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Significant differences in parameters of glucose metabolism in children of hypertensive and normotensive parents

Istotne różnice w parametrach metabolizmu glukozy wśród zdrowych dzieci rodziców z nadciśnieniem i rodziców normotensyjnych

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Abstract

Introduction. In the recent years, alterations in the carbohydrate metabolism, including insulin resistance, are considered as risk factors in the development of hypertension and its complications in young age. Hypertension is associated with significant cardiovascular morbidity and mortality. The onset of pathology responsible for the development of hypertension, as well as levels of biomarkers specific for early stages of atherosclerosis are poorly understood. **Aim.** To compare a group of children whose parents have a history of hypertension (study group) with a group of children with normotensive parents (reference group), with consideration of typical risk factors for atherosclerosis, parameters of lipid and carbohydrate metabolism, anthropometric data and new biomarkers of early cardiovascular disease (hsCRP, adiponectin, sICAM-1). **Material and Methods.** The study population consists of 84 children. Of these, 40 children (mean age 13.6±2.7 years) had a parental history of hypertension, and 44 aged 13.1±3.7 yrs were children of normotensive parents. Anthropometric measurements were taken, and measurements of blood pressure, lipid profile, glucose and insulin levels were carried out. The insulin resistance index (HOMA IR) was calculated. Levels of hsCRP, soluble cell adhesion molecules (sICAM) and adiponectin were measured. **Results.** There were no statistically significant differences in anthropometric parameters (body mass, SDS BMI, skin folds) between groups. Values of systolic blood pressure were statistically significantly higher in the study group (Me 108 vs. 100 mmHg, p= 0.031), as were glycaemia (Me 80 vs. 67 mg/dl p<0.001) and insulinaemia levels (Me 8.89 vs. 5.34 μIU/ml, p=0.024). Higher, statistically significant values of HOMA IR were found in the study group (children of hypertensive parents) (Me 1.68 vs. 0.80 mmol/l × mU/l, p=0.007). Lower adiponectin levels (Me 13959.45 vs. 16822 ng/ml, p=0.020) were found in children with a family history of hypertension. No significant differences were found in the levels of sICAM, hsCRP, and parameters of lipid metabolism. **Conclusions.** Family history of hypertension is correlated with higher values of systolic blood pressure and higher values of parameters for carbohydrate metabolism in children. Hypertension in parents is a risk factor for cardiovascular disease in their children.

Key words

children, family history, hypertension, glucose metabolism, adiponectin, hsCRP, sICAM

Streszczenie

Wstęp. W ostatnich latach zwraca się uwagę na udział zaburzeń przemiany węglowodanów, w tym insulinooporności, w rozwoju nadciśnienia i jego powikłań już w młodym wieku. Znaczny odsetek chorobowości i śmiertelności z przyczyn sercowo-naczyniowych ma związek z nadciśnieniem tętniczym. Kwestią dyskusyjną pozostaje moment rozpoczęcia procesu chorobowego odpowiedzialnego za rozwój nadciśnienia tętniczego, a także jego związek ze specyficznymi dla wczesnych stadiów rozwoju miażdżycy biomarkerami. **Cel.** Porównanie grupy dzieci obciążonych obecnością nadciśnienia tętniczego u rodziców (grupa badana) do grupy dzieci, których rodzice nie chorują na nadciśnienie tętnicze (grupa referencyjna) w zakresie występowania klasycznych czynników ryzyka miażdżycy:

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parametrów przemiany lipidowej, węglowodanowej, pomiarów antropometrycznych, jak również nowych biomarkerów wczesnego ryzyka chorób układu sercowo-naczyniowego (hsCRP, adiponektyna, sICAM-1). **Materiał i metody.** Badaniami objęto 84 dzieci pacjentów lekarza rodzinnego: 40 dzieci (śr. wieku 13,6 lat ± 2,7lat) z obciążonym wywiadem w kierunku nadciśnienia tętniczego i 44 dzieci w wieku średnim 13,1±3,7 lat bez obciążonego wywiadu rodzinnego w kierunku nadciśnienia. U wszystkich dzieci wykonano badanie antropometryczne, badanie ciśnienia tętniczego krwi, oznaczono lipidogram, glikemię oraz insulinemię. Obliczono wskaźnik insulinooporności HOMA-IR. Wykonano oznaczenie hsCRP, stężenie cząsteczek adhezyjnych sICAM i adiponektyny. **Wyniki.** Masa ciała, wskaźnik SDS BMI i pomiary fałdów skórno-tłuszczowych nie różniły się istotnie statystycznie pomiędzy grupami. Wartości ciśnienia skurczowego były istotnie statystycznie wyższe w grupie badanej (Me 108 vs 100mmHg; p= 0,031). Zaobserwowano istotnie statystycznie wyższe stężenie glikemii (Me 80 vs. 67 mg/dl p<0,001) oraz insuliny (Me 8,89 vs. 5,34μUI/ml; p=0,024) w grupie dzieci rodziców z nadciśnieniem. Wskaźnik insulinooporności HOMA wykazywał wartości istotnie statystycznie wyższe w przypadku grupy badanej (dzieci rodziców z nadciśnieniem) (Me 1,68 vs 0,80 p=0,007). Dzieci z dodatnim wywiadem rodzinnym nadciśnienia charakteryzowało niższe stężenie adiponektyny (Me 13959,45 vs. 16822 ng/ml; p=0,020). Nie wykazano istotnych różnic w stężeniu sICAM i hsCRP oraz w zakresie parametrów przemiany lipidowej. **Wnioski.** Dodatni wywiad rodzinny w kierunku nadciśnienia tętniczego koreluje z wyższymi wartościami ciśnienia skurczowego oraz zaburzeniami przemiany węglowodanowej u dzieci. Obciążenie nadciśnieniem tętniczym u rodziców jest czynnikiem ryzyka rozwoju chorób sercowo-naczyniowych u ich potomków.

