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Outcome of Sofosbuvir and Ribavirin based treatment in genotype 3 of cirrhotic chronic hepatitis C patients

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Abstract
Introduction: *Hepatitis C virus is a leading cause of chronic liver disease in both industrialized and developing countries. Considering the high prevelance of chronically infected individuals, the burden of disease and the absence of a vaccine, treatment forms part of the control of the disease. Sofosbuvir is a pyrimidine nucleotide analogue with high anti-viral activity against all genotypes and shows a high genetic barrier to resistance*
Aims and Objectives: *The aim of this study is to assess the Outcome of Sofosbuvir and Ribavirin based treatment in genotype 3 of cirrhotic chronic hepatitis C patients.*
Materials and Methods*: This was a prospective study carried in the department of Gastroenterology Sheri Kashmir Institute of medical sciences soura between 2015 to 2016 involving chronic cirrhotic hepatitis C patients of Genotype 3 with age more than 18yrs. Data analysis was performed using the IBM SPSS version 22.*
Results and Observations: *In this prospective study the total number of patients was (n=29). The mean age (in years) of patients was (41.2 ±11.77). The number of male patients was 11 (37.93%) and of female patients wa18s (62.06%). The number of cirrhotic patients in treatment naïve group was (n=23) while that in treatment experienced group was (n=6).On comparison on the basis of sustained virological response at twelve weeks of the completion of treatment (SVR12) we observed that treatment naïve cirrhotic patients had (SVR12=100%) while in the treatment experienced non cirrhotic patients (SVR12=66.7%).Sustained virological response (SVR12) among male and female patients was statistically not significant.*
Conclusion: *The sofosbuvir and ribavirin based therapy shows potentially good rates of sustained virological response in patients with chronic hepatitis C genotype 3 patients and is cost effective and easy to adminster.*
Keywords: *Hepatitis C; Genotype 3;treatment.*

Introduction

HCV was discovered to be the major cause of non-A non-B hepatitis in 1989, and is now known to be a leading cause of chronic liver disease in both industrialized and developing countries. Considering the high prevalence of chronically infected individuals, the burden of disease and the absence of a vaccine, treatment will form part of the control of the disease. Even considering the all majority of those with persistent infection are unaware of the infection and screening programs to identify patients will be required to prevent silent progression of the disease[1,2].

HCV genome, comprises six genotypes and several subtypes[3]. In populous countries such as India and Pakistan, HCV-3 is the predominant genotype[4]. Peginterferon (PEG-IFN) a-2b (1.5 mg/kg/week) plus ribavirin (RBV) (800–1400 mg/day) or PEG-IFN a-2a (180 mg/week) plus RBV (800 mg/day) for 24 weeks have been the established standard of care regimens for patients with HCV-3[5]. Sofosbuvir is a pyrimidine nucleotide analogue with high anti-viral activity against all genotypes and shows a high genetic barrier to resistance[6]. Regardless of HCV genotype sofosbuvir based triple therapy resulted in SVR rates of 83–100%[7]. The combination of sofosbuvir (200 mg or 400 mg once daily) and PEG-IFN/RBV for 12 weeks demonstrated efficacy, reaching SVR12 of 91% in HCV-1 and 92% in HCV-2/ HCV-3[8]. The tremendous improvement in SVR rates in genotype 1 and genotype 2 has rendered genotype 3 HCV the major challenge, as it continues to globally afflict a large population of patients. Sofosbuvir and ribavirin is the first all-oral therapy regimen that has been approved in the US by the FDA for use in Genotype 2 and 3 patients[9].

Aims and Objectives

The aim of this study is to assess the outcome of sofosbuvir and ribavirin in cirrhotic chronic hepatitis C patients with Genotype 3.

Materials and Methods

This was a prospective study carried in the department of Gastroenterology Sheri Kashmir Institute of medical sciences soura between 2015 to 2016.

The study was an interventional study involving chronic hepatitis C patients of Genotype 3.

Cirrhotic patients were included in this study to receive Sofosbovir 400mg and Ribavirin weight based (1000mg/day for <75kgs and 1200mg/day for > 75kgs weight) for 24 weeks duration,

Inclusion Criteria:

Chronic hepatitis C genotype 3 Cirrhotic patients.

Treatment Naive and experienced patients.

Age more than 18 years

Both male and female.

Non pregnant and non lactating females.

Diagnosis of cirrhosis was based on Fibroscan showing cirrhosis or results >12.5 kPa.

Statistical Analysis

Data analysis was performed using the IBM SPSS version 22.Continous variables were expressed as mean±SD. Two sided unpaired test was performed for continuous variables and x^2 test for discrete variables.

Results and Observations

In this prospective study carried in the department of Gastroenterology Sheri Kashmir Institute of medical sciences Soura, Srinagar between 2015 to 2016 involving chronic hepatitis C patients of Genotype 3,the total number of patients was(n=29). The mean age (in years) of patients was (41.2 ±11.77). The age distribution of study patients is depicted in (Table1). We observed that the number of male patients in our study was 11 (37.93%) and the number of female patients was 18(62.06%). This observation showed predominance of female patients (Table 2). We observed that in our patients the baseline hepatitis C RNA load (iu/ml) had a mean of 163131891 IU/ml (±1146556279). The range of baseline RNA Load (IU/mL) is depicted in (Table3). Baseline laboratory parameters observed in our patients is presented in (Table4). In our study we

observed that the number of cirrhotic patients in treatment naïve group was (n=23) while the number of cirrhotic patients in treatment experienced group was (n=6).On comparison on the basis of sustained virological response at twelve weeks of the completion of treatment (SVR12) we observed that treatment naïve cirrhotic patients had (SVR12=100%) while in the treatment experienced non cirrhotic patients (SVR12=66.7%).

