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Value of Genetic Risk Factors with Chronic Cerebrovascular Complications at Patients with the Arterial Hypertension

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Abstract

Background and Objectives: The arterial hypertension remain to one of the most widespread diseases of cardiovascular system now. Human APOE is polymorphic protein which interacts with a receptor of a lipoprotein of the low density, provides delivery of cholesterol from lipoproteins of very low density in cages and thus participates in exchange of lipids in blood and in exchange of cholesterol in a brain. Thus, the purpose of our research it to define the importance of APOE genes and lipid metabolism in development of chronic cerebrovascular diseases of a brain in patients with arterial hypertension.

Material and Methods: 145 sick men and women, at the age of 55, 6±9, 8 years, suffering AH with chronic cerebrovascular diseases are examined. The diagnosis of was established on gradation of stages of discirculation encephalopathy based on classification of Schmidt EW.

Result: According to our data, among patients with cerebrovascular encephalopathy, in comparison with group healthy the occurrence ε4-allele was more often, 8,6% and 5,9% respectively. At all patients it was observed tendency to excess body weight, at carriers ε3/ε3 and ε3/ε4-genotype was observed the highest coefficient of BMI which has made 29,8±4,0 and 28,9±4,5 kg/sq. m respectively. Office SBP and DBP value were high at carriers ε2/ε4 and ε3/ε4-genotypes. The analysis of clinical indicators on alleles has shown existence of high SBP and DBP in group of carriers ε4 - allele. We have shown the research IMT that the carriage ε4-allele at patients with cerebrovascular encephalopathy is associated with increase in thickness of IMT carotids (p=0,02). Severe forms of chronic cerebrovascular diseases were more often observed at persons with carriage ε2/ε3 and ε3/ε4 APOE gene genotypes.

Conclusion: The carriage of ε4 allele and ε2/ε4 and ε3/ε4 - genotypes of the APOE gene causes the tendency to a hypercholesterolemia and giperlipoproteinemiya, violation of a daily profile of BP in the form of high variability and insufficient night decrease arterial pressure that is high risk of development of atherosclerosis and cardiovascular diseases.

Keywords: APOE Gene; Metabolic Disorder; Arterial Stiffness; Arterial Hypertension Ah; Chronic Cerebrovascular Diseases CCVD

Abbreviations: BMI: Body Mass Index; BP: Blood Pressure; AH: Arterial hypertension; APOE: Apolipoproteins E; IMT: Intima-Media Thickness; CCVD: Chronic Cerebrovascular Diseases DE: Discirculation Encephalopathy

Introduction

The Arterial Hypertension (AH) remains to one of the most widespread diseases of cardiovascular system now. Frequent damage of target organs by AH and as a result the high percent of disability and lethal outcomes do this disease socially important and demand careful approach to treatment of such patients [1]. First, it belongs to cerebrovascular complications of AH [2]. Cerebrovascular pathology takes the second place among the leading causes of death and disability of the population in economically developed countries that defines it as one of the major medical and social problems. So, in Russia the number of patients with chronic ischemia of a brain, makes not less than 700 on 100 000 population. Development and deployment of new methods of stroke therapy can't significantly improve all anymore the indicators of survival and restoration after brain accident, in this connection there is obvious a need of searching new markers which would allow to allocate groups of patients with high risk of an adverse current. Human APOE is polymorphic protein which interacts with a receptor of a lipoprotein of the low density (LDL-C), provides delivery of cholesterol from lipoproteins

of very low density (VLDL-C) in cages and thus participates in exchange of lipids in blood and in exchange of cholesterol in a brain [3-7]. Thus, the purpose of our research it to define the importance of APOE genes and lipid metabolism in development of chronic cerebrovascular diseases of a brain in patients with AH.

Material and Methods

145 sick men and women, at the age of 55, 6±9, 8 years, suffering AH with chronic cerebrovascular diseases (CCVD) are examined. The diagnosis of CCVD was established on gradation of stages of discirculation encephalopathy based on classification of Schmidt EW.