Słowa kluczowe
dzieci, wywiad rodzinny, nadciśnienie tętnicze, metabolizm węglowodanów, adiponektyna, hsCRP, sICAM

Introduction

Hypertension has been the subject of many studies because of the high incidence and association with cardiovascular mortality. According to the WHO report of 2009, 12.8% of all cardiovascular deaths globally, and 26% in Europe, are associated with hypertension. However, the onset of pathology responsible for the development of hypertension and concomitant disorders of lipid and carbohydrate metabolism, as well as the correlation between the levels of biomarkers specific for early stages of atherosclerosis and hypertension are still poorly understood The pathological mechanism of hypertension is multifactorial and, about 20-40% of individuals with hypertension are genetically predisposed [1]. Population studies demonstrated that the incidence of hypertension is higher in offspring of hypertensive parents. Fuentes et al. found that when a parent is hypertensive, their child has an up to approximately 3.5-fold more chance of developing hypertension when compared to a child whose parents are normotensive [2]. In addition, there are over 10 gene mutations responsible for the development of hypertension [3, 4], and the structure (thickness and rigidity) and function of arterial walls are determined by genetic factors [5]. Intergenerational lifestyle habits also affect cardiovascular risk factors within biological families [6]. Schwandt et al. carried out the PEP Family Heart Study and found that hyper-caloric nutrition of the parents predicted the energy intake of the children [6]. Many studies revealed the offspring of hypertensive parents to have a number of metabolic abnormalities and humoral factors (concerning adrenalin, noradrenalin, ANP, aldosterone, endothelin) whose increased activity in early childhood predisposes them to the development of hypertension [1]. Increasing attention is paid to the role of chronic vascular inflammation in the pathogenesis of hypertension. Adhesive molecules are markers of inflammation specific for the vascular endothelium. Results of clinical studies indicated increased levels of adhesive molecules (ICAM-1, VCAM-1) in patients at risk of cardiovascular disease and in hypertensive patients [7, 8]. Adhesion of leukocytes to epithelial cells due to the increased expression of adhesins is considered to be the earliest disorder causing the onset of atherosclerosis. There are also single reports linking family history of hypertension with increased levels of inflammatory markers and abnormal platelet levels in healthy normotensive offspring of hypertensive patients[9]. In addition, a correlation between increased levels of C-reactive protein (CRP) and the risk of myocardial infarction, stroke and sudden cardiac death in asymptomatic women and men was also proven [10]. High-sensitivity C-reactive protein (hsCRP) is also a marker of the inflammatory process found at early stages of hypertension [11, 12].

The problem of hypertension concerns a growing number of children. It has recently been estimated that about 1–3% of children aged less than 18 years are hypertensive. This figure continues to increase, and it is clearly associated with the epidemics of obesity found in younger age groups. Growing attention is also paid to the role of cytokines released from fatty tissue (e.g. adiponectin), whose protective, anti-inflammatory and anti-atherosclerotic effect is reduced alongside the increase in the amount of fatty tissue [13].

So far, data published on cardiovascular risk factors has concerned mainly adults and have been obtained from clinical centers where patients had more advanced stages of disease and presented with complications. We focused our interest on a group of healthy children with hypertensive parents. So far, such studies have not been carried out in Poland by family doctors.

Aim

The aim of this study is to compare a group of children whose parents had a history of hypertension with a group of children with normotensive parents, with consideration of typical risk factors for atherosclerosis, parameters of glucose metabolism and new biomarkers of early cardiovascular disease (hsCRP, adiponectin, sICAM-1).

Material and Methods

Patients were recruited from a Family Doctor Practice in Białystok, Poland. The main inclusion criterion for the study waspreviously known good health status of a child (not recognized with hypertension or any disease influencing glucose metabolism). Recruited children were divided into two groups: the study group (healthy children of parents with recognized hypertension)that consisted of 84 children. Forty participants (24 boys and 16 girls) aged 7–18 years (mean age 13.6±2.7 years), had a family history of hypertension in at least one parent (data from medical records). The control group consisted of forty-four healthy children of normotensive parents, matched for age, sex and puberty stages (mean age 13.1±3.7 years). The height of patients was measured with a stadiometer (accuracy up to 0.1 cm). Body weight was measured under standard conditions, with accuracy up to 0.1 kg. Data obtained from measurements were used for the calculation of body mass index (BMI) according to the formula: body weight/height^2 (kg/m^2). Children with BMI adjusted for sex and age over 97 centile were considered to be obese, and those with BMI within 90–97 centile were considered overweight. Obtained data were compared to standards for Polish children, including centile charts for relevant sex and age of subjects. Distribution of fatty tissue was specified based on skinfold thickness measured for the biceps skinfold, triceps skinfold, abdominal skinfold and subscapular skinfold. Measurements were taken with skinfold callipers with accuracy up to 1mm. Waist and hip circumference were measured with a non-elastic measuring tape, with accuracy up to 1mm, and then waist-to-hip ratio (WHR) was calculated. Blood pressure was measured three times under standard conditions and interpreted as a mean from measurements expressed in mmHg. The pulse was then measured three times and mean values were calculated. Samples of venous blood were taken for laboratory tests from fasting subjects after 8–12 hours' night rest. Levels of lipids (triglycerides – TG, total cholesterol – TC, HDL cholesterol), glucose and insulin were measured using routine laboratory methods, and LDL cholesterol level was calculated from the Friedewald equation. Levels of hsCRP were measured using reagents from Roche and the immunoturbidimetric technique. Levels of adhesion molecules (sICAM) and adiponectin were determined using kits for enzyme-linked immunosorbent assay (ELISA) from R&D Systems. Insulin resistance was identified based on the HOMA IR index (homeostasis model assessment insulin resistant) according to the equation: fasting blood insulin level (mU/ml) x fasting blood glucose level (mmol/l)/22.5 [14]. The protocol of this study was approved by the Local Bioethical Committee of the Medical University of Bialystok. All children included in the study expressed their spoken consent to participate in the study, and written consent was given by their parents.

