

EVALUATION OF CARDIAC INVOLVEMENT IN HCV PATIENTS RECEIVING NEW HEPATITIS C ANTIVIRAL THERAPIES

Scientific background

The global burden of hepatitis C infection (HCV) amounts around 2, 5%. In Germany suffer around 0, 5% of the population from such infection. Egypt has higher rates of HCV than neighboring countries as well as other countries in the world. The strong homogeneity of HCV subtypes found in Egypt (mostly 4a) suggests an epidemic spread of HCV. Since a history of drug injection has been implicated as one of the most important risk factors for HCV infection so a prime candidate to explain the high prevalence of HCV in Egypt is the past practice of parenteral therapy for schistosomiasis. (1)

Hepatic effects of HCV

The usual progression of liver disease in patients with hepatitis is a process of inflammation accompanied by periportal necrosis and fibrosis. The viral inflammation causes stimulation of stellate cells, which ultimately leads to the deposition of collagen with subsequent fibrosis progression within the liver. (2)

Many patients with chronic HCV are noted to have a degree of steatosis based on their liver biopsies. Chronic HCV infection can lead to hepatic scarring and ultimately to cirrhosis. In some cases, patients will go on to develop liver failure, portal hypertension, ascites, easy bruising or bleeding, life-threatening esophageal and gastric varices, jaundice, liver cancer, and the syndrome of cognitive impairment known as hepatic encephalopathy (3).

Extrahepatic complications of HCV

1-The most common extrahepatic manifestation of HCV is mixed cryoglobulinemia (usually the type II form), an inflammation of small and medium-sized blood vessels. (4)

2-Sjögren's syndrome : a chronic autoimmune disease through which the body's white blood cells destroy the exocrine glands, specifically the salivary and lacrimal glands.

3-Thrombocytopenia is estimated to occur in 0.16% to 45.4% of people with chronic hepatitis C. (5)

4-Porphyrria cutanea tarda : characterized by onycholysis and blistering of the skin in areas receiving higher levels of exposure to sunlight.

5- Insulin resistance and type two diabetes mellitus with the concomitant complication

6- Autoimmune thyroiditis

7-B-cell lymphoproliferative disorders.

8- Membranoproliferative glomerulonephritis.

Cardiovascular complications of HCV

1 -Myocarditis.

2- Dilated cardiomyopathy.

3- Hypertrophic cardiomyopathy.

4- Arrhythmogenic right ventricular cardiomyopathy.

5- Left ventricular aneurysm.

Pathogeneses:

HCV can lead to acute myocarditis which progresses to chronic inflammation resulting in myocardial fibrosis. This cascade can process to dilated cardiomyopathy attributable to necrosis and loss of myocytes. However, proliferative stimuli induced by HCV infection may promote myocyte hypertrophy and hypertrophic cardiomyopathy. (5) HCV has been associated with athrosclerosis and coronary artery disease as well. (7), (8) The increased risk of CAD in HCV-infected persons might be related to cytokines production, which result in inflammation, thrombosis, and endothelial dysfunction. (9),(10).

New oral anti-HCV drugs

Gilead's Sovaldi (Sofosbuvir), Gilead's Harvoni (Ledipasvir / Sofosbuvir) and AbbVie's Veikira Pak (Ombitasvir / Paritaprevir / Ritonavir tablets ; Dasabuvir tablets) the long-awaited reality of highly effective, interferon-free, Hepatitis C treatment was finally introduced. The addition of these new Hepatitis C drugs to the FDA approved list will greatly benefit Hepatitis

C patients by making treatment not only safer and more effective but also increasing the competition to keep treatment more affordable.

1-Gilead's Sovaldi (Sofosbuvir): Is a new anti HCV drug indicated for the treatment of genotypes 1,2,3 or 4 chronic HCV infections which should be taken in combination with Ribavirin . Its dose is 400 mg once daily for 12 weeks except for genotype 3 for 24 weeks .

2-Gilead Harvoni (Ledipasvir 90 mg / Sofosbuvir 400 mg) : The second new anti HCV drug which is indicated for the treatment of geotype 1 chronic HCV infecation . When it is combined with Ribavirin it gives better results and it can shorten the duration of therapy . Its dose is one tablet once daily for 12 weeks in non-cirrhotic patients but in cirrhotic patients it should be given for 24 weeks .

3-AbbVie's Veikira Pak (Ombitasvir / Paritaprevir / Ritonavir tablets ; Dasabuvir tablets) : Is tha third new anti HCV drug indicated for the treatment of genotype 1 chronic HCV infection. It should be taken with Ribavirin in patients with genotype 1a with or without cirrhosis and in patients with genotype 1b with cirrhosis but not in patients with genotype 1b without cirrhosis . Its dose is one tablet containing Dasabuvir 250 mg twice a day OR two tablets containing (Ombitasvir 12.5 mg / Paritaprevir 75 mg / Ritonavir 50 mg) once daily for 12 weeks except for genotype 1a with cirrhosis for 24 weeks .

Side effects of Sovaldi

-More common:

- 1- Chills
- 2- Fever
- 3- Lower back or side pain
- 4- Pale skin
- 5- Ulcers, sores, or white spots in the mouth.
- 6- Unusual tiredness or weakness

Rare side effects:

- 1- Behavior changes
- 2- Discouragement
- 3- Suicidal tendency

Cardiovascular complications of Sovaldi

Serious symptomatic bradycardia has been reported in patients combining amiodarone with Harvoni or Sovaldi. (2015 Mar 24) (11)

Aim of work

To evaluate the cardiovascular sequelae of new antiviral therapy in HCV patients with different genotypes.

Methodology

The study will be conducted at the internal medicine department in Cairo University, Cardiology department of scientific research academy in Egypt as well as gastroenterology department of Klinikum Coburg in Germany.

The study will last one year starting from November 2015 to November 2016.

The aim is to enroll 200 patients in this prospective study.

Inclusion criteria

-All HCV patients candidate for receiving the new antiviral HCV therapy.

Exclusion criteria

-HBsAg positive patients.

-Patients with known cardiac diseases.

-Patients over 70 years old who are already prone to cardiac events without application of the new therapy.

-Patients with past history of receiving Interferon or HCV treatment modality.

-Cardiac patients already receiving amiodarone.

All enrolled patients will be subjected to the following diagnostic measures:

- 1-Liver function tests : ALT , AST .
- 2-CBC .
- 3-Quantitative HCV RNA by PCR .
- 4-Hepatitis markers .
- 5-Cardiac Troponin I .
- 6-NT Pro BNP .
- 7-Highly sensitive CRP .
- 8-Abdominal US .
- 9-Fibroscan .
- 10-ECG .
- 11-Echocardiography including Tissue Doppler and speckle tracking .
- 12-Carotid duplex .

-These tests will be carried on before starting the therapy. Follow up study will be repeated at the 3rd month. The last follow up study will be underwent after completing the therapy.

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