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rs78726532 TLR3 gene polymorphism with susceptibility to hepatitis C virus infection

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Abstract

HCV is a blood pathogen that affects approximately 180 million people worldwide. It has the ability to escape its host's defense mechanism and is considered a resistant species. Toll-like receptors (TLRs) are a family of evolutionary receptors that have been identified by the diagnosis of pathogens as the main regulators of innate and acquired immune responses. Studies have shown that genetic changes in the TLR3 gene are associated with high susceptibility or resistance to immune and infectious diseases. In this study, the effects of the TLR3 gene single nucleotide polymorphism rs78726532 on susceptibility to HCV infections were examined. The association between this polymorphism and the risk of hepatitis C in 50 patients and 50 healthy subjects was investigated. The results revealed a significant relationship between polymorphism rs78726532 and hepatitis C infection ($p = 0.002$). Thus, it could have a therapeutic and predictive potential.

INTRODUCTION

Hepatitis C is an enveloped virus with single-stranded RNA that infects liver cells (hepatocytes) (1). It is a blood pathogen that affects approximately 180 million people worldwide (2). The virus belongs to the family Flaviviridae and is a member of the hepatitis virus. Because HCV has the ability to escape its host's defense mechanism, it is considered a resistant species (3). People with chronic liver infections suffer from diseases such as fibrosis and liver cirrhosis, and 3% to 5% of people with liver cirrhosis will develop liver cancer in the future. Hepatitis C-related diseases are usually treated with antivirals such as interferon alpha and ribavirin, which are standardized for the care of chronic HCV patients (4); however, such treatment is only effective on 50-60% of patients. In addition to the development of drugs that stimulate cellular immunity in the host, significant progress has been made in the treatment and management of the hepatitis C virus through antiviruses that directly affect it (5).

Toll-like receptors (TLRs) are a family of evolutionary receptors that have been identified by the diagnosis of pathogens as the main regulator of innate and acquired immune responses (6). TLRs are a group of molecules essential for the innate immune response to pathogens (7). Recently, cellular immune activation using TLR agonists and stimulation of interferon production has been developed for the treatment of HCV infections (8). There are 10 types of these receptors in humans that are expressed in the various organs of the immune system (8). Specifically, TLR3 is encoded by a gene located in the 4q35.1 region and expressed intracellularly (9). TLR antitumor activity has recently been described by inhibiting HCC growth and development (10). A number of studies have shown that genetic changes in the TLR3 gene are associated with high susceptibility or resistance to immune and infectious diseases, including AIDS, liver disease in people with HCV infection, herpes simplex virus infection (Herpes virus) Type 2, viral infection hepatitis B, type 1 diabetes, and autoimmune diseases. In this study, the effect of TLR3 gene single nucleotide polymorphism rs78726532 on susceptibility to HCV infections was examined.

MATERIALS AND METHODS

The association of rs7872653 polymorphism with hepatitis C in the blood samples of 50 persons with hepatitis C and 50 healthy individuals was examined. The average age of the study population was 43.8 years. Serum factors ALT, AST, and ALP were measured. About 5 ml of peripheral blood was collected in EDTA tubes. To determine the genotype of this polymorphism, the sequencing method was used. For this purpose, the DNA of the samples was extracted using a GeneAll Blood DNA extraction kit. Then PCR was performed using specific primers (Table). The PCR product was sequenced after purification, and the results were analyzed using ChromasPro software.

Table1. primer sequences

Primer	Sequence
rs78726532	5’-GCTGGAAAATCTCCAAGAGC-3’ 5’-AGAGACCAAGCCAGCTAACC-3

RESULTS

The results revealed a significant relationship between rs78726532 polymorphism and hepatitis C infection (p = 0.002). It was also observed that old age and gender can be significantly associated with hepatitis C. Liver enzyme testing (AST, ALP, ALT) and body mass index also showed significant associations with hepatitis C infection. It was found that the GG genotype of this polymorphism could be associated with the risk of hepatitis C (p = 0.037), so that 8% of patients and 11% of healthy individuals with this genotype had this polymorphism.

Table2. Genotype frequency of polymorphism rs78726532 in groups of patients with hepatitis C and control group

SNP	Genotype/allele frequency	Control	HCV patients	*p*-value
rs78726532	GG	11%	8%	0.037
	AG	14%	15%	0.756
	AA	75%	77%	0.623

DISCUSSION

Infections caused by the hepatitis C virus can be very dangerous and can sometimes lead to hepatocellular carcinoma (11). According to the latest statistics, only 0.5% of the Iranian population has the virus, which is much lower than the rate of hepatitis B, but due to the lack of vaccines, preventive measures are of great importance. It is important to have biomarkers that can predict the risk of people getting the disease (12). In this study, the association of rs78726532 polymorphism with the risk of hepatitis C virus infection was examined. The results indicated a significant association between this polymorphism and the risk of hepatitis C infection, 8% of patients and 11% of healthy individuals with the GG genotype having this polymorphism. Previous studies have shown a significant association between other polymorphisms in this gene (rs1879026 and rs3775290) and hepatitis C in Chinese and Arab populations (13). Al-Anazi reported a significant association between rs78726532 polymorphism and the risk of hepatitis C compared to the healthy population (14). Other studies have suggested that the polymorphisms in the TLR3 gene’s promoter sequence may influence the expression of this gene. On the other hand, it has been observed that HCV virus can affect the transcription of TLR3 gene through the p53 factor (15). Studies have also shown that the TLR3 gene and its polymorphisms are significantly associated with hepatitis C infection, and thus, they could have therapeutic and predictive potential.

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