Statistical Analysis

The Chi-square test of independence was used to test the correlation between quantitative parameters. Normality of distribution was assessed using the Kolmogorov-Smirnov test, Lillefors test and Shapiro-Wilk test. Normal distribution was not found for the analysed quantitative variables. Quantitative variables with non-normal distribution were compared using a non-parametric U Mann-Whitney test on two groups. The Spearman's rank correlation coefficient was also calculated. Results are presented as a median and quartile range. Statistical significance of results was adopted at $p<0.05$. Statistical analysis was carried out using the Statistica 10.0 software package from StatSoft.

Results

Study group characteristics

The general characteristics of the study group are presented in table I. Mean age in the study group was 13.6±2.7 (6.5 to 17.3) years, and 13.1±3.7 (6.5 to 17.8) years in the control group.

Table I. Characteristics of study groups
Tabela I. *Charakterystyka badanej grupy*

	Study group N=40	Control group N=44	p
Age*	13.5 ± 2.7 years	13.1±3.7 years	0.505
Sex			
Boys (%)	24 (60)	20 (45.5)	
Girls (%)	16 (40)	24 (54.5)	
Body weight [kg]**	56.50 [47–71]	49.50 [37–68]	0.083
Height [cm]**	1.65 [158–1.72]	1.55 [1.41–1.66]	0.009

* Data presented as the mean and standard deviation ** Data presented as median and quartile range

Anthropometric measurements

There were no statistically significant differences in body weight (Me 56.50 vs. 49.50 kg, p=0.083), body mass index (BMI) (Me 20.57 vs. 20.81 kg/m^2, p=0.654), SDS-BMI (0.30vs.0.47, p=0.233), waist circumference (Me 69.5vs.68cm p=0.209), WHR (Me 0.78vs.0,77; p=0,189) and measurements of skinfolds. However, in the study group there were 6 children (15% of the study group) with obesity (BMI>97 centile), and 8 (20% of the study group) overweight children (BMI 90–97 centile), while in the control group overweight children accounted for 13.6%, and children with obesity accounted for 4.5%. Children from the group of hypertensive parents were higher than children from control group.

Blood pressure

Of all the evaluated parameters statistically significant differences were only found for values of systolic blood pressure, which were higher in the study group (Me 108 vs. 100 mmgHg, p= 0.031) (tab II). There was no significant difference in diastolic blood pressure (Me 67vs 60mmHg; p=0.218).However higher were the values of systolic blood pressure in some children in the study group, nobody had been recognized with hypertension during the study.

Carbohydrate metabolism

Significant differences were found in all evaluated parameters of carbohydrate metabolism. In the study group, statistically significant higher values were found for glycaemic levels (Me 80 vs. 67 mg/dl, p<0.001), insulinaemia (Me 8.89 vs. 5.34 μIU/ml, p=0.024) and insulin resistance index HOMA IR (Me 1.68 vs. 0.80 mmol/l × mU/l, p=0.007) (tab III).

Lipid metabolism

The analysis of lipid metabolism revealed a number of differences close to the limit of statistical significance. Children of hypertensive parents were found to have higher, but not statistically significant, levels of total cholesterol (Me 156 vs.150 mg/dl, p=0.232), TG (Me 73.5 vs.59 mg/dl, p=0.079), LDL cholesterol (Me-86.5vs.81 mg/dl, p=0.072, and lower levels of HDL cholesterol (Me 51 vs.58 mg/dl, p=0.069) (tab III).

New biomarkers of cardiovascular disease

The markers measured were sICAM, adiponectin and hsCRP. No significant difference was detected in sICAM levels (Me 386 vs. 338 ng/ml, p=0.528) or hsCRP levels (Me 0.54 vs. 0.48 mg/l, p= 0.964 (tab III). Lower adiponectin levels (Me 13959 vs. 16822 ng/ml, p=0.020) were found in children with a family history of hypertension (fig. 1, table III).

Correlations

Statistical analysis demonstrated that the insulin resistance index HOMA IR was positively correlated with BMI (R= 0.692, p<0.05) (fig. 2) and with values of systolic blood pressure (R=0.26, p<0.05) (fig. 3). Adiponectin levels were negatively correlated with BMI (R= -0.269, p<0.05), (fig. 4) and with insulin resistance index HOMA IR (R= -0.425, p<0.05) (fig. 5).

