EVALUATION OF ANGIOTENSIN-II RECEPTOR ANTAGONIST (LOSARTAN) ON HEMODYNAMICS OF PORTAL CIRCULATION IN PATIENTS WITH CHRONIC LIVER DISEASES

Thesis
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بسم الله الرحمن الرحيم
وَأَنْزَلَ اللهُ
عَلَيْكَ الْكِتَابَ
والْحِكْمَةَ
وَعَلَّمَكَ مَا لَمْ
تَكُنْ تَعْلَمُ
وَكَانَ فَضْلُ
اللهِ عَلَيْكَ
عَظِيمًا
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List of Abbreviations

Abbrev.	Meaning
ALB	Albumin
ALT	Alanine transaminases
AST	Aspartate aminotransaminases
AT1	Angiotensin receptor type I
AT2	Angiotensin receptor type II
BUN	Blood urea nitrogen
CI	Congestive index
Creat	Creatinine
CSA	Cross sectional area
DBil	Direct bilirubin
DUL	Doppler ultrasonography
HAPI	Hepatic-artery pulsatility-index
HARI	Hepatic artery resistive index
Hb	Hemoglobin
HSC	Hepatic stellate cells
IHCT	Intrahepatic circulatory time
IUC	Inferior-vena cava
K	Potassium
LVI	Liver-vascular index
Na	Sodium
No	Nitric oxide
PHT	Portal hypertension
PI	Pulsatility index

List of Abbreviations

Abbrev.	Meaning
PV	Portal vein
PVV	Portal vein velocity
RAAS	Rennin-angiotensin aldosterone system
RAS	Rennin angiotensin system
RBCs	Red blood corpusles
RI	Resistive index
SBP	Spontaneous bacterial peritonitis
SV	Splenic vein
TBil	Total-bilirubin
TIPS	Transjugular intrahepatic portosystemic shunt
V mean	Portal vein velocity
WBCs	White blood corpusles

تقييم دور مناهضات مستقبلات انجيوتنسن II على ديناميكة الدورة البابية لمرضى الكبد المزمن

رسالة

توطئة للحصول على درجة الماجستير فى طب المناطق الحارة

مقدمة من الطبيب

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INTRODUCTION

Portal hypertension is responsible for the development of oesophageal varices and for the formation of ascites. Therefore establishing its presence is an important step in the management of patients with chronic liver disease, both when the disease is first diagnosed and during follow-up ***(Piscaglia et al., 2001).***

Medical treatment to prevent fist variceal bleeding must be considered as soon as varices are detected ***(Grace et al., 1998)*** because oosopahgeal bleeding is a life-threatening complication, with a mortality rate around 15-20% ***(Burroughs et al., 1989).***

Beta blockers and vasopressin are drugs with a portal hypotensive effect; they are used to treat portal hypertension. Plasma angiotensin II concentrations are elevated in cirrhosis and have been implicated as a cause of portal hypertension. It has been reported that angiogesnin Ii receptor antagonists, which were developed as antihypertensive agents, also have a portal hypotensive effect ***(Wagatsuma et al., 2006).***

The administration of losartan in a doses of 25 mg per day may be effective in lowering portal pressure in patients with compensated cirrhosis, particularly in those

with more severe portal hypertension ***(Hülagü et al., 2002 and Castaňo et al., 2003).***

But other studies showed that chronic administration of low-dose losartan does not lead to a significant reduction in the portal pressure gradient ***(Tripathi et al., 2004).***

Duplex Doppler sonography, is a suitable method for diagnosis of portal hypertension. It detects changes in portal flow velocity, portal vein diameter and impedance indices of hepatic and splenic arteries in portal hypertension ***(Bolognesi et al., 1996).***

Duplex Doppler sonography, is a suitable method for diagnosis of portal hypertension. It detects changes in portal flow velocity, portal vein diameter and impedance indices of hepatic and splenic arteries in portal hypertension ***(Bolognesi et al., 1996).***

AIM OF THE WORK

Assessment of the value of Losartan as angiotension II receptor antagonist on portal circulation by usage of Doppler ultrasononography in cirrhotic patients.

ANATOMICAL CONSIDERATIONS

Normal anatomy of portal venous system

Portal vein is formed by the union of superior mesenteric vein and the splenic vein just posterior to the head of pancreas at about the level of the second lumbar vertebra ***(Hegab and Luketic, 2001).*** It extends slightly to the right of the midline for a distance of 5.5-8 cm before entering the liver at the porta hepatis ***(Sherlock and Dooley, 2002)***.

