CURRENT UNDERSTANDING OF THE PEDIATRIC METABOLIC SYNDROME (REVIEW)

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Abstract

According to the World Health Organization, 68% of the causes of global mortality are due to noncommunicable diseases that include cardiovascular pathology, obesity, atherosclerosis and diabetes mellitus. The combination of abdominal obesity, hypertension, hyperglycemia and hyperlipidemia against a background of insulin resistance and chronic subclinical inflammation are components of metabolic syndrome (MetS). MetS in pediatric population is also a complex problem associated with the potential cardiovascular risk in young adults. There are lots of debates around definitions and diagnostic cut-offs for the MetS components due to age dependent fluctuations of the metabolic and cardiovascular parameters. This leads to the unclear incidence of the syndrome in children. Meantime, healthy lifestyle, nutrition and sleep are best strategies for both preventing and treating MetS in children and adolescents. Despite the large number of studies in this area, pediatric metabolic syndrome remains the subject of controversy.

Keywords: *Metabolic syndrome, diagnosis, children.*

According to the World Health Organization, the prevalence of overweight and obesity among children and adolescents aged 5 to 19 years increased dramatically from 4% in 1975 to more than 18% in 2016, when the number of children with obesity and overweight reached 340 million [1]. 17.77% children in Ukraine were obese in 2014 [2] with an annual upward trend in the incidence of new cases [3].

Overweight and obese children have a high probability to become obese adults and develop cardiovascular problems [4] and diabetes in the early adulthood [5]. The combination of abdominal obesity, insulin resistance, hyperglycemia, hypertension, violation of hemostasis was combined into the concept of "metabolic syndrome" (MetS). The main concept of the MetS theory is in the timely patient stratification into a group of high cardiovascular risk [6].

Despite numerous studies, common criteria for diagnosing MetS in childhood are still under debates. Current diagnostic criteria for the pediatric practice were published in the IDF report in 2007 and were based on similar MetS criteria for adults. These criteria include: waist circumference > 90 percentile, triglycerides level > 1.7 mmol/l, high-density lipoproteins (HDL) level < 1.03 mmol/l, fasting glucose level > 5.6 mmol/l or diagnosed diabetes mellitus, systolic blood pressure > 130 mm Hg and diastolic blood pressure > 85 mm Hg [7].

Unfortunately, these cut-offs do not meet modern requirements for the parameters included and it has been shown in the results of the investigation in the IDEFICS study [8]. That is why the prevalence of MetS differs in dependently on the definition (ranged from 6 to 39%) [9]. Furthermore, there are lot of controversies around the pediatric MetS diagnosis [10, 11]. Despite confirmed association between childhood and adolescent MetS with long-term outcomes, further prospective studies are needed to clarify the true value of diagnosing MetS in youth [12].

Insulin Resistance was mentioned as a main background for all MetS components development [13]. Homeostasis model assessment-insulin resistance (HOMA-IR) was proposed to evaluate insulin resistance [14] and became the most

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popular for both adults and children despite the fact that many other surrogate indices were elaborated [15–18].

Meanwhile, there is still unknown how to properly measure Insulin Resistance in children, according to the conclusion of the Insulin Resistance in Children Consensus Conference Group (2010) [19].

The problems of determining the clinical criteria for MetS in children include physiological changes that occur throughout childhood and puberty. For example, insulin resistance increases in early puberty, but stabilizes in the middle of adolescence as well as lipids and can also vary depending on gender [20].

Insulin secretion is affected well before blood glucose concentrations are within the range of prediabetes and diabetes. It is well established that abnormal β-cell function and peripheral insulin resistance are associated with elevated 2-h glucose levels, even within the normal glucose tolerance range, without meeting the criteria for impaired glucose tolerance and impaired fasting glucose [21, 22]. There is a linear dependence of fasting and average insulin concentration on BMI. Thus, there is a strongest insulin response at the standard glucose load at the second phase in overweight and obese subjects that differs from normal weight and skinny children [23].

It may well explain why the elevated blood glucose 2 hours after the standard load is a strong predictor for the development of T2DM in adults [22], but not in children [24].

According to the European Society of Cardiology elevated triglycerides and LDLs and decreased HDLs are direct cause of cardiovascular disease in adulthood [25]. Decreased HDL and elevated triglycerides are components of the metabolic syndrome in children according to the IDF Consensus [7]. It is estimated that about 42% of obese children have lipid abnormalities, particularly those with visceral obesity [26].

The leading document that allows assessment of the level of lipid metabolism, taking into account the age of the child are the recommendations of the National Cholesterol Education Program (NCEP) [27]. These recommendations effectively establish variants of hyperlipidemia in obese children [28].

Associations between MetS and non-alcoholic fatty liver disease, hyperuricemia, sleep apnea, and several other potential biomarkers, useful for early identification of patients with a higher cardiometabolic risk, have been described in obese children. But these are still not considered when MetS is defined [29].

A number of recent studies also indicate that epigenetic mechanisms may play an important role in MetS initiation [30] and its course in both adults [31, 32] and children [33]. Meanwhile, excessive nutrition, low physical activity, social environment and stress have even stronger influence on the development of obesity and related metabolic disorders, that can be preventable [1].

Regardless of many different approaches to treating metabolic syndrome (MetS) in children and adolescents, early screening and treatment of the individual components that contribute to its development play a key role in reducing cardiometabolic risk. Therefore weight loss and lifestyle interventions can have a positive effect on the components of MetS [34].

Also, according to numerous studies, special attention should be paid to the sleep duration as poor or insufficient quality of sleep (less than 8 hours) in children and adolescents are associated with MetS elements such as hypertension with/or non-dipping profiles of BP [29]. Furthermore, acute sleep restriction increases food intake associated with the deteriorated lipid content [35].

Conclusions

Metabolic syndrome in pediatric population is a complex of problems associated with the potential cardiovascular risk. There are lots of debates around definitions and diagnostic cut-offs for the MetS components due to age dependent fluctuations of the metabolic and cardiovascular parameters. This leads to the unclear incidence of the syndrome in children. Healthy lifestyle, nutrition and sleep are best strategies for preventing and treating MetS in children and adolescents.

Despite the large number of studies in this area, pediatric metabolic syndrome remains the subject of controversy.

Conflict of interests

The authors of the article declare no conflict of interests.

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