Table II. Anthropometric and blood pressure measurements
Tabela II. *Pomiary antropometryczne i wartości ciśnienia krwi*

Parameter	Study group N=40	Control group N=44	p
BMI [kg/m^2]	20.57 [17.67–3.77]	20.81 [17.59–23.63]	0.654
SDS-BMI	0.30 [-0.38–1.70]	0.47 [0.004–1.23]	0.233
Waist circumference [cm]	69.5 [63.7–79.2]	68 [60–81]	0.209
Hip circumference [cm]	91.5 [85.5–99]	90.5 [77.5–100.5]	0.428
WHR	0.78 [0.74–0,84]	0.77 [0.73–0.8]	0.189
Systolic blood pressure [mmHg]	108 [100–123]	100 [91.5–116]	0.031
Diastolic blood pressure [mmHg]	67 [60–72.5]	60 [60–70]	0.218
Biceps skinfold thickness [mm]	12.5 [8.5–18.5]	10.00 [6–20.5]	0.594
Triceps skinfold thickness [mm]	17 [10–23]	15 [10–24.5]	0.703
Subscapular skinfold thickness [mm]	15.5 [10–23]	12 [9–17.5]	0.168
Abdominal skinfold thickness [mm]	20.5 [14–29]	20 [12–28]	0.257

Data presented as median and quartile range

Table III. Results of laboratory tests
Tabela III. *Wyniki badań laboratoryjnych*

Parameter	Study group N=40	Control group N=44	p
Glucose [mg/dl]	80 [70–90]	67 [59.5–78.5]	<0.001
Insulinaemia μIU/ml	8.89 [5.45–12]	5.34 [2.47–8.93]	0.024
HOMA IR [mmol/l × mU/l]	1.68 [0.97–2.58]	0.80 [0.41–1.8]	0.007
Total cholesterol [mg /dl]	156[142–169.5]	150 [136–162]	0.232
HDL [mg/dl]	51 [46–60]	58 [52–62]	0.069
LDL [mg/dl]	86.5 [76.5–100]	81 [71.5–92.5]	0.072
TG [mg/dl]	73.5 [55–105]	59 [54–75]	0.079
hsCRP [mg/l]	0.54 [0.33–1.13]	0.48 [0.36–0.86]	0.964
sICAM-1 [ng/ml]	386 [282–484]	338 [317–412]	0.528
Adiponectin [ng/ml]	13959 [9591–18037]	16822 [12117–23203]	0.020

Data presented as median and quartile range

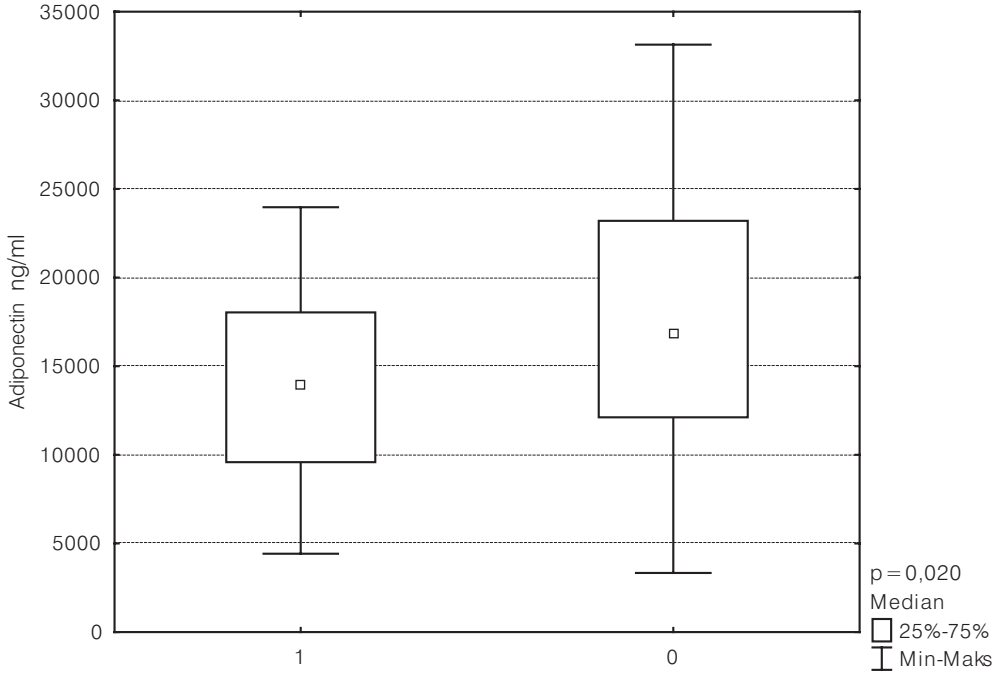

Fig. 1. Adiponectin levels in both groups; 1 – study group (children of hypertensive parents), 0 – control group (children of normotensive parents)
Ryc. 1. *Stężenie adiponektyny w badanych grupach; 1 grupa badana (dzieci rodziców z nadciśnieniem), 0 grupa kontrolna (dzieci rodziców normociśnieniowych)*

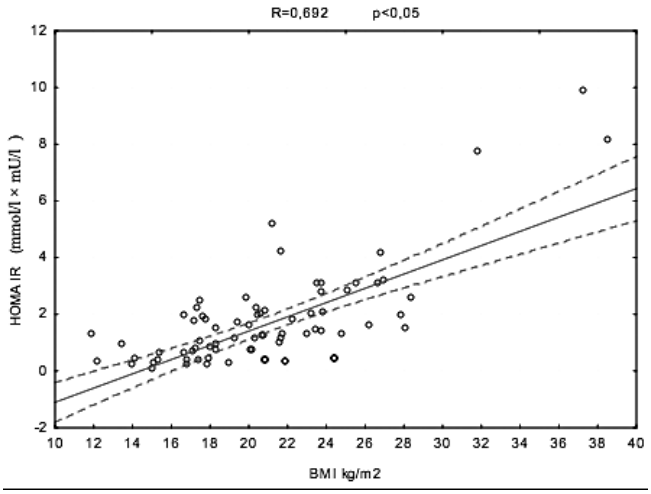

Fig. 2. The correlation between HOMA IR and BMI
Ryc. 2. *Korelacje pomiędzy HOMA IR i BMI*

