variants of the GNB3 gene (rs5443, 825C>T) did not differ significantly between groups. The wild C-allele statistically significantly prevails over the mutated T-allele in both groups according to the AGT (rs4762) and GNB3 (rs5443) genes ($p<0.001$).

Binary logistic regression confirmed an increase in the risk of hypertension inheritance according to dominant and additive models in minor T-allele carriers of the AGT gene (rs4762) almost 3 times higher than in C-allele homozygotes ($p = 0.04$ and $p = 0.03$). Inheritance of EAH is not associated with polymorphic variants of the GNB3 gene (rs5443).

Conclusions: The T-allele of the AGT gene (rs4762) increases the risk of hypertension almost 3 times, whereas, polymorphic variants of the GNB3 gene (rs5443) are not predictors of EAH in the observed.

POLYMORPHIC VARIANTS OF AGT (RS4762) AND GNB3 (RS5443) GENES AS RISK FACTORS FOR SEVERE ARTERIAL HYPERTENSION

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Objective: The aim of our study was to evaluate the role of AGT (rs4762) and GNB3 (rs5443) gene polymorphisms as risk factors for severe hypertension.

Design and method: The case-control study involved 100 patients with EAH stage II, 1-3 degrees of blood pressure (BP), high and very high cardiovascular risk. Among the patients there were 21% (21) men, 79% (79) women. The mean age of patients was 59.86±6.22 y.o. The control group consisted of 60 almost healthy individuals with relevant age (49.13±6.28y.o.) and gender distribution (63% - women, 37% - men). The AGT (rs4762) gene polymorphism was studied by a qualitative polymerase chain reaction (PCR) in real time.

Results: Severity of EAH does not depend on polymorphic variants of AGT (rs4762) and GNB3 (rs5443) genes. The distribution showed no statistically significant differences in the aforementioned distribution. Individuals with the first degree of hypertension met more often with the CC genotype of the GNB3 gene (rs5443) by 22.23% than among patients with the T allele ($x2 = 3,66$; $p = 0,055$) in patients with EAH.

Conclusions: Epidemiological analysis did not confirm the polymorphic variants of the AGT (rs4762) and GNB3 (rs5443) genes as predictors of the severe course of EAH according to the degrees of BP elevation.

IMMUNE AND METABOLIC DISORDERS IN HYPERTENSION, OBESITY, AND HEPATIC STEATOSIS ASSOCIATE WITH PPAR-GAMMA2 PRO12ALA AND ACE I/D GENES' POLYMORPHISMS

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Objective: Metabolic changes and obesity play important roles in arterial hypertension pathogenesis and progression. Whereas hepatic steatosis (HS) and AH have multiple common mechanisms of development involving metabolic and immune changes, the aim of study was to investigate the influence of Pro12Ala polymorphism of PPAR-γ2 gene and I/D polymorphism of ACE gene on metabolic profile and cytokines in obese patients with HS and AH.

Design and method: Study involved 154 AH patients with HS (87 males, 67 females, age 50.06±7.34). Duration of HS 1-5 years, AH 3-21 years. Metabolic disorders were defined with body mass index (BMI), glycaemia, immunoreactive insulin (IRI), total cholesterol (TC), low and high density cholesterol (LDL-C, HDL-C), triglycerides (TG), C-peptide (CP) levels and HOMA-IR index. TNF- α and leptin plasma levels were assessed by ELISA. Genes' polymorphism of PPAR-γ2 (Pro-12Ala), and ACE (I/D) alone or in combination was studied with PCR.

Results: Differences of BMI, plasma glucose, IRI, HOMA-IR, CP and leptin are independent from ACE gene genotypes ($p>.05$). Pro-allele carriers of PPAR-γ2 gene have higher BMI than AlaAla carriers (32.7±2.1 and 27.9±1.1 kg/m² vs 25.6±0.8 kg/m², accordingly ($p<.05$), leptin level – 14.3±0.41 and 8.6±0.25 ng/ml vs 3.7±0.22 ng/ml, ($p<.001$), glucose level – to 10.2% and 10.9% accordingly ($p<.05$); CP level was higher in ProPro-genotype than in Ala-allele carriers to 15.7% ($p<.05$). Risk group of dyslipidemia are ProPro-genotype carriers of PPAR-γ2 gene with higher level of TC, TG and LDL-C to 16.4%, 17.3% and 27.9% ($p<.05$) and lower level of HDL-C in women to 25.6% ($p = .038$). Lipids levels are independent on ACE I/D polymorphism. Baseline TNF-α plasma levels did not significantly deviate between genotypes of PPAR-γ2 gene, but D-allele carriers (I/D+DD) of ACE gene had higher baseline TNF-α plasma levels (91.61 and 109.11 pg/ml, accordingly $p<.01$).

