GASTRIC MUCOSAL BLEEDING TIME IN EGYPTIAN CIRRHOTICS

Thesis
Submitted for the partial fulfilment of
the Msc. Degree of Internal Medicine

Presented by

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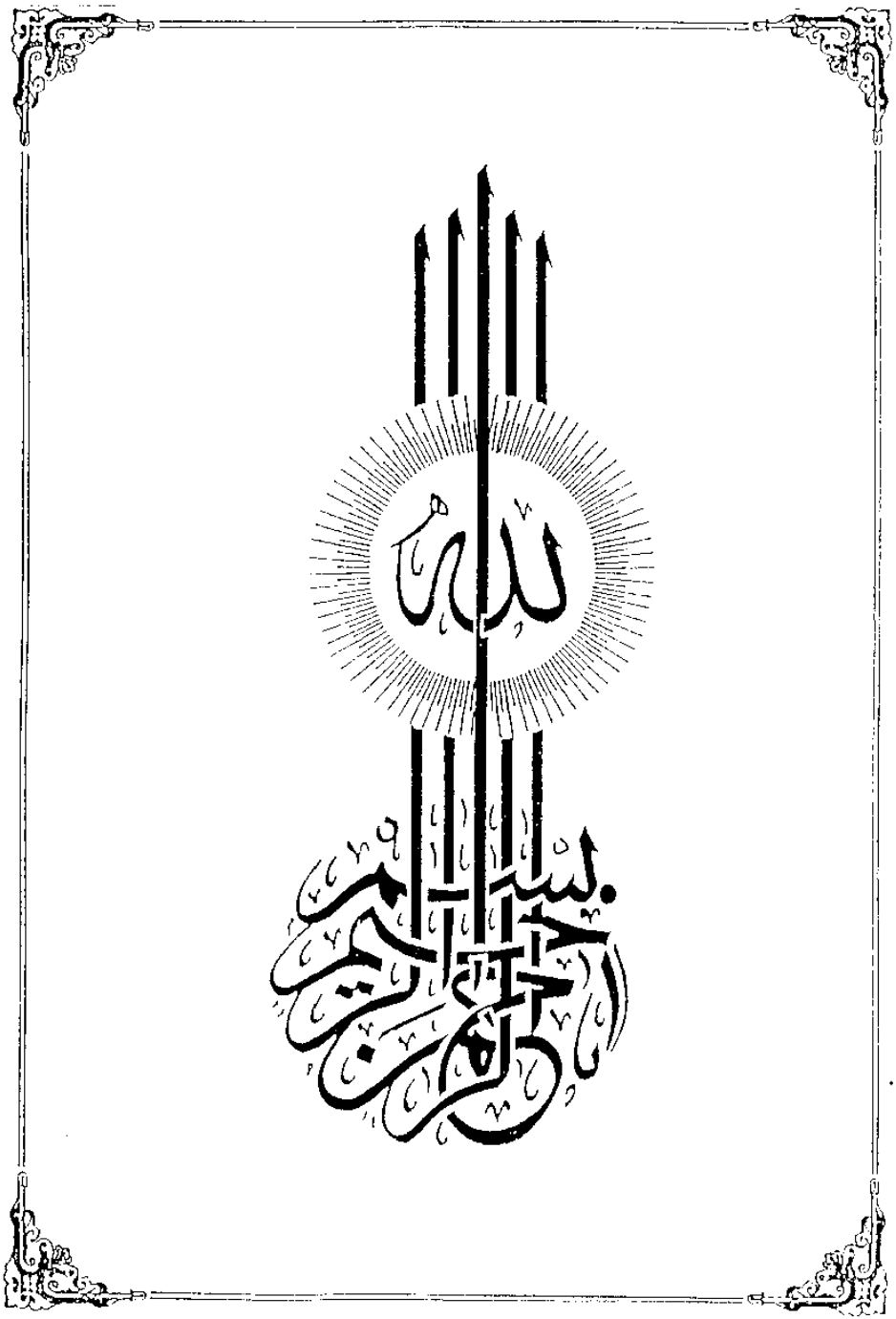

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INTRODUCTION
AND
AIM OF THE WORK

INTRODUCTION

Before undertaking liver biopsy in patients with cirrhosis, prothrombin time (PT) and platelet count are routinely measured (Zakim and Boyer, 1990). It has been stated that the skin bleeding time (SBT) is probably a more important predictor of bleeding time than PT or platelet count with respect to liver biopsy in cirrhosis (Jalan et al., 1994). It has been suggested that prolonged bleeding time is common in patients with cirrhosis, even in those with prothrombin time and platelet count within safe limits for invasive procedures and that the severity of liver disease as assessed by the bilirubin concentration plays an important part in determining the bleeding time in cirrhosis (Blake et al., 1990).

