Metabolic and endocrine consequences of childhood obesity

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Abstract

Introduction. *Nowadays, childhood obesity is an epidemic problem with significant complications and it represents an important risk factor for adult morbidity and mortality.*

Objectives. *The authors of this study aimed to evaluate the pediatric patients diagnosed with obesity and their metabolic and endocrine complications.*

Material and method. *Obese patients (BMI > percentile 97%) admitted in 2012-2013 in 1st Pediatric Clinic, Timisoara were included in the study. They were examined clinically, anthropometric (weight, height, BMI and abdominal circumference), endocrine (cortisol, insulin, peptide C, TSH, vitamin D), metabolic (glucose, oral glucose tolerance test, Hb1c, lipids, HOMA index), abdominal ultrasound and DXA examination.*

Results. *We studied 112 patients aged 5 to 17 years (61.60% girls). OGTT was changed in 40.17% of cases and hyperinsulinemia has been described in 18.75% of children. 3 patients were diagnosed with Cushing's syndrome and 2 boys had Prader Willi syndrome. TSH level was increased in 40 children. Changes of lipids were found in 22.32% of children. DXA examination revealed the presence of osteopenia in 3 patients, while 2 teenagers associated liver steatosis. Metformin was prescribed to children with insulin resistance (29).*

Conclusions. *Obesity in children is an important risk factor for diabetes and atherosclerosis of adult, fact that requires drastic sanction of it in childhood.*

Keywords: *obesity, children, complications*

BACKGROUND

The rise in the prevalence of obesity in children and adolescents is one of the most alarming public health issues facing the world today. As the prevalence of childhood obesity increases, its health implications are becoming more evident. Obesity is associated with significant health problems in children and is an early risk factor for much of adult morbidity and mortality. (1)

In the 2010, the International Obesity Taskforce estimates that almost 40-50 million school children are classified as obese and in Europe around 12 million children are overweight or obese (2). In the UK, the Health Survey for England recorded that 30% of children with their age between 2-15 years were overweight and 16% of all children were obese (3).

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Childhood obesity is the most common chronic disease of pediatric age. It is associated with many adverse consequences, including cardiac problems (hypertension), respiratory problems (obstructive sleep apnea), orthopedic disorders (slipper upper femoral epiphysis and joints), cancer, polycystic ovarian syndrome and non-alcoholic fatty liver disease (4). It is also associated with type 2 diabetes, pre-diabetes and the metabolic syndrome, known as insulin-resistance syndrome, which consists in a combination of abnormalities characterized by central obesity, dyslipidemia, hypertension and changes in glucose levels. Many years it was thought the type 2 diabetes is a disorder characteristic of overweight and elderly people, but latterly many articles report the increasing number of children diagnosed with this pathology.

Childhood obesity tends to track to adulthood and thus represents an early beginning of a potentially lifetime pathological process. There are many evidence demonstrate that childhood obesity can be associated with premature mortality and physical morbidity in adulthood. (5,6)

OBJECTIVES

The authors of this study aimed to evaluate the pediatric patients diagnosed with obesity and their metabolic and endocrine complications.

MATERIAL AND METHOD

Obese patients with the age less than 18 years old admitted and diagnosed in the Endocrinology Department of the 1st Pediatric Clinic of "Louis Turcanu" Children Hospital Timisoara between the years 2012 and 2013 were included in this study. They were diagnosed as being obese if the body mass index (BMI) was less the 97th percentiles standard for age and sex. If their BMI was between the 85th and 97th percentiles they were considered overweight patients and were excluded from this study. We used the percentiles recommended according to the Centers for Disease Control and Prevention (CDC) growth charts.

These patients were strictly analyzed after the following protocol. All children were clinically examined very carefully. The anthropometric data such as weight, height and abdominal circumference were measured and then the BMI (weight in kilograms divided by the square of height in meters) were calculated. The puberty stage was defined according to the Tanner classification.

