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ASSESSMENT OF INFLUENCING FACTORS IN ADOLESCENT HYPERTENSION

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1. INTRODUCTION

The clinical manifestation of hypertension mostly appears in adulthood, but might easily evolve in adolescence. Furthermore, the existence of target-organ damage can already be substantiated at this age. The prevalence of adolescent hypertension is much lower than that of adulthood hypertension. According to international epidemiological tests the occurrence ranges from 0.4% to 12%, while the Hungarian tests produced a result of 2.53 %. High importance is attributed to adolescent hypertension as adolescents with high blood pressure are likely to have hypertension in their adulthood.

There is a substantial distinction between the adult and adolescent hypertension. For adults epidemiological tests resulted a marked threshold between healthy normotension and clinical hypertension, which is 140/90 mmHg. In adolescence the young ones go through physical growth and maturity and neither the degree nor the rhythm of these changes are alike in the case of the two genders. Both the normal and the clinical blood pressure values vary according to genders. Blood pressure is also significantly influenced by one's height and age, therefore when determining the normal and clinical blood pressure values percentile diagrams are to be applied, which are widely used in paediatrics. According to this method the blood pressure of the tested young individual is to be compared to the blood pressure values of young ones' of the same gender, age, and height. Blood pressure is certified to be normal if neither the systolic nor the diastolic value exceed the 90th percentile value of the relevant subsample. In case of adolescents clinical hypertension is diagnosed if the average values of blood pressure recorded at least three different regular times in the day exceed the 95th percentile value typical of the given age, sex and height.

While for decades auscultator mercury blood pressure measurers were considered as standard, in the past two decades digital oscillometry manometers have been also spreading. By applying this new device ambulatory blood pressure monitors started to be used widely. In contrast with casual blood pressure measuring in the GP's office this new device enabled the patients to test themselves at home and it also allowed of ambulatory blood pressure monitoring as well as more in-depth study of the changes in blood pressure.

Using Ambulatory Blood Pressure Monitoring (ABPM) device is expressly wide-spread in the treatment of adult hypertension. The variations of blood pressure value recorded this way more clearly correlate with the target-organ damages, therefore ABPM plays a crucial role in defining cardiovascular risks as well as in their precise measuring. The device, which has been used extensively in the past decade, also allows of distinguishing the white coat hypertension and the masked hypertension. By white coat hypertension we mean that the blood pressure measured in the GP's office is constantly higher while the values measured at home are normal. In case of masked hypertension just the opposite is true: the values are normal in the GP's office and high at home. Considerably poorer is the scientific data in the available literature on the ABPM tests performed on adolescents, though – just like in the case of adults – it can provide useful information on episodic hypertension, hypotonic episodes and medicine resistance.

2. STUDY AIMS

In case of adult hypertension target-organ damage is often recorded. The most widely known – also meaning a separate cardiovascular risk factor – is the left ventricular hypertrophy and the thickening of the intima-media layer measured over the carotid arteries. Earlier tests already proved that adolescent hypertension also produces detectable target-organ damage.

Distinction between genders in adolescent hypertension

1. Is there a detectable difference between hypertensive male and female adolescents regarding
    a) anthropometric data,
    b) laboratory test results,
    c) blood pressure values,
    d) the concentration of nitric oxide and endothelin-1 in plasma,
    e) in the left ventricular mass index or in the intima-media thickness of common carotid arteries?
2. Is there a recordable difference between hypertensive and normotensive female adolescents with respect to
    a) anthropometric data,

b) laboratory test results,
c) blood pressure values,
d) the concentration of nitric oxide and endothelin-1 in plasma,
e) in the left ventricular mass index or in the intima-media thickness of common carotid arteries?

3. Is there a recordable difference between hypertensive and normotensive male adolescents with respect to
   a) anthropometric data,
   b) laboratory test results,
   c) blood pressure values,
   d) the concentration of nitric oxide and endothelin-1 in plasma,
   e) in the left ventricular mass index or in the intima-media thickness of common carotid arteries?

