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ARTERİAL HİPERTENZİYA VƏ PİYLƏNMƏ OLAN XƏSTƏLƏRDƏ IRS-1 VƏ ADIPOQ GENLƏRİ POLİMORFİZMİNİN HEMODİNAMİK VƏ NEYROHUMORAL PARAMETRLƏRLƏ ƏLAQƏSİ

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Xülasə. *Məqalədə I insulin reseptorunun (İRS-1) G972R geninin polimorfizmi ilə adiponektinin (ADİPOQ) G276T geninin polimorfizmi arasında mümkün olan assosiasiyaları və onların Ukrayna populyasiyasında arterial hipertenziyası (AH) və piylənməsi olan şəxslərdə kardiovaskulyar remodelləşdirmə və neyrohumoral pozuntularla kombinasiyalarını aydınlaşdırmaq məqsədilə aparılmış tədqiqat haqqında məlumat verilir.*

Tədqiqata II dərəcəli AH və I-II dərəcəli piylənməsi olan 45-55 yaşlı 200 nəfər cəlb edilmişdir. Tədqiqatda antropometrik, biokimyəvi metodlardan, avtomatlaşdırılmış immunoloji analiz üsullarından, spektrofotometrik, molekulyar-genetik, instrumental və statistik metodlardan istifadə edilmişdir.

Tədqiqat göstərmişdir ki, xəstələrdə ADİPOQ substratının G276T geninin G/T + T/T genotipləri olan şəxslərdə G/G geninin daşıyıcılarına nisbətən aldosteronun və plazmada renin aktivliyinin (PRA) daha yüksək səviyyəsi, adipokin və karbohidrat səviyyələrinin disbalansı, antioksidant mühafizə sisteminin zəifləməsi, qanda malon dialdehidinin, dien konyuqatlarının, triqliseridlərin səviyyəsinin artması, eyni zamanda ümumi yuxu arteriyasının intima-media qişalarının qalınlaşması və həmin arteriyada nəbz dalğasının tezləşməsi müşahidə edilir.

İRS-1 substratına uyğun gələn G972R geninin G/R +R/R genotiplərinin daşıyıcıları yuxarıda göstərilən parametrlərlə birgə, endotelidən asılı vazodilatasiyanın zəifləməsi və plazmada C-reaktiv zülalın, həm də interleykin 6-nın səviyyəsinin artdığı diqqəti cəlb edir.

G276T geninin G/T +T/T genotipləri ilə İRS-1-ə uyğun gələn G972R geninin G/R + R/R genotiplərinin kombinasiyası neyrohumoral parametrlərin daha dərin neqativ xarakterli dəyişiklikləri ilə və ürək-damar sisteminin remodelləşməsinin çətinləşməsi ilə xarakterizə edilir; bu dəyişikliklər hər iki polimorf markerlərin G/G genotiplərinə malik olan şəxslərdəkinə nisbətən daha artıq dərəcədə olur.

Beləliklə, tədqiqat nəticəsində müəyyənləşdirilmişdir ki, AH və piylənməsi olan Ukrayna populyasiyasiyalı şəxslərdə ADİPOQ geninin G276T və İRS-1 geninin G972T geninin polimorfizmi ürək remodelləşməsinə nisbətən damar remodelləşməsinin daha artıq dərəcədə pozulması ilə assosiasiya edir.

Açar sözlər: *arterial hipertenziya, piylənmə, I insulin reseptoru substratının geni, adiponektin geni, genetik polimorfizm*

Ключевые слова: *артериальная гипертензия, ожирение, ген субстрата инсулинового рецептора-1, ген адипонектина, генетический полиморфизм*

Key words: *arterial hypertension, obesity, insulin receptor substrate-1 gene, adiponectin gene, genetic polymorphism*

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ASSOCIATION OF POLYMORPHISMS IRS-1 AND ADIPOQ WITH HEMODYNAMIC AND NEUROHUMORAL PARAMETERS IN OBESE HYPERTENSIVE PATIENTS

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The article presents the results of a study conducted to determine possible associations of polymorphism G972R of the insulin receptor substrate gene - 1 (IRS-1) and polymorphism G276T of the adiponectin gene (ADIPOQ) and their combination with cardiovascular remodeling and neurohumoral disorders in patients of the Ukrainian population with arterial hypertension (AH) and obesity (OB).

