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بسم الله الرحمن الرحيم

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

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علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

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تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

Efficacy of the new Direct Acting Antiviral drugs in the treatment of Thalassemic HCV patients

Thesis

Submitted for partial fulfillment of the MD degree
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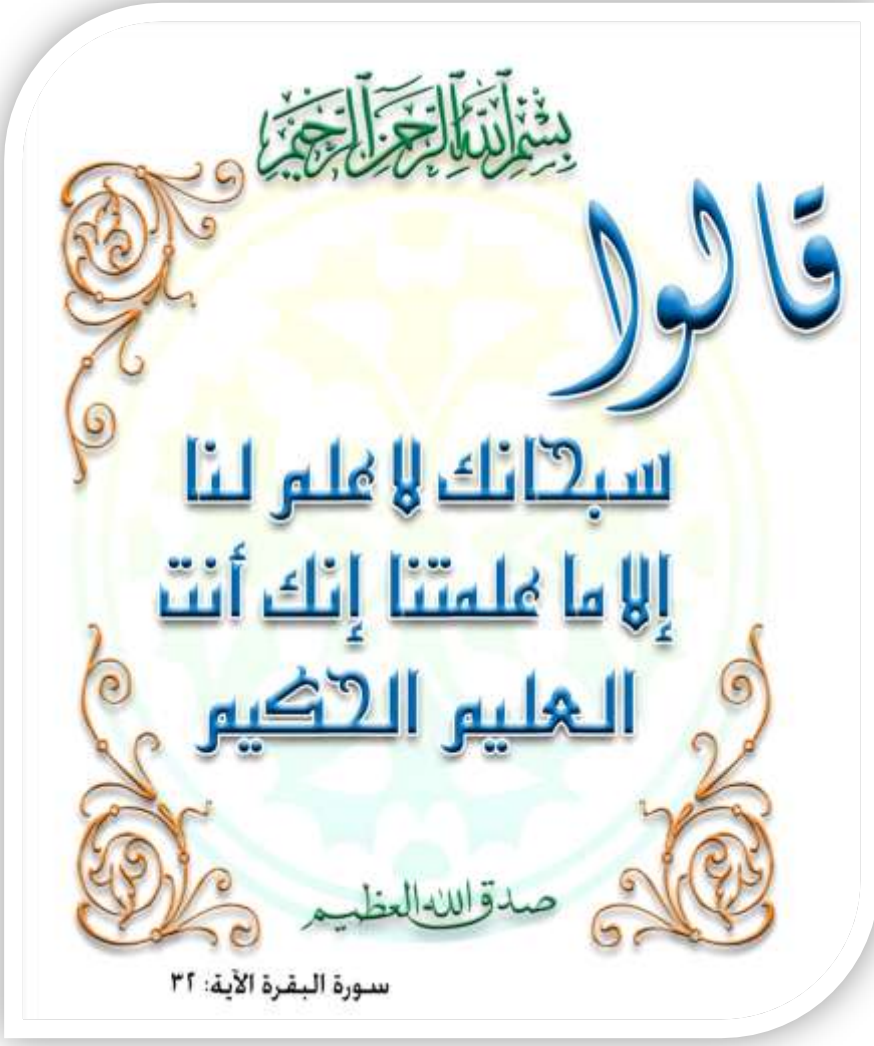
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List of Abbreviations

Abbr.	Full-term
A.A.	Amino acids
ALD	Alcoholic liver disease
Apo	Apolipoproteins
APRI	Aspartate aminotransferase to platelet ratio index
ART	Antiretroviral therapy
BMT	Bone marrow transplantation
BTM	β-thalassemia major
CHC	Chronic hepatitis C
CMV	Cytomegalovirus
DAAs	Direct acting antivirals
DDIs	Drug–drug interactions
DM	Diabetes mellitus
EASL	European Association for the Study of the Liver
EDHS	Egyptian Demographic Health Survey
EPO	Erythropoietin
eGFR	Estimated glomerular filtration rate
EHIS	Egyptian Health Issues Survey
EIA	Enzyme immunoassay
ESCRT	Endosomal-sorting complex required for transport
ER	Endoplasmic reticulum
ESRD	End stage renal disease
FIB4	Fibrosis 4
GIT	Gastrointestinal tract
HAV	Hepatitis A virus
HAMP	Hepcidin antimicrobial peptide
HB	Hemoglobin
HBV	Hepatitis B virus
HCC	Hepatocellular Carcinoma
HCV	Hepatitis C virus
HIV	Human Immunodeficiency Virus
HSC	hepatic stellate cells
HTN	Hypertension

