OBESITY, HYPERTENSION AND INSULIN RESISTANCE IN CHILDHOOD - A PILOT STUDY

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Background. Obesity and arterial hypertension are a serious risk factor for insulin resistance patients leading to diabetes and other disorders. Obesity is one of the most common nutritional problems in developed countries. Actually the incidence of obesity is increasing considerably, obesity is emerging in alarming rates between the last 10 years. Obesity and hypertension beginning in childhood often precedes the hyperinsulinemic state. The metabolic syndrome is rapidly increasing in prevalence with rising childhood obesity and sedentary lifestyles worldwide. The aim of this study was to compare average levels of the homeostatic indices HOMA and QUICKI in obese children compared to healthy and hypertonic children in order to find convenient markers for insulin sensitivity in clinical pediatric practice.

Methods. 49 obese children (11 girls, 38 boys), 42 children healthy (33 boys and 9 girls) and 37 hypertensive children (4 girls, 33 boys) were selected.

Results. The average level of HOMA in obese children was 4.58; in healthy children 1.8 and in the group of hypertonic children the level was 2.75. The average level of QUICKI in obese children was 0.22; in healthy children 0.29 and in hypertonic children 0.28.

Conclusions. The results demonstrate the possibility of insulin sensitivity assessment using these indices in pediatric practice. QUICKI has a narrower confidence interval and thus a lower variability. QUICKI and HOMA indexes are useful predominantly for epidemiological purposes, mainly for mapping the scope of insulin resistance among children.

INTRODUCTION

Simple fasting methods to measure insulin resistance, such as the homeostasis model assessment (HOMA), and quantitative insulin sensitivity check index (QUICKI) methods, have been widely promoted for adult studies but have not been evaluated formally among children and adolescents. The aim of this study was to compare the HOMA, and QUICKI methods for measuring insulin resistance, in a group of children with primary hypertension and with obesity and to compare them to the indices of healthy children with the aim of establishing the usefulness of the indices for prediction insulin resistance development.

In recent years, the increasing number of children in the Czech Republic are manifesting the first signs of disorders which earlier only used to be seen predominantly in adults, for example a high blood pressure and the insulin resistance syndrome leading to diabetes type 2 (DT2)¹. (The associations between elevated blood pressure and overweight, on one hand, and the increasing prevalence over time of pediatric overweight, on the other hand, sug-

gest that the prevalence of elevated blood pressure could have increased in children over the last few decades. Obesity itself needs not always mean overweight but an accumulation of fatty tissue. In childhood, it is obvious that the continuous increase in weight is not merely caused by the increase of fat tissue but also by the development of the body frame and the muscle mass. The share of this component differs according to the individual age group and gender.

Obesity. One of the most common nutritional disorder worldwide, affecting virtually both developed and developing countries of all socio-economic groups, irrespective of age, sex or ethnicity, clearly associated with the metabolic syndrome, condition with implications for the development of many chronic diseases as obesity and hypertension, type 2 diabetes mellitus, dyslipidemia, obstructive sleep apnoe, and orthopedic problems. In the Czech Republic, childhood obesity is now a serious epidemiological problem: 20% of children aged 6–12 and 11% of children aged 13–17 years are already overweight or obese. These data were provided by the study of the Czech Obesity Association entitled “Life Style and

Obesity 2005". This enormous increase in the prevalence of obesity is mainly caused by modern lifestyle and the consumption of high-calorie fast food. Overweight results from long-term positive energy imbalances². Naturally, it is one of the most serious risk factors in the development of insulin resistance and other disease conditions which are connected with this syndrome.

Hypertension. The 2004, the American Academy of Pediatrics (AAP) study defined hypertension in children as mean systolic and diastolic pressure above 95th percentile adjusted for sex, age and height.

As children grow, their blood pressure increases, depending on gender. Therefore, when evaluating the measured levels, the age, gender and the height of a child must be taken into account. Percentile graphs for blood pressure values in children were compiled by measuring blood pressure in tens of thousands of healthy children. The graphs currently in use by most doctors in developed world are those published by an American group for a child's hypertension in 1987 and published as the "Report of the Second Task Force".