Blood samples were taken in the morning on fasting for the study of endocrine markers such as cortisol, C peptide, the thyroid hormones and D vitamin. The blood level of glucose and lipids, the fasting insulin, the Hb1c the oral glucose tolerance test (OGTT) and homeostasis model assessment of insulin resistance (HOMA-IR) index are useful for the characterization of the metabolic profile of these children.

Karyotypes were done in the cases of patients with specific phenotypes. Abdominal ultrasound was used for the evaluation of liver structure, while DXA examination was performed in order to identify the presence of osteopenia or osteoporosis at hip or lumbar level.

RESULTS

During the study period, we analyzed 112 obese pediatric patients (mean BMI 34.6 ± 6.6 kg/m^2). Their age ranged between 5 to 17 years, with a majority of the girl patients (61.60%). 15.17% of patients were prepubertal, while the remaining were at puberty (Tanner stages II-V). The karyotypes performed revealed the presence in the lot of three patients with Down syndrome (2.67%) and two with Prader Willi syndrome (1.78%) (Fig. 1.)

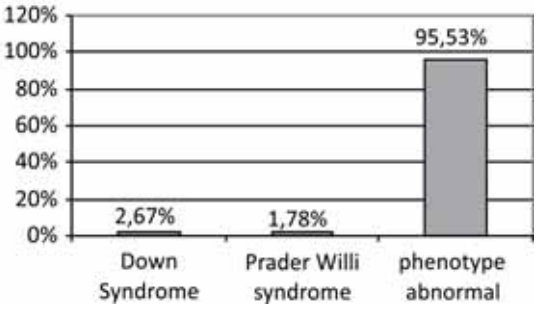

FIGURE 1. *The phenotypes of the study cases*

Abnormal glucose profile consisted in the presence of an altered OGTT in 40.17% of cases or increased value of HbA1c outside the normal range (20.53%), while hyperinsulinemia was identified in 18.75% of obese children. Dyslipidemia (increased cholesterol or triglyceride values) were identified in 22.32% of studied patients. According to the ultrasound imagines, 2 teenagers were diagnosed with liver steatosis (Fig. 2).

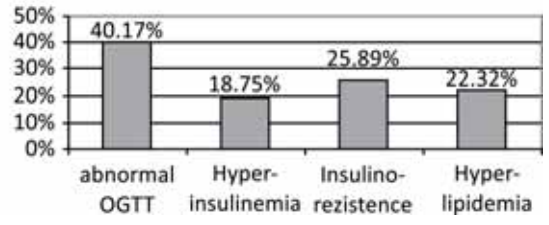

FIGURE 2. *Metabolic syndrome identified in the study lot*

Concerning the endocrine complications diagnosed in this study, 2.67% of patients were diagnosed with

Cushing's syndrome, while the TSH level was increased in 35.71% of children with normal or slightly elevated free T4 and/or free T3 levels. The presence of the T score (hip or lumbar) lower than -2.5 reveled during DXA examination was very suggestive for osteopenia in 3 (2.67%) obese children (Fig. 3.)

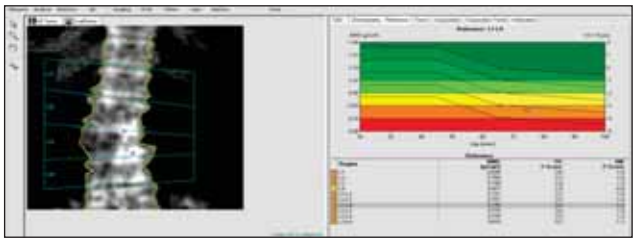

FIGURE 3. *RR, 14 years old, with scoliosis and osteoporosis*

A low calories diet containing low glucoses and lipids and sustained exercises were suggested to all the patients. The medical treatment of obesity was recommended to all patients aged up to 10 years old and imparement of glucose metabolism. Fibers were recommended in 74.10% of children, while Metformin was prescribed to children diagnosed with insulin resistance (25.89%) with the age up to 12 years old.

