Original Article

End Treatment Response of Chronic Hepatitis C with Directly Acting Oral Antivirals at 12 Weeks

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ABSTRACT

Objective: To determine the end treatment response of directly acting antivirals (DAAs) in chronic hepatitis C patients with reduced adverse effects.

Study Design: Prospective study

Place and Duration of Study: This study was conducted at the Department of Medicine of Al-Nafees Medical College and Hospital, Islamabad from 26th March 2019 to 26th September 2019.

Materials and Methods: The study was conducted after approval from hospital ethical committee. The chronic hepatitis C patients with detectable viral load on PCR with genotype 3 between ages 30-60 years were included in the study after taking informed written consent. Demographic data like age, gender and co-morbid were taken. Baseline investigations and USG abdomen were done to exclude the patients having pregnancy, renal failure, cirrhosis, portal hypertension and suspected hepatocellular carcinoma. The PCR for HCV RNA was done at 12 weeks to look for end treatment response of directly acting antivirals. The collected data was analyzed by using SPSS 23 version.

Results: In study total 60 patients were enrolled and divided in two groups of 30 each. In group A Sofosbuvir and Daclatasvir was given to patients and in group B Sofosbuvir with Velpatasvir was given to patients. The mean age of the patients in group A was 43.23±8.87 year and in group B was 43.53±10.10 year. Primary outcome of the study was end treatment response at 12 weeks in group A (Sofosbuvir and Daclatasvir) and In group B (Sofosbuvir with Velpatasvir) 90.0% and 93.3% with undetectable PCR respectively. Secondary outcome was of adverse effects that in group A 16.7% patients had nausea, 13.3% patients had vomiting, 20.0% patients had fatigue, 16.7% patients had allergic reactions, 16.7% patients had decreased appetite, 6.7% patients had oral ulcer, 23.3% patients had headache, 3.3% patient had diarrhea and 10.0% patient had fever. In group B 10.0% patients had nausea, 6.7% patients had vomiting, 16.7% patients had fatigue, 10.0% patients had allergic reaction, 13.3% patients had decreased appetite, 6.7% patients had oral ulcers, 10.0% patients had headache, 6.7% patients had diarrhea and 6.7% patients had fever. In group A and B no patients had pancytopenia and jaundice.

Conclusion: Newer Directly acting oral antivirals are better and safe treatment option for chronic Hepatitis C. It is found that combination of Velpatasvir plus Sofosbuvir though expensive has a marginal edge over Sofosbuvir plus Daclatasvir combination.

Key Words: Directly acting oral antivirals, sustained viral response, chronic hepatitis C, cirrhosis of liver, hepatocellular carcinoma

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INTRODUCTION

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Hepatitis C is HCV RNA and is a developing health problem currently in the world and estimated more than 71 million people are affected.[1]

Hepatitis is among the primary cause of death ranked 7th globally and Pakistan has 2nd most affected population of chronic hepatitis C. Pakistan has 10 million chronically infected hepatitis C virus (HCV) carriers. [2]

In Pakistan, the most common HCV genotype is 3a and 3b and genotype 1a and 2a is present in less population. In Khyber Pakhtunkhwa, Punjab, and Sindh, genotypes 3a and 3b occurred the most prevalent, while most of the patients from Baluchistan suffered with genotypes 1a and 2a.[3]

The most common causes are non-sterilized equipment during the procedures and widespread in rural areas.[4]

Conventional interferon therapy was introduced in 1991 and pegINF in 2001 with very low sustained viral response (SVR) and about 50% to 60 % patients were having treatment failure, and adverse effects like thrombocytopenia, pancytopenia, neurotoxicity, depression and myalgia were more common.[5]

The latest treatment guidelines of HCV infection depends on IFN-free treatment. Direct-acting antivirals (DAAs) target non-structural proteins of HCV resulting in the arrest of viral replication[5] with highly positive results.[6]

It was difficult to achieve sustained viral response (SVR) for genotype 3 with conventional mode of treatment. Patients had to use the treatment regimen repeatedly, which carried financial burden as well as increased adverse effects.[7]

Directly acting antivirals have increased the treatment response of the chronic hepatitis C and are effective against all genotypes (1-6) with sustained viral response >90% with few side effects and can be used in decompensated chronic liver disease (DCLD) patients as well.[8]

The current study is meant to evaluate the response of drug regimens in our population and its future prospective for the treatment of chronic hepatitis C.