The bleeding time should be measured when assessing patients for invasive procedures who have a raised bilirubin concentration or poor hepatic function, even if the platelet count and PT are considered adequate. The bleeding time is not only influenced by the platelet count but may also be affected by the platelet volume, the packed cell volume, blood urea concentration, and nature of the connective tissue. Both the platelet count and the serum bilirubin concentration were independently correlated with bleeding time, suggesting that liver function has an important role in determining primary haemostasis in patients with cirrhosis (Greaves et al., 1990).

Haemorrhage is a common event in severe liver failure. It has generally been associated with reduced blood levels of clotting factors or with a low platelet count, caused by the liver disease. Severe bleeding does occur also in the absence of these recognised haemostatic defects. The balance between the concentration of clotting factors and inhibitors may influence the overall effect on haemostasis (Boks et al., 1986).

Gastric mucosal lesions are common in portal hypertension, and they are an important cause of blood loss, which may be slow and insidious causing anaemia or sudden and severe causing massive and occasionally fatal haemorrhage. Gastric mucosal biopsies are regularly performed during upper gastrointestinal endoscopy and rarely bleed significantly even in patients with chronic liver disease and deranged haemostatic mechanisms (Iwao et al., 1993).

It has been suggested that the measurement of gastric mucosal bleeding time (GBT) is a clinically valid and useful parameter for studying mechanisms of gastric mucosal haemostasis in patients with portal hypertension due to liver cirrhosis (Jalan et al., 1994).

AIM OF THE STUDY

The aim of this study was to assess the gastric mucosal bleeding time (GBT) in patients with cirrhosis in relation to the severity of liver disease, presence of oesophageal varices, degree of portal hypertensive gastropathy, skin bleeding time (SBT), platelet count, and degree of haemodynamic changes in portal vein.

REVIEW OF LITERATURE

PORTAL HYPERTENSION

DEFINITION:

It is persistent elevation of the portal vein pressure above normal. Normal pressure in the portal vein is low (10-15 cm saline or 7-10 mmHg) because the vascular resistance in the hepatic sinusoids is minimal (Isselbacher, 1982).

Direct portal system pressure - at surgery - over 22 mmHg, intra-splenic pressure over 17 mmHg, and wedged hepatic pressure more than 4 mmHg above inferior vena caval pressure are reliable indications of portal hypertension (Schiff, 1975).

CLASSIFICATION:

Westaby and Williams (1985) classified the causes of portal hypertension, based on the site of the underlying lesion, into:

A. <u>Intra-hepatic</u>:

1- Schistosomiasis.

2- Cirrhosis.

3- Congenital hepatic fibrosis.

4- Idiopathic non-cirrhotic portal hypertension.

5- Chronic active hepatitis.

6- Alcoholic hepatitis.

7- Viral hepatitis.

8- Veno-occlusive disease.

9- Partial nodular transformation of the liver.

10- Myelo- and lympho-proliferative disorders.

11- Hepato-portal arteriovenous fistula.

B. Pre-hepatic:

1- Portal vein thrombosis.

2- Splenic vein thrombosis:

a)Neonatal umbilical infection and intra-abdominal sepsis.

b) Haematologic disorders as polycythaemia rubra vera.

c) Intra-abdominal malignancy, abdominal trauma, pancreatitis.

d) Unknown cause.

3- Tropical splenomegaly.

4- Spleno-portal arteriovenous fistula.

C. Supra-hepatic:

1- Budd-Chiari syndrome.

2- Right ventricular failure.

3- Constrictive pericarditis.

From the practical point of view, **Sherlock and Dooley (1997)** classified portal hypertension into:

I. Presinusoidal group of causes.

II. Hepatic group of causes.

I- Presinusoidal Causes

Obstruction in the presinusoidal venous compartment may be anatomically outside the liver (extra-hepatic) e.g. portal vein thrombosis, or within the liver itself (intra-hepatic) but at functional level proximal to the hepatic sinusoids so

that the liver parenchyma is not exposed to the elevated pressure e.g. Schistosomiasis (Isselbacher, 1982).

A) Extra-hepatic presinusoidal causes:

1- Portal vein obstruction:

a) Infection: Septicaemia or intra-abdominal infection e.g. acute appendicitis and peritonitis are the commonest causes. Umbilical vein infection may be responsible in neonates **(Thompson and Sherlock, 1964).**

b) **Post-operative:** The portal and splenic veins commonly block after splenectomy, especially when pre-operatively the patient had a normal platelet count which, however, rises post-operatively. The thrombosis spreads from the splenic vein into the main portal vein. It is especially likely in patients with myeloid metaplasia (Broe et al., 1981).

c) **Trauma:** Portal vein injury may follow automobile accidents or stabbing (Sherlock and Dooley, 1997).

d) Hypercoagulable state: Enhanced clotting may be a factor, particularly in the older age group, myeloproliferative disease, especially polycythaemia rubra vera are the commonest associations (Sherlock and Dooley, 1997).

e) Invasion and compression: Hepatocellular carcinoma, carcinoma of the pancreas, usually of the body, and of other adjacent organs may lead to portal vein block (Sherlock and Dooley, 1997).

f) Congenital : Congenital obstruction can be produced any where along the line of the right and left vitelline veins from which the portal vein develops (Morse et al., 1986).

g) **Miscellaneous:**

* Portal vein thrombosis may occur with pregnancy and long use of oral contraceptives, especially in older women (Capron et al., 1981).