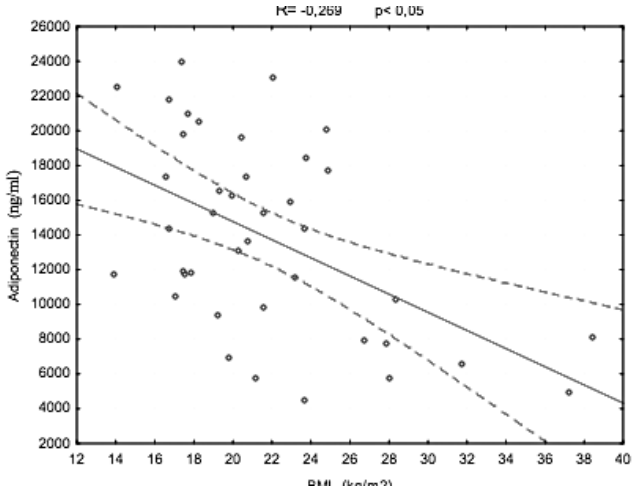

Fig. 4. The correlation between adiponectin level and BMI
Ryc. 4. *Korelacja pomiędzy stężeniem adiponektyny i BMI*

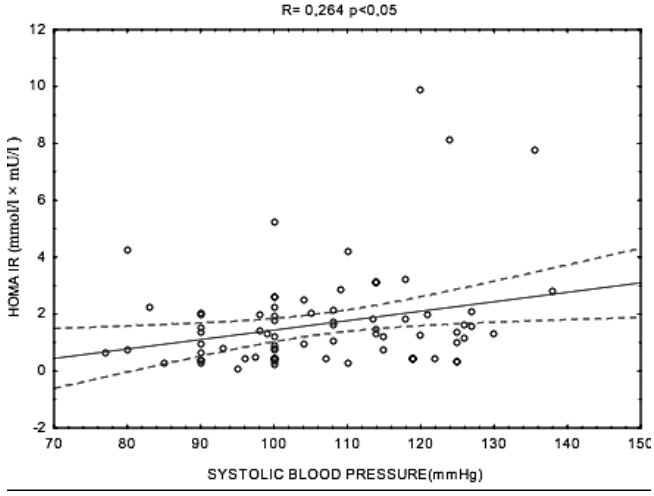

Fig. 3. The correlation between HOMA IR and systolic blood pressure (SBP)
Ryc. 3. *Korelacja pomiędzy HOMA IR i ciśnieniem skurczowym krwi*

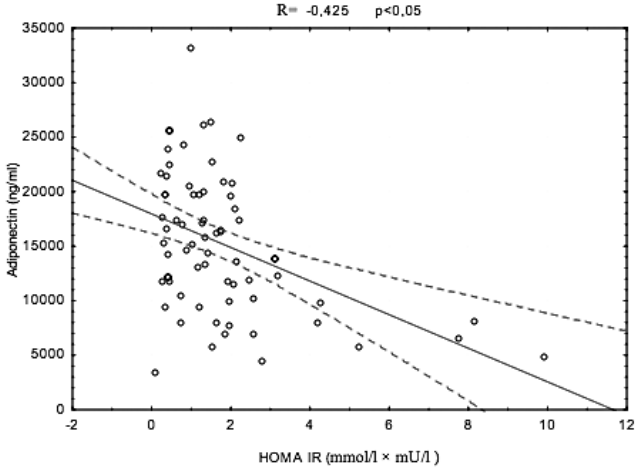

Fig. 5. The correlation between adiponectin level and HOMA IR
Ryc. 5. *Korelacja pomiędzy stężeniem adiponektyny i HOMA IR*

Discussion

Population studies carried out over the years have confirmed that parental hypertension affects blood pressure values in their children.

Our research demonstrated that children from the study group had higher values of systolic blood pressure when compared to the control group. Similar results were reported by Kucerova et al. [15], while Loster et al. reported significant differences in diastolic blood pressure [16]. The studies by Yasmin et al. and Zizek et al. found that systolic blood pressure, diastolic blood pressure and glucose blood levels were significantly higher in the offspring of hypertensive parents [17, 18]. This study did not show any significant differences in diastolic BP but this must be treated with caution because of the small sample size and the potential inaccuracies of office based BP monitoring reported in the adult population [19, 20]. Differences found in the values of blood pressure in children having hypertensive or normotensive parents seem to be significant with respect to the proven linear correlation between the values of blood pressure and increased cardiovascular risk [21] and so earlier recording of childrens' blood pressure may pick up some of those at risk.

Statistically significant differences were found in the parameters of carbohydrate metabolism, such as glucose and insulin blood levels, and the higher value of the insulin resistance index HOMA IR in the hypertensive group, and lack of differences in body weight, were in line with findings by Ohno et al., who also observed reduced sensitivity to insulin in young lean offspring of hypertensive parents [22]. Measurement of these biomarkers may also identify chidren at risk.

