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ENDOTHELIAL NITRIC OXIDE SYNTHASE GENE POLYMORPHISM (894G>T, 786T>C) CONTRIBUTE TO HYPERTENSION RISK AND LIPIDS PROFILE DISORDERS

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Objective: Endothelial nitric oxide synthase (eNOS) gene meet the criteria for candidate genes of cardiovascular disease, including essential arterial hypertension (EAH). The aim of the study was to evaluate the association of eNOS gene polymorphism (894G>T, 786T>C) with EAH risk, lipids profile and some concomitant diseases.

Design and method: 100 EAH patients with target-organ damage, moderate, high/very high cardiovascular risk were involved in the case-control study. 79.0% females and 21.0% males, mean age 59.87 ± 8.02 ; disease duration 6–25 years. Control included 48 practically healthy persons of relevant age. eNOS gene polymorphisms (894G>T, 786T>C) was examined by Real-Time PCR. Lipids' profile was studied by total cholesterol (TC), high-, low density cholesterol (HDL-C, LDL-C), triglycerides (TG) and atherogenic index (AI).

Results: eNOS gene mutants' T-allele of 894G>T and C-allele of 786T>C were observed in 34.2% and 32.2% patients, that was almost 2 times less, than G-allele carriers ($p = 0.006$) and T-allele patients ($p = 0.004$) respectively. eNOS gene T-allele (894G>T) and C-allele (786T>C) were associated with increased relative risk of EAH 1.8 times [OR = 2.43; 95%CI:1.20–4.95] and 2.15 times [OR = 3.48; 95%CI:1.58–7.68], also with higher risk of concomitant Diabetes Mellitus type 2, cerebrovascular disease and acute myocardial infarction in anamnesis 1.53–1.72 times ($p < 0.05$). eNOS gene haplotype analysis proved the contribution of -894G/786C and -894T/786C haplotypes to EAH risk increase 2.05 times [OR95%CI:1.18–4.04] and 3.18 times [OR95%CI:1.27–7.29], elevation of TG level and atherogenic index by 10.5–18.7% ($p < 0.05$) and 12.65–14.19% ($p < 0.05$) accordingly. The HDL-C level was significantly lower in -894G/786C and -894T/786C carriers by 18.16% ($p < 0.01$) and 22.07% ($p < 0.001$). -894G/786T genotypes combination played a protective role against EAH [OR = 0.55; 95%CI:0.39–0.76; $P < 0.001$].

Conclusions: eNOS gene -894G/786C and -894T/786C increased the EAH risk and lipids profile metabolism disorders.

DEPENDENCE OF METABOLIC DISORDERS ON ALDOSTERONE SYNTHASE CYP11B2 (-344C/T) GENE POLYMORPHISM IN HYPERTENSIVE PATIENTS

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Objective: The aim of the study was to analyze the association of CYP11B2 (-344C/T) gene polymorphism with lipids profile and aldosterone level changes in patients with essential arterial hypertension (EAH).

Design and method: One-hundred subjects with EAH and target-organ damaging (2nd stage), moderate, high or very high cardiovascular risk were involved in the case-control study. Among them 79.0% females and 21.0% males, mean age 59.87 ± 8.02 ; disease duration from 6 to 25 years. Control group included 48 practically healthy persons of relevant age. Gene polymorphism of aldosterone synthase gene CYP11B2 (-344C/T) was examined by polymerase chain reaction. Lipids' profile in serum was studied by total cholesterol (TC), high- and low density levels cholesterol (HDL-C, LDL-C), triglycerides (TG) concentration and atherogenic index (AI). Aldosterone plasma concentration was assessed by ELISA.

Results: The TG level and atherogenic index were higher in T-allele carriers than in CC-genotype of CYP11B2 gene: in patients by 22.61–56.2% ($p < 0.05$), in control group by 31.16–77.42% ($p < 0.05$). Contrary, the HDL-C level was lower T-allele carriers in both groups: by 12.23% and 12.95% ($p < 0.05$) in patients and by 18.34% and 27.22% ($p < 0.05$) in control group, respectively. Significant differences in lipids profile data between patients and control groups depending on genotypes were not observed. Aldosterone concentration elevated also in T-allele carrier's patients by 53.62% ($p < 0.001$) and 26.90% ($p = 0.015$), than in CC-genotype and was 2.14–2.72 times higher, than in control group ($p < 0.001$). TG level in CC-genotype males was higher, than in CC-genotype's women by 68.57% ($p = 0.028$), but in TT-genotype males HDL-C was reliably lower by 18.40%

($p = 0.008$) than in TT-carriers' women with higher atherogenic index by 25.84% ($p = 0.031$). Otherwise, aldosterone concentration was certainly higher in women, than in men regardless the genotypes of CYP11B2 gene. But aldosterone level prevailed in T-allele carriers of both genders over CC-genotype patients' data: by 27.01% and 49.64% ($p < 0.05$) for women and by 20.93% and 43.11% ($p < 0.05$) for men.