The portal vein divides within the liver into right and left branches that serve the right and left lobes respectively ***(Boyer and Henderson, 2000)***. It is without valves in its larger channels and it has a segmental intra-hepatic distribution accompanying the hepatic artery ***(Sherlock and Dooley, 2002)***.

The portal venous blood (low pressured, low oxygenated, nutrient-riched blood) mixes with blood which come from the hepatic arteries (high pressured and well oxygenated blood), either in portal venules or in the sinusoids. The blood is collected from the sinusoids by the hepatic veins. The right and left hepatic veins enter the inferior vena cava separately just before it penetrates the diaphragm, while the caudate lobe may drain into the inferior vena cava via a separate hepatic vein. So portal venous system begins as capillaries of intestine and ends as

capillaries in the liver i.e. hepatic sinusoids ***(Boyer and Henderson, 2000)***.

The superior mesenteric vein is formed by tributaries from the small intestine, right colon and head of the pancreas and irregularly from the stomach via the right gastroepiploic vein. The splenic veins (5-15 channels) originate at the splenic hilum and join near the tail of pancreas with the short gastric vessels to form the main splenic vein, which proceeds in a transverse direction of the body and head of pancreas. The left gastro-epiploic vein joins the main splenic vein near the spleen. The inferior mesenteric vein, bringing blood from left part of the colon and rectum, usually enters its medial third. Occasionally, however, it enters the junction of superior mesenteric and splenic veins ***(Luketic and Sanyal, 2000).***

Additional contribution to the portal venous blood flow is provided by the left gastric (coronary) vein which drains the lesser gastric curvature to the proximal part of portal vein ***(Boyer and Henderson, 2000)***.

The venous drainage of the esophagus begins in a submucosal venous plexus. From this plexus, branches pass through the muscular walls to the surface of the esophagus to form a periesophageal plexus. The esophagogastric junction and abdominal portion of the esophagus drain into the right and left gastric veins, which normally form the coronary vein, and into short gastric vein which drain into splenic vein.

When portal hypertension exists, or when there is thrombosis of the splenic vein, backflow through the coronary vein and short gastric veins into the lower esophageal branches occurs, causing dilation and producing varices ***(Pelot, 1995).***

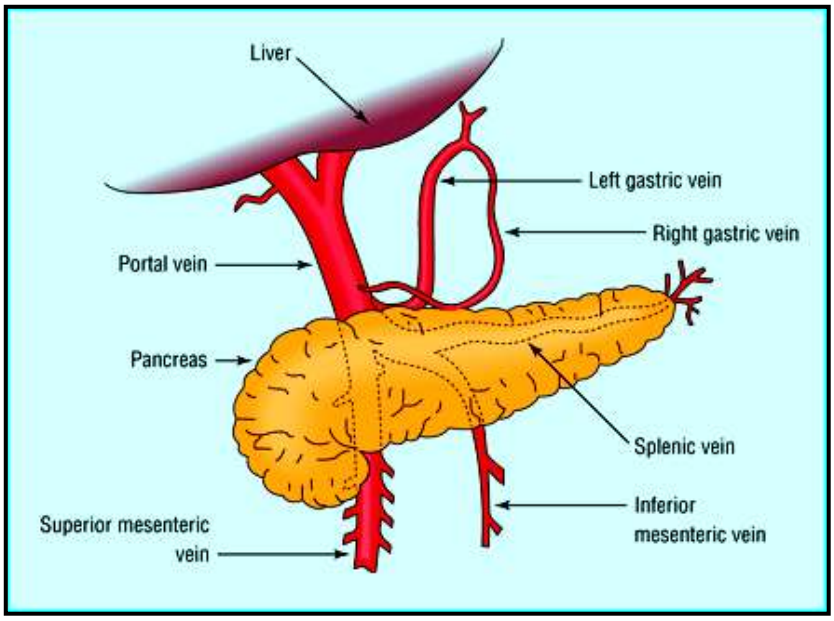

Figure (1): Anatomy of portal venous system
(Krige and Beckingham, 2001)

The portal system includes all veins that carry blood from the abdominal part of the alimentary tract (with the exception of the lower part of the rectum), and from the spleen, pancreas and gallbladder ***(Sherlock and Dooley, 2002).***

Hepatic blood flow is normally about 1500 ml/minute, representing 15-20% of cardiac output, one third of this flow is provided by the hepatic artery and two