Relation between Interleukin-10 polymorphism and the efficacy of interferone–based therapies in HCVpatients

Thesis submitted for fulfillment of Master Degree in Medical Biochemistry

By

Omayma Owees Abdelaleem
M.B.,B.ch

Under supervision of

Professor Dr. Olfat Gamil Shaker
Professor of Medical Biochemistry
Faculty of Medicine, Cairo University

Professor Dr. Yasser Hussien Nassar
Professor of Medical Biochemistry
Faculty of Medicine, Cairo University

Dr. Amr Aly Zahra
Assistant Professor of Medical Biochemistry
Faculty of Medicine, Fayoum University

Faculty of Medicine
Cairo University
2011

SUMMARY

Infection with hepatitis C virus (HCV) affects millions of people HCV infection may often .worldwide and leads to chronic liver disease progress to cirrhosis and hepatocellular carcinoma.

The most effective current standard of care in patients with chronic hepatitis C is a combination of PEG-IFN-α with ribavirin, but unfortunately it does not produce SVR in all treated patients , expensive and associated with significant side effects.

To avoid these side effects in patients who will not be helped by the treatment, as well as to reduce the substantial cost of PEG-IFN-α/RBV treatment, it would be useful to be able to predict an individual's response before or early in treatment.

IL-10 is a cytokine with potent anti inflammatory properties. It acts to surpass the release and function of a number of pro-inflammatory cytokines including TNF-α and IL-6. The elevated serum levels of IL10 have been observed in patients with untreated chronic HCV infection. Numerous disease association studies using IL-10 promoter marker have shown that IL-10 is important in susceptibility to inflammatory disease **.**

The aim of the present study is to detect the single nucleotide polymorphism of IL-10 gene at nt - 1082 and its protein level in the blood of hepatitis C patients under treatment with interferon (responders and non-responders).

The present study was conducted on 120 subjects divided into 100 patients with chronic hepatitis C received PEG-IFN alpha-2b plus ribavirin for 24 weeks and 20 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 protein level of interleukin -10 by ELISA.

Statistical analysis showed that there was significant difference in the prevalence of single nucleotide polymorphism (SNP) in the promotor region of the interleukin-10 gene (IL-10) at nucleotide (nt) -1082 (p=.004) and its protien level (p=.001) between responders and non responders to interferon therapy of chronic hepatitis C patients**.**

Also there were significant differences between responders and non responders to interferon therapy of chronic hepatitis C patients before treatment as regards the mean values of [T.bil , D.bil , ALK , ALB, AFP , PT , fibrosis, and viremia].

By univariate logistic regression the significant predictors affecting response to combined therapy in hepatitis C patients were T.bil , D.bil , ALK , ALB, PT, fibrosis, IL-10 protein, and IL-10 SNP nt(-1082) .

And by multivariate logistic regression D.bil, fibrosis and SNP(-1082) were found to be significant predictors for response.