Research questions coming up while studying adolescent white coat hypertension:

1. Is adolescent hypertension diagnosed via repeated measurements performed by using ABPM verifiable? What is the prevalence of white coat hypertension in adolescence?
2. Are the adolescents with white coat hypertension healthy or ill?
   a) Is there a detectable difference between the anthropometric data and the laboratory test results of the normotensives and the white coat hypertensives?
   b) What types of distinction can be detected between the ABPM test results of the white coat and the sustained hypertensives?
   c) Is the target-organ damage (left ventricular hypertrophy, thickening of intima-media) detectable in case of adolescent white coat hypertension?

3. PATIENTS AND METHODOLOGY

3.1. The „Debrecen Hypertension Study”

Our working group performed a series of screening tests in order to measure the occurrence of clinical hypertension among secondary school pupils in Debrecen. 10 359 adolescents (aged between 15 and 18) were involved from 26 secondary schools of the town. 22 refused participation, and in case of 19 individuals the hypertension had been already detected and known therefore they could not be included in the sample.

3.2. Selection of the examined individuals

***Hypertensive sample*:** according to blood pressure values measured three times at three different points in the day in this sample the average systolic and/or diastolic blood pressure exceeded the 95th percentile value of the relevant subsample by age, sex and height. We found 216 hypertensive adolescents. The prevalence of hypertension was 1.97% in the female and 2.27% in the male adolescent sample. 61.3% (133 pupils) of the original sample of 216 agreed to go on with the examinations. In 13 cases secondary hypertension was verified, therefore these data were not used in the analyses.

Having asked for approval in the sample of 120 individuals (64 male and 56 female) we went beyond the routine examinations and determined the intima-media thickness of the common carotid artery (IMT). By using echocardiography we calculated the left ventricular mass index (LVMI) and also conducted 24-hour ambulatory blood pressure monitoring.

Normotensive sample: both systolic and diastolic blood pressure values were lower than the 90th percentile value of the relevant subsample selected by age, sex and height. Control subsamples of students in identical age, sex and height were randomly selected, following a written agreement from the individuals. Besides the routine laboratory examinations we determined the concentration of nitric oxide and the endothelin-1 in plasma, the thickness of intima-media in the common carotid artery, we calculated the left ventricular mass index (LVMI) by using echocardiography, and 24-hour ABPM was also performed.

In both samples measuring height and weight happened before taking the blood pressure, BMI calculation was performed on the basis of this data set.

3.3. Blood pressure measuring

Testing always happened between 8 a.m. and 13 p.m. in the classroom of the young individuals according to the international ethical norms. We considered the average of the systolic and diastolic values of 3 measurements carried out with five minutes intervals on the right arm, in sitting position after 10 minutes resting. We used validated OMRON M4 digital oscillometric manometer (OMRON Healthcare GmbH, Germany). One hour before the measurement the tested young individuals were not allowed to smoke and to have drinks with caffeine.

The adolescents were grouped according to their sex and age. The age categories: aged 15 (between 14.5 and 15.49 years of age), aged 16 (between 15.5 and 16.49 years of age), aged 17 (between 16.5 and 17.49 years of age), aged 18 (>17.5 years of age).

After the determination of the 25, 50 and 75th percentile value of these eight groups further subsamples were formed according to the quartels of height. Finally, altogether 32 subsamples were formulated. In each subsample we determined the blood pressure percentiles focusing on the 90th and 95th baseline percentiles. As long as the systolic and diastolic blood pressure value exceeded the 90th percentile value of the relevant subsample, at two different occasions three repeated blood pressure measurings were performed the average of which were finally taken for analyses.

3.4. 24-hour ambulatory blood pressure monitoring

The ambulatory blood pressure monitoring happen by using oscillometric ABPM-04 (Meditech Ltd. Budapest, Hungary) device. The placement of the devices took place between 8-9 a.m. and were removed 24 hours later. The measurements were performed with 15 minutes intervals during daytime (between 6 a.m. and 22 p.m.), and with 30 minutes intervals during nighttime (between 22 p.m. and 6 a.m.). For calculating the daytime average the values measured between 10 a.m. and 20 p.m. were used, while for gaining the nighttime average blood pressures measured between midnight and 5 a.m. were considered.

