Relation between Osteopontin gene polymorphism & its protein level and the efficacy of interferon-based therapies in HCV patients

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By

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SUMMARY

Chronic infection with hepatitis C virus (HCV) is responsible for substantial morbidity and mortality worldwide. Approximately 170 million people are estimated to suffer from chronic hepatitis C at risk of long-term complications such as liver cirrhosis and hepatocellular carcinoma.

Hepatitis C virus genotype 4 (HCV-G4) is prevalent in the Middle East and Africa and has spread to several regions in Europe. HCV-G4 represents a major health problem in Egypt, with a prevalence rate 28%.

HCV-G4 has been considered a difficult-to-treat genotype because of the poor sustained virological response (SVR) rates reported with a conventional interferon (IFN)-based regimen. Pegylated IFN and ribavirin combination therapy was associated with significant improvements in SVR rates that currently exceed 60%, particularly with individualized therapy.

The aim of our study is to detect the single nucleotide polymorphism (SNP) in the promotor region of the osteopontin gene (OPN) at nucleotide (nt) -155 and its protein level in the blood of chronic liver disease patients under treatment with interferon (responders and non-responders). Also, to compare the results with non infected patients.

This study was conducted on 100 subjects classified into 2 groups: Group I which included 80 with chronic hepatitis C received PEG-IFN alpha-2b plus ribavirin for 24 weeks; Group II (controls) which included 20 healthy subjects. A detailed history taking, thorough physical and clinical examination and 10 ml of blood were collected from each

subject. The following was done; Liver function tests, hepatitis markers, HCV quantitation by real time PCR, DNA extraction from whole blood, agarose gel electrophoresis followed by sequence analysis and quantitation of protein level of osteopontin by ELISA.

Statistical analysis was performed to demonstrate any relation between single nucleotide polymorphism (SNP) in the promotor region of the osteopontin gene (OPN) at nucleotide (nt) -155, its protein level in blood and efficacy of interferon-based therapies in chronic hepatitis C patients.

Concerning single nucleotide polymorphism (SNP) in the promotor region of the osteopontin gene (OPN) at nucleotide (nt) -155 (G/G homozygote ,G/- heterozygote deletion, -/- homozygote deletion) show significant difference between responders and non responders by univariate simple analysis.

Also, there was a significant difference between responders and non responders as regards serum osteopontin level by univariate simple analysis (p=.000).

Analyzing prognostic viral and host for the therapeutic efficacy of INF revealed that, higher serum albumin (P=.000), lower pre-treatment AST levels (P=.000), lower pretreatment AFP levels (P=.006), lower pretreatment Tbil levels (p=.000), lower pretreatment Dbil levels (p=.000), lower pretreatment ALK levels (p=.001), lower PT (p=.003) and lower stage of fibrosis (p=.000) were correlated with better response.

A univariate and multivariate logistic regression analysis was also performed to show the significant predictors affecting response to interferon therapy. By univariate logistic regression analysis predictors of response includes Tbil, Dbil, ALK, ALB, PT, Fibrosis grades (1,2,3 vs 4,5,6), OPN protein and SNP -155 (-/- vs G/G&G/-). But by

multivariate logistic regression analysis only pretreatment fibrosis stage (1,2,3 vs 4,5,6) (p= .047) and pretreatment serum OPN level (p= .015) were independent predictors of response.