The update of this Report is the Third Report in 1996 and also the Fourth Report in 2004. The output of the Fourth Report are tables according to which the blood pressure is examined not only by judging the age and the gender of a child. The third criteria became to be the child's height.

MATERIAL AND METHODS

49 obese children (11 girls, 38 boys) with a body mass index (BMI) greater than the 95th percentile for age and gender, of an average age of 16.5 were being given an

advice on losing weight at the Ambulance of children obezitology in Department of Sports Medicine, University Hospital in Olomouc. 37 hypertensive children (4 girls, 33 boys) with mean systolic blood pressure above 95th percentile according to their height and sex formed the patient group. Another 42 children (33 boys and 9 girls) of an average age of 16.2 who showed normal physiological parameters, were used as the control group of healthy children. For each child, the following parameters were measured: blood pressure, body mass index (BMI) and laboratory concentrations of total cholesterol, triglycerides, HDL and LDL cholesterol, glycemia and insulinemia. The values of glucose and insulin concentration were used to calculate homeostasis model assessment (HOMA) of insulin resistance (HOMA-IR), quantitative insulin-sensitivity check index (QUICKI). Simple fasting sample methods to measure insulin sensitivity such as HOMA and QUICKI have been widely promoted in adult studies but have not been formally evaluated in children.

The homeostatic index for insulin resistance, HOMA IR was calculated according to the homeostatic model^{3,4} as:

$$\text{HOMA IR} = \text{insulin fasting } (\mu\text{IU/ml}) \times \text{glycemia fasting } (\text{mmol/l}) / 22.5$$

Homeostatic index insulin resistance QUICKI was calculated according to Katz et al.⁵

$$\text{QUICKI} = 1 / [\log \text{insulin fasting } (\mu\text{IU/ml}) + \log \text{glycemia fasting } (\text{mg}/100 \text{ ml})]$$

$$\text{QUICKI} = 1 / [\log \text{insulin fasting } (\mu\text{IU/ml}) + \log \text{glycemia fasting } (\text{mmol/l}) \times 18.182]$$

Insulin resistance is defined as values of HOMA index greater than or equal to 2.68 and QUICKI as values less than or equal to 0.34.

Fig. 1. Means and 95% confidence intervals of HOMA.

Fig. 2. Means and 95% confidence intervals of QUICKI.

Statistical evaluation was done using the programme Statistics version 6.0 program for analysis of means, medians and standard deviations. T-test was calculated to determine statistical significance ($p < 0.05$) in clinical and biochemical characteristics.

RESULTS

Table 1 shows the results of the examination in the control group of children as means and SD. The results could be calculated as physiological parameters for each following value. Table 2 shows the results for each parameter in the obese group. Individuals in this group also

showed normal physiological values. Only the insulin resistance was higher. Table 3 shows the results for hypertensive children.

Fig. 1 and 2 depict mean values for homeostatic indices with their 95% confidence intervals. Fig. 1 shows the mean HOMA index of 1.8 in healthy children, compared with 4.58 in obese children and 2.75 in hypertensive children. Fig. 2 shows a QUICKI mean value of 0.29 in healthy children, as compared with 0.22 in obese children and 0.26 in hypertensive children. The QUICKI values in obese children may indicate a shift towards the insulin resistance. Fig. 1 and 2 show that the levels in the control group are different from those in the obese group (HOMA $p < 10^{-6}$). This is because confidence intervals do not over-

Table 1. Results of parameters in healthy children.

Parameters	Mean	Standard deviation
Cholesterol mmol/l	3.87854	0.65160
TAG mmol/l	1.11707	0.66698
HDL mmol/l	1.29366	0.22555
LDL mmol/l	2.07512	0.64105
Glycemia mmol/l	4.85049	0.39236
Inzulinemia mIU/l	8.13415	6.07382
BMI percentile	47.71250	24.24505
HOMA	1.80761	1.36812
QUICKI	0.29628	0.056

Table 2. Results of parameters in obese children.

Parameters	Mean	Standard deviation
Cholesterol mmol/l	4.07939	0.817427
TAG mmol/l	1.47970	0.919166
HDL mmol/l	1.25121	0.513717
LDL mmol/l	2.16212	0.734825
Glycemia mmol/l	4.83030	0.657878
Inzulinemia mIU/l	21.07212	8.850644
BMI percentile	98.40313	1.725984
HOMA	4.58321	1.918997
QUICKI	0.22524	0.028777

lap. The confidence intervals in the control group and hypertensive group overlap only partly (HOMA $p < 0.005$).