The following derived parameters were used:

- diurnal index (%) – the degree of nighttime blood pressure decrease;
- percent time elevation (%) – period of increased blood pressure;
- hypertensive load (mmHg x h) – degree of pressure load.

The daytime and nighttime systolic and diastolic blood pressure average values were determined.

Hypertension was verified if the average of at least one of the blood pressure parameters (daytime systolic, daytime diastolic, nighttime systolic, nighttime diastolic) exceeded the recommended 95th percentile value of the relevant group for the given individual.

The teenager was considered to be ***white coat hypertensive*** (i.e. besides occasionally recorded higher blood pressure, ABPM test results are normal) as long as the average of all the examined parameters was lower than the recommended 95th percentile value.

3.5. Laboratory tests

Blood samples were taken in the morning hours before meals by the closed vacationer technique (Beckton & Dickinson). The determination of the routine laboratory parameters (serum sodium, potassium, glucose, urea, creatinine, triglyceride, LDL-, HDL- and total cholesterol) happened with validated laboratory automatic devices by using methods standardized and validated in the DE OEC Clinical Biochemistry and Molecular Pathological Institute.

To gain the endothelin-1 (ET-1) concentration within the plasma we used a kit produced by Biomedica (Biomedica Group, Vienna, Austria). The samples were stored at -70^{o}C until processing. The results were given in fmol/ml.

The measuring of the active nitric oxide (NOx) occurred by determining the nitric oxide ratio (NOx = NO_2 + NO_3), (which is widely discussed by international literature). This was determined immediately after the blood sample had been taken by modifying Green's method. According to this method the plasma proteins were precipitated in 100 µl 35 % sulfo-salicil acid beforehand, then by separating in the Eppendorf centrifugal machine (10 minutes, 10000xg) 0.4 ml protein-free plasma was put into a test-tube filled with cadmium granules. This substance makes the NO_3 – NO_2 reduction possible, 0.3 ml of this solution is mixed with 0.3 ml Griessa reagent (one unit of 0.1 % concentration naftil-ethilen-diamid and 1 unit of 1 % concentration sulfanilamid) and it was incubated in 60 C^{o} warm water for 20 minutes. The absorption of the samples was determined by using spektrophotometre (Hewlett Packard 8453, USA) on 546 nm. The NOx value of the plasma was given in µmol/l.

3.6. Ultrasound diagnostic methods

3.6.1. Determining the intima-media thickness of the common carotid artery

Measuring intima-media thickness in the common carotid artery happened by using 7 MHz linear array probe (Hewlett-Packard Sonos 2000, USA).

The transducer was placed behind muscle of sternocleidomastoideus, first bifurcation of the carotid artery was found, followed by the flow divider between the internal and external carotid arteries. Flow divider means the area on ultrasound picture seeming as “flow divider”, from where proximal at 2 cm distance a measurement on the common carotis section opposite to the probe was performed. The IMT was determined as the distance between the lumen-intima layer and the media-adventitia interface. Three measurings were performed, and evaluation considered the mean averages.

3.6.2. The determination of the left ventricular hypertrophy (LVH)

In each subsample transthoracic M-mode and bidimensional echocardiography happened (2.0-2.2 MHz transducer, Hewlett-Packard Sonos 2000, USA). We calculated left ventricular mass (in grams) by ways of the method and according to the formula proposed by Devereux:

0.8 x [1.04 x (interventricular septum + left ventricular end-diastolic diameter + left ventricular end-diastolic posterior wall diameter)^3- (left ventricular end-diastolic diameter)^3] + 0.6.

By the correction of left ventricular mass – produced as described above – to the total body surface we gained the left ventricular mass index (LVMI). In order that we can make the influential role of the body size independent in the case of adolescents, the LVMI calculated with the Devereux – formula needed to be raised to the power of 2.7 of the height expressed in meters. Left ventricular hypotrophy was justified if the left ventricular mass exceeded the 95th percentile of the control group.