This difference in sustained virological response (SVR12) was statistically significant (P-value0.037).These results are presented in (Table5). In our study we observed and compared sustained virological response (SVR12) among male (n=11) and female (18) patients. The sustained virological response in male patients (SVR12=90.9) and among female patients (SVR12=88.8%).This difference was however statistically not significant. These observations are shown in (Table 6).

Table 1: Age distribution of study patients

Age (years)	Frequency	Percentage
19-29	4	13.7
30-39	12	41.37
40-49	8	27.5
50-59	3	10.34
≥ 60	2	6.8
Mean±SD=(41.2 ±11.77).		

Table 2: Gender distribution of study patients

Gender	Frequency	Percentage
Male	11	37.93
Female	18	62.06
Total	29	100

Table 3: Showing baseline RNA load (IU/ML) among study patients

	Baseline RNA Load (IU/ML)
Mean	163131891
SD	1146556279
Min	470
Max	9797701497

Table 4: Showing descriptive statistics of baseline laboratory parameters

Parameter	Mean	SD	Min	Max
HB	12.82	1.93	8.5	17.77
TLC	5.42	2.0	2.4	12.07
PLT	28.12	40.33	1.0	165
BIL	1.47	1.17	0.3	6.95
AST	51.41	25.66	9	111
ALT	112.01	93.10	17	655
PRO	7.66	0.75	4.9	9.5
ALB	3.76	0.47	2.32	4.82
INR	1.22	0.12	1.07	1.78

Table 5: Comparison based on SVR12 among treatment naïve and treatment experienced cirrhotic patients

SVR12	Treatment Naïve		Treatment Experienced		P-value
	Number (n).	%age	Number (n).	%age	
Yes	23	100	4	66.7	0.037*
No	0	0.0	2	33.3	
Total	23	100	6	100	

Table 6: Comparison based on SVR12 as per gender

SVR12	Male		Female		P-value
	Number (n).	%age	Number (n).	%age	
Yes	10	90.9	16	88.8	0.622
No	1	9.09	2	11.11	
Total	11	100	18	100	

Discussion

In our study of 29 patients of cirrhotic chronic hepatitis C genotype 3 we found that all the patients in treatment naïve group achieved sustained Virological response at 12 weeks of completing treatment (SVR12=100%). In Valence study[10] Among the treatment naïve patients with cirrhosis(n=13) sustained virological response was achieved by twelve patients(SVR12=92%). In treatment experienced patients with cirrhosis (n=47) sustained virological response was achieved by twenty nine patients (SVR12=61.7%). In our study we found that among 6 treatment experienced patients sustained virological response was achieved by 4 patients (SVR12=66.7%).Therefore the observations regarding sustained virological response (SVR12) in our study are in agreement with the Valence study.

In ASTRAL-3[11] study the patients with genotype 3 when treated with sofsobuvir and ribavirin for twenty four weeks among the treatment naïve cirrhoticgroup (n=45) sustained virological response was achieved by thirty three patients (SVR12=73%). The higher sustained virological response in our study can partly be explained by small patient number as compared to ASTRAL 3 study.

In BOSON study[12] among treatment naïve patients (n=94) who received sofosbuvir and ribavirin for twenty four weeks sustained virological response was achieved by 58%, while as in treatment experienced patients (n=88) sustained virological response was achieved by seventy patients (SVR12=80%). In our study of chronic hepatitis C genotype 3 we found that all the patients in treatment naïve achieved sustained Virological response at 12 weeks of completing treatment (SVR12=100%). In treatment experienced group those patients with cirrhosis (n=6) sustained virological response was achieved by four patients (SVR12=66.7%).The sustained virological response at 12 weeks of completing (SVR12) in our study was higher in treatment naïve group as compared to those in BOSON study. However in treatment experienced group the SVR12 was almost similar as those in BOSON study.

In POSITRON study[13] sofosbuvir and ribavirin was given for only twelve weeks in genotype 3 patients .Among treated patients (n=98) sustained virological response was achieved by 21%.

The high sustained virological response in our study as compared to the POSITRON study can be explained by the fact that extending the treatment duration from twelve weeks to twenty four weeks significantly increases the sustained virological response. These observations are in accordance with the published literature.

The FUSION study[14] in treatment experienced patients with genotype three observed that patient who received sofosbuvir and ribavirin for twelve weeks only had sustained virological response (SVR12=19%) in cirrhotics. The higher sustained virological response in our study can be explained by increased duration of treatment .This observation of improved sustained virological response on increasing the treatment duration from twelve and sixteen weeks to twenty four weeks is in agreement with the published data. In Valence study[6] among female patients (n=95) sustained virological response at twelve weeks of completion of treatment was(SVR12=93.7%) and among the male patients(n=155) the sustained virological response rate at twelve weeks of completion of treatment was(SVR12=80.0%).The sustained virological response (SVR12) was slightly more in male patients in our study however it was statistically insignificant. The higher sustained virological response (SVR12) in female population in Valence Study can partly by explained higher number of male patients(n=155) and non significant difference in (SVR12) among male and female patients in our study can partly be explained on the basis of small sample size.

Summary and Conclusion

The oral sofosbuvir and ribavirin results in high rates of sustained virological response in patients with chronic hepatitis C genotype 3 patients. This treatment is cost effective, easy to adminster and will help in better outreach with less frequent monitoring of patients treated.

Conflict of interest: None

Acknowledgment: None

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