SERUM GASTRIN LEVEL IN PATIENTS WITH BILHARZIAL HEPATIC FIBROSIS

THESIS

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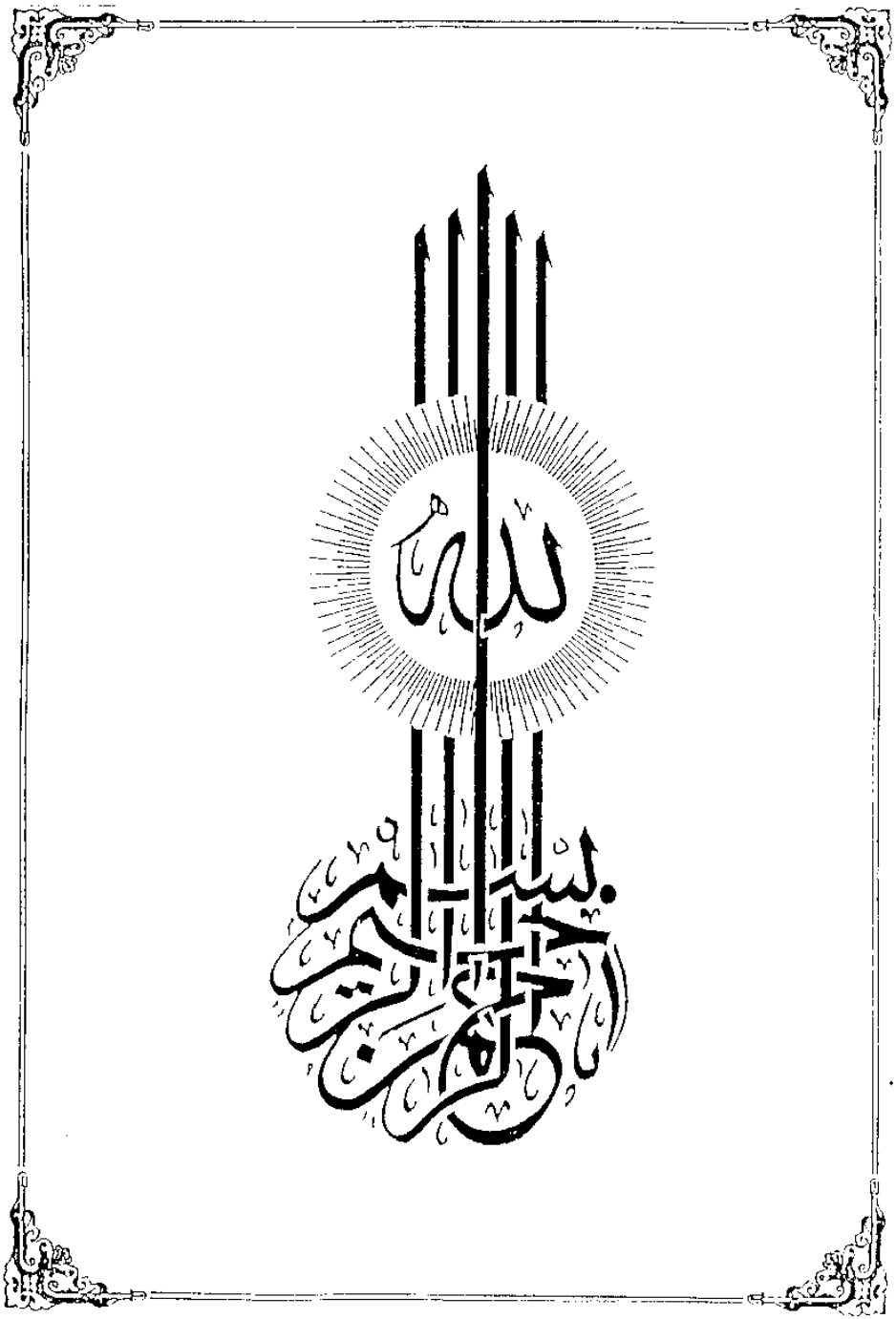

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INTRODUCTION

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Interest in gastric function in liver diseases has been stimulated by reports of an increased incidence of peptic ulcer in hepatic cirrhosis and after porta-caval shunts. More intruiguing, however, is the conjecture that the liver may play a role in the regulation of gastric secretion.

