Response and Tolerability of Sofosbuvir Plus Velpatasvir in Patients With Hepatitis C Related Liver Cirrhosis

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Abstract

Objective: To determine the response and tolerability of Sofosbuvir plus Velpatasvir in patients with hepatitis C related liver cirrhosis in the studied Pakistani population. Our study also compared cirrhotic patients with non-cirrhotic ones in terms of treatment effectiveness as well as safety.

Material and Methods: This was a prospective observational study[11] performed at Department of Medicine, Hepatology and Gastroen-terology, SIMS/Services hospital, Lahore, from January 2022 to December 2022. The enrolled 100 patients were grouped into Group A (non-cirrhotic hepatitis C patients) and Group B (compensated cirrhotic hepatitis C patients). Sofosbuvir plus Velpatasvir was given to group A patients for 12 weeks & to group B patients for 24 weeks. Laboratory findings, response and adverse effects were recorded four weekly. The data was analysed using SPSS version 27. Comparisons were done between two studied patient's groups in terms of effectiveness and tolerability of the treatment. The p-values were significant if <0.05.

Results: ETR and SVR-12 were 98.1% and 94.3% in group A and 95.7% and 93.6% in group B. SVR-12 was comparable in two groups (p= 0.602). No adverse event leading to treatment withdrawal was reported in either group. However, mild worsening of abdominal was seen in one patient of group B (p= 0.470). Deterioration in blood indices was seen in 2 patients of group B while 3 patients of group A (P= 0.557). Mild ALT flare was seen in one patient of each group (p= 0.722).

Conclusion: Sofosbuvir plus Velpatasvir therapy was highly efficacious and safe in non-cirrhotic and compensated cirrhotic patients with chronic viral hepatitis C. The response and tolerability of treatment was comparable in both studied groups.

Keywords: Hepatitis C, Liver cirrhosis, Sofosbuvir, Velpatasvir, Sustained Virological Response.

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Introduction

Chronic hepatitis C is a major root-cause of liver cirrhosis in Pakistan[1], affecting about 3-13% people.[2] Without treatment, it leads to liver cirrhosis in upto 75% patients.[3] Sofosbuvir plus Velpatasvir is an excellent treatment modality for hepatitis C, with higher response and negligible adverse events as compared to previously available direct acting antiviral regimens especially ribavirin based.[4] The treatment duration of Sofosbuvir plus velapatasvir is 12 weeks for non-cirrhotic patients. The duration is extended to 24 weeks or ribavirin has to be added if patient has cirrhosis.[5] The response of treatment is checked at the end of treatemt (ETR) and 12 weeks after end of treatment (SVR-12)[6] using real time HCV-RNA Polymerase chain reaction (PCR) test.[7] In the era of interferons, cirrhotic patients were in great problem regarding active viremia eradication.[8] Now, oral medicines have emerged to a level where effectiveness and tolerability of treat-

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ment is better. However, liver cirrhosis patients have many symptoms routinely.[9] Headache, nausea and fatige are the most commonly observed side effects with sofosbuvir use.[10] The knowledge about the efficacy of sofosvuvir plus velpatasvir therapy as well as its tolerability in cirrhotic patients is scarce in our people. This made the author keen to choose this topic for research. Hence, the objective of our study was to determine the response and tolerability of Sofosbuvir plus Velpatasvir in patients with hepatitis C related liver cirrhosis in the studied Pakistani population. Our study also compared cirrhotic patients with non-cirrhotic ones in terms of treatment effectiveness as well as safety.