We examined 200 class II hypertensive patients with obesity I-II degrees aged 45-55. Anthropometric, biochemical, automated methods of immune analysis, spectrophotometric, molecular genetic methods, instrumental, statistical methods were used.

It was established, in obese hypertensive patients, the presence of G/T + T/T genotypes G276T of the ADIPOQ gene was associated with higher levels of aldosterone and plasma renin activity (PRA), more pronounced adipokine and carbohydrate imbalance, decreased overall antioxidant protection, increased levels of malonic dialdehyde (MDA), diene conjugates (DC), triglycerides and intima-media thickness (CIMT), an increase of the pulse wave velocity of carotid artery (cPWV) compared with carriers of G/G genotype. Carriers of G/R + R/R genotypes G972R of the IRS-1 gene, along with the above mentioned changes in parameters, are characterized by an additional decrease in endothelium-dependent vasodilatation (EDVD) and an increase in plasma levels of C-reactive protein (CRP) and also interleukin - 6 (IL-6). The presence of combination of G/T + T/T genotypes G276T of the ADIPOQ gene with G/R + R/R genotypes G972R of the IRS-1 gene is associated with more pronounced negative changes in neurohumoral parameters and indicators of cardiovascular remodeling compared with patients, carrying a combination of G/G genotypes of both polymorphic markers.

Thus, the study found that in patients of the Ukrainian population with AH and OB, polymorphisms G276T of the ADIPOQ gene and G972R of the IRS-1 gene are associated with profound neurohumoral disorders and, to a greater extent, with the progression of vascular remodeling than the cardiac one.

For a long time hypertension (AH) remains the most common non-communicable disease, as well as one of the most influential risk factors for cardiovascular diseases (CVD), with a leading position in terms of prevalence and overall mortality [1, 2]. Hypertension is also the most common disease associated with obesity, which acts as a risk factor for its development, and as a factor determining the global cardiovascular risk in hypertensive patients. The association of obesity with hypertension is characterized by two main consequences: higher morbidity and mortality from CVD, as well as an increase in the number of cases resistant to treatment of hypertension [3-5]. This is mainly due to the presence of additional metabolic disorders (prediabetes and diabetes) in these patients, multifactorial lesions of the cardiovascular system (CVD), which significantly contribute to the deterioration of the prognosis of comorbidity and life of patients [6-9]. Lipotoxic lesions of the cardiovascular system with the development of structural and functional changes, including left ventricular hypertrophy, contractile dysfunction, cardiomyocyte fibrosis, are possible with obesity.

Most links in the mechanisms of hypertension with obesity development are still poorly understood. According to the researchers,

hereditary risk factors are the most significant predictors of hypertension and obesity [10-12]. Genetic predisposition to hypertension is manifested under the influence of environmental factors - high-calorie diet, excessive fat intake and low physical activity. These environmental factors contribute to the development and progression of the metabolic syndrome components with hypertension because of the impairment of genes expression controlling insulin signal, polymorphic lipid disorders, defects in glucose metabolism enzymes [13, 14]. Insulin resistance considered being a major factor that determines the incidence of cardiovascular complications. Gly972Arg-polymorphism is one of the most recognized polymorphisms of the IRS-1 gene, which has been linked to the IR development in many populations. Numerous studies of IRS-1 polymorphism have shown its association with the development of type 2 diabetes in different populations, but there is insufficient data on its influence on the formation of hypertension and obesity comorbidity, in particular, at the stage of IR absence [15]. It is still unclear how the substances synthesized by adipose tissue affect insulin signal transmission and the IR development in obese patients at the stage of prediabetes [16, 17]. Adiponectin is the only protective factor that reduces IR in the liver, muscles, adipose tissue. With obesity, its secretion is reduced; as a result the protective role in relation to the risk of IR developing and metabolic disorders is lost [16, 17].

