

CHARLES UNIVERSITY IN PRAGUE
FACULTY OF PHARMACY IN HRADEC KRÁLOVÉ
DEPARTMENT OF BIOCHEMICAL SCIENCES

HUMAN PARAOXONASE (PON1) Q192R POLYMORPHISM IN HEMODIALYSIS PATIENTS

RENATA PŠIKALOVÁ

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. The decrease of PON1 activity is a possible mechanism of developing CHD.

Aim: To determine the relationship of PON1 Q192R polymorphism, atherogenic biochemical markers, CRP and PAF serum levels, and PON1 activity to hemodialysis treatment.

Methods: HD-patients (N=45, M/F=25/20, age=61±14years) and control (healthy) subjects (N=47, M/F=27/20, age=61±15years) from area of Split, Croatia were included in this study. PON1 Q192R polymorphism was detected by polymerase chain reaction (PCR) and restriction fragments length polymorphism (RFLP) method. Lipid profile, CRP and PAF serum concentrations were determined by methods routinely used in clinical biochemistry laboratories. Paraoxon was used as a substrate for measuring PON1 activity.

Results: The distribution of PON1 Q192R genotypes in HD-patients (4% RR, 16% RQ, and 80% QQ) did not differ significantly from control subjects (4% RR, 17% RQ, and 79% QQ). Atherogenic serum markers (TC, TAG, LDL, and oxLDL) were significantly higher in HD-patients. HDL and ApoA levels were lower as compared with control subjects independent of the PON1 genotype. Serum PON1 activities in both HD-patients and control subjects seemed to be regulated by PON1 Q192R polymorphism: RR > RQ > QQ.

Conclusion: The distribution of PON1 Q192R genotypes was similar in HD-patients as compared with control subjects. The lipid profile of HD-patients is more atherogenic as compared to control subjects independently of genotype. Serum PON1 activity is regulated by PON1 Q192R polymorphism.

(VII + 85 pages including 11 tables, 41 figures and 146 references; original in English)

Keywords: paraoxonase, polymorphism, genotype, hemodialysis

Supervisors: Prof. Dr. sc. Karmela Barišić,
Prof. MUDr. Jaroslav Dršata, Csc.

Reviewer: PharmDr. Tomáš Šimůnek, Ph.D.