Coronary artery disease association with serum concentration and genetic variation of MMP-9 in Ukrainian population

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Introduction: Coronary artery disease (CAD) is one of the main cause of death in European countries. The mortality associated with CAD has been rising for the past 30 years in Central and Easten Europe (including Ukraine). It is known that atherosclerosis is the primary risk factor of CAD development and Matrix metalloproteinase-9 (MMP-9) is involved in all stages of atherosclerosis and thus may contribute to CAD aggravation. It is very important to find specific mechanisms of atherosclerosis progression, the impact of genetic and external factors which influence on the development of CAD in different populations. Therefore, the aim of this study was to investigate the influence of MMP-9 concentration and functional rs17576 single nucleotide polymorphism (SNP) on risk of CAD development in Ukrainian population.

Materials and methods: In our study 128 patients were recruited. All of them we divided into three groups: 1 - with angiogrphically normal (intact) coronary arteries; 2 - patients with acute coronary syndrome (ACS) and 3 - with chronic coronary syndrome (CCS). The study protocol was approved by the Institutioal Ethics Committee and each participant was required to provide a writing informed consent. We recorded clinical data, biochemical analysis, performed electrocardiogram, coronary angiography and echocardiography. Blood for detection of MMP-9 and rs 17567 MMp-9 polymorphism was draw under standardized conditions before coronary angiography. Levels of MMP-9 were assessed using commercial ELISA immunoassay following manufacturer's instruction. The genotyping for MMP-9 rs17567-single nucleotide polymorphism was done by Real-time PCR. All statistical calculations were done using Statistical Package for the Social Sciences software.

Results: The results of analysis of association between MMP-9 rs17576 and CAD development demonstrate a weak link with borderline significance between MMP-9 concentration and ACS presence both before (Pc=0.026; ORc=1.003, 95% CI: 1–1.006) and after the adjustment for covariates (Pa=0.04; ORa=1.003, 95% CI: 1–1.006). In contrast, no significant association was detected for CCS group (Pa>0.05). There were no statistically significant differences in genotype and allele frequencies in compared groups (P>0.05) and association between MMP-9 serum concentration and MI occurrence. But we found the statistically significant differences in genotypes distribution (P=0.025) while the alleles distribution was similar (P>0.05) among compared groups. Additionally, AG-carriers had the lower risk of MI development in crude (Pc=0.033; ORc=0.359, 95% CI: 0.14–0.922) and adjusted (Pa=0.023; ORa=0.299, 95% CI: 0.106–0.848) overdominant model of inheritance.

Conclusion: In the present research we have analyzed the link of MMP-9 serum concentration and MMP-9 rs17567-polymorphic variant with CAD development among Ukrainians. We found lower risk of MI occurrence for AG-carriers.