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Tamara Turlyun

Department of Internal
Medicine, State Establishment
“Dnipropetrovsk Medical
Academy of Health Ministry of
Ukraine,” Dnipropetrovsk,
Ukraine.

Natalya Pertseva

Department of Endocrinology,
State Establishment
“Dnipropetrovsk Medical
Academy of Health Ministry of
Ukraine,” Dnipropetrovsk,
Ukraine.

Clinical laboratory features of arterial hypertension in patients with different cardiovascular risk at the beginning of the research

Tamara Turlyun and Natalya Pertseva

Abstract

The issue of studying features of endothelial dysfunction of vessels in patients with arterial hypertension (AH) and different cardiovascular risk remains essential. While studying two groups of patients with moderate and a high risk for developing cardiovascular conditions it has been determined that, body mass index (BMI) increased significantly more expressed in the group with AH with the high risk for cardiovascular conditions ($p < 0.01$ in comparison with the first group). Ratio WC/HC and WC/height exceeds the recommended indices, which confirms the presence of overweight in the main part of the studied patients in general. DBP in the second group has been reliably higher than the indices of the first group ($p < 0.001$). The average value of TC exceeds the recommended values, level of high-density lipoproteins (HDL) has been confirmed to be different in both groups at the beginning of the research and it has been higher in the first group ($p < 0.05$). In the group of the high risk, irrefutable increase in endothelin-1 (ET-1) and vWF (von Willebrand factor) has been observed compared to indices in the group with a moderate risk ($p < 0.001$), which testifies to more expressed vasoconstriction and progressive blood clots in vessels.

Keywords: arterial hypertension, endothelial dysfunction, moderate cardiovascular risk, high cardiovascular risk, Diabetes Mellitus type 2, endothelin-1, thrombomodulin, von Willebrand factor

Introduction

Despite the increase in control over arterial pressure around the world, the increase in a number of patients with hypertonic disease alarms. Further study of clinical-functional features of AH in patients with different clinical groups with the research on ways of correcting not only arterial hypertension itself but also associated microcirculatory, endothelial and metabolic disorders with determination of additional organs-targets with the development of the differentiated approach to therapy and evaluation of anti-hypertension treatment effectiveness criteria, remains actual [4].

The issue of studying features of endothelial dysfunction of vessels in patients with AH and different cardiovascular risk is of current importance [5]. Vulnerability of endothelial cells to pathogenic factors of the system blood flow is defined by their unique position on the edge between circulating blood and tissues. Dysfunction of endothelium causes disorder in control over vascular tone, blood clots, fibrinolysis [1,3].

According to Framingham study, the main factors of endothelial dysfunction of arteries are increased body mass index (BMI), AH, age, smoking, dyslipidemia, DM and so on, they intensify the processes of oxidative stress, which violates the balance between protective and damaging influence on the vascular wall and leads to initiation and progression of pathological changes in vessels [7].

The purpose of the research is to study features of endothelial dysfunction in patients with AH, associated with a moderate and a high risk for cardiovascular conditions.

Materials and methods.

102 patients with DM 2 type aged 42-73 were under observation; they were distributed into two groups by the risk for development of cardiovascular conditions: I group – 48 patients with AH and a moderate risk, II group – 54 patients with AH and a high cardiovascular risk (DM 2 type). Among the studied patients 34 (33.3%) were men and 68 (66.7%) women. Average duration of AH was 10.09 ± 0.59 years.

Both groups of patients were compared by gender, age and duration of AH – in all comparisons $p > 0.05$ (Table 1).

Correspondence

Tamara Turlyun

Department of Internal
Medicine, State Establishment
Dnipropetrovsk Medical
Academy of Health Ministry of
Ukraine,” Dnipropetrovsk,
Ukraine.

Table 1: General and clinical characteristics of patients of main groups at the beginning of the research (M±m)

Index		Total (n=102)	I group (n=48)	II group (n=54)	p between groups
Gender	males	34 (33.3%)	19 (39.6%)	15 (27.8%)	>0.05
	females	68 (66.7%)	29 (60.4%)	39 (72.2%)	
Age, years		56.2±0.62	55.4±0.95	56.9±0.80	>0.05
BMI, kg/m ²		27.8±0.23	27.1±0.37	28.4±0.25	<0.01
Duration of AH, years		10.09±0.59	9.48±0.77	10.64±0.88	>0.05
Duration of DM, years		4.89±0.40	–	4.89±0.40	<0.001

The control group was 15 clinically healthy by the main disease people who were compared by age (average age was 58.0±1.2 years old; $p>0.05$) and gender (6 males and 9 females; $p>0.05$). Level of endothelin-1 (ET-1) in blood of practically healthy people was 0.37±0.06 fmol /ml, vWF - 0.7±0.2 U/ml, triglycerides 2.5±0.07 ng/ml, which is considered to be a norm for the region.

