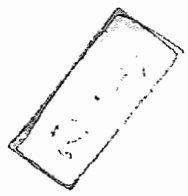
FIBRINOLYTIC ACTIVITY OF GASTRIC JUICE IN PATIENTS WITH ESOPHAGEAL VARICES: A COMPARATIVE STUDY BETWEEN BLEEDERS AND NON-BLEEDERS



THESIS
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BY
ALAA MOHAMED ALI EL- MELIGY
M.B., B. CH.

Supervisors

PROF. DR. NADIA LOTFY EL- ANSARY
Professor of Internal Medicine and Gastroenterology
Faculty of Medicine-Ain Shams University

DR. MOHAMED ABD EL- HAMID EL- BOKL
Ass. Professor of Internal Medicine and Gastroenterology
Faculty of Medicine-Ain Shams University.

DR. AZZA MOHAMED SADEK
Lecturer of Clinical Pathology
Faculty of Medicine-Ain Shams University

FACULTY OF MEDICINE
AIN SHAMS UNIVERSITY

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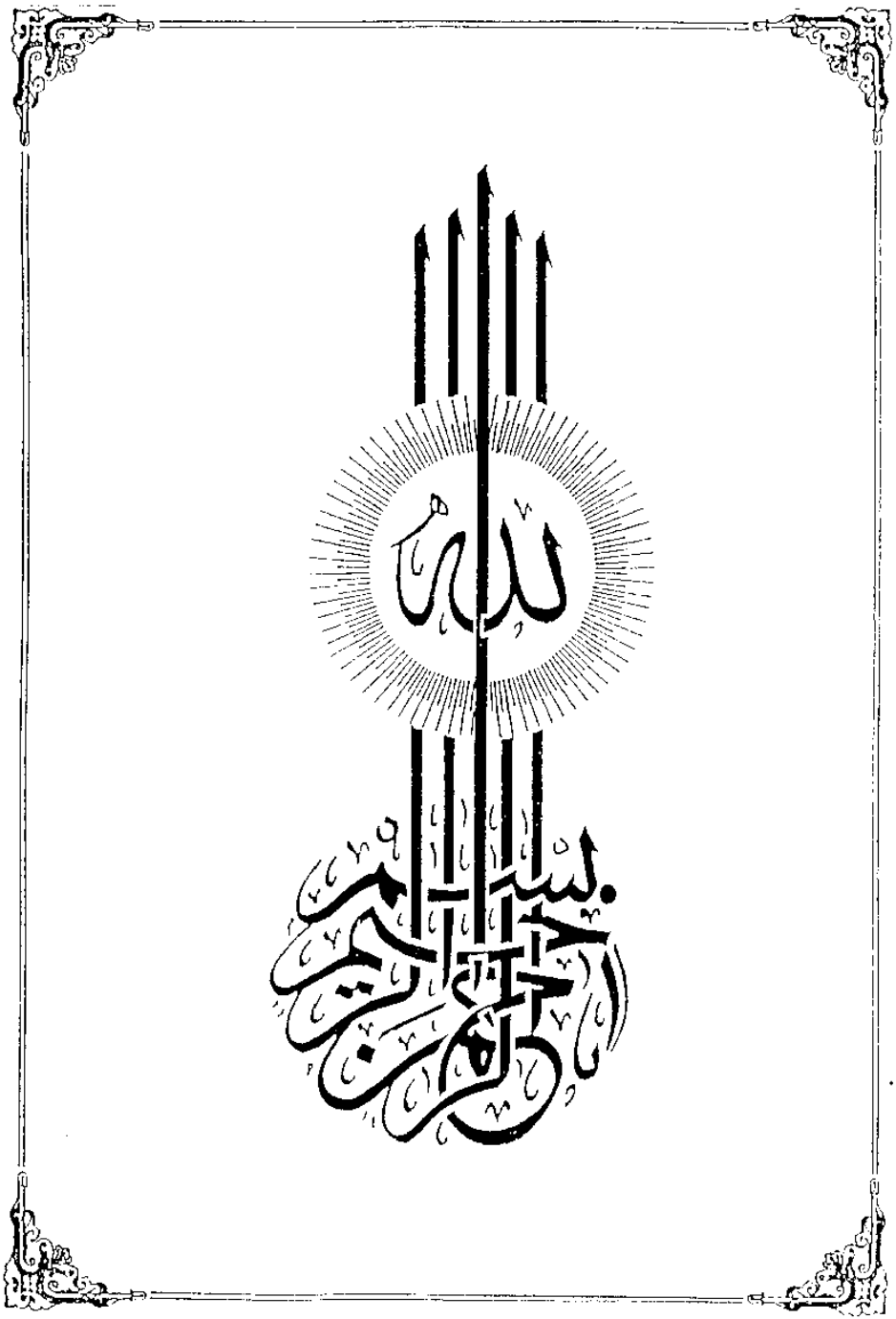