IFN	Interferon
INR	International normalised ratio
LDs	Lipid droplets
LIM	Liver iron concentration
MASRI	Faculty of medicine Ain shams university research institute
MELD	Model End Stage Liver Disease
MRI	Magnetic resonance imaging
MSM	Men who have sex with men.
NAFLD	Non-alcoholic fatty liver disease
NAT	nucleic acid testing
NCCVH	National Committee for the Control of Viral Hepatitis.
NHL	Non Hodgkin lymphoma
NPIs	Nucleoside polymerase inhibitors
NS	Non Structural
NTDT	Non-transfusion dependent thalassaemias
NTPase	Nucleoside triphosphatase
NTPI	Non-transferrin-bound iron
OST	Opioid substitution therapy
PIs	Protease inhibitors
PWID	People who inject drugs
RBV	Ribavirin
RDTs	Rapid diagnostic tests
RNA	Ribonucleic acid
ROS	Reactive oxygen species
SVR	Sustained viral response
SQUID	Superconducting quantum interference device
TDT	Transfusion dependent thalassaemia
US	United states of America
WHO	World Health Organization

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Abstract

Background and Objectives: B-thalassemia major patients are susceptible to Hepatitis C Virus (HCV) infection owing to life-long dependency for blood-transfusion. Moreover, this patient population is at risk of progression of liver fibrosis or development of cirrhosis as a consequence of both iron overload and HCV infection. However, patients with haemoglobinopathies and CHC have been excluded from the major clinical trials that led to the approval of DAAs, Hence, at present, limited experience is available regarding the safety and efficacy of DAAs in this population which is traditionally considered difficult to treat. Hence, this study was carried out to evaluate efficacy and safety of the combination regimen of sofosbuvir and daclatasvir for HCV infection in B-thalassemia major patients.

Methods: This study was conducted on 200 subjects divided into two groups, first group contains150 HCV-Thalassemic patients while the second group contains 50 HCV only patients. Each group was classified into easy to treat or difficult to treat and received sofosbuvir 400mg + daclatasvir 60mg once/day for the duration of 12 or 24 weeks according to the NCCVH Hepatitis C treatment protocol 2015. Sustained virological response at post-treatment week-12 (SVR-12) was defined as negative HCV-RNA at week-12 post treatment.

Results: In group (I), successful SVR was achieved in all patients (100%) in subgroup (Ia) while in subgroup (Ib) 12 patients didn't achieve SVR (15.38%), 4 patients stopped due to side effects(5.13%) and 62 patient achieved SVR (79.49) with overall successful SVR of 134 out of 150 HCV-Thalassemic patients in group (I) (89.33%). in group (II), 2 patients didn't achieve SVR (5.71%)and 33 patients achieved SVR (94.29%) in subgroup (IIa) while in subgroup (IIb) 2 patients didn't achieve SVR (13.33%) and 13 patients achieved SVR (86.67%) with overall successful SVR of 46out of 50 HCV only patients in group (II) (92%). few patients suffered from minor side effects that didn't require cessation of treatment but 4 patients developed major side effects in group (Ib) that required cessation of treatment. There were marked improvement in liver enzymes, Fib4 score, hemoglobin level and transfusion requirements in HCV-Thalassemic group after treatment.

Conclusion: A combination of sofosbuvir and daclatasvir is an efficacious and tolerable treatment regimen with negligible side effects for patients with thalassemia major and HCV infection.

Key words: Hepatitis C, Thalassemia, HCV Treatment, Sofosbuvir, Daclatasvir.

Introduction

Hepatitis C virus (HCV) infection is a public health problem worldwide and is a leading cause of cirrhosis and liver cancer ***(Messina et al., 2015),*** In Egypt, hepatitis C virus (HCV) infection has the highest prevalence rate in the world, which is estimated at 14.7% nationally ***(Mohlman et al., 2015).*** More than 90% of HCV infection in Egypt is due to genotype 4 which is the most common genotype in the Middle East and Africa ***(Gower et al., 2014).***

Thalassemia is an autosomal recessive inherited blood disorder characterized by abnormal hemoglobin production due to genetic disorder leading defects in either the α or β globin chain, causing production of abnormal red blood cells that necessitate frequent blood transfusion and iron overload ***(Weatherall, 2015).***

Hepatitis C virus infection has been reported in 4.4% to 85.4% of thalassemia patients that might be acquired through blood transfusion. The incidence of chronic hepatitis C was higher among thalassemia patients transfused before 1992, when screening of blood donors was still not available ***(Nawfal, 2016).***

As chelation therapy with new drugs seems to prevent cardiac damage and improve survival, the chronic liver