The level of AH in patients of both groups corresponded to criteria of moderate and high AH, according to recommendations of Annual European Conference on Arterial Hypertension, edited and amended in 2013. [2, 6].

Apart from general clinical examination, the following special clinical-laboratory parameters have been studied: concentration in blood serum of markers of endothelial dysfunction (endothelin-1, trombomodulin and von Willebrand factor), concentration of total cholesterol (TC), high and low density lipoprotein cholesterol (HDL and LDL), triglycerides (TG) and atherogenic index (AI), calculated according to the well-known formula for TC and HDL. Besides the speed of glomerular filtration rate (GFR) and levels of creatinine and urea have been estimated. All laboratory examinations have been carried out considering recommendations of manufacturing companies based on contemporary principles of laboratory technologies. Immunoassay analysis of markers of endothelial dysfunction (ED) was carried out on the base of the diagnostic center of LLC “Apteky Medychnoyi Akademiyi” (Dnipropetrovsk) with the help of reagent kits made by “Technoclone GmbH” and “Biomedica Medizinprodukte” (Austria).

Statistic processing of results of the research has been done with the help of the licensed software Statistica, version 6.1®. Reliability assessment of differences between means has been carried out according to Student’s test (t) considering homo or heteroskedasticity variance (Fisher’s exact test), relative measures – Pearson’s chi-squared test (χ^2).

Results and discussions.

Level of systolic blood pressure (SBP) in the first group was 166.9±0.6 mmHg, in the second group – 167.7±0.8 mm Hg, without reliable differences between them ($p>0.05$) (Table 2). At the same time, indices of diastolic blood pressure (DBP) in patients with AH and a high cardiovascular risk were 6.0 mmHg or 7.5% higher than those of the patients from the first group ($p<0.001$).

Table 2: Level of arterial pressure in patients of main groups at the beginning of the research (M±m)

Index	I group (n=48)	II group (n=54)	p between groups
SBP, mmHg	166.9±0.60	167.7±0.83	>0.05
DBP, mmHg	79.7±1.20	85.7±1.05	<0.001

One of the major predictors of developing cardiovascular conditions is overweight. BMI on average was 27.8±0.23

kg/m², which means overweight in all groups of the studied patients (Table 1). At that in the group with AH and DM 2 type BMI was 4.8% higher than indices of the first group ($p<0.01$), which implies additional factor of developing cardiovascular conditions.

It is worth noting that in case of sportsmen, children and gender BMI does not necessarily define overweight. Among additional parameters are indices of waist circumference (WC) and hip circumference (HC), height and their ratio WC/HC, WC/height. The recommended waist circumference for evaluating the distribution of fat tissue in women is 80 cm, in men – 94 cm. Indices higher than 88 cm in women and 102 cm in men indicate a higher risk of developing cardiovascular complications and diabetes mellitus in future (WHO, 1997). According to the results of our research indices of WC in women of both groups significantly exceed the norm – 98.0±2.06 cm in the first group and 97.1±1.13 cm in the second group ($p>0.05$ between groups) (Table 3).

Table 3: Indices of WC, height and their ratio depending on gender of patients in main groups at the beginning of the research (M±m)

Index		I group (n=48)	II group (n=54)	p between groups
WC	males	94.5±1.9	95.9±1.51	>0.05
	females	98.0±2.06	97.1±1.13	>0.05
WC/HC	males	0.91±0.010	0.89±0.015	>0.05
	females	0.85±0.009	0.88±0.007	<0.01
WC/height	males	0.54±0.011	0.55±0.008	>0.05
	females	0.60±0.014	0.60±0.007	>0.05

Ratio WC/HC characterizes the possibility of developing abdominal overweight as a predictor of developing cardiovascular conditions in future. In females of the second group ratio WC/HC was 3.5% higher than that one of the first group- 0.88±0.007 compared to 0.85±0.009 ($p<0.01$). Overall the increase in norms of ratio WC/HC was observed in 42.2% (43 patients) cases, including in the first group- 22.9% (11 patients out of 48), in the second group – 59.3% (32 out of 54 patients) ($p<0.001$ between groups), which indicates additional risk factor in patients with AH, especially in combination of AH with DM 2 type.

