Osteopontin gene polymorphism as marker predicting the efficacy of interferon-based therapies in patients with chronic hepatitis C

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ABSTRACT

Background and aim: viral hepatitis is T cell – mediated and Osteopontin induce T cell chemotaxis, support adhesion, proliferation**,** and also enhance expression of T helper 1 (Th1) cytokines. Genetic polymorphisms in the osteopontin gene (OPN) determine the magnitude of immunity against rickettsial infection in mice. Similar polymorphisms, if present also in human beings, might affect hepatitis activity and the response to treatment by interferon and ribavirin in those infected with HCV. This study aimed to detect SNP in -1748 in the promoter of Osteopontin gene and Osteopontin protein serum level and their relation to responsiveness and non-responsiveness to interferon treatment.

Subject and Methods: the study included 80 patients with chronic viral hepatitis C and 20 healthy subjects serving as control. Osteopontin protein was measured with enzyme-linked immunosorbent assay. SNP -1748 in promoter region of Osteopontin gene was detected by direct sequencing with both forward and reverse primer.

Results: show that By univariate analysis SNP -1748 in OPN protein gene (A/A vs G/A,G/G) (P =.073 ,odd ratio = .382) did not predict the response of hepatitis C patient to interferon but Osteopontin serum protein level, Tbil , Dbil, ALK, ALB , PT, fibrosis and vireamia represent predictor for treatment response . And by step wise multivariate logistic regression T bil, AST, and ALB represent independent predictor for treatment.

A significant difference (P = .002) in the level of OPN protein between the patients of chronic hepatitis C in the different allele of SNP –1748 of OPN gen , and a significant difference between the responder and non-responder in each allele of SNP –1748 of OPN gene AA (P =.001)), GA (P=.021) and GG (.004), and a negative correlation between OPN

protein and AST6, ALB6 and HCV RNA titer 6(AST, ALB , HCV RNA titer measured six months after treatment completion).

Conclusion: While SNP in the promoter of Osteopontin gene at –1748 can not be used as a marker to predict the response of chronic hepatitis C patient to treatment by interferon and ribavirin, Osteopontin serum protein level could be used as a marker to predict responsiveness. Also the level of Osteopontin protein is affected by the polymorphism in –1748 in OPN gene which is significantly lower in AA allele and higher level in GA and GG alleles. A negative correlation between Osteopontin protein and AST6, ALB6 and HCV RNA titer 6 was found in patients.