Laminin and Chromogranin A levels in Patients with liver cirrhosis

A Protocol of Thesis submitted for partial fulfillment of Master Degree in Medical Biochemistry

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SUMMARY

Liver cirrhosis is a pathologic condition characterized by fibrosis of the liver parenchyma and evidence of regenerative activity. The

epidemiology of cirrhosis is linked to both alcohol consumption and the prevalence of hepatitis B and hepatitis C virus infections. Worldwide, cirrhosis is the cause of thousand deaths per year.

Laminin is one of the main glycoproteins of the basement membrane. In normal liver, laminin is found around the vessels and biliary ducts, where basement membranes are identified. Under some inflammatory stimuli, Ito cells can transform into myofibroblast like cells, thus increasing the synthesis of the different components of the extracellular matrix. Accordingly, laminin has been considered to be a marker of fibrogenesis.

Chromogranin-A (CgA) is a 50-kD acid glycoprotein originally described in catecholamine storage vesicles of the adrenal medulla. Elevated CgA in patients with cirrhosis and superimposed HCC suggesting that raising CgA levels, likely due to a neuroendocrine component of the tumor, might be a useful prognostic marker for HCC in cirrhotic patients. However, high serum CgA values are also found in patients with hepatic failure, possibly because of inadequate hepatic metabolization and neuroendocrine activation. This finding suggests that determination of CgA serum values is useful in monitoring patients with cirrhosis of the liver for early detection of HCC.

The aim of the present study was to determine the relationship between laminin and chromogranin-A levels and severity of liver dysfunction, and whether these parameters could be used as novel markers in assessing liver function.

This study was conducted on 50 subjects classified into 2 groups: Group I which included 30 cirrhotic patients and Group II (controls) which included 20 healthy non-cirrhotic subjects. A detailed history taking, thorough physical and clinical examination and abdominal

ultrasound were performed for each subject included in the study. 10 ml of blood were collected from each subject for the measurements of laminin, ChromograninA, ALT, AST, GGT, Total Bilirubin , Albumin and Alpha fetoprotein.

Statistical analysis was performed to demonstrate any relation between liver cirrhosis and those laboratory profiles.

Concerning laminin and chromogranin, ALT, GGT, albumin and bilirubin were significantly higher in group I when compared to group II.

There was a statistically significant positive correlation between laminin and ALT and bilirubin in cirrhotic patients. There was also a statistically significant positive correlation between chromogranin and AFP in cirrhotic patients.

A linear regression was also performed to show the significant predictors affecting laminin level. Only ALT (P=0.034), albumin (P = 0.02) and bilirubin (P = 0.009) were found to be significant predictors for laminin. As regard the liner regression of chromogranin, ALT, AFP and albumin were found to be significant predictors for chromogranin level in cirrhotic patients

The diagnostic performance of plasma laminin showed a sensitivity of 96.7 %, a specificity of 75%, positive predictive value of 85.3%, negative predictive value of 93.3% and overall accuracy value of 88% for the diagnosis of liver cirrhosis. ROC curve was performed to show the diagnostic value of laminin in diagnosis of cirrhotic patients taking a cut-off level 242 ng/ml. It was found to be significant with AUC was 0.981. The combined use of laminin with AFP improved the specificity of diagnosis of cirrhotic patients up to 90%.

As regards chromogranin, it was found that the diagnostic performance of plasma chromogranin showed a sensitivity of 100% , a specificity of 85%, positive predictive value of 90.9 %, negative predictive value of 100% and overall accuracy value of 94% for the diagnosis of liver cirrhosis. ROC curve was performed to show the diagnostic value of chromogranin in diagnosis of cirrhotic patients taking a cut-off level 75.6 ng/ml. It was found to be significant with AUC was 1.000. The combined use of CgA with AFP improved the specificity of diagnosis of cirrhotic patients up to 95%.