STUDY OF THE PREVELANCE OF URTICARIA IN CHRONIC RENAL DIALYSIS EGYPTIAN PATIENTS WITH HCV INFECTION

Thesis

Submitted for Partial Fulfillment of Master Degree in Internal Medicine

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2012

دراسة معدل انتشار الأرتيكاريا في مرضى الاستصفاء الدموي المزمن المصابين بالألتهاب الكبدي الوبائي سي بمصر

رساله

توطئة للحصول على درجة الماجستير في طب الأمراض الباطنيه

مقدمة من

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بكالوريوس الطب والجراحة جامعة عين شمس ٢٠٠٤

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INTRODUCTION

Hepatitis C virus (HCV) is a major health problem; it is the main cause of transfusion-associated hepatitis and is also seen in intravenous drug abuse, organ transplant and hemodialysis patients, and health care workers ***(Neil et al., 2003).***

In addition to hepatitis, cirrhosis and hepatocellular carcinoma (HCC), several extrahepatic manifestations (EHM) have been reported in the natural history of HCV infection. According to different studies, 40-74% of patients infected with HCV might develop at least one EHM during the course of the disease ***(Galossi et al., 2007).***

A significant proportion of these extrahepatic manifestations (EHM) disorders involve the skin (***Davis et al., 2003).*** Various cutaneous eruptions have been described in the setting of HCV infection ***(Neil et al., 2003).***

Urticaria is a common disorder that affects up to 20% of the population at some point during their lifetime. Aggravating factors include drugs, foods, additives, connective tissue disorders and infections. It is well established that Hepatitis B virus causes urticaria. Whether Hepatitis C infection causes urticaria or not is still debated with reports both in favor of and against this **(*Siddique et al., 2004).***

AIM OF THE WORK

To analyze the frequency of urticaria in chronic renal dialysis Egyptian patients with HCV infection.

LIST OF ABBREVIATIONS

AASLD	American Association for the Study of Liver Diseases
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
CDC	Center of Disease Control
CDNA	Complementary DNA
CG	Cryoglobulinemia
CI	Confidence Interval
CKD	Chronic kidney disease
CLD	Chronic liver disease
DNA	Deoxyribonucleic acid
EDHS	Egyptian Demographic Health Survey
EIA	Enzymatic immune assay
EHM	Extra hepatic manifestations
ERBP	European Renal Best Practice Guidelines
ESRD	End stage renal disease
ETR	End of treatment response
EVR	Early viral response
FDA	Food and Drug Administration
GFR	Glomerular filtration rate
GN	Glomerulonephritis
HAI	History activity index
HAV	Hepatitis A virus
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma

HCM	Hypertrophic cardiomyopathy
HCV	Hepatitis C virus
HCVcAg	Hepatitis C core antigen
HD	Hemodialysis
HIV	Human immune deficiency virus
HTLV	Human T-lymphotropic virus
IDE	Integrated development environment
IDSA	Infectious Disease Society of America
IFN	Interferon
Ig	Immunoglobulin
IR	Insulin resistance
IRES	Internal ribosome entry site
IVDU	Intra venous drug users
KDIGO	Kidney disease improving global outcome
KDOQI	Kidney disease outcomes quality initiative
LHF	Lassa haemorrhagic fever
MENA	Middle East North Africa
MHD	Maintenance hemodialysis
MICS	Malnutrition inflammation cachexia syndrome
MIEC	Medanta independent ethics committee
MPGN	Membrano proliferative glomerulonephritis
MPGN	Mesangio proliferative glomerulo nephritis
MU	Million units
NANB	Non- A Non – B
NAT	Nucleic acid testing
NHANES	National Health and Nutrition Examination Survey

NHL	Non-Hodgkin lymphoma
NSAID	Non steroid anti- inflammatory drugs
OR	Odd ratio
PAT	Parentral antischistosomal therapy
PBMC	Peripheral blood monocytes
PBMC	Periphral blood mononuclear cell
PCR	Polymerase chain reaction
PCT	Porphyria cutanea tarda
PD	Peritoneal Dialysis
PN	Peripheral neuropathy
RA	Rheumatoid arthritis
RBV	Ribavirin
RdRp	RNA dependant RNA polymerase
RF	Rheumatoid Factor
RIBA	Reverse immuno- blot assay
RNA	Ribonucleic acid
RR	Relative risk
RRT	Renal replacement therapy
RT-PCR	Reverse transcriptase polymerase chain reaction
RVR	Rapid virological response
SLE	Systemic lupus eryromatosus
SOC	Standard of care
SPT	Skin prick test
SS	Sjogren's syndrome
SVR	Sustained viral response
TIPSS	Transjugular intrahepatic portosystemic shunt

