Insulin Resistance in Chronic Hepatitis B virus infection

Thesis

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in Internal Medicine

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Summary

This study was carried out in the department of internal medicine, Ain Shams University hospital.

50 subjects were included and were divided into two groups: Group (A) 35 patients with chronic hepatitis B virus infection and Group (B) 15 healthy volunteers.

The aim of this study was to determine whether insulin resistance occurs in patients with chronic hepatitis B virus infection.

HOMA insulin resistance index was found to be within normal range among chronic HBV infected patients, and all variables (except serum ALT level) were comparable between patients and control group.

Insignificant differences were found between average weight and overweight chronic HBV infected patients as regards all parameters exploring insulin resistance.

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List of Abbreviations

α1 ATD	: α1 antitrypsin deficiency
αFP	: Alpha fetoprotein
Akt	: Alpha serine/threonine protein kinase
ALT	: Alanine transaminase
AMP	: Adenosine mono phosphate
AST	: Aspartate transaminase
BMI	: Body mass index
BUN	: Blood urea nitrogen
cccDNA	: Covalently closed circular DNA
CD	: Cluster of differentiation
CHB	: Chronic hepatitis B
CHC	: Chronic hepatitis C
CK	: Cretinine kinase
CLD	: Chronic liver disease
DCs	: Dendritic cells
DM	: Diabetes Mellitus
DPP-4	: Dipeptidyl peptidase-4
ELISA	: Enzyme linked immune sorbant assay
FFA	: Free fatty acids
FSIVGTT	: Frequently sampled IV glucose tolerance test
HAI	: Histologic activity index
HAV	: Hepatitis A virus
HBc Ab	: Hepatitis B core antibody
HBe Ab	: Hepatitis B envelope antibody
HBe Ag	: Hepatitis B envelope antigen
HBV	: Hepatitis B virus
HBVsAb	: Hepatitis B surface antibody

HBVsAg : Hepatitis B surface antigen
HBX : Hepatitis B virus X protein
HCC : Hepatocellular carcinoma
HCV : Hepatitis C virus
HCVAb : Anti hepatitis C virus antibody
HDV : Hepatitis D virus
HIV : Human immunodeficiency virus
HOMA-IR : Homeostasis Model assessment
IFNs : Interferons
IL : Interleukin
INR : International normalization ratio
IR : Insulin resistance
IRS : Insulin receptor substrates
MHC : Major histocompatibility complex
mRNA : Messenger RNA
MS : Metabolic syndrome
NAFLD : Non alcoholic fatty liver disease
NAs : Nucleoside or nucleotide analogs
NASH : Non Alcholic Steato Heptitis
NFKB : Nuclear Factor-KappaB
NK : Natural killer cells
OGTT : Oral glucose tolerance test
ORF : Open reading frame
OS : Oxidative stress
PBC : Primary biliary cirrhosis
PCR : Polymerase Chain Reaction
PEG : Polyethylene glycol
PI3K : Phosphatidylinositol- 3-kinase
PPARγ : Peroxisome proliferator activated receptor gamma
PSC : Primary sclerosing cholangitis

PT : Prothrombin time
SOCS3 : Suppressor of cytokine signaling-3 gene
T2DM : Type 2 diabetes mellitus
TGF-β1 : Transforming growth factor-beta 1
Th17 : T helper 17
TNF : Tumor necrosis factor
ULN : Upper Limit of Normal
USFDA : United States Food and Drug Administration
WBISI : Whole-body insulin sensitivity index

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Amira Isaac

Introduction

Incidence of diabetes mellitus in adults with chronic hepatitis B virus infection is four times higher than that in the general population (22.5%) ***(Custro et al., 2001).***

Prospective studies have shown that insulin resistance precedes the onset of diabetes by 10-20 years; also the presence of diabetes may be associated with increased rate of progression of fibrosis in patients with chronic hepatitis C and chronic hepatitis B virus infection ***(Hui et al., 2003).***

Patients with chronic hepatitis have impaired glucose metabolism with hyperinsulinemia and insulin resistance, this hyperinsulinemia has been shown to be due to decreased insulin catabolism rather than increased pancreatic insulin secretion ***(Greco et al., 2002).***

Persico et al. (2009) reported higher prevalence of metabolic syndrome and diabetes mellitus in patients with hepatitis C virus than in patients with hepatitis B virus related chronic liver disease.

Recent years have seen numerous studies devoted to the relationship between chronic hepatitis C virus infection and insulin resistance. However no sufficient data are available for the relationship between chronic hepatitis B virus infection and insulin resistance.

Aim of the work

The aim of this study is to determine whether insulin resistance occurs in patients with chronic hepatitis B virus infection.

Hepatitis B Virus Infection

Hepatitis B virus (HBV) infection is highly prevalent worldwide and is a major cause of morbidity and death. Two billion people globally have been infected with HBV, 350 to 400 million are chronic carriers, and tens of millions of new cases occur annually ***(Carey, 2009).***

Some individuals can develop acute HBV infection and achieve complete immune clearance of virus, yielding a life-long immunity, while others can develop chronic HBV infection depending on the host immune response. Chronic HBV infection is associated with a wide range of clinical manifestations, from an asymptomatic carrier state with a normal liver histology to severe and chronic liver diseases, including cirrhosis and hepatocellular carcinoma ***(McMahon, 2005).***

Geographic Distribution of Chronic HBV Infection:

The global prevalence of HBV varies widely. Regions are divided into areas of low, intermediate, and high prevalence, defined as follows:

High prevalence implies that at least 8% of the population is currently infected. About 45% of the world's population lives in regions of high prevalence. Among this group, early childhood infections are common, with the virus usually transmitted from mother to infant during the perinatal period. These regions include South East Asia, China, the Amazon area, and sub-Saharan Africa ***(Heathcote et al., 2008).***