

Hormonal predictors of arterial blood hypertension in obese adolescent boys*



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The aim of the study is to investigate the role of hormonal factors in formation of arterial hypertension and insulin resistance in obese adolescent boys.

Materials and methods. The total study cohort included 187 obese (BMI > 95 %) adolescent boys (aged 12–17 y. o.). Physical examination included height, weight, total subcutaneous fat mass, waist circumference and blood pressure measurements as well as assessment of pubertal development (Tanner stage). The control group involved boys with same age without somatic and endocrine diseases. Fasting glucose, insulin (IRI), cortisol (C), TSH, leptin, triglyceride (TG) and HDL-cholesterol (HDH-C) blood samples were undertaken with using of commercial kits (Roche Diagnostics GmbH). Insulin sensitivity and β -cell function were assessed by HOMA Calculator v.2.2.

Statistical (ANOVA, multivariate and univariate regression) analysis was done with using SPSS program, version 9.0. Data are presented as mean and 95 % confidence interval (CI). P-value less than 0.05 was considered as statistically significant.

Results and discussion. By the results of univariate regression analysis it was found that elevated leptin, insulin and cortisol levels play the determination role in the formation of hypertension in obese boys. Leptin concentration above 40.0 ng/ml is an independent factor in increasing of systolic (SBP) and diastolic blood pressure (DBP) in adolescents, besides patients with leptin-deficient forms of obesity: $SBP \approx 128.4 + 0.15 \cdot L$ ($r = 0.24$, $p = 0.0001$) and $DBP \approx 82.5 + 0.09 \cdot L$ ($r = 0.21$, $p = 0.0001$). Hyperinsulinemia (basal insulin levels in blood above 20 mU/L) was also associated with high blood pressure in obese adolescent boys: $SBP \approx 130.2 + 0.25 \cdot IRI$ ($r = 0.19$, $p = 0.0001$) and $DBP \approx 76.6 + 0.17 \cdot IRI$ ($r = 0.15$, $p = 0.0001$).

Conclusions. Multivariate linear regression analysis was performed to find out that in obese adolescent boys without puberty deviation elevated blood pressure closely associated with elevated leptin, cortisol and insulin levels ($SBP \approx 0.92 \cdot IRI + 1.09 \cdot L + 0.14 \cdot C$ ($R^2 = 90.1$ %, $p = 0.0001$); $DBP \approx 0.65 \cdot IRI + 0.69 \cdot L + 0.07 \cdot C$ ($R^2 = 90.5$ %, $p = 0.001$)). It was shown that elevated levels of TG and low HDH-C are the major metabolic syndrome components, which are associated with decreased sensitivity of target tissues to insulin and voltage secretory β -cells function in obese adolescent boys.

Key words: obesity, metabolic syndrome, insulin resistance, puberty.

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Childhood obesity is reaching epidemic proportions and represents the most important chronic disease in this age group [28]. At the same time, urbanization, unhealthy diet and increasingly sedentary lifestyle are major contributors to such disorders and have contributed to increasing the prevalence of childhood obesity, particularly in developing countries. In the USA 15.8 % of children between 6 and 11 years and 16.1 % of adolescents have a body mass index (BMI) in the range of overweight [13, 32]. Similar trends have also been observed in many European countries, where, based on the latest International Task Force criteria, overweight and obesity are present in 31.8 % of school-aged children [26]. Furthermore, the recent phenomenon of «nutritional transition» with a «westernization» of food, typical of many developing countries, has caused a significant rise in obesity even among populations that were unaware of this problem until some years ago [28].

Childhood obesity is associated with an increased risk for several metabolic complications, such as insulin resistance, glucose intolerance and type 2 diabetes mellitus (T2DM). In particular, insulin resistance is the most common metabolic alteration related to obesity [2], and it represents an important link between obesity and other metabolic as well as cardiovascular complications [24]. As cardiovascular disease is the first cause of morbidity and mortality in adulthood, the epidemic of childhood obesity will cause a real burden for the future of the society. Obese children are also at risk of developing psychological problems, orthopedic and respiratory disorders and also certain malignancies. Furthermore, childhood obesity frequently tracks into adulthood, thus representing a major contributor to the adult obesity epidemic and to the increased cardiovascular morbidity and mortality in adult life. All these data are alarming and underline how obesity is a real threat for the health of children and adolescents.

Obesity, particularly in the central (abdominal) region, is associated with an increase in risk of cardiovascular disease and has been determined as a key precipitating factor for T2DM. It is a key component in the IDF definition of metabolic syndrome in adults. Each of these children is at increased risk of developing metabolic syndrome and subsequently progressing T2DM and cardiovascular disease in later life.

