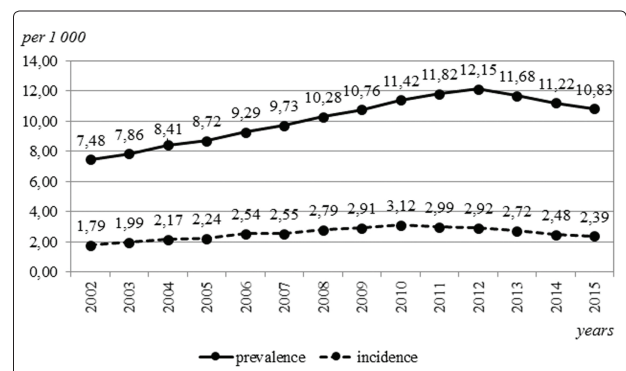


Figure 1: The dynamics of the prevalence and morbidity of obesity among children aged 0 to 17 years per 1,000 of the relevant population (2002 – 2016) [1].

The increase of body weight can be conditioned by violation of synthesis or products of hormones that participate in adjusting of food behavior. There are two basic groups of hormones regulative food behavior: orexigenic (increase the consumption of meal) and anorexigenic (diminish a consumption to the meal) [2]. A table 1. Monoamines, peptids that influence on adjusting of appetite [2].

Hormones of energy balance

Orexigenic effect	Anorexigenic effect
Norepinephrine (alpha2 receptors)	Norepinephrine (alpha2-, Beta-receptors)
Neuropeptide Y	Serotonin
Beta-endorphin	Cholecystokinin
Somatoliberin	Melanocyte-stimulating hormone
Galanin	Corticoliberin

The hormone Leptin belongs with an anorexigenic effect - one of most studied to present of адіпокинів tense, hormone of peptide nature, the basic mestome of synthesis of that is white fatty fabric [3, 4].

Leptin

Leptin is a hormone of peptide nature, and white fat tissue is the main place of its synthesis [5, 6]. This hormone was revealed in 1994. Nowadays the measurements of this hormone tended to be used even in clinical practice [7, 8].

The main effects of leptin:

- Increased hepatic gluconeogenesis and glucose uptake by skeletal muscle;
- Increase in the rate of lipolysis and a decrease in triglycerides of the white adipose tissue;
- Strengthening of thermogenesis;
- Stimulation of CNS;
- Decrease in triglyceride level in the liver, skeletal muscles and the pancreas without an increase in plasma NEFAs;
- Increases the sensitivity of muscles and adipose tissue to insulin;
- Lowers an appetite;
- Increases the tone of the sympathetic nervous system;
- Decreases the tonus of the parasympathetic nervous system;
- Increases energy expenditure;
- Activates metabolism of fats and glucose

To the hormones with a orexigenic effect Ghrelin (Ghr) belongs is a peptid hormone, that is influences on the synthesis of different enzymes, processes of digestion, level of sugar at blood, insulin, efficiency of work of heart and many other physiology indexes [9, 10].

Ghrelin

Is produced by P / D1 cells of the mucous membrane of the stomach fundus. This hormone was revealed in 1999, and until now the role of this hormone is not clear [11, 12].

The main effects of ghrelin:

- Stimulates the production of neuropeptide Y (NPY);
- Stimulates the secretion of growth hormone;
- Promotes the activation of endothelial nitric oxide synthase isoform;

- Promotes adaptation, the antidepressant effect;
- Affects memory, cognitive functions of the brain, sleep and wakefulness processes, inhibits the production of leptin, and regulates the level of adrenaline (hormone of stress) in the blood. Completely unclear the role of Ghr in the etiopathogenesis of obesity in adolescents with HD.

We have chosen from a variety of peptides orexigenic ghrelin and anorexigenic leptin, taking into account their probable opposite effect on the development of obesity. Some studies indicate a connection of ghrelin with metabolic characteristics [13].

The level of ghrelin in obese children has not been studied. That is why we studied the level of this peptide in obese children in Ukraine. Low plasma ghrelin is associated with insulin resistance, hypertension, and the prevalence of type 2 diabetes.

Material and Methods

The study involved 39 children (14 boys / 25 girls 15.1 ± 1.4 years) with hypothalamic dysfunction. The control group consisted of 14 healthy children (mean age 14.6 ± 1.2 years).

Obesity classification in children

Diagnosing overweight /obesity: SDs of BMI by age and gender (between 1- 2 SD's and more 2 SD overweight/obesity respectively). All children had some signs of hypothalamic dysfunction according to Morrison J.A., Friedman L.A., Harlan W.R., 2005.

