Assessment of the Role of Serum Zinc in Patients with Different Stages of Chronic Viral Hepatitis C

Thesis

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LIST OF ABBREVATIONS

Abbreviation	Meaning
• **AFP**	… Alpha-fetoprotein
• **AIDS**	… Aquired immune deficiency syndrome
• **ALD**	….Alcoholic liver disease.
• **ALP**	… Alkaline phosphatase.
• **ALT**	… Alanine aminotransferase.
.AST	….Aspartate aminotransferase.
• **Ca**	…. Calcium.
• **cAMP**	…. Cyclic adenosine monophosphate.
• **CCl4**	…. Carbon tetrachloride
• **Cd**	…. Cadmium.
• **cGMP**	…. Cyclic guanosine monophosphate.
• **CH**	…. Chronic hepatitis.
• **CLD**	…. Chronic liver disease.
• **Cr**	…. Creatinine.
• **CT**	…. Computed tomography.
• **Cu**	…..Copper
• **CYP 450**	…..Cytochrome P450.
• **D. bilirubin.**	…. Direct bilirubin.
. DM	…. Diabetes mellites
• **ELISA**	…. Enzyme linked immunosorbent assay

Abbreviation	Meaning
• **FAD**	…. Flavin adenosine dinucleotide.
• **FasL**	…. Fas ligand.
• **Fe**	…. Iron.
• **GABA**	…. Gamma amino butyric acid.
• **GGT**	…. Gamma glutamyl-transpeptidase.
• **GSH**	…. Glutathione.
• **HAV**	…. Hepatitis A virus
• **HBsAg**	…. Hepatitis B surface antigen.
• **HBc Ab**	…. Hepatitis B core antibody
• **HBV**	…. Hepatitis B virus.
• **HCC**	…. Hepatocellular carcinoma.
• **HCV**	…. Hepatitis C virus.
• **HE**	…. Hepatic encephalopathy
• **HFL**	…. Hepatic focal lesion.
• **HAI**	…. Histology Activity Index.
• **HIV**	…. Human immune deficiency virus
• **HLA**	…. Human leuckocytic antigen
• **INF**	…. Interferone.
• **IL**	…. Interlukin.
• **ICAM**	…. Intracellular adhesion molecule.
• **INR**	…. International normalized ratio
• **K**	…. Potassium.

Abbreviation	Meaning
• **LCF signs**	…. Liver cell failure signs.
• **LDH**	…. Lactate dehydrogenase.
• **LEC**	…..Long-Evans Cinnamon.
• **LFA**	…..Leukocyte function associated antigen
• **MMPs**	…. Metalloprotiens.
• **m RNA**	…. Messenger RNA.
• **MSM**	…. Men having sex with men
• **MTs**	…. Metallothioneins
• **MT-KO**	…..Metallothionine-knockout
• **Na**	…. Sodium.
• **NF**	…. Nuclear factor.
• **NO**	…. Nitric oxide.
• **NS5A**	…..Non-structional 5A.
• **NS3**	…..Non-structional 3.
• **OCP**	…. Oral contraceptive pills.
• **PBC**	…..primary biliary cirrhosis
• **PCR**	…. Polymerase chain reaction
• **PG**	…. Prostaglandin
• **PMBC**	…. peripheral blood mononuclear cells
• **ROC**	…. Receiver Operator Curve.
• **ROS**	…. Reactive oxygen species.

Abbreviation	Meaning
• **SE** • **SGOT** • **SGPT** • **SOD**	…. Selenium. …. Supper oxide dismutase …. Serum glutamic oxaloacitic transaminase. …..Serum glutamic pyruvic transaminase.
• **TAA** • **T. bilirubin** • **TE** • **TGF** • **TNF** • **TPEN**	…..Thioacetamide. …. Total bilirubin. …. Trace elements …. Transforming growth factor …. Tissue necrosis factor. …. Tetrakis pyridilmethyl ethyle nediamine
• **U/l** • **US**	…..Unit per liter …. Ultrasonography.
• **VEGF** • **VIP**	…. Vascular endothelium growth factor. …. Vasoactive intestinal peptide.
• **ZINC T** • **ZIP** • **ZN**	…. Zinc tranporter …..Zrt-, Irt-like Protein …. Zinc.

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CONTENTS

Aim of the Work

This study aims to evaluate the levels of serum Zinc in patients with chronic HCV, and investigate its relation with different stages of the post hepatitic liver damage including HCC (as one of its complications).