Intrauterine events for the unborn child and factors during early development years predispose a child to disorders such as obesity, prediabetes, and metabolic syndrome. The presence of maternal gestational diabetes, low birth weight, and infant feeding practices for example contribute to a child's future level of risk. Other factors can be genetic, socio-economic or environmental (an obesogenic environment for example). Early identification of children at risk and preventive action are therefore very important.

Insulin resistance is a state in which a given amount of insulin produces a subnormal biological response. In

particular, it is characterized by a decrease in the ability of insulin to stimulate the use of glucose by muscles and adipose tissue and to suppress hepatic glucose production and output. Furthermore, it accounts a resistance to insulin action on protein and lipid metabolism and on vascular endothelial function and genes expression.

IDF suggests that the metabolic syndrome should not be diagnosed in children younger than 10 years, but that a strong message for weight reduction should be delivered for those with abdominal obesity. For children age 10 years or older, metabolic syndrome can be diagnosed with abdominal obesity and the presence of two or more other clinical features (i. e. elevated triglycerides, low HDL-cholesterol, high blood pressure, increased plasma glucose). In the absence of contemporary definitive data, the criteria adhere to the absolute values in the IDF adult definition, except that waist circumference percentiles are recommended and one (rather than a sex-specific) cut-off is used for HDL-cholesterol levels. For children older than 16 years, the IDF adult criteria can be used. Further research is needed to identify optimum criteria for the definition of the syndrome.

Puberty is a crucial time for metabolic syndrome development because, during puberty, insulin resistance is increased, and insulin sensitivity is reduced in both nondiabetic and diabetic children. It was found by recent epidemiologic study that adolescent males are three times as much at risk to develop metabolic syndrome than adolescent females [21]. In pediatric population obesity and hypertension are principle components of clinical manifestation of the metabolic syndrome. As it is thought, metabolic syndrome is caused by inheritable and/or acquired resistance to insulin.

The role of fatty acids and adipocytokines. Obesity represents the major risk factor for the development of insulin resistance in children and adolescents [3], and insulin resistance/hyperinsulinemia is believed to be an important link between obesity and the associated metabolic abnormalities and cardiovascular risk [30]. Several studies suggested that approximately, 55 % of the variance in insulin sensitivity in children can be explained by total adiposity, after adjusting for other confounders, such as age, gender, ethnicity and pubertal stage [3]. Obese children have hyperinsulinemia and peripheral insulin resistance with a ≈ 40 % lower insulin-stimulated glucose metabolism than non-obese children. In a recent population-based study conducted in American adolescents, insulin resistance was detected in ≈ 50 % obese subjects and adiposity was also confirmed to be the most important factor affecting insulin sensitivity [18]. Adipose tissue seems to play a key role in the pathogenesis of insulin resistance through several released metabolites, hormones and adipocytokines that can affect different steps in insulin action [20]. Adipocytes produce non-esterified fatty acids, which inhibit carbohydrate metabolism via substrate competition and impaired intracellular insulin signaling. In

children, both and in adults, several «adipocytokines» have been related to adiposity indexes as well as to insulin resistance.

The identification of the hormone leptin by Friedman et al in 1994 has proved to be a seminal observation in biomedical science. The discovery that a circulating protein secreted almost exclusively by adipocytes could regulate body weight through its effects on food intake and energy expenditure represented a remarkable breakthrough in our understanding of the molecular components of the systems involved in energy homeostasis [7]. Leptin associated clinical phenotype of congenital leptin deficiency, which includes hyperphagia, morbid obesity, hypogonadism, and impaired immunity, has provided insights into the role of leptin-responsive pathways in the regulation of eating behavior, intermediary metabolism, and the onset of puberty. There are also data showing a close relationship between leptin levels and insulin resistance in children [4].

The next most significant cytokines is adiponectin which produced by adipose tissue, and has an important insulin sensitizing and anti-atherogenic properties [5, 9]. Whereas obesity is generally associated with an increased release of metabolites by adipose tissue, levels of adiponectin are inversely related to adiposity. Therefore, reduced levels of this adipocytokine have been implicated in the pathogenesis of insulin resistance and metabolic syndrome [20].

Decreased levels of adiponectin have been detected across pathways of insulin resistance in children and adolescents [29], where it is an independent predictor of insulin sensitivity, independently of adiposity. Adipose tissue also produces tumour necrosis factor- α , an inflammatory factor, which can alter insulin action at different levels in the intracellular pathway. Interleukin-6 (IL-6) is another inflammatory cytokine released by adipose tissue and its levels are increased in obesity [20]. IL-6 stimulates the hepatic production of C-reactive protein and this can explain the state of inflammation associated with obesity, and could mediate, at least partially, obesity-related insulin resistance. Data based mainly on animal studies also suggest that increased levels of resistin, another molecule produced by adipose tissue, could impair insulin sensitivity. Recently, it has also been shown that serum levels of retinol-binding protein 4 (RBP4) correlate with insulin resistance in subjects with obesity as well as in those with impaired glucose tolerance (IGT) or T2DM, therefore suggesting that it could be useful in assessing insulin resistance and the associated risk for complications [10].

