Snezana Lesovic[1]

METABOLIC SYNDROME IN THE PARTICIPANTS OF THE CIGOTICA PROGRAMME

INTRODUCTION

Obesity is the leading cause of the metabolic syndrome in pediatric population. The prevalence of metabolic syndrome in children and adolescents of average weight in the USA is considerably lower (1-4%) in comparison to the obese ones (24-51%). Regardless of the evaluation criteria, children and adolescents suffering from the metabolic syndrome have visceral obesity, elevated waist circumference, elevated blood pressure, dyslipidemia and hyperinsulinemia. Metabolic complications and metabolic syndrome in obese children and adolescents very often remain undiagnosed.

AIM

To establish the prevalence of metabolic syndrome in adolescent participants of Cigotica Programme.

METHODOLOGY

504 adolescents were examined (256 girls and 248 boys), aged 12 to 18, diagnosed with primary obesity and hospitalised at the Special Hospital for Thyroid Gland Diseases and Metabolism Zlatibor from August 2008 to November 2009. The obesity criterion was the body mass index (BMI) ≥ 97 percentiles. Apart from the clinical examination, the body mass, the height and the blood pressure were also measured. The status of lipids and glycemia were established using standard procedures after a 12-hour fasting period. IDF criteria were used to diagnose the metabolic syndrome.

* Snežana Lešović, MMedSc, pediatrician The Special Hospital for thyroid Gland Diseases and Metabolism Zlatibor, e-mail: lsnez@eunet. rs

RESULTS

The criteria for diagnosing the metabolic syndrome were met by 65 (13%) adolescents (23 girls and 42 boys). Four adolescents had four risk factors, and 61 of them had three risk factors. The most common risk factor for the metabolic syndrome was visceral obesity (WC>90 percentils), which was evident in all examinees (100%). The blood pressure was elevated in 61 adolescents (12.10%). Systolic hypertension was registered in 52 (10.31%), and diastolic hypertension was registered in 9 (1.78%) adolescents. Triglycerides were elevated in 25 (4.96%) adolescents. The reduced level of HDL cholesterol was observed in 78 (15.48%) adolescents. Glucose intolerance was the least common risk factor, and it was registered in 7 (1.39%) adolescents. 140 (28%) adolescents had two risk factors for the metabolic syndrome.

CONCLUSION

The identified risk factors for the metabolic syndrome in children and adolescents emphasize the need for screening obese children in order to begin treatment in time and prevent obesity complications. The Cigotica Programme, an intensive change of lifestyle that comprises a balanced, hypocaloric diet and intensified physical activity but only with the support of the family and social environment, may contribute considerably to the prevention of obesity complications.

Key words: obesity, metabolic syndrome, adolescents

INTRODUCTION

Obesity prevalence in children and adolescents is on the increase throughout the world. Obesity is becoming the most important chronic disease in pediatric population. The causes of obsity epidemics are new nutrition patterns 'nutrition transition' (changes of eating habits, types of food and its availability), changes of lifestyle and reduced energy consumption. Obesity is connected with major health problems in pediatric population and is a significant risk factor in morbidity and mortality in adulthood (1). Obesity in children can cause insulin resistence, diabetes type 2, liver steatosis, hypertension, glomerusclerosis, increased growth and bone maturation, gynecomastia in boys, ovarian hyperandrogenism in girls, cholecystitis and pancreatitis. Obese children are at a greater risk of suffering from othopedic and respiratory disorders, incontinence stress, psychological problems (2,3). The Bogalusa study showed that 50% of obese children have at least one risk factor for the development of cardiovascular diseases (hypercholesterolemia, hyperinsulinemia, hypertrygliceridemia, hypertension), which are all linked to an early appearance of atherosclerosis. Cardiovascular diseases are the major cause of morbidity and mortality in adulthood, which makes obesity epidemics significant not only in terms of health but from the economic, social and demographic points of view as well.

Raven and his associates noticed that the most common risk factors for cerebrovascular diseases and imbalanced glucose metabolism may be registered in the same people, and they called this constellation of risk factors 'insulin resistence syndrome', which was later called the metabolic syndrome. According to the World Health Organization (WHO), National Cholesterol Education Programs (NCEP) and Adult Treatment Panel III (ATP III) , the metabolic syndrome is registered in those adults who have at least three out of five criteria (4):

– Elevated blood pressure

– High trygliceride levels

– Low levels of HDL cholesterol

– Glucose intolerance (elevated fasting level of glucose, disbalanced glucose tolerance, diabetes type 2)

– Obesity (of central, abdominal type).

