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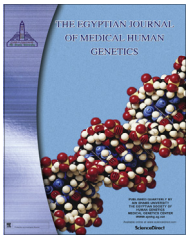

ORIGINAL ARTICLE

Lipoprotein lipase gene variants: Association with acute myocardial infarction and lipid profiles

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KEYWORDS

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Abstract *Background:* Studies showed that lipid metabolism disorders are significant risk factors for myocardial infarction and coronary artery disease (CAD). Therefore, genes involved in lipid and lipoprotein metabolism pathways such as lipoprotein lipase (*LPL*), are proper candidates for susceptibility to CAD.

Aim: To investigate the possible association between *LPL* gene variants (HindIII (rs320) and PvuII (rs285)), acute myocardial infarction (AMI) and serum lipid levels.

Subjects and methods: The study population consisted of 211 patients with a diagnosis of premature AMI, and 203 age-matched individuals with normal coronary angiograms as controls. Genotyping of HindIII and PvuII polymorphisms was done by the PCR-RFLP technique.

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Results: Although the H^+ and P^+ alleles were more observed among the patients, there were no significant differences in genotype distributions and allele frequencies of HindIII and PvuII polymorphisms between patient and control subjects ($P > 0.05$). Triglyceride levels were found to be significantly elevated in H^+H^+ and P^+P^+ genotypes compared to others ($P < 0.05$). However, there was no association between HindIII and PvuII genotypes and HDL-C, LDL-C and cholesterol levels.

Conclusion: Our findings indicate that LPL-HindIII and PvuII polymorphisms are not associated with acute myocardial infarction but with triglyceride levels.

1. Introduction

Epidemiological and clinical studies showed that lipid metabolism disorders such as elevated levels of total cholesterol (TC), triglycerides (TGs), low density lipoprotein cholesterol (LDL-C) and low levels of high-density lipoprotein cholesterol (HDL-C) are significant risk factors for myocardial infarction and coronary artery disease [1,2]. Therefore, genes involved in lipid and lipoprotein metabolism pathways including lipoprotein lipase (*LPL*), are proper candidates for susceptibility to CAD [3].

The human LPL (EC 3.1.1.34) is a 448 amino acid glycoprotein that is synthesized and secreted by many tissues and then transported to the luminal surface of vascular endothelial cells. LPL hydrolyzes triglyceride-rich lipoproteins including chylomicrons and very-low-density lipoprotein (VLDL) and hence plays a central role in lipid metabolism [4,5]. Accordingly, any deficiency in LPL activity could lead to disturbance in lipid metabolism associated with clinical hyperlipidemia and coronary artery diseases [6].

LPL gene spans over 30 Kb on chromosome 8p22 and composed of 10 exons and 9 introns [7]. The association between several polymorphic sites of *LPL* gene including the T-93G (rs1800590), D9N (rs1801177), G188E, N291S (rs268), PvuII (rs285), HindIII (rs320), and S447X (rs328) and CAD risk was investigated in several studies [8–10]. The HindIII polymorphism (rs320) is located in position 495 of *LPL* gene's intron 8th. In this single nucleotide polymorphism (SNP) the ancestral allele (T) is substituted by (G) allele [11]. This nucleotide substitution abolished a restriction site for HindIII. There are supporting evidences which suggest that the common allele (H^+) is significantly associated with high TG and low HDL levels compared to the H^- allele [12,13]. The PvuII polymorphism (rs285) is the result of C into T transition in the LPL gene intron 6th [11]. Previous studies showed that The P^+ allele is associated with high TG and low HDL-C levels [14,15]. However, the association of HindIII and PvuII variants with CAD and serum lipid levels remained to be controversial.

We aimed here to investigate the possible association between LPL gene variants (HindIII (rs320) and PvuII (rs285)), acute myocardial infarction (AMI) and serum lipid levels in an Iranian population through a case-control study.

2. Subjects and methods

2.1. Subjects

The study population consisted of 211 patients with a diagnosis of premature AMI and the age of $\leqslant$50 years who were hospitalized at the Shaheed Rajaei Cardiovascular Center, Tehran, Iran between September 2011 and August 2013. As a control group, 203 age-matched individuals with normal coronary angiograms were recruited from the same demographic area. Two cardiologists confirmed diagnosis of AMI according to the new criteria of the American College of Cardiology and the European Society of Cardiology definition [16]. To obtain clinical information including MI type (STEMI or NSTEMI) and cardiac markers (troponin and creatine kinase-MB) we inspected the medical records. Diabetic patients were excluded from the study. The study adhered to the principles of the Declaration of Helsinki in 1995 (as revised in Edinburgh 2000) and has been approved by Tehran University of medical sciences Ethics Committee and all subjects gave their written informed consent.

2.2. Biochemical analysis

We took blood samples after fasting for 12 h. Serum levels of lipid parameters including TC, TG and HDL-cholesterol were measured enzymatically. We calculated LDL-cholesterol levels by Friedewald equation.

2.3. DNA analysis

We extracted total genomic DNA from EDTA anticoagulated whole blood by Miller's method [17]. Genotyping of HindIII and PvuII polymorphisms was done by the PCR-RFLP technique. For HindIII variant, PCR amplification was performed by following primers: 5′-ACATAAGCACTGAATCGCTC AC-3′ (forward primer) and 5′-CTTCAGCTAGACATTGC TAGTGT-3′ (reverse primer). The cycling condition was as follows: 94 °C for 5 min followed by 30 cycles comprising of 95 °C for 45°s, annealing time at 62 °C for 40 s and extension at 72 °C for 35 s with final extension time of 7 min at 70 °C. For determination of HindIII genotypes, the PCR products (476 bp) were digested by 10 U of HindIII restriction enzyme at 37 °C for 16 h. The resulting fragments separated on a SYBR Green stained 2.5% agarose gel included 476 bp fragment for H^-H^- (GG), 476, 259 and 217 bp fragments for H^+H^- (GT) and 259 and 217 bp fragments for H^+H^+ (TG).

Amplification of the PvuII polymorphism carried out by the forward 5′-AAACCTGAGGGAAGGGATGATA-3′ and reverse 5′-TGCTGCTTTAGACTCTTGTCCA-3′ primers. The cycling condition was as follows: 94 °C for 5 min followed by 30 cycles comprising of 95 °C for 45 s, annealing time at 62 °C for 40 s and extension at 72 °C for 40 s with final extension time of 7 min at 70 °C. The PCR product (529 bp) was