Ratio WC/height is another sign of abdominal obesity. It is even more qualitative than BMI, since while calculating features of skeleton, muscular features of a certain person, distribution of fat tissue are not considered. Normal ratio is 0.42-0.49 for women and 0.43-0.53 for men. The increase in its value means overweight. At the beginning of the research this index was higher than norm in 55.9% males (19 out of 34) and in 97.1% females (66 out of 68), without reliable differences between the studied groups ($p>0.05$) (Table 3).

Thus during estimation of indices of abdominal obesity as an additional factor of developing cardiovascular conditions, we can note that BMI is increased both in the first and in the second group, but it is more expressed in the group of AH with

a high risk for cardio-vascular conditions ($p < 0.01$ compared to the first group). Ratio WC/HC, WC/height exceeds the recommended indices, which confirms overweight in the main part of the studied patients in general. In the process of observation the patients are reasonable to be recommended to control their weight.

All patients at the stage of the research had general clinical, laboratory and special methods of examination.

Level of Hb in the first group at the beginning of the research was 130.6 ± 0.51 g/l, in the second group – 135.9 ± 1.91 g/l, and was reliably different ($p < 0.05$ according to Student's test), however, clinically significant decrease of index compared to norm has not been determined in any group (Table 4).

Table 4: Level of Hemoglobin in patients of main groups at the beginning of the study (M±m)

Index	Total (n=102)	I group (n=48)	II group (n=54)	p between groups
Hb, g/l	133.4±1.07	130.6±0.51	135.9±1.91	<0.05

The direct and indirect inclusion of dyslipidemia into the mechanism of development and progression of ED has been confirmed. Therefore all patients were examined by the lipid profile in dynamics of the research (Table 5).

Table 5: Level of indices of lipid profile in patients of main groups at the beginning of the research (M±m)

Index	Total (n=102)	I group (n=48)	II group (n=54)	p between groups
TC, mmol/l	5.57±0.10	5.70±0.12	5.46±0.16	>0.05
HDL, mmol/l	1.29±0.03	1.35±0.05	1.23±0.04	<0.05
LDL, mmol/l	3.35±0.08	3.44±0.11	3.28±0.12	>0.05
TG, mmol/l	2.00±0.09	1.82±0.10	2.16±0.15	>0.05
AI	3.50±0.11	3.42±0.17	3.57±0.15	>0.05

At the initial stage of the research the analysis of lipid profile did not determine statistically significant differences in patients of the first and second groups by the level of TC: in the first group this index was 5.70 ± 0.12 mmol/l, in the second group – 5.46 ± 0.16 mmol/l ($p > 0.05$). The average value of TC by groups was 5.57 ± 0.10 mmol/l, which exceeds the values indicated by recommendations of ESC (2013) [2, 5].

Level of HDL reliably differs in two groups of the research and it was 9.8% higher in the first group ($p < 0.05$), which indicates more expressed antiatherogenic features and less progressive dysfunction of endothelium in future (Table 5).

Level of cholesterol LDL in both groups was high – 3.44 ± 0.11 mmol/l in the first group and 3.28 ± 0.12 mmol/l in the second group but without reliable differences between them ($p > 0.05$).

Level of TG at the beginning of the research in the second group was increased (2.16 ± 0.15 mmol/l) compared to patients of the first group (1.82 ± 0.1 mmol/l) with $p = 0.061$ according to Student's test, which characterizes DM as the predictor of a high risk of cardiovascular condition.

Index AI has been estimated based on TC and HDL, therefore it is directly connected with these indices. In the first group this index was 3.42 ± 0.17 , in the second group – 3.57 ± 0.15 without reliable differences ($p > 0.05$). (Table 5) Since the defining index in calculation of this index is HDL, despite the fact that TC is higher in the first group, AI is higher in the group with a high cardiovascular risk.

