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Efficacy of Velpatasvir and Sofosbuvir Combination Therapy in Chronic HCV Patients

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ABSTRACT

Background: Chronic Hepatitis C is a prevalent infection in Pakistan. It can lead to complications like cirrhosis of liver, liver failure, hepatocellular carcinoma and death. Oral antiviral therapy has revolutionized the treatment of Hepatitis C. It can achieve eradication of HCV in the form of sustained virological response in HCV patients. **Objective:** We conducted a study to analyze the efficacy of Sofosbuvir, Velpatasvir combination therapy with Ribavirin except when there was a contraindication. **Study Design:** Prospective single Centre cohort study. **Settings:** Ather gastro liver Centre, Faisalabad Pakistan. **Duration:** The study duration was one year from January 2019 to December 2019. **Methods:** Study including all chronic Hepatitis C patients who underwent treatment for Chronic hepatitis C virus (HCV) with Sofosbuvir (SOF) and Velpatasvir (VELPA) combination therapy with Ribavirin (Rib). All patients were more than 18 years old. **Results:** 64% patients were male and 36% were females. 8.5 % patients were cirrhotic and all patients received Ribavirin. SVR was achieved in 115 / 117 (98.29%) patients. **Conclusion:** Sofosbuvir, Velpatasvir combination therapy with Ribavirin is an effective antiviral therapy for the treatment of chronic hepatitis C.

Keywords: *Hepatitis C, Sofosbuvir, Velpatasvir, Ribavirin, Naïve, HCV treatment in faisalabad, Cirrhosis, Sustained virological response.*

INTRODUCTION

Chronic HCV is a worldwide problem and about 71 million people are infected worldwide. In Pakistan the prevalence of chronic HCV is about 6.5% and, in some areas, it is about 14%.[1]

Chronic HCV is caused by RNA Flavivirus. It is a silent infection and many people are diagnosed when already have a number of complications. The active or passive vaccination does not exist till date. Intravenous drug abuse, unscreened blood products, needle stick injury to health care professionals and vertical transmission from mother to baby are major risk factors for transmission. The untreated cases have a risk of progression. Risk factors for progression of disease are male gender, immunosuppressive therapy, prothrombotic states and alcohol abuse.[2]

20% of chronic HCV patients present after developing cirrhosis. The survival rates of cirrhosis of liver are 95 % and 81% for 5 years and 10 years respectively. About 25% of cirrhotics develop complications within 10 years. Cirrhotics develop HCC by 2-5% per year.[3] It takes 6-12 weeks for antibodies to develop in the blood. PCR for HCV RNA can be detected in blood as early as 2-4 weeks after acute infection. There are six genotypes. Genotype has no effect on progression of disease but does affect response to treatment.[4] With the help of new antivirals, SVR is achieved in 90% to 100% of patients with new drugs. There are 4 major classes of DAAs: Protease Inhibitors (PI), Nucleoside polymerase inhibitors, non-Nucleoside polymerase inhibitors, NS5A replication complex inhibitors and host targeting antiviral agents.

Velpatasvir has been in use since 2018 in Pakistan. It has gained much importance because of very high anti-viral

activity due to NS5A inhibition against all Hepatitis C Genotypes. The patients with cirrhosis of liver can also be treated for 3 months along with non-cirrhotics. Sofosbuvir and Velpatasvir treatment is also very effective in patients with decompensated cirrhosis. Sofosbuvir and Velpatasvir is recommended for chronic HCV predominantly Genotype III population. It is a Pan-genotypic NS5A inhibitor and achieves 99% SVR rate in naïve, non-cirrhotic patients.[5]

The Sofosvbuvir/Velpatasvir combination therapy efficacy has been not been studied extensively in general HCV patients of Faisalabad. Our study is the first in this city with a population of more than 10 million people. The studies of Shahid *et al*. and Mehmood *et al* on SOF and VELPA combination therapy, in chronic hepatitis C patients with chronic renal failure and majority patients were on hemodialysis and large studies are lacking on in this subject.[6,7]

We conducted a study on Velpatasvir / Sofosbuvir combination therapy in hepatology clinics of Ather Gastro Liver Centre, Faisalabad. We hereby share our experience of treating chronic HCV patients with Sof/Velpa combination therapy.

