

# HEPATORENAL FAILURE

## Essay

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Abbreviations:

- ERPF : effective renal plasma flow.
- GFR : glomerular filtration rate.
- HRS : hepatorenal syndrome.
- PCA : portocaval anastomosis.
- PGE<sub>2</sub> : prostaglandin E<sub>2</sub>.
- RPF : renal plasma flow.
- Tx A<sub>2</sub> : thromboxane A<sub>2</sub>.
- Tx E<sub>2</sub> : thromboxane E<sub>2</sub>.

### INTRODUCTION & AIM OF THE WORK

The hepatorenal syndrome is one of the primary causes of death in patients with liver cirrhosis. In this syndrome patients with decompensated cirrhosis develop acquired, functional renal failure in which none of the usual causes of renal insufficiency are present and in which the kidneys themselves are normal. This disorder stubbornly resists attempts to improve renal function and usually ends in death. The single most frustrating aspect of this unique disorder is that the kidneys are anatomically and histologically normal and capable of normal function. The kidneys from patients who have died of the hepatorenal syndrome can be transplanted into patients with chronic uremia, where they function promptly and well. Conversely, transplantation of a liver into a patient with the HRS promptly restores renal function to normal (Conn, 1982). When clinical evidence of renal insufficiency such as oliguria or azotemia develops in a patient with cirrhosis and ascites, the process is probably only reversible, if at all, when liver function can be improved, (Arief and Chidsey, 1974). The onset of the HRS frequently follows diuretic therapy, paracentesis or gastrointestinal hemorrhage in cirrhotic patients who have decompensated liver disease characterized by jaundice, ascites, hypoalbuminemia, portal hypertension, and hepatosplenomegaly. Reversal of impaired renal function will reduce the enteropatic circulation of nitrogen derived from ureolysis within

the intestine. (Holtzapple, 1979).

There is a number of diverse disorders which affect both the liver and kidney and, in effect, give rise to a variety of hepatorenal syndromes. Clearly, however, these pseudo-hepatorenal disorders can be readily differentiated from the true HRS by recognition of the precipitating event or by characteristic clinical, laboratory, or functional features of the hepatic or renal lesions, or both.

However, the prior presence of chronic renal disease, such as glomerulonephritis, should exclude the diagnosis of the HRS.

This syndrome appears to be a disorder of reduced glomerular filtration rate and decreased renal blood flow, which probably precede by months the appearance of overt renal failure and perhaps set the stage for its development. Paradoxically, this evidence of decreased renal blood flow usually exists in the presence of increased plasma volume and cardiac output. (Conn, 1982).

Our aim in this work is to give a broad scope on this syndrome with its hemodynamics, its clinical picture, complications and management if possible.

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LIVER ANATOMY AND PHISIOLOGY

### Anatomy:

The liver of the full-term infant weighs 120 to 160gm at birth. The weight is doubled at 2 years and tripled at 3 years; at 9 years it has increased six times, and at puberty, ten times. The liver of the adult is twelve to thirteen times as large as that of the newborn infant. The relative sizes of the lobes of the liver change with age; at birth the right lobe is twice as large as the left lobe, in young children and adolescents it is about three times as large. In the newborn infant the liver edge is usually less than 2 cm below the costal margin in the right midclavicular line. The upper border of hepatic dullness is at the level of the fifth or sixth rib in the mammillary line and extends nearly horizontally. In the axillary line it is usually in the seventh intercostal space and posteriorly in the ninth space. The lower border of the liver may be normally palpable about 1 cm below the costal margin throughout childhood (Kaye and Holtzapple, 1975).

### Histology:

Histologically, the liver is divided into lobules based on a central vein and peripheral portal tracts with regular radiating sinusoids and plates of liver cells between them. The central veins are tributaries of the hepatic veins which drain to the inferior vena cava; the portal tracts contain branches of the hepatic artery, the portal vein, lymphatics and the bile ducts. The sinusoids are channels lined by endothelial and phagocytic (Kupffer) cells, which receive

blood separately from the hepatic arterial and portal venous systems and convey it to the central veins. The liver cells (hepatocytes) are arranged in single-cell plates which lie between and separate the sinusoids from one another. Between the liver cells and the sinusoidal cells is the space of Disse which contains fluid draining to the lymphatics in the portal tracts. There are bile canaliculi forming networks between ducts which link the intralobular bile canaliculi to the larger interlobular bile ducts in the portal tracts.

The liver has arterial and venous blood supply and its total blood flow is normally about 1500ml/min. In man the hepatic artery supplies about 35 % of the total liver blood flow and about 40 % of its total oxygen supply. The portal vein drains its blood from the alimentary tract, spleen, pancreas and gall bladder. It enters the liver in the porta hepatis and is distributed throughout the liver via the portal tracts and empties its blood into the sinusoids. The oxygen content of portal blood varies and is lowest during digestion. (Finlayson and Richmond, 1981).

#### Liver Function:

The liver has the following important functions:

1. It produces bile and through the bile salts contained in this digestive secretion it facilitates the absorption of fat and fat-soluble vitamins.
2. The liver produces a large number of proteins and is

- the site of synthesis of all the plasma proteins except the immunoglobulins. Of the hepatic proteins albumin is the most important; 10-15g. of albumin are synthesized in the liver per day. The liver is also the site of production of important binding globulins as transferrin, caeruloplasmin and various combinations of globulin and lipid called lipoproteins. The liver is also the site of production of the proteins concerned in blood coagulation and of amino acid degradation to alpha keto-acids and ammonia. Ammonia is then converted in the liver to urea by a series of enzymes acting in the Krebs urea cycle.
3. Carbohydrates in the form of glucose and galactose are metabolized in the liver and the end result of this process is the synthesis of glycogen. The polymer, glycogen, is stored in the liver and breakdown of this substance (glycogenolysis) is facilitated by several series of enzymes. (Price, 1975).

The hepatic glucostat: There is a net uptake of glucose by the liver when the blood glucose is high and a net discharge when it is low, thus maintaining a constant circulating glucose levels. This function is not automatic; glucose uptake and glucose discharge are affected by the actions of numerous hormones. (Ganong, 1981).

Effects of glycogen on hepatic function:

When the hepatic glycogen level is high, the rate of deamination of amino acids is depressed, and the amino acids are thus preserved for other uses. Ketone body formation is also depressed when the liver glycogen content is high. Acetylation and glucoronide conjugation of various substances in the liver progress at a faster rate when the glycogen content is high, and the glycogen-rich liver is more resistant to toxic agents and pathologic processes. This is why it is important in the treatment of infectious hepatitis to maintain a high carbohydrate intake. (Ganong, 1981).

4. The liver plays an essential part in fat metabolism. It is able to utilize free fatty acids released from fat depots in order to provide energy. It also converts free fatty acids to triglyceride and other lipids. Neutral fat can be split by the liver to glycerol and free fatty acid. Free fatty acid is in turn oxidized to acetyl CoA units which either undergo complete oxidation or recombine to form aceto-acetic acid. This latter compound is important because it is one of the ketone bodies appearing in the blood and urine in severe diabetes and because it is unable to be further metabolized in the body. The normal liver contains fat-usually about 5 percent of its weight.

In certain circumstances such as diabetes, starvation, and alcoholic liver disease this amount is much increased. (Price, 1975).