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HUMAN PARAOXONASE (PON1) L55M ALLELIC POLYMORPHISM AND HEMODIALYSIS

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ABSTRACT

Background: Patients on maintenance hemodialysis (HD) are at high risk of coronary heart disease. Human paraoxonase (PON1, EC 3.1.8.1) is a high-density lipoprotein (HDL) associated enzyme that protects low-density lipoprotein (LDL) from oxidation and also protects against atherosclerosis. PON 1 L55M polymorphism can take a part in the mechanism of development of CHD.

Aim: To map genotype distribution of PON 1 L55M allelic polymorphism in Croatia and to determine the relationship of PON1 L55M polymorphism and hemodialysis treatment.

Methods: HD-patients (N=51, M/F=28/23, age=60±12 years) and control (blood donors) subjects (N=95, M/F=48/47, age=49±17 years) from area of Slavonski Brod, Croatia were included in this study. PON1 L55M polymorphism was detected by polymerase chain reaction (PCR) and restriction fragments length polymorphism (RFLP) method.

Results: The distribution of PON1 L55M genotypes in hemodialysis patients (11% MM, 40% LM, and 49% LL) differs from control subjects (12% MM, 48% LM, and 40% LL). The allele frequency for PON1 L55M allelic polymorphism did differ in 5% in hemodialysis patients (69% L allele, 31% M allele) and control subjects (64% L allele, 36% M allele). The most common is L allele for both the HD and CS subjects.

Conclusion: There were approximately 55.5% PON1 L55M polymorphic subjects and 44.5% subjects with no PON1 L55M polymorphism in this study. L allele is the most common allele for PON 1 L55M polymorphism in hemodialysis patients as well as in group of control subjects. The allele frequency for PON1 L55M allelic polymorphism did differ in 5% of hemodialysis patients (69% L allele, 31% M allele) and control subjects (64% L allele, 36% M allele). This study suggested that hemodialysis is associated rather with M allele appearance than with MM genotype for PON 1 L55M allelic polymorphism.

(VII + 91 pages including 8 tables, 43 figures and 128 references; original in English)

Keywords: paraoxonase, genotype, polymorphism, hemodialysis

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7 SUMMARY

This research takes part in a complex genotypisation for human paraoxonase PON 1 allelic polymorphisms in Croatian population of blood donors. Some results of this thesis are summarised in following paper „Genetic Frequencies of Paraoxonase 1 Gene Polymorphisms in Croatian Population", authors Marija Grdić, Karmela Barišić, Lada Rumora, Ilza Salamunić, Milena Tadijanović, Tihana Žanić Grubišić, Renata Pšikalová, Zlata Flegar-Meštrić, and Dubravka Juretića; published in Croatica Chemica Acta. The hemodialysis patients' genotypisation is used in research of comparison of human paraoxonase allelic polymorphism in hemodialysis patients and control subjects in Croatia (not published yet).

I have summarized almost all available information in the field of paraoxonase research in theoretical part of my Master Thesis. Brief characteristics of hemodialysis are presented in theoretical part too. I used Internet, especially database Medline, and Scientific Library in Hradec Králové to collect all information.

I have done genotypisation for human paraoxonase PON 1 L55M allelic polymorphism of hemodialysis patients (HD) and control subjects (CS) using polymerase chain reaction (PCR) and restriction fragments length polymorphism (RFLP) technique in experimental part of thesis. I tried to determine the relationship of PON1 L55M allelic polymorphism and hemodialysis. I mapped gender and age distribution of studied population and compared it.

There were approximately 55.5% PON1 L55M polymorphic subjects and 44.5% subjects with no PON1 L55M polymorphism. The distribution of PON1 L55M genotypes in HD (11% MM homozygote, 40% LM heterozygote, and 49% LL wild type) did differ from control subjects (12% MM homozygote, 48% LM heterozygote, and 40% LL wild type).

I have determined that L allele is the most common allele for PON 1 L55M polymorphism in hemodialysis patients as well as in group of control subjects. The allele frequency for PON1 L55M allelic polymorphism did differ in 5% of hemodialysis patients (69% L allele, 31% M allele) and control subjects (64% L allele, 36% M allele).

This study suggested that hemodialysis is associated rather with M allele appearance than with MM genotype for PON 1 L55M allelic polymorphism.