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PATHOGENETIC MECHANISMS OF DYSLIPIDEMIA IN PUBERTY IN GIRLS: THE CONTRIBUTION OF HORMONAL RECONSTRUCTION TO THE INCREASE IN ATHEROGENICITY

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Abstract
The article examines the pathogenetic mechanisms of lipid spectrum disorders in girls during puberty . The role of hormonal changes, insulin resistance , obesity and inflammatory processes in the formation of the atherogenic profile and metabolic syndrome is highlighted. Particular attention is paid to clinical studies of recent years demonstrating the relationship between changes in lipid metabolism and increased cardiometabolic risks in adolescents.

Keywords: puberty, adolescent girls, lipid spectrum, dyslipidemia, atherogenicity, metabolic syndrome, insulin resistance

Introduction

Puberty is a critical stage of development characterized by intense hormonal and metabolic changes. In girls, it is during this age period that the reproductive system is formed, growth accelerates, body proportions change, and adipose tissue is formed. These processes are accompanied by a significant impact on lipid and carbohydrate metabolism. [1.2].

It is known that lipid profile disorders in adolescence are associated with an increased risk of early formation of atherosclerotic changes in blood vessels. Against the background of hormonal changes and increased tissue sensitivity to insulin, some girls develop the opposite situation - insulin resistance , which becomes the starting point for the formation of dyslipidemia and metabolic syndrome [2.4].

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Modern studies show that during puberty girls often experience changes such as increased levels of triglycerides (TG), total cholesterol (TC), low-density lipoproteins (LDL), and decreased concentrations of high-density lipoproteins (HDL). These changes increase blood atherogenicity and create conditions for the early development of cardiovascular diseases [3].

Thus, the study of the mechanisms of lipid spectrum disorders during puberty in girls is of not only scientific but also clinical interest, since it is during this period that the first markers of future cardiovascular and endocrine diseases can be identified and preventive measures can be carried out in a timely manner.

Pathogenetic mechanisms of lipid metabolism disorders in girls during puberty

The puberty period in girls is accompanied by profound hormonal and metabolic changes that have a direct effect on lipid metabolism and determine the level of atherogenicity of the blood. These changes are associated with changes in the production of sex hormones, the development of insulin resistance , the accumulation of visceral fat, the activation of inflammatory processes and oxidative stress. The combination of these factors forms the basis for the development of dyslipidemia and metabolic syndrome.

1. Hormonal changes and lipid profile

With the onset of puberty in girls, there is a sharp increase in the secretion of estrogens and progesterone, as well as a moderate increase in androgen production. Estrogens are traditionally considered cardioprotective hormones, since they contribute to an increase in the concentration of high-density lipoproteins (HDL) and a decrease in the level of low-density lipoproteins (LDL). However, under conditions of hormonal imbalance, especially with relative hyperandrogenism , this protective effect is leveled, which can lead to an atherogenic shift in the lipid spectrum [4].

Progesterone, on the contrary, is able to reduce tissue sensitivity to insulin and stimulate the accumulation of visceral fat, which is accompanied by an increase in the concentration of triglycerides (TG) and total cholesterol (TC) in the blood [5]. Excessive secretion of androgens, observed in some girls (for example, with polycystic ovary syndrome), increases lipolysis in adipose tissue and increases

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the level of free fatty acids (FFA). This leads to their entry into the liver, where they are used to synthesize triglycerides and LDL, contributing to the formation of severe dyslipidemia [6].

Thus, hormonal changes during puberty are the primary link that triggers a cascade of metabolic changes that increase the risk of atherosclerotic processes.

2. Insulin resistance as a key link in pathogenesis

A physiological phenomenon of puberty is a decrease in tissue sensitivity to insulin, which is compensated by increased secretion by β-cells of the pancreas. Normally, this process is temporary and gradually levels out as puberty is completed. However, in the presence of excess body weight, abdominal obesity or genetic predisposition, physiological insulin resistance (IR) acquires a pathological character [7].

IR has a multifaceted effect on lipid metabolism. Increased lipolysis in adipocytes is accompanied by the release of a large amount of FFA into the systemic bloodstream. These acids actively enter the liver, where they are used to synthesize triglycerides, which increases the production of very low density lipoproteins (VLDL). At the same time, the activity of lipoprotein lipase decreases , which prevents the utilization of TG and leads to their accumulation in the blood plasma. As a result, the concentration of TG and LDL increases, while the level of HDL decreases [6.8].

