Duplex-Doppler Ultrasonography Versus 24 Hours Urinary Na, Serum Creatinine and Serum Na in Diagnosis of Renal Dysfunction and Hepatorenal Syndrome in Patients with Chronic Hepatitis C

Thesis

Submitted for Partial Fulfillment of Master Degree
In Internal Medicine

By

Mohamed Hussein Galal
M.B.B.Ch - Ain Shams University

Under Supervision Of

Prof. Dr. Samir Abd El-hameed Ghait
Professor of Internal Medicine
Faculty of Medicine-Ain Shams University

Dr. Hanan Mahmod M. Badawy
Assistant professor of Internal Medicine
Faculty of Medicine-Ain Shams University

Dr. Zainab Ahmed Ahmed Ali EL-Din
Lecturer of Internal Medicine
Faculty of Medicine-Ain Shams University

Faculty of Medicine
Ain Shams University
2009

List Of Contents

Acknowledgement

First of all, all gratitude is due to **Allah** *the Almighty who guided and helped me in bringing this thesis to light which would have never been crowed by success without blessing of Allah to whom my faithful loyalty will remain however beyond any compromises.*

It is a pleasure to express my deepest appreciation, gratitude and sincere thanks to my teacher and supervisor ***Prof. Dr. Samir Abd El-hameed Ghait,*** *Professor of Internal Medicine, Faculty of Medicine, Ain Shams University, for his constructive suggestions, excellent guidance and eminent supervision which tided me over difficulties I met with throughout this work.*

I wish to express my deep and extreme appreciation and greatest thanks to ***Dr. Hanan Mahmod M. Badawy,*** *Lecturer of Internal Medicine, Faculty of Medicine, Ain Shams University, for her valuable instructions, kind support, continuous help, and giving me unlimited effort for very close supervision throughout this work.*

With considerable appreciation, I express my great indebtedness to ***Dr. Zainab Ahmed Ahmed Ali EL-Din,*** *Lecturer of Internal Medicine, Faculty of Medicine-Ain Shams University, for her keen supervision, fruitful discussion, significant*

encouragement, and magnificent assistance throughout this work.

List of Abbreviations

ADH	: Antidiuretic hormone
ALT	: Alanine aminotransferase
ANP	: Atrianatriuretic peptide
ARF	: Acute renal failure
AST	: Asparate aminotransferase
ATN	: Acute tubular necrosis
B	: Brightness
GFR	: Glomerular filtration rate
HBs	: Hepatitis B surface
HCC	: Hepatocellular carcinoma
HCV	: Hepatitis C virus
HPF	: High power field
HRS	: Hepatorenal syndrome
INR	: International normalized ratio
MARS	: Molecular adsorbent recirculating system
MELD	: Model for end-stage liver disease
NO	: Nitric oxide
OLT	: Orthotopic liver transplantation
RAAS	: Rennin-angiotensin-aldosterone system
RI	: Resistive index
SBP	: Spontaneous bacterial peritonitis
SNS	: Sympathetic nervous system
TIPS	: Transjugular intravenous portosystemic shunt
UOP	: Urinary out put
US	: Ultrasound
VC	: Renal Vasoconstrictors
VD	: Renal vasodilators

List Of Tables

List Of Figures

Page

INTRODUCTION

Liver Cirrhosis is defined as the histological development of regenerative nodules surrounded by fibrous bands in response to chronic liver injury, the etiology of cirrhosis can usually be identified by the patient's history combined with serologic and histologic evaluation. Alcoholic liver disease and hepatitis C are the most common causes in the Western world, while hepatitis B prevails in most parts of Asia and sub-Saharan Africa. After the identification of the hepatitis C virus in 1989 and of nonalcoholic steatohepatitis in obese and diabetic subjects, the diagnosis of cirrhosis without an apparent cause is rarely made. It is important to know the etiology of cirrhosis, since it can predict complications and direct treatment decisions. It also allows the discussion of preventive measures, e.g., with family members of patients with alcoholic cirrhosis or chronic viral hepatitis, and consideration of (genetic) testing and preventive advice for relatives of patients with genetic diseases, such as hemochromatosis or Wilson's disease ***(Farrell and Larter, 2006).***

The association between liver disease and renal dysfunction was reported more than a century ago when patients with chronic liver disease and normal renal histology were found to develop oliguric renal failure. This led to proposed links between renal dysfunction and the derangement in systemic circulation secondary to the liver failure ***(Turban et al., 2007).***

The International Ascites Club defined hepatorenal syndrome HRS as: “a syndrome that occurs in patients with advanced chronic liver disease and advanced hepatic failure and portal hypertension characterized by impaired renal function and marked abnormalities in the arterial circulation ***(Ruiz-del-Arbol et al., 2005)***

Duplex Doppler ultrasound can be used to assess vascular resistance in small renal intraparenchymal through analysis of the Doppler wave form by a parameter termed resistive index (RI) which is a non-invasive predictor of kidney dysfunction and hepatorenal syndrome in liver disease ***(Bardi et al., 2002).***

AIM OF THE WORK

The aim of the work to assess the value of renal arterial resistive index measured by Duplex Doppler ultrasonography as anon invasive technique in comparison with 24 hours urinary sodium, serum creatinine and serum sodium in detection of renal dysfunction in patients with advanced chronic liver disease and its possible use in early detection of patients with risk of developing hepatorenal.

