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Risk factors for cardiovascular diseases in children and adolescents with arterial hypertension

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A group of 70 children of 12–17 years old with stable and labile forms of arterial hypertension and prehypertension hospitalized to cardiopulmonary department with high blood pressure was observed.
In 27.1% cases arterial hypertension was associated with various cardiovascular risk factors: hyperinsulinemia and insulin resistance revealed in 72.9% children with stable and labile forms of arterial hypertension and prehypertension, overweight or obesity were detected in 64.3%, dyslipidemia was registered in 51.4 % cases.
It was shown, that arterial hypertension more frequently was associated with multiple risk factors of cardiovascular diseases (3 and more) and revealed in 37.1% children with arterial hypertension that testifies to the beginning of high risk formation for cardiovascular diseases already in childhood.
Key words: *arterial hypertension, insulin resistance, cardiovascular disease, cardiometabolic risk, risk factors, children.*

Arterial hypertension (AH) is an important risk factor for early development of cardiovascular complications and mortality [4, 8].

Until recently, children and adolescents with arterial hypertension were traditionally attributed to a low risk of cardiovascular disease [3].

However, as shown in prospective studies, AH, starting in childhood, may be associated with cardiovascular risk factors that persist into adulthood and are adverse prognostic factors for cardiovascular complications of hypertension [11, 13, 15].

The high frequency of hypertension association with cardiovascular and metabolic risk factors in adults [2, 4, 8] identifies the need to study possible existence of such an association in children.

Relevance of early detection of risk factors is very important because their correction, starting from infancy, can prevent the development of disease or its progression [4].

In this context, the aim of study was to investigate the association of hypertension with cardiometabolic risk factors in children and adolescents.

MATERIALS AND METHODS

The study included 70 children (boys – 61, girls – 9) with various forms of hypertension – stable (n=37), labile (n=20), prehypertension (n=13) aged 12–17 years old admitted to Dnipropetrovsk city pediatric cardio-pulmonary department due to increased blood pressure (BP) level revealed at a single outpatient measurement.

Ambulatory blood pressure monitoring (ABPM) [3, 10] was conducted for all children in order to establish a diagnosis of hypertension and to determine its clinical and pathogenic forms. To determine the risk factors for cardiovascular disease, indicators of physical development of children were assessed, lipid profile was determined, evaluation of carbohydrate metabolism was

carried out (levels of venous blood glucose and serum basal insulin, as well calculation of homeostatic model assessment of insulin resistance – HOMA-IR were identified).

ABPM was carried out by the registrar Cardiotens-01 of "MEDITECH" company (Hungary) with brachial cuff according to age. In analyzing the ABPM data, the following quantitative parameters were evaluated: daily average, maximum and minimum values of systolic blood pressure, diastolic blood pressure, average blood pressure, pulse blood pressure, heart rate, increased systolic and diastolic blood pressure load indexes during the day and night [3, 7].

Stable AH was diagnosed when the average daily level of blood pressure was above the 95th percentile and hypertension time index was more than 50%, labile AH was determined if hypertension time index was 25% to 50%, but the average daily blood pressure was lower than the 95 percentile. Prehypertension was defined if the level of the average daily blood pressure was 90 to 95 percentile [3, 13].

Physical development of the children was assessed using anthropometric parameters: body weight and height, waist circumference (WC) and body mass index (BMI). Body mass index (BMI, kg/m²) in children surveyed was measured by nomograms based on age and sex of the child. BMI was considered as a normal, if it was within 15–85 percentiles. BMI between 85 and 95 percentile were regarded as excess body weight, BMI above the 95th percentile – as obese. The criterion for abdominal obesity was considered if WC was equal to or greater than 94 cm to 80 cm for boys and girls of 16–18 years and above 90 percentile for children under 15 years (IDF, 2005) [3,5].

The level of glucose in venous blood was determined by GOD-PAP using a set of Glucose liquicolor (Human, Germany) and Microlab 200 photometer.

The solid phase enzyme-linked immunosorbent assay (ELISA) method with a set of DRG insulin ELISA (Germany) was used to quantify the level of basal immunoreactive insulin in serum. Hyperinsulinemia was diagnosed if insulin levels increase above the reference value of 25 µU/ml. Insulin level 20–24.9 µU/ml was considered borderline.

