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INDICATORS OF LIPID METABOLISM DISORDERS IN THE BLOOD SERUM OF ADOLESCENTS WITH METABOLIC SYNDROME

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Atherogenic dyslipidemia is one of the main and early indications of adolescents with metabolic syndrome. Because there is not enough information about the nature of dyslipidemia in adolescents and the possibilities of its correction and prevention, the study of this problem is relevant. The goal of the study was to estimate the indexes of lipid metabolism in blood serum of adolescents with metabolic syndrome. We examined 200 obese patients aged 14–18 years, who were divided into two groups with and without metabolic syndrome. The control group consisted of 30 adolescents of similar age with normal body weight. The lipid profile of blood was studied by standardized methods using semi-automatic photometer. The level of β-lipoproteins in blood serum was determined by the turbidimetric method. Elevated levels of triglycerides, low and very low density lipoprotein cholesterol, β-lipoproteins and a tendency to decreased high density lipoprotein level cholesterol were found in the blood serum of adolescents with metabolic syndrome as the signs of atherogenic dyslipidemia. Reliable correlations both between the indexes of lipid profile and between atherogenic dyslipidemia indicators and anthropometric indexes were established, indicating an increased risk of lipid metabolic disturbances in individuals with abdominal obesity.

K e y w o r d s: adolescents, metabolic syndrome, dyslipidemia.

One of the most important issues in modern medical science is the metabolic syndrome (MS), which combines such important components as the phenomenon of insulin resistance (IR), abdominal obesity, decreased carbohydrate tolerance or diabetes type 2, dyslipidemia, arterial hypertension and other criteria according to the recommendations of the International Diabetes Federation (IDF, 2007) and the WHO [1]. Currently, there is no doubt that the origins of metabolic disorders begin in childhood, are characterized by high prevalence and progressive course [2, 3]. And this makes it important to study this problem and develop approaches to the treatment and prevention of MS, starting from childhood, which will prevent the development of future complications, social maladaptation, disability and mortality. The prevalence of MS in children ranges from 4 to ~ 30% of cases in the general population, is much higher among children and adolescents with obesity [4, 5]. However, in pediatric science, the concept of MS has no scientific basis, as there are only a few scientific developments in this direction. It is known that atherogenic dyslipidemia is one of the main and early criteria of MS [6], which plays an important role in the pathogenesis of atherosclerotic process and related cardiovascular diseases [7, 8]. Due to the lack of information, lack of vigilance about dyslipidemia as a component of MS in obese children and adolescents, the study of the nature of the lipid spectrum in this category of patients is relevant.

The purpose of the study: to study the features of the lipid profile in adolescents with metabolic syndrome.

Materials and Methods

The study was conducted among adolescents aged 14 to 18 years who needed medical attention for obesity and overweight with the following examination by the Institute of Children and Adolescents Health Care of the National Academy of Medical Sciences of Ukraine. 200 patients (114 boys and 86 girls) were examined, of which 2 groups were formed: 1st - 100 adolescents with MS on the background of obesity, 2nd - 100 adolescents with obesity and no signs of MS. The control group consisted of 30 adolescents with normal body weight of the same age without any acute and chronic pathology. The diagnosis of MS was performed according to the recommendations of IDF (2007): in the presence of abdominal obesity, hypertension, IR, hyperglycemia, elevated triglycerides and low cholesterol levels of high-density lipoprotein. The threshold point for the diagnosis of abdominal obesity in children under 16 years of age was the waist circumference > 90th percentile of the distribution according to age and sex, for children over 16 years - for girls > 80 cm, for boys - > 94 cm. The cut-off points for hypertension were blood pressure values of 130/85 mm Hg, hypertriglyceridemia - 1.7 mmol/l, fasting hyperglycemia - 5.6 mmol/l, low cholesterol levels of high-density lipoprotein - 1.03 mmol/l for boys and 1.29 mmol/l for girls over 16 years of age [1]. The spectrum of examination of patients included clinical examination, anthropometric measurements: body weight, height, waist and hip circumference, body mass index (BMI), the waist circumference to height ratio (WC/height) (in case of exceeding the value of 0.5 diagnosed abdominal type), waist circumference to hip circumference ratio (WC/HC), according to which the abdominal type of obesity in adolescents was diagnosed at a value of ≥ 0.9 for boys, ≥ 0.8 for girls), which was carried out by conventional methods. Determination of blood pressure was performed by the traditional Korotkov method using a sphygmomanometer three times with an interval of 5 minutes. The average values of three measurements were taken as an indicator of blood pressure. Determination of serum lipids (total cholesterol (5-cholesterol-3β, (mmol/l)), triglycerides (TG (triacyl glycerol, (mmol/l)), high-density lipoprotein cholesterol (HDL cholesterol, mmol/l), were performed by unified methods in accordance with IFCC recommendations on a semi-automatic photometer "Cormay Multi" using standard kits "Cormay" (Poland). The level of β-lipoproteins in the serum (β-LP, the norm for adults and adolescents - 3.5-6.6 g/l), which is the total amount of low density lipoprotein cholesterol (LDL cholesterol) and very low density lipoprotein cholesterol (VLDL cholesterol) and was determined by turbidimetric method of Burstein M. and Samaille F.M. This method is based on the ability of β-LP to form a complex with heparin in the presence of calcium chloride, followed by the formation of a precipitate. The calculation of lipid fractions was performed according to the formulas of W.T. Friedewald et al.: LDL cholesterol, mmol/l = total cholesterol – (HDL cholesterol – (0.45×TG); VLDL cholesterol, mmol/l = TG/2.2. The atherogenic coefficient (AC) was calculated by the formula: AC = (total cholesterol – HDL cholesterol)/ HDL cholesterol. Phenotyping of dyslipoproteinemia was performed according to the Frederickson classification [9]. The criterion for IR was the homeostatic model HOMA – IR (Homeostasis model assessment of Insulin Resistance, Matthews D.R., 1985). The calculation was carried out according to the formula: HOMA = (G_0×Ins_0)/22.5; (G_0 – fasting glucose level of the blood serum, mmol/l; Ins_0 – the content of insulin in blood serum, mkU/ml. The result of more than 3.5 units testified to IR presence.