3.7. The methods of statistical assessment

For the analysis of the data we used the software called Statistica for Windows (Statsoft, Tulsa, USA). For each parameter mean average and standard deviation were calculated. The parameters were assessed with the Shapiro-Wilk test first in order to conclude if we talk about normal or abnormal distribution samples. In case of normal and abnormal

distribution the data were compared by using ANOVA and Kruskal-Wallis ANOVA tests respectively. The non-parametric data were processed by using the khi-square test. The link between the thickness of the intima-media and the laboratory test results (parameters) was examined with linear regression or Spearman-correlation test. In the case one-direction hypothesis we made a test of one side significance. For the tests the level of significance was determined in 5%.

4. RESULTS

4.1. Difference between genders in adolescent hypertension

4.1.1. The characteristics of the young hypertensive population

When comparing the two sexes 114 young hypertensives, 58 males and 56 females were examined, whose age 16.5 y ± 1.2 vs. 16.4 ± 0.8 y and body mass index (23,7 ± 3,9 kg/m^2 vs. 23,7 ± 4,3 kg/m^2; p=0,8) did not show any difference. Significant distinction was found among adolescent hypertensives regarding height (179,4 ± 6,7 cm vs. 166,6 ± 6,5 cm; p<0,001) and weight (76,3 ± 14,8 kg vs. 65,8 ± 15,7 kg; p<0,001), young male hypertensives were 13 cm taller and their weight was 11 kg greater than that of the examined female individuals. Examining metabolism parameters the total (3,9 ± 0,7 mmol/l vs. 4,6 ± 0,7 mmol/l; p<0,001), HDL- (1,1 ± 0,3 mmol/l vs. 1,1 ± 0,3 mmol/l; p<0,001) and LDL-cholesterol (2,2 ± 0,7 mmol/l vs. 2,5 ± 0,6 mmol/l; p<0,01) level was significantly higher in case of girls but stayed within the normal range. There was no difference between sexes regarding nitric oxide and endothelin-1 plasma concentration. When comparing the blood pressure values the casual systolic blood pressure (148,1 ± 5,9 mmHg vs. 133,8 ± 8,0 mmHg; p<0,001) measured with the mean arterial pressure and the ambulatory blood pressure monitoring – also considering the daytime (138,88 ± 8,66 Hgmm vs. 130,68 ± 9,51 Hgmm; p<0,001) , nighttime (119,76 ± 9,66 mmHg vs. 112,5 ± 11,38 mmHg; p<0,001) and 24-hour values (132,42 ± 8,51 mmHg vs. 124,65 ± 9,31 mmHg; p<0,001)– the mean systolic blood pressure was significantly higher in case of male hypertensives. From the examined target-organ damages the left ventricular mass index was higher for male than for female hypertensives ($1.8x10^{-4}$ ± $5.4x10^{-5}$ g/m^2 vs. $1.4x10^{-4}$ ± $4.57x10^{-5}$ g/m^2; p<0.001). The intima-media thickness of carotid arteries was the same for both sexes.

4.1.2. Comparative analyses of young female normotensives and hypertensives

Data gained from the examination of 56 hypertensive girls were compared to the test results of the randomly selected 30 normotensive ones. The weight of the hypertensive girls exceeded that of the normotensive ones by 10 kg, besides, their BMI (19,7 ± 2,3 kg/m^2 vs. 23,7 ± 4,3 kg/m^2; p<0,001) was also higher. The serum glucose (4,6 ± 0,5 mmol/l vs. 5,5 ± 1,7 mmol/l; p<0,001), total- (4,0 ± 0,6 mmol/l vs. 4,6 ± 0,7 mmol/l; p<0,001) and LDL-cholesterol (2,1 ± 0,5 mmol/l vs. 2,5 ± 0,6 mmol/l; p<0,001) concentration were significantly higher with hypertensive girls than with normotensive ones. In spite of the facts that the cardiovascular risk factors stayed within the normal range in case of the hypertensives, the difference can be still taken as considerable. Both systolic and diastolic blood pressure values and also the mean arterial pressure were significantly high in the sample of the hypertensive girls (110,7 ± 8,7 mmHg vs. 133,8 ± 8,0 mmHg; p<0,001 and 64,7 ± 7,2 mmHg vs. 83,3 ± 4,9 mmHg; p<0,001). No marked difference could be recorded regarding endothelin-1 plasma concentration between the two subsamples of girls. Sharp distinction was detected however in the plasma nitric oxide concentration: it was lower in the case of hypertensive girls (38.4 ± 7.9 umol/l vs. 27.1 ± 14.0 umol/l; p<0.001).