DISCUSSIONS AND CONCLUSIONS

Prevention of the complications of obesity represents the main objective when you are facing with obese children. In these cases, the primary medical goal consists in the weight-reduction therapy.

This medical fact is very important because excessive body fat in children is associated with insulin resistance and dysglycemia (7) and predicts development of the metabolic syndrome in adulthood (8). Insulin resistance is of particular concern because it is independently associated with metabolic abnormalities during childhood (9) and development of type 2 diabetes (10).

There are much evidence for lifestyle intervention with dietary changes and exercises. The pediatric patients need to avoid of the consumption of energy-dense, high-carbohydrate beverages and snack foods rich in sugar or fat. They have to practice increase physical activities and sports by at least 30 minutes daily and it is indicated to limit exposure to television and video or computer games to no more than 1.5 hours a day (11).

Pharmacological intervention is variously recommended upon failure of lifestyle with Orlistat as the only licensed drug for obesity in children and adolescent (12). There are currently no medications that are approved by the U.S. Food and Drug Administration to treat obesity in children less than 12 years of age.

Metformin was used to reduce weight gain, hyperinsulinemia and hyperglycemia in adults diagnosed with type 2 diabetes (13) and to reduce progression from impaired glucose tolerance to diabetes in those without diabetes (14) with remarkable results. These benefits have led to an increase in the use of Metforminin obese children with hyperinsulinemia.

Metformin is approved by the Food and Drug Administration to treat type 2 diabetes in adults and children over 10 years old. It is a first line drug for type 2 diabetes, and has been used for many decades. In adults metformin delays the onset of type 2 diabetes, but there is no evidence that the drug has a similar effect on children. It is clinically useful, safe and well-tolerated in obese children who are at risk for type 2 diabetes. (15)

Kendall and co studied the effect of Metformin on BMI-SD score, metabolic risk factors, and adipokines on a lot consisted in one hundred fifty-one obese children and young people (aged ranged 8-18 years and mean age 13.7 years) diagnosed with hyperinsulinemia and/or impaired fasting glucose or impaired glucose tolerance. The results of MOCA trial revealed a reduction in BMI-SDS at 6 months and insulin and glucose levels from oral glucose tolerance tests and alanine aminotransferase at 3 months (16).

Mauras's study demonstrated that a six months of Metformin therapy improved weight loss and reduced abdominal adiposity in adolescent, but unfortully does not influence the inflammation, thrombosis, or hepatic fat in obese children with normal glucose tolerance (17).

In the meta-analysis of Park and collaboration is presented the beneficial effect of Metformin on obesity among hyperinsulinemic children and adolescents. A 6 months treatment with Metformin (1,000-2,000 mg/day) may be efficacious in reducing BMI, in total cholesterol level (a small reduction) and had an important effect on the homeostasis model assessment of insulin resistance. (18)

Childhood obesity can be frequent associated with elevated TSH concentrations sometimes with normal or slightly elevated free T4 and/or free T3 levels. This fact was observed in our study The mechanisms underlying these thyroid hormonal changes are still unclear. Whether higher TSH in childhood obesity is adaptive, increasing metabolic rate in an attempt to reduce further weight gain, or indicates subclinical hypothyroidism or resistance and thereby contributes to lipid and/or glucose dysmetabolism, remains

controversial. (19) It is considered that the elevated TSH levels in obesity is a consequence rather than a cause of obesity (20).

Osteopenia described at DXA examination in the two obese children from the study is secondary to the low 25 hydroxivitamin D blood level. Different studies reported that the apparent decrease in vitamin D bioavailability with increased adiposity has been hypothesized to be due to the increased sequestration of vitamin D in fat, and so, decreased bioavailability from cutaneous sources (21,22). So we can state that in obese children, adiposity increases the risk of vitamin D deficiency with the secondary development of osteopenia.

As we already mentioned obesity in children is an important risk factor for type 2 diabetes of adult and other important complications, fact that requires a drastic sanction of it since childhood

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