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Sofosbuvir-Containing Regimen for the Treatment of Hepatitis C Virus in a Patient With Sickle-Thalassemia: The First Case Report

Nawfal R Hussein[1,*]

[1]Department of Internal Medicine, College of Medicine, University of Duhok, Duhok, Iraq

[*]*Corresponding author*: Nawfal R Hussein, Department of Internal Medicine, College of Medicine, University of Duhok, Duhok, Iraq, E-mail: nawfal.hussein@yahoo.com

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Abstract

Introduction: Chronic HCV could be treated with classical interferon-containing regimen. However, it was previously shown that the success rate with such a regimen is around 50% in patients with hemoglobinopathy and HCV. Although directly acting antivirals (DAAs) are potent for the treatment of HCV, such drugs have not been approved for the treatment of HCV in patients with hemoglobinopathy.

Case Presentation: We described a 16- year-old male patient with sickle-thalassemia who was infected with a HCV. Treatment was started with sofosbuvir, ribavirin and pegylated interferon and continued for 12 weeks. Rapid virologic response was achieved and liver enzymes decreased gradually. Sustained virologic response was achieved as HCV reverse transcription-polymerase chain reaction (RT-PCR) was negative 12 weeks after stopping treatment. The patient reported no side effect during the course of treatment.

Conclusions: If such a regimen is approved, it would be a breakthrough in the treatment of HCV in subjects with hemoglobinopathy. More prospective, randomized control trial studies are needed to investigate the efficacy and safety profile of such a regimen.

Keywords: HCV, Hemoglobinopathy, Thalassemia, Iraq, DAA, Sofosbuvir

1. Introduction

Hepatitis C virus (HCV) infection is a public health problem worldwide and is a leading cause of cirrhosis and liver cancer (1). 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. In Duhok city, Iraq, the screening for HCV was only started in 2000 and most of the patients caught the infection before the screening era. Currently, the transmission of virus by blood transfusion is rare because of the strict regulations that mandate screening of blood products. Interferon alpha and ribavirin combination was the classical approved standard treatment for chronic hepatitis C (2). However, the use of ribavirin was controversial in hemoglobinopathic patients because of hemolytic complications (3). It was previously shown that [16] treatment with interferon monotherapy resulted in a sustained biochemical response (SBR) in 40% - 50% of thalassemia patients with HCV-related chronic hepatitis (3). In Iraq, we previously reported that sustained virologic response (SVR) was achieved in about 50% of our patients (4). Outstanding development has been made in the treatment of chronic HCV with the development of potent DAA (5). These drugs may represent a promising approach for the treatment of HCV in patients with hemoglobinopathy. There is a need for clinical trials for the use of DAA in such patients. Here, we report a case of hemoglobinopathy with HCV that achieved SVR after receiving 12 weeks sofosbuvir-containing regimen.

2. Case Presentation

A16-year-old male was referred to the infectious disease unit in Azadi teaching hospital, Duhok City, with sickle thalassemia and was positive for HCV antibodies test. Blood tests showed elevated ALT (89 U/L) and AST (110 U/L), normal serum albumin (4.8) and international normalized ratio (INR) (1.2) while CBC showed mild anemia and normal platelet count. The patient was sent for HCV RT-PCR analysis and results showed that HCV load was 159450 IU/mL. Hepatitis C virus genotyping showed that the patient was infected with HCV genotype 4 and the patient refused to conduct liver biopsy. The patient discussed the new options of treatment of HCV with a multidisciplinary team. The patient decided to take treatment and informed consent was taken from him for the treatment with new drugs not approved for treatment of HCV in thalassemia patients.

Approval for treatment protocol was taken from the hospital's ethics committee. Sofosbuvir was started at a dose of 400 mg qd plus RBV at the dose of 14mg/kg in two divided doses plus pegylated interferon alpha 180μg once a week for 12 weeks. After starting treatment, the patient was followed up every 4 weeks. Rapid virologic response was achieved; liver enzymes began to decrease gradually (Table 1). Sustained virologic response was achieved as HCV RT-PCR was negative 12 weeks after stopping treatment with improvement of ALT and AST. The patient reported no side effect during the course of treatment.

Table 1. Patient Monitoring and Selected Laboratory Values

Test	Before Treatment	During the Treatment			12 Weeks After Treatment
		4 Weeks	8 Weeks	12 Weeks	
ALT	89	33	38	47	35
AST	110	48	46	61	39
Albumin	4.8	4.6	4.5	4.6	4.5
INR	1.2	1.1	1.2	1.2	1.1
HCV RT-PCR	159450	Undetected	Undetected	Undetected	Undetected
Hb (%)	10.1	10.4	10.2	10	10.2

Abbreviations: ALT, alanine transaminase; AST, aspartate transaminase; Hb, hemoglobin; HCV RT-PCR, hepatitis C virus reverse-transcription polymerase chain reaction; INR, international normalized ratio.

3. Discussion

In thalassemia, the classical treatment of HCV included pegylated interferon with or without ribavirin. We previously studied the treatment of HCV infection in patients with hemoglobinopathy including thalassemia. It was shown that the SVR was achieved in 50% of the patients and the HCV genotype was a major determinant of treatment success. In the same study, it was shown that HCV genotype 4 was the most common and most difficult to treat (4). Worldwide, several studies recruiting thalassemia patients showed that SVR was achieved in a range of 24% for interferon monotherapy to 51% in patients receiving a combined therapy (6, 7). The approval of DAA for the treatment of HCV infection represented a major breakthrough with more than 90% success rate. However, these medications have not been approved for the use in patients with hemoglobinopathy. Our patient was diagnosed with HCV genotype 4 with high levels of ALT and AST. To the best of our knowledge, this is the first case of HCV genotype 4 to be treated with sofosbuvir-containing regimen. The patient was stable throughout the course of the treatment and no blood transfusion was required. Sustained virologic response was achieved as the viral load was undetectable 12 weeks after the treatment. Additional follow-up time and subjects will be needed to show that the viral clearance in such cases is durable. If such a regimen is approved, it would be a breakthrough in the treatment of HCV in subjects with hemoglobinopathy and may prevent HCV-related complications in this group of patients. However, it would be premature to draw solid conclusions about the optimal regimen, recalling the multitude of new DAAs anticipated in the very near future. More prospective randomized control trial studies are needed to investigate the efficacy and safety profile of such a regimen taking into account the viral, histological and clinical characteristics of patients.

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Footnote

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