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THE ROLE OF RISK FACTORS IN THE DEVELOPMENT OF INSULIN RESISTANCE IN CHILDREN

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Abstract: According to the World Health Organization (2016), 1.9 billion people worldwide (every fourth) are overweight or obese. Insulin resistance is a complex multifactorial process based on the interaction of genetic, hormonal and external factors. Insulin resistance is called one of the main causes of obesity and a trigger for type 2 diabetes mellitus, hypertension, coronary heart disease, liver and kidney disease, infertility in women, erectile dysfunction in men and even Alzheimer's disease. Modern lifestyle characterized by a sedentary lifestyle, high-calorie diet and stress increases the risk of developing insulin resistance. It is important to study how these factors affect children in order to develop effective preventive measures.

Key words: Insulin resistance, pathogenesis, etiological factors, obesity, insulin, risk factor.

INTRODUCTION

Insulin resistance in school-aged children is becoming increasingly important in light of the growing incidence of metabolic disorders. The prevalence of metabolic syndrome in children and adolescents is growing in parallel with the growth of obesity rates. According to the World Health Organization (2016), 1.9 billion people worldwide (every fourth) are overweight or obese. In the United States and Canada, 60% of the population suffers from it, in Europe - 44%, and in Russia - about 50%; obesity is less common in Asia - 27% and in Africa - 19% of the total population. By 2025, the WHO predicts that another 167 million people worldwide will be obese. The prevalence of overweight among children and adolescents aged 5 to 19 has increased sharply from 4% in 1975 to just over 18% in 2016. This increase is evenly distributed among children and adolescents of both sexes: in 2016, 18% of girls and 19% of boys were overweight. The study of risk factors for insulin resistance is an important task in pathophysiology and hygiene, since these factors can significantly affect the health of the younger generation. Insulin resistance (IR) is a condition in which body tissues lose sensitivity to the hormone insulin. It is produced by beta cells in a special area of the pancreas - the islets of Langerhans. A minimal amount of insulin is constantly

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present in the blood, but it is especially actively synthesized when sugar levels rise. Normally, this happens every time after a meal: carbohydrates are converted into glucose during digestion and enter the bloodstream in this form. The blood carries glucose to all organs and tissues, where it is converted into energy. This process is called glycolysis. Glucose penetrates without hindrance into the cells of the brain, nerve fibers, retina, kidneys and adrenal glands - these organs are called insulin-independent. In other cells, sugar needs a mediator - this function is performed by insulin [1]. Insulin resistance is called one of the main causes of obesity and the trigger for type 2 diabetes, hypertension, coronary heart disease, liver and kidney disease, infertility in women, erectile dysfunction in men and even senile dementia - Alzheimer's disease [2]. Therefore, it is so important to identify the risk factors for insulin resistance at an early age.

A number of researchers conducted a cohort study in collaboration with the international BioSHaRE-EU project in seven European countries (Estonia, Finland, Germany, Italy, the Netherlands, Norway and the United Kingdom), involving ten populations. The highest prevalence of obesity was found in Germany - 26.3% (average age of participants 59.6 years), in Finland - 25.7% (57.3 years), in Estonia - 23% (52.6 years) and in the United Kingdom - 22.9% (44.0 years), and the lowest prevalence of obesity was noted in the Italian studies CHRIS (11.6%, 53.6 years) and MICROS (14.8%, 54.9 years) [3]. The risk of insulin resistance in children with obesity at 11-14 years of age compared to younger schoolchildren increased sharply regardless of gender [4]. The most important result of the study by Malyavskaya and Lebedev is the established fact that metabolic atherogenic disorders in a high percentage of cases (43.82%) are

detected in individuals without abdominal obesity, who may represent part of the spectrum of children and adolescents with insulin resistance syndrome. At the same time, three or more components of metabolic syndrome were detected in 5.62% of children with normal body weight and waist circumference [5].

The key mechanism for the development of IR and, consequently, IR-related chronic diseases is mitochondrial dysfunction, which contributes to the ectopic accumulation of lipids and their metabolites [6]. Various factors influence tissue sensitivity to insulin. Many physiological conditions predispose to IR: puberty, pregnancy, old age, night sleep, physical inactivity. However, IR is most often caused by pathological conditions other than type 2 diabetes mellitus (T2DM), which most often occurs against the background of existing IR, there are a number of other diseases and conditions associated with this phenomenon.

Elevated levels of sex hormones, growth hormone and cortisol, characteristic of puberty, contribute to the development of IR in adolescents. IR in adolescents is a physiological feature of puberty and can be transient. With sufficient adaptive reserve provided by a complex of neuroendocrine reactions, the balance between incoming and outgoing energy is maintained at a constant level [7]. In children with background IR during puberty, more pronounced IR develops, which often does not disappear after puberty, but continues to progress. The onset or exacerbation of acne is associated with IR during puberty. Thus, physiological and pathological IR can represent a continuous spectrum of conditions [6]. The period of puberty is accompanied by an abrupt change in the level of various hormones, an increase in the number of adipocytes and physiological

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insulin resistance. In particular, evidence has been obtained that the level of insulin resistance determined in eight-year-old children is 2 times lower than at the age of 15. In this regard, some researchers believe that puberty itself is associated with the progression of abnormal metabolic processes [8].

