Study of Anaemia & Thrombocytopenia in adult Egyptian patients with HCV infection treated with Interferon & Ribavirin in relation to virological response

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List of Abbreviations

AFP……ALPHA-FETOPROTEIN

ALT……ALANINE AMINOTRANSFERASE

ANC……ABSOLUTE NEUTROPHIL COUNT

AST……ASPARTATE AMINOTRANSFERASE

BMI…..BODY MASS INDEX

DNA…..DEOXY RIBONUCLEIC ACID

ECG……ELECTRO-CARDIOGRAPHY

ELISA ……ENZYME LINKED IMMUNOSORBANT ASSAY

HAI……..HISTOLOGICAL ACTIVITY INDEXGENERAL HEALTH

HBV……HEPATITIS B VIRUS

HCC…….. HEPATOCELLULAR CARCINOMA

HCV……..…..HEPATITIS C VIRUS

INF…….…. INTERFERON

IVDU…… ... INTRAVENOUS DRUG USER

LC…… …. ... ……. ….. ……..LIVER CIRRHOSIS

PRE TTT……PRE-TREATMENT

RNA…… …… ... RIBONUECLIEC ACID

US…… …….. ULTRASOUND

WHO ……..…..WORLD HEALTH ORGANIZATION

Abstract

Background: Egypt is a country that has one of the world's highest hepatitis burdens. It is estimated that 10% of the population between 15 and 59 years is chronically infected with hepatitis C. Peg-Interferon and Ribavirin (combined therapy) used for treatment of HCV infected patients for 48 months that cause anaemia ,thrombocytopenia and neutropenia as documented by many studies.

Aim of work: The aim of this study is to assess the predictive value of hematological toxicity mainly thrombocytopenia in adult Egyptian patients with HCV treated by Peg-interferon and ribavirin in relation to virological response

Patients and methods: This Cohort study will include 204 patients infected with HCV and treated by Peg-Interferon and Ribavirin who developed hematological toxicity during treatment.

Result: There is significant reduction in hemoglobin (HB%) level, platelet (Plt)count and Leucocytic (WBC)count during 48weeks of treatment and after finishing the treatment course, the drop of Hemoglobin(HB%)level and Platelet(Plt)count stop but didn't reach the baseline level, but the level of neutrophils count did not show any improvement.

Conclusion: Anemia and thrombocytopenia are the most common side effects of treatment with pegylated interferon and ribavirin with incidence about 23-25%. Anemia is mainly due to hemolysis of RBCs as a result of ribavirin intake, and also interferon shared by minimizing the correction of anemia by suppression of the bone marrow, Thrombocytopenia caused by bone marrow suppression and there is no correlation between PCR results and severity of complications.

Key Words: (HCV) hepatitis c virus, (HB%) hemoglobin, (Plt) Platelet, (WBC) White blood count, Peg-Interferon and Ribavirin.

Chapter 1

HCV

1.1- Introduction

Hepatitis C virus (HCV) infection is the leading cause of chronic liver disease including cirrhosis and hepatocellular carcinoma (HCC), It is also the most common reason for liver transplantation in the Western World.

The actual estimated incidence is 1-3 per 100,000 person per year, which is markedly decreased in the last decades .This fact is attributable to the identification of the virus in the late ’80 of the past century, which has allowed the development of a correct transfusion’s screening policy thus permitting a dramatically decrease of the onset of new infections ***(Lawson A, Hagan S, et al.2007)***

1.2- REVALENCE AND INCIDENCE

Hepatitis C is an infectious disease caused by the hepatitis C virus (HCV). There is a global epidemic of hepatitis C, with approximately 185 million people estimated to be infected in 2005 (***WHO guidelines for screening of HCV 2014***) and 350 000–500 000 deaths estimated annually. Over 80% of those affected by the disease live in low- and middle-income countries, especially in central, north and west Africa. (***Graham CS&SwanTA,2014***) Several middle-income countries such as Egypt, Nigeria and Pakistan have a high burden of hepatitis C. (***Gower E,EstesC,et al 2014)***

The epidemiology of HCV transmission in Egypt has been the subject of intense study in the two decades since HCV diagnostic assays became available. Recent study shows that the prevalence rate of HCV infection in north Africa and middle east is 3.6% of the population (>15milion people) , the highest prevalence rate is in Central Asia 3.8 %(>50 million) of the population.(***Mohamed HanafiahK,GoergerJ,et al 2013***)

It is generally accepted that the high prevalence of HCV infection is in part attributed to parenteral anti-schistosomal treatment campaigns that were conducted in the 1970s. However, epidemiologic studies suggest that HCV continues to be transmitted at relatively high rates (***Pybus, OG, Drummond AJ, et al 2003***). Monitoring the incidence of HCV infections is difficult because most infections are asymptomatic and available assays do not distinguish acute from chronic or resolved infections (***KlimashevskayaS,ObrindinaA,et al 2007***). Prospective cohort studies monitoring HCV seroconversion among susceptible persons have identified incidence rates ranging from 3.1 - 5.2 per 100,000 Based on these studies (***Saleh DA,SheblF,et al 2008***), it is projected that 248,000 - 416,000 infections may occur each year in Egypt.

