

Genes of vascular tone polymorphism and PE risks in Uzbek population

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Purpose: To study the relationship among mostly studied polymorphisms of 4 genes responsible for vascular tone regulation: angiotensinogen (AGT) rs4762 and rs699, angiotensin II receptor type 1 receptor (AGTR1) rs5186 and angiotensin II receptor type 2 receptor (AGTR2) rs1403543.

Method: Preeclampsia's (PE) ISSHP definition was used to identify women with hypertension and proteinuria. Control group matched parity and anamnesis excluded hypertension. Genotyping was done by amplification of corresponding genome regions using qPCR methods (DNA technology DT-96, RF) and pyrosequencing (PyroMark Q24, Qiagen, Germany) using PyroMark Gold Q24 reagents (Qiagen, Germany) and PCR kits. Statistical analysis was done using statistical packages "SPSS 13", "PLINK" and "Haploview 4.2", haplotypes formation and evaluation of their link with APS syndrome was done using "THESIAS" program. Results were statistically significant at $P < 0.05$.

Patients: 78 cases of PE and 26 women in control group were included in Ob&Gyn RSSRMC.

Results: Genotypes distribution of all 4 polymorphisms was in the Hardy-Weinberg equilibrium in both groups. Allele frequencies distribution and genotypes of polymorphism rs4762, rs699, rs5186, rs1403543 regulators of vascular tone genes in PE and control groups revealed risk and protective markers for this disease. Relative polymorphism of relative risk r and 4762 genotype was 2.69 ($P=0.005$) and 3.1 respectively ($P=0.02$); G-allele ($OR=0.37$, $P=0.005$) and genotype GG ($OR=0.29$, $P=0.02$) of this polymorphism can be considered as protective marker in this pathology development. Disequilibrium of connection between loci of polymorphic AGT genes ($r^2=0.937$, $D=0.89$, $P=0.0000$) was observed in patients with PE and control group. Comparing haplotypes frequencies between patients with PE and control group showed risky haplotype of CC (64% versus 3.5% in control group, $\chi^2=6.66$, $p=0.009$, $OR=1.57$, $CI: 1.04-2.36$) and protective haplotype of TC ($\chi^2=5.8$, $p=0.015$, $OR=0.29$, $CI: 0.22-0.42$). There were no statistically significant differences for other haplotypes.

Conclusion: Polymorphisms of "vascular tone" genes have great importance for development of hypertensive disorders during pregnancy. Genetic associations performed in the study can be used as genetic markers of PE susceptibility, which will allow patients with temporary group risk, to develop preventive measures.

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