Views on the contribution of the G972R polymorphisms of the IRS-1 gene and G276T of the ADIPOQ gene to the development of IR, as the common pathophysiological mechanism of AH and obesity, remain controversial, despite advances in genome research [15]. There is also no data on the relationship between the combination of these polymorphisms with the development of the heart and blood vessels remodeling and neurohumoral disorders in this category of patients. This necessitates further research on the role of these polymorphisms in the development of hypertension and obesity comorbidity.

The purpose of our study was to determine possible associations of polymorphism G972R of the insulin receptor substrate gene-1 (IRS-1) and polymorphism G276T of the adiponectin gene (ADIPOQ) and their combination with cardiovascular remodeling and neurohumoral disorders in patients of the Ukrainian population with arterial hypertension and obesity.

Material and research methods: We examined 200 class II hypertensive patients with obesity I - II degrees aged 45-55. Patients had a history of hypertension for less than 5 years, medicated with antihypertensive drugs non-systemically and/or did not reach target BP levels when prescribing drug therapy. 120 patients were diagnosed with insulin resistance and 80 had no insulin resistance. Insulin resistance (IR) was determined by calculating the HOMA index.

Clinical-anamnestic methods with office measurement and home blood pressure monitoring were used to assess the clinical manifestations of AH and study the etiological factors of the disease. Average BP was calculated by the formula: $Average\ BP = 0.42 \times (SBP - DBP) + DBP$. Anthropometric methods used to assess the degree of obesity and diagnose abdominal obesity, height, body weight, body mass index, waist circumference, thigh volume, index "waist – thigh".

In this study, using standard biochemical methods, we defined the degree of carbohydrate metabolism disorders (fasting glycemia, glycosylated hemoglobin (HbA_{1c}), glucose tolerance test) and lipid metabolism (total cholesterol, triglycerides, LDL (low-density lipoprotein) cholesterol and HDL (high-density lipoprotein) cholesterol).

The activity of the renin-angiotensin-aldosterone system (RAAS) was evaluated by the levels of aldosterone and plasma renin activity (PRA) and their ratio (ARR). The functional state of adipose tissue was assessed by leptin and adiponectin, the state of proinflammatory activity by IL-6 and CRP. To determine the above parameters, automated methods of immune analysis were used. The spectrophotometric method was used to determine the intensity of lipid peroxidation. The prooxidant activity was assessed by the levels of malondialdehyde (MDA) and diene conjugates (DC), and the state of the antioxidant system was assessed by the index of total antioxidant activity.

Molecular genetic methods, using polymerase chain reaction, established the presence of genetic polymorphisms G276T gene ADIPOQ and G972R gene IRS-1. Three genotypes of the IRS-1 gene (G/G, G/R and R/R) and three genotypes of the ADIPOQ gene (G/G, G/T, T/T) were identified.

Morphofunctional properties of the myocardium were evaluated during ultrasound examination of the heart in one-dimensional, two-dimensional and Doppler modes by conventional methods («IMAGIC Agile» («Kontron Medical», France)).

The ejection fraction (EF) was calculated by the formula: $EF = (EDV – ESV) / EDV$, where ESV and EDV are the end-systolic and end-diastolic LV volumes, respectively.

The relative wall thickness of the LV (RWT) was calculated by the formula: $RWT = (TPWd + TIVSd) / LVEDD$, where TPWd – thickness of the posterior wall of the left ventricle in diastole, TIVSd – thickness of the interventricular septum (diastole), LVEDD – end-diastolic diameters.

