METABOLIC SYNDROME IN CHILDREN
(LITERATURE REVIEW)
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One of the most important issues of modern medical science is metabolic syndrome (MS) — insulin resistance syndrome — that combines such important components as abdominal obesity, reduced carbohydrate tolerance or type 2 diabetes mellitus, dyslipidemia, arterial hypertension, and other criteria according to the recommendations of the World Health Organization’s (WHO). These components cause rapid development of complications that lead to the social exclusion, disability, and mortality. There is no doubt now that the origins of metabolic disorders date back to childhood, and the high prevalence of metabolic syndrome components determines the relevance of studying this problem and the development of approaches to treatment and prevention of MS since childhood. The prevalence of MS in childhood ranges from 4% to 30% among the total population; it is much higher among children and adolescents with obesity. However, a notion of MS in pediatrics has no scientific justification, as there is only scarce scientific research and development in this area [1].

Metabolic syndrome is a compound interconnected complex of regulatory, neuroendocrine, and metabolic disorders that result in the formation of abdominal visceral type of obesity and insulin resistance with compensatory hyperinsulinemia, which in turn contribute to the progression of arterial hypertension (AHT), the development of dyslipidemia (DL) of atherogenic nature, cause impaired glucose tolerance or type 2 diabetes and hyperuricemia, alteration of hemostasis of prothrombinic orientation and a number of related hormonal disorders that lead to the maintenance of pathological inclination of metabolism [27].

It is proved that in the development of obesity and metabolic syndrome, dyslipidemia is one of the most important mechanisms, which results in the formation and progression of atherosclerosis and leads to the vicious circle: obesity — insulin resistance — hyperinsulinemia — obesity. At the same time in the scientific literature, there are only a few reports of studies of this pathology [24].

In 1988, Reaven described the interaction of insulin resistance, AHT, DL, and other related metabolic disorders and introduced in the scientific medical literature the term «metabolic syndrome». It is known that each of its components is a clear risk factor for the development and progression of cardiovascular diseases. The prevalence of metabolic syndrome in the population aged over 30 years in industrialized countries is 10% to 40%; recent epidemiological studies show that incidence of MS among children and adolescents is 47.6%, while under overweight this figure of MS increases dramatically, reaching 30-50% [25].

The main etiological factors of MS are considered genetic predisposition, poor diet, physical inactivity, and syndrome of obstructive sleep apnea. Hyperinsulinemia and insulin resistance, dysfunction of endocrine activity of internal fat, excessive activity of sympathetic-adrenal (SAS) and renin-angiotensin-aldosterone systems (RAAS), and endothelial dysfunction are important in the pathogenesis of metabolic syndrome and its complications, thus developing atherogenic DL, AHT, and other metabolic disorders [18].

The development of hyperinsulinemia and insulin resistance with overweight means increasing body fat mass, accompanied with an increase in the size of fat cells, and adipocyte becomes less sensitive to insulin. Insulin secretion and insulin receptor signaling disrupt, regulation of glucose and damaged proinflammatory cytokines breaks, and insulin accumulates in adipose tissue. Intensive lipolysis in visceral adipocytes leads to the release of large amounts of free fatty acids (FFA) and glycerol in the granule circulation. Muscle cells and liver cells enhance capture and oxidation of free fatty acids, insulin depending glucose transport reduces — insulin resistance develops. Once in the liver, FFA, on the one hand, become a substrate for the formation of atherogenic lipoproteins, on the other hand, they prevent insulin from the binding of hepatocytes and its degradation, potentiating insulin resistance at liver level, inhibiting the suppressive effect of insulin on glucose production by the liver. Insulin resistance of hepatocytes leads to lower glycogen synthesis, activation of glycogenolysis and gluconeogenesis. Compensating for these violations, the pancreas increases insulin production, hyperinsulinemia develops, thus promoting the development of peripheral insulin resistance [3].

In terms of hyperinsulinemia and insulin resistance in the liver, the synthesis of triglycerides increases; the content of ultra low density lipoprotein (ULDLP) increases; and the lipoprotein lipase activity decreases that leads to lower catabolism of ULLPD and lipids coming from the gut as part of chylomicrons and their remnants; the hepatic lipase activity increases and the hydrolysis of saturated triglycerides, high density lipoprotein (HDLP), and low density lipoprotein (LDLP) accelerates, the modified LDLP forms, and the cholesterol level of HDLP, especially the cholesterol level of cardioprotective subtraction of the cholesterol level of HDLP decreases [5].
The content of visceral or intra-abdominal fat correlates with inflammation, as a large amount of signal substances synthesizes in white adipose tissue, such as leptin, tumor necrosis factor-α, interleukin-6, interleukin-8, and the corresponding soluble receptors. White adipose tissue also secretes important regulators of metabolism LP, such as lipoprotein lipase, apolipoprotein E, and protein carrier of cholesterol ester. In addition, white adipose tissue secretes angiotensinogen, angiotensin II, plasminogen activator inhibitor-1, transforming growth factor-β, and adiponectin.