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INTRODUCTION

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Patients suffering from portal hypertension frequently bleed from esophageal varices. This is a dramatic event accompanied by a high incidence of mortality which is about 50% after the first hemorrhage *(Rigo et al 1992).*

The factors that predispose to and precipitate variceal hemorrhage have still not been clearly identified *(MacMathuna et al 1992).*

In normal individuals bleeding can result from localized hyperfibrinolysis. Any amount of localized fibrinolysis could exaggerate local bleeding and favorably influenced by fibrinolytic inhibitors *(Prentice 1975)*. Certain lesions that cause upper or lower gastrointestinal bleeding have been associated with increased local fibrinolytic activity e.g. cirrhosis of the liver and bleeding due to esophageal varices *(OKa and Tanaka 1979).*

The aim of this work is to study the relationship between local fibrinolytic activity (i.e. in gastric juice) and bleeding tendency in cases of esophageal varices. This relationship, if present, will be very useful in management and prophylaxis against bleeding episodes which are very dangerous.

REVIEW

PORTAL HYPERTENSION

Portal venous system:

The portal system includes all veins that carry blood from the abdominal part of alimentary tract, the spleen, pancreas and gallbladder. The portal vein enters the liver at the porta hepatis in two main branches, one to each lobe; it is without valves in its larger channels.

The portal vein is formed by the union of the superior mesenteric vein and the splenic vein just anterior to the head of the pancreas at about the level of the second lumbar vertebra. Its length is about 5.5-8cm.

Portal blood flow in man is about 1000-1200 ml/min. Portal pressure is normally about 7 mmHg in man *(Sherlok 1993).*

Definition of portal hypertension:

Portal hypertension is defined as portal vein pressure in excess of the normal 5-10 mmHg *(Genecin and Groszmann 1993).*

Clinical consequences of portal hypertension:

These include the evolution of portosystemic collaterals, plasma volume expansion, the hyperdynamic circulation, varices and congestive gastropathy, and splenomegally. Ascites, portosystemic encephalopathy,

and renal failure result from the hemodynamic derangements of portal hypertension *(Genecin and Groszmann 1993).*

Collateral circulation:

When the portal circulation is obstructed, whether it be within or outside the liver a remarkable collateral circulation develops to carry portal blood into the systemic veins *(Sherlok 1993).* Normally 100% of the portal venous blood flow can be recovered from the hepatic veins, whereas in cirrhosis 13% is obtained *(McIndoe 1928).* The remainder enters collateral channels which form four main groups *(Sherlok 1993).*

1- Group I:

Where the protective epithelium adjoins absorptive epithelium:

A) At the cardia of stomach:

Where the left gastric vein, posterior gastric and short gastric veins of the portal system anastmose with intercostal, diaphragmo-esophageal and azygos minor veins of the caval system. Deviation of blood into these channels lead to the formation of esophageal varices at the lower end of esophagus and gastric varices and congestive gastropathy at the fundus of the stomach.

B- At the anus:

Where the superior hemorrhoidal vein of the portal system anastmoses with the middle and inferior hemorrhoidal veins of the caval

system. Deviation of blood into these channels may lead to rectal varices. These collaterals are thought to be distinct from hemorrhoids *(Hosking et al 1989).*

2- Group II:

In the falciform ligament through the paraumblical veins. These dilated paraumblical veins are know as the caput medusae.

3- Group III:

Where the abdominal organs are in contact with retroperitoneal tissues or adherent to the abdominal wall. These include veins from the liver to the diaphragm.

4- Group IV:

Portal venous blood is carried to the left renal vein. Large spontaneous anastmoses between the portal system and the left renal vein may evolve; these may be large enough to simulate a surgical shunt *(Genecin and Groszmann 1993).*

Pathogenesis of portal hypertension:

1- Increased resistance to venous flow.

It is the most common mechanism for the development of portal hypertension. Liver disease accounts for the majority of cases; however, occlusion of the portal or hepatic veins and cardiac disease

also cause increased resistance to flow and increase in portal pressure *(Boyer 1992).*

2- Increased portal venous blood flow.

