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Predictive Factors for Interferon and Ribavirin Combination Therapy in Patients with Chronic Hepatitis C Genotype 4

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Summary and conclusion

Hepatitis C is a viral disease caused by the hepatitis C virus (HCV) that belongs to the genus Hepacivirus a member of the family Flaviviridae characterized by the inflammation of the liver. The infection is often asymptomatic, but chronic infection can lead to scarring of the liver and ultimately to cirrhosis, which is generally apparent after many years. In some cases, those with cirrhosis will go on to develop liver failure, liver carcinoma. HCV is a small enveloped positive single-stranded RNA genome that is composed of 9600 nucleotide base pair open reading frame, when translated produces a single large pre-protein consists of about 3000 amino acids subsequently proceed to form ten small proteins by action of cellular and viral proteases.

Up to 85% of individuals who are initially (acutely) infected with HCV will fail to eliminate the virus and will become chronically infected. Hepatitis C becomes a global health problem for 170 million of infected people worldwide (~3%). Egypt has recorded the highest prevalence of HCV-infected people among the world (~22%).There are about seven genotypes of HCV distributed widely over the world. The most predominant genotype in Egypt is genotype 4.

Many studies are carried out for evaluating the predictive genetic factors on the response of the treatment of combination PEG-IFN and Ribavirin therapy for chronic hepatitis C among different genotypes of HCV such as ISDR sequences or ……..etc. Interferon sensitivity determining region (ISDR) is a sequence of 40 amino acids stretch (2209-2248 a.a) located in the NS5A protein, one of the non-structural proteins of HCV that is reported, to have an effect on IFN treatment response on HCV.

In this study, a great effort was done for predicting the effect of the sequence of NS5A-ISDR and its mutation on the response of IFN and ribavirin combination therapy on patients with chronic hepatitis C genotype 4.

This study was established on 50 patients infected with chronic HCV. Interferon sensitivity determining region (ISDR) was sequenced from 40 HCV-RNA only, as five samples was from other genotypes and another five samples failed to be sequenced. Treatment of patients is based on PEG-IFN-α and ribavirin according to the standard regime "48 weeks". We classified our samples into two groups' responder and non-responder on the effectiveness of the therapy.

Our results show that the responsiveness of chronic HCV genotype 4 patients is not related to the ISDR type or its amino acid substitutions first developed by Entomto et al. in 1996. Therefore, we cannot consider it as a predictor genetic factor for early correlation of therapy outcome for HCV genotype 4. In addition, we found that response is influenced by HCV-RNA titer, but not by age, or gender.