Sample Collection and Study Design

All samples were extracted from human whole blood collected in EDTA or sodium citrate Eppendorf tubes. The study was approved by the medical ethical committee of the center of cardiology, Tashkent Uzbekistan. Informed consent was obtained from everyone recruited.

Statistical Analyses

Associations between alleles and AH were sought using odds ratios (OR) with 95% confidence intervals. The significance level for all the analyses was set at p<0.05. Statistical analyses were performed using Gene Pop and Statistical v6.0 software (Stat Soft, USA).

Genotyping

Genotyping of the SNP was performed by polymerase chain reaction and restriction fragment length polymorphism PCR-RFLP. Sense primer was F 5′- TCC AAG GAG CTG CAG GCG GCG CA -3′ R 5′-ACA GAA TTC GCC CCG GCC TGG TAC ACT GCC A-3′ The PCR primer was synthesized by EVROGEN Corporation. The conditions of amplification reaction were as follow: 94ºC for 5 min (initial denaturation); 65ºC for 30 s (denaturation); 70ºC for 90s (annealing); 94ºC for 30 s (extension); 40 cycles; 70ºC for 10 min (extension); 4ºC (conservation). Enzyme reaction system: a total volume of materials was 25 mL within 10 mL PCR products, 2.5 mL 10. buffer solution, 0.2 IU restriction endonuclease Hua I and 12.3 mL sterilization deionized water. Reaction condition: a warm bath (37ºC) for 16h was designed. The digests were then subjected to electrophoresis on a 12% polyacrylamide gel and visualized under ultraviolet illumination, where the undigested product e2-allele showed a band of 81 and 91 bp, e3- allele showed a band of 91bp, and e4- allele showed a band of 72 bp (Lancet 1991 May11 VOL337) [8].

Results

Distribution of patients on a stage of discirculation encephalopathy (DE) has shown that DE an I-stage was observed at 38 patients (26,6%), an II stage at 59 patients (40,8%), DE of an III stage at 48 patients (32,5%). On AH degree in the general population has shown degree AH 1 at 25,7%, to degree AH 2 at 37,2% and 3- degrees at 37,2%. Accumulation of genotype ε3/ε3-genotype APOE gene authentically prevailed among population as healthy (p>0,0001), and among sick AH with CCVD (p<0,0001). Among patients with encephalopathy in comparison with group of healthy the occurrence ε4-allele was more often than 8,6% and 5,9% respectively. Carriage of ε4-allele at patients with discirculation encephalopathy was associated with increase of thickness of a complex IMT carotids (p=0,02). Violation of lipid metabolism at carriers ε4-allele were authentically than at carriers ε3 and ε2 - allele. Analyzing the frequency of risk factors occurrence of surveyed risk factors as - a sex, age - 44% have made males at the age of ≥55 years and 45% of the woman at the age of ≥65 years, with the family anamnesis of early cardiovascular diseases have made 89% of the examined patients. Smoking has made 31,8%, a hypercholesterolemia of 62,4%, the excess body weight of 85,7%, improper feeding of 59,2%. At 40,8% the hypercholesterolemia, 81,2% psycho-emotional overloads were observed. The headache, dizziness, a ring or noise in ears, a sleep disorder, irritability and fast fatigue were the main complaints of patients. It should be noted that, the frequency of complaints increased with increase of severity of encephalopathy. Accumulation ε3/ε3-genotype authentically prevailed as at healthy (OR 12,5; 95%CI 5,24-29,9; p <0,0001), and at sick AH with CCVD (OR 9,88; 95%CI 5,77-16,9; p>;0,0001) (Figures 1 & 2).

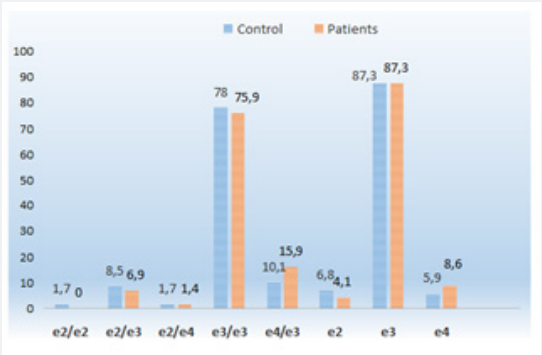

Figure 1: Case-Control study: genetic association analysis in Uzbekistan Genotype/allele frequencies.