The LV myocardial mass index (LVMI) was calculated as the ratio of the LV myocardial mass (LVM) to the surface area of the body (S):

$$LVMI = LVM / S$$

Left ventricular diastolic function was evaluated by pulmonary artery blood flow and transmitral diastolic blood flow in pulsed Doppler. For studying endothelial function, the degree of endothelium-dependent vasodilation (EDVD) in reactive hyperemia was determined in all patients according to the method of Celermajer D.S. in the modification of the method by O.V. Ivanova [18, 19]. Simultaneously, we measured the intima media thickness (CIMT) of the carotid artery. The pulse wave velocity (PWV) in the carotid artery (cPWV) was determined by the W-Track method; determination of the PWV in the abdominal aorta (aPWV) was performed using a phased sensor.

The statistical processing of the obtained data was carried out using the package of statistical software "SPSS 17" (IBM), Microsoft Office Exel-2003. The data are presented as mean values ± standard deviation. Significance was set at a p value of <0.05 in all cases.

The study protocol was approved by the Ethics Committee. All participants were informed about the aim of the study and signed a written consent form.

Research results. In patients with AH with obesity, the presence of G/T and T/T genotypes of the polymorphic marker G276T of the ADIPOQ gene is associated with an increase in BMI, CIMT, cPWV, higher levels of aldosterone and plasma renin activity, lower ARR ($p<0.01$ for all indicators), higher leptin levels ($p<0.001$), and lower adiponectin ($p<0.01$), more pronounced insulin resistance, higher carbohydrate levels profile ($p<0.001$ for all indicators), triglycerides ($p<0.05$), a decrease in the overall antioxidant protection ($p<0.01$) and increasing levels of MDA and DC ($p<0.001$ for both indicators).

Carrying of G/R and R/R genotypes in the G972R polymorphism of the IRS-1 gene in patients with AH and obesity alongside the above-mentioned changes is characterized by an additional decrease in EDVD ($p<0,05$) and an increase of both CRP and IL-6 ($p<0.001$ and $p<0.01$ respectively) in blood and more negative indicators of cardiac remodeling (LVEDD, $p<0,05$; LVESD, $p<0,01$; EDV, $p<0,05$; ESV, $p<0,05$; LVM, $p<0,05$).

Carriers of the combination of G/T or T/T-genotype G276T of the ADIPOQ gene in combination with G/R or R/R genotype G972R of the IRS-1 gene (41% of the total number of AH group with obesity) differ from carriers of the combination G/G genotype of the polymorphic marker of the ADIPOQ gene and G/G genotype of the polymorphic marker of the IRS-1 gene with large changes in vascular remodeling (larger CIMT ($p<0.001$), cPWV ($p<0.01$)), parameters of carbohydrate and lipid metabolism, system of oxidative stress – antioxidant protection, systemic inflammatory response factors, components of RAAS, leptin, as well as the presence of progression of heart remodeling - an increase in the size of the left ventricle and its MM ($p<0.05$ for all indicators) (Tables 1, 2).

Discussion. According to studies, numerous polymorphisms of the IRS-1 gene localized in 2q36-37 are associated with insulin resistance in various population groups. At the same time, these data are quite contradictory. Some have shown that the Gly972Arg polymorphism contributes to the development of diabetes mellitus in patients in Europe and Mexico, while other studies have not confirmed the role of this polymorphism in the formation of diabetes mellitus in the population of Turkey and India. The nucleotide polymorphism of Gly972Arg in the IRS-1 gene was found to be associated with decreased phosphatidylinositol-3-kinase (PI3-K) activity in some populations, leading to varying degrees of IR expression. In a study by CM Taniguchi and co-authors, a decrease in IRS-1 phosphorylation and phosphatidylinositol-3-kinase (PI3-K) activity in patients with type 2 diabetes with varying body weight and in