Insulin resistance was assessed by indirect indicators: the level of basal insulinemia and homeostatic model of insulin resistance with calculation of parameters HOMA-IR, which was calculated by the formula:

(Fasting Glucose Level, mmol/l) × (Fasting Insulin Level, µU/ml) : 22.5

The level of HOMA-IR more than 3.6 was the criterion of high insulin resistance. The level of HOMA-IR 2.77–3.59 was considered as borderline level of insulin resistance. Retained insulin sensitivity (absence of insulin resistance) was diagnosed at a level less than 2.77 HOMA-IR [9].

Metabolic syndrome (MS) was defined according to criteria ATP III (2001), IDF (2005) and pediatric criteria [5, 12, 14].

Statistical processing of research materials was conducted using methods of biostatistics implemented in software packages EXCEL-2003, STATISTICA 6.0 (Statsoft Inc., USA) [1, 9]. Student's t test and Mann-Whitney test have been applied for assessing the reliability of differences in quantitative traits, as well, criteria consent chi-square (χ^2) and Fisher's exact tests to assess the reliability of differences in qualitative features. Spearman's rank correlation coefficient (r) and odds ratio (OR) were calculated to assess the contingency [1].

Fig. 1. The incidence of hyperinsulinemia in children with hypertension

Normal insulin levels (<20 μU/ml), n = 35
Borderline insulin levels (20-24,9 μU/ml), n = 16
Hyperinsulinemia (> 25 μU/ml), n = 19

RESULTS AND DISCUSSION

Analysis of risk factors in children with arterial hypertension showed a high frequency of family history for hypertension in hypertensive children (78.0%), especially in stable form of hypertension (83.3%) and prehypertension (88.9%).

Reliable (P<0.05) prevalence of hereditary burdening with hypertension in relationship line 1, namely maternal, in children with stable form of hypertension (65.0%) compared with groups of children with labile form of hypertension (42.5%), prehypertension (33.3%) and normotension (23.1%) observed.

In addition to genetic predisposition, a number of modifiable risk factors affects the occurrence and progression of hypertension, and these factors should be the point of application of the system of prevention [3, 4, 8].

One of the most important risk factors is the presence of excess body weight and obesity [14]. It was found that the value of BMI was higher than normal values in almost 2/3 of children with hypertension (n=71 – 60.2%), including excess body weight in 34.8% (n=41) of children, obesity – in 25.4% (n=30). In the comparison group, only four children (30.8%) had a BMI deviation from normal values (P<0.05, compared with children with AH), of which 23.1% (n=3) had an excess of body weight (P>0.30) and in one case – obesity (P>0.10).

Statistical analysis showed that a number of children with overweight and obesity was significantly higher in the group of stable systolic AH (71.7%), as compared with groups of labile systolic AH (37.5%; P<0.001) and normotension (30.8%; P<0.01).

Dyslipidemia is another modifiable risk factor for cardiovascular disease of adults [2]. Dyslipidemia was observed in 55.1% surveyed children with combined disorders in lipid profile in 34.7% children, being presented by atherogenic types of hyperlipoproteinemia: in 14.4% by type IIa, in 11.9% – type IIb and 8.5% – type IV. Increased total cholesterol was found in 21.7% children with stable systolic AH, 12.5% – labile systolic AH, 16.7% – prehypertension and in 15.4% of children with normotension. Increased triglycerides above 1.7 mmol/l were
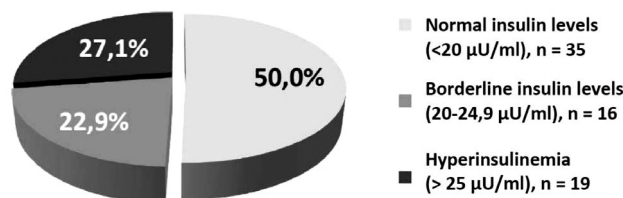

