

بسم الله الرحمن الرحيم



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شبكة المعلومات الجامعية التوثيق الالكتروني والميكرو فيلم



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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

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Cardiac Safety of Direct Acting Antiviral Agents among Egyptian Patients with Chronic Hepatitis C Infection

A Thesis

*Submitted for Partial Fulfillment of M.D. Degree in
Cardiology*

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

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List of Abbreviations

Abb.	Full term
AASLD	<i>American Association for the study of Liver Diseases</i>
ACS	<i>Acute Coronary Syndrome</i>
AFP	<i>Alpha-Feto-Proteins</i>
ALB	<i>Albumin</i>
ALT	<i>Alanine Aminotransferase</i>
AST	<i>Aspartate Transaminase</i>
ATP	<i>Adenosine Triphosphate</i>
B-NHL	<i>B Cell non-Hodgkins Lymphoma</i>
BOC	<i>Boceprevir</i>
BSA	<i>Body Surface Area</i>
CAD	<i>Coronary Artery Disease</i>
Cr	<i>Creatinine</i>
CVD	<i>Cardiovascular Disease</i>
DAA	<i>Direct Acting Anti-viral drugs</i>
DCM	<i>Dilated Cardiomyopathy</i>
DCV	<i>Daclatasvir</i>
EASL	<i>European Association of Study of Liver Diseases</i>
ECG	<i>Electrocardiogram</i>
EF	<i>Ejection Fraction</i>
FIB-4	<i>Fibrosis-4</i>
FMD	<i>Flow Mediated Dilatation</i>
FS	<i>Fraction Shortening</i>
Hb	<i>Hemoglobin</i>
HBA1c	<i>Glycated Hemoglobin</i>

List of Abbreviations (Cont...)

Abb.	Full term
HCC	<i>Hepatocellular Carcinoma</i>
HCM	<i>Hypertrophic Cardiomyopathy</i>
HCV	<i>Hepatitis C Virus</i>
HCV-G4	<i>Hepatitis C Virus Genotype 4</i>
HS	<i>Highly Significant</i>
IDSA	<i>Infectious Diseases Society of America</i>
IHD	<i>Ischemic Heart Disease</i>
INF	<i>Interferon</i>
INR	<i>International Standardized Ratio</i>
IR	<i>Insulin Resistance</i>
LA	<i>Left Atrium</i>
LDV	<i>Ledipasvir</i>
LV	<i>Left Ventricle</i>
LVEDD	<i>Left Ventricle End Diastolic Diameter</i>
LVEF	<i>Left Ventricular Ejection Fraction</i>
LVESD	<i>Left Ventricle End Systolic Diameter</i>
LVMI	<i>Left Ventricular Mass Index</i>
MACE	<i>Major Adverse Cardiovascular Events</i>
MAPHR	<i>Maximum Age Predicted Heart Rate</i>
Max HR	<i>Maximum Heart Rate</i>
MELD	<i>Model for End-Stage Liver Disease</i>
Mets	<i>Metabolic Equivalent</i>
MOH	<i>Ministry of Health and Population</i>
NCCVH	<i>National Committee for Control of Viral Hepatitis</i>
NK	<i>Natural Killer</i>

List of Abbreviations (Cont...)

Abb.	Full term
NNIs	<i>Non-Nucleoside Inhibitors</i>
NS	<i>Non Significant</i>
PCR	<i>Polymerase Chain Reaction</i>
peg-INF	<i>Pegylated Interferon</i>
PI	<i>Protease Inhibitor</i>
PIH	<i>Post Ischemic Hyperemia</i>
Plt	<i>Platelets</i>
QTc	<i>Corrected QT Interval</i>
RA	<i>Right Atrium</i>
RBV	<i>Ribavirin</i>
RTE	<i>Real-Time Elastography</i>
RVSP	<i>Right Ventricular Systolic Pressure</i>
S	<i>Significant</i>
SIM	<i>Simeprevir</i>
SOF	<i>Sofosbuvir</i>
SVR	<i>Sustained Virologic Response</i>
TIME	<i>Exercise Time</i>
TVR	<i>Telaprevir</i>
VEL	<i>Velpatasvir</i>
WBC	<i>White Blood Cells</i>
WHO	<i>World Health Organization</i>

Abstract

Background: Hepatitis C virus (HCV) is a major health problem in Egypt. Direct-acting antivirals (DAA) have markedly improved the treatment of HCV. However data regarding cardiovascular performance and safety are limited. The aim of our work was to assess cardiovascular performance and cardiac safety of direct acting antiviral agents in patients with chronic hepatitis C virus infection.

Results: Our study was a prospective cohort involving 64 HCV patients treated with DAA for 3 weeks. All patients performed surface electrocardiogram (ECG), stress ECG test and transthoracic echocardiography before and after treatment. The end point of this study was the development of major adverse cardiovascular event (MACE). 12% of the studied patients showed improved cardiovascular performance after successful treatment of HCV with DAA. Predictors of improved cardiovascular performance included lower baseline alanine aminotransferase, lower baseline resting heart rate and higher maximum heart rate during exercise post treatment. DAA had no significant effect on resting ECG or transthoracic echocardiographic parameters. No major adverse cardiovascular event or complication occurred during or 3 month after treatment. None of the enrolled patients developed any signs of ischemia.

Conclusion: Direct acting antiviral agents were associated with an improvement in cardiovascular performance and exercise related symptoms. DAA proved its cardiac safety in patients with chronic hepatitis C virus infection receiving DAA

Keywords: HCV, Direct Acting, Antiviral, Cardiac Safety, cardiovascular performance, stress electrocardiogram.

INTRODUCTION

Hepatitis C Virus (HCV) infection is considered one of the most important health problems worldwide, approximately affecting 185 million patients. Globally, it was found that liver cirrhosis and hepatocellular carcinoma (HCC) were attributed to HCV in 27% and 25% of cases respectively. Egypt has one of the highest prevalence of HCV worldwide (*Mormile, 2016; Gomaa et al., 2017*).

Although HCV is considered major contributor to different liver diseases, it also has extra-hepatic affection on the cardiovascular, kidney, lymph nodes, bone marrow, thyroid, and other organs (*Dou et al., 2017*).

HCV infection and cardiovascular affection are concomitant conditions observed in a large proportion of the general population. Therefore, it is difficult to establish whether a simple association exists between the two conditions or other pathogenic mechanisms directly or indirectly link chronic HCV infection to cardiovascular disorders. A recent systematic review concluded that HCV infection was associated with twofold increase in carotid intima thickness, increased cerebrovascular and cardiovascular events (*Petta, 2017*).

The combination of pegylated interferon (peg-INF) with Ribavirin (RBV) was the main treatment regimen for chronic HCV infection. Many concerns about this regimen were raised