Renal excretory function has been estimated for 12 months with the help of glomerular filtration rate (GFR) as well as with the help of additional indices – urea and creatinine. The

function of kidneys has been preserved, it has been proved by the following data: GFR as the most sensitive index of functional and tissue work of kidneys in the first group was 86.4 ± 1.89 ml/min./ $1.73m^2$, in the second group – 86.1 ± 1.95 ml/min./ $1.73m^2$ without reliable differences between them ($p > 0.05$).

Level of urea in blood serum in the first group was – 5.85 ± 0.23 mmol/l, in the second group – 5.97 ± 0.19 mmol/l (Table 6). No reliable differences between groups were revealed ($p > 0.05$).

Table 6: Biochemical indices of kidney metabolism in patients of main groups at the beginning of the research (M±m)

Index	I group (n=48)	II group (n=54)	p between groups
Urea, mmol/l	5.85±0.23	5.97±0.19	>0.05
Creatinine, mkmmol/l	81.6±2.27	73.5±2.17	<0.05
GRF, ml/min/1.73m ²	86.4±1.89	86.1±1.95	>0.05

The second marker of renal work is creatinine. In the first group it was 81.6 ± 2.3 mkmmol/l, in the second group – 73.5 ± 2.2 mkmmol/l, which is 8.1 mkmmol/l, or 11.0% higher in the first group ($p < 0.05$). However, the increase of the index above norm has not been noticed.

Specific markers for defining endothelial function of vessels in our research were: endothelin-1 (ET-1), vWF and thrombomodulin. In the group of a high risk, reliable increase of ET-1 and vWF ($p < 0.001$) has been noticed compared to groups with moderate risk (Table 7).

Table 7: Level of markers of ED of all studied groups of patients at the beginning of the research (M±m)

Index	Total (n=102)	I group (n=48)	II group (n=54)	p between groups
ET-1, fmol/ml	1.29±0.11	0.87±0.048	1.66±0.198	<0.001
Thrombomodulin, ng/ml	3.32±0.09	3.27±0.121	3.37±0.133	>0.05
vWF, U/ml	1.05±0.03	0.95±0.037	1.17±0.029	<0.001

ET-1 in the first group was 0.87 ± 0.048 fmol/ml, in the second 1.66 ± 0.198 fmol/ml, average index by groups was 1.29 ± 0.11 fmol/ml. The groups were reliably different by the level of ET-1 ($p < 0.001$ according to Student's test), which indicates strong vasoconstriction of vessels in the group with a high cardiovascular risk at the beginning of the research.

Thrombomodulin in the first group at the beginning of the research was 3.27 ± 0.121 ng/ml, in the second one – 3.37 ± 0.133 ng/ml. Despite the fact that this marker is responsible for athrombogenic features of the vascular wall, binding thrombin and later it significantly changes its features, there were no evident reliable differences between groups ($p > 0.05$ according to Student's test).

Von Willebrand factor in the first group was 0.95 ± 0.04 U/ml, in the second group 1.17 ± 0.03 U/ml ($p < 0.001$ according to Student's test). The reliable exceed of this factor grounds the intensified influence of AH with a high risk for cardiovascular conditions in the vascular wall.

Conclusions

1. Increasing BMI is more pronounced in the hypertensive group at high risk of cardiovascular events ($p < 0,01$ compared with the first group). Ratio WC/HC, WC/height exceeds the recommended indices, it confirms the

overweight in the main part of the studied patients in general. In the process of observation, it has been concluded that IT is reasonable to control the weight of the body.

2. DBP in the second group at the beginning of the research was reliably higher than that of the first group ($p < 0.001$), which indicates vascular changes in the group with a high cardiovascular risk.
3. The mean value of TC by groups is 5.57 ± 0.10 mmol/l, which exceeds values recommended by ESC (2007), and it is an additional factor of cardiovascular conditions in future.
4. The level of HDL in the first group is $1,35 \pm 0,05$ mmol/L, the second - $1,23 \pm 0,04$ mmol/L, indicating a more pronounced antiatherogenic properties and less progression of endothelial dysfunction in the future ($p < 0.05$) in a group with moderate risk of cardiovascular events.
5. In the group of a high risk, the reliable exceed in ET-1 and vWF has been revealed compared to indices of the group with a moderate risk ($p < 0.001$), which indicates more expressed vascular constriction and progressing blood clots in vessels.
6. Prospect for further research is connected with dynamic monitoring over indicators of ED markers in the selected groups of patients, administration of anti-hypertensive medicines and analysis of their influence on endothelium of vessels within twelve months.

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