ORIGINAL ARTICLE

ARTERIAL HYPERTENSION ASSOCIATED WITH HYPERURICEMIA: FEATURES OF HEART DAMAGE

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ABSTRACT

The aim is the analysis of hyperuricemia influence on the heart features in patients with arterial hypertension.

Materials and methods: We include 75 patients with arterial hypertension which were divided in two groups according to the level of uric acid in the blood, 30 practically healthy people. Patients from the I group (n = 40) had arterial hypertension and coexistent hyperuricemia; II (n = 35) – arterial hypertension. Left ventricular mass index was determined for left ventricular hypertrophy confirmation.

We used clinical, anthropometric, biochemical, instrumental, statistical method. Serum uric acid level was observed by the reaction with uricase. Left ventricular mass index was calculated as left ventricular mass to body surface area ratio. The results were analyzed statistically by SPSS 21 and Graphpad.

Results: Left ventricular mass index was significantly higher (p = 0,0498) in patients from the I group (109,7 ± 3,21) g/m^2 comparable with the II (97,6 ± 5,35) g/m^2 and increased in proportion to the biggest level of uric acid (r = 0,31; p = 0,04) in patients with arterial hypertension and hyperuricemia.

Conclusions: Concentric and excentric left ventricular hypertrophy, increased left ventricular mass index proportionally to uric acid levels (r = 0,31; p = 0,04) is the confirmation of important role of hyperuricemia in the left ventricular hypertrophy development in patients with arterial hypertension.

KEY WORDS: arterial hypertension, hyperuricemia, left ventricular mass index

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INTRODUCTION

A new wave of the interest in hyperuricemia is associated not only with the significant role of uric acid level elevation as an independent and modifiable risk factor of gout but also as an indicator of cardiovascular and chronic kidney disease (CKD) [1].

Hyperuricemia is determined in 26 % of patients with arterial hypertension (AH). The increased uric acid level is associated with decline control of blood pressure (BP) [2].

Hyperuricemia leads to the kidney function disorders. It is connected with the adhesion of sodium monourate crystals on the surface of kidney epithelial cells followed by activation of inflammatory mechanisms [3].

On the other hand, a lot of publications are devoted to the effects of hyperuricemia on cardiac function disorders. The high levels of free radicals which are results of uric acid synthesis and progressive endothelial dysfunction leads to the heart failure. It is associates with the reduction of myocardium perfusion, increase of vascular tonus, decrease of the blood flow in the coronary arteries. All these mechanisms lead to the myocardium contractile dysfunction [2].

Relaxation of the myocardium is changed at first during AH. Left ventricular (LV) hypertrophy is determined as a criterion of heart disorders in patients with AH [4] and one of the indicators of heart failure with reserved ejection fraction [5]. Hyperuricemia is associated with the increased risk of LV hypertrophy on 75 % [6]. In conclusion, the assessment of relationship between hyperuricemia and LV hypertrophy is important nowadays.

As a result the actual internal medicine problem is the determination of increased uric acid level influence on the severity of heart and kidney disorders in hypertensive patients.

THE AIM

The aim is the analysis of hyperuricemia influence on the features of heart damage in patients with arterial hypertension. Study had aim to estimate the LV geometry in patients with AH and coexistent hyperuricemia; to define the influence of increased uric acid levels on the LV hypertrophy progress by the detail analysis of relationship between hyperuricemia and LV mass index (LVMI) in hypertensive patients.

MATERIALS AND METHODS

We observed 75 patients with AH in the clinical trial treated in Sumy Central Regional Clinical Hospital during 2018-2019 years and 30 practically healthy people. They were divided in two groups according to the level of uric acid in the blood. Patients from the I group (n = 40) had AH and coexistent hyperuricemia; II (n = 35) – AH.

Patients were enrolled in the study after informed consent obtained in accordance with the Helsinki Declaration of the World Medical Association on the Ethical Principles of Scientific and Medical Research. The study was approved

by the Bioethics Committee for experimental and clinical studies at Sumy State University Medical Institute.

The diagnosis, the stage, the degree of AH were confirmed according to the Unified clinical guidelines of primary, emergency and secondary care of arterial hypertension (2016) developed by the working group of the Ministry of Health of Ukraine [7] and guidelines of Ministry of Health of Ukraine №384 (24.05.2012 year) [8]. Hyperuricemia was determined by European League Against Rheumatism (EULAR, 2016 p.) if the uric acid level was more than 360 mcmol/l (6 mg/dl) [9]. Asymptomatic hyperuricemia was the coexistent pathology in hypertensive patients.

