Study of IL28B gene variation as a predictor of response to Directly Acting antiviral therapy in Hepatic transplantation Hepatitis C Egyptian Patients

Thesis
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List of Contents

List of Tables

List of Tables Cont...

List of Tables Cont...

List of Figures

List of Figures

List of Figures

List of Abbreviations

Abb.	Full term
AIDS	aquired immune deficiency response
AKI	Acute Kidney Injury
AR	Acute rejection
CKD	Chronic kidney disease
CMV	Cytomegalovirus
CNIs	Calcineurin inhibitors
DAAs	Direct acting antivirals
Dac	Daclatasvir
EBV	Epstein Barr virus infection
GWAS	Genome-wide association study
HA	Hepatic artery
HAS	Hepatic artery stenosis
HAT	Hepatic artery thrombosis
HBIG	HBV immuneglobulin
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
IFN-λ3	Interferon lambda-3
IL28A	Interleukin 28A
IL28B	Interleukin 28B
INR	International normalized ratio
LDLT	Living Donor Liver Transplantation
Led	Ledibasvir
LT	Liver transplantation
MELD	Model for End Stage Liver Disease
NASH	Nonalcoholic steatohepatitis
NPV	Negative predictive value

List of Abbreviations Cont...

Abb.	Full term
PBC	Primary Biliary Cirrhosis
PEI	Percutaneous ethanol ablation
PPV	Positive predictive value
PSC	Primary Sclerosing Cholangitis
PTA	Percutaneous transluminal angioplasty
PTLD	Post transplantation lymphoproliferative disease
PV	Portal vein
PVS	Portal vein stenosis
PVT	Portal vein thrombosis
RBV	Ribavirin
RFA	Radiofrequency ablation
RI	Resistance index
SAT	Systolic ascending time
SNP	Single nucleotide polymorphism
Sof	Sofosbuvir
SVR	Sustained virological response
TACE	Transarterial chemoembolization
UCSF	University of California, San Francisco criteria

ABSTRACT

Background: IL28B gene polymorphisms are associated with the response to antiviral therapy in hepatitis C patients in the non-transplant setting.

Objective: To determine the prevalence and impact on clinical outcomes of donor and recipient IL28B genotypes among liver transplant recipients receiving directly acting antiviral therapy compared to those of HCV non-transplant patients.

Patient and Methods: This study included 60 patients divided into 2 groups: group 1 included 30 patients subjected to living donor liver transplantation and group 2 included 30 patients of HCV infection. Each group was subdivided into group A and group B according to the regimen of directly acting antiviral therapy (sofosbuvir-ledibasvir, sofosbuvir-daclatasvir). Liver transplantation was done between January 2016 and April 2018. Genotyping of the polymorphism was performed on DNA collected from all donors and recipients in group 1 before and after liver transplantation and also collected from all patients of group 2. Sustained virological response was found in 28 patients in group 1 (transplanted group) and 29 patients in group 2 (non-transplanted group) with no significant difference.

Results: No significant difference also was found in both groups according to the type of regimen. Also the type of genotype CC, CT and TT of IL28B in donors and recipients were not significantly associated or affecting the results of SVR in both groups of patients.

Conclusion: Our results support no role of recipient IL28B genotype in the response to directly acting antiviral drugs for hepatitis C recurrence. Interestingly, donor genotype seems not to influence the response pattern in recipients who have different IL28B genotype.

Keywords: IL28B: interleukin 28B, SVR: sustained virological response , sof : sofosbuvir , dac : daclatasvir , led : ledibasvir , HCV : hepatitis C virus.

INTRODUCTION

Hepatitis C virus (HCV) is an important etiology of chronic hepatitis and cirrhosis and is a leading indication for liver transplantation in adults around the world ***(Ghani et al., 2009).***

HCV infection may lead to significant liver injury. Viral, environmental and host factors, including immunologic and genetic susceptibilities, may contribute to differences in the disease expression and treatment response. This genetic susceptibility has a significant part in developing of HCV infection, from viral antigen recognition and presentation to the type of immune response developed against the pathogen ***(Promrat et al., 2003).***

The predictive factors of treatment response are also related to the virus and they can be classified as clinical, immunologic, and genetic factors ***(Seeff and Hoofnagle, 2002).***

Gene polymorphisms that encode or regulate the host molecular expression may be useful as disease evaluation markers and therapy response predictors, moreover they could provide helpful information for understanding the complex mechanisms underlying the virus-host interaction and the variations observed in antiviral therapy responses ***(Ge et al., 2009).***

The IL28B polymorphisms were considered the strongest baseline identified predictors of viral kinetics and spontaneous