It is an unusual cause of portal hypertension for two reasons *(Siato et al 1987).*

a) Increase in portal vein flow causes a reflex decrease in hepatic artery flow, thereby tending to maintain relatively normal sinusoidal pressure.
b) The outflow resistance from the liver is so low that increase in portal vein flow must be very large to cause a significant increase in portal venous pressure.

Causes of portal hypertension *(Boyer 1992).*

I- Increased resistance

1-Liver diseases

Cirrhosis - all causes.
Congenital hepatic fibrosis.
Schistosomiasis.
Idiopathic portal hypertension.
Sarcoidosis.
Alcoholic hepatitis.
Partial nodular transformation.

2- Diseases of the cardiovascular system.

Portal vein occlusion.

Splenic vein occlusion.

Hepatic vein occlusion.

Veno-occlusive disease.

Web lesion or thrombosis of the inferior vena cava

Congestive heart failure.

Constrictive pericorditis.

II Increased portal blood flow.

Splenomegally not due to liver disease.

Arteriovenous fistula.

ESOPHAGEAL VARICES (E.V.)

To understand the mechanism of development of esophageal varices we should at first study the normal venous anatomy of the lower part of esophagus. We can classify the normal venous anatomy of this area by 2 ways i.e. From above downwards or from inside outwards.

Normal venous anatomy of the lower part of esophagus:

Vianna et al. (1987) using radiology, corrosion casting and morphometry studied the normal venous anatomy of this area and have defined 4 distinct zones of venous drainage.

1- Gastric zone.
2- Palisade zone.
3- Perforating zone.
4- Truncal zone.

Spence, (1984) studied the normal venous anatomy of the same area before but using image analysis systems. He defined 3 zones.

zone 1: corresponds to gastric zone.

zone 2: corresponds to palisade and perforating zones.

zone 3: corresponds to truncal zone.

1- CASTRIC ZONE:

It is present in the proximal part of the stomach. The veins in this area occupy a much greater proportion of the submucosa than in the lamina propria. *(Spence, 1984).* It consists, of 2-3 cm circular band of

veins in the proximal stomach with the upper border at gastroesophageal junction. This zone drains distally into:

1- Portal vein through left gastric vein.

2- Splenic vein through short gastric veins *(Vianna et al 1987).*

2- PALISADE ZONE:

This zone begins at gastroesophageal junction and extends for 2-3 cm in the lower part of esophagus. The veins in this region lie mainly in lamina propria. They resemble a palisade *(Vianna et al. 1987).* The veins in gastric zone pierce the muscularis mucosa at gastroespphageal junction and run in lamina propria in palisade zone. The transition from gastric zone to palisade zone is sudden and occurs at Gastroesophageal junction (at the point of change of epithelium from columnar to squamous). In portal hypertension the vessels in lamina propria in this zone become varicosed. As they are more superficial, this explains the frequency of rupture of esophageal varices at this zone *(Spence, 1984).* The blood flow in this area is bidirectional. This bidirectional flow is attributed to the presence of perforating veins *(McCormack et al. 1983).*

3- PERFORATING ZONE:

This zone occupies the area between 3-5cm above the gastro esophageal junction. This zone is formed as a continuation of the palisade zone by confluence of palisade veins to form longitudinal trunks changing their direction to run inferioly then piercing the muscle coat of esophagus

to reach its outer surface. On the outer surface of the esophagus these vessels fuse to form the extrinsic esophageal veins (adventitial veins) *(Vianna et al. 1987).* Many of the perforating veins that connect the intrinsic veins (i.e. superficial and deep intrinsic = subepitheleal and submucosal veins) to extrinsic (adventitial) veins have valves that direct blood flow away from esophageal lumen ***(Butler, 1951).*** Venous dilatation occurring with increased pressure causes these valves to become incompetent allowing retrograde flow. Turbulent blood flow in the varix caused by the perforating veins may explain why variceal rupture commonly occurs just above gastroesophageal junction. ***(McCormack et al. 1983).***

4- TRUNCAL ZONE:

It extends for about 8-10 cm with its inferior border about 5 cm above gastroesophageal junction. The veins in this area drains into the proximal extremity of perforating zone *(Vianna et al. 1987).* The veins in this area occupy a much greater proportion of the submucosa than the lamina propria ***(Spence, 1984).***

Layers of veins in the lower esophagus:

Kitano et al. (1986) studied the normal venous anatomy of the lower esophagus using a refined resin casting technique. Four layers of veins were described.