1.3- MODES OF TRANSMISSION

1 - Persons who inject drugs have the highest risk of infection: Globally, the prevalence of HCV is 67% among drug abusers. ***(Nelson PK, Mathers BM,et al 2011).***

2 - Recipients of infected blood products or invasive procedures in health-care facilities with inadequate infection control practices. Risk of HCV infection varies depending upon the frequency of medical procedures (i.e. number of injections/person/year) and level of infection-control practices. High frequency of injections and low level of infection control can result in high prevalence of HCV in the general population (e.g. prevalence of chronic HCV infection confirmed by nucleic acid testing was 9.8% in Egypt in 2008). ***(ElzantyF,WayA,et al 2008)***

3 - Children born to mothers infected with HCV have estimated risk of transmission around 4–8% among mothers without HIV infection. Transmission risk is estimated as 17-25% among mothers with HIV infection. ***(Mast EE,HwangLYet al 2005)***

4 - People with sexual partners who are HCV-infected have low or no risk of sexual transmission of HCV among HIV-uninfected heterosexual couples and HIV-uninfected men who have sex with men (MSM). The risk of sexual transmission is strongly linked to pre-existing HIV infection. ***(Terrault NA , Dodge JL, et al 2013).***

5 - People with HIV infection, in particular men who have sex with men (MSM) , are at increased risk of HCV infection through unprotected sex. ***(Taylour LE, Swan T 2012).***

6 - People who have used intranasal drugs. Non-injecting drug use (e.g. through sharing of inhalation equipment for cocaine) is associated with a higher risk of HCV infection. ***(Scheinmann R , Hagan H.et al 2007)***

7 - People who have had tattoos or piercings have higher prevalence of HCV compared with persons without tattoos. ***(Jafari S, Copes R ,et al2010)***

8 - Health-care associated transmission:

Hepatitis C virus infection is strongly associated with health inequity in low- and middle-income countries, infection with HCV is most commonly associated with unsafe injection practices and procedures such as renal dialysis and unscreened blood transfusions. ***(de Oliveira T, Pybus O G ,et al 2006)***
(Between 8 - 12 billion injections are administered yearly around the world and 50% of these are considered to be unsafe (mainly in sub- Saharan Africa and Asia). In low- and middle-income countries.

Infection with HCV is frequently associated with unsafe injection practices and unscreened (or inadequately screened) blood transfusions. ***(Marincovich B, Castilla J, et al 2003).*** According to the latest WHO report on blood safety, countries do not routinely screen blood transfusions for blood-borne viruses. ***(Global database on blood safety. Geneva: WHO; 2011).***

The most well documented example of health-care associated transmission is the generalized epidemic of HCV infection resulting from unsafe injection practices in Egypt, where HCV prevalence is 25% in some regions countries do not routinely screen blood transfusions for blood-borne viruses. ***(Frank C, Mohamed MK, et al 2000)***

1.4- Co-infections

A) HIV and HCV co-infection

HIV and HCV have common routes of transmission, and it is estimated that, globally, 4 –5 million persons are co-infected with these two viruses. With the widespread ***(Alter MJ. 2006)*** Use of antiretroviral therapy (ART), which reduces the risk of HIV-associated opportunistic infections, HCV-related liver disease has started to overtake AIDS defining illnesses as a leading cause of death in some high-income countries. (***Bica I, McGovern B,et al2001)***

B) HBV and HCV co-infection

Hepatitis B virus (HBV) and HCV co-infection is commonly found in HBV-endemic countries in Asia, sub-Saharan Africa and South America. Up to 25% of HCV infected persons may be co-infected with HBV in some areas***. (Potthoff A, Manns M P, et al2010)***

1.5- Natural history of HCV infection

Hepatitis C virus causes both acute and chronic infection. Acute HCV infection is defined as the presence of HCV within six months of exposure to and infection with HCV. It is usually clinically silent, and is only very rarely associated with life-threatening disease. Spontaneous clearance of acute HCV infection occurs within six months of infection in 15–45% of infected individuals in the absence of treatment. ***(Thomson EC, Fleming VM, et al 2011).***