Table 1. *Comparative assessment of anthropometric and neurohumoral parameters in patients with hypertension and obesity in the presence of two unfavorable or two protective genotypes of ADIPOQ and IRS-1 genes*

Indicators	G/G genotype of ADIPOQ and G/G genotype of IRS-1	G/T+T/T genotypes of ADIPOQ and G/R + R/R genotypes of IRS-1
	n = 67	n = 81
BMI [kg/m^2]	33,62 ± 2,93	36,57 ± 1,53***
Waist circumference [cm]	107,54 ± 6,76	109,23 ± 7,32
Hip [cm]	116,12 ± 9,79	113,83 ± 7,42
Waist-to-hip ratio	0,93 ± 0,11	0,97 ± 0,10
HOMA-IR	2,56 ± 0,94	4,03 ± 1,35***
HbA_{1c} (%)	5,01 ± 0,32	5,47 ± 0,50***
Blood glucose [mmol/L]	4,87 ± 0,26	5,18 ± 0,55**
Insulin [μU/mL]	11,89 ± 4,48	17,36 ± 4,97***
Total cholesterol [mmol/L]	6,08 ± 0,53	6,14 ± 0,48
Triglycerides [mmol/L]	1,95 ± 0,37	2,02 ± 0,39
LDL cholesterol [mmol/L]	4,69 ± 0,73	4,98 ± 0,51*
HDL cholesterol, [mmol/L]	0,99 ± 0,10	0,99 ± 0,09
Overall antioxidant protection [mmol/L]	1,09 ± 0,06	1,01 ± 0,04***
MDA [nmol/mL]	33,99 ± 3,70	36,44 ± 3,15***
DC [nmol/mL]	30,35 ± 2,26	33,28 ± 4,11***
IL-6 [pg/mL]	137,16 ± 7,98	140,75 ± 8,27*
CRP [mg/L]	7,14 ± 1,02	7,99 ± 1,24***
Aldosteron [ng/dl]	15,84 ± 3,20	17,84 ± 1,81**
PRA , ng/ml/hour	2,03 ± 1,02	2,65 ± 0,49**
ARR	11,22 ± 7,38	7,03 ± 1,73**
Adiponectin [ng/mL]	6,43 ± 0,33	6,40 ± 0,54
Leptin [ng/mL]	13,71 ± 2,38	16,20 ± 2,29***

Notes: * – p<0,05; ** – p<0,01; *** – p<0,001: Significance of differences between the combination of G/T + T/T genotypes G276T of the ADIPOQ gene and G/R + R/R genotypes G972R of the IRS-1 gene and the combination of G/G genotypes of both polymorphic markers of the ADIPOQ and IRS-1 genes.
BMI – body mass index; HbA_{1c} – glycated hemoglobin; HDL – high density lipoprotein; LDL – low-density lipoprotein; CRP – C-reactive protein; IL-6 – interleukin 6; HOMA-IR – Homeostatic Model Assessment for Insulin Resistance; MDA – malonic dialdehyde; DC – diene conjugates; PRA – plasma renin activity; ARR – aldosterone-renin ratio

obese patients without type 2 diabetes in 50-60% of cases were accompanied by decreased expression of IRS-1 and PI3-K]. In addition, it was noted that Gly972Arg polymorphism also affects hyperinsulinemia and fatty acid composition [15].

Genetic variants of the ADIPOQ gene are known to affect the circulation of adiponectin, the only known protective factor that can reduce IR in the liver, muscle, and adipose tissue. For example, in Asian and European populations, the rs1501299 T-allele carriers have higher levels of adiponectin [17, 20]. A meta-analysis of the Chinese Han population reported a higher frequency of G alleles in people with metabolic syndrome. In addition, in the Spanish population of persons homozygous for the GG genotype, impaired glucose tolerance was found [16]. The study by S.Kumar et al. determined associations of the ADIPOQ gene with the development of IR and visceral obesity [21].

