



CODEN [USA]: IAJPBB

ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

<http://doi.org/10.5281/zenodo.3457177>

Available online at: <http://www.iajps.com>

Research Article

END TREATMENT RESPONSE OF CHRONIC HEPATITIS C VIRUS GENOTYPE 3 INFECTION WITH SOFOSBUVIR AND RIBAVIRIN AT 24 WEEKS

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Article Received: June 2019

Accepted: July 2019

Published: September 2019

Abstract:

Background: Chronic hepatitis C is a global problem and is particularly concentrated in the developing world. There is paucity of literature regarding management of chronic hepatitis C in lower- & middle-income countries.

Objectives: The aim of this study was to present management strategies in chronic hepatitis C virus infections using the novel chemotherapeutic drugs.

Methods: This is a prospective cohort study of six months duration which was conducted at the department of internal medicine, Mufti Mehmood Teaching Hospital, Dera Ismail Khan. We included adult (14-75 Years) hepatitis C positive naive patients detected on PCR from both genders. Follow up PCR was performed at 12 weeks and 24 weeks. Excluded cases were recurrent hepatitis C infection, cirrhotic, Hepatocellular Carcinoma, hypersensitivity to the chemotherapeutics and those with multiple hepatic viral infections. Data was collected about patient demographics, inclusion PCR results, treatment details, and follow-up PCR readings.

Results: A total of 115 patients were included in this study. There were 60 (52.2%) males and 55 (47.8%) females. The age range was 14 to 75 years with a mean age of 40.02 ± 13.09 years. Among the 111 patient's data which was available for analysis, 106 (92.2%) patients PCR was negative for viral RNA, while it was positive for 5 (4.3%) cases.

Conclusion: Sofosbuvir and Ribavirin combination is very effective in treatment naive chronic hepatitis C patients with Genotype 3 in Pakistani population with minimal side effects and is cost effective.

Key Words: Sofosbuvir, Ribavirin, HCV infection, ETR (End Treatment Response).

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Please cite this article in press Taj Muhammad Khan et al., End Treatment Response Of Chronic Hepatitis C Virus Genotype 3 Infection With Sofosbuvir And Ribavirin At 24 Weeks., Indo Am. J. P. Sci, 2019; 06[09].

INTRODUCTION:

Chronic hepatitis C is a worldwide disease which can further lead to various complications like cirrhosis of liver and hepatocellular carcinoma. Worldwide 130-150 Million people have chronic hepatitis C infection.¹ In developing countries like Pakistan chronic Hepatitis C prevalence is increasing.² In Pakistan around 8-10 Million people are affected with chronic Hepatitis C.³⁻⁴

There are six genotypes of Hepatitis C virus with various different subtypes.⁵ The most common genotype in Pakistan is Genotype 3a.⁶

Previously interferon was the main therapy for the treatment of chronic Hepatitis C but interferon was associated with unsatisfactory results and many side effects.⁷⁻⁸ Sofosbuvir is a direct acting nucleotide polymerase inhibitor and is recommended for the treatment of chronic hepatitis C.⁹ Sofosbuvir is given orally with daily dose of 400mg and has a very good response.¹⁰⁻¹¹ Sofosbuvir has very good results against Hepatitis C with high potency, fewer side effects and has a very good efficacy against Genotype 3.¹²⁻¹³

Most of our population live in Rural area(66% of Pakistani population) and the prevalence of hepatitis C is also high in these rural area.¹⁴ Our study is also based in the Rural areas of Khyber Pakhtunkhwa.

In low and middle-income countries like Pakistan Hepatitis C is very prevalent and Pakistan ranks No 2 in such countries with prevalence of 6.7%.¹⁶ There is paucity of studies on this topic in whole country especially in the southern districts of Khyber Pakhtunkhwa. We want to present our management strategies for these patients which have not previously been reported in the literature from our community and to determine the clinical efficacy of Sofosbuvir and Ribavirin among patients with Chronic Hepatitis C infection.