Ostrow et al. (1960) measured the gastric secretory function in patients with hepatic cirrhosis by means of uropepsin excretion, blood pepsinogen level and gastric acid output, both basally and after histamine. He found that all the above secretory parameters were significantly reduced to below normal; in addition to histamine achlorohydria in one third of decompensated cirrhotics. The same reduction in gastric secretion was found in cirrhotics who were not malnourished or decompensated. This suggests that chronic illness is not the cause of the diminution in gastric function.

In addition, uropepsin and blood pepsinogen values were as low in post necrotic and biliary cirrhosis as in alcohol cirrhosis, indicating that alcoholism itself was not responsible for the decreased gastric acidity.

Moreover, he found that gastric acid output, both basally and after histamine, was higher in cirrhotics with porta-caval shunting than in cirrhotics without shunting.

Osborne et al. (1966) reported that extensive small bowel resection in man was followed by excessive acid secretion and a high incidence of peptic ulceration. They suggested that the small bowel produced an inhibitor of acid secretion. The loss of this inhibitor was considered the cause of gastric hypersecretion.

Temperley et al. (1971) also noticed increased incidence of peptic ulceration following extensive small bowel resection in man. They found that the biological activity of synthetic human gastrin I was unaffected by transit through the liver. Their experiments showed that the small bowel was, indeed, an important site of gastrin inactivation; both in dogs and in rats. They also found different enzymes in homogenates of liver and small bowel mucosa which inactivate pentagastrin and gastrin respectively. Pentagastrin and gastrin have the same C-terminal tetrapeptide sequence in which all their biological activity appears to reside.

The biologically inactive part of gastrin molecule (residues 1-13) is not, however, without function. It Protects the molecule from inactivation in the liver.

Furthermore, it allows inactivation of gastrin in the small bowel. The results of Temperley suggest that a specific enzyme exists in the small bowel to cause such an inactivation.

El Rooby (1967) reported the presence of intestinal lymphangiectasia in patients with Hepato splenic Schistosomiasis (HSS). Shafei (1975) added the presence of moderate mucosal atrophy of intestinal villi with marked cellular infiltration.

Dencker et al. (1973) studied the gastrin levels in the portal and peripheral venous blood after feeding in man. They suggested that endogenous gastrin in man, as measured by radioimmuno assay, were not to any great extent inactivated by the liver. The slightly lower gastrin levels, noticed in peripheral blood, were most likely caused by dilution only. They were probably not to be considered a result of degradation or inactivation of endogenously released gastrin by the liver.

In conclusion, passage through the liver has not been found to affect the concentration or molecular size of immunoreactive gastrin in serum. These findings, however, do not disprove the hypothesis that gastrin may be one factor responsible for the hypersecretion of acid

after porta-caval shunting. The possibility still remains that the shunting rpocedure as such, augments the release of gastrin from its cellular stores in the gastro intestinal mucosa.

Lam (1976) studied hypergastrinaemia in cirrhosis of liver. His results indicated that the hypergastrinaemia, in cirrhotic patients, was a reflection of gastric hypo-acidity and beared no relationship to hepatic dysfunction. Although no relashionship was found between basal acid output and fasting serum gastrin; a significant relation-ship was present between the acid secretory capacity (as expressed in maximal acid output/kg total body weight) and the post prandial gastrin response.

Lam also suggested that the gastric hypoacidity did not accure solely from mucosal abnormality, the most cons-istent picture of which was mucosal congestion with occa-sional atrophic gastritis. This hypoacidity may result from the presence ofexcessive amounts of circulating acid-inhibiting intestinal peptides, which the diseased liver fails to metabolise. Vasoactive inhibitory peptide (VIP) has been observed to be present in the serum in abnormally high concentration in patients with cirrhosis (Said et al, 1974). However, Rayford et al., (1974) found that VIP only inhibited gastrin release in unphysiological high doses.