MATERIALS AND METHODS

This prospective study (interventional study design) was conducted at the outpatient department, Department of Medicine, Al- Nafees Medical College & Hospital Islamabad from 26th March 2019 to 26th September 2019 after approval from the hospital's ethical committee. The sample size was calculated (n=60) with confidence interval 95%, estimated true proportion 50% by Epitools software.

Detailed history regarding the illness was obtained from each patient. A complete clinical examination was performed and informed written consent was taken from each patient. Patients with chronic hepatitis C with detectable viral load on quantitative PCR with genotype 3 between ages 30-60 years were selected and have not received oral antiviral treatment previously. Baseline investigations and USG abdomen were done to exclude the patients having pregnancy, renal failure, cirrhosis, portal hypertension and suspected hepatocellular carcinoma. The PCR for HCV RNA was done at 12 weeks to look for end treatment response of directly acting antivirals.

After collecting the data, it was entered in a specially designed performa. Data was analyzed by the Statistical Package for Social Sciences (SPSS) version 23. Quantitative variables like age, gender, mean and SD was calculated. P-value ≤ 0.05 was considered as significant.

RESULTS

In study total 60 patients were enrolled and divided in two groups of 30 each. In group A Sofosbuvir and Daclatasvir were given to patients and in group B Sofosbuvir with Velpatasvir were given to patients. The mean age of the patients in group A was 43.23±8.87 year and in group B was 43.53±10.10 year. In group A 16(53.3%) were male and 14(46.7%) were female and in group B 18(60.0%) were male and 12(40.0%) were female. Males were more than females and in group B male patients were more than group B as shown in Figure-1.

Primary outcome of the study was end treatment response at 12 weeks in group A (Sofosbuvir and Daclatasvir) and in group B (Sofosbuvir with Velpatasvir) 90.0% and 93.3% with undetectable PCR respectively as shown in Table-1.

Secondary outcome was of adverse effects that in group A 16.7% patients had nausea, 13.3% patients had vomiting, 20.0% patients had fatigue, 16.7% patients had allergic reactions, 16.7% patients had decreased appetite, 6.7% patients had oral ulcer, 23.3% patients had headache, 3.3% patient had diarrhea and 10.0% patient had fever. In group B 10.0% patients had nausea, 6.7% patients had vomiting, 16.7% patients had fatigue, 10.0% patients had allergic reaction, 13.3% patients had decreased appetite, 6.7% patients had oral ulcers, 10.0% patients had headache, 6.7% patients had diarrhea and 6.7% patients had fever as shown in Table-2. In group A and B no patients had pancytopenia and jaundice.

Table No.1: Results of PCR quantitative for HCV RNA at 12 weeks in study groups (n=60)

PCR Quantitative for HCV RNA at 12 weeks	Groups		Total	p value
	Group A (Sofosbuvir and daclatasvir)	Group B (Sofosbuvir with velpatasvir)		
Detectable	3	2	5	**0.640**
	10.0%	6.7%	8.3%	
Undetectable	27	28	55	
	90.0%	93.3%	91.7%	
Total	30	30	60	
	100.0%	100.0%	100.0%	

Table-2: Results of adverse effects at 12 weeks in study groups (n=60)

Adverse Effects	Groups		Total	p value
	Group A (Sofosbuvir and daclatasvir) n=30	Group B (Sofosbuvir with velpatasvir) n=30		
Nausea	16.7%	10.0%	13.3%	0.448
Vomiting	13.3%	6.7%	10.0%	0.389
Fatigue	20.0%	16.7%	18.3%	0.739
Allergic Reactions	16.7%	10.0%	13.3%	0.448
Decreased Appetite	16.7%	13.3%	15.0%	0.718
Oral Ulcers	6.7%	6.7%	6.7%	1.000
Headache	23.3%	10.0%	16.7%	0.166
Diarrhea	3.3%	6.7%	5.0%	0.554
Fever	10.0%	6.7%	8.3%	0.640