3. The role of inflammation and oxidative stress

Current research shows that adolescents with metabolic disorders often have a state of chronic low-level inflammation. It is manifested by increased levels of C-reactive protein, interleukins (IL-6, IL-17A) and tumor necrosis factor-α (TNF-α), which have a damaging effect on the vascular endothelium and increase the expression of adhesion molecules.

oxidative stress develops , leading to modification of low-density lipoproteins. The resulting oxidized forms of LDL (ox -LDL) have pronounced atherogenicity : they easily penetrate the intima of blood vessels, stimulate absorption by

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macrophages and the formation of "foam cells", which is an early stage in the formation of an atherosclerotic plaque.

Thus, the combination of hormonal changes, insulin resistance , inflammation and oxidative stress during puberty in girls creates conditions for the formation of an unfavorable lipid profile and increases the likelihood of developing metabolic syndrome and cardiovascular pathology in the future.

Clinical studies of recent years demonstrate that it is precisely at puberty that girls begin to develop the first markers of atherogenicity and metabolic syndrome. These changes are both biochemical and clinical in nature, and if detected in a timely manner, they can serve as a basis for prevention.

One of the most studied aspects is the disturbance of lipid metabolism in girls with precocious puberty . A meta-analysis that included more than 2,500 adolescents showed that girls with precocious puberty had significantly higher levels of triglycerides (TG), total cholesterol (TC), and low-density lipoproteins (LDL) compared to their peers [11]. At the same time, the level of high-density lipoproteins (HDL) did not differ significantly between the groups.

These data allow us to conclude that even without obesity or pronounced insulin resistance, girls with accelerated sexual development already have an atherogenic blood profile.

Longitudinal observations of adolescents of different ethnic groups show that with the onset of puberty there is a gradual increase in the prevalence of metabolic syndrome. In one European study, the frequency of MS increased from 9.1% in prepuberty to 11.9% in the period of active puberty [10].

The main risk factors were:

- body mass index (BMI-z),
- waist circumference,
- insulin resistance indicators (HOMA-IR),
- systolic blood pressure.

It has been established that these predictors are the ones that most strongly correlate with changes in the lipid spectrum.

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Prevalence of dyslipidemia in adolescents

A large study conducted in China among more than 9,000 schoolchildren aged 10–18 years showed that the most common lipid abnormalities in girls were low HDL and elevated TG . Moreover, the proportion of adolescents with combined lipid abnormalities increased significantly from prepuberty to late puberty [4]. These data highlight the need for early screening and dynamic monitoring of the lipid profile during puberty.

Table 1. Average lipid profile values in girls depending on the stage of puberty

Indicator	Prepuberty	Puberty	Late puberty	p-value
Triglycerides (TG), mmol /l	0.85 ± 0.12	1.12 ± 0.18	1.25 ± 0.20	<0.05
Total cholesterol (TC), mmol /l	4.2 ± 0.3	4.8 ± 0.4	5.0 ± 0.5	<0.05
LDL, mmol /l	2.3 ± 0.2	2.8 ± 0.3	3.0 ± 0.4	<0.05
HDL, mmol /l	1.4 ± 0.2	1.2 ± 0.2	1.1 ± 0.1	<0.05

Note: data are averaged from several population studies [9–11].

Puberty in girls is a critical period in which a combination of hormonal changes, insulin resistance , obesity and inflammatory processes leads to significant changes in the lipid profile. These disorders gradually transform into a state of increased atherogenicity and create the basis for the formation of metabolic syndrome.

Atherogenic imbalance of the lipid spectrum. Atherogenic changes in lipid metabolism are understood as an increase in the concentration of triglycerides, low-density lipoproteins and total cholesterol with a simultaneous decrease in high-density lipoproteins. Such an imbalance is typical for girls at puberty, especially in conditions of insulin resistance and excess body weight [1].

The atherogenicity of the lipid profile is enhanced by:

- an increase in the number of small and dense LDL particles, which have a high ability to penetrate the vascular wall;
- reducing the concentration of antiatherogenic HDL, which normally ensures the reverse transport of cholesterol from tissues to the liver;

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- an increase in the content of oxidized forms of LDL (ox -LDL), which trigger inflammatory reactions in the vascular wall [3].

Insulin resistance and obesity as catalysts. Insulin resistance not only disrupts carbohydrate metabolism, but also stimulates lipotoxicity . Excess free fatty acids in plasma enhance hepatic lipogenesis , which leads to hypertriglyceridemia and an increase in VLDL levels. In turn, the accumulation of visceral fat in the body of a teenage girl forms a vicious circle: obesity → insulin resistance → dyslipidemia → even greater obesity [5].