According to recommendations for future research of the IDF consensus definition of the metabolic syndrome in children and adolescents the main keys include the following:

- Improved understanding of the relation between body fat and its distribution in children and adolescents.
- Investigation of whether early growth patterns predict future adiposity and other features of the

syndrome; and whether low birth weight predicts future metabolic syndrome, diabetes and cardiovascular disease.

- Factor analysis in children and adolescents to establish grouping of metabolic characteristics such as adiposity, dyslipidemia, hyperinsulinemia, hypoadiponectinemia and insulin resistance.
- Investigation of how obesity in children should be better defined, e. g. weight/height, waist circumference, etc.
- Development of ethnic specific age and sex normal ranges for waist circumference, ideally based on healthy values.
- Ethnic specific studies of waist circumference versus visceral fat based on imaging.
- Studies of adiponectin, leptin, etc in children and adolescents as predictors of metabolic syndrome in adulthood.
- Initiation of long-term studies of cohorts of children of different ethnic origin into adulthood to define the natural history and effectiveness of interventions, particularly those relating to lifestyle.

Puberty is a crucial time for metabolic syndrome development because, during puberty, insulin resistance is increased in this critical period in both non-diabetic and diabetic children. It was found by recent epidemiological study that adolescent males are three times as much at risk to develop metabolic syndrome than adolescent females. In pediatric population obesity and hypertension are principle components of diagnostic criteria of metabolic syndrome.

Thus, studying correlations between leptin, insulin, cortisol, parameters of carbohydrate and lipid metabolism in obese children, in our opinion, is relevant and has such scientific interest.

The aim of the present study is to investigate association between arterial blood pressure components and hormonal determinants of the insulin resistance in euthyroid adolescent obese boys.

Materials and methods

Eligibility criteria: obese (BMI > 95 percentile) and overweight (BMI = 85th – 95th percentile) adolescent (age 12–17) boys were eligible for this study.

The total study cohort thus included 187 boys, 32 from the Pediatric Department of Rudolfstiftung Hospital (Vienna, Austria) under leadership of Prim. Univ.-Prof. Dr. M. Minkov and 155 boys of the Department of Age-Related Endocrinology in Institute of Endocrine Pathology Problems Ukrainian Academy of Medical Science (Ukraine, Kharkiv) under leadership of Prof. Dr. O. Khyzhnyak.

Exclusion criteria: boys with fetal or congenital diseases that could affect fetal growth were excluded (e. g. TORCH infections, congenital malformation, chromosomal aberrations). Children born below 34 weeks of gestation and those who had a severe neonatal condition were also not included in the study.

Physical examination included height, weight, total subcutaneous fat mass, waist circumference, blood pressure measurements, pubertal development (Tanner stage) estimation. To assess the anthropometric characteristics control group consisted of boys of the same age without somatic and endocrine diseases.

Blood samples for glucose, insulin (IRI), cortisol (C), leptin, TSH, triglyceride and HDL-cholesterol measurements were taken in fasting state and were measured using commercial kits (Roche Diagnostics GmbH).

Ideally, hyperinsulinemia is defined if insulin level exceeds the normal value according to the pubertal stage, due to the impact of physiological insulin resistance of puberty [17]. Thus, standard values of normal, borderline, and high fasting insulin levels proposed by the American Heart Association scientific statement were chosen [31]. HOMA-IR is a proxy for insulin resistance and is widely used in clinical settings and research, with high reliability in determining insulin resistance [17]. There is still a debate about the appropriate cutoff point for HOMA-IR, with proposed values of ≥ 2.5 [19, 25], ≥ 1.77 , and > 3.16 [17]. Keskin et al. found that HOMA-IR was the most sensitive and most specific of three proxies for defining insulin resistance, and the cutoff point for insulin resistance diagnosis based on HOMA-IR was 3.16, so that definition was used in the present study [18]. The homeostatic model assessment index (HOMA index = fasting glucose [mmol/L] · fasting insulin [mU/L]/22.5) was used as a measure of insulin sensitivity. Insulin sensitivity and β -cell function were estimated by HOMA Calculator v.2.2.

Assessment of lipid profile for the participants included fasting TG, fasting cholesterol, fasting LDL,

and fasting HDL. Jolliffe and Janssen developed age- and sex-specific percentiles for lipoproteins and cholesterol, starting from age 12 years to age 20 years [14]. However, our participants were aged 12–17 years, and it was not possible to use these lipoprotein percentiles for the whole sample. Therefore, the reference values for these parameters were taken from the National Cholesterol Education Program, with fixed cutoff points for normal, borderline, and high values regardless of sex and age [22]. Low Density Level cholesterol (LDL-C) was calculated using the Friedewald formula [8].