The left ventricular mass index was quite similar (1,4 x 10^{-4} ± 4,57 x 10^{-5} g/m^2 vs. 1,4 x 10^{-4} ± 3,6 x 10^{-5} g/m^2, p = 0.80), while regarding the intima-media thickness of the carotid artery there was detectable difference in case of hypertensive girls (0.046 ± 0.01 cm vs. 0.054 ± 0.01 cm; p<0.001).

4.1.3. Comparative analyses of young male normotensives and hypertensives

Data gained from the examination of the 58 hypertensive boys were compared to the test results of the randomly selected 30 male normotensive adolescents. From among the anthropometric parameters weight was markedly different as it was 8 kg more in the case of hypertensive male adolescents, and their BMI was also higher (20,7 ± 2,9 kg/m^2 vs. 23,7 ± 3,9 kg/m^2; p<0,001).

In case of hypertensive boys the serum glucose concentration were significantly (4,9 ± 0,5 mmol/l vs. 5,6 ± 0,6 mmol/l; p<0,001), but stayed within the normal range, total- and LDL-cholesterol concentration was similar.

In the hypertensive group the casual blood pressure values and the mean arterial pressure values were also considerably higher (31/14 mmHg). The nitric oxide level playing an important role in vasodilatation was lower in the case of hypertensive boys (39,3 ± 7,4 umol/l vs. 33,4 ± 23,4 umol/l; p<0,001), however the endothelin-1 plasma level was higher (3,6 ± 4,1 fmol/ml vs. 1,1 ± 0,9 fmol/ml; p<0,01) relative to the male normotensive subsample.

Comparing the hypertensive and normotensive male subsamples with respect to the examined target-organ damage there were significant deviations found both for left ventricular mass index and intima-media thickness of the carotid artery in the group of hypertensives (LVMI: 1,8 x 10^{-4} ± 5,4 x 10^{-5} g/m^2 vs. 1,4 x 10^{-4} ± 4,7 x10^{-5} g/m^2; p<0,01 and IMT: 0,056 ± 0,01 cm vs. 0,049 ± 0,01 cm; p=0,008).

4.2. The importance of the adolescent white coat hypertension

From the participants of the Debrecen Hypertension Study – described above – 133 individuals turned up to go on with further examinations. In the sample, in 13 cases secondary form of hypertension was justified, therefore their data were left out of the analyses. 24-hour blood pressure monitoring was performed with the 120 adolescents (64 male, 56 female), which justified hypertension in 73 cases: half of the girls (28 individuals) and 70% of the boys (45 individuals). Besides, in 47 cases white coat hypertension was diagnosed. As a consequence the diagnosis of hypertension needed to be revised in the case of the 120 adolescents involved in our study: the sufficient diagnosis is white coat hypertension in 47 cases: 28 girls (50%) and 19 boys (30%).

There was no deviation between the average age 15.8 ± 0.6 vs. 16.3 ± 1.1 year, or the distribution between sexes (30/29 vs. 19/28) in the normotensive and the white coat hypertensive subsamples. The white coat hypertensives weighted 6 kg more (58,3 ± 11,5 kg vs. 64,1 ± 13,8 kg; p<0,05) and the value of their BMI was higher than in the normotensive group (20,2 ± 2,7 kg/m^2 vs. 21,8 ± 3,5 kg/m^2; p<0,05). The risk factors examined (serum glucose and lipids) in the two groups did not show any difference.

The systolic and diastolic blood pressure values were quite similar for the hypertensive adolescents and the white coat adolescents. Considering the 24-hour (125,2 ± 9,3 mmHg vs. 130,8 ± 9,5 mmHg; p<0,01), the daytime (131,3 ± 9,1 mmHg vs. 137,2 ± 10,0 mmHg; p<0,001) and nighttime values (112,3 ± 9,8 mmHg vs. 118,7 ± 11,1

mmHg; p<0,001)the average systolic values, the percent time elevation referring to systolic blood pressure and also the hypertensive load were significantly higher in the group of adolescents with sustained hypertension. However, there were no distinctions between the two groups regarding diastolic blood pressure values and pulse rate.

