شبكة المعلومات الجامعية

بسم الله الرحمن الرحيم

HOSSAM MAGHRABY

شبكة المعلومات الجامعية

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

HOSSAM MAGHRABY

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها

علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

HOSSAM MAGHRABY

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

By

Housam Magdy Said Mohamed Hassan
M.B.B.Ch, Master degree in Cardiology, Ain Shams University

Under Supervision of

Dr. Ahmed Ibrahim Nassar
Professor of Cardiology
Faculty of Medicine, Ain Shams University

Dr. Ossama Ashraf Ahmed
Professor of Internal Medicine
Faculty of Medicine, Ain Shams University

Dr. Ahmad Elsayed Yousef
Associate Professor of Cardiology
Faculty of Medicine, Ain Shams University

Dr. Diaa Eldin Ahmed Kamal
Associate Professor of Cardiology
Faculty of Medicine, Ain Shams University

Dr. Ahmed Elsayed Gaafar
Lecturer of Cardiology
Faculty of Medicine, Helwan University

Faculty of Medicine
Ain Shams University
2021

سورة البقرة الآية: ٣٢

Acknowledgment

*First and foremost, I feel always indebted to **Allah**, the Most Kind and Most Merciful.*

*I'd like to express my profound gratitude to **Dr.Ahmed Nassar**, Professor of Cardiology, Faculty of Medicine, Ain Shams University for his keen guidance, kind supervision, continuous encouragement, which made completion of this work possible. I had the honor to complete this work under his supervision*

*I am deeply thankful to **Dr.Ossama Ashraf**, Professor of Internal Medicine, Ain Shams University for his great help, active participation, kind support and guidance. This work would not have been done without him*

*I also express my deepest gratitude to **Dr.Ahmad Elsayed** Associate Professor of Cardiology, Ain Shams University for his kind care, genuine support, granting me much of his time and continuous training setting a role model in professorship.*

*I would like to thank **Dr.Diaa Eldin Kamal**, Associate Professor of Cardiology, Ain Shams University for his outstanding dedication, continuous support, and his patience in reviewing and correcting this work. He has always been there for me in every step.*

*I would like to thank **Dr.Ahmed Gaafar**, Lecturer of Cardiology, Helwan University, who sincerely guided and supported me in every step in this work and in my career. His valuable ethics will be kept in my mind forever.*

*Finally I thank **my parents and brother** for always pushing me forward and for their unconditional support.*

*As ever, I thank **my loving wife** for her constant encouragement and patience. I owe her for putting up with my busyness without any sign of discomfort.*

Housam Magdy Hassan

List of Contents

Title Page No.

List of Tables

List of Tables *(Cont...)*

List of Figures

List of Abbreviations

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

List of Abbreviations *(Cont...)*

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

List of Abbreviations *(Cont...)*

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

Abstract

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

Results: Our study was a prospective cohort involving 64 HCV patients treated with DAA for 3weeks. All patients performed surface electrocardiogram (ECG), stress ECG test and trans-thoracicechocardiography before and after treatment. The end point of this study was the development ofmajor adverse cardiovascular event (MACE).12% of the studied patients showedimprovedcardiovascular performance after successful treatment of HCV with DAA. Predictors of improvedcardiovascular performance included lower baseline alanine aminotransferase, lower baseline restingheart rate and higher maximum heart rate during exercise post treatment. DAA had no significanteffect on resting ECG or transthoracic-echocardiographic parameters. No major adversecardiovascular 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 incardiovascular performance and exercise related symptoms. DAA proved its cardiac safety inpatients with chronic hepatitis C virus infection receiving DAA

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

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