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Short Communication

Association of adiponectin gene functional polymorphisms (–11377C/G and +45T/G) with nonalcoholic fatty liver disease ☆,☆☆

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ABSTRACT

Adiponectin levels are reduced in NAFLD patients and genetic variants of adiponectin have been frequently associated with type 2 diabetes and insulin resistance. To determine the genotypic frequencies of adiponectin functional polymorphisms (–11377C/G and +45T/G) and their subsequent effect on disease progression and plasma adiponectin levels in the patients with NAFLD. A total of 137 NAFLD patients and 250 matched controls were enrolled in the study. DNA sequencing and genotyping were performed to identify the genetic variants. The plasma adiponectin levels were assessed by ELISA. Homozygous mutant genotype of adiponectin SNPs, –11377C/G and +45T/G, were significantly more prevalent in NAFLD patients than controls (Bonferroni corrected $p = 0.014$ and 0.018 , respectively). Plasma adiponectin levels were significantly lower in the NAFLD patients as compared to controls. Moreover, presence of 'G' allele at position –11377C/G and +45T/G was found to be associated with necroinflammatory grade and reduced adiponectin levels, (p values 0.02 and 0.01) respectively. –11377G and +45G alleles are associated with severity of liver disease and hypoadiponectemia, in the patients with NAFLD, respectively.

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1. Introduction

Nonalcoholic fatty liver disease (NAFLD) is one of the most common forms of chronic liver disease worldwide, affecting nearly 20–40% of the population in western countries and becoming increasingly prevalent in Asian subcontinent as well. NAFLD encompasses a spectrum of conditions ranging from simple steatosis, nonalcoholic steatohepatitis (NASH), to advanced fibrosis and cirrhosis (Adams et al., 2005; Angulo, 2002; Clark et al., 2002; Chitturi et al., 2004). NAFLD is recognized as a common cause of cryptogenic cirrhosis due to its delayed

diagnosis as compared to other chronic liver diseases and thus confers a higher mortality rate (Clark and Diehl, 2003). Obesity, insulin resistance and metabolic syndrome are the major risk factors associated with NAFLD pathophysiology (Angulo et al., 1999; Farrell and Larter, 2006). It is strongly believed that both genetic and environmental factors influence disease pathogenesis and progression (Chitturi et al., 2002; Sanyal, 2002; Pagano et al., 2002). Genetic polymorphisms are known to influence predisposition of individuals to various monogenic and polygenic diseases (Butte et al., 2005; Patsulaia et al., 2009). Genome-wide scanning mapped a susceptibility locus for type 2 diabetes and metabolic syndrome to chromosome 3 (3q27) in humans which includes adiponectin gene spanning a 17 kb region consisting of three exons (Vionnet et al., 2000). Adiponectin is an adipose tissue-derived cytokine playing an important role in the regulation of glucose homeostasis and insulin sensitivity (Wolf, 2003). Hypoadiponectinemia is considered a key factor in development of insulin resistance and reduced adiponectin levels have been frequently reported in obese and type 2 diabetes patients (Virsaladze et al., 2007; Weyer et al., 2001). Previous studies have shown that adiponectin improves insulin sensitivity and possesses anti-inflammatory and anti-atherosclerotic properties (Yamauchi et al., 2003; Pajvani et al., 2003). Genetic variants of adiponectin gene were identified in the promoter and exonic regions and these SNPs, alone or in haplotype, are associated with obesity, diabetes and metabolic syndrome (Gu et al., 2004; Heid et al., 2006).

Abbreviations: NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; SNP, single-nucleotide polymorphism; AST, aspartate transferaminase; ALT, alanine transferaminase; HOMA-IR, homeostasis model assessment of insulin resistance; BMI, body mass index; bp, base pairs; SP, stimulatory protein.

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☆☆ The authors declare no conflict of interest.

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