When comparing the target-organ damages examined in the study, it was found that the intima-media thickness of the carotid artery was significantly greater in the groups of white coat and sustained hypertensive adolescents than in the group of normotensives. The difference compared to the values of the healthy group was similar (0.048 ± 0.01 cm vs. 0.056 ± 0.01 cm vs. 0.054 ± 0.012 cm). Regarding left ventricular mass index in the normotensive and white coat hypertensive adolescent groups there was no distinction (37,7 ± 11,2 $g/m^{2,7}$ vs. 35,5 ± 10,3 $g/m^{2,7}$; p=0,87). With respect to this target-organ damage the white coat hypertensive adolescents can be considered as healthy. Compared to these two groups marked differences can be traced in the group of hypertensives (35.5 ± 10.3 $g/m^{2,7}$ vs. 37.7 ± 11.2 $g/m^{2,7}$ vs. 44.1 ± 14.1 $g/m^{2,}7$; p<0.001 and p<0.05).

When examining factors causing target-organ damages for adolescents it was found that in the case of both left ventricular mass index (p=0.192) and the intima-media thickness of the carotid artery (p=0.202) independently from BMI and the lipid parameters hypertension alone is an explaining cause.

5. DISCUSSION

5.1. Difference of genders in adolescent hypertension

The cardio- and cerebrovascular diseases are considered as classic problems of the male population and women in post menopause. Nevertheless, in the United States analyzing the data of the hospitalized population aged under 45 a sharp increase in the number of ischemic stroke cases was found, which was most probably caused by overweight and hypertension. Scrutinising the distinctions between gender the male population proved to suffer from hypertension more frequently than the female population of the same age. This suggests that physiological control over blood pressure varies for the two sexes. Nowadays the available data is scarce for the gender-dependent distinctions in adolescent hypertension.

In our analyses comparing the sexes in the hypertensive adolescent group in case of male individuals the average systolic blood pressure was significantly higher. Also in the mean arterial pressure and ambulatory blood pressure monitoring the male subgroup produced increased average systolic blood pressure. In the total sample of adolescents examined in our program the difference was less marked than it is recorded in adulthood.

5.1.1. The significance of nitric oxide and endothelin-1

According to former analyses it might be assumed that in the hypertensive adult population sexual hormones might have a role in modifying the vascular function as they influence the endothelium dependent vasoconstriction factors, e.g. the level of ET-1 and NO production.

Contrasting hypertensive male and female adolescent subsamples the level of both NO and ET-1 was alike in our examination, therefore Khalil's statements could not be attested. Nevertheless, we need to note that our observations and measurements were performed in the group of adolescents aged between 15 and 18 years and in their case the balance of sexual hormones is not comparable with that of the adults. In our former examination programs on adolescent hypertension we observed that the activity of the ET-1 system was increased, while that of the NO system was decreased. Comparing healthy and hypertensive girls in the second case the NO plasma concentration decreased, while ET-1 concentration did not show significant deviation. In the male subgroup in the hypertensive subsample the NO plasma concentration also decreased, while the ET-1 concentration was elevated. Some research results suggest that vasoconstriction evolves as the consequence of a change in the NO/ET-1 ratio. Other research findings stress the role of vasoconstriction dominance evolving as the result of decrease in the basal vasodilatation tone in the diseases characterized with different vein and endothelium damages. According to observations, in case of hypertension the NO concentration was decreased in the subsamples of both sexes, which – in line with earlier studies – is continuously produced in the endothelium and plays an important role in the evolving of the basal tone of the veins. The deviations observed suggest that disturbance in the balance of NO and endothelin-1 has importance in the

pathophysiological mechanisms of hypertension in adolescents as well, and NO might have a notable role in this phenomenon.

Nevertheless, differences between hypertensive boys and girls cannot only be explained by deviations occurring in the concentration of vasoactive substances caused by sexual hormones.