Reference values of blood lipid profile in children are regulated by NCEP and American Association of Clinical Endocrinologist' Guidelines (2012) [7]. Normally, in children and adolescents aged 1 to 19 years, the levels of total cholesterol and LDL cholesterol do not exceed the 75th percentile of the distribution, which is 4.25 mmol/l for total cholesterol, and 2.75 mmol/l for LDL cholesterol. Limit levels are considered to be in the range of 75-95th percentile: 4.25–4.99 mmol/l for total cholesterol and 2.75–3.24 mmol/l for LDL cholesterol. Elevated levels are values greater than 5.0 mmol/l for total cholesterol and 3.25 mmol/l for LDL cholesterol.

The database creation and the statistical processing of the results were performed on IBM-Pentium III using application packages 'Stadia-6' (serial number of license certificate 1218 May 24, 2000, version 'Prof'), Microsoft 'Access', 'Excel'. The *t*-criterion of the Student (p), Fisher (φ), Mann-Whitney test were used to assess the likelihood of differences, as well as the correlation analysis. The critical significance level for checking statistical hypotheses when comparing groups was assumed to be 0.05. Ethical norms at all stages of the survey were observed. The work was conducted taking into ac-

count the requirements of the European Convention (Strasbourg, 1986), the provisions of the ICH GCP (2008), GLP (2002). The studies did not cause psychological discomfort in patients. Patients and their parents were provided with the information on the methods and scope of the research, signed informed consent to participate in the study.

Results and Discussion

A comprehensive clinical and laboratory-instrumental study of 200 adolescents with obesity allowed dividing patients into 2 groups: I (MS+) - with the main features of MS (50.0% of patients with the presence of IR, abdominal type of obesity, dyslipidemia), II (MS-) - patients with obesity and without IR, borderline changes in lipidogram (also 50.0%). In patients of group I, when determining BMI, its values were statistically significantly higher than those of group II (36.25 ± 4.45 kg/m^2 and 28.0 ± 3.73 kg/m^2, respectively, $P < 0.01$). Group I was characterized by statistically significantly higher WC/height ratios compared with patients in group II (0.69 ± 0.07 U and 0.59 ± 0.04 U, respectively, $P < 0.05$). The WC/HC ratio in obese adolescents also indicated an abdominal type of obesity, but did not differ significantly in the groups ($P > 0.05$). Thus, the WC/height index was more sensitive to establishing the type of adipose tissue distribution, which is consistent with the world literature [10]. Adolescents with MS also showed borderline and elevated blood pressure (≥ 130/85 mm Hg), and in the group of adolescents without MS this indicator was within the age norm. That is, half of the patients surveyed had MS by the main criteria. Characteristics of the lipid profile of obese patients showed (Table) that the patients had signs of atherogenic dyslipidemia, which manifested itself in the form of increased levels of LDL cholesterol, VLDL cholesterol, AC, increased TG content and tendencies to decrease the level of HDL cholesterol, more pronounced among those surveyed with MS ($P < 0.05$). What exactly was one of the criteria for dividing patients into groups. There was no statistically significant difference depending on gender in the lipid profile ($P \geq 0.05$). According to the results of the Helsinki Heart Study [11], these changes are independently associated with high proatherogenic potential, so the lack of high values of total cholesterol in the examined contingent can not be a marker of "atherogenic safety".