Data analysis: ANOVA, multivariate and univariate regression analysis were performed. Data are given as mean and 95 % CI, and best-fitting model equations. All analyses were conducted using SPSS version 9.0 (IBM Corporation, New York, USA). A P-value of less than 0.05 was considered significant.

Results

The mean values of blood pressure hormonal parameters, carbohydrate and lipids metabolism are provided for group of obesity boys in Tables 1 and 2. The mean values for obese boys have significantly higher systolic blood pressure (SBP) and diastolic blood pressure (DBP) compared with control ($p < 0.05$). The frequency of diagnosed hypertension depended on the age of patients. Thus, in boys younger age (12–13 years) an increased blood pressure was registered in 14.7 % of patients and in the group of adolescents 14–17 years – already at 64.6 % ($p < 0.01$). Data on the incidence of high blood pressure in obese boys are presented in Figure 1.

Table 1
The mean values of systolic and diastolic blood pressure in obese boys

Age, years	SBP, mm Hg		DBP, mm Hg	
	Obese boys	Control group	Obese boys	Control group
10	123.6 \pm 3.61*; 17.49	98.3 \pm 0.9; 9.20	75.71 \pm 4.29*; 11.33	56.5 \pm 0.8; 8.30
11	120.0 \pm 3.87*; 12.24	97.0 \pm 1.0; 10.70	79.30 \pm 2.75*; 8.71	56.3 \pm 0.7; 7.60
12	120.0 \pm 3.25*; 11.28	102.0 \pm 1.2; 12.00	77.50 \pm 3.04*; 10.55	57.7 \pm 0.9; 8.80
13	126.73 \pm 3.24*; 16.54	108.5 \pm 1.2; 13.50	79.65 \pm 0.97*; 10.05	60.3 \pm 0.8; 9.10
14	138.37 \pm 2.55*; 16.75	112.8 \pm 1.3; 14.10	87.56 \pm 1.69*; 11.15	61.5 \pm 0.8; 8.70
15	144.08 \pm 2.73*; 19.14	114.6 \pm 1.3; 14.20	90.24 \pm 1.90*; 13.51	63.0 \pm 0.8; 8.50
16	141.48 \pm 3.14*; 16.34	118.2 \pm 1.1; 13.50	91.29 \pm 2.28*; 11.89	66.3 \pm 0.7; 9.10
17	142.94 \pm 2.98*; 16.49	118.8 \pm 1.4; 13.50	91.76 \pm 2.74*; 11.31	65.9 \pm 0.9; 8.80

Data are expressed as Mean \pm m; SD.

SBP indicates systolic blood pressure; DBP – diastolic blood pressure;

* $p < 0.05$ statistically significant differences between control group.

Table 2
The mean values of hormonal parameters, carbohydrate and lipids metabolism in obese boys

Subjects: Males (n = 187)	M ± m	SD	Min—Max	P*
Cholesterol, mmol/l	4.42 ± 0.09	0.98	2.4–7.3	> 0.05
HDL-C, mmol/l	1.25 ± 0.03	0.30	0.75–1.92	> 0.05
LDL-C, mmol/l	2.81 ± 0.1	0.98	0.49–5.9	< 0.01
Triglycerides, mmol/l	1.11 ± 0.06	0.61	0.47–3.74	> 0.05
Fasting blood glucose (FBG), mmol/l	4.6 ± 0.1	0.7	3.3–5.8	> 0.05
Insulin, mU/L	21.47 ± 2.15	17.87	1.0–100.0	< 0.001
Leptin, ng/ml	46.76 ± 2.7	30.11	0.01–193.0	< 0.001
HOMA	8.37 ± 1.30	2.40	1.35–25.38	< 0.001
HOMA-%S	63.32 ± 15.61	78.07	8.9–341.8	–
HOMA-%B	227.80 ± 20.85	104.25	48.4–425.9	–