After criteria for adults were identified in 2005, in 2007, the International Diabetes Federation (IDF) defined the risk factors for the metabolic syndrome in children, with an aim to estimate the risk of the appearance of diabetes type 2 by registering children at the risk of developing the metabolic syndrome at an early stage. The criteria for diagnosing the metabolic syndrome in children and adolescents aged 10 to 16 are: abdominal obesity defined on the basis of the waist circumference WC ≥90 percentiles (the standards for waist circumference in adults cannot be applied in pediatric population due to excessive variations in terms of age, racial and ethnic background) and two or more typical clinical, i.e. laboratory analyses:

– Tryglicerides ≥ 1.7 mmol/l

– HDL cholesterol ≤ 1.03 mmol/l

– Sistolic pressure ≥ 130 or diastolic ≥ 85 mm Hg.

– Glycemia ≥ 5.6 mmol/l or type 2 diabetes melitus

Adult criteria may be applied in adolescents over 16 years of age. Children aged 6-10 who are obese and have a positive family anamnesis for obesity, diabetes, dyslipidemia, hypertension, cardiovascular diseases need to be examined regularly and recommended on how to reduce the body mass. The metabolic syndrome may be found in 4% of all adolescents and 30% of obese adolescents in the USA (7,8,9).

Insulin resistence, diabetes type 2 and liver steatosis in adults

Insulin resistence is a reduced capacity of insulin to enable peripheral usage of glucose in ordinary amounts, to reducee glucose production in the liver and to inhibit the secretion of lipoproteins of very low density (3).

Diabetes melitus type 2 is the ultimate outcome of metabolic decompensation which develops for months and years. The disease appears in childhood with the peripheral resistence to insulin with fasting hyperinsulinemia. The risk for the ap-

pearance of diabetes melitus type 2 depends on genetic predisposition, development, nutritive factors and energy consumption. The prevalence increases in adolescence due to anti insulin activity of growth hormones and sex hormones, but the risk of having the disease is greater in mothers with gestational dibetes, in children born too small in comparison to their gestational age, especially in those with a more prominent growth momentum in early childhood (5). Insulin sensitivity is reversely proportional to the body mass index (BMI) and the percentage of body fat. In the USA, the imbalanced glucose tolerance can be noticed in 21-25% of extremely obese children in pre-adolescence and adolescence, while diabetes melitus type 2 can be found in about 4 % of them (6,7).

The risk for glucose intolerance is determined by fat distribution as well. The accumulation of visceral and abdominal subcutaneous fat is connected with insulin resistence, whereas insulin sensitivity does not correlate with the accumulated femoral and gluteal subcutaneous fat. The accumulation of visceral fat is followed by the resistence of fat tissue to insulin and increased sensitivity to catecholamines.

Changes in the activity of adipocyte cytochines also affect the development of insulin resistence. There is an excessive activity of the tumor necrosis factor (TNF-α) and interleukin (IL-6) in the fat tissue of obese people, whereas the secretion of adiponectin is reduced. TNF-α inhibits the acceptance of glucose and free fatty acids, and trygliceride synthesis in the fat tissue, and, just like catecholamines, it induces lipolysis and the release of free fatty acids from the fat tissue. The lipolitic effect is emphasised by the activity of IL-6, which inhibits lipoprotein lipase and accumulation of triglycerides in the fat tissue. IL-6 and TNF-α reduces the activity of adiponectins in developing preadipocytes, which partly accounts for the reduced activity of adiponectins in obese people (1,5). The levels of adiponectins in the plasma are reversely proportional to the BMI, waist circumference and abdominal fat, and they are higher in women than in men.

Tryglicerides and free fatty acids released from the fat tissue accumulate in the liver, skeletal muscles, pancreas and the heart. The accumulation is alleviated by leptine resistence or by a relatively small amount of leptine, which normally stimulates the oxidation of free fatty acids and inhibits lipogenesis. The accumulation of tryglicerides in the liver (steatosis) may cause steatohepatitis and an increased serum transaminases.

Direct activity of TNF-α and IL-6, with the reduction in adiponectin levels, may increase insulin resistence in the liver, which then leads to elevated glucose production in the liver through gluconeogenesis and contributes to elevated blood glucose levels and increased insulin secretion in the fat tissue. The replacement of cholesterol in lipoproteins of very low density (VLDL-TG) with cholesterol estres in lipoproteins of high density (HDL) causes an increased kidney clearance HDL and reduced levels of HDL in blood.