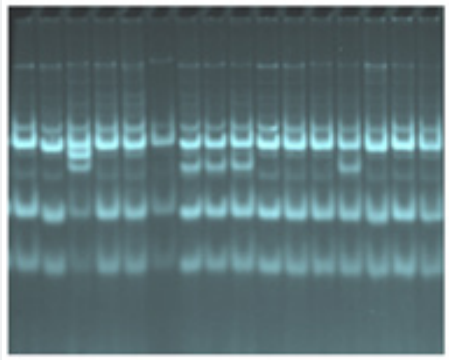

Figure 2: Visualization of the genotypes for e2/e4 polymorphism of the APOE gene, under ultraviolet illumination.

According to our data, among patients with cerebrovascular encephalopathy, in comparison with group healthy the occurrence ε4-allele was more often, 8,6% and 5,9% respectively. At all patients it was observed tendency to excess body weight, at carriers ε3/

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ε3 and ε3/ε4-genotype was observed the highest coefficient of BMI which has made 29,8±4,0 and 28,9±4,5 kg/sq. m respectively. Office SBP and DBP value were high at carriers ε2/ε4 and ε3/ε4 -genotypes. The analysis of clinical indicators on alleles has shown existence of high SBP and DBP in group of carriers ε4-allele. We have shown the research IMT that the carriage ε4-allele at patients with cerebrovascular encephalopathy is associated with increase in thickness of IMT carotids (p=0,02) (Table 1). It was observed tendency to increase in the levels total cholesterol, VLDL-C and triglycerides in group of carriers ε2/ε4, ε3/ε3 and ε3/ε4-genotypes by results the of lipid range analysis. At carriers ε4-allele the average level of Total cholesterol and LDL-C in blood it is reliable above than at carriers ε3 and ε2. 226, 7±41,1mg/dl (p=0,04) (Total cholesterol) and 134,1±35,1mg/dl (LDL-C) (p=0,02). The HDL-C level in group of carriers ε4 was the lowest and was 37, 4±6, 2 mg/dl (p =0, 04) (Table 2).

Table 1: The clinical characteristic and alleles (M±SD).

Parameters	e2, n=12	e3, n=253	e4, n=25	p1-2	p1-3	p2-3
AGE	51,3±7,4	54,0±9,6	55,2±8,3	0,34	0,18	0,55
BMI	28,0±3,3	29,6±4,0	28,7±4,4	0,17	0,63	0,29
Duration AH	10,1±6,1	10,7±7,3	11,6±8,3	0,78	0,58	0,56
SBP mm.Hg	164,2±22,8	166,5±21,4	170,6±23,9	0,72	0,44	0,37
DBP mm. Hg	95,8±13,1	95,8±10,3	99,6±7,9	1,0	0,28	0,07
IMT	0,91±0,3	0,89±0,3	1,04±0,3	0,82	0,23	0,02
Glucose	5,3±0,5	5,7±0,7	5,6±0,5	0,05	0,10	0,49

p1-2; p1-3- In comparison with data of group e2; p2-3- In comparison with data of group e3.

Table 2: Cholesterol status (M±SD).

Parameters	e2, n=12	e3, n=253	e4, n=25	p1-2	p1-3	p2-3
Total cholesterol mg/dl	198,1±33,3	218,0±36,3	226,7±41,1	0,23	0,04	0,26
TG, mg/dl	174,8±61,6	204,5±84,2	174,1±68,3	0,23	0,98	0,08
HDL-C mg/dl	42,2±6,6	39,4±6,5	37,4±6,2	0,15	0,04	0,14
VLDL-C mg/dl	35,1±12,4	41,4±17,2	34,4±13,7	0,21	0,88	0,05
LDL-C, mg/dl	120,3±32,2	117,9±33,6	134,1±35,1	0,74	0,26	0,02
KA	3,8±0,9	4,9±2,7	4,4±1,0	0,16	0,09	0,36

p1-2; p1-3- In comparison with data of group e2; p2-3- In comparison with data of group e3.

