THE NEW ARMENIAN MEDICAL JOURNAL
Vol.12 (2018), No 2, p.39-44

CHANGES OF THE CAROTID INTIMA-MEDIA COMPLEX THICKNESS AND COGNITIVE FUNCTIONS IN PATIENTS WITH ARTERIAL HYPERTENSION

Dotsenko N.Ya.[1*], Boev S.S.[1], Gerasimenko L.V.[1], Shekhunova I.A.[1], Molodan A.V.[1], Malynovskaya A.Ya.[1], Yatsenko O.V.[2]

[1] Department of Cardiology, State Institute "Zaporozhye Medical Academy of Postgraduate Education Ministry of Health of Ukraine", Zaporozhye, Ukraine
[2] Department of Internal Medicine No 3, Zaporozhye State Medical University, Zaporozhye, Ukraine

Received 14/01/2018; accepted for printing 11/05/2018

Abstract

Arterial hypertension is one of the most significant medical and social problems. In recent years, numerous studies have demonstrated the role of hypertension as an independent risk factor in the development and progression of cognitive impairment in the general population. At present, the relationship between blood pressure and cognitive impairment has been confirmed in a number of clinical studies. Decline of the cognitive functions is one of the modern medicine actual problem.

The study aimed to analyze the relationship between cognitive impairment and subclinical changes in carotid arteries in hypertensive patients.

Totally 69 patients with hypertensive disease of II stage with average age of 51.38±0.94 years were examined. Patients were divided into 2 groups with absence and presence of cognitive impairment. The control group consisted of 12 healthy, normotensive individuals aged 54.25±2.74, without cognitive impairment. To assess cognitive functions, the Montreal Evaluation Scale (MoCA-test) was used, which is recommended by most modern experts in the field of cognitive impairment for broad use in everyday clinical practice.

The average thickness of the intima-media complex in patients of I and II groups was not significantly different. The proportion of people with intima-media complex thickness exceeding normal values was significantly higher in persons with cognitive impairment (71%) than in persons without it (39.5%).

In patients with II stage of hypertensive disease, the thickness of the intima-media complex of the carotid artery was increased. A positive correlation of increased thickness of the intima-media complex with hypertensive crises was found only in patients with cognitive impairment.

Keywords: *hypertonic disease, cognitive function, thickness of the intima-media complex.*

Introduction

Arterial hypertension is one of the most common and socially significant diseases in clinical medicine [*Lim S et al., 2013*]. Arterial hypertension is an independent factor in the development of cognitive impairment. The relationship between blood pressure and cognitive impairment is confirmed in a number of clinical studies. Even in relatively young people with white coat and borderline hypertension, cognitive impairment is already noted in some cases [*Shehab A, Abdulle A, 2011*]. For long-term follow-up, a high level of blood pressure in middle-aged patients is associated with a future decline in cognitive functions (from mild cognitive impairment to dementia) [*Qiu C et al., 2005; Whitmer R et al, 2005*]. These additional clinical conditions change the course of the underlying disease [*Preobrazhenskaja I, Gromova D, 2014*] and have a very negative impact on the life quality of the patient, make it difficult to

Address for Correspondence:
Nikolay Ya. Dotsenko
Department of Cardiology
20 Vintera Blvd, Zaporozhye 69096, Ukraine
Tel.: (061) 224-37-37
E-mail: zmapo40@gmail.com

treat co-occurring diseases and carry out rehabilitation measures [*Zakharov V, 2016*]. From a practical point of view, assessment of cognitive abilities in hypertension can be considered as one of the promising ways of early prognosis of cognitive impairment, which for a long time can be asymptomatic against the background of the underlying disease of the cardiovascular system [*Osipov E et al., 2015*]. Therefore, in the new European recommendations (2013) on the diagnosis and treatment of hypertension, it is emphasized that elderly patients with elevated blood pressure should be tested for the state of cognitive functions [*Mancia G et al, 2013*]. At the same time, cognitive disorders are characteristic for patients of working age with hypertension, even with adequate control of blood pressure level [*Krotova V, 2016*]. The question when to start testing the cognitive function with arterial hypertension remains open.

Much attention is paid to the evaluation of the atherosclerotic process in the carotid arteries, which plays an important role in cerebrovascular diseases and cognitive deficits [*Heiss G et al., 1991*]. The most informative early (subclinical) marker of atherosclerosis is an increase in carotid intima-media thickness (CIMT) complex in the common carotid artery [*Stulin I, 2003; Sojkova J et al., 2010*]. A number of studies have shown that an increase in TIM (translocase of the inner membrane) complex is associated with a reduction in regional cerebral blood flow and a violation of cognitive functions [*Cabeza R, Nyberg L, 2000; Grady C, 2000*]. However, many mechanisms of these relationships are unclear.

Therefore, the influence of subclinical changes in the carotid arteries on cognitive impairment with arterial hypertension still remains a topic under discussion.

The purpose of this study is to analyze the relationship between cognitive impairment and subclinical changes in carotid arteries in patients with essential hypertension.

