Assessment of Serum Level Cholinesterase as a Biomarker of Post Viral Liver Cirrhosis

Thesis

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List of Abbreviations

Abb.	Full term
Ach	*Acetylcholine*
ALP	*Alkaline Phosphatase*
ALT	*Alanine aminotransferase*
AN	*Anorexia nervosa*
AST	*Aspartate aminotransferase*
CBC	*Complete blood count*
CD	*Crohn's disease*
ChE	*Cholinesterase*
DN	*Dibucaine number*
FN	*Fluoride number*
GGT	*Gamma Glutamyl Transferase*
HCV	*Hepatitis C virus*
MHE	*Minimal encephalopathy*
MRI	*Magnetic resonance imaging*
NAFLD	*Nonalcoholic fatty liver disease*
PBC	*Primary biliary cirrhosis*
PCHE	*Pseudocholinesterase*
PSC	*Primary sclerosing cholangitis*
PT	*Prothrombin time*
TIPS	*Transjugular intrahepatic portosystemic shunt*
WHO	*World Health Organization*

INTRODUCTION

Liver cirrhosis is a late stage of progressive hepatic fibrosis is characterized by distortion of the architecture and formation of regenerative nodules and different degrees of liver function impairment; these patients are prone to a variety of complications reducing life expectancy markedly ***(Sørensen et al., 2003).***

Cirrhosis represents the final common histologic pathway for a wide variety of chronic liver diseases. The term cirrhosis was first introduced by Laennec in 1826. It is derived from the Greek term *scirrhus* and refers to the orange or tawny surface of the liver seen at autopsy. Cirrhosis is defined histopathologically as a diffuse hepatic process characterized by fibrosis and the conversion of normal liver architecture into structurally abnormal nodules ***(Tsochatzis et al., 2014).***

The World Health Organization (WHO) indicates that 10% of the world population has chronic liver disease; this represents approximately 500 million people, Two million people worldwide die each year from hepatic failure ***(Schuppan and Afdhal, 2008).***

The prognosis of cirrhosis is highly variable since it is influenced by a number of factor, including etiology, severity, presence of complications, and comorbid diseases. One of the earliest models (the Child's classification) continues to be a useful method for stratifying disease severity, surgical risk, and overall prognosis but it has limited discriminatory capacity and does not

adequately segregate patients with progressively abnormal lab results. So the MELD score was developed for prediction of short term survival within three months, while the predictivity for the survival of more than three months is much weaker Therefore the evaluation of new markers is an important task in patients with liver cirrhosis ***(Kamath et al., 2007)***.

However, the cirrhotic patients, particularly those with Child grades B and C with ascites or hemorrhagic tendency, are usually treated with albumin or blood transfusion, which may affect the real numerical value for calculating the Child-Pugh score additionally; serum cholinesterase is not easily affected by this treatment ***(Meng et al., 2013)***.

Cholinesterase is a family of enzymes that catalyze the hydrolysis of the neurotransmitter acetyl choline into choline and acetic acid. The 2 types of cholinesterase found in the human blood are acetyl cholinesterase ("true" cholinesterase) in red cells and butyryl cholinesterase (non-specific, pseudo cholinesterase) in serum ***(Brimijoin and Koenigsberger, 1999)***.

Cholinesterase (ChE) is synthesized mainly in hepatocytes and released into the blood. Serum ChE activity is reduced in liver dysfunction due to reduced synthesis, the marked decrease in its synthesis with hepatocyte dysfunction and restoration of synthesis with hepatocyte recovery suggests that serum cholinesterase activity might be a more specific indicator of liver dysfunction than the traditional liver function tests ***(Ruchi et al., 2014)***.

Aim of the Work

The aim of this work is to assess the value of serum cholinesterase in evaluating liver reserve function in post viral cirrhotic patients.

Chapter One

LIVER CIRRHOSIS

Definition:

Liver cirrhosis is a frequent consequence of the long clinical course of all chronic liver diseases and is characterized by tissue fibrosis and the conversion of normal liver architecture into structurally abnormal nodules ***(Massimo et al., 2011).***

Epidemiology:

Because many patients with cirrhosis are asymptomatic until decompensation occurs, it is very difficult to assess the real prevalence and incidence of cirrhosis in the general population. The prevalence of chronic liver disease or cirrhosis worldwide is estimated to be 100 (range, 25 to 400) per 100,000 subjects, but it varies widely by country and by region ***(Goldman and Schafer, 2012).***

Cirrhosis is an important cause of morbidity and mortality worldwide. According to the World Health Organization, about 800,000 people die of cirrhosis annually. In the United States, cirrhosis accounts for about 27,500 deaths each year, or a death rate of 9.3 per 100,000, making it the 12th leading cause of death overall. Importantly, chronic liver disease and cirrhosis are the seventh leading cause of death in the United States in individuals between 25 and 64 years of age. Because chronic liver disease affects people in their most

productive years of life, it has a significant impact on the economy as a result of premature death, illness, and disability ***(Goldman and Schafer, 2012).***

Causes of cirrhosis:

Main factors causing cirrhosis:

- Chronic Hepatits C
- Alcoholic liver disease
- Nonalcholic fatty liver disease
- Chronic Hepatits B

Other causes of cirrhosis

- Cholestatic and autoimmune liver disease
  - Primary biliary cirrhosis
  - Primary sclerosing cholangitis
  - Autoimmune hepatitis
- Intrahepatic or extrahepatic biliary obstruction
  - Mechanical obstruction
  - Biliary atresia
  - Cystic fibrosis
- Metabolic disorders
  - Hemochromatosis
  - Wilson's disease

- Glycogen storage disease
- α1 –antitrypsin deficiency
- Porphyria
- Abetalipoprotienemia

- Sinusoidal obstruction syndrome
  - Budd-chiari syndrome
  - Veno-occlusive disease
  - Right-side heart failure
- Drugs and toxins
- Intestinal bypass
- Indian childhood cirrhosis

Chronic viral hepatitis C and alcoholic liver disease are the most common causes of cirrhosis worldwide, followed by nonalcoholic fatty liver disease and chronic hepatitis B ***(Goldman and Schafer, 2012).***

Viral hepatitis:

Hepatitis B is a DNA virus, unlike the other common hepatotropic viruses, which are RNA viruses. It may occur as a discrete entity or as co-infection with hepatitis D, or delta infection. Although hepatitis B usually presents as a mono-infection, its presence is necessary for the delta virus to be