According to a Degree of Obesity:

- BMI SDS 2.0 - 2.5 – degree I
- BMI SDS 2.6 - 3.0 – degree II
- BMI SDS 3.1 - 3.9 – degree III
- BMI SDS ≥ 4.0 – morbid
- Abdominal visceral form of obesity –
Waist circumference (WC)/Hip circumference (HC)
WC/HC > 0.85 in girls
WC/HC > 0.9 in boys
- Gluteofemoral form of obesity –
WC/HC < 0.85 in girls
WC/HC < 0.9 in boys

16 patients (41.03 %) had visceral abdominal obesity (VAO) (waist-to-thigh circumference ratio was as following

- > 0.85 in girls, and > 0.9 in boys) and 23 patients (58.97 %) had gluteo-femoral obesity (GFO). The levels of immunoreactive insulin (IRI), ghrelin (Ghr), leptin in blood plasma, and HOMAIR were determined. The levels of leptin were determined by the immune enzyme method (Roche Diagnostics GmbH Mannheim).
- The levels of ghrelin were determined by the immune enzyme method (Baysurzen, Belgium). The obtained data were expressed as ng / ml. Student's t-test was used for statistical processing.

Aim: To study the levels of anorexigenic and orexigenic hormones in the blood of children and adolescents with obesity.

Results

Overweight was revealed in 15 (38, 5 %) patients with HD, ObI – in 8 (20, 5 %) people, ObII – in 10 (25, 6 %) persons, ObIII – in 6 people (15, 4 %). The signs of insulin resistance (HOMA-IR > 2,77; IRI > 20 μIU/mL) were noted in 60 % patients. Serum Ghr

level was found significantly lower in obese adolescents compared to that of control group and was dependent on the degree of Ob.

The Ghrelin level was significantly lower in obese children than in the control group, and depended on the obesity degree. The lowest level of Ghrelin was in obesity of third degree. Leptin levels demonstrates the opposite relation (Figure 2).

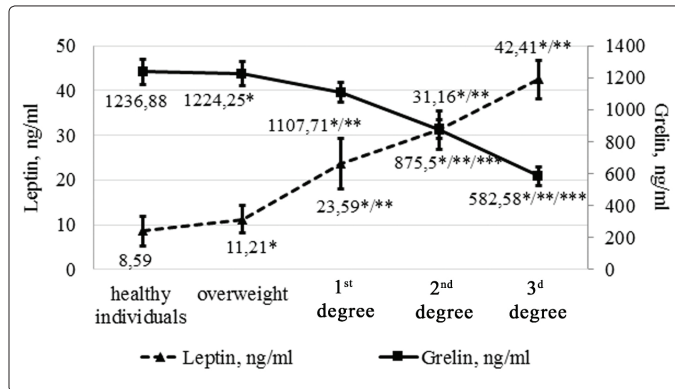


Figure 2: Correlation of levels of Leptin and Ghrelin for children and adolescents with obesity depending on the degree of obesity

Obesity children had Signs of insulin resistance (HOMA > 2.77, IRI > 20 mcU / ml). The level of hyperinsulinemia and insulin resistance increased with the degree of obesity. The higher the degree of obesity, the higher the insulin values (Figure 3).

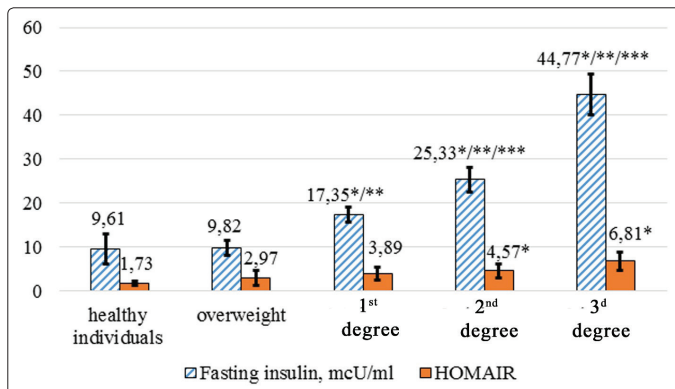


Figure 3: Levels of insulin and index of HOMAIR for children and adolescents with obesity depending on degree obesity

Notes:

- *The difference is significant comparing to the index in healthy individuals (p < 0.05);
- **The difference is significant comparing to the index in children with overweight (p < 0.05);
- ***The difference is significant comparing to index in children with obesity of the 1st degree (p < 0.05).

Conclusions

- Obesity in children is associated with a low level of ghrelin and a high level of leptin in the blood.
- This phenomenon depends on the degree and form of obesity in children.
- The higher the degree of obesity, the lower the level of ghrelin and the higher the level of leptin in the blood.
- The level of ghrelin is lower but insulin and leptin are higher

than in the case of gluteofemoral form in visceral abdominal obesity.

- Future epidemiological studies are needed for studying childhood obesity in Ukraine.

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