Relatively recently the term 'metabolic obesity' was introduced to the literature. This term refers to obesity manifested by excessive deposits of visceral fat in subjects with normal body weight and normal BMI. Both metabolic obesity and abdominal obesity are associated with disorders of lipid and carbohydrate metabolism. The importance of dietary and exercise advice is further highlighted because visceral fatty tissue, in comparison to subcutaneous, releases lower amounts of adiponectin (increasing sensitivity to insulin and uptake and use of glucose by muscles), but is also the source of resistin, an adiponectin antagonist. Individuals with metabolic obesity are at much higher risk of carbohydrate metabolic disorders, dyslipidaemia and hypertension [23, 24]. Exercise and a good diet can reduce insulin resistance. Hyperinsulinaemia have an atherogenic effect, directly stimulating epithelial dysfunctions, local inflammation in vascular walls, and the formation of atherosclerotic plaque, as well as indirectly inducing or stimulating typical risk factors for atherosclerosis [25]. Increased insulin levels also cause increased activity in the sympathetic system, resulting in increased cardiac output and increased tone of resistance blood vessels, and is associated with the effects of cortisol, which becomes more bioavailable in insulin-resistant subjects [26]. The higher levels of insulin and higher values of HOMA index that we found in the group of healthy children of hypertensive parents may indicate an existing predisposition to the development of insulin resistance, with consequent oxidative stress and subclinical inflammation which contributes to an increase in blood pressure in these young subjects [27].

Insulin resistance is also accompanied by lipid profile disorders, called atherogenic dyslipidaemia (increased TG level, reduced HDL cholesterol level, slightly increased LDL cholesterol level) [28]. Similar differences (close to the level of statistical significance) were also found in our group of children.

Subjects with hypertensive parents had lower levels of adiponectin than the control group, and the difference was statistically significant. Similar findings were reported by Hoffman et al. [29]. A number of studies on adiponectin have revealed that this hormone, synthesized in the fatty tissue, has a very positive effect on lipid and carbohydrate metabolism, e.g. by improving the sensitivity of tissues to insulin and protecting the vascular epithelium against inflammation and atherosclerosis. Experimental studies demonstrated a negative correlation between adiponectin level and activity of the sympathetic nervous system, and positive correlation with the increased activity of the epithelial nitric oxide synthase [30]. Such activity of adiponectin may be associated with an antihypertensive effect. The low adiponectin level is an independent risk factor for metabolic syndrome, diabetes type 2 and cardiovascular disease, including hypertension [31]. Studies demonstrated that children with the metabolic syndrome have lower adiponectin levels [32]. On the other hand, in children with diabetes type 1 higher adiponectin level was found [33]. American researchers suggested that this substance can function as a biomarker of the metabolic syndrome in children. They also demonstrated a strong association with an inflammatory marker (CRP). A high adiponectin level is correlated with the low level of CRP [34], and in our study we also found the same statistically significant negative correlation.

CRP is an active factor in atherogenesis, and CRP detected with high-sensitivity analytical methods (hsCRP) allows for the estimation of cardiovascular risk, i.e. myocardial infarction, stroke or sudden cardiac death [35]. Levels of hsCRP in the paediatric population are positively correlated with obesity markers, high values of blood pressure and insulin resistance index (HOMA IR) [36, 37, 38]. The inflammatory process can also be partly responsible for familial hypertension [39]. Lieb et al. and Diaz et al. found higher levels of CRP in the offspring of hypertensive parents. In our study children from the study group also had slightly higher levels of hsCRP than controls, but in this small sample the significance of the difference was not shown[40, 41].

Endothelial cell dysfunction is another factor important in the development of atherosclerotic diseases. An inflammatory reaction develops in hypertension and sICAM adhesion molecules play a significant role in this inflammatory process. The sICAM level can be used as a marker of epithelial cell activity at an early stage of atherosclerosis. Many large-scale studies demonstrated the close correlation between sICAM levels and cardiovascular risk [42] including hypertension, dyslipidaemia, diabetes and the metabolic syndrome [43]. In our study no significant differences for this inflammation marker were found

between the studied groups, perhaps because neither of the groups included individuals with diagnosed hypertension [41]. The children included in our study had only hypertensive parents, but presented no clinical symptoms of the disease. We found no significant differences in anthropometric parameters (body weight, BMI, skinfold thickness), but statistical analysis revealed significant differences in parameters of carbohydrate metabolism and adiponectin levels. Considering the fact that reduced adiponectin level is increasingly regarded as an independent risk factor for CVD and raised HOMA-IR and decreased adiponection may indicate insulin resistence, these children may be potentially at risk of earlier development of cardiovascular disease and disorders of carbohydrate metabolism.

This study highlights the need to identify children at risk of future cardiovascular disease. There is no easy way to identify these children by anthropomorphic measurement and a standard office based BP measurement may be misleading. There is evidence to support the targeting of children with a hypertensive parent and the need for a larger population based study to test the use of biomarkers. There is of course a research burden from screening children and may not be universally acceptable unless finger prick near patient testing was developed. The role and form of preventive therapy is not addressed in this paper but with statins having an anti-inflammatory action [44, 45] and biguanides countering insulin resistance [46], solutions may already exist.

Conclusions

1. Children of hypertensive parents have higher values of systolic blood pressure than children with normotensive parents.

2. Parameters of carbohydrate metabolism, i.e. glycaemia, insulin level and HOMA IR have higher values in the group of children with hypertensive parents, but no differences in body weight and BMI are found when compared to the control group.

3. Children of hypertensive parents have lower levels of adiponectin than children with normotensive parents and so it is important to offer lifestyle advice to reduce visceral adipose tissue.

