Study of Paraoxonase -1 Gene Polymorphism in a Healthy Population of Khorramabad, Iran

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Abstract

Human serum paraoxonase (HuPON1; EC 3.1.8.1.), a calcium-dependent esterase, is synthesized in the liver and widely distributed in tissues including liver, kidney, intestine, and serum, where it is associated exclusively with high-density lipoprotein. Human paraoxonase-1 plays an important role in prevention of atherosclerosis and also protection against organophosphate-induced neurotoxicity. Paraoxonase-1 shows 2 common polymorphisms: Q/R at position 192 and M/L at position 55. In this study, paraoxonase-1 192 and 55 polymorphisms were investigated in 64 healthy Iranian individuals. Genomic DNA was isolated from whole blood by the Bartlett method, and paraoxonase-1 genotypes were determined by polymerase chain reaction amplification followed by restriction isotyping and gel electrophoresis. The chi-square test was used to evaluate the Hardy-Weinberg equilibrium. The genotype frequencies for paraoxonase 1-Q192R were approximately 47% (QQ), 41% (QR) and 12% (RR) and for paraoxonase-1 M55L, 44% (LL), 44% (ML) and 12% (MM). Thus, the frequency of alleles R, L, Q, and M were 0.33, 0.66, 0.67, and 0.34 respectively. In conclusion, the frequencies of paraoxonase-1 192 and 55 polymorphisms in this group of Iranian population were different from those seen in other Asian populations from Japan and China but similar to European (Caucasians).

Keywords: Atherosclerosis, Haplotype, Paraoxonase, Polymorphism, Polymerase Chain Reaction.

Introduction

Human paraoxonase-1 (PON1) belongs to the family of serum paraoxonases consisting of PON1, PON2, and PON3. The 3 human PON genes are located adjacent to each other at bands q21-q22 on chromosome7 [1]. Paraoxonase 1 (PON1) is a calcium-dependent esterase composed of 354 amino acids (45 kDa), which is synthesized in the liver and secreted into the plasma where it is associated with high-density lipoproteins (HDL) [2-4]. The concentration of PON1 in human plasma is ~50 mg/L, but can vary by as much as 13-fold from one individual to another [5]. PON1 hydrolyzes many active metabolites of organophosphorus insecticides, including paraoxon (a catabolite of the insecticide parathion), diazoxon and chlorpyrifosoxon, detoxifies various neurotoxic agents like sarin and soman and hydrolyses the aliphatic lactones such as y-butyrolactone and homocysteine-thioiactone [6-8].

Increased enzyme activity has been associated with higher HDL levels in some populations, but not in all studies [9, 10]. The PON 192 and 55 polymorphisms have been associated with risk of ischemic stroke in a small study of younger adults and older patients respectively [11, 12]. PON1 is assumed to be involved in the lipid metabolism and to be a protective factor against atherosclerosis. It prevents the formation of oxidized LDL, inactivates LDL-derived oxidized phospholipids once they are formed and prevents oxidation of HDL phospholipids [6]. Genetic factors include polymorphisms in the coding and promoter regions of the PON1 gene that might influence the PON1 expression and its catalytic activity [13-16]. Two common polymorphisms in the coding region of the PON1 gene have been identified, Q192R glutamine to arginine substitution at position 192 and L55M leucine to methionine substitution at position 55[17]. Q192R polymorphism affects PON1 activity towards paraoxon, diazoxon, soman and sarin and is associated with coronary artery disease, familial hypercholesterolemia, type 2 diabetes and Parkinson’s disease [18]. L55M polymorphism can affect the PON1 mRNA and protein levels and its activity.

Since there are not enough data for the Iranian population, this study was undertaken to investigate the distribution of the PON1-192 and -55 polymorphisms in healthy individuals of Khorramabad in west of Iran.

Materials and Methods

Subjects

The study included 64 healthy unrelated individuals (28 male and 36 female subjects), aged 55 years [35-75]. Healthy volunteers in the central laboratory of Khorramabad were screened for the study. The protocol was approved by Razi University Ethical Committee, and