Conclusions: Thus, TT-genotype or T-allele of aldosterone synthase gene CYP11B2 (-344C/T) associated with higher blood level of triglycerides and aldosterone concentration (especially in females), elevated atherogenic index and lower HDL-C rate (preferably in males).

ARE METABOLIC DISORDERS IN HYPERTENSIVE PATIENTS ASSOCIATED WITH GNB3 (RS5443) GENETIC POLYMORPHISMS?

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Objective: Primary/essential hypertension (PH) is the most common cause of left ventricular hypertrophy (LVH) and is often associated with metabolic disorders. The aim of the study was to analyse dependence of metabolic parameters on the guanine nucleotide binding protein (G-protein) $\beta 3$ subunit gene polymorphism (GNB3, rs5443) in hypertensive patients.

Design and method: A cross-sectional study involved 72 PH patients of high and very high cardiovascular risk (29.16% men and 70.84% women); the average age 59.87 ± 7.98 y. The control group included 48 healthy individuals (aged 49.13 ± 6.28 y) and sex distribution (62.5% women and 37.5% men). GNB3 (C825T) polymorphism was investigated by Real Time PCR. LVH was assessed by EchoKG. Metabolic disorders were studied by lipids panel (Total cholesterol (TC), Triglycerides (TG), Low-, and High- density lipoprotein cholesterol (LDL-C, HDL-C) levels) and Glucose blood value. The atherogenic index (AI) was calculated by the formula: $(TC - HDL-C) / HDL-C$.

Results: In CC-genotype carriers of the GNB3 gene metabolic parameters were as follows: TC 5.50 ± 0.79 mmol/L, TG 2.10 ± 0.8 mmol/L, HDL-C 1.22 ± 0.22 mmol/L, LDL-C 4.03 ± 0.76 mmol/L, AI 3.66 ± 0.84 U, Glucose 7.7 ± 2.34 mmol/L. In PH patients with TC-genotype the concentration of TC was 5.82 ± 1.15 mmol/L ($pCC > 0.05$), TG 1.73 ± 0.55 mmol/L ($pCC > 0.05$), HDL-C 1.30 ± 0.21 mmol/L ($pCC > 0.05$); LDL-C 4.39 ± 1.07 mmol/L ($pCC > 0.05$), AI 3.61 ± 0.95 ($pCC > 0.05$), Glucose 7.37 ± 2.34 mmol/L ($pCC > 0.05$). In TT-genotype carriers the concentration of TC was 6.6 ± 0.64 mmol/L (it was higher than in C-allele carriers by 20.0% ($pCC > 0.05$) and 13.79% ($pTC = 0.016$) as much), TG 2.6 ± 1.27 mmol/L, that was higher than in C-allele patients by 23.81% ($pCC > 0.05$) and 52.94% ($pTC = 0.038$), respectively. The other parameters did not differed significantly between genotypes' carriers and in mutation homozygous T-allele carriers were as follows: HDL-C 1.3 ± 0.05 mmol/L ($pCC, TC > 0.05$), LDL-C 4.7 ± 0.69 mmol/L ($pCC, TC > 0.05$), AI 4.0 ± 0.69 ($pCC, TC > 0.05$), Glucose 6.20 ± 1.2 mmol/L ($pCC, TC > 0.05$).

Conclusions: Therefore, the metabolic disorders in hypertensive patients do not depend on the GNB3 (rs5443) gene polymorphism.

LINKAGE BETWEEN NOS3 (RS2070744) AND GNB3 (RS5443) GENES' POLYMORPHISM, CAROTID ARTERIES STRUCTURAL CHANGES AND ENDOTHELIAL DYSFUNCTION IN ESSENTIAL HYPERTENSION

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Objective: This study aims to verify the risk of endothelial dysfunction (ED) and carotid intima media thickness (IMT) changes depending on GNB3 (rs5443) and NOS3 (rs2070744) genes' polymorphism in essential arterial hypertensives (EAH).

Design and method: One-hundred EAH patients (moderate-very high cardiovascular risks, aged 45–65 years) and 48 practically healthy (control) participated in the case-control study. Soluble Vascular Cell Adhesion Molecule (sVCAM-1), total NO metabolites, transcriptional activity of NOS3 gene, Endothelium-Dependent Flow-Mediated Dilation of the Brachial Artery (FMD BA) and carotid IMT were studied. GNB3 (rs5443) and NOS3 (rs2070744) genotyping performed by TaqMan probes (CFx96QReal-Time PCR).

Results: C-allele of NOS3 gene elevates the risk of atherosclerotic plaques on the carotid arteries over 3.5 times [OR95%CI:1.24–11.20; $p = 0.019$ and OR95%CI:1.22–10.18; $p = 0.018$], ED – by total NO metabolites decrease ($< 25 \mu\text{mol/l}$) and sVCAM-1 value raise ($> 1050 \text{ ng/ml}$) – 12 and 4 times