Introduction

The relationships between chronic liver diseases and trace element (TE) contents are debated. Particularly, no defined data are available about the TE levels in viral liver disease patients with or without malnutrition.

Essential micronutrients are involved in many metabolic pathways in the liver, such as enzymatic functions and protein synthesis, oxidative damage and anti-oxidant defense, immunological competence, interferon therapy response regulations, and alterations of the virus genomes ***(Ozcelik et al., 2003).*** The oxidant production associated with immune reactions against viral hepatitis has a role in the formation of hepatocellular carcinoma (HCC) ***(Jain et al., 2002).*** Therefore, the changes in micronutrients and their demolishing effects against oxidative stress are factors for viral hepatitis pathogenesis.

HCV is a major cause of chronic liver disease. HCV infection frequently leads to chronic hepatitis with increasing risk of developing liver cirrhosis and HCC ***(Wang-Sheng et al., 2005)***.

On the other hand, patients with chronic liver disease exhibit metabolic imbalances of trace elements such as high levels of iron and copper, and low levels of Zinc, selenium, phosphorus, calcium and magnesium ***(Loguercio and federico, 2003).***

Viral hepatic diseases, can progress into more serious pathological outcomes and eventually to hepatocellular carcinoma. A growing number of evidence indicates that many trace elements play important roles in a number of carcinogenic processes that proceed through various mechanisms ***(Ching-Chiang et al., 2006).***

The levels of some trace elements, such as selenium, iron, copper, and Zinc, and Cu:Zn ratios, might serve as biomarkers for the increased severity of viral hepatic damage ***(Ching-Chiang et al., 2006).***

Many of the clinical features of liver cirrhosis have been linked to Zinc deficiency, including loss of body hair, testicular atrophy, poor appetite, immune dysfunction, altered taste and smell, reduced vitamin A and thyroid hormone metabolism, altered protein metabolism, delayed wound healing, and diminished drug elimination capacity ***(Grüngreiff, 2004)***.

One of the most interesting and novel aspects concerning the presumable role of Zinc in producing the clinical features of liver cirrhosis is the possible relationship between Zinc deficiency and hepatic encephalopathy (HE). Zinc may be involved in the pathogenesis of HE either by altering nitrogen and ammonia metabolism or by directly influencing brain functions ***(Grüngreiff, et al., 2004)***.

To our knowledge, few Egyptian studies have assessed the role of Zinc as one of the micronutrients in patients with chronic HCV, and its relation to different stages of post hepatitic liver damage.

Chronic viral hepatitis C

* Epidemiology:

The hepatitis C virus (HCV) is a major public health problem and a leading cause of chronic liver disease. An estimated 180 million people are infected worldwide ***(Williams, 2006).***

In the United States (U.S.), the prevalence of HCV infection between the years 1999 and 2002 was 1.6%, equating to about 4.1 million persons positive for antibody to hepatitis C (anti-HCV), 80% of whom are estimated to beviremic. Some calculations suggest that mortality related to HCV infection (death from liver failure or hepatocellular carcinoma) will continue to increase over the next two decades ***(Deuffic-Burban et al., 2007).***

The highest prevalence rate of HCV is among Egyptians (14% - 18%; approximately 10-fold greater than in the United States and Europe) ***(Mohamed et al., 2005)***. Because of the very high prevalence rate of HCV in the general Egyptian population, it accounts for most chronic liver disease and HCC cases in Egypt ***(Hassan et al., 2001 and Strickland et al., 2002)***. Progressive hepatic fibrosis with the development of cirrhosis is

a feature of almost all chronic liver diseases ***(Mohsen et al., 2003).***

* Major routes of transmission:

Parentral exposure to the hepatitis C virus is the most efficient means of transmission. Accordingly, the majority of patients infected with HCV in Europe and the United States acquired the disease through intravenous drug use or blood transfusion. The latter has become rare since routine testing of the blood supply for HCV began in the early 1990s. Other types of parentral exposure are important in specific regions in the world. It is important to notice that very often in patients with newly diagnosed HCV infection no clear risk factor can be identified ***(Sutton et al., 2008).***

Injection drug use:

Injection drug use has been the most commonly identified source of acute HCV infection. It is estimated that most newly acquired infections occur in individuals who have injected illegal drugs. The sero-prevalence of anti-HCV antibodies in groups of intravenous drug users may be up to 70% with considerable variation depending on factors such as region, risk behavior, socioeconomic status and others, underscoring the efficiency of transmission via direct blood contact ***(Sutton et al., 2008).***