Increased synthesis of free fatty acids in MS leads to hyperuricemia because activation of pentose way of glucose oxidation promotes the formation of ribose-5-phosphate, from which purine nucleus are synthesized. Circulating FFA cause inflammation through direct activation of NF-κB and TLR4, reinforcing the development of atherosclerosis. The state of hyperleptinemia is a significant factor in the development of oxidative stress and oxidative modification of lipoproteins in blood plasma. Hiperleptinemia stimulates adreno-corticotropic releasing-factor hormone, so light hypercorticoidism is often observed in MS. In chronic hyperinsulinemia SAS and RAAS are stimulated. Through mitohenaktive protein kinase insulin enhances pathological vascular effects by stimulating various growth factors (platelet, insulin, fibroblast transforming growth factor, etc.), leading to the proliferation and migration of smooth muscle cells, to the fibroblast proliferation of the vascular wall, and to the extracellular matrix accumulation. These processes cause remodeling of the cardiovascular system, resulting in loss of elasticity of the vascular wall, microcirculatory disorders, atherogenesis progression and, finally, to the increase of vascular resistance and stabilization of arterial hypertension [20]. Deteriorating blood supply of myocytes, which are the main consumer of glucose in the body, leads to an increase in insulin resistance and hyperinsulinemia (the vicious circle closes). AHT against the backdrop of normoglycemia usually indicates the presence of insulin resistance. For the diagnosis of insulin resistance one important to identify tolerance violations towards glucose. Hyperinsulinemia against the backdrop of normoglycemia, increased level of triglycerides, and reduced cholesterol level of HDLP — for boys and girls [8]. Given that the anthropometric parameters in children and adolescents depend on age and sex, for the diagnosis of overweight there were used protsentyl tables of distribution of body mass index (BMI) of the populace according to age and gender. There is a disagreement as to which BMI should be associated with overweight and obesity. Children and adolescents, whose BMI is in the range between the 85th and 90th percentile, are at risk of overweight development. Some authors suggest diagnosing overweight/obesity with a BMI equal to the 90th percentile, while others advise the 95th percentile. Undoubtedly, for the diagnosis of excessive body weight and obesity in children and adolescents it is more appropriate to use standardized criteria for BMI adjusted for age and sex and eligible for the criteria of overweight (25 kg/m²) and obesity (30 kg/m²) in adults, because these parameters define high risk of cardiovascular diseases [15].

The study received shows common criteria for the diagnosis of main components of metabolic syndrome — obesity, arterial hypertension, hyperglycemia, increased level of triglycerides, and reduced cholesterol level of HDLP — for boys and girls [8]. Given that the anthropometric parameters in children and adolescents depend on age and sex, for the diagnosis of overweight there were used protsentyl tables of distribution of body mass index (BMI) of the populace according to age and gender. There is a disagreement as to which BMI should be associated with overweight and obesity. Children and adolescents, whose BMI is in the range between the 85th and 90th percentile, are at risk of overweight development. Some authors suggest diagnosing overweight/obesity with a BMI equal to the 90th percentile, while others advise the 95th percentile. Undoubtedly, for the diagnosis of excessive body weight and obesity in children and adolescents it is more appropriate to use standardized criteria for BMI adjusted for age and sex and eligible for the criteria of overweight (25 kg/m²) and obesity (30 kg/m²) in adults, because these parameters define high risk of cardiovascular diseases [15].

However, BMI does not give a complete picture of the distribution of adipose tissue in the body. There are two main types of distribution of adipose tissue in obesity: hinosaur and android. The hinosaur type is characterized by predominant accumulation of fat on the hips, while the android type presupposes the accumulation of fat in the abdominal area, with the largest amount vescically (abdominal obesity) [22]. The evaluation of insulin resistance should take into account not only insulin level but also compare it with the level of glucose, which is important to identify tolerance violations towards glucose. Hyperinsulinemia against the backdrop of normoglycemia usually indicates the presence of insulin resistance. For the diagnosis of insulin resistance one
can use the oral glucose ratio calculation of correlation between insulin and plasma glucose at the beginning and after two hours [6,26].

