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EARLY VIROLOGICAL RESPONSE OF CHRONIC HEPATITIS C GENOTYPE 3 VIRUS INFECTION TO SOFOSBUVIR AND RIBAVIRIN AT 12 WEEKS (EVR).

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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.*

Materials &Methods:*This is a prospective cohort study of six months duration which was conducted at the department of internal medicine, Mufti Mehmood Teaching Hospital, Dear Ismail Khan. We included adult (14-75 Years) hepatitis C positive patients detected on PCR from both genders. Follow up PCR was performed at 12 weeks. Hepatitis C virus genotyping was also done before starting antiviral therapy. Excluded cases were recurrent 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 114 cases who underwent PCR at 12 weeks, 111 (96.5%) cases were clear and no viral RNA was detected.*

Conclusion: *Sofosbuvir and ribavirin combination treatment is very effective in chronic hepatitis C genotype 3 patients, associated with negligible side effectsand tolerated much better.*

Key Words:*Sofosbuvir, HCV infection, Early Virologic Response (EVR)*

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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 theprevalence of hepatitis C is also high in these rural areas.[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 countries 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 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 the second stage we will assess treatment response by ETR (End TreatmentResponse) 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), Sofobuvir 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 without any cirrhosis on the Liver Ultrasound.

Inclusion and exclusion criteria: The following Inclusion criteria was used

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

The following patients were excluded from the study

a) Age below 14 years
b) Child-Pugh Score of B or worse
c) 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 12 weeks follow-up, we lost 1 (0.9%) patient to follow-up. Among the 114 cases who underwent PCR at 12 weeks, 111 (96.5%) cases were clear and no viral RNA was detected. In three (2.6%) patients (all males), the PCR detected viral load at the 12th week. On chi-square analysis, we did not find significant difference for association of gender groups with PCR positivity (p = 0.150).

DISCUSSION:

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

A total of 115 patients were included in this study. In this study there was very rapid fall of the hepatitis C RNA and we achieved EVR of 96.5% which is very encouraging and in agreement with other studies.[11]In our study all the patients were treatment naïve patients and without cirrhosis. In One national Study treatment of chronic Hepatitis C with Sofosbuvir and Ribavirin at 12 weeks achieved 88.57 % of the response rate which is slightly inferior to our study.[17]Another international study conducted by Lawitz E, etal the response of the combination treatment sofosbuvir and Ribavirin was 67% at 12 weeks which was discouraging and inferior to our study.[18]

Regarding the treatment of hepatitis C virus, a local study at Karachi showed a response of 92.3% which is comparable with our study.[19] In ELECTRON study the response rate of HCV genotype 3 was 100% treated with Sofosbuvir plus Ribavirin. [20] This is very close and better than our result. In another local studyconducted at holy family Rawalpindi EVR was achieved in 90% of the patients.[21]Again this result was slightly inferior to our study.
In one real life Scandinavian HCV treatment study of patients with genotype 3 the response rate was 96% at 12 weeks of treatment with sofobuvir and Ribavirin which is almost the exact results our study produced.

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 combination is a very effective treatment for hepatitis C virus genotype 3 infection. It is cost effective for low- and middle-income countries like Pakistan. It is also safe with no major side effects.

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