Evaluation of HbA1c level in diabetic patients with chronic HCV infection treated with sofosbuvir plus daclatasvir with or without ribavirin regimen

Thesis

Submitted for Partial Fulfillment of the Master Degree in Internal Medicine

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2018

تقييم مستوى الهيموجلوبين السكري في مرضى السكري مع الالتهاب الكبدي الفيروسي المزمن "سي" الذين يتم علاجهم بعقار سوفوسبوفير بالإضافة إلى دكلاتسفير مع أو بدون ريبافيرين

رسالة

توطئة للحصول على درجة الماجستير في الباطنة العامة

مقدمه من

الطبيب/ محمود مصطفى محمود خاطر

بكالوريوس الطب والجراحة– جامعة المنصورة

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جامعة عين شمس

٢٠١٨

سورة البقرة الآية: ٣٢

Acknowledgement

First of all, thanks to Allah whose magnificent help was the main factor in completing this work.

I cannot find sufficient words to express my gratitude to **Prof. Mohamed Abd El-Fattah El-Maltawy,** Professor of Internal Medicine- Faculty of Medicine, Ain Shams University, for his continuous generous supervision, help, kind guidance and encouragement throughout the whole work, without him, this work could never be completed.

Deepest appreciation and thanks to **Prof. Marcel William Keddeas,** Professor of Internal Medicine, Faculty of Medicine, Ain Shams University, for her great help, patience and valuable advice during the conduction of this work

I am greatly indebted to **Dr. Ahmed Samir Allam,** Lecturer of Internal Medicine ،Faculty of Medicine, Ain Shams University, for his guidance and valuable suggestions and kind Supervision.

Deep thanks to our patients without their cooperation this work couldn't be completed & to all members of the Viral Hepatitis unit - Ahmed Maher Teaching Hospital and Ain Shams University Hospital for their kind moral support as well as to my Parents for their support to me all the time.

Mahmoud Khater

Contents

List of Abbreviations

AFP	Alpha feto protein
AIDS	Acquired immunodeficiency syndrome
ALT	Alanine transferase
ARFI	Acoustic radiation force impulse
AST	Aspartate transferase
BMI	Body mass index
CHC	Chronic hepatitis C
CLD	Chronic liver Disease
CTGF	Connective tissue growth factor
DAAs	Direct antiviral agents
DCV	Daclatasvir
E1 & E2 Proteins	Envelope proteins 1 & 2
EASL	European Association for the Study of the Liver
EBR	Elbasvir
ECM	Extra Cellular Matrix
ELISA	Enzyme Linked Immunosorbent Assay
F2, F3 &F4	Fibrosis 2,3 &4
FBS	Fasting blood sugar
FDA	Food and drug administration
G	Gram
GFR	Glomerular filtration rate
GGT	Gamma Glutamyl Transferase
GI	gastro intestinal
GT1	Genotype 1
GT4	Genotype 4
GU	Genitourinary
GZR	Grazoprevir
HA	Hyaluronic acid

Hb	Heamoglobin
HbA1c	Glycated hemoglobin
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV-4	Hepatitis c virus genotype 4
HIV	Human immunodeficiency virus
HSC	Hepatic stellate cells
IFNα	Interferon alpha
Ig G	Immunoglobulin G
IIT	Interferon-induced thyroiditis
INF	Interferon
INR	International randomized ratio
IR	Insulin resistance
IV	Intravenous
LDV	Ledipasvir
MELD Score	Model for end-stage liver disease Score
MFAP-4	Microfibril-associated glycoprotein 4
MMPS	Metalloproteinases
MRE	Magnetic Resonance Elastography
NAFLD	Non Alcoholic Fatty Liver Disease
NAT	Nucleic acid test
NICE	National institute for health and care excellence
NNIs	Non-nucleoside inhibitors
NPIS	Nucleotide polymerase inhibitors
NS	Nonstructural proteins
NS5A	Nonstructural 5 A protein
NS5B	Nonstructural 5 B protein
OBV	Ombitasvir
PCR	Polymerase chain reaction
Peg INF	Pegylated interferon
PICP	Procollagen type I carboxy terminal peptide