DISCUSSION

The standard technique for assessment of insulin sensitivity is the hyperinsulinemic euglycemic clamp; it is often combined with the hyperglycemic clamp to determine the adequacy of compensatory β -cell hypersensitivity. Although clamp technology has been applied to the study of insulin sensitivity and insulin secretion during childhood, it is too invasive for general epidemiologic studies. Because no intravenous access is needed, the oral glucose tolerance test (OGTT) is better suited for assessment of large populations. Although OGTTs are more difficult to perform than simple measurements of fasting glucose and insulin levels, the OGTT is a minimal-risk procedure that is applicable for large-scale screening and for repeat studies for individual subjects⁶.

These methods currently used for the diagnosis of the insulin resistance are very demanding and completely unsuitable for the investigation of large number of people. In the case of epidemiologic studies, validated models like HOMA or QUICKI model are much more suitable. Other approaches are therefore sought, such as the easy way to assess homeostatic relations between insulin and glycaemia. An increase in concentration of insulin can be a physiological terms guide to glycaemia and vice versa. Disorders in this relationship show insufficient insulin activity and are the basis of the homeostatic model used to appraise the insulin resistance. Among indices and results, the "clamping technique" has repeatedly verified the highly significant correlation^{7,8}.

In the table of the results, it can be seen that the mean value for the HOMA index which can characterise the insulin resistance, in healthy non-obese children of mentioned age, it is 1.8 while the QUICKI value in these children is 0.29. These values can be considered as a standard in healthy children⁹.

Adolescent obesity may result from growth in the infantile age. Most studies on infant size has shown that infants who were recognised as "obese" or who were in the higher range of the body mass index were more inclined to the development of obesity in their childhood, adolescence or an early adulthood in comparison to other children. Infants who grew quickly were more inclined to obesity in their childhood, puberty and an early adulthood than other children. A large size or a rapid phase of growth in the intervals between the first and the second year of their life are predictive of an inclination to later obesity¹⁰. In the obese or hypertensive groups, HOMA and QUICKI indices changed, suggesting possible development of insulin resistance. Currently, no visible increase in other metabolic parameters apart from insulinemia is seen. If these children experienced negative changes in metabolic parameters, the development of the insulin resistance

Table 3. Results of parameters in hypertensive children.

Parameters	Mean	Standard deviation
Cholesterol mmol/l	3.74111	0.71601
TAG mmol/l	1.05917	0.57561
HDL mmol/l	1.39583	0.27902
LDL mmol/l	1.95722	0.51779
Glycemia mmol/l	4.76667	0.32950
Inzulinemia mIU/l	12.91944	12.32512
BMI percentile	72.88889	25.79488
HOMA	2.75378	2.66460
QUICKI	0.26832	0.047745

could be accelerated in the near future. Obesity should no longer be viewed as a cosmetic or body-image issue. There is compelling evidence that overweight people are at increased risk of a variety of health problems, including type 2 diabetes, hypertension, dyslipidemia, coronary artery disease, stroke, osteoarthritis and certain forms of cancers. Treatment of the complication and comorbidity should be focused on preventing progression, reversing the disease process, and, ultimately, achieving control of obesity with family-based lifestyle changes that will allow the child to maintain a healthy balance between genetic predisposition and the environment. Weight control of obese children should be recommended as the first-line intervention to decrease metabolic syndrome in children, adolescents and adults.

CONCLUSIONS

The results show the possibility of evaluating insulin sensitivity from the levels of glycaemia and insulinaemia with the help of the homeostatic indices HOMA and QUICKI which is for the use in pediatric practice. In reality, index QUICKI which has narrower confidence intervals and hence less variability may be more useful^{1,11}. Healthy children have values of QUICKI index around 0.29. Obese and hypertensive children have lower values^{12,13}.

QUICKI and HOMA indexes are useful predominantly for epidemiological purposes, mainly for mapping the scope of insulin resistance among children.

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