METHODS

117 patients were included in this prospective cohort study. The study duration was one year from January 2019 to December 2019. The study was approved by ethical committee of Ather gastro liver Centre vide letter No 123/2018. Minimum sample size was calculated assuming 95 % confidence interval and 5 % margin of error. The patients received velpatasvir and sofosbuvir combination therapy in addition to ribavirin. The duration of treatment was three months for both cirrhotics and non cirrhotics. The standard criteria for being cirrhotic was low platelets, high total bilirubin in absence of other causes, high Prothrombin time and low albumin, reverse ALT to AST ratio, presence of splenomegaly, dilated portal vein and nodular liver on ultrasound or ascites. Presence of varices in esophagus, stomach and duodenum also indicate cirrhosis of liver or portal hypertension. Although Fibro scan is available as non invasive test for diagnosis of cirrhosis of liver but it was not available to all patients.

All patients having chronic HCV infection evidence by positive qualitative or quantitative PCR were included. Cirrhotics and non-cirrhotics, renal failure patients who were treated with sofosbuvir and velpatasvir were also included in the study.

Patients with hepatocellular carcinoma, advance cirrhotics having MELD score more than 18 and Child score more than 9 and patients with evidence of acute hepatitis and severe organ failure were excluded from study. Patients having other chronic liver diseases were also excluded from the study.

It was a Prospective cohort study. Outpatient clinic visits were scheduled at the end of weeks 4, 8 and 12 during treatment and 12 weeks after end of treatment. Patients were checked for safety and adverse effects. Data collected on prescribed Proforma from our medical record. Data entry as well as data analysis was done on SPSS version 22. Data analyzed and percentage of patients having SVR was calculated.

RESULTS

A total of 117 patients were studied. 64 (54.71%) were male and 53(45.29%) were female. 8.5 % were Cirrhotics. Most prevalent age group was from 40-50 years and mean age was 43 years (Range from 22 to 76 years). Non-Cirrhotic patients had SVR 99 %. Patients with Cirrhosis had SVR of 90%.

Table 1: Gender distribution of population

	Frequency	Percentage
Male	64	54.71%
Female	53	45.29 %
Total	117	100

Table 2: Frequency of different complications of cirrhosis

Variable	Frequency	Percent
Ascites	10	8.5 %
Hepatic Encephalopathy	5	4.38 %
Low Platelets	10	8.5 %
Decompensated Cirrhosis	10	8.5 % (fibroscan not done)
Non-Cirrhosis	107	91.45 %
Upper GI Bleeding	9	7.69 %

Table 3:

	SVR	No SVR
Decompensated Cirrhosis	9/10 (90%)	1/10
No-Cirrhosis	106 / 107 (98%)	1/107

DISCUSSION

In our study 8.5% were cirrhotics. This calculation was done on the basis of overt complications including ascites, varices, upper GI bleeding and low platelets on complete blood count readings. SVR among cirrhotics was 90%, lower than that of non-cirrhotics which was 98%. Our study results showed SVR of above 97%. Now in this study with Sof / Velpa combination therapy SVR is 92%.[10]

The efficacy of Velpatasvir in combination with Sofosbuvir has been studied in ASTRAL-I study done by Feld JJ and colleagues. In this study 53% patients were genotype -1, 19 % were cirrhotics and 32% were previously treated. The overall SVR was 99%.[8]

Foster and colleagues studied the effect of sof/velpa combination therapy in ASTRAL II and ASTRAL III studies. 134 patients were Genotype-II and 277 patients were Genotype-III. 29% patients were cirrhotics. 71(26%) patients were previously treated. Among them 20 were null responders and 51 were relapsers or partial responders. SVR was 99 % in genotype-II patients. In ASTRAL-III study the efficacy of Sofosvbuvir / Velpatasvir combination was confirmed in genotype-III patients and SVR was 95%.SVR for naïve non-cirrhotic patients was 98% and for naive cirrhotics it was 93%. The SVR was 91% in treatment experienced patients without cirrhosis and 89 % in treatment experienced cirrhotics.[9]

We already published a study on SOF / daclatasvir ribavirin combination therapy done in HCV population of Faisalabad study. The clinical setting was same as of our present study and SVR was 97.5 %.[10] In ASTRAL-V study done by Wayeles and colleagues and was mainly on HCV and HIV-I co-infected patients were studied. Among 106 patients, 18% were cirrhotics. The overall SVR was 95 % and the SVR among genotype-III patients was 92%.[11]

