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EFFICACY OF SOFOSBUVIR AND RIBAVIRIN IN NON CIRRHOTIC CHRONIC HEPATITIS C PATIENTS WITH GENOTYPE 3

Gastroenterology

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ABSTRACT

Introduction: HCV is a leading cause of chronic liver disease in both industrialized and developing countries. The high number of chronically infected individuals, the burden of disease and the absence of a vaccine indicates that treatment will form part of the control of the disease.

Aims and objectives : The aim of this study is to assess the efficacy of sofosbuvir and ribavirin in non 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 involving chronic non 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: The total number of patients was(n=50). The mean age was (40.2 ±11.62) yrs with male patients being 20 (40%) and female patients 30 (60%). In treatment naïve group we had 40 while in treatment experienced group we had 10 patients. Sustained virological response at twelve weeks of the completion of treatment (SVR12) in treatment naïve was 100% while in the treatment experienced it was 80.0%. Sustained virological response (SVR12) difference among male and female patients was statistically not significant.

Discussion: The results of our study were consistent with other studies although some differences were there due to difference in sample size . The final results were very encouraging regarding the efficacy of the drugs.

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 offers an alternative to pegylated interferon based regimen, is cost effective , easy to adminster as the therepy is oral and also convenient.

KEYWORDS

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. The high number of chronically infected individuals, the burden of disease and the absence of a vaccine indicates that treatment will form part of the control of the disease. However the 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]

AIMS AND OBJECTIVES:

The aim of this study is to assess the efficacy of sofosbuvir and ribavirin in non cirrhotic chronic hepatitis C patients with Genotype 3.The primary objective is a sustained virologic response at 12 weeks after the end of treatment. This response is defined as a level of HCV RNA below the lower limit of quantification (25 IU per milliliter).

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.Non 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 Non 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.

STATISTICALANALYSIS:

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 our study which was a prospective study carried in the department of Gastroenterology Sheri Kashmir Institute of Medical Sciences Soura between 2015 to 2016 involving chronic hepatitis C patients of Genotype 3.The total number of patients was(n=50). The mean age (in years) of patients was (40.2 ±11.62). The age distribution of study patients is depicted in (Table1). We observed that the number of male patients in our study was 20 (40%) and the number of female patients was 30 (60%). This observation showed predominance of female patients in our study (Table 2). We observed that in our patients the baseline hepatitis C RNA load (iu/ml) had a mean of 163131981 IU/ml (±1146556310). The range of baseline RNA Load (IU/mL) is depicted in (Table3). Baseline laboratory parameters observed in the patients is presented in (Table4) In our study we observed that the number of non cirrhotic patients in treatment naïve group was (n=40) while the number of non cirrhotic patients in treatment experienced group was (n=10).On comparison on the basis of sustained virological response at twelve weeks of the completion of treatment (SVR12) we observed that treatment naïve non cirrhotic patients had (SVR12=100%) while in the treatment experienced non cirrhotic patients it was (SVR12=80.0%). These results are presented in (Table5). In our study we observed and compared sustained virological response (SVR12) among male (n=20) and female (30) patients. The sustained virological response in male patients (SVR12=96.9) and among female patients (SVR12=93.6%).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	7	13.9
30-39	20	39.2
40-49	13	26.6
50-59	6	12.7
≥ 60	4	7.6
Mean±SD=40.2±11.62		

Table 2: Gender distribution of study patients		
Gender	**Frequency**	**Percentage**
Male	20	40
Female	30	60
Total	50	100

Table 3: Showing baseline RNA load (IU/ML) among study patients	
	Baseline RNA Load (IU/ML)
Mean	163131981
SD	1146556310
Min	488
Max	9797701586

Table 4: Showing descriptive statistics of baseline laboratory parameters				
Parameter	**Mean**	**SD**	**Min**	**Max**
HB	12.88	1.97	8.5	17.8
TLC	5.91	2.01	2.6	12.2
PLT	28.32	40.36	1.01	174
BIL	1.37	1.14	0.3	6.5
AST	48.41	25.76	10	105
ALT	114.01	93.23	18	612
PRO	7.86	0.78	6	10.5
ALB	4.16	0.53	2.4	4.9
INR	1.19	0.16	1	1.85

Table 5: Comparison based on SVR12 among treatment naïve and treatment experienced non cirrhotic patients					
SVR12	**Treatment Naïve**		**Treatment Experienced**		**P-value**
	Number (n).	%age	Number (n).	%age	
Yes	40	100	8	80	0.037*
No	0	0.0	2	20	
Total	40	100	10	100	

Table 6: Comparison based on SVR12 as per gender					
SVR12	**Male**		**Female**		**P-value**
	Number (n).	**%age**	**Number (n).**	**%age**	
Yes	31	96.9	29	93.6	0.643
No	1	3.1	3	6.4	
Total	20	100	30	100	

DISCUSSION:

In our study of 50 patients of non 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 among treatment naïve genotype 3 patients (n=105) Sustained virlogical response at 12 weeks of completion of treatment was achieved by ninety nine patients(SVR12=94%).[6] In our study we found that in treatment experienced patients (n=10) sustained virological response was achieved by eight patients (SVR12=80%).Therefore the observations regarding sustained virological response (SVR12) in our study are in agreement with the Valence study.

In ASTRAL-3 study the patients with genotype 3 when treated with sofsobuvir and ribavirin for twenty four weeks among the treatment naïve non cirrhotic patient(n=156) sustained virological response was achieved by one hundred forty one patients(SVR12=90%). In treatment experienced non cirrhotic (n=31) sustained virological response was achieved by twenty two patients (SVR12=71%) .The higher sustained virological response in our study can partly be explained by small patient number as compared to ASTRAL 3 study.[7]

In BOSON study among treatment naïve patients (n=94) who received sofosbuvir and ribavirin for twenty four weeks sustained virological response was achieved by eighty three patients (SVR12=88%) while as in treatment experienced patients (n=88) sustained virological response was achieved by seventy patients (SVR12=80%).Further non cirrhotics patients (n=126) had sustained virological response of eighty seven percent (SVR12=87%).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.[8]

In POSITRON study sofosbuvir and ribavirin was given for only twelve weeks in genotype 3 patients .Among treated patients (n=98) sustained virological response was achieved by (SVR12=68%).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.[9]

The FUSION study in treatment experienced patients with genotype three observed that patient who received sofosbuvir and ribavirin for twelve weeks only had sustained virological response (SVR12=37%) in non cirrhotics.[10]

SVR12 after treatment of G3 patients without cirrhosis for 16 weeks revealed a SVR12 of 63%.

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 offers an alternative to pegylated interferon based regimen, is cost effective , easy to adminster as the therepy is oral and also convenient. Further it will help in better outreach with less frequent monitoring of patients treated.

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