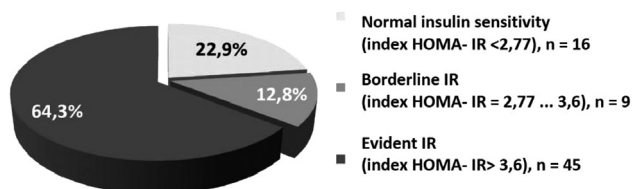Fig. 2. The frequency of insulin resistance in children with hypertension

Normal insulin sensitivity (index HOMA- IR <2,77), n = 16
Borderline IR (index HOMA- IR = 2,77 ... 3,6), n = 9
Evident IR (index HOMA- IR> 3,6), n = 45

observed in 21.7%, 12.5%, 16.7% of children with stable systolic AH, labile systolic AH and prehypertension, respectively, and were absent in normotensive children. Increased LDL levels were observed in 25.0% of children with stable systolic AH, 15.0% of children with labile systolic AH, 33.3% of prehypertension and 15.4% of normotensive children. Reduction of HDL levels were observed in 23.3% of children with stable systolic AH, 15.0% of labile systolic AH, 44.4% of prehypertension and 23.1% of children with normotension.

Analysis of changes in lipid profile in children with hypertension showed reliably more frequent association of hypertension, compared with normotension, with higher levels of triglycerides and VLDL, which are key markers of atherogenic dyslipidemia [12].

Hyperinsulinemia (over 25 μU/ml) was observed in 27.1% (n=19) children with stable, labile forms of hypertension and prehypertension; the borderline insulin levels (20-24.9 μU/ml) in serum were recorded in 22.9 % (n=16) cases, normal insulin levels were observed in 50.0% (n=35) children (Fig. 1.)

The state of evident insulin resistance (HOMA index more than 3.6) was observed in 45 children (64.3%), normal insulin sensitivity (HOMA index less than 2.77) was determined in 16 children (22.9%; p<0,001) (Fig. 2).

The highest incidence of hyperinsulinemia was observed in

Combination of hypertension with different cardiometabolic risk factors in children

Variant No	Risk factors				Number of children	
	AH	Dyslipid-emia	Excess body weight/obesity	Hyper-insulinemia/ insulin resistance	abs.	%
1	+	-	-	-	10	14.3
2	+	+	-	-	2	2.9
3	+	-	+	-	3	4.3
4	+	-	-	+	9	12.9
5	+	+	+	-	4	5.7
6	+	+	-	+	4	5.7
7	+	-	+	+	12	17.1
8	+	+	+	+	26	37.1
Total	Abs.	70	36	45	51	70
	%	100	51.4	64.3	72.9	100

the group of children with stable systolic AH (32.4%), which is consistent with data of several studies [15].

However, significant differences were observed only when compared with the group of children with normotension, in which increase of insulin levels were not found (P=0.087 by Fisher's exact criterion).

The average level of basal insulin in the blood serum of children with various forms of hypertension was within the normal range and amounted 23.34±1.77 µU/ml in children with stable hypertension, 20.00±2.62 µU/ml with labile hypertension and 21.27±2.41 µU/ml with prehypertension. The average level of HOMA insulin resistance index was increased and amounted to 5.21±0.41, 4.26±0.63 and 4.64±0.53 in children with stable, labile hypertension and prehypertension, respectively (p>0,05).

The state of evident insulin resistance (by index HOMA) in children with stable form of hypertension was observed in 1.6 times more frequently than in labile hypertension (73.0% and 45.0%, respectively; P<0.05), and almost 3 times more often than in children with normotension (25.0%; P<0.05). At the same time, the group of children with stable systolic AH and prehypertension were compared for this indicator (73.0% and 69.2%, respectively; P>0.40).

The level of glucose in venous blood was within the normal range and had no significant differences ($P_H>0.05$).

Cases of fasting hyperglycemia (blood glucose above 5.6 mmol/l) were observed in almost every tenth child with stable systolic AH and labile systolic AH (9 people out of 100). The frequency of hyperglycemia was comparable in groups of stable systolic AH – 8.3% (n=5) and labile systolic AH – 10.0% (P>0.70). Fasting hyperglycemia was not observed (P>0.10 compared with the previous groups) in children with systolic prehypertension and normotension. However, impaired glucose tolerance was found in one child (5.6%) with systolic prehypertension.

It was found that hypertension was combined with various risk factors for cardiovascular disease in 85.7% (n=60) cases.