*p < 0.05 statistically significant differences between control group

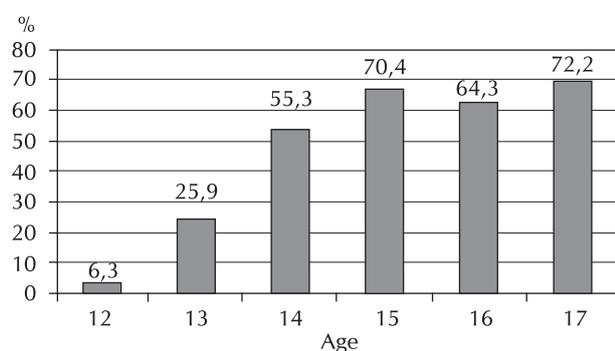


Fig. 1. Data on the incidence of high systolic blood pressure in obese boys

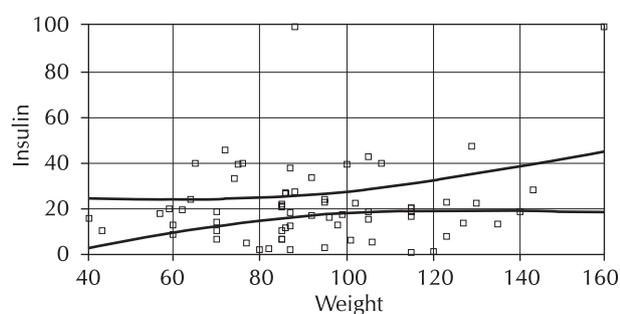


Fig. 2. Plasma insulin (mU/L) and body weigh (kg) in obese boys

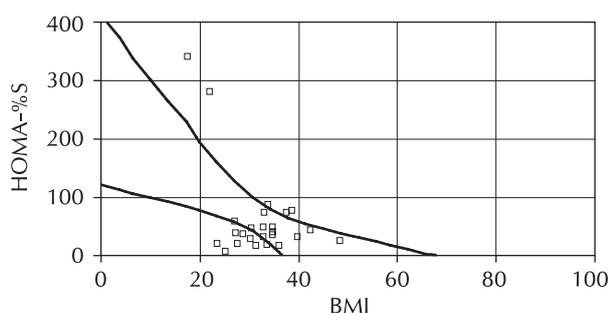


Fig. 3. Insulin sensitivity (Index HOMA-%S) and BMI in obese boys

The adolescent males have marginally higher LDL-C ($p < 0.05$) compared with the healthy subjects. Analysis of the results revealed that boys in the youngest age group, i. e. the early stages of the disease, found the increase of TG in (23.4 %) and reduced HDL-C (18.3 %). In the whole group was found increasing levels LDL-C (68.0 %), TG (42.0 %), and low levels HDL-C in 32.7 % of patients.

In the group of obese boys the average value of HOMA were (8.37 ± 1.30), in the control group – (3.32 ± 0.27) ($p < 0.05$). The highest values of this index were observed in adolescents 15–17 of age: in the range [2.54–25.38], (7.77 ± 1.20). Regression analysis showed that it is a positive significant correlation between body weight and insulin levels ($r = 0.42$; $p < 0.05$) and negative significant correlation between BMI and insulin sensitivity HOMA-%S index ($r = -0.52$, $p = 0.007$) (Fig. 2 and 3).

Univariate regression analysis showed that leptin concentration above 40.0 ng/ml is associated with high systolic (SBP) $SBP \approx 128.4 + 0.15 \cdot L$ ($r = 0.24$, $p = 0.0001$) and diastolic (DBP) $DBP \approx 82.5 + 0.09 \cdot L$ ($r = 0.21$, $p = 0.0001$) blood pressure (Fig. 4 A, B).

Fasting IRI was also associated with high blood pressure: $SBP \approx 130.2 + 0.25 \cdot IRI$ ($r = 0.19$, $p = 0.0001$) and $DBP \approx 76.6 + 0.17 \cdot IRI$ ($r = 0.15$, $p = 0.0001$) (Fig. 5 A, B).

Multivariate linear regression analysis was performed to find out association between blood pressure components, as dependent variables, and a set of hormones, as independent variables. It was found that in obese individuals without puberty deviation, elevated blood pressure is strongly associated with elevated hormone levels: $SBP \approx 0.92 \cdot IRI + 1.09 \cdot L + 0.14 \cdot C$ ($R^2 = 90.1\%$, $p = 0.0001$); $DBP \approx 0.65 \cdot IRI + 0.69 \cdot L + 0.07 \cdot C$ ($R^2 = 90.5\%$, $p = 0.001$).

It was found that in insulin resistant individuals ($HOMA\text{-}\%S < 100\%$) there was significant dyslipoproteinemia ($TG \geq 1.7$ mmol/l) – OR = 16.6

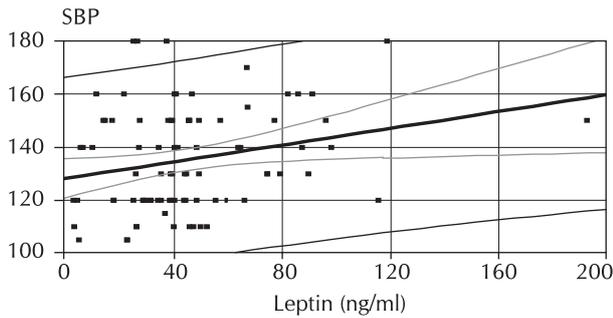


Fig. 4A. Plasma leptin (ng/ml) and systolic blood pressure (SBP, mm/Hg) in obese boys