In the study of Alessandra one thousand four hundred twenty-nine patients were included. Majority patients were naive and fibrosis score was F0 / F1. The study of Alessandera showed SVR of 95.7% after treatment with Sofosbuvir and Velpatasvir. SVR was 87% in cirrhotic patients and 97% among non-cirrhotic patients and no additional benefits of ribavirin use were observed in non-cirrhotics. The overall SVR was 98.5% and in genotype-III patients it was 97.3%.[12] In the study of Ajit Sood and colleagues 129 patients were included. Majority of patients were of genotype-III 70 % and 22% were of genotype-I. The overall SVR rate was 93%.[13]

In the study of Rafael Esteban efficacy of sof-velpa therapy in chronic HCV patients with cirrhosis of liver was studied. SVR was 91% in patients treated with Sof / Velpa and 96% in patients treated with Sof / Velpa and Ribavirin respectively. In the patients who were positive for RAS had less effect on SVR.[14]

In the study of Michael P Curry the genotype-III patients were 15 % and majority were genotype-I. The overall SVR was 83%. It was 94% when Ribavirin was added. The SVR was 86% among those who received 24 weeks therapy.[15] The study of Hussein *et al*, was a meta-analysis of previous studies done on Sofosbuvir Velpatasvir, including six RCTs and showed SVR rate of 94.7% in genotype-III patients.[16]

In the study of Namiki Izumi 117 patients were treated with oral antivirals. Overall SVR was 97% and with genotype-I patients, it was 98%.[17] The study of Pianko *et al*, was done in Australia showed SVR of 100 % in non-cirrhotics with and without Ribavirin. The SVR was 88% in cirrhotics without Ribavirin and 96%in cirrhotics who were treated with SOF/ Velpa and Ribavirin.[18]

The study done by Isakov and colleagues was on genotype 1-6 on both naïve and treatment experienced patients. Study was done on 122 patients. Majority were genotype-I (66%) and 29% were genotype-III. Overall SVR was 99%.[19] Begovac did this case study on a patient infected with HCV genotype-III and also co-infected with HIV and on hemodialysis and treated with sofosbuvir and velpatasvir therapy. The patient achieved SVR.[20] M. Omata in APASAL guidelines published in 2015 mentioned velpatasvir as effective antiviral drug. These guidelines were published in Hepatology International in 2016.[21] Di Biago and colleagues studied different trials on DAA therapy for genotype-IV chronic HCV patients and concluded that Sof / Velpa combination therapy is very effective.[22]

Hussain Fathi and colleagues did systemic review of last 5 years publications data and concluded that sofosbuvir/ velpatasvir combination therapy is very effective.[23] N But *et al* treated 113 patients were with Sof/Velpa combination therapy.72% patients were non-cirrhotics and among them 91% achieved SVR. Among compensated cirrhotics SVR was achieved by 92% patients.[24] In the study of Arif Qayyum and colleagues on Sof / Velpa combination therapy the SVR was 97 %. In cirrhotics it was 95 % and in non-cirrhotics it was 100%.[25] The study of Saima Mushtaq was done on 1400 patients treated with Sof / Dacla and Sof/Velpa combinations in Islamabad. The SVR was 95% among those who received Sof / Velpa combination therapy. Among cirrhotics the SVR was 88% at week 24.[26] Our results are in comparison with these studies.

CONCLUSION

Among the patient with chronic hepatitis C virus, Velpatasvir is very effective when used with combination with Sofosbuvir. And Ribavirin. It is effective in Cirrhotics as well as Non-Cirrhotics as shown in many trials. Our study shows that Velpatasvir is effective also in genotype-III population which is prevalent in our country.

LIMITATIONS

It was a single arm study. Sample size was small and design was open-label. There was lack of resistance

testing and study population was not uniform. Adverse effects were not documented. A few patients did perform fibroscan. Fibroscan was not done on all patients due to availability and affordability issue, so few compensated cirrhosis patients might be grouped among non-cirrhotics. The benefits of adding ribavirin was given to patients where it was not contraindicated. Furthermore, record of CRF and HCC patients is not documented.

SUGGESTIONS / RECOMMENDATIONS

Large studies need to be done to confirm results and conclusions of our study. Ribavirin addition to chronic HCV patient treatment needed to be evaluated in our population.

CONFLICT OF INTEREST / DISCLOSURE

No conflict of interest nothing to disclose.

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