Table 2. *Comparative assessment of hemodynamic parameters in patients with hypertension and obesity in the presence of two unfavorable or two protective genotypes of ADIPOQ and IRS-1 genes*

Indicators	G/G genotype of ADIPOQ and G/G genotype of IRS-1	G/T+T/T genotypes of ADIPOQ and G/R + R/R genotypes of IRS-1
	n = 67	n = 81
SBP [mm Hg]	171,90 ± 4,13	170,33 ± 4,77
DBP [mm Hg]	101,72 ± 3,08	101,05 ± 2,91
Average BP [mm Hg]	131,01 ± 4,99	130,75 ± 3,12
CIMT [mm]	0,88 ± 0,08	0,95 ± 0,08***
CIMT bifurcation [mm]	1,32 ± 0,16	1,38 ± 0,15*
cPWV [m/s]	8,24 ± 1,05	8,89 ± 1,12**
aPWV [m/s]	8,41 ± 0,92	8,70 ± 1,13
EDVD (%)	6,97 ± 1,10	6,72 ± 1,05
TIVSd [cm]	1,16 ± 0,13	1,20 ± 0,12
TIVSs [cm]	1,43 ± 0,17	1,49 ± 0,14
TPWd [cm]	1,17 ± 0,14	1,20 ± 0,16
TPWs [cm]	1,60 ± 0,32	1,66 ± 0,40
LVEDD[cm]	4,82 ± 0,32	4,97 ± 0,36**
LVESD[cm]	3,18 ± 0,23	3,29 ± 0,28*
EDV [mL]	109,38 ± 17,82	117,45 ± 20,28**
ESV [mL]	40,70 ± 7,64	44,23 ± 9,49*
LVEF (%)	62,71 ± 3,85	62,50 ± 2,85
LVM [g]	252,95 ± 64,68	278,04 ± 71,47*
LVMI [g/m^2]	120,59 ± 30,80	129,42 ± 33,66
RWT	0,48 ± 0,05	0,48 ± 0,05
Mean pulmonary AP [mm Hg] by Kitabatake	16,16 ± 3,71	16,49 ± 2,86
e´ [cm / s]	11,75 ± 2,27	11,54 ± 2,12
E [cm / s]	70,39 ± 11,14	66,88 ± 7,23*
A [cm / s]	80,53 ± 12,21	78,05 ± 9,14
E/A	0,89 ± 0,15	0,86 ± 0,11
E/e´	6,12 ± 1,08	5,97 ± 1,14

Notes: * – p<0,05; ** – p<0,01; *** – p<0,001: Significance of differences between the combination of G/T + T/T genotypes G276T of the ADIPOQ gene and G/R + R/R genotypes G972R of the IRS-1 gene and the combination of G/G genotypes of both polymorphic markers of the ADIPOQ and IRS-1 genes.
DBP – diastolic blood pressure; SBP – systolic blood pressure; A – maximum late (atrial) filling speed; AP – artery pressure; E – filling rate in spectral mode; e – maximum early LV filling rate at tissue mode; E/A – ratio of maximal rates of early and late filling of LV at spectral mode; E/e – ratio of E and e; EDVD – endothelium-dependent vasodilatation; EF – ejection fraction; CA – carotid artery; IMT – intima-media thickness; LVM – left ventricular mass; LVMI – left ventricular mass index; PWV – pulse wave velocity (cPWV – carotid artery, aPWV – abdominal aorta); TIVSd – thickness of the interventricular septum (diastole); TIVSs – thickness of the interventricular septum (systole); TPWs – the thickness of the posterior wall of the left ventricle in systole; TPWd – the thickness of the posterior wall of the left ventricle in diastole; LVEDD – end-diastolic diameters; LVESD – end-systolic diameters; EDV – end-diastolic volume; ESD – end-systolic volume; RWT – relative wall thickness