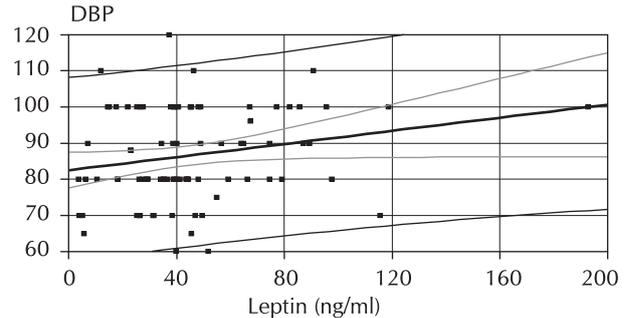


Fig. 4B. Plasma leptin (ng/ml) and diastolic blood pressure (DBP, mm/Hg) in obese boys

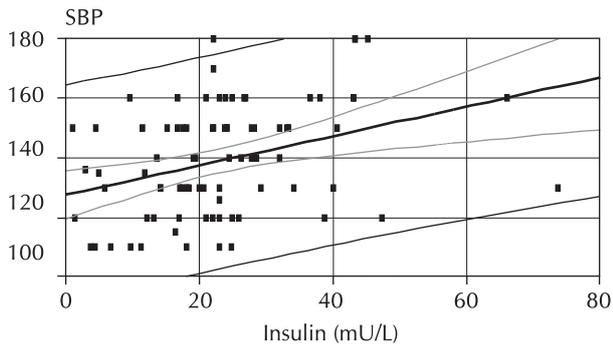


Fig. 5A. Plasma insulin (mU/L) and systolic blood pressure (SBP, mm/Hg) in obese boys

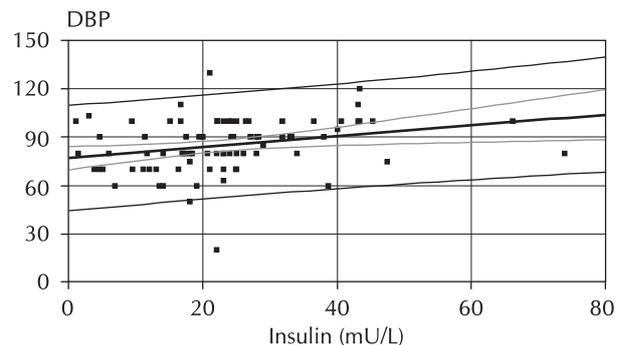


Fig. 5B. Plasma insulin (mU/L) and diastolic blood pressure (DBP, mm/Hg) in obese boys

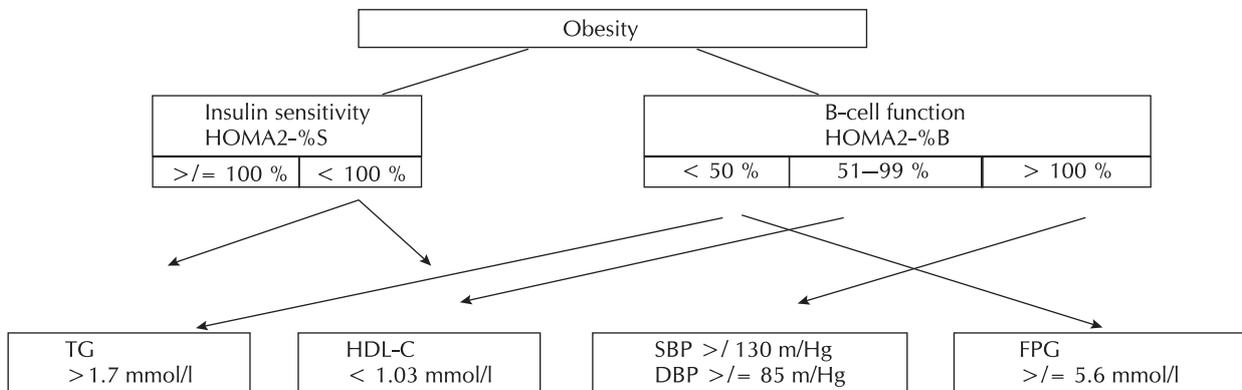


Fig. 6. Association between Metabolic syndrome components, and insulin sensitivity, and β -cell function which estimated by HOMA Calculator v.2.2. in adolescent obese boys

[16.4–16.8]; HDL ($< 1.03 \text{ mmol/l}$) – OR = 3.36 [1.9–5.2] and elevated blood pressure (SBP $> 130 \text{ mm/Hg}$, DBP $> 85 \text{ mm/Hg}$) – OR = 2.13 [1.2–6.09]. Fasting glucose intolerance ($\geq 5.6 \text{ mmol/l}$) was associated with β -cell dysfunction ($50 \% < \text{HOMA-}\%B < 100 \%$) – OR = 14.7 [10.3–19.1] (Fig. 6).

Conclusions

1. In obese adolescent boys with metabolic syndrome leptin, insulin and cortisol are determinants of

hypertension in the range has been determined by last IDF MS' diagnostic criteria.