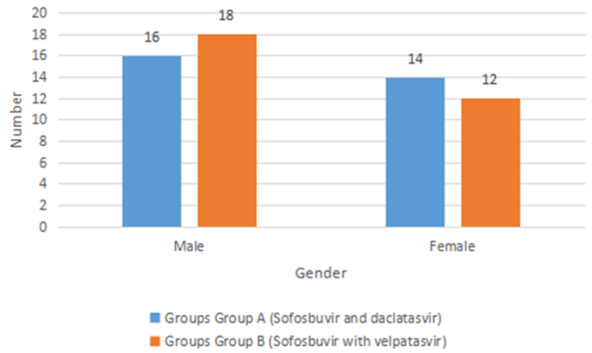

Figure No.1: Distribution gender in study groups (n=60)

DISCUSSION

The development of DAAs as cures for HCV infection was a revolution in biomedical research.

A fewer DAAs regimens are available and effective for the treatment of HCV genotype 3 infection, which is the second most prevalent HCV genotype globally, infecting approximately 54 million persons.

The European Association for the Study of the Liver (EASL) recommends sofosbuvir/daclatasvir ± ribavirin or sofosbuvir/velpatasvir ± ribavirin (ribavirin addition dependent upon treatment-experienced and cirrhosis status) for genotype 3.[9]

In the same way, the American Association for the Study of Liver Diseases (AASLD) recommends 12 weeks of sofosbuvir/daclatasvir or sofosbuvir/ velpatasvir for treatment-naïve and experienced patients without cirrhosis and addition of ribavirin for experienced patients with cirrhosis. [10]

These agents have shown high SVR rates of ~ 90% in clinical trials, shorter therapies, less toxicity, and regimens free of interferon.[11] In our study, treatment response in group A (sofosbuvir/daclatasvir) was 90.0% which is similar to the study of Salama and colleagues, included 475 patients with chronic HCV infection was 91% [11] and another study by Sulkowski MS et al. study efficacy of daclatasvir/sofosbuvir was found to be 92%.[12]

A study was done in Pakistan on 1,388 participants showed efficacy of 94.4% with sofosbuvir/daclatasvir and 94.7% with sofosbuvir/velpatasvir at 12 weeks which had better efficacy than our study which may be due to the reason that few patients were given ribavirin in combination too. The study was conducted on only genotype 3 infected patients.[13]

In a study conducted by Pamel S et al. on genotype 2 and 3 showed efficacy of 94.5% with sofosbuvir/ daclatasvir and 94.4% with sofosbuvir/velpatasvir in genotype 2. In genotype 3 showed 90.8% with sofosbuvir/daclatasvir and 92% with sofosbuvir/ velpatasvir which is comparable with our study as well.[14]

In a phase 3 RCT with 552 patients velpatasvir–sofosbuvir for 12 weeks (95%) was larger to sofosbuvir plus ribavirin for 24 weeks (80%) and was related with fewer adverse events, mainly less anemia which is also comparable with our results as well. [15]

In another actual observational study, among 4257 patients treated with sofosbuvir-based DAAs, and different genotypes and SVR achieved were 93–98% and 88%-98% for the different combinations which are comparable with our study as well.[16]

In summary, the results of this study support that these generic DAAs were effective in eradication of hepatitis C virus specifically genotype 3 and found to be safe and well-tolerated.

CONCLUSION

Newer Directly acting oral antivirals are better and safe treatment option for chronic Hepatitis C. It is found that combination of velpatasvir plus sofosbuvir though expensive has a marginal edge over sofosbuvir plus daclatasvir combination.

Recommendations: We recommend more studies with large sample size to be conducted to see the effectiveness and safety of DAA for treatment of hepatitis C with genotype 3 in different regions of Pakistan.

Author's Contribution:

Concept & Design of Study:	Danish Zia
Drafting:	Syed Saif Ur Rehman, Safdar Hussai
Data Analysis:	Muhammad Irshad Khan, Abida Mateen
Revisiting Critically:	Muhammad Wajad Munir
Final Approval of version:	Syed Saif Ur Rehman

Conflict of Interest: The study has no conflict of interest to declare by any author.

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