In order to detect insulin resistance, there are also calculated indexes: index of insulin sensitivity — QUICKI Index (QUantitative Insulin sensitivity ChecK Index) and insulin resistance index HOMAR (Homeostatic Model Assessment), which is calculated by the formula: Go?INSO/22.5, where Go is glucose concentration in plasma on an empty stomach (mmol/l), INSO is insulin concentration in serum on an empty stomach (mkOD/ml) [9,17].

Based on examination of children of all ages who were at different stages of puberty, there were proposed cutting points in children and adolescents, corresponding to the 90th percentile: insulin – 15.05 mkOD/ml, C-peptide – 2.85 ng/ml, HOMA-index – 3.43, and QUICK-index – > 1.10 [14,19].

In children and adolescents, comprehensive treatment of this syndrome includes a complete lifestyle change, together with passing obesity, abnormalities of carbohydrate metabolism, hypertension, and dyslipidemia. The aim of any doctor in this case is to form a stable patient motivation, which helps him continue to implement the recommendations on diet, normalized physical activity, and strict medicine taking [13]. Inistent persuasion in success enables the patient to cope easily with difficulties in order to change his/her traditional way of life. This change provides prompt normalization of regime and diet of the child, optimization of physical activity, comprehensive psychotherapy, problem-targeted training programs, and rigid self-control [2].

The main approach to the treatment of metabolic syndrome in children is a lifestyle change. The child should walk more, engage in various sports, and spend more time outdoors. At the same time, it is necessary to limit the child in a computer monitor or TV.

Since excessive accumulation of visceral adipose tissue is one of the major pathogenetic factors in the formation of MS, the main place in complex treatment of patients should be taken by measures to combat obesity (lifestyle optimization with increased physical activity and diet prescription). Weight loss by 10-15% is accompanied with weight reduction of visceral adipose tissue. It usually improves insulin sensitivity, reduces systemic hiperinsulinism, makes better lipid and carbohydrate metabolism, and lowers blood pressure. According to the recommendations of the American Heart Association, to maintain a satisfactory health condition of adults and children (aged over 5 years) they should spend at least 30 minutes daily for moderate dynamic (aerobic) loading and 30 minutes 3-4 times a week for intense physical activity [12].

The examples of moderate physical activity can be fast walking (3 km for 30 minutes), cycling (8 km for 30 minutes), dancing at a moderate pace (during 30 minutes), playing basketball (for 15-20 min), and volleyball game (for 45 minutes). It is proved that a daily 50-minute physical activity (70% of maximal oxygen consumption) for 7 days in patients with type 2 diabetes significantly increases the sensitivity of peripheral tissues (skeletal muscle) to insulin. The diet consists of taking into account body weight, age, gender, level of physical activity, and food preferences of patients. The diet should be highly caloric — with restriction of refined fats and easily digestible carbohydrates. Consumption of fat is limited to 20-30% of daily calories.

The next step in the treatment of metabolic syndrome in children should be diet food. It is necessary for a child to reduce the use of refined fats (butter, mayonnaise, and sauces) and «empty» carbohydrates (chocolate, sweet drinks, candy, and sugar). It is necessary to enrich the diet of baby with fruit and vegetables, as they are the main source of fiber. Meals should bring to 4-5 times a day, with breakfast must be complete. If possible, one should try to protect children from stress, because they, as adults, actually ‘stick’ stress, which also leads to obesity [7].

There can be applied the system of dietary approach to treating arterial hypertension in children — DASH (The Dietary Approaches to Stop Hypertension). Such a diet includes fruit and vegetables, is rich in fiber and low in fat (saturated and total) compared with the usual diet, and therefore it contains more potassium magnesium, calcium, flavonoids, flavin, beta-carotene, beta-cryptoxanthin, lycopene, lutein-zexantyn, and phytosterol. It is known that the DASH lowers blood pressure and lipid level in blood [23]. Admission of potassium to the body plays a big role in reducing glucose tolerance. Metformin is notable among medications that increase sensitivity of tissues to insulin action. Metformin has also hypolipidemic, hypotensive and antiatherogenic action, inhibits glumoneogenesis and glycoenzolysis in the liver. The drug is taken with meals 2-3 times a day [8,11].

The main areas of MS prevention are sufficient physical activity and a diet that meets the physiological needs. Metabolic syndrome in children should be treated even with the first signs of the disease until it begins to develop as a complication of disorders of the cardiovascular or digestive systems. Metabolic syndrome in both children and adults is easier to prevent than to cure, and this should lead to a healthy life [10].