5.1.2. Target-organ damage, left ventricular hypertrophy

In an earlier research program performed among adolescents the left ventricular mass index was found increased in the healthy male subsample compared to the healthy females. In our present study in the sample of hypertensive adolescents when dealing with the target-organ damages the left ventricular mass index was also higher compared to the hypertensive female subsample. These findings make us conclude that the difference of LMVI in the hypertensive male and female samples also originates from the general distinctions of sexes. At the same time this statement is not supported by the fact that in the course of contrasting the normotensive adolescents no difference was found in the left ventricular mass index of the male and female subsamples. No deviation could be detected between the left ventricular mass index of the healthy and the hypertensive girls, which indicates that myocardium was not yet affected regarding target-organ damage. When contrasting the test results of the male sample major increase was recorded in the group of hypertensive boys.

Examinations of younger (9-11 years old) children were closed with conclusions quite similar to ours: left ventricular hypertrophy, significantly increased left ventricular mass index were found in the hypertensive sample and among boys.

5.1.3. Target-organ damage, intima-media thickness of the carotid arteries

According to the relevant literature the intima-media thickness of the carotid artery was greater in the adolescent hypertensive subsample compared to the healthy one. The significance of this is emphasized by Sorof et al. in their study on carotid doppler examinations: in the case of young hypertensives by measuring the intima-media thickness of the carotid artery the early artery wall deformation and cardiovascular consequences can be forecast.

According to a prospective observation performed in Finland, while the cardiovascular risk factors measured in adolescent in both gender showed coherence with the intima-

media thickness recorded in adulthood, the cardiovascular risk factors measured at earlier ages and the intima-media thickness showed coherence only in case of boys. This makes us assume that the increased intima-media thickness of the carotid arteries is a possible risk factor of men too.

In contrast with this no difference could be found when contrasting sexes in the hypertensive sample: the intima-media thickness proved to be similar for the male and female samples. One possible explanation of this is that in their case both the systolic and the diastolic blood pressure was 10-10 Hgmm higher than as it was described in Raitakari's study.

The higher blood pressure values and the consequential chronically higher shear stress on the vessel walls probably caused an increased IMT was similar magnitude in boys and girls.

5.2. The significance of the white coat hypertension

In the last proposal of the European Hypertension Society concluded that childhood and adolescent high blood pressure is more prevalent, than it was found earlier. The term "tracking" phenomenon was formulated for this young population: i.e. young individuals with constantly high blood pressure will most probably be hypertensive in their adulthood. In the earlier proposals to formulate the diagnosis of adolescent hypertension repeated casual blood pressure measuring is required, performing ambulatory blood pressure monitoring is not obligatory.

In our research program 216 adolescent hypertensives were found in the total sample of the secondary school pupils of Debrecen, the prevalence of hypertension was 1.97% in the female and 2.27% in the male subsample. From among the 216 hypertensives 133 entered the further examinations. In 120 cases of adolescent primer hypertension (64 boys and 56 girls) beyond the routine examinations 24-hour ambulatory blood pressure monitoring was performed. In 60.8% of the sample of these pupils the diagnoses of hypertension was justified, in 39.2% of the sample white coat hypertension was found. The results support the statement that before starting off the medical treatment of adolescent hypertension 24-hour ambulatory blood pressure monitoring would be expedient, as the diagnosis of white coat hypertension can also be formulated by using

this method. In our current research program the focus was placed on that part of the secondary school age group in which white coat hypertension was justified.

We intended to find out if their representative parameters are more like those of the normotensive or of the hypertensive adolescents.

5.2.1. Anthropometric values and laboratory test results

Regarding the anthropometric characteristics of white coat hypertensives compared to the data of the healthy subsample elevated values were recorded for height, weight and BMI, but these values did not reach the levels experienced in the group of hypertesnsives. In the laboratory test results the values of the risk factors included in our examinations did not show any difference.