The role of these peptides in the genesis of gastric hypoacidity in cirrhosis is only speculative and remains to be defined.

Before discussing the gastrin response to insulin in patients with cirrhosis of the liver, it is necessary to stress on the role of neural influences on the release of gastrin using the potent autonomic nerve stimulus of hypoglycemia.

Mechanism of Acetyl Choline (AC) in Stimulating the Gastric Acid Secretion and Gastrin :

Cholinergic nerves supply both parietal cells and antral G cells. These cholinergic nerves are activated both by vagal impulses and by the so called short reflexes that are completed within the wall of the stomach. Vagal activation occurs as a result of stimuli acting in the head(cephalic phase) and in the stomach (gastric phase).

1- Cephalic stimuli include chewing, tasting and swallowing food (as in Sham feeding), through sight, smell or thought of food (conditioned reflex), hypoglycemia induced by insulin and interference with glucose utilization by non metabolizable sugars such as 2 deoxy glucose.

2- Gastric stimuli include distention of the stomach and the action of chemical agents, particularly partially digested proteins, on the gastric mucosa.

The gastric stimuli initiate both vasovagal reflexes and short intramural reflexes; the long reflexes are more effective. All these mechanisms activate cholinergic fibres to both the parietal cells and the gastrin cells.

Atropine blocks the direct vagal stimulation of oxyntic cells and markedly inhibits the response to gastrin. Thus, vagotomy does not reduce the capacity of the stomach to secrete acid but takes away one of the stimulants required to fully activate the capacity. Antrectomy reduces the response to vagal stimulation. Antrectomy and vagotomy have additive effect on reducing the gastric acid secretion (Beeson, 1979).

McLoughin (1978) claimed that catecholamines play a part in recovery from hypoglycemia. He also demonstrated that the onset of vagal stimulation in hypoglycemia occurs later than that of sympathetic activity. He concluded that the vagus contains fibres both to enhance and inhibit gastrin release. The stimulation of gastrin release by the vagus may, therefore, be under the influence of adrenergic vagal fibres found in many species including man.

REVIEW OF LITERATURE

STRUCTURE OF THE GASTRIC MUCOSA

Based on the distribution of the gastric glands, the stomach can be divided into three regions :

1- Cardiac area : a zone of one to four centimeters wide of mucosal glands that guard the oesophageal orifice.

2- Fundic area (oxyntic glands area): it is the largest surface interposed between the cardiac and the pyloric areas. The lower limit of the fundic area is marked by the incisura angularis on the lesser curvature and a line extending diagonally towards the pylorus to the greater curvature.

3- Pyloric area : comprising 15 to 20 % of the total gastric mucosal area.

The Gastric Mucosa contains Three Types of Cells :

1- Main gastric glands : These constitute the main bulk of the gastric mucosa. Each gland consists of a short duct and a long alveolus. The alveolus contains chief or peptic cells which secrete pepsin, and less numerous ovoid oxyntic cells (parietal cells) which secrete HCl. The surface of the gastric mucosa consists of columnar cells which secrete mucus. This surface is

pitted by the openings of the gastric glands. Some 100 pits are found per cubic mm, each pit being formed by the openings of the ducts of several glands. Gastric HCl secretion is solely a property of the oxyntic cells in the mammalian stomach (Keel and Neil, 1971).

In addition to pepsinogen and HCl, the main gastric glands secrete a heat labile mucoprotein, the intrinsic factor which combines very firmly with dietary Vit.B_{12}.

2- Pyloric glands : They are present in the mucosa between the level of incisura angularis on the lesser curvature and the pylorus; and to a lesser extent on the greater curvature. These glands resemble the duodenal glands of Brunners in having long ducts and short alveoli. They secrete mucus rich alkaline viscid juice which is poor in enzyme content. The mucus is supposed to lubricate the surface over which a large volume of chyme moves back and forth during digestion. The pyloric glands elaborate the hormone gastrin (Bockus, 1974).

3- Cardiac tubular glands : Consisting of cells which secrete mucus are found in the gastric mucosa which immediately surrounds the oesophagus .