TMA	Transcription mediated amplification
USPHS	United States Public Health Service
UTR	Untranslated region

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HEPATITIS C VIRUS (HCV)

Definition

HCV, first identified in 1989, is strictly a blood-borne RNA viral infection in the family Flaviviridae. Humans are the only reservoir for this viral infection. HCV infection most often leads to an asymptomatic chronic state, which can later progress to active liver disease, liver failure, or primary hepatocellular carcinoma. Treatment of HCV is costly, beyond the reach of most patients in less-developed countries, requires 48 or more weeks to complete, and has serious adverse effects and low efficiency. HCV in a family member can be socially and economically detrimental ***(Millera and Abu Rhaddad, 2010).***

Egypt reports the highest prevalence of HCV worldwide, ranging from 11% to more than 14% among regions and demographic groups. In the U.S., the number of new cases of infection with HCV has declined over the last 10 years from a peak of some 200,000 annually to about 19,000 in 2006. Up to 85% of newly infected people fail to clear the virus and become chronically infected. In the U.S., more than three million people are chronically infected with HCV. Infection is most common among people who are 40 to 60 years of age, reflecting the high rates of infection in the 1970s and 1980s. There are 8,000 to 10,000 deaths each year in the U.S. related to HCV. HCV is the leading cause of liver transplantation in the U.S and is a risk factor for liver cancer ***(Dubuisson, 2007)***

HCV is a small single-stranded RNA virus with a lipid envelope (E) containing glycoproteins (E1 and E2) and a core with a genome consisting of 9500 nucleotides. HCV components are both structural (core, E1, and E2) and nonstructural (NS; P7, NS2, NS3, NS4A, NS4B, NS5A, and NS5B). The nonstructural genes encode various enzymes including a polymerase responsible for replication of HCV ***(KDIGO Guidelines, 2008).***

The structural proteins include the core (C), which forms the viral nucleocapsid, and the envelope glycoproteins E1 and E2. They are released by host-cell signal peptidases. The structural proteins are separated from the nonstructural proteins by the short membrane peptide p7, thought to be a viroporin. The nonstructural (NS) proteins NS2 to NS5B are involved in polyprotein processing and viral replication. The proteolytic processing of NS polyprotein part is complex and requires two distinct proteinases: the NS2- NS3 zinc-dependent metalloproteinase, and the NS3 serine proteinase located in the N-terminal region of NS3. The NS2-NS3 proteinase appears to be dedicated solely to cleavage at the NS2/NS3 site that occurs rapidly and by a conformation-dependent, autocatalytic mechanism ***(Penin et al., 2004).***

The remaining NS proteins are released by the NS3 proteinase associated with its cofactor, NS4A. The C-terminal region of NS3 protein includes RNA helicase and NTPase activities. NS4B is an integral membrane protein of unknown function. NS5A is a polyphosphorylated protein of unknown function, and NS5B is the RNA-dependent RNA polymerase

(RdRp). The existence of one or more previously unknown HCV proteins potentially synthesized by ribosomal frame shift has been suggested recently ***(Choi et al., 2003).***

Although this basic structure is common to all hepatitis C viruses, there are at least six distinctly different strains of the virus which have different genetic profiles (genotypes). In Egypt genotype 4 is the most common form of HCV. In the U.S., genotype 1 is the most common form of HCV. Even within a single genotype there may be some variations (genotype 1a and 1b, for example). Genotyping is important to guide treatment because some viral genotypes respond better to therapy than others. The genetic diversity of HCV is one reason that it has been difficult to develop an effective vaccine since the vaccine must generate viral proteins from each genotype ***(Dev et al., 2002).***

HCV Prevalence in Egypt

The highest HCV prevalence in the world occurs in Egypt, where the prevalence of infection increases steadily with age, and high rates of infection are observed among persons in all age groups ***(Perz et al., 2006).*** This pattern indicates an increased risk in the distant past followed by an ongoing high risk for acquiring HCV infection, although there are regional differences in average overall prevalence ***(Medhat et al., 2002).***

In 1992, when HCV antibody testing became widely available, the prevalence of HCV in Egypt was reported to be 10.8% among first-time blood donors ***(Millera and Abu Raddad, 2010)***. Since this discovery, many prevalence estimates of HCV