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Resistant Arterial Hypertension, Questions of Diagnostics and Pathogenetic Therapy

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Abstract: Arterial hypertension, which largely causes high cardiovascular morbidity and mortality, in Uzbekistan and in all countries with developed economies, is one of the most urgent medical and social problems. At the same time, AH, despite its wide prevalence, is characterized by the lack of effective control.

In developed countries, as a result of preventive measures, the mortality of patients with hypertension has significantly decreased due to the systematic control of blood pressure levels, timely drug correction and achievement of its target level [9]. This control is carried out by general practitioners or family doctors. Many studies have been devoted to evaluating the effectiveness of the use of various groups of antihypertensive drugs; recommendations have been developed for the diagnosis, prevention and treatment of hypertension. Many doctors know and apply the recommendations, but the rates of cardiovascular morbidity (CVD) and especially mortality continue to grow, more often death occurs from developed complications at the prehospital stage; according to the literature, death from stroke is recorded in patients at home in 56.3% of cases, in a hospital much less often - in 18.9% [3,7].

Diseases of the circulatory system are one of the most common diseases in the Republic of Uzbekistan, the mortality from which in the structure of the causes of general mortality of the population is 51.1%.

A number of studies have convincingly shown that hypertension is accompanied by hypercoagulation and slowing down of fibrinolysis, which increases the risk of atherothrombosis. In addition, in patients with hypertension, disturbances in the hemostasis system can be expressed to varying degrees, depending on the presence and severity of dyslipoproteinemia. Some researchers believe that the lack of adequate decrease in blood pressure reduction in mortality from heart attack and stroke in hypertension may be due to disorders in the blood coagulation system. Meanwhile, information concerning the study of the blood coagulation system in young people is still controversial. A number of authors testify to the presence of hypercoagulability and DLP in young people with hypertension and obesity. While other researchers refute the increase in blood thrombogenic potential in young patients with hypertension.

Materials and methods

In accordance with the set goal and objectives, a prospective controlled study with elements of a nested case-control study was planned and carried out, which included three stages. The study was conducted in family clinics in the Bukhara region.

Diagnosis of hypertension was based on the detection of systolic blood pressure of 140 mm Hg. and more and or diastolic blood pressure 90 mm Hg. and more registered by N.S. Korotkov after a 30-minute rest in time for at least two visits with intervals between them of at least a week.

Exclusion of the diagnosis of symptomatic hypertension and stratification of cardiovascular risk was carried out on the basis of complaints, anamnesis, study of lifestyle, as well as the results of a comprehensive examination, which included general clinical methods:

- anthropometric measurements with calculation of body mass index and determination of waist circumference;
- measurement of blood pressure in the upper and lower extremities (to exclude aortic coarctation);
- Examination of the skin to exclude café-au-lait spots, neurofibromatous nodes (neurofibromatosis), livedo reticularis (nodular, periarteritis); striae (Itsenko - Cushing's syndrome), increased skin moisture (thyrotoxicosis, pheochromocytoma);
- examination of the neck area: noise over the carotid artery during auscultation; swelling of the jugular veins; enlargement of the thyroid gland;
- examination of the cardiovascular system: assessment of the pulse on both hands (to exclude nonspecific aortoarteritis (disease, Tokayasu)); frequency and rhythm of heart contractions; apical impulse; cardiac impulse; auscultation of the heart - clicks, noises, III and IV tones (coarctation of the aorta, defects);
- examination of the abdominal organs: an increase in the size of the kidneys on palpation (polycystic kidney disease, volumetric formations), pathological, pulsation; noises over the area of the abdominal aorta, renal arteries during auscultation of the abdomen (renal artery stenosis);
- Examination of the extremities: pulse on the peripheral arteries; noise on the femoral artery (coarctation of the aorta, Takayasu's disease).

In addition, laboratory (general blood and urine tests, determination of fasting plasma glucose, creatinine, uric acid, total cholesterol, potassium, sodium, calcium) and instrumental (ECG, echocardiography, ultrasound of the kidneys and adrenal glands) methods were used.

The level of prothrombin ratio of the blood was determined by the unified thromboplastin-calcium method according to Quick in a hemocoagulometric thermostat TPS (Russia). The analysis of indicators of the platelet link of hemostasis was carried out using a laser analyzer of platelet aggregation (BIOLA Ltd., model 230 LA).