Eight combinations of hypertension with different cardiometabolic risk factors in children were identified (Table).

It was found that the isolated AH without metabolic risk factors was observed only in 14.3% children (n=10).

Hyperinsulinemia and insulin resistance were the most frequent components of cardiometabolic risk factors combinations (72.9%).

A preferred combination (37.1%) was the association of hypertension with multiple risk factors including excess body weight or obesity, dyslipidemia, and hyperinsulinemia and/or insulin resistance, the frequency of hyperinsulinemia in this combination amounted 92.3%.

Combination of hypertension with excess body weight or obesity and hyperinsulinemia and/or insulin resistance took second place (17.1%); the incidence of hyperinsulinemia was 50.0%.

Association of hypertension with hyperinsulinemia and/or insulin resistance was on the third place (12.9%) with 55.6% frequency of hyperinsulinemia in it.

The incidence of metabolic syndrome in children with hypertension in the whole group was 10 to 15% depending on the criteria used. Moreover, in the group of children without insulin resistance, metabolic syndrome frequency for all criteria (ATP III, 2001; IDF, 2005; and pediatric criteria) was 6.3% and in the group of children with metabolic syndrome, insulin resistance was observed in 13.3%, 15.6%, and 17.8% of cases, respectively.

CONCLUSIONS

1. Arterial hypertension in childhood should not be considered as an isolated state but as a component of a cluster of metabolic and hemodynamic risk factors for cardiovascular diseases, which are observed in 85.7% of children with hypertension.

2. A high frequency of combination of hypertension in children with hyperinsulinemia (27.1%) and insulin resistance (64.3%) was found.

3. Most often, hypertension in children associates with multiple risk factors (three or more) – 37.1%, indicating the beginning of a high risk formation for cardiovascular disease as early as in childhood.

Фактори ризику кардіоваскулярних захворювань у дітей та підлітків з артеріальною гіпертензією
О.І. Гайдук, Л.Р. Шостакович-Корецька, Т.А. Гайдук

Обстежено 70 дітей з різними формами артеріальної гіпертензії (АГ) – стабільною, лабільною формами і прегіпертензією у віці 12–17 років, яких було госпіталізовано до дитячого міського кардіопульмонологічного відділення у зв'язку з підвищенням артеріального тиску під час його разового вимірювання на амбулаторному етапі. Виявлено, що у 85,7% випадків АГ поєднувалася з різними факторами ризику кардіоваскулярних захворювань (гіперінсулінемією та інсулінорезистентністю – у 72,9%, надмірною масою тіла або ожирінням – у 64,3%, дисліпідемією – у 51,4% випадків). Установлено, що АГ у дітей найбільш часто асоціюється з множинними факторами ризику (трьома і більше) – 37,1%, що свідчить про початок формування високого ризику кардіоваскулярних захворювань уже у дитячому віці.
Ключові слова: артеріальна гіпертензія, інсулінорезистентність, серцево-судинні захворювання, кардіометаболічний ризик, фактори ризику, діти.

Факторы риска кардиоваскулярных заболеваний у детей и подростков с артериальной гипертензией
О.И. Гайдук, Л.Р. Шостакович-Корецкая, Т.А. Гайдук

Обследовано 70 детей с различными формами артериальной гипертензии (АГ) – стабильной, лабильной формами и прегипертензией в возрасте 12–17 лет, госпитализированных в детское городское кардиопульмонологическое отделение в связи с повышением артериального давления при его разовом измерении на амбулаторном этапе. Выявлено, что в 85,7% случаев АГ сочеталась с различными факторами риска кардиоваскулярных заболеваний (гиперинсулинемией и инсулинорезистенцией – в 72,9%, избыточной массой тела или ожирением – в 64,3%, дислипидемией – в 51,4 % случаев). Установлено, что АГ у детей наиболее часто ассоциируется с множественными факторами риска (три и более) – 37,1%, что свидетельствует о начале формирования высокого риска кардиоваскулярных заболеваний уже в детском возрасте.
Ключевые слова: артериальная гипертензия, инсулинорезистентность, сердечно-сосудистые заболевания, кардиометаболический риск, факторы риска, дети.

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