Severe forms of CCVD were more often observed at persons with carriage ε2/ε3 and ε3/ε4 APOE gene genotypes. The allele ε4 meets more often at degree AH 2 (10,9% of OR 2,18; 95%CI 0, 74-6,43; p=0,24) and degree AH 3 (9,3% OR 1,83; 95%CI 0,57-5,81; p=0,46), in comparison with degree AH 1 (5,3%). The allele ε4 meets more often at DE II (10,3% OSH 2,19; 95%DI 0,59-8,09; p=0,36) and DE III (8,8% OR 1,83; 95%CI 0,48-6,91; p=0,55), in comparison with DE I a stage (5,5%). It was observed the high index of loading BP in the afternoon and at night on all groups of patients (Table 2). It once again confirms features of a daily profile of arterial blood pressure at sick AH with cerebrovascular insufficiency. Also, according to the index of extent of night decrease in BP sick "non-dippers" prevailed, 5,8% among carriers ε4 – allele have made "night-speakers", "over-dippers" meets only at 1 patient.

Conclusion

The carriage of ε4 allele and ε2/ε4 and ε3/ε4 - genotypes of the APOE gene causes the tendency to a hypercholesterolemia and giperlipoproteinemiya, violation of a daily profile of BP in the form of high variability and insufficient night decrease arterial pressure that is high risk of development of atherosclerosis and cardiovascular diseases.

Discussion

Our results match with data of large-scale researches. So, it has been established that ε3-allele the most often met in human population according to Framing research. In work of the American scientist's interaction of the APOE genotype and gender on risk of development atherosclerosis has been shown. Men with ε3/ε4-genotype was associated with 1,79 multiple increase in risk of emergence of carotid plaques in comparison with other individuals. The multi alternative analysis has shown that at women ε2/ε3-genotype has been associated with decrease in risk of carotid plaques formation in comparison with ε3/ε3-genotype. Best of all contacts a receptor of LDL-C–ε2-allele, worst of all–ε4. It is found in most of representatives of European race ε3-allele. Frequency ε4-allele in the European populations varies from 5% in the southern populations (population of Italy, Spain) up to 30% in northern populations. The allele ε2 is met approximately at 5% of representatives of the European populations.

References

1. P Kirchhof, R Sipido, R Cowie, T Eschenhagen, A Fox, et al. (2014) The continuum of personalized cardiovascular medicine: a position paper of the European Society of Cardiology. Eur Heart J 35(46): 3250-3257.

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2. Williams O, Brust JC (2004) Hypertensive encephalopathy. Curr Treat Option Cardiovasc Med 6(3): 209-216.

3. Aydogan H, Isbir S, Kurnaz O, Gormus U, Isbir T (2009) Association of lipoprotein lipase s 447x and apoliprotein E genotypes with Low-density lipoprotein subfractions in Turkish patient with coronary artery disease. *In vivo* 23(1): 155-161.

4. Singh P, Singh, Bhatnagar DP, Kaur TP, Gaur SK (2008) Apoliprotein E polymorphism and its relation to plasma lipids in coronary heart disease. Indian Journal of medical science 62(3): 105-112.

5. Kawakami K, Okumura K, Matsui H, Tomida T, Sakai Y, et al. (2001) The apoliprotein E genotype influences the risk for vasospatic angina. Canadian Journal in cardiology 17(6): 660-666.

6. Kolovou G, Panagiotakos D, Kolovou V, Katsiki N, Mavroqeni S, et al. (2015) Common variants of apoliprotein E and cholesteryl ester transport protein genes in male patients with coronary heart disease and variable body mass index. Angiology 66(2): 169-173.

7. Davignon J, Gregg R, Sing C (1988) Apolipoprotein E polimorphism and atherosclerosis. Arteriosclerosis 8(1): 1-21.

8. Zhu L, Fratiglioni L, Guo Z, Basun H, Corder EH, et al. (2000) Incidence of dementia in relation to stroke and the apolipoprotein E epsilon4 allele in the very old. Findings from a population-based longitudinal study. Stroke 31(1): 53-60.

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