Results and discussion

In the course of our study, it was found that the international normalized ratio characterizing phases I and II of blood coagulation was 14.3% higher in young people with hypertension compared with the group of normotensive peers (p=0.018), the thrombin time index was 14.3% higher. 5.31% higher in the control group (p=0.015), indicating an increase in blood thrombogenic activity in young patients with hypertension (Table 1). Meanwhile, there were no significant differences in APTT, which also characterizes the phases of prothrombin and thrombin formation.

Table 1Comparative characteristics of the main parameters of the hemostasis system in the studied groups

Indicators	M+SE	V0.25	V0.75	M+SE	V0.25	V0.75	U	Z	p level
	Study group (n=83)			Control group (n=23)					
INR, units	1.28±0.05	1.33	2.03	1.12±0.07	0.89	1.45	1305.5	2.11	0.018
Thrombin time, sec	15.24±0.19	14.00	17.00	16.05±0.25	15.00	17.00	2783.5	-2.47	0.015
APTT, sec	33.38±0.48	29.00	37.00	32.97±0.57	29.00	37.00	3412.5	0.55	0.584
Fibrinogen, g/l	3.45±0.10	2.46	3.78	2.75±0.07	2.30	3.23	2171.0	4.35	0.011
PAT, %	94.38±0.55	90.00	98.00	93.42±0.58	90.00	96.00	2957.0	1.94	0.052

Note: M is the sample mean, SE is the standard error of the mean, the 25th (V0.25) and 75th percentiles (V0.75) are indicated due to the non-normal distribution of values in the series, U is the Mann-Whitney test for comparing numerical data of two independent groups, Z-value of the

variation of the normal distribution (normal distribution variate value), p-level - critical level of significance.

More pronounced differences were found in the study of a number of indicators that determine phase III (fibrin formation) of blood coagulation. Thus, in the representatives of the main group, the level of fibrinogen was statistically significantly higher than in the control group - by 25.5% ($p<0.011$) and coagulation factor XIII - by 5.0% ($p=0.024$).

At the same time, none of the parameters of the blood coagulation system exceeded the allowable values, both in the main group and in. Control group. Despite this, the data obtained indicated the need for preventive measures in young people with AH, aimed, among other things, at preventing thrombotic complications. So, according to a number of authors, the positive effect of normalizing body weight at a young age is accompanied by an improvement in the lipid spectrum and indicators of the blood coagulation system. Moreover, Zanettini R. (1997) showed that regular physical training in patients with AT I - II degree, not receiving antihypertensive therapy, leads to a significant decrease in fibrinogen levels. The cessation of training is accompanied by the return of fibrinogen values to the initial level.

The concentration of one of the main components of the anticoagulant blood system - plasma antithrombin did not have statistically significant differences in the studied groups and did not exceed the maximum allowable values (94.38±0.55 vs. 93.42±0.58; $p=0.052$), which indicated about the absence of changes in the anticoagulant system in young people of the studied groups (Table 4.3.1). The decrease in fibrinolytic activity of blood plasma in the representatives of the main group was also unreliable. Thus, the data obtained indicated the absence of a violation of the fibrinolytic activity of the blood in young people with AH and their healthy peers.

Conclusions

1. In young people at the stage of developing hypertension, statistically significant differences were revealed, compared with healthy peers, in the parameters of the lipid spectrum: an increase in the level of total cholesterol, LDL cholesterol, TG, VLDL cholesterol, CA and a decrease in HDL cholesterol ($p<0.05$); the main indicators of the hemostasis system: an increase in the level of fibrinogen, XIII factor, thrombin time, as well as an increase in the level of leptin ($p<0.05$).
2. In young patients with hypertension, a significant relationship was established between the levels of total cholesterol, LDL cholesterol and fibrinogen with the intensity of smoking ($rs=0.77$; $rs=0.53$; $rs=0.63$, respectively; $p<0.05$), BMI ($rs=0, 61$; $rs=0.54$; $rs=0.45$; $p<0.05$); the degree of increase in SBP ($rs=0.41$; $rs=0.51$; $rs=0.56$, $p<0.05$). The level of leptin statistically significantly correlates with the degree of development of PFA ($rs=0.78$; $p<0.05$), BMI ($rs=0.77$; $p<0.05$), the level of total cholesterol ($rs=0.68$; $p<0.05$), LDL-C ($rs=0.63$; $p<0.05$), fibrinogen ($rs=0.57$; $p<0.05$).

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