Assessment of Nutritional State in HCV Chronic Liver Disease Before and After Treatment with Direct Acting Antivirals Therapy in Egyptian Patients

Thesis

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Contents

List of Abbreviations

(BT) ratios	: Branched-chain amino acid / tyrosine ratio
(I-SMI)	: Increased skeletal muscle index
AMAs	: Antimitochondrial antibodies
ANA	: Anti-nuclear antibodies
ASH	: Alcoholic steatohepatitis
ASMA	: Anti-smoot muscle antibodies
BCAA/ AAA	: Branched-chain amino acid / aromatic amino acid
BMI	: Body mass index
BTR	: Branched-chain amino acid to tyrosine ratio
CHC	: Chronic hepatitis C
DAAs	: Direct-acting antivirals
DAC	: Daclatasvir
GI	: Gastrointestinal
Hb	Hemoglobin
HbA1C	: Glycated hemoglobin
HCC	: Hepatocellular carcinoma
HCV	: Hepatitis C virus
HDL	: High density lipoproteins
HE	Hepatic encephalopathy
HGS	: Hand grip strength
HOMA-IR	: Homeostasis model assessment of insulin resistance
HRQOL	: Health- Related Quality of life
HRS	Hepatorenal syndrome
IBD	: Inflammatory bowel disease
IFN	: Interferon
INR	: International normal range
IR	: Insulin resistance
IV	Intravenous
LC1	: anti-liver cytosol
LDL	: Low density lipoproteins
LKM1	: Anti-liver kidney microsomes
LPS	: lipopolysaccharide
LSM	: Low Skeletal muscle mass
MAC	: Mid arm circumference
MELD	: Model for end-stage liver disease
NASH	: Non-alcoholic steatohepatitis
PAUS	: Pelvi-abdominal ultrasound
PBC	: Primary biliary cholangitis
PCR	: Polymerase chain reaction
PSC	: Primary sclerosing cholangitis

RBV	: Ribavirin
SD	: Standard deviation
SGA	: Subjective global assessment
SIM	: Simprevier
SMI	: Skeletal muscle index
SML	: Skeletal muscle loss
SMM	: Skeletal muscle mass
SOF	: Sofosbuvir
SPSS	: Statistical program for social science
SVR	: Sustained virologic response
TC	: Total cholesterol
TG	: Triglycerides
TLR	: Toll-like receptor
TNF-a	: Tumor necrosis factor - alpha
tTG	: Tissue transegluitamase
TTT	: Treatment
UGI	Upper gastrointestinal
WHO	: World Health Organization

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Abstract:

Egypt own the highest prevalence rate of HCV infection worldwide, so the government launched a national HCV treatment program targeted a prevalence of <2% by 2025.

Malnutrition in cirrhosis characterized by progressive loss of muscle mass with simultaneous occurrence of lipid compartments consumption to satisfy a higher energetic demand of the hypercatabolic state of the cirrhotic patients affecting their (HRQOL) as they became physically and mentally impacted by fatigue, depression and anxiety. It's evaluated by many tools e.g. Anthropometric tools including BMI, and MAC and Functional tests such as HGS which represent a reliable and easy-to-perform method that can predict sarcopenia in the cirrhotic patient with overall better sensitivity and specificity than other tools.

DAA therapy is a treatment that promises improved quality of life and a favorable prognosis in HCV- infected patients, as in contrast to interferon-based treatment, lead to a high viral eradication rate, less or mostly no side effects.

Inadequate nutrition worsens severity of liver disease and also affects the HRQOL. So, nutritional interventions are important beside DAAs.

INTRODUCTION

Viral hepatitis was estimated to be the 7th leading cause of mortality worldwide. In many cases, it is attributed to hepatitis C virus (HCV), which is the main causes of liver fibrosis, cirrhosis and cancer worldwide, however, Egypt own the highest prevalence rate in the world. ***(Mohd, et al., 2013).***

It is widely accepted that the widespread of infection in Egypt was due to implementation of mass population antischistosomal treatment with "tartar emetic injections" (from 1950s to 1980s) beside the usual modes of transmission, such as IV drug usage, shared or reused needles, poorly sterilized surgical or dental equipment, and blood transfusions. ***(Ahmed, et al., 2016).***

It is well known that there has been a spectrum of treatments to target the public health disaster represented by the hepatitis C problem in Egypt ranging from the use of PEGylated interferon to the recent use of direct acting antiviral drugs. ***(Ahmed, et al., 2016).***

The era of recent direct-acting antivirals (DAAs) provides possibility of reducing disease burden and eliminating this blood-borne virus as a public health concern. (***World Health Organization, 2017).***

The prevalence of hepatitis C in Egypt has a historical and cultural context in response to that the public health measures encouraged by Egyptian health authorities and World Health Organization officials were serious in a period spanning over three decades in the latter half of the last century. ***(Ahmed, et al., 2016).***

World Health Organization has recently formulated the "Global Health Sector Strategy on Viral Hepatitis", Egyptian government following successful negotiations for 99% discounted DAA prices, it launched a national HCV treatment program aiming to treat over 250,000 chronically infected individuals per year, with the goal of achieving a national chronic infection prevalence of <2% by 2025. ***(Silva. et al., 2018).***

About 180 million people worldwide are infected with (HCV) that causes both acute and chronic infection. Although the acute stage is largely asymptomatic with little visible symptoms, it's required 20-40 years harboring the infection to develop chronic hepatitis when noticeable symptoms or signs of the disease will occur (***Struthers, 2007)***.

The Approximately 55–85% of infected individuals will develop chronic hepatitis C virus and about 15-30% of the chronically infected by HCV will develop cirrhosis ***(Webster et al., 2015), (Ponziani, et al., 2017).***

HCV is a significant "precursor" for fibrosis, cirrhosis, and even hepatocellular carcinoma, but it is important to understand that this is only in chronic cases. Advanced liver disease and its complications such as ascites, HE, UGI bleeding , hepatopulmonary syndrome, HRS and hepatocellular carcinoma and *"sarcopenia"* , which is defined as progressive loss of muscle mass representing frequently unseen complication is also common, reflecting the poor nutritional status in cirrhotic cause significant morbidity and mortality, which definitely affect the Health- Related Quality of life (HRQOL) of the patients as they are physically and mentally impacted by fatigue, depression and anxiety ***(Barboza, et al. ,2016) (Nitin, et al., 2016)*** .

HCV is a hepatotropic RNA virus of the genus Hepacivirus in the Flaviviridae family. It's exists as an enveloped, positive-stranded RNA virus which is ~50 nm in size and is made up of ~9600 nucleotide bases covered by an icosahedral nucleocapsid which is further surrounded by a lipid bilayer and glycoproteins. ***(Zhao, et al., 2014).***

HCV is grouped into 6 major genotypes that exhibit at least 30% variation in nucleotide sequence from one another. (Fig.1)