LV hypertrophy is the objective feature of heart damage for patients with AH [7]. The indicators were analyzed in hypertensive persons with and without hyperuricemia.

We observed patients with written consent of participation in our study, presence of confirmed AH and coexistent hyperuricemia or AH without increased uric acid levels.

The clinical characteristic of patients is presented in table I.

All observed patients were comparable by age with predominance of men.

The significant difference between the level of systolic and diastolic BP were absent in patients from the I and II group (p = 0,8467; p = 0,9171).

The duration of AH was respectively (4,3 ± 2,31) and (4,0 ± 2,11) year (p = 0,9247) for patients with AH and coexistent hyperuricemia comparable with hypertensive persons.

Firstly we determined AH in all persons with comorbidity. Hyperuricemia was the coexistent pathology.

We collected anamnesis, made the objective and physical examination of all participants.

Measurement of height (m) was made by centimeter tape; weight (kg) – by electronic scales. Body surface area was calculated by Mosteller formula as square root of the height (cm) multiplied by the weight (kg) divided by 3600 [10].

Serum uric acid level was observed by enzymatic photocolorimetry. The biggest level of uricemia is associated with increased the color intensity of the product resulted by the reaction with uricase [11].

The echocardiography was done. LVMI was calculated as a LV mass (LVM) (g) to body surface area (m^2) ratio [12].

LVM was calculated according to the American Society of Echocardiography's Guidelines:

$LVM\ (g) = 0,8 \cdot \{1,04 \cdot [(LVIDd + LVPWTd + IVSTd)^3 - (LVIDd)^3]\} + 0,6$ [27]. We estimated LV internal dimension at end diastole (LVIDd), LV posterior wall thickness at end diastole (LVPWTd), intraventricular septal thickness at end diastole (IVSTd).

Table I. Clinical characteristic of all observed patients

Indicator		I group (n = 40)	II group (n = 35)	control (n = 30)	p
age (years)		52,4 ± 0,69	54,1 ± 0,61	53,3 ± 0,4	$p_1 = 0,0725$ $p_2 = 0,3045$ $p_3 = 0,2941$
gender	m	27 (70 %)	24 (68,6 %)	21 (70 %)	
	f	13 (30 %)	11 (31,4 %)	9 (30 %)	
Systolic BP (mmHg)		146,4 ± 5,38	144,7 ± 7,07	120,8 ± 6,48	$p_1 = 0,8467$ $p_2 = 0,0032$ $p_3 = 0,0166$
Diastolic BP (mmHg)		94,8 ± 6,05	93,9 ± 5,93	80,1 ± 2,6	$p_1 = 0,9162$ $p_2 = 0,0495$ $p_3 = 0,0482$
Uricemia (mcmol/l)		401,6 ± 3,93	304,5 ± 4,95	265,0 ± 8,38	$p_1 < 0,0001$ $p_2 < 0,0001$ $p_3 < 0,0001$
Duration of AH (years)		4,3 ± 2,31	4,0 ± 2,11	–	$p_1 = 0,9247$
Duration of hyperuricemia (years)		4,1 ± 0,35	–	–	–
Glucose in blood, mmol/l		4,4 ± 0,7	4,3 ± 0,59	4,04 ± 0,53	$p_1 = 0,9147$ $p_2 = 0,7000$ $p_3 = 0,7476$

Notes:
1. p_1 – the significance of differences between the indicators of the I and II groups;
2. p_2 – the significance of differences between the indicators of the I group and control;
3. p_3 – the significance of differences between the indicators of the II group and control;
4. n – the number of persons;
5. f – female;
6. m – male

Table II. Echocardiographic indicators, which are necessary for left ventricular mass index calculation