2. Leptin is independent predictor of high systolic and diastolic blood pressure in its concentration more than 40 ng/ml. Leptin doesn't affects blood pressure in obese but leptin-deficient individuals.

3. Hyperinsulinemia (fasting IRI $> 20 \text{ mU/L}$) is other predictor of hypertension in obese adolescent boys with MS.

4. Cortisol is minor predictor of hypertension in obese adolescent boys with MS.

5. According to our results triglyceride and HDL levels are the major MS components which are strongly associated with resistance to insulin in young patients.

Discussion

Obesity-related insulin resistance is highly prevalent in children and adolescents, and is associated with the increased lifetime risk of type 2 diabetes and cardiovascular disease. The obtained equations enable to conclude that the main mechanism of high blood pressure in young people who are overweight and determine role of hyperinsulinemia-hyperleptinemia. On one side a significant increase in insulin levels in insulin resistance may lead to the activation of renal afferent nerves. On the other side, leptin, through the central melanocortin pathway regulation of energy balance in the body can also activate the sympathetic section of the hypothalamus, reinforcing fibers of the sympathetic tonus in the kidney, which leads to increased sodium reabsorption.

This is due to the ability of insulin and leptin to increase the tone of the sympathetic nervous system [1]. In recent years, we considered a number of possible mechanisms for the formation of essential hypertension in the cardiometabolic syndrome [23].

In addition to the animal experiments and clinical studies have convincingly shown that the basal blood pressure is regulated via the central mechanisms of energy balance in the body [11, 12, 15]. The hormones

leptin and melanocortin are the links of transmission humoral information on reserves of energy to the hypothalamic centers of the sympathetic nervous system, and their hyperproduction or deficiency may increase or decrease the sympathetic tonus of whole organs and systems.

This pattern is broken in genetically-modified mice and people with «genetic breakdown» in one of the links of melanocortin pathway. These include the modification of regions of genes encoding receptors of the structure or synthesis of insulin, leptin, melanocortin [6, 27]. For this reason, high blood pressure is not recorded in all individuals with obesity. As reported in leptin-deficient individuals despite the severe form of obesity recorded normal blood pressure [27]. In the most common form of monogenic obesity associated with genetic modification to the melanocortin receptor (MC4-R), is also not observed hypertensive syndrome [16]. The local renin-angiotensin system adipose tissue is also seen as one possible mechanism for the development of hypertension in obesity. Like many adipokines, the level of production of angiotensin depends adipose tissue mass [16]. That is, not be excluded high blood pressure in individuals with genetic forms of obesity.

Thus, it should be a differentiated approach to obesity as a risk factor, cardiovascular syndrome, because without all the possible reasons is difficult to find effective treatment and to make a long-term forecast of possible complications of the pathological condition.

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Гормональні предиктори артеріальної гіпертензії у хлопчиків-підлітків з ожирінням

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Мета роботи — вивчити роль гормональних чинників у формуванні артеріальної гіпертензії та інсулінорезистентності у хлопчиків-підлітків з ожирінням.

Матеріали та методи. Обстежено 187 хлопчиків з ожирінням (ІМТ > 95 %) віком 12–17 років. Оцінка антропометричних показників охоплювала вимірювання зросту, маси тіла, загальної маси підшкірного жиру, окружності талії, артеріального тиску, визначення статевого дозрівання (стадії за Таннером). Контрольну групу склали хлопчики такого ж віку без соматичних і ендокринних захворювань. Зразки крові брали в стані натще для визначення рівня глюкози в плазмі, інсуліну (ІРІ), кортизолу (С), ТТГ, лептину (L), тригліцеридів (TG) і холестеролу ЛПВЩ (HDL) у сироватці крові з використанням комерційних наборів (Roche Diagnostics GmbH). Чутливість до інсуліну і функцію β-клітин підшлункової залози оцінювали з використанням НОМА — калькулятора v.2.2.

Статистичний аналіз з використанням сертифікованої програми SPSS (версія 9.0.) проводили багатовимірний, одно-вимірний регресійний і дисперсійний аналізи. Дані наведені у вигляді середнього і 95 % довірчого інтервалу (СІ). Р-значення менше 0,05 вважалося статистично достовірним.

Результати та обговорення. За результатами одномірного регресійного аналізу встановлено, що детермінаційна роль у формуванні артеріальної гіпертензії у хлопців з ожирінням належить підвищеному рівню лептину, інсуліну та кортизолу в крові. Концентрація лептину в сироватці крові вище 40 нг/мл слугує незалежним чинником підвищення систолічного (SBP) і діастолічного артеріального тиску (DBP) у підлітків, крім пацієнтів з лептин-дефіцитними формами ожиріння: $SBP \approx 128.4 + 0.15 \cdot L$ ($r = 0.24$, $p = 0.0001$) і $DBP \approx 82.5 + 0.09 \cdot L$ ($r = 0.21$, $p = 0.0001$). Гіперінсулінемія (базальний рівень інсуліну в крові вище 20 мОД/л) виступає ще одним предиктором розвитку артеріальної гіпертензії у хлопчиків-підлітків з ожирінням: $SBP \approx 130.2 + 0.25 \cdot IRI$ ($r = 0.19$, $p = 0.0001$) і $DBP \approx 76.6 + 0.17 \cdot IRI$ ($r = 0.15$, $p = 0.0001$).