It should be noted that the average values of the level of β-LP (g/l), as an indicator of the total amount of LDL cholesterol and VLDL cholesterol by the method of Burstein M. and Samaille F.M., in obese adolescents were above normal (3.5-6.6 g/l), and were statistically significantly higher in the 1st group of adolescents (7.57 ± 0.05) g/l than in the 2nd group (6.97 ± 0.08) g/l, ($P < 0.05$).

Thus, this indicator was very informative and reliable in determining the dangerous fractions of lipids and can be recommended as an early diagnostic criterion for atherogenic dyslipidemia in metabolic syndrome in adolescents.

At the same time, the severity of abnormalities in the lipid profile found in adolescents was significantly lower than typical disorders of lipid metabolism in obese adults [11], and had no significant differences by gender. Thus, all obese adolescents showed signs of moderate dyslipidemia, more pronounced in patients with MS. This confirms the fact that for patients with MS the most characteristic are hypertriglyceridemia, increased LDL cholesterol, decreased HDL cholesterol, while hypercholesterolemia is a persistent sign of lipid metabolism disorders and therefore is not included in the criteria of MS, according to consensus IDF (2007) [1].

The Bogalusa Heart Study, conducted in children and adolescents, also showed that atherosclerotic process, which was confirmed by elevated levels of LDL cholesterol and VLDL cholesterol, against the background of normal levels total cholesterol, be-

Blood lipid spectrum in adolescents with obesity, ($M \pm \sigma$)

Groups	Total cholesterol, mmol/l	TG, mmol/l	HDL cholesterol, mmol/l	LDL cholesterol mmol/l	VLDL cholesterol, mmol/l	AC, Units
MS+	4.12 ± 0.08*	1.84 ± 0.07*,**	1.02 ± 0.03*	3.67 ± 0.12*	0.58 ± 0.03*,**	3.18 ± 0.18*
MS-	4.17 ± 0.08*	1.66 ± 0.07*	1.11 ± 0.03*	3.50 ± 0.12*	0.41 ± 0.03*	3.01 ± 0.16*
Control	3.7 ± 0.03	0.84 ± 0.04	1.4 ± 0.03	2.2 ± 0.01	0.17 ± 0.01	1.4 ± 0.03

*Difference between the patients from the main group (MS+ та MS-) and the control group ($P < 0.05$); **Difference between the patients from group1 (MS+) and 2 (MS-) ($P < 0.05$)

gins in childhood, develops during adolescence and leads to cardiovascular disease in adulthood and old age [12-15].

To resolve additional questions about the relationship between lipid profile and specific anthropometric characteristics in adolescents with obesity, a correlation analysis was made that found that children with MS and without MS had different relationships between these parameters. A direct statistically significant correlation was found between WC/HC ratio and the level of β-LP (r = 0.270; P < 0.001) in adolescents with MS (Group I) and without MS (Group II) (r = 0.211; P < 0.05).

Also direct statistically significant correlations were observed in adolescents with MS (Group I) between WC/HC ratio and the content of total cholesterol (r = 0.189; P < 0.05); WC/height ratio and the level of β-LP (r = 0.238; P < 0.05), LDL cholesterol (r = 0.279; P < 0.05), VLDL cholesterol (r = 0.253; P < 0.05) and TG (r = 0.250; P < 0.05).

In the examined patients direct statistically significant correlations were established between BMI and VLDL cholesterol (group I: r = 0.246; P < 0.05; group II: r = 0.249; P < 0.05); between BMI and TG levels (group I: r = 0.255; P < 0.05; group II: r = 0.252; P < 0.05). Also in the group of adolescents without MS there was an inverse statistically significant correlation between BMI and HDL cholesterol (r = -0.266; P < 0.05).

Correlation analysis also revealed a direct statistically significant association of obesity with immunoreactive insulin (group I: r = 0.241; P < 0.001; group II: r = 0.239; P < 0.05), and direct statistically significant correlation between obesity and HOMA index (group I: r = 0.297; P < 0.05; group II: r = 0.267; P < 0.05).

According to the correlation analysis, no correlations were found between levels of blood glycemia and anthropometric parameters (BMI, WC/HC and WC/height ratios).