Conclusions: In HS hypertensive patients metabolic disorders are clearly associated with PPAR-γ2 Pro-allele (carbohydrates) and ProPro-genotype (lipids). Presence of D-allele of ACE gene is associated with reliably higher level of TNF-α plasma levels.

ENDOTHELIAL NITRIC OXIDE SYNTHASE (NOS3) AND GUANINE NUCLEOTIDE-BINDING PROTEIN (GNB3) GENES' POLYMORPHISMS PORTEND OBESITY IN HYPERTENSIVE PATIENTS: THE GENDER ASPECT

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Objective: Obesity is a major risk factor of essential arterial hypertension (EAH) because of neuro-hormonal, sympathoadrenal and renin-angiotensin-aldosterone system activation, as well as endothelial dysfunction and systemic low grade inflammation. However, genetic mechanisms of obesity development in EAH patients remained unclear. Therefore, we studied the guanine nucleotide-binding protein-β3 (GNB3, rs5443) and endothelial nitric oxide synthase (NOS3, rs2070744) genes' polymorphisms as possible genetic harbingers of obesity in EAH patients particularly focusing on gender.

Design and method: One-hundred EAH patients with hypertensive-mediated organ damage (moderate-very high cardiovascular risks, aged 45-65 years) and 48 practically healthy (control) participated in the cohort case-control study. Obesity was determined by body mass index (BMI) >30 kg/m2. GNB3 (rs5443) and NOS3 (rs2070744) genotyping performed by TaqMan probes (CFX96 Real-Time PCR).

Results: The NOS3 gene mutation in the homozygous state occurs in 16.67% of EAH patients and for the GNB3 gene in 8.33% of cases, which does not differ from the control group. The relative frequency of obese prevailed among EAH patients with the mutated C-allele carriers of the NOS3 gene by 31.94% ($\chi^2 = 13.58$; $p<0.001$) and T-allele of the GNB3 gene (30.56%) in the absence of such among healthy control. The risk of obesity increases in EAH patients in C-allele carriers of the NOS3 gene almost 6 times [OR 95%CI:2.11-14.82; $p<0.001$] and in T-allele patients of the GNB3 gene – more than 10 times [OR 95%CI:2.25-45.44; $p<0.001$], 1.3 times more often in women than men ($p<0,05$), regardless the genes' allelic state. The TT-genotype of the NOS3 gene and the CC-genotype of the GNB3 gene play a protective role against obesity.

Conclusions: The C-allele of the NOS3 gene (rs2070744) and the T-allele of the GNB3 gene (rs5443) increase the obesity risk in hypertensive patients 6-10 fold ($p<0.001$) as well, 1.3 times more often in women, than men.

RISK CONFERRED BY POLYMORPHIC VARIANTS OF VITAMIN D RECEPTOR (VDR) AND ANGIOTENSIN II TYPE 1 RECEPTOR (AGTR1) GENES FOR ESSENTIAL HYPERTENSION

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Objective: The aim of this study was to establish the role of 1166A>C polymorphism of the AGTR1 gene (rs5186) and A/G polymorphism of the VDR gene (rs2228570) in risk prediction of essential hypertension (EH).

Design and method: The study included patients with EH and hypertensive-mediated organs damage (2nd stage), moderate, high/very high cardiovascular risk. 100 subjects were involved in the case-control study. There were 70.84% females, 29.16% males among them, the mean age was 57.86±7.81 yo. Age- and gender-matched controls ($n = 60$) whose blood pressure measurements were in normal range and without any apparent diseases were randomly selected to compare with the patient data. In order to detect AGTR1 (rs5186) and VDR (rs2228570) gene polymorphism the qualitative real-time polymerase chain reaction was done. AGTR1 gene genotyping was performed for 72 patients and 48 healthy individuals and VDR gene – for 100 patients and 60 healthy subjects.

Results: The distribution of genotypes and alleles AGTR1 (rs5186) and VDR (rs2228570) in the study and control groups did not differ significantly ($p>0.05$). C-allele of AGTR1 gene (rs5186) increases the risk of EAH more than 2 times [OR–2.31; 95% CI OR:1.19–4.47; $p = 0.011$], as well as AC- and the combination of AC- + CC-genotypes [OR–2.09; 95% CI OR:1.03–4.25; $p = 0.038$ and OR–2.30; 95% CI OR:1.14–4.64; $p = 0.017$]. The epidemiological analysis showed that polymorphic variants VDR (rs2228570) genes are not the risk factors of EH in the observed. Although, the combination of wild alleles of both genes in the homozygous state (AAAGTR1/AAVDR) makes a protective effect [OR = 0,42; OR 95%CI:0,18-1,0; $\chi^2 = 3,74$; $p = 0,05$], the combination of minor alleles (C-allele