The Effect of the Polymorphism in IL-28B Gene on the Treatment Response of a Combined Therapy by Sofobuvir and Daclatasvir with and without Ribavirin in HCV Egyptian Patients

Thesis

Submitted for partial fulfillment of master degree in

Clinical and Chemical Pathology

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Summary

Hepatitis C virus infection is a global health problem, about 130-150 million persons suffer from chronic HCV infection worldwide.Hepatitis C virus (HCV) is a spherical, enveloped, positive-strand RNAvirus.It is a member of the family Flaviviridae. Seven genotypes .67 confirmed subtypes.

Diagnosis of HCV infection is based principally on the detection of antibodies to recombinant HCV polypeptides and by assays for HCV RNA.

Functional gene polymorphisms have been identified in cytokines such as interferon-gamma (**IFNγ**) which shows possible relationships between these genotypes and the clinical outcome of HCV-related liver disease.

In the prior interferon era of treatment, genotype was the strongest predictor of obtaining a SVR. In the current DAA era, the role of HCV genotype in predicting treatment response has decreased significantly given the high efficacy of different DAA combinations across all genotypes and the introduction of pangenotypic agents.Among the three genotypes of IL-28B, CC genotypes associated with 2 to 3 fold increase in SVR as compared with either CT or TT genotypes.

One hundred HCV cases compared to 100 age and sex matched healthy control subjects. Two ml blood was collected in EDTA sterile vacutainer. Genomic DNA was extracted from peripheral white blood cells then all samples were genotyped by real-time PCR using TaqMan SNP allelic discrimination assays.

All patients was subjected to the following:Personal history including patient BMI, blood chemistry (ALT,AST, total bilirubin, albumin), Full blood

examination (TLC, Hb and platelets), coagulation profile, HCV RNA level in HCV cases, presence or absence of diabetes and FIB4 .

We found that the biochemical profiles including the serum ALT, AST and total bilirubin in the patients with chronic hepatitis C were higher than those in healthy control.Additionally,P value of HB,TLC and platelets were very highly statistically significant (p value <0.001). Both the genotype and allele frequency of IL-28B gene in controls and HCV patients were found to be statistically insignificant .

The responders had a higher frequency of the wild allele “C” compared to non-responders (22% versus 10%), and a lower frequency of the mutant allele “T” compared to non-responders (6 versus 22%).The non-responder group has a higher frequency of T allele.The TT genotype of IL-28B was found to be present in much higher frequency in non-responders (22%), when compared with SVR patients (6%).

We concluded that TT genotype may be responsible for the failure of combined DCV and SOF ±RBV for maintaining the SVR in chronic HCV patients.CC genotype is a good indicator SVR in chronic HCV patients.