PIIINP	Procollagen type III aminoterminal peptide
PIs	Protease inhibitors
PLTS	Platelets
PPV	Positive predictive values
PTV/r	Ritonavir
PVD	peripheral vascular disease
R	Ratio
RBS	Random blood sugar
RBV	Ribavirin
RIBA	Recombinant Immunoblot Assay
RNA	Ribonucleotide
SC	Sub-cutaneous
SD	Standard variation
SMV	Simeprevir
SOF	Sofosbuvir
SVR	Sustained virologic response
SVR12	Sustained virologic response 12 weeks
SVR24	Sustained virologic response 24 weeks
T1DM	Type 1 diabetes mellitus
T2DM	Type 2 diabetes mellitus
TGF-β1	Transforming growth factor-β1
TIMPS	Tissue inhibitors of matrix metalloproteinases
TMA	Transcription-mediated Amplification
U/S	Ultra sound
VEL	Velpatasvir
WBCs	White blood cells

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Abstract

Background: Hepatitis C is an infectious disease caused by hepatitis C virus (HCV) which mainly attacks the liver cells**.** The acute stage of the disease passes mostly without manifestations, but the chronic stage can cause hepatic fibrosis and cirrhosis, that has mostly occurred after several years. Some cirrhotic patients may develop liver failure, hepatocellular carcinoma (HCC) or fatal bleeding from esophageal or gastric varices. HCV_4 is prevalent among Middle East and Africa causing more than 80% of HCV infections and has recently spread to several European countries. In Egypt, HCV-4 responsible for almost 90% of the infections. **Aim:** The aim of this study is to evaluate the glycemic control in diabetic patients with chronic HCV infection after eradication of HCV by sofosbuvir plus daclatasvir with or without ribavirin regimen through HbA1c measurement before the start of treatment, at the end of treatment, and 3 months after the end of treatment. **Methodology:** This study has been conducted at Viral Hepatitis unit - Ahmed Maher Teaching Hospital and Ain Shams University Hospital - the National Committee to Combat Viral Hepatitis (NCCVH) in Egypt during period from October 2016 to September 2017. One hundred (100) Egyptian diabetic patients with chronic HCV infection eligible for treatment were recruited in this study and were divided as follows: Group I: 50 patients recieving oral hypoglycemic drugs. Group II: 50 patients recieving insulin therapy. Both groups received sofosbuvir (400mg) plus daclatasvir (60mg) daily for 12 weeks with or without ribavirin. **Results:** No hypoglycemic attacks were reported throughout our study. In our study mean values of baseline alanine transaminase (ALT) and aspartate transaminase (AST) in both groups was significantly decreased at end of treatment. In both groups, there is a significant decline of HbA1C value at the end of treatment and 3 months after end of treatment. **Conclusion:** The glycemic control is significantly improved in diabetic patients after eradication of HCV by new DAAs regimens.

Keyword: HbA1c, HCC, HCV, Sofosbuvir plus daclatasvir, Ribavirin regimen

Introduction

Hepatitis C virus (HCV) infections has been identified as one of the leading causes of chronic liver disease with serious sequelae such as end-stage cirrhosis and liver cancer (**Lauer and Walker, 2001).**

Chronic hepatitis C infection has a global prevalence of 2%-3%. Approximately 170 million people are thought to be currently infected (approximately 3% of the world's population), and an additional 3-4 million are infected each year **(Alter, 2007).**

The suggestion that HCV may be associated with type 2 diabetes mellitus (type 2 DM) was first made by (**Allison et al., 1994).** The liver plays an important role in carbohydrate metabolism, and liver diseases such as chronic hepatitis are associated with impaired glucose tolerance, and insulin resistance (IR) **(Weinman and Belalcazar 2004).** Which can eventually lead to DM **(Bugianesi et al., 2005).**

Liver dysfunction exerts a ‘‘toxic" effect on pancreatic islets, playing a major pathophysiological role in the development of diabetes (**Grancini et al., 2015).**