CHRONIC HEPATITIS C AND LIVER CIRRHOSIS

Hepatitis C is caused by the hepatitis C virus (HCV) infection. According to World Health Organization data, 3% of the world population (approximately 170 million people) is infected with HCV. Over 70% of those infected manifest no symptoms in the acute phase of the disease, and in about 70–80% the acute phase progresses into a chronic form. Patients with symptoms in the acute phase of HCV infection most commonly present with unspecific signs and symptoms that may develop in other viral liver infections, e.g. malaise, fatigue, abdominal pain, mild hepatomegaly and splenomegaly and arthralgia. These symptoms usually persist for 2 to 12 weeks. In the chronic phase a subset of patients complain of malaise, nausea, abdominal pain and itching. With time, chronic hepatitis C may develop into liver cirrhosis ***(Czepiel et al., 2008).***

Cirrhosis can be caused by many things, some known and others unknown ***(Schuppan and Nezam, 2008):***

- Alcohol: Using alcohol in excess is the most common cause of cirrhosis in the United States.
- Chronic Viral Hepatitis: Type B and Type C hepatitis, and perhaps other viruses, can infect and damage the

liver over a prolonged time and eventually cause cirrhosis.

- Chronic Bile Duct Blockage: This condition can occur at birth (biliary atresia) or develop later in life (primary biliary cirrhosis). The cause of the latter remains unknown. When the bile ducts outside the liver become narrowed and blocked, the condition is called primary sclerosing cholangitis. This condition is often associated with chronic ulceration of the colon (colitis).

- Abnormal Storage of Copper (Wilson's disease) or Iron (Hemochromatosis): These metals are present in all body cells. When abnormal amounts of them accumulate in the liver, scarring and cirrhosis may develop.

- Drugs and Toxins: Prolonged exposure to certain chemicals or drugs can scar the liver.

- Autoimmune Hepatitis: This chronic inflammation occurs when the body's protective antibodies fail to recognize the liver as its own tissue. The antibodies injure the liver cells as though they were a foreign protein or bacteria.

- Cystic Fibrosis and Alpha l-antitrypsin Deficiency -- These disorders are inherited.

Cirrhosis is an expanding problem and has multiple etiologies. Most of the morbidity and mortality of chronic liver

diseases is due to its progression to cirrhosis and complications of cirrhosis. Ascites is the most common major complication of cirrhosis.When liver damage progresses to an advanced stage, signals are sent to the kidneys to retain salt and water in the body with fluid collection in the legs and in the abdominal cavity between the abdominal wall and the abdominal organs (ascites) ***(Runyon, 2004).***

Fluid in the abdominal cavity is the perfect place for bacteria to grow. Normally, the abdominal cavity contains a very small amount of fluid that is able to resist infection well, and bacteria that enter the abdomen (usually from the intestine) are killed or find their way into the portal vein and to the liver where they are killed. In cirrhosis, the fluid that collects in the abdomen is unable to resist infection normally. In addition, more bacteria find their way from the intestine into the ascites. Therefore, infection within the abdomen and the ascites, referred to as spontaneous bacterial peritonitis, is likely to occur. Spontaneous bacterial peritonitis is a life- threatening complication. Some patients with spontaneous bacterial peritonitis have no symptoms, while others have fever, chills, abdominal pain and tenderness, diarrhea, and worsening ascites ***(Menon and Kamath 2000).***

In the cirrhotic liver, the scar tissue blocks the flow of blood returning to the heart from the intestines and raises the pressure in the portal vein (portal hypertension). When pressure in the portal vein becomes high enough, it causes blood to flow

around the liver through veins with lower pressure to reach the heart. The most common veins through which blood bypasses the liver are the veins lining the lower part of the esophagus and the upper part of the stomach. As a result of the increased flow of blood and the resulting increase in pressure, the veins in the lower esophagus and upper stomach expand and then are referred to as esophageal and gastric varices; the higher the portal pressure, the larger the varices and the more likely a patient is to bleed from the varices into the esophagus or stomach ***(Carbonell et al., 2004).***

Bleeding from varices usually is severe and, without immediate treatment, can be fatal. Symptoms of bleeding from varices include vomiting blood (the vomitus can be red blood mixed with clots or "coffee grounds" in appearance, the latter due to the effect of acid on the blood), passing stool that is black and tarry due to changes in the blood as it passes through the intestine (melena), and orthostatic dizziness or fainting (caused by a drop in blood pressure especially when standing up from a lying position). Bleeding also may occur from varices that form elsewhere in the intestines, for example, the colon, but this is rare. For reasons yet unknown, patients hospitalized because of actively bleeding esophageal varices have a high risk of developing spontaneous bacterial peritonitis ***(Jutabha et al., 2005).***

Some of the protein in food that escapes digestion and absorption is used by bacteria that are normally present in the

intestine. While using the protein for their own purposes, the bacteria make substances that they release into the intestine. These substances then can be absorbed into the body. Some of these substances, for example, ammonia, can have toxic effects on the brain. Ordinarily, these toxic substances are carried from the intestine in the portal vein to the liver where they are removed from the blood and detoxified. When the toxic substances accumulate sufficiently in the blood, the function of the brain is impaired, a condition called hepatic encephalopathy. Sleeping during the day rather than at night (reversal of the normal sleep pattern) is among the earliest symptoms of hepatic encephalopathy. Other symptoms include irritability, inability to concentrate or perform calculations, loss of memory, confusion, or depressed levels of consciousness. Ultimately, severe hepatic encephalopathy causes coma and death ***(Cordoba et al., 2004).***

Cirrhosis due to any cause increases the risk of primary liver cancer (hepatocellular carcinoma). Primary refers to the fact that the tumor originates in the liver. The most common symptoms and signs of primary liver cancer are abdominal pain and swelling, an enlarged liver, weight loss, and fever. In addition, liver cancers can produce and release a number of substances, including ones that cause an increased in red blood cell count (erythrocytosis), low blood sugar (hypoglycemia), and high blood calcium (hypercalcemia) ***(Heidelbaugh and Bruderly, 2006).***