Material and methods

Totally 69 patients with arterial hypertension of II stage who did not receive antihypertensive therapy or were treated irregularly (without achieving target blood pressure), among whom 48 men (69.6%) and 21 women (30.4%) aged 51.38±0.94 were examined; 40.6% of arterial hypertension patients had blood pressure level 2, 59.4% had blood pressure level 3, the average duration of the disease was 8.31±0.58. The control group consisted of 12 healthy, normotensive individuals aged 54.25±2.74, without cognitive impairment.

The diagnosis of essential hypertension was established according to the recommendations of the European Society of Cardiology (2013) [*Mancia G et al., 2013*]. The blood pressure level was estimated at the office measurement and daily monitoring of blood pressure: the average daily systolic blood pressure (av. SBP) and the average daily diastolic blood pressure (av. DBP).

To assess cognitive functions, the Montreal Evaluation Scale (MoCA-test) was used, which is recommended by most modern experts in the field of cognitive impairment for broad use in everyday clinical practice. The system of formalized assessment of the MoCA-test does not provide for a gradation in terms of the severity of the violations, depending on the scores (26 points or more are considered normal) [*Molchanova J et al., 2013*].

The examination of the right common carotid artery in the supine position after 10 minutes of rest was performed using an ultrasonic multifunctional “Megas”-scanner by Esaote S.p.A with the LA 523 (13-4 *MHz*) sensor.

The study did not include patients who underwent craniocerebral trauma, with a permanent form of atrial fibrillation, chronic obstructive pulmonary diseases (respiratory failure of grade 2-3), coronary heart disease, diabetes mellitus, severe liver, kidney impairment, obesity.

The research study is performed in accordance with the provisions of Council of Europe Convention for Protection of Human Rights and biomedicine.

Statistical processing of the study results was carried out by the IBM SPSS Statistics 22 computer program. The distribution of the studied indicators in the groups was checked for normality, in most cases the type of distribution correspond to the normal one. To describe the variables we used the average value of the characteristic (M) and standard error (m). Obtained data considered as significant at $p<0.05$. Relationship between parameters was assessed by means of Pearson rank correlation method.

Results

The examined patients of II stage essential hypertension were divided into 2 groups. The first group included 38 patients with the absence of cognitive impairment, and the second – 31 patients with the detected cognitive impairment (according to the MoCA-test) (Table 1). We also evaluated the duration of training and the number of hypertensive crises for the previous year before the survey began (retrospective analysis of medical records and patient questioning). A sudden worsening in the patient's state of health caused by elevation of blood pressure relative to the usual level, which accompanied by the appearance of "cerebral", "cardiac" and other complaints, was attributed to the hypertensive crises.

In patients of II group, hypertensive crises (2.81±0.38 and 1.37±0.22, respectively, $p<0.05$) were noted more frequently than in I group, and a larger number of patients in the previous year had hypertensive crises (77.4% and 36.9%, respectively) (Table 1).

As a rule, the experts of the European Society of Arterial Hypertension and the European Society of Cardiology chose wall thickness <0.9 *mm*, thickening of CIMT complex 0.9-1.3 *mm*, and the criterion for plaques is CIMT complex, more than 1.3 *mm*. The average value of CIMT in the patients examined by us was significantly higher in both groups of essential hypertension relative to the control group ($p<0.05$). In patients of II group, the CIMT index was greater by 8.5% than in I group, although it did not reach reliable values ($p=0.065$). Moreover, the proportion of people with CIMT exceeding normal values (CIMT complex > 0.9 *mm* and <1.3 *mm*) was significantly greater in those with cognitive impairment (71%) than in those without cognitive impairment (39.5%) (Table 2).

The conducted correlation analysis showed the existence of an interrelation between a number of indicators in the surveyed patients. Thus, a negative correlation was established with the frequency of crises in patients with essential hypertension in the presence of cognitive impairment and the sum of the MoCa-test scores ($r=-0.51$, $p<0.05$) and positive correlation with the TIM complex value, both in I and II group of patients ($r=+0.64$, $p<0.05$ and

Table 1

Clinical characteristics of patients with II stage essential hypertension, depending on the level of cognitive dysfunction

Indicators, units of measurement	Groups with Essential hypertension	
	I group (n=38) without cognitive impairment	II group (n=31) with cognitive impairment
Age (*years*)	50.84±1.11	52.03±1.59
Duration of the disease (*years*)	7.36±0.75	9.48±0.88
Body mass index (kg/m^2)	27.31±0.66	28.01±0.59
Duration of training (*years*)	12.97±0.34	13.00±0.44
average daily systolic blood pressure (*mmHg*)	141.42±2.25	143.48±2.73
average daily diastolic blood pressure (*mmHg*)	86.47±1.48	88.58±1.88
MoCA test (*scores*)	27.66±0.23	24.48±0.12º
Number of hypertensive crises for the year before the survey	1.37±0.22	2.81±0.38º
Hypertensive crises	24 (63.1%)	7 (22.6%)
Without hypertensive crises	14 (36.9%)	24 (77.4%)

Note: *º – differences in the indices while comparing I and II groups are significant ($p<0.05$)*