4. Parental hypertension is a risk factor for the development of cardiovascular disease in children.

References

1. Horký K, Jáchymová M, Jindra A, Savliková J, Peleska J, Umnerová V et al. *Metabolic, humoral and haemodynamic characteristics of normotensive offspring from hypertensive families*. J Hum Hypertens. 1996;10 suppl 3:S85-87.
2. Fuentes RM, Notkola IL, Shemeikka S, Tuomilehto J, Nissinen A. *Familial aggregation of blood pressure: a population-based family study in eastern Finland*. J Hum Hypertens. 2000;14:441-445.
3. Lifton RP. *Molecular genetics of human blood pressure variation*. Science. 1996;272:676-680.
4. Camci L, Kilic Z, Dinleyici EC, Muslumanoglu H, Tepeli E, Ucar B. *Angiotensin-converting enzyme gene insertion/deletion polymorphism frequency in normotensive children with a positive family history of essential hypertension*. J Paediatr Child Health. 2009;45:742-746.
5. Sayed-Tabatabaei FA, van Rijn MJE, Schut AFC, Aulchenko YS, Croes EA, Zillikens MC et al. *Heritability of the function and structure of the arterial wall – Findings of the erasmus rucphen family (ERF) study*. Stroke. 2005;36:2351-2356.
6. Schwandt P, Haas GM, Liepold E. *Lifestyle and cardiovascular risk factors in 2001 child-parent pairs: the PEP Family Heart Study*. Atherosclerosis. 2010;213:642-648.
7. Damnjanović G, Jelić M, Dindić B, Ilić S. *[Serum concentration of soluble adhesive molecules in patients with different forms of coronary artery disease]*. Vojnosanit Pregl. 2009;66:265-270.
8. Shavelle DM, Katz R, Takasu J, Lima JA, Jenny NS, Budoff MJ et al. *Soluble intercellular adhesion molecule-1 (sICAM-1) and aortic valve calcification in the multi-ethnic study of atherosclerosis (MESA)*. J Heart Valve Dis. 2008;17:388-395.
9. Solini A, Santini E, Passaro A, Madec S, Ferrannini E. *Family history of hypertension, anthropometric parameters and markers of early atherosclerosis in young healthy individuals*. Journal of Human Hypertension. 2009;23:801-807.
10. Danesh J, Whincup P, Walker M, Lennon L, Thomson A, Appleby P et al. *Low grade inflammation and coronary heart disease: prospective study and updated meta-analyses*. BMJ. 2000;321:199-204.
11. Niskanen L, Laaksonen DE, Nyyssönen K, Punnonen K, Valkonen VP, Fuentes R et al. *Inflammation, abdominal obesity, and smoking as predictors of hypertension*. Hypertension. 2004;44:859-865.
12. Sesso HD, Buring JE, Rifai N, Blake GJ, Gaziano JM, Ridker PM. *C-reactive protein and the risk of developing hypertension*. JAMA. 2003;290:2945-2951.
13. Goldstein BJ, Scalia R. *Adiponectin: A novel adipokine linking adipocytes and vascular function*. J Clin Endocrinol Metab. 2004;89:2563-2568.
14. Szurkowska M, Szafraniec K, Gilis-Januszewska A, Szybiński Z, Huszno B. *Wskaźniki insulinooporności w badaniu populacyjnym i ich wartość predykcyjna w określeniu zespołu metabolicznego*. Przegl Epidemiol. 2005;59:743-751.
15. Kucerová J, Filipovský J, Staessen JA, Cwynar M, Wojciechowska W, Stolarz K et al. *Arterial characteristics in normotensive offspring of parents with or without a history of hypertension*. Am J Hypertens. 2006;19:264-269.
16. Loster M, Stolarz-Skrzypek K, Olszanecka A. *Składowe zespołu metabolicznego u dorosłych z prawidłowym ciśnieniem, potomków pacjentów z nadciśnieniem tętniczym*. Nadciśnienie tętnicze. 2010;14:201-207.