The mechanism with which lipids affect the function of beta cells (lipotoxicity) remains unclear. Free fatty acids and cytochines can, just like TNF-α and IL-6, directly damage beta cells with apoptosis. Alternatively, free fatty acids may induce the creation of inflammatory cytochines with the help of macrophage in the pancreas cells. Cytochines increase the production of nitrous oxide in beta cells, which inhibit the glucose-stimulated secretion of insulin and cause the apoptosis of pancreas beta cells. The resistence to the activity of leptines can lead to lipotoxicity since leptine reduces the activity of the synthetase of nitrous oxide and maintains the expression of anti-apoptotic genes. The apoptosis of beta cells can resut from chronic exposure to elevated levels of glucose (glucotoxicity). The loss in weight and functions of beta cells under the influence of nutrients and cytochines in people who are resistent to insulin causes glucose intolerance and diabetes melitus type 2 (1,4,5).

Insulin resistence and other obesity complications

Obesity and insulin resistence in children create a predisposition for cardiovascular complications later in life. Extreme obesity at the age 9 - 11 results in reduced elasticity of carotid arteries, and obesity in adolescence causes the thickness of intima and media of carotid arteries in young adults (10).

Reduced sensitivity to insulin results in high blood pressure in children. Some studies report that obesity otself is the reason for this, whereas others emphasize that insulin resistence is a sign of high blood pressure irrespective of BMI. Affecting the sympathetic neuro system and reabsorbtion of natrium through insulin are the key mechanisms of the potential link between insulin resistence and elevated blood pressure. Insulin resistence is connected with the development of the polycystic ovarian syndrome (PCOS) in obese girls, which is characterised by unovulatory disorders and hyperandrogenemia (11).

In the pathogenesis of vascular diseases hormones, growth factors, vasoactive materials, cytochines, oxidative radicals and adhesive molecules act together. A relative increase in sex steroids may lead to increased growth and bone maturation of obese children. Increased levels of insulin and IGF-1 with adrenocorticotropic (ACTH) and luteinizing hormone (LH) stimulate the production of androgen from adrenocortical cells and ovarian theca cells (12).

Biological availability of ovarian and adrenalin androgens is increased due to the insulin- reduced SHBG (sex hormone binding globuline) and reduced <SHBG levels in the serum. Free androgens increase the pulsatile activity of LH-RH and the relation between LH and FSH and increase the androgen production in theca cells (13).

Elevated levels of adrenal androgens may result in the appearance of premature andrenarche and cause annovulation and hirsutsm in girls and young women. The aromatisation of androstenedione in the fat tissue increases the levels of estrone in the

plasma and results in gynecomastia in adolescent boys. Insulin resistence is a possible risk factor for the development of respiratory disorders, such as asthma, in extremely obese children and adolescents. Children with asthma have a higher insulin resistence than children without respiratory problems. Inflamation connected with insulin resistence is considered to be a potential agent in this link (14).

AIM OF THE STUDY:

To establish the prevalence of metabolic syndrome in adolescent participants of the Cigotica programme.

METHODOLOGY:

504 children were examined (248 boys and 256 girls) of the average age of 12.7 (12-18), and diagnosed with primary obesity. All examinees were hospitalised at the Centre for prevention, treatment and rehabilitation of obesity in children and adolescents within the Special hospital 'Cigota' on Zlatibor in the period between August 2008 and November 2009. The obesity criterion was BMI higher than 97th percentile. Apart from clinical examination, the body mass (tanita scales for determining body composition using the impendance method) and body height (stadiometre with the range of up to 2 m and precision of 0.1 cm) were also measured. The blood pressure was measured at the right arm of the patient sitting and lying. Total trygliceride levels, HDL-h and LDL-h as well as glycemia were measured after a 12-hour fasting period. IDF criteria were used for diagnosing the metabolic syndrome.

The metabolic syndrome in the participants of the Cigotica Programme

Obesity epidemics in children and adolescents has an increasing in annual prevalence (in European countries up to 30%). According to UNICEF, in Serbia it is 19% in children to the age of 5, and ot is considered that there are around 100,000 of overweight and obese children at the age of 12-18. Obesity is linked with various and numerous health problems in childhood. Around 60-85% of obese school children remain ovese in adulthood. The alarming spread of obesity epidemics in children and adolescents, as well as the lack of tested and efficient measures and programmes for obesity prevention point out the necessity for bulding the Centre for the prevention, treatment and rehabilitation of obesity in children and adolescents and the Cigotica Programme at the Special hospital 'Cigota' on Zlatibor.

The participants of the Cigotica Programme are children and adolescents aged 12-18. The multidisciplinary measures and activities of the Cigotica Programme em-

phasise the importance of a balanced hypocaloric diet, planned and organized physical activity, educational lectures and psychological support in the body mass reduction within the obesity treatment and prevention of obesity complications. By particiapting in the Cigotica Programme for 21 days, adolescents are given the opportunity to choose between a healthy and unhealthy lifestyle – an opportunity to reject the inadequate and adopt the adequate and healthy nutrition style and physical activity.