Висновки. За допомогою багатофакторного лінійного регресійного аналізу встановлено, що у хлопчиків з ожирінням без порушень темпів статевого дозрівання підвищений артеріальний тиск тісно пов'язаний з підвищеними рівнями лептину, кортизолу, інсуліну: $SBP \approx 0.92 \cdot IRI + 1.09 \cdot L + 0.14 \cdot C$ ($R^2 = 90.1\%$, $p = 0.0001$); $DBP \approx 0.65 \cdot 0.69 + IRI \cdot L + 0.07 \cdot C$ ($R^2 = 90.5\%$, $p = 0.001$). Показано, що підвищений рівень TG і знижений — HLLH-C асоційовані зі зниженою чутливістю тканин-мішеней до інсуліну й напругою секреторної функції β-клітин підшлункової залози у підлітків з ожирінням.

Ключові слова: ожиріння, метаболічний синдром, інсулінорезистентність, пубертат.

Гормональные предикторы артериальной гипертензии у мальчиков-подростков с ожирением

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Цель работы — изучить роль гормональных факторов в формировании артериальной гипертензии и инсулинорезистентности у мальчиков-подростков с ожирением.

Материалы и методы. Обследовали 187 мальчиков с ожирением (ИМТ > 95 %) в возрасте 12–17 лет. Оценка антропометрических показателей включала измерение роста, массы тела, общей массы подкожного жира, окружности талии, артериального давления, оценку полового созревания (стадии по Таннеру). Контрольную группу составили мальчики того же возраста без соматических и эндокринных заболеваний. Образцы крови брали в состоянии натощак для определения уровня глюкозы в плазме, инсулина (ІРІ), кортизола (С), ТТГ, лептина (L), триглицеридов (TG) и холестерола ЛПВП (HDL-C) в сыворотке крови с использованием коммерческих наборов (Roche Diagnostics GmbH). Чувствитель-

ность к инсулину и функцию β -клеток поджелудочной железы оценивали с использованием НОМА — калькулятора v.2.2.

Статистический анализ проведен с использованием сертифицированной программы SPSS (версия 9.0.), проводили многомерный, одномерный регрессионный и дисперсионный анализы. Данные приведены в виде среднего и 95 % доверительного интервала (CI). P-значение менее 0,05 считали статистически достоверным.

Результаты и обсуждение. По результатам одномерного регрессионного анализа установлено, что детерминирующую роль в формировании артериальной гипертензии у мальчиков с ожирением играют повышенные уровни лептина, инсулина и кортизола в крови. Концентрация лептина в сыворотке крови выше 40 нг/мл является независимым фактором повышения систолического (SBP) и диастолического артериального давления (DBP) у подростков, кроме пациентов с лептин-дефицитными формами ожирения: $SBP \approx 128.4 + 0,15 \cdot L$ ($r = 0,24$, $p = 0,0001$) и $DBP \approx 82.5 + 0,09 \cdot L$ ($r = 0,21$, $p = 0,0001$). Гиперинсулинемия (базальный уровень инсулина в крови выше 20 мЕД/л) является еще одним предиктором развития артериальной гипертензии у мальчиков-подростков с ожирением: $SBP \approx 130.2 + 0,25 \cdot IRI$ ($r = 0,19$, $p = 0,0001$) и $DBP \approx 76.6 + 0,17 \cdot IRI$ ($r = 0,15$, $p = 0,0001$).

Выводы. С помощью многофакторного линейного регрессионного анализа установлено, что у мальчиков с ожирением без нарушений темпов полового созревания повышенное артериальное давление тесно связано с повышенными уровнями лептина, кортизола, инсулина: $SBP \approx 0,92 \cdot IRI + 1,09 \cdot L + 0,14 \cdot C$ ($R^2 = 90,1\%$, $p = 0,0001$); $DBP \approx 0,65 \cdot 0,69 + IRI \cdot L + 0,07 \cdot C$ ($R^2 = 90,5\%$, $p = 0,001$). Показано, что повышенный уровень TG и пониженный — HLH-C ассоциированы со сниженной чувствительностью тканей-мишеней к инсулину и напряжением секреторной функции β -клеток поджелудочной железы у подростков с ожирением.

Ключевые слова: ожирение, метаболический синдром, инсулинорезистентность, пубертат.