MATERIAL AND METHODS:

After approval from the ethical review board this study was conducted in Mufti Mehmood Teaching Hospital Dera Ismail Khan. This study was observational Cohort study and the time period of the study was six months (February 2017 to July 2017). The study is a 2 stage observational cohort study. In the first stage we assessed the treatment response by EVR (Early Virological Response) by doing HCV RNA PCR at 12 weeks. In this second stage we assessed treatment response by ETR (End Treatment Response) by doing PCR at 24 weeks. Selection of the patients was by consecutive sampling

from the outpatient department with informed consent and inclusion criteria satisfied. Screening of the patients was done by standard laboratory tests, HCV RNA PCR and genotype of HCV. Drugs were given to the patients according to Asia Pacific Association for the Study of Liver (APASL), Sofosbuvir 400 mg daily once a day and Ribavirin according to the weight (1000 mg in divided doses with weight of less than 75 Kg and 1200 mg with weight more than 75Kg). All the patients included in this study were above 14 years with HCV positive on PCR.

Inclusion and exclusion criteria:**The following Inclusion criteria was used**

- All patients with Positive PCR and Genotype 3.
- Age above 14 years
- Patients with no ultra sound abnormalities of the liver or Child-Pugh Score A Patients.
- Patients not previously treatment for hepatitis C (Treatment Naïve Patients).

The following patients were excluded from the study

- Age below 14 years
- Child-Pugh Score of B or worse
- Patients with Concomitant Hepatitis B or HIV infection

RESULTS:

A total of 115 patients were included in this study. There were 60 (52.2%) males and 55 (47.8%) females. The age range was 14 to 75 years with a mean age of 40.02 ± 13.09 years. There were 94 (81.7%) patients below 50 years of age, while the rest of 21 (18.3%) were between 51 to 70 years.

At 24 weeks follow-up, 4 patients were lost to follow-up. Among the 111 patients data which was available for analysis, 106 (92.2%) patients PCR was negative for viral RNA, while it was positive for 5 (4.3%) cases. In the five positive cases at 24 weeks, there were 3 males & 2 females. On chi-square analysis the gender difference was non-significant ($p = 0.935$).

DISCUSSION:

In this Observational Cohort study, we administered Sofosbuvir plus Ribavirin in previously untreated and non-cirrhotic patient with chronic Hepatitis C Genotype 3. Hepatitis C is a worldwide disease more concentrated in developing countries. The main objectives of treating Hepatitis C infection is to prevent or minimize complications like liver cirrhosis, Hepatocellular Carcinoma etc.

Extraordinary achievements have been made in the development of antiviral therapy against Hepatitis C virus in the form of direct acting antiviral agent which attack those viral encoded proteins that are necessary for replication like NS5A, NS5B and NS3/4A.²²

A total of 115 patients were included in this study. In this study in the stage 1 there was very rapid fall of the hepatitis C RNA and we achieved RVR of 96.5% which was very encouraging and in agreement with other studies.¹¹ In this second stage of the study we will assess ETR (End Treatment Response) at 24 weeks. In this study all the patients were treatment naïve patients and without cirrhosis. In One international Study treatment of chronic Hepatitis C with Sofosbuvir and Ribavirin achieved 90-96% response rate at 24 weeks of treatment which is similar with the results of our study.¹⁷ Another local study conducted by Zahid Azam, et al showed 98% response in chronic Hepatitis C patients treated with Sofosbuvir.¹⁸

Regarding the treatment of hepatitis C virus VALENCE study showed 85% Response rate treated with sofosbuvir at 24 weeks.¹⁹ That was a bit discouraging and inferior to our results. In another Quasi experimental study conducted in Rawalpindi Response Rate (ETR) was 96.5% in HCV genotype 3 treated with Sofosbuvir.²⁰ This is very close to our result and much better than Zeuzem et al., 2014. In another local study conducted at Holy Family Rawalpindi ETR was achieved in 96.5% of the patients.²¹ This result was slightly quite similar to our study.

So far as the treatment of chronic Hepatitis is concerned our study results are quite encouraging. The safety concerns of sofosbuvir and Ribavirin are minimal in our population. No serious side effects were observed during the study. Most of the patients reported only headache, fatigue, Myalgias and weakness which was easily managed without any difficulties. None of our patients required blood transfusions.

CONCLUSIONS:

Sofosbuvir and ribavirin combined treatment is very effective in chronic hepatitis C genotype 3 patients in our population. It is cost effective and very well tolerated with fewer side effects.

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