17. Yasmin, Falzone R, Brown MJ. *Determinants of arterial stiffness in offspring of families with essential hypertension*. Am J Hypertens. 2004;17:292-298.
18. Zizek B, Poredos P, Videcnik V. *Endothelial dysfunction in hypertensive patients and in normotensive offspring of subjects with essential hypertension*. Heart. 2001;85:215-217.
19. Pickering TG, White WB; American Society of Hypertension Writing Group. *ASH Position Paper: home and ambulatory blood pressure monitoring. When and how to use self (home) and ambulatory blood pressure monitoring*. J Clin Hypertens (Greenwich) 2008;10:850-855.
20. White WB. *Ambulatory Blood Pressure Monitoring for the Evaluation of Antihypertensive Therapy*. In: White WB (ed) *Blood Pressure Monitoring in Cardiovascular Medicine and Therapeutics*. Totawa, NJ, Humana Press, 2007, ed 2, 437-462.
21. MacMahon S, Peto R, Cutler J. *Blood pressure, stroke,and coronary heart disease. Part 1. Prolonged differences in blood pressure: prospective observational studies corrected for the regression dilution bias*. Lancet. 1990;335:765-774.
22. Ohno Y, Suzuki H. *Impaired insulin sensitivity in young, lean normotensive offspring of essential hypertensives: possible role of disturbed calcium metabolism*. Journal of Hypertension. 1993;11:421-426.
23. St-Onge MP, Janssen I, Heymsfield SB. *Metabolic syndrome in normal-weight Americans: new definition of the metabolically obese, normal-weight individual*. Diabetes Care. 2004;27:2222-2228.
24. Milewicz A, Kubicka E. *Otyłość metaboliczna z prawidłową masa ciała*-implikacje terapeutyczne. Przewodnik Lekarza. 2011;14:68-71.
25. Steinberger J, Daniels SR. American Heart Association Atherosclerosis Hp, and Obesity in the Young Committee (Council on Cardiovascular Disease in the Young), American Heart Association Diabetes Committee (Council on Nutrition PyA, and Metabolism). *Obesity, insulin resistance, diabetes, and cardiovascular risk in children: an American Heart Association scientific statement from the Atherosclerosis, Hypertension, and Obesity in the Young Committee (Council on Cardiovascular Disease in the Young) and the Diabetes Committee (Council on Nutrition, Physical Activity, and Metabolism)*. Circulation. 2003;107:1448-1453.
26. Scherrer U, Sartori C. *Insulin as a vascular and sympathoexcitatory hormone: implications for blood pressure regulation, insulin sensitivity, and cardiovascular morbidity*. Circulation. 1997;96:4104-4113.
27. Mazzone T, Chait A, Plutzky J. *Cardiovascular disease risk in type 2 diabetes mellitus: insights from mechanistic studies*. The Lancet 2008; 371, Pages 1800-1809.
28. Lillioja S, Mott DM, Spraul M, Ferraro R, Foley JE, Ravussin E et al. *Insulin resistance and insulin secretory dysfunction as precursors of non-insulin-dependent diabetes mellitus*. *Prospective studies of Pima Indians*. N Engl J Med. 1993;329:1988-1992.
29. Hoffman K, Bryl W, Stażyńska A, Miczke A, Cymers M, Kramer L et al. *Ocena stężenia adiponaktyny, insuliny, wybranych parametrów metabolicznych, wywiadu rodzinnego i wskaźników antropometrycznych u młodych osób z pierwotnym nadciśnieniem tętniczym*. 2008;12:359-66.
30. Hattori Y, Suzuki M, Hattori S, Kasai K. *Globular adiponectin upregulates nitric oxide production in vascular endothelial cells*. Diabetologia. 2003;46:1543-1549.
31. Gola M, Grzeszczak W. *Adiponektyna- mechanizm działania,aktywność biologiczna i nadzieje terapeutyczne*. Diabetologia Doświadczalna i Kliniczna. 2011;11:11, 2: 78-83.
32. Głowińska-Olszewska B, Urban M, Koput A. *Adipocytokiny i markery zapalenia w zespole metabolicznym u młodzieży*. Endokrynologia Pediatryczna. 2008;7:33-43.
33. Peczyńska J, Urban M, Głowińska B, Florys B. *Evaluation of adiponectin level in children and adolescents with diabetes type 1*. Pediatr Endocrinol Diabetes Metab. 2008;14(2):77-81.
34. Winer JC, Zern TL, Taksali SE, Dziura J, Cali AM, Wollschlager M et al. *Adiponectin in childhood and adolescent obesity and its association with inflammatory markers and components of the metabolic syndrome*. J Clin Endocrinol Metab. 2006;91:4415-4423.
35. Podręcznik Polskiego Forum Profilaktyki. Kraków: Medycyna Praktyczna; 2007.
36. Wasilewska A, Tenderenda E, Taranta-Janusz K, Zoch-Zwierz W. *High-sensitivity C-reactive protein and mean platelet volume in paediatric hypertension*. Pediatr Nephrol. 2010;25:1519-1527.
37. Głowińska-Olszewska B, Tołwińska J, Urban M. *Relationship between endothelial dysfunction, carotid artery intima media thickness and circulating markers of vascular inflammation in obese hypertensive children and adolescents*. J Pediatr Endocrinol Metab. 2007; 20:1125-1136.
38. Głowińska-Olszewska B, Urban M, Peczyńska J, Koput A. *hsCRP protein in children and adolescents with diabetes type 1*. Pediatr Endocrinol Diabetes Metab. 2007;13(2):79-84.
39. Ross R. *Atherosclerosis – an inflammatory disease*. N Engl J Med. 1999;340:115-126.
40. Lieb W, Pencina MJ, Wang TJ, Larson MG, Lanier KJ, Benjamin EJ et al. *Association of parental hypertension with concentrations of select biomarkers in nonhypertensive offspring*. Hypertension. 2008;52:381-386.
41. Díaz JJ, Arguelles J, Málaga I, Perillán C, Diéguez A, Vijande M, Málaga S. *C-reactive protein is elevated in the offspring of parents with essential hypertension*. Arch Dis Child. 2007 Apr;92(4): 304-308.
42. Machnica L, Deja G, Polanska J, Czupryniak L, Szymanska-Garbacz E, Loba J, Jarosz-Chobot P. *Blood pressure disturbances and endothelial dysfunction markers in children and adolescents with type 1 diabetes*. Atherosclerosis 2014;237:129-134.
43. Bogdański P, Pupek-Musialik D, Dytfeld J, Miczke A, Bryl W, Jabłecka A et al. *Ocena wybranych wykładników stanu zapalnego u chorych z nadciśnieniem tętniczym i klinicznymi cechami zespołu metabolicznego*. Arterial Hypertension 2005;9:192-201.
44. Libby P. *Inflammation in atherosclerosis.* Nature 2002;420:868-874.
45. Libby P, Ridker PM, Maseri A. *Inflammation and atherosclerosis*. Circulation 2002; 105:1135-1143.
46. Landin K, Tengborn L, Smith U. *Treating insulin resistance in hypertension with metformin reduces both blood pressure and metabolic risk factors*. Journal of Internal Medicine 1991; 229:181-187.