Changes in Blood Sugar Level in Relation to the Degree of Liver Cell Failure and development of Hepatocellular Carcinoma in Cirrhotic patients

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بسم الله الرحمن الرحيم

(قَالُوا سُبْحَانَكَ لَا عِلْمَ
لَنَا إِلَّا مَا عَلَّمْتَنَا إِنَّكَ
أَنْتَ الْعَلِيمُ الْحَكِيمُ)

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Khaled Mohamed Mamdouh

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LIST OF ABBREVIATION

HCC	hepatocellularcarcinoma
HGP	hepatic glucose production
PEPCK	phosphoenol pyruvate carboxykinase
G-6Pase	glucose-6 phosphatase
FP2ase	fructose-1 6 biphosphatase
PEP	phosphoenol pyruvate
G6P	glucose 6 phosphate
MIRKO	muscle specific insulin receptor knock out
LIRKO	liver specific insulin receptor knock out
GK	gluco-kinase
ACC	acetyle-co-A carboxylase
FAS	fatty acid synthase
PI3K	phosphatidyle inositol 3-kinase
IGT	impaired glucose tolerance
NALFD	non alcoholic fatty liver disease
IGF-I	insulin like growthfactor I
GH	growth hormone
GH-IGF-I	growth hormone insulin like growth factor I

TNF	tumor necrosis factor
IL	interleukin
AKT	serine-threonin protein kinase
Tyr-k	tyrosine kinase
PKC	protein kinase c
ECM	extra cellular matrix
HCV	hepatitis C virus
HBV	hepatitis B virus
HbsAg	hepatitis B surface antigen
DM	diabetes mellitus
OGTT	oral glucose tolerance test
CHC	chronic hepatitis C
MELD sco	models for end stage liver disease
ALT	alanine transaminase
AST	aspartate transaminase
--FP	alpha-foeto protein
FBS	fasting blood sugar
PPBS	post prandial blood sugar
S.alb	serum albumin
LFT	liver function tests
KFT	kidney function tests

PT	prothrombine time
HOMA-IR	Homeostasis model assessment for insulin resistanc
BMI	Body mass index
IR	insulin resistance
IRE	insulin responce element
IRS1	insulin receptor substrate 1
NASH	non alcoholic steatohepatitis
PKA	protein kinase A
ChoRE	carbohydrate responce element
ChREBP	carbohydrate responce element binding protein
SRE	sterol regulatory element
SREBP	sterol responce element binding protein
TIPS	Trans-jugular intra hepatic porto-systemic shunting
AASLD	American association for study of liver diseases.
IFG	Impaired fasting glucose.
HSC	Hepatic stellate cells.
NMR	Nuclear magnetic resonance.

Contents

Introduction

Hepatitis C is a major cause of liver related morbidity and mortality worldwide and represents a major public health problem ***(Alberti and Benvegnu, 2003).*** The World Health Organization has detected hepatitis C virus aglobal health problem with approximately 3% of the world population(rougly 170-200 million people) infected with HCV **(Mohamed,2004)**

The prevalence of HCV infection in Egyptians is the highest worldwide. Many reports showed high rates of HCV seropositivity among Egyptian blood donors (9.7-24.8%) ***(Saeed et al., 1991; Kamel et al., 1992 ; Darwish et al., 1993 and El-Zayadi et al., 2001)***, as well as patients with chronic liver disease (67%) ***(El-Zayadi et al., 1992; Fathalla, 1992; and Mohamed et al., 1996).*** Most cases of HCV-related HCC occur in the setting of cirrhosis which generally occurs after at least one decade of infection ***(Di Bisceglie, 1999).***

The liver plays a central role in control of the serum blood sugar by balancing the uptake and storage of glucose via glycogenesis and the release of glucose both from hepatic glycogen stores via glycogenolysis and de novo through gluconeogenesis ***(Nurdlie et al., 1999).***

Glucose intolerance is well known to be frequently present in patients with chronic liver diseases, especially cirrhosis. It has been documented that 60-80% of cirrhotic patients have glucose intolerance and 10-30% eventually develop overt Diabetes mellitus when their impaired insulin secretion cannot meet the increased demand for insulin due to insulin resistance ***(Aoki et al., 2000).***

Hypoglycemia is found in 30% of patient with HCC because of malnutrition and a decrease of gluconeogenesis in the liver ***(Margolis & Homcy, 1972)***. Another explanation is that hypoglycemia may be due to increase demand for glucose by an enormous tumour mass and so is often associated with an undifferentiated, rapidly progressive tumour ***(Sherlock and Dolley, 2002).*** In patients with severe recurrent hypoglycemia, the tumour tissue contains 10-20 folds more high molecular weight insulin like growth factor II than normal liver and this might mediate the hypoglycemia ***(Shapiro et al., 1990).***