Vitamin D serum level and CYP27B1-1260 promoter polymorphism in chronic hepatitis C patients treated with interferon.

Thesis

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SUMMARY

Hepatitis C virus (HCV)-related chronic liver disease is a major health problem and a key issue in antiviral research. Approximately 170 million people are infected with HCV worldwide. Chronic HCV infection commonly induces immune reactive inflammation, which results in continuous liver tissue damage and progression of liver fibrosis to cirrhosis. Part of the problem relates to the fact that the current standard of care treatment for HCV, combination pegylated interferon-alpha (PegIFNa) and ribavirin (Rib), is expensive, associated with significant side effects, and results in only a 50% rate of sustained virological response (SVR) ***(Selzner and McGilvray , 2008).*** Predicting the likelihood of response to treatment prior to initiating therapy (or soon after starting therapy) would be very useful ***(Dogra et al., 2011).***

One, twenty-five-dihydroxyvitamin D, the activated hormonal form of vitamin D, is an important immune modulator that has an impact on innate and adaptive immune pathways. In a previous study, vitamin D deficiency was associated with poor response to pegylated interferon-alfa and ribavirin in HCV genotype 1 ***(Petta et al.,2009, Lange et al., 2011)***. Furthermore, an in vitro analysis in the replicon model revealed an inhibitory effect of vitamin D on HCV replication ***(Yano et al., 2007)***.

In the present study we aimed to determine the incidence of vitamin D deficiency in patients with chronic hepatitis C. In addition, we evaluated associations of vitamin D serum levels as well as polymorphisms within gene encoding the 1α-hydroxylase with the virologic response of interferon-alfa based treatment in patients chronically infected with HCV genotypes 4.

The present study was conducted on 133 subjects divided into 2 groups: Group I which included 103 patients with chronic hepatitis C received PEG-IFN alpha-2b plus ribavirin for 24 weeks and Group II (controls) which included 30 healthy subjects.

The following were done: history taking, general examination, liver function tests, hepatitis markers, HCV quantitation by real time PCR , DNA extraction from whole blood, PCR for gene amplification, agarose gel electrophoresis and quantitation of serum level of Vit D by ELISA.

Statistical analysis showed that there was a significant difference in the prevalence of vitamin D deficiency between responders and non responders to interferon therapy of chronic hepatitis C patients (P=0.003).

Also there were a significant difference as regards the relation between Vit D serum level and 1α- hydroxylase promoter polymorphism CYP27B1-1260 in chronic HCV patients (AA, CA, CC) (p=0.000)

also there was a highly statistically significant difference between responders and non responders to interferon therapy of chronic hepatitis C patients before treatment as regards the mean values ± SD of AST (P= 0.009), D.bil (P = 0.001), AFP (P= 0.000), PC (P = 0.000), Vit D (P = 0.001), and fibrosis (P = 0.001).

By stepwise multivariate logistic regression analysis the significant predictors affecting response to combined therapy in hepatitis C patients were: ALT (P= 0.04), AST (P= 0.009), D.bil (P = 0.013), ALB (P = 0.012), AFP (P=0.001), PC (P = 0.012), Vit D (P = 0.002), and CYP27B1-1260 genotype AA (P = 0.009).

Conclusion:

Serum levels of Vitamin D and1α- hydroxylase promoter polymorphism CYP27B1-1260 are significant predictors for response to interferon therapy of hepatitis C patients.