Influence of Gene Polymorphisms for IL-10 and TNF alpha on Cardiovascular Morbidity in Haemodialysis Patients

Jelena Tosic1, Jovan Popovic2, Aleksandar Jankovic2, Petar Djuric2, Ana Bulatovic2, Marko Barovic3, Vera Pravica3 and Nada Dimkovic4,5

1. University Medical Centar Zvezdara, Clinical Department for Renal Diseases, Belgrade, Serbia, 2. University Medical Centar Zvezdara, Department for Nephrology and Dialysis, Belgrade, Serbia, 3. Medical Faculty, Belgrade University, Institute for Microbiology and Immunology, Belgrade, Serbia, 4. University Medical Centar Zvezdara, Department for Nephrology and Dialysis, Belgrade, Serbia, 5. Medical Faculty, Belgrade University, Internal Medicine, Belgrade, Serbia

Introduction and Aims: Uraemia related inflammation is prone to be a key factor to explain the persistent high cardiovascular morbidity rate in patients on chronic haemodialysis. Much recent interest has therefore focused on the role of cytokine genetic polymorphisms (such as IL-10 and TNF alpha) that may influence the immune response, balance between pro and anti-inflammatory markers, as well as the prevalence of atherosclerosis, which is recognized as inflammatory disease. The aim of the study was to analyze cardiovascular morbidity in regard to gene polymorphism for IL-10 and TNF alpha in patients on chronic haemodialysis.

Methods: This cross-sectional study included 95 patients on regular haemodialysis, three times per week on polysulphone membranes for more than six months. Genomic DNA was isolated from whole blood and gene polymorphisms (TNF alpha -308/A and IL 10 -1082 G/A) were determined by using polymerase chain reaction (PCR). TNF-alpha GA and AA genotype were analyzed together due to a small number of patients with AA genotype. These findings were correlated with the cardiovascular morbidity data from patients history.

Results: Out of 95 patients 18% had GG, 50% had GA and 32% had AA IL-10 genotype respectively. Regarding TNF alpha genotype, GG had 76% of patients, while GA and AA together were present in 24% of our patients. Our results have shown significant influence of TNF alpha A allele on incidence of cardiovascular events \( (p = 0.03) \) with 3 folds higher risk regarding GG homozygots. Although without statistical significance patients with A allele of this gene experienced twice higher risk for cerebrovascular insult and 1.6 higher risk for coronary artery disease. Regarding IL 10 gene polymorphism AA homozygots have shown 1.7 folds higher risk for developing coronary artery disease and peripheral vascular disease, but without statistical significance.

Conclusions: Patients with AA TNF alpha genotype have significantly higher risk for cardiovascular events, but we need further studies with larger number of patients for definitive conclusion. Early interventions in haemodialysis patients with high risk genotypes may decrease cardiovascular morbidity and mortality.