Indicator	I group (n = 40)	II group (n = 35)	control (n = 30)	p
Left ventricular internal dimension at end diastole, cm	4,9 ± 0,06	4,7 ± 0,1	4,6 ± 0,04	$p_1 = 0,0819$ $p_2 = 0,0002$ $p_3 = 0,3849$
left ventricular posterior wall thickness at end diastole, cm	1,1 ± 0,02	1,04 ± 0,02	0,81 ± 0,02	$p_1 = 0,0381$ $p_2 < 0,0001$ $p_3 < 0,0001$
intraventricular septal thickness at end diastole, cm	1,1 ± 0,02	1,02 ± 0,04	0,78 ± 0,01	$p_1 = 0,0673$ $p_2 < 0,0001$ $p_3 < 0,0001$
left ventricular mass, g	205,2 ± 5,41	175,9 ± 9,02	117,8 ± 2,72	$p_1 = 0,0054$ $p_2 < 0,0001$ $p_3 < 0,0001$
weight, kg	75,9 ± 1,79	69,9 ± 1,4	60,2 ± 0,1	$p_1 = 0,0117$ $p_2 < 0,0001$ $p_3 < 0,0001$
height, cm	169,1 ± 0,01	170,6 ± 0,01	163,3 ± 0,01	$p_1 < 0,0001$ $p_2 < 0,0001$ $p_3 < 0,0001$
body surface area , kg/m^2	1,9 ± 0,02	1,8 ± 0,02	1,7 ± 0,02	$p_1 < 0,0001$ $p_2 < 0,0001$ $p_3 = 0,0008$
left ventricular mass index, g/m^2	109,7 ± 3,21	97,6 ± 5,35	71,4 ± 1,6	$p_1 = 0,0498$ $p_2 < 0,0001$ $p_3 < 0,0001$

Notes:
1. p_1 – the significance of differences between the indicators of the I and II groups;
2. p_2 – the significance of differences between the indicators of the I group and control;
3. p_3 – the significance of differences between the indicators of the II group and control;
4. n – number of persons

LV hypertrophy was determined if the LVMI was more then 115 g/m^2 for men and 95 g/m^2 for women [5].

The hypothesis of normal samples distribution was tested by Kolmagorov-Smirnov criterion used SPSS 21.

If there was no reason for rejection of hypothesis about normal distribution law, the significance of the difference between the mean values was analyzed by Student's t-test for independent samples with the help of GraphPad.

This research was adopted by the Ethics Committee of Sumy State University, Sumy, Ukraine. Research was conducted keeping to the main issues of the Convention of the Council of Europe on Human Rights and Biomedicine of Declaration of Helsinki of the World Medical Association on the ethical principles of conducting medical research involving human beings (1975, with further amendments, including version of 2000) and Order of Ukrainian Ministry of Health № 690 on 23.09.2009.

RESULTS AND DISCUSSION

LV hypertrophy is the marker of heart disorders in hypertensive persons. LVMI was calculated in all observed patients. Indicators, which are necessary for this calculation, performed in table II.

LVMI was significantly higher (p = 0,0498) in patients from the I group (109,7 ± 3,21) g/m^2 comparable with the II (97,6 ± 5,35) g/m^2.

There was the absence of significant relationship between uricemia and LVMI in persons from II group. LVMI increased in proportion to the biggest level of uricemia (r = 0,31; p = 0,04) in the I group.

The analysis of LV geometry in patients from the I group showed the confirmation of concentric remodeling in 14 (35 %) persons, concentric hypertrophy – in 16 (40 %), excentric hypertrophy – in 7 (17,5 %), normal sizes – in 3 (7,5 %). The analysis of LV geometry in patients from the II group showed the confirmation of concentric remodeling in 20 (57,14 %) persons, concentric hypertrophy – in 4 (11,43 %), excentric hypertrophy – in 5 (14,29 %), normal sizes – in 6 (17,14 %).

The level of uric acid in patients with concentric remodeling was (397,7 ± 23,22) mcmol/l; concentric hypertrophy – (407,5 ± 29,7) mcmol/l, p = 0,8; excentric hypertrophy – (401,0 ± 20,66) mcmol/l, p = 0,9283. The significant difference between uricemia in coexistent patients from the I group with concentric and excentric hypertrophy (p = 0,8922).

LVMI increased in proportion to the biggest level of uricemia (r = 0,31; p = 0,04) in the I group. Other investigators had similar results connected with positive correlation be-

tween uricemia and LVMI in patients with AH (r = 0,346, p < 0,001) [13].

Finally, concentric and excentric hypertrophy were observed often in patients with AH and coexistent hyperuricemia. Furthermore normal type of LV geometry was present more often in hypertensive persons from the II group.

The significant difference between uricemia in coexistent patients from the I group with concentric and excentric hypertrophy. It means that hyperuricemia is associated with all types of LV hypertrophy.

CONCLUSIONS

1. Concentric and excentric left ventricular hypertrophy was determined often in patients with arterial hypertension which have increased uric acid levels. Concentric remodeling and normal type of left ventricular geometry were observed more often in hypertensive persons without hyperuricemia.
2. The significantly increased left ventricular mass index proportionally to uric acid levels (r = 0,31; p = 0,04) is the confirmation of important role of hyperuricemia in the left ventricular hypertrophy development in patients with arterial hypertension.

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