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A prospective study of the pathogenesis and the management of portal hypertension

ESSAY

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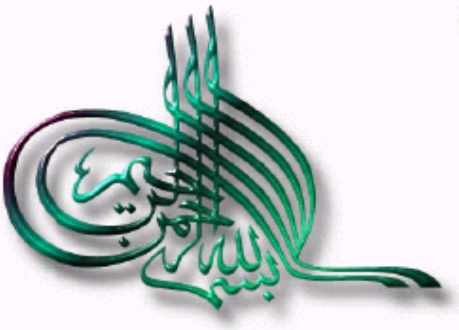

قالوا سبحانك لا علم لنا إلا ما

علمتنا إنك أنت العليم الحكيم

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LIST OF ABBREVIATIONS

[Ca21]i	Intracellular calcium
AASLD	American Association for the Study of Liver Diseases
ACE	Angiotensin converting enzyme
Ad5LacZ	Control adenovirus (lack the pro-human MMP-1 DNA)
Ad5MMP-1	Adenovirus infected with pro-human matrix metalloproteinase-1 complementary DNA
AST	Aspartate aminotransferase
A–V shunts	Arterio-venous shunts
AzBF	Azygos blood flow
BCS	Budd-Chiari syndrome
BH4	Tetrahydrobiopterin
B-RTO	Balloon occluded retrograde transvenous obliteration
cAMP	Cyclic adenosine monophosphate
CB1 and CB2	Cannabinoid receptors
CD-EUS	Color Doppler endoscopic ultrasound
cGMP	Cyclic guanosin mono phosphate
CGRP	Calcitonin gene related protein
CLD	Chronic liver disease
CO	Carbon monoxide
COX	Cyclooxygenase enzyme
CSPH	Clinically significant portal hypertension
CT	Computed tomography
CTGF	Connective tissue growth factor
CYP2E1	Cytochrome P450 2E1
DDUS	Duplex doppler ultrasound
ECM	Extracellular matrix
EGD	Esophago-gastro-duodenoscopy
EGF	Epidermal growth factors
EIS	Endoscopic injection sclerotherapy
EMT	Epithelial mesenchymal transition
ET-1	Endothelin-1
EUS	Endoscopic ultrasound
EVL	Endoscopic variceal ligation
Fas/FasL	Apoptotic mediators

FGF	Fibroblast growth factor
FHVP	Free hepatic venous pressure
FXR	Farnesoid X receptor
GEV	Gastro-esophageal varices
GPCR	G-protein-coupled receptors
GPCR	G-protein-coupled receptors
GRK-2	G-protein-coupled receptor kinase 2
H2S	Hydrogen sulfide
HCV	Hepatitis C virus
HE	hepatic encephalopathy
HGF	Hepatocyte growth factor
HMGCO	Hydroxymethyl glutaryl coenzyme A
HO	Heme oxygenase
HRS	Hepatorenal syndrome
HSC	Hepatic stellate cells
HVPG	Hepatic venous pressure gradient
IHVR	Intra-hepatic vascular resistance
IL	Interleukin
INR	International normalized ratio
IP3	Inositol triphosphate
IV	Intravenous
IVC	Inferior vena cava
JNKs	c-jun N-terminal kinases
LPS	Lipopolysaccharide
LVP	Large volume paracentesis
MAPK	Mitogen activated protein kinase
MCP-1	Monocyte chemo-attractant protein 1
MCP-1	Monocyte chemo-attractant protein 1
MCTE	Multidetector computer tomographic esophagography
MDA	Malondialdehyde
MELD	Model of end stage liver disease
MLC	Myosin light chain
MMP	Matrix-metalloproteinases
MRI	Magnetic resonance imaging
mRNA	Messenger RNA
NK	Natural killer