There are reliable risks in the development of insulin resistance in children with obesity - relative and attributable - recorded with a two-year history of the disease and high anthropometric indicators: excess body weight - body mass index (kg / m2) over 30, sagittal abdominal diameter > 20 cm, waist circumference > 94 cm in boys and > 80 cm in girls [9]. According to P. Gluckman et al., a child born against the background of a difficult pregnancy predicts unfavorable development after birth, when the body builds a strategy to prepare for survival: in particular, short stature, early puberty, hormonal axis disorders, behavioral changes, increased insulin resistance, a tendency to accumulate adipose tissue [10]. Also, low-birth-weight newborns (body weight less than 2500 g) with signs of prenatal hypotrophy and intrauterine growth retardation are at risk for the development of insulin resistance. Although genetic predisposition has a limited influence on the development of MS, modifiable risk factors such as maternal weight during pregnancy, children's lifestyle, obesity, IR, sedentary behavior, vitamin D deficiency, sleep disorders, hypercortisolism, chronic inflammation and changes in the intestinal microbiota play a decisive role in the development of MS [11].

Insulin resistance is a complex multifactorial process based on the interaction of genetic, hormonal and external factors. The main cause of impaired insulin sensitivity is excess body weight, especially visceral obesity, which

contributes to inflammatory processes and deterioration of glucose metabolism. Hormonal changes, especially during puberty, can temporarily increase the manifestations of IR, which requires special attention to adolescents. Stress, nutritional factors and lack of physical activity also play an important role.

Among the risk factors for overweight and obesity, endogenous and exogenous ones are distinguished. The leading component of endogenous factors is the genetic component, which determines congenital genetic mutations and various variations of insulin resistance. Exogenous factors include behavioral risk factors, including excessive consumption of high-calorie foods with excess salt and sugar content [12].

In recent years, many researchers have given preference to genetic factors that characterize rare genetic mutations in individuals and families with obesity. Rui-Rui Gao et al. investigated the biological function of rs283 polymorphism in adolescents of Han ethnicity and concluded that Chinese adolescents with obesity of Han ethnicity with the GG genotype of rs283 polymorphism were more sensitive to exercise-induced reduction in body fat, insulin resistance and plasma TG [13]. A study was conducted that was devoted to studying the effect of LPL gene polymorphism on insulin resistance in adolescents of the Kazakh population. The obtained data showed that rs328 polymorphism of the LPL gene is associated with the risk of hyperinsulinemia and insulin resistance [14]. It was revealed that in patients with T2DM with obesity in the Azerbaijani population, the normal variant of the insulin-induced gene polymorphism in homozygous form (GG), the mutant variant in the heterozygous form of the leptin gene, the mutant variant of the adiponectin gene in homozygous form and

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the normal variant of the TNF-α gene in homozygous form are more common [15]. According to a number of studies, single nucleotide polymorphisms of the UBE2E2 gene (rs6780569, rs7612463, rs9812056) are associated with an increased risk of developing T2DM in residents of Japan, Korea and China [16]. Analysis of epidemiological data shows that insulin resistance in children is becoming an increasingly common problem due to lifestyle changes, increasing obesity and low physical activity. It has been revealed that children with excess body weight have a higher risk of developing IR, which in the future can lead to metabolic disorders and chronic diseases. Studies confirm that the prevalence of insulin resistance is higher in countries with a high level of urbanization and availability of high-calorie food. Gender and age also play a role: in adolescents during puberty, the level of IR increases, which is associated with hormonal changes. For effective prevention, a comprehensive approach is needed, including changing eating habits, increasing the level of physical activity and early diagnosis of metabolic disorders. As recent decades have shown, the prevailing understanding of the causes and mechanisms of IR and MS in many ways does not allow us to effectively combat them, which requires a deeper and more accurate understanding of the key pathogenetic mechanisms and cause-and-effect relationships of this pathology and the factors leading to its development. Conclusion. The modern lifestyle, characterized by a sedentary lifestyle, high-calorie diet and stress, increases the risk of developing insulin resistance. It is important to study how these factors affect children in order to develop effective preventive measures. Insulin resistance in childhood can lead to serious long-term health consequences, including chronic diseases that manifest later in life.

Understanding the risk factors allows us to minimize these consequences. Despite the growing problem, there is a lack of research on risk factors for insulin resistance in the pediatric population, especially when compared to adults. This highlights the need for more in-depth analysis of this problem.

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