That is, the correlation analysis showed that abdominal obesity is more associated with early atherogenic changes in blood lipid profile, which is very important for predicting the course of the disease, possible future consequences and developing strategies for their prevention.

Therefore, the obtained results fully correspond to the literature data about lipid profile in patients with obesity and indicate in favor of proatherogenic potential, more pronounced on the background of MS [16-18]. In particular MS is characterized by a lipid triad, which is represented by high values of TG, LDL cholesterol and low values of HDL cholesterol, which increase the risk of cardiovascular diseases even in the absence of carbohydrate metabolism disorders and hypertension [19, 20]. Experts from the National Cholesterol Education Program (NCEP) recommend targeted screening for dyslipidemia in children and adolescents with early-stage cardiovascular disease or high cholesterol in their families. Based on the proposed criteria, it can be assumed that screening for dyslipidemia should cover up to 40% of children [12]. Data from Pathobiological Determinants of Atherosclerosis in Youth and Bogalusa Heart Study showed that the severity of coronary artery atherosclerosis correlates strongly with age, hypertension, BMI, obesity, hyperglycemia, dyslipidemia: LDL cholesterol, HDL cholesterol, TG and over time gains a prognostic threat [12, 13, 21, 22].

According to the study, atherogenic dyslipidemia is detected in adolescence against the background of obesity, which progresses over time and leads in the future, along with other risk factors, to socially significant cardiovascular diseases. This should justify vigilance regarding the early detection of disorders of lipid metabolism as a component of the metabolic syndrome in adolescents, their correction and dynamic monitoring.

Conclusions.

1. According to a comprehensive clinical and laboratory study in 50% of patients were detected signs of metabolic syndrome (insulin resistance, abdominal obesity, atherogenic dyslipidemia, border levels of glycemia, high blood pressure).

2. It was found that patients with metabolic syndrome showed statistically significantly higher values of BMI, the degree of abdominal obesity than adolescents without signs of metabolic syndrome.

3. Adolescents with metabolic syndrome showed signs of atherogenic dyslipidemia, manifested as elevated levels of triglycerides, low- and very low-density lipoprotein cholesterol, β-lipoproteins, a tendencies to lower high-density lipoprotein cholesterol, the degree of brightness of which is lower than in adult patients, which is more prognostically favorable, as it allows early therapeutic intervention and prevention of consequences.

4. The level of β-LP showed high informativeness about atherogenic changes of lipid profile, which allows to recommend its use in general practice, and β-LP indicator should be considered as an early diagnostic criterion of atherogenic dyslipidemia as a component of metabolic syndrome.

5. Significant correlations have been established between atherogenic dyslipidemia and anthropometric measurements, which indicates an increased risk of lipid metabolism disorders in individuals with abdominal obesity, and in adolescents without metabolic syndrome, these pathophysiological relationships are few, which leaves a more prognostic and favorable greater reserve for therapeutic correction and prevention.

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ПОКАЗНИКИ ПОРУШЕННЯ ЛІПІДНОГО ОБМІНУ В СИРОВАТЦІ КРОВІ ПІДЛІТКІВ ІЗ МЕТАБОЛІЧНИМ СИНДРОМОМ

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Атерогенна дисліпідемія є одним з основних та ранніх критеріїв метаболічного синдрому в підлітків. Дослідження характеру дисліпідемії в підлітків, можливостей її корекції й профілактики наразі є актуальним. Мета роботи – дослідити особливості порушення ліпідного обміну в підлітків із метаболічним синдромом. Обстежено 200 хворих на ожиріння віком 14–18 років, яких було розподілено на дві групи: з метаболічним синдромом та без нього. У контрольній групі було 30 підлітків з нормальною масою тіла. Ліпідний профіль у крові підлітків вивчали уніфікованим методом відповідно до рекомендацій IFCC на напівавтоматичному фотометрі. Рівень β-ліпопротеїнів у сироватці крові вимірювали турбідиметричним методом. Встановлено підвищення рівня тригліцеридів, холестеролу ліпопротеїнів низької та дуже низької щільності, β-ліпопротеїнів та тенденцію до зниження холестеролу ліпопротеїнів високої щільності в крові підлітків із метаболічним синдромом як ознаки гетерогенної дисліпідемії. Вірогідні кореляційні зв'язки як між показниками ліпідного профілю, так і між показниками атерогенної дисліпідемії та антропометричними значеннями, вказують на підвищений ризик порушення метаболізму ліпідів в осіб з абдомінальним ожирінням.

Ключові слова: підлітки, метаболічний синдром, дисліпідемія.

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