Our study conducted in the Ukrainian population found that in patients with hypertension with obesity G/T and T/T genotypes of the polymorphic marker G276T of the ADIPOQ gene, as well as G/R and R/R genotypes of the polymorphic marker G972R of the IRS-1 gene were unfavorable in the development of this comorbidity and were

associated with distinction in anthropometric parameters, with more pronounced violations of carbohydrate and lipid spectra of blood and activation of RAAS, imbalance of adipokines and proinflammatory parameters, activity of oxidative stress – antioxidant protection, negative changes in cardiovascular remodeling compared with GG genotypes of both polymorphic markers, which requires better and polysystemic monitoring of clinical, functional and laboratory conditions in this category of patients.

Concomitant presence of the G/T or T/T genotype G276T of the ADIPOQ gene and the G/R or R/R genotype of the G972R of the IRS-1 gene in patients with hypertension with obesity was associated with profound neurohumoral disorders associated with progression of the cardiac and blood vessels remodeling.

Thus, the study found that in patients of the Ukrainian population with AH and OB, polymorphisms G276T of the ADIPOQ gene and G972R of the IRS-1 gene are associated with profound neurohumoral disorders and, to a greater extent, with the progression of vascular remodeling than the cardiac one.

Conflict of interest

All authors declare no conflict of interest

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АССОЦИАЦИЯ ПОЛИМОРФИЗМОВ IRS-1 И ADIPOQ С ГЕМОДИНАМИЧЕСКИМИ И НЕЙРОГУМОРАЛЬНЫМИ ПАРАМЕТРАМИ У ПАЦИЕНТОВ С АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ И ОЖИРЕНИЕМ

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Резюме. В статье приведены результаты исследования, проведенного с целью определения возможных ассоциаций полиморфизма G972R гена субстрата инсулинового рецептора-1 (IRS-1) и полиморфизма G276T гена адипонектина (ADIPOQ) и их комбинации с кардиоваскулярным ремоделированием и нейрогуморальными расстройствами у пациентов украинской популяции с артериальной гипертензией (АГ) и ожирением (ОЖ).

Обследовано 200 больных с АГ II степени и ожирением I - II степени в возрасте 45-55 лет. Использовались антропометрические, биохимические, автоматизированные методы иммунного анализа, спектрофотометрические, молекулярно-генетические методы, инструментальные, статистические методы.

Установлено, что присутствие генотипов G/T + T/T G276T гена ADIPOQ у пациентов с АГ и ОЖ ассоциировано с более высокими уровнями альдостерона и плазменной активности ренина, более выраженным адипокиновым и углеводным дисбалансом, снижением общей антиоксидантной защиты, повышением уровня малонового диальдегида, диеновых конъюгатов, триглицеридов, увеличением толщины интима-медиа общей сонной артерии и скорости пульсовой волны сонной артерии (СПВ ОСА) по сравнению с носителями G/G генотипа.

Носители G/R + R/R генотипов G972R гена IRS-1, наряду с вышеуказанными изменениями параметров, характеризуются дополнительным снижением эндотелий-зависимой вазодилатации (ЭЗВД) и повышением плазменных уровней С-реактивного белка, а также интерлейкина-6.

Наличие комбинации G/T + T/T генотипов G276T гена ADIPOQ с G/R + R/R генотипами G972R гена IRS-1 ассоциировано с более глубокими негативными изменениями нейрогуморальных параметров и показателей сердечно-сосудистого ремоделирования по сравнению с носителями комбинации G/G генотипов обоих полиморфных маркеров.

Таким образом**,** в результате исследования установлено, что у пациентов украинской популяции с АГ и ОЖ полиморфизмы G276T гена ADIPOQ и G972R гена IRS-1 ассоциированы с глубокими нейрогуморальными расстройствами в большей степени связанными с прогрессированием сосудистого ремоделирования, чем ремоделирования сердца.

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