5.2.2. The blood pressure values of the adolescent white coat hypertensives

The casual systolic blood pressure values were alike for the white coat and sustained hypertensive adolescent groups. The systolic values recorded in the course of the ambulatory blood pressure monitoring were higher in the sustained hypertensive adolescent group. In this research the difference of the casual blood pressure values was 6.5 mmHg, which statistically was not significant, however the difference recorded by using ABPM was marked ($p < 0.01$) 5.6 mmHg. A possible explanation is that data gained from the ambulatory blood pressure monitoring can more easily be reproduced, consequently the deviation turned out to be statistically significant, the value of the deviations were similar for the two blood pressure measuring techniques.

In line with what is found in the relevant literature, in the adolescent subsample where hypertension was diagnosed, isolated systolic hypertension was also justified. In the research the values of the diastolic blood pressure were similar in both hypertensive groups and they stayed in the normal range.

5.2.3. Target-organ damage, the intima-media thickness of the carotid arteries

In an earlier examination of carotid artery in adult white coat and borderline hypertensive samples the intima-media was found thicker than in the control group. The research outcomes of other authors also indicate that the IMT measured in pre-hypertensive state falls in between values measured in normo- and hypertensive samples. The examinations first mentioned were performed among the adult population, no similar examination for adolescent samples were completed.

Our working group was focusing on the comparison of target-organ damage occurring in the adolescent population. It was recorded that the IMT was increased in the white coat hypertensive group compared to what was found in the sample of healthy adolescents and was quite similar to values recorded in the hypertensive group.

5.2.4. Target-organ damage, left ventricular hypertrophy

When examining the healthy, pre-hypertensive and hypertensive children and adolescents aged between 5-18 Stauboli et al. found that in case of higher blood pressure values left ventricular hypertrophy occurred and the left ventricular mass index was also increased.

In our present study left ventricular mass index measured in the white coat hypertensive group hardly differed from the normotensives, and having applied the Bonferroni correction this deviation turned out to be non- statistically significant. This suggests that in the population examined by ourselves the white coat hypertensive adolescents can be considered as healthy. However, marked differences were experienced in the hypertensive subsample compared to the other two groups, i.e in the case of sustained hypertension the left ventricular was thicker than in either the white coat hypertensive or in the normotensive sample.

All these considered we think that the development of target-organ damage commences already in the early stage of hypertension, therefore it can be detected in the case of white coat hypertension. Puato et al. reported similar results for adult samples: the intima-media thickness of carotid artery was similarly higher in the grade-1 and white coat hypertensive subsamples than in the normotensive group. In line with our research findings the left ventricular mass index was higher only in the case of justified first garde-1 hypertension compared to healthy control group.

Formerly white coat hypertension was considered as benignus state but the results of the follow-up examinations published recently indicate that white coat hypertensives already produce the signs of cardiovascular risks.

6. SUMMARY

Hypertension is the most prevalent cardiovascular disorder affecting 35-45% of the adult population. The new guideline for adolescent hypertension of European Society of Hypertension emphasizes the fact that increased blood pressure during childhood is more common that was previously recognized.

1. Our results indicate that there are differences in the blood pressure values of adolescent hypertensive girls and boys. Both casual and 24-hour systolic blood pressure values were higher in boys.

2. We were unable to detect any difference in IMT of hypertensive adolescent boys and girls.

3. The potential role of an NO/ET-1 imbalance in adolescent hypertensives is well-known. We found the activity of the NO is decreased in both gender groups and the activity of the endothelin-1 system is increased in boys. We showed there are no difference between plasma NO and ET-1 concentrations of female and male hypertensive teenagers.

4. In case of repeated elevated casual blood pressure ABPM is required just to differentiate white-coat hypertension.

5. We found that IMT values of the carotid arteries are higher in WCH subgroup than in healthy controls and similar to sustained hypertensive adolescents. On the other hand the LVMI of white coat hypertensives are similar to normotensives. Our results indicate that target-organ damage develops in stepwise fashion in adolescent hypertension. We emphasize the importance of regular blood pressure measurements also in adolescents, just to diagnose hypertension in time.

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List of publications related to the dissertation

1. **Juhász, M.**, Katona, É., Settakis, G., Paragh, G., Molnár, C., Fülesdi, B., Páll, D.: Gender-related differences in adolescent hypertension and in target organ effects.
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