The Incidence Of Occult Hepatitis B Among HCV Chronic Patients (Responders and Non-responders) Receiving Combined Therapy

Thesis

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AIM OF THE WORK

1. Determine the incidence of occult HBV DNA with absent HBsAg among chronic HCV patients receiving combination therapy.
2. Relation to response to treatment will be studied.

Contents

List of Abbreviations

α-INF	Alpha interferon
µg	Microgram
µmol/L	Micro mill mol
AA	Amino acids
AASLD	American Association for Study of Liver Diseases
ALP	Alkaline phosphates
ALT	Alanine aminotransferase
Anti-HBc	Hepatitis B core antibody
Anti-HBe	Hepatitis B e antibody
Anti-HBs	Hepatitis B surface antibody
Anti-HCV	Antibodies against hepatitis C virus
AST	Aspartate aminotransferase
BMI	Body mass index
cccDNA	Covalently closed circular DNA
CTLs	Cytotoxic T lymphocytes
DNA	Deoxyribonucleic acid
ELISA	Enzyme linked immunosorbant assay
EVR	Early virological response
g/dl	Gram per deciliter
HBcAg	Hepatitis B core antigen
HBeAg	Hepatitis e antigen
HBIG	Hepatitis B Immune Globulin
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HDV	Hepatitis Delta virus
HLA	Human leukocyte antigen
HS	Highly significant
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IU/ml	International unit per milliliter

Kd	Kilo Dalton
Kg	Kilogram
LCF	Liver cell failure
mg/dL	Milligram per deciliter
MIU	Million international unit
Ml	Milliliter
ng	Nanogram
NK	Natural killer
NS	Non significant
OAS	oligo-adenylate synthetase
PBMCs	periphral blood mononuclear cells
PC	Prothrombin concentration
PCR	Polymerase chain reaction
PEG	Polyethylene glycol
Pg	Pico gram
QN	Quantitative
RNA	Ribonucleic acid
S	Significant
SC	Subcutaneous
SD	Standard deviation
STD	Sexually transmitted diseases
SVR	Sustained virological response
T3	triiodothyronine
T4	thyroxine
TP	Total proteins
TSH	Thyroid stimulating hormone
WHO	World Health Organization
β	Beta

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INTRODUCTION

Hepatitis B & C are the most common causes of chronic liver disease world wide. Acute infection with hepatitis B virus (HBV) or hepatitis C virus (HCV) may result in chronic infection. Co-infection of both viruses can occur because of shared routes of infection e.g. blood Transfusion, hemodialysis or organ Transplant ***(Crockett and Keeffe, 2005)***.

Hepatitis B virus infections in patients who lack detectable hepatitis B surface Ag (HBsAg) with or without serologic markers of previous infection (HBsAb or hepatitis B core Ab) are called occult infection. Lack of circulating HBsAg in such patients are unknown but recent observation have suggested that the lack of HBsAg may be due to rearrangement of HBV genome that interfere with gene expression or lead to production of an antigenically modified S protein. Occult HBV infection has been frequently identified in patients with HCV related chronic hepatitis; considerable data suggests that this occult infection may contribute to chronic liver damage, development of hepatocellular carcinoma and diminished response to interferon. ***(Cacciola et al., 1999)***.

Detection of occult HBV infection is done by detection of HBV DNA through PCR in serum or liver biopsy, since viral DNA levels in occult HBV are very low, the identification of occult HBV is strongly dependant on specificity and sensitivity of the assay ***(Torbenson and Thomas, 2002)***.

In patients chronically infected with HCV, combination therapy with ribavirin plus alpha 2 interferon has greatly

improved the rate of sustained biochemical and virological response compared to those achieve with interferon monotherapy ***(Larrat et al., 2003)***.

The clinical significance of occult hepatitis B alone or in combination with HCV infection remains unsettled, previous epidemiologic and molecular studies have indicated that persistence of HBV infection may be associated with the development of HCC in HBsAg negative patients ***(Kao et al., 2002)***.

CHAPTER I
THERAPY OF CHRONIC HEPATITIS C

Introduction

Hepatitis due to hepatitis C virus (HCV) infection is an important public health problem worldwide ***(Andreone et al., 1999)***. HCV causes hepatitis, cirrhosis, and hepatocellular carcinoma (HCC), and globally reported anti-HCV prevalence ranges between 1% and 3% ***(Leung, 2002)***. Its prevalence varies from 0.01% in United Kingdom to 17%-20% in Egypt ***(Abdel-Wahab et al., 1994)***.

Despite the introduction of laboratory tests to screen national blood supplies, HCV remains the most common cause of post-transfusion hepatitis worldwide because unscreened blood and blood products are still used in many developing countries or economies in transition ***(Kim, 2002)***.

The WHO has estimated that 170 million people worldwide are infected with hepatitis C virus (HCV). Reports indicate that the prevalence rates for anti-HCV ranges from 0.5–1% in low prevalence areas such as North America to >20% in high prevalence areas such as Egypt ***(World Health Organization, 1999)***. Acute infection with HCV is followed by chronic infection in 80% of cases with increased risk for liver cirrhosis and hepatocellular carcinoma ***(Liang et al., 2000)***.

HCV genotype differences are of considerable clinical significance because they affect responses to antiviral therapy. Genotype 4 predominates throughout the Middle East and parts of Africa ***(Abdel-Aziz et al., 2000)***, often in association with high population prevalence as in Egypt ***(Habib et al., 2001)***,