References
ОГЛЯДИ ЛІТЕРАТУРИ


УДК 616.12-008.331.1-056.5-053.5 МЕТАБОЛІЧНИЙ СИНДРОМ У ДІТЕЙ (ОГЛЯД ЛІТЕРАТУРИ) Фастовець М. М.

Резюме. В оглядовій статті наведені результати багаторічних досліджень вітчизняних та іноземних науковців стосовно метаболічного синдрому, який є одним із найважливіших питань сучасної медичної науки. Dana patologia поєднує такі важливі складові, як абдомінальне ожиріння, зниження толерантності до вуглеводів, інсулинорезистентність, дисліпідемію, гіперінсулінемію, хронічну або гостру артеріальну гіпертензію, гіперандростендреному, знижену фібринолітичу активність, мікральбуменію, гіперурікемію, які спричиняють швидкий розвиток ускладнень, призводять до соціальної дезадаптації, інвалідності та смертності.

Ключові слова: метаболічний синдром, ожиріння, інсулинорезистентність, дисліпідемія, артеріальна гіпертензія.

УДК 616.12-008.331.1-056.5-053.5 МЕТАБОЛІЧНИЙ СИНДРОМ У ДІТЕЙ (ОБЗОР ЛІТЕРАТУРИ) Фастовець М. Н.

Резюме. В обзорной статье представлены результаты многолетних исследований отечественных и иностранных ученых касательно метаболического синдрома, который является одним из самых важных вопросов современной медицинской науки. Данная патология объединяет такие важные составляющие, как абдоминальное ожирение, снижение толерантности к углеводам, инсулинорезистентность, дислипиде-
METABOLIC SYNDROME IN CHILDREN (LITERATURE REVIEW)

Fastovets M. M.

Abstract. The review article presents the results of years of research of domestic and foreign scientists regarding the metabolic syndrome, which is one of the most important issues of modern medical science. This pathology combines such important components as abdominal obesity, reduced tolerance to carbohydrates, insulin resistance, dyslipidemia, hyperinsulinemia, chronic or acute arterial hypertension, hyperandrohenia in girls, reduced fibrinolytic activity, microalbuminuria, and hyperuricemia, which cause rapid development of complications leading to social exclusion, disability, and mortality.

The main etiological factors of the metabolic syndrome are considered a genetic predisposition, poor diet, and lack of physical exercise. Hyperinsulinemia and insulin resistance, endocrine dysfunction of internal fat, excessive activity of sympathoadrenal and reninangiotensin-aldosterone systems, endothelial dysfunction, thus developing metabolic disorders, are important in the pathogenesis of the metabolic syndrome and its complications.

The only criteria for the diagnosis of major components of the metabolic syndrome are obesity, hypertension, hyperglycemia, increased triglycerides, reduced levels of HDLP (high-density lipoprotein) in boys and girls. Anthropometric parameters in children and adolescents depend on age and gender, so for the diagnosis of overweight there are used percentage tables of BMI (body mass index) distribution in the population according to the age and gender.

The evaluation of insulin resistance should consider not only the insulin level but also the level of glucose, which is important to identify the violations of glucose tolerance. Hyperinsulinemia against the backdrop of normoglycemia usually indicates the presence of insulin resistance. For the diagnosis of insulin resistance one can use the oral glucose ratio calculation of correlation between insulin and plasma glucose at the beginning and after two hours. In order to detect insulin resistance one can also use calculated indices of insulin sensitivity and insulin resistance.

In children and adolescents, comprehensive treatment of the metabolic syndrome should include a complete change of lifestyle, concomitant treatment of obesity, abnormalities of carbohydrate metabolism, hypertension, and dyslipidemia. This change provides prompt normalization of regime and diet of the child, optimization of his/her physical exercise, comprehensive psychotherapy, problem-targeted training programs, and strict self-control.

The main approach to the treatment of the metabolic syndrome in children is to optimize their lifestyle with increased physical activity and diet destination. The child should walk more, engage in various sports, and spend more time outdoors. At the same time, the child should be limited with a computer or TV.

The diet should be highly caloric—with restriction of refined fats and «empty» carbohydrates (chocolate, sweet drinks, candy, and sugar). It is necessary to enrich the diet of the child with fruit and vegetables, as they are the main source of fiber. Meals should bring to 4-5 times a day, with breakfast must be complete.

The metabolic syndrome in children and adults is easier to prevent than to cure, and to this should lead a healthy lifestyle.

Keywords: metabolic syndrome, obesity, insulin resistance, dyslipidemia, hypertension.