NO	Nitric oxide
NOS	Nitric Oxide Synthetase
NPY	neuropeptide Y
OLT	Orthotopic liver transplant
para-GCV	Para gastric collateral veins
para-OCVs	Para-esophageal collateral veins
PDGF	Platelet derived growth factor
PGI2	Prostaglandin I 2
PHG	Portal hypertensive gastropathy
PHT	Portal hypertension
PLCβ	Phospholipase C β
PlGF	Placental growth factor
PPAR-γ	peroxisome proliferators activated receptors gamma
PTFE	Polytetrafluoroethylene
PTVE	Percutaneous trans-hepatic embolization of varices
PVT	Portal vein thrombosis
Rho	A small, monomeric guanosine triphosphate–binding protein from the ras super family
ROS	Reactive oxygen species
RTUS	Real time ultrasound
SAAG	Serum to ascites albumin gradient
SBP	Spontaneous bacterial peritonitis
SEC	Sinusoidal endothelial cells
SHP	Small heterodimer partner
SOD	Super oxide dysmutase
TGF	Transforming growth factor
TGF-β	Transforming growth factor beta
Th1	T-lymphocyte helper cell type 1
TIMP	Tissue inhibitors of metalloproteinase
TIPS	Transjugular intrahepatic porto-systemic stent shunts
TNFα	Tumor necrosis factor alpha
TRAIL	Tumor necrosis factor-related apoptosis-inducing ligand
TXA2	Thromboxane A2
TXA2	Thromboxane A2
US	ultrasound
VEGF	Vascular endothelial cell growth factor

VEGFR	VEGF receptor
VEGFR2	Vascular endothelial growth factor receptor 2
Vs.	Versus
WHVP	Wedged hepatic venous pressure
α-SMA	Alpha smooth muscle actin

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INTRODUCTION AND AIM OF WORK

Introduction and Aim of the Work

Introduction:

Portal hypertension (PHT) is a common clinical syndrome consequence of almost all chronic liver diseases. It is defined as the pathologic increase of portal pressure, in which the gradient between portal vein and the inferior vena caval pressure is increased above the upper normal limit of 5 mmHg ***(Sanyal et al., 2008).***

The importance of this syndrome is defined by the frequency and severity of its complications (Porto-systemic collaterals, variceal hemorrhage, ascites, hepato-renal syndrome, porto-systemic encephalopathy and hepato-pulmonary syndrome) with the rupture of esophageal varices representing the main and most lethal complications. The appearance of these complications defines the progression from compensated to decompensated liver disease ***(D'Amico and de Franchis, 2003).***

PHT is initiated by increased hepatic outflow resistance as a result of chronic activation of hepatic stellate cells (HSC) and the mediator action on it. An increase in the portal blood inflow occurs as a result of the increasing vascular tone, expanded plasma volume and splanchnic vasodilatation in response to many mediators. This maintains and aggravates portal hypertension ***(Cichoz-Lach et al., 2008).***

The most common world wide cause of PHT is cirrhosis due either to alcoholic hepatitis, in western countries, or due to post hepatitic cirrhosis

specially due to HCV in developing countries like Egypt. While bilharzial periportal fibrosis represents another important cause in Egypt ***(Gryseels et al., 2006).***

Morbidity and mortality associated with these treatment strategies are still high, which should direct our attention for developing mew screening methods and diagnostic tools, specially the non invasive of them, for early detection of the disease. Also, to find out new, effective therapeutic modalities that can have better outcome when implied early in the course of the disease ***(D'Amico and de Franchis, 2003, Bosch et al., 2010 and Thabut and Shah, 2010).***

Current treatment modalities for PHT rely on decreasing portal blood inflow to reduce the elevated portal venous pressure ***(D'Amico et al., 1999).*** While future therapy for portal hypertension is expected to be more causal in nature as it should be able to stop the progression of, or even revert, the original liver disease like fibrosis and hepatic stellate cell (HSC) activation as well as interfering with any other pathologic state that can maintain or aggravate PHT like angiogenesis and the state of endothelial dysfunction ***(Bosch et al., 2010 and Thabut and Shah, 2010).*** This prospective therapy seems promising, offering portal hypertensive patients more hope about the possibility of better treatment in the future.