Chronic inflammation and oxidative stress. Girls with dyslipidemia at puberty show signs of chronic low-level inflammation: increased levels of C-reactive protein, interleukin-6, and TNF-α. These cytokines damage the vascular endothelium and stimulate monocyte migration, which accelerates the formation of atherosclerotic plaques [8].

oxidative stress develops : under the influence of active forms of oxygen, low-density lipoproteins are oxidized, turning into ox -LDL. These modified particles are highly atherogenic , provoke the accumulation of foam cells and the formation of fatty streaks in the intima of blood vessels [11].

Mechanisms of connection with metabolic syndrome. Metabolic syndrome (MS) in girls at puberty is a complex of disorders: abdominal obesity, hypertriglyceridemia , low HDL, hyperglycemia and arterial hypertension. All these components are interconnected and have a common pathogenetic basis - insulin resistance and dyslipidemia [10].

Table 2. The main mechanisms of formation of atherogenicity and metabolic syndrome in girls during puberty

Pathogenetic factor	Effect on lipid spectrum	Consequences
Hormonal imbalance (estrogen/androgen)	Increased TG, LDL, decreased HDL	Early signs of dyslipidemia
Insulin resistance	Increased lipolysis , increased free fatty acids, hypertriglyceridemia	Increased atherogenicity of blood
Visceral obesity	Decreased LP-lipase activity, increased VLDL	Increased risk of metabolic syndrome
Chronic inflammation	Endothelial damage, cytokine expression	Acceleration of atherogenesis
Oxidative stress	Education ox -LDL	Formation of atherosclerotic plaques

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Thus, atherogenicity in girls during puberty is formed under the influence of a complex of factors. The central place is occupied by hormonal changes and insulin resistance, while inflammation and oxidative stress accelerate the progression of vascular disorders. Against this background, early formation of metabolic syndrome occurs, which in the future significantly increases the risk of cardiovascular and endocrine diseases.

Prevention and ways of correction of lipid metabolism disorders in puberty

Early detection and correction of lipid profile disorders in girls during puberty is of key importance for the prevention of metabolic syndrome and cardiovascular diseases in adulthood.

1. Screening and diagnostics

In accordance with international and national recommendations, girls from risk groups (with obesity, family history of dyslipidemia , precocious puberty, signs of insulin resistance) are recommended to undergo:

- biochemical blood test with determination of lipid spectrum (TC, TG, LDL, HDL),
- calculation of atherogenic indices (for example, the Castelli index , ApoB /ApoA1),
- fasting glucose levels and HOMA-IR [8].

Early screening allows us to identify an atherogenic shift in lipid metabolism at the preclinical stage and begin correction in a timely manner.

2. Non-drug preventive measures

Lifestyle correction is the first and most effective stage of prevention. It includes: Rational nutrition - limiting saturated fats, trans fats and simple carbohydrates, increasing consumption of vegetables, fruits, foods rich in fiber and polyunsaturated fatty acids.

Regular physical activity - at least 60 minutes of moderate to vigorous activity per day (walking, swimming, dancing, team sports).

Weight loss in obesity is gradual and controlled, with an emphasis on reducing visceral fat, which plays a key role in the pathogenesis of insulin resistance [2].

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3. Drug prevention and treatment

In some cases (severe dyslipidemia , PCOS, severe insulin resistance) drug correction may be required. The most commonly used drugs in adolescent girls are:

- metformin - improves tissue sensitivity to insulin, reduces the level of TG, LDL and increases the concentration of HDL;
- Statin drugs are used to a limited extent in adolescent practice in cases of severe hypercholesterolemia and high risk of CVD;
- hormonal therapy - girls with hyperandrogenism and PCOS are prescribed combined oral contraceptives, which can partially normalize the lipid spectrum [3].

4. Educational and organizational measures

An important area is health education work with teenagers and their parents, aimed at developing healthy eating habits, reducing physical inactivity and early diagnostics of health disorders. At the level of the healthcare system, programs for screening schoolchildren and the introduction of early MS prevention protocols are relevant.

Conclusion

Puberty in girls is a critical "window of vulnerability" when, against the background of hormonal changes and physiological insulin resistance, the first signs of dyslipidemia and atherogenicity are formed . In this age period, even moderate changes in the lipid profile are of great importance, since they predetermine the risk of developing metabolic syndrome and cardiovascular diseases in adulthood.

The central place in the pathogenesis is occupied by insulin resistance , which increases lipid disorders and leads to the activation of inflammation and oxidative stress. The combination of these factors forms the "metabolic soil" for atherosclerosis.

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Early prevention—including screening, lifestyle modification, healthy diet, and increased physical activity—is the most effective method for preventing the progression of metabolic disorders. In special cases, drug correction is required. Thus, puberty is a period when it is necessary to pay special attention to monitoring the lipid spectrum in girls , since it is during this age period that one can most effectively influence future health and reduce the risk of cardiovascular diseases.

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