* Portal vein block has been associated with general disease of veins and in particular with thrombophlebitis migrans (Sherlock and Dooley, 1997).

h) **Unknown:** Even after full investigations, the aetiology may remain obscure. Some of these patients have associated autoimmune disorders such as thyroiditis, diabetes, pernicious anaemia, dermatomyositis or rheumatoid arthritis (Webb and Sherlock, 1979).

2- <u>Splenic vein obstruction</u>:

Isolated splenic vein obstruction causes sinistral (left sided) portal hypertension. It may be due to any of the factors causing portal vein obstruction. Pancreatic disease such as carcinoma, pancreatitis, pseudocyst and pancreatectomy are particularly important (Sherlock and Dooley, 1997).

3- <u>Hepatic arterial-portal venous fistulae</u>:

These fistulae are usually congenital, traumatic, or related to adjacent malignant neoplasms (Sherlock and Dooley, 1997).

4- <u>Portal-hepatic venous shunts</u>:

They are probably congenital. They may be between the main portal and hepatic veins or between the right or left portal vein and the hepatic veins (Sherlock and Dooley, 1997).

B) Intra-hepatic presinusoidal causes:

1- Portal tract lesions:

a) **Schistosomiasis** : Schistosomiasis is one of the major health problems in Egypt. It is estimated that about 20 million individuals are infected by schistosoma mansoni and/or schistosoma haematobium (Abdel-Wahab, 1982). The pathology of hepatic schistosomiasis is periportal fibrosis of two types, coarse and fine according to whether the large or small portal tracts are affected (Hashem, 1947). The main complication of such fibrotic process is portal hypertension (Mousa, 1975). In schistosomiasis, the portal hypertension results from the ova causing a reaction in the minute portal venous radicles (Sherlock and Dooley, 1997). The eggs reach the liver via the portal blood and become extravascular in the portal tracts where they initiate a cellular reaction that ends in periportal fibrosis leading to presinusoidal block. This interferes with the flow of blood in the portal system resulting in portal hypertension, development of porto-systemic collaterals, and eventually upper gastrointestinal haemorrhage from oesophageal varices (Abdel-Wahab et al., 1978).

b) **Congenital hepatic fibrosis:** The portal hypertension is probably due to deficiency of the terminal branches of the portal vein in the fibrotic portal zones (Sherlock and Dooley, 1997).

c) **Myeloproliferative diseases:** Including myelosclerosis, myeloid leukaemia and Hodgkin's disease. The mechanism is related to infiltration of the portal zones with haemopoietic tissue, but thrombotic lesions in the major and minor portal vein radicles and nodular regenerative hyperplasia contribute (Wanless et al., 1990).

d) **Systemic mastocytosis :** Portal hypertension is related to increased intra-hepatic resistance secondary to mast cell infiltration (Grundfest et al., 1980).

e) **Primary biliary cirrhosis:** Portal hypertension may be a presenting feature long before the development of the nodular regeneration characteristic of cirrhosis (Sherlock and Dooley, 1997).

f) **Sarcoidosis:** Portal hypertension is presinusoidal due to portal granulomas. Sinusoidal block may be superimposed due to fibrosis (Valla et al., 1987).

g) Acute alcoholic fatty infiltration (Sherlock and Dooley, 1997).

2- Toxic causes:

The injurious substance is taken up by endothelial cells mostly lipocytes (Ito cells) in Disse's space; these are fibrogenic. Minute portal vein radicles are obstructed and intra-hepatic portal hypertension results (Sherlock and Dooley, 1997).

a) Reversible portal hypertension may follow vitamin A intoxication (Guarascio et al., 1983).

b) Portal hypertension complicates the treatment of psoriasis with arsenic (Sherlock and Dooley, 1997).

c) Exposure to the vapour of the polymer of vinyl chloride.

d) Prolonged use of cytotoxic drugs, such as methotrexate, 6-mercaptopurine and azathioprine, can lead to presinusoidal fibrosis and portal hypertension (Sherlock and Dooley, 1997).

3- Hepato-portal sclerosis:

It is also called non-cirrhotic portal fibrosis, non-cirrhotic portal hypertension and idiopathic portal hypertension. The injury may be infectious, toxic or in many instances unknown. This is marked by splenomegaly,