TABLE 2

Carotid ultrasonic data

Indicators, units of measurement	Control group (n=12)	Groups with Arterial hypertension	
		I group (n=38)	II group (n=31)
		without cognitive impairment	with cognitive impairment
CIMT complex (*mm)*	0.68±0.03	0.82±0.02▪	0.89±0.03*
CIMT complex according to *European Society for arterial hypertension and European Society of Cardiology.*			
-normal CIMT <0.9 *mm*	-	23 (60.5%)	9 (29%)
-Thickened CIMT (≥0.9 *mm* and <1.3 *mm*)	-	15 (39.5%)	22 (71%)

Notes: *▪ – the differences between the indices when comparing I group and the control group are significant (p<0.05)*
** – differences in the indices when comparing II group and the control group are significant (p <0.05)*

r=+0.75, p<0.01, respectively). However, when patients with normal size and with carotid artery thickening were divided, positive correlation was found only in persons with cognitive impairment (r=+0.62, p<0.05).

Statistically significant correlation dependencies were not obtained between the results of the MoCA-test and av. SBP, av. DBP, duration of the disease and level of education.

Thus, in essential hypertension patients, there is an increase in carotid CIMT complex, which depends on the frequency of hypertensive crises, but the dependence of the presence of cognitive impairment on the frequency of hypertensive crises is observed only in patients with elevated values of CIMT complex.

DISCUSSION

AP accelerates the development of cerebral artery atherosclerosis, which leads to a decrease in cerebral blood flow and disrupts the function of neurons, because the brain tissue is highly sensitive to the level of incoming oxygen and glucose [*Torre J, 2012; Bilchenko A, Matyukha L, 2014*]. In a longitudinal population study, AGES-Reykjavik (2,430 elderly people) has shown that an increase in CIMT complex as an early marker of atherosclerosis is associated with a decrease in brain volume and gray matter by magnetic resonance imaging [*Sabayan B et al., 2016*].

The relationship between CIMT complex and cognitive function among middle-aged and older people is confirmed in a recent study of the Chinese population (2016) [*Wang A et al., 2016*]. Carrington R. and co-authors note that subclinical atherosclerosis (CIMT complex) can be differently informative among various demographic subgroups of the population as a cognitive impairment predictor [*Carrington R et al., 2016*].

Gulkevych O. and co-authors observed 118 patients with essential hypertension (av. age 66.8 years) for 10 years. They found that the severity of damage to the structure of the carotid artery and CIMT complex is associated with cognitive impairment. This association was independent of age, body mass index and duration of hypertension [*Gulkevych O et al., 2015*].

The generic aspect of our work was the study of the interconnection of CIMT complex and the features of the course of essential hypertension (the frequency of hypertensive crises) on cognitive functions.

The inverse correlation between the carotid imaging of the carotid artery and the cognitive impairment (by the number of points of the MoCA-test) in patients with exceeding the normal values of CIMT complex in both patients with cognitive impairment and without it (r=-0.73, p<0.01 and r=-0.56, p<0.05, respectively) has been found. However, in patients without cognitive impairment, according to the MoCA-test, the score is ≥26, and with the cognitive impairment the sum is <26 points. In order to explain these results, further studies on specific domains of cognitive functions are required, since no statistically significant correlation associations were obtained with CIMT complex values of less than 0.9 *mm*.

Pathophysiological studies on the modeling of repeated hypertensive crises, according to which the disruption of autoregulation during recurrences of crises did not have a diffuse character and occurred in the same segments of the arteries as in the first increase in blood pressure [*MacKenzie E et al., 1976*]. In all likelihood, this is the basis of progressive damage to perivascular tissue with myelin death. On the other hand, the growing damage to the vessel wall due to its repeated impregnation with plasma and the loss of the muscular scaffold at a certain stage cannot provide an autoregulatory reaction with a second increase in blood pressure. This leads to a shift in the disruption of autoregulation to the more distal sections of the arteries and, as a consequence, to the appearance of foci of white matter damage in the deep sections [*Varakin Yu et al., 2014*]. Progressive atherosclerotic cerebral vascular disease associated with hypertension aggravates the above-described processes, which can cause both acute vascular (lacunar strokes, hemorrhages) and chronic diffuse brain damage with cognitive impairment, that is, the "crisis" course of hypertension accelerates the progression of brain damage [*Denishhuk I, 2006*]. We have identified the relationship between early atherosclerotic changes and cognitive functions in patients with a characteristic essential hypertension course associated with hypertensive crises ("crisis current").

These results show that patients who exceed CIMT complex values require more intensive monitoring. Therefore, for the purpose of early detection of cognitive dysfunction, it is necessary to begin testing for the state of cognitive functions in patients with essential hypertension with frequent crises and increased values of CIMT complex (0.9-1.3 *mm*).

Conclusion

1. In patients with II stage arterial hypertension with uncontrolled blood pressure, CIMT complex values are increased.
2. With increased CIMT complex values (≥0.9 *mm* and <1.3), a positive correlation with hypertensive crises was detected only in persons with cognitive impairment (r=+0.62, p<0.05).
3. Hypertensive crises are more frequent in patients with cognitive impairment.

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