504 obese children were examined (248 boys and 256 girls) of an average age of 12.7 (12-18), and diagnosed with primary obesity. The criteria for diagnosing the metabolic syndrome were met by 65 (13%) adolescents (23 girls and 42 boys). Four adolescents had four risk factors, and 61 of them had three risk factors. The most common risk factor for the metabolic syndrome was visceral obesity (WC>90 percentils), which was evident in all examinees (100%). The blood pressure was elevated in 61 adolescents (12.10%). Systolic hypertension was registered in 52 (10.31%), and diastolic hypertension was registered in 9 (1.78%) adolescents. Triglycerides were elevated in 25 (4.96%) adolescents. The reduced level of HDL cholesterol was observed in 78 (15.48%) adolescents. Glucose intolerance was the least common risk factor, and it was registered in 7 (1.39%) adolescents. 140 (28%) adolescents had two risk factors for the metabolic syndrome.

CONCLUSION:

The increase in the number of obese children and adolescents raises a lot of concern. The problem of obesity in children has not been adequately analysed so far. Metabolic complications, such as imbalanced glucose tolerance, dyslipidemia, hypertension, liver fat infiltration and inflammatory changes of a lower degree, appear in a large number of obese children at an early age. The prevalence of metabolic syndrome in obese adolescents, participants of the Cigotica Programme is 13%, and 140 of them (28%) have two of components of the metabolic syndrome. These patients are at a greater risk of cardiovascular disease and diabetes type 2 in adulthood. We hope that the team work and the results of the Cigotica Programme, the observation of staturo ponderal development and BMI in children and adolescents will considerably contribute to obesity treatment and prevention of obesity complications.

Literature:

1. Caprio S, Weiss R. The metabolic consequences of childhood obesity. Best practice and Research Clinical Endocrinol Metab 2005; 19(3): 405–19.
2. Anemiya K, Duhashi K, Unkam T, Sugihara S, Obzeki T, Tajina N. Metabolic syndrome in youth. Pediatric Diabetes 2007; 8(9) 48–54.

3. Maffeis C, Banzato C, Talamini G. Waist-to-Height Ratio, a Useful Index to Identify High Metabolic Risk in Overweight Children. J Pedatr 2008; 152: 207–13.

4. Hassink Gibson S. Insulin Resistance, the Metabolic Syndrome and Type 2 Diabetes. U: A Clinical Guide to Pediatric Weight Management and Obesity. Lippincot Williams and Wilkins, 2007; 86–103.

5. Freemark M. Metabolic consequences of obesity and their management. U: Kronenberg ur. Williams Textbook of Endocrinology – 11th ed. Philadelphia: Saunders Elsevier 2007; 419–35.

6. Klein S. Romijn JA. Obesity. U Kronenberg : Williams Textbook of Endocrinology, 11 th ed. Saunders, Philadelphia, 2008; 1563–80.

7. Weiss R, Dziura J, Burgert T, Tamborlane W, Taksali S, Yeckel CW, ET AL. Obesity and the metabolic syndrome in children and adolescents, N Engl J Med 2004; 350: 2362–74.

8. Vener RM, Segal TY, Lichtarovitz-Krynska E, Hindmarsh P. Prevalence of the insulin resistance syndrome in obesity. Arch Dis Child 2005; 90:10–4.

9. Lee SL, Bacha F, Gungor N, Arslani S. Comparison of Different Definitions of Pediatric Metabolic Syndrome: Relation to Abddminal adiposity, Insulin Resistance, Adiponectin and inflammatory Bio markers J Pediatr 2008; 152: 177–84.

10. Bokor S, Frelut ML, Vania A, Hadjiathanasiou CG, Anastasakou M, Malecka-Tendera E, et al. Prevalence of metabolic syndrome in European obese children. Int J Pediatr Obes 2008; 3 Suppl 2:3–8.

11. Freemark M. Metabolic consequences of obesity and their management. U: Kronenberg ur. Williams Textbook of Endocrinology – 11th ed. Phyladelphia : Saunders Elsevier 2007; 419–35.

12 Cook S, Alinger P, Chaoyang MS, Ford ES. Metablic Syndrome Rates in United States Adolescents, from the National Health and Nutrition Examination Survery, 1999–2002. J Pediatr 2008; 152: 165–70.

13. Cail AM, Bonadonna RC, Tromberta M, Weiss R, Caprio S. Metabolic abnormalities Underlzng the Different Prediabetic Phenotzpes In Obese Adolescents. J Clin Endocrinol Metab 2008; 93: 1765–73.

14. Hang T. Nansel TR, Belshem AR, Morrison JA. Sensitivity, Specificity and Predictive Values of Pediatric Metabolic Syndrome Components in Relation to Adult Metabolic Syndrome. The Princeton LRC Follow-up Study. J Pediatr 2008; 152: 185–90.