Material and Methods

This was a prospective observational study[11] performed at Department of Medicine, Hepatology and Gastroenterology, SIMS/Services hospital, Lahore, from January 2022 to December 2022. A total of 100 patient of chronic hepatitis C aged 12 years and above, from both gender with positive HCV-RNA were enrolled in the study. The sample size was estimated using 90% confidence interval, 5% margin of error & expecting outcome of 90%. Both non-cirrhotic and compensated cirrhotic patients were included. The patients suffering decompensated liver disease, pregnancy, renal dysfunction with creatinine clearance <50 mL /minute, HIV or HBV co-infection, on anticonvulsant drugs and patients who had already used Sofosbuvir plus Velpatasvir were excluded from the study. Ultrasonographic findings (coarse liver, dilated portal vein, splenomegaly), AST to platelet ratio index with cut-off of 2.0 and METAVIR score F4 were used for detection of cirrhosis.[12] Liver cirrhosis with Child-Pugh A was taken as compensated while liver cirrhosis with Child-Pugh B or C was labelled as decompensated cirrhosis.[13] After ethical approval, written informed consent was taken from each patient. Demographic features and laboratory data were noted. The enrolled patients were grouped into Group A (non-cirrhotic hepatitis C patients) and Group B (compensated cirrhotic hepatitis C patients). Sofosbuvir plus Velpatasvir was given to group A patients for 12 weeks & to group B patients for 24 weeks. Laboratory findings, response and adverse events were recorded four weekly. Effectiveness of the treatment was defined by the end treatment response (ETR) and sustained viral response 12 weeks post-therapy (SVR-12) by finding undetected serum HCV-RNA by a PCR with a lower limit of detection < 15IU/ml.[14] Comparisons were done between two studied patient's groups in terms of effectiveness and tolerability of the treatment. The data was analysed using SPSS version 27. To find significant association with specified groups, qualitative variables were subjected to Chi-square test and quantitative ones to independent sample T-test. The p-values were significant if <0.05.

Results

Out of a total 100 patients, 54% were male and 46% were female. Amongst 53 patients of group A, 52 patients (98.1%) achieved ETR while 50 patients (94.3%) achieved SVR-12. Amongst 47 patients of group B, 45 patients (95.7%) achieved ETR, while 44 patients (93.6%) achieved SVR-12 (Figure 1). The mean age was 48.89 + 19.10 years in group A and 49.98 + 18.29 years in group B. Gender (p= 0.235), age (p= 0.558), weight (p= 0.318), initial haemoglobin (p= 0.747), ALT (P= 0.472) and viral load (p= 0.783) had no confounding effect on studied groups. However, thrombocytopenia in group B was due to defining feature of liver cirrhosis (Table 1). No adverse event leading to treatment withdrawal was reported in either group. However, worsening of abdominal ascites from mild to moderate was seen in one patient of group B (p= 0.470). Worsening blood cytopenia was seen in 2 patients of group B and three patients of group A (P= 0.557). ALT flare less than 15 times upper normal limit (UNL) was seen in one patient of each group (p= 0.722). Out of 53 patients of group A, 7 patients (13.2%) reported minor complaints including headache, nausea, vomiting, abdominal comfort, fatigue, while out of 47 patients of group B, 6 patients (12.8%) also reported similar minor complaints (p= 0.593). Overall tolerability of Sofosbuvir plus Velpatasvir was excellent and comparable in both groups of the patients (Table 2).

Table 1: *Demographic and clinical characteristics of the patients (n = 100) **

Qualitative variables	Group A (Non-cirrhotic patients) n=53	Group B (Cirrhotic patients) n=47	p-value
1. Age (years)	48.89 ± 19.10	49.98 ± 18.29	0.558
2. Weight (kg)	73.06 ± 1.60	73.74 ± 14.16	0.318
3. Hb (g/dl)	13.34 ± 1.81	12.14 ± 1.72	0.747
4. Platelet count ($x10^3$ /ml)	295.98±102.41	104.28± 28.63	<0.01
5. ALT (IU/ml)	84.47 ± 85.76	85.51 ± 84.46	0.472
6. Serum HCV load (IU/ml)	9283479 ± 21573112	9943458 ± 21186361	0.783

Table 2: *Associations of parameters of response and adverse events of therapy with presence and absence of liver cirrhosis in studied population (n = 100) **

Quantitative variables	Group A (Non-cirrhotic patients) n=53	Group B (Cirrhotic patients) n=53	p-value
Gender:			
Male	25 (47.2%)	28 (59.6%)	0.235
Female	28 (52.8%)	19 (40.4%)	
End treatment response:			
Achieved	52 (98.1%)	45 (95.7%)	0.599
Not-achieved	01 (1.9%)	02 (4.3%)	
Sustained viral response:			
Achieved	50 (94.3%)	44 (93.6%)	0.602
Not-achieved	03 (5.7%)	03 (6.4%)	
Liver disease decompensation during therapy:			
Yes	00 (0.0%)	1 (2.1%)	0.470
No	53 (100%)	46 (97.9%)	
Worsening of cytopenias during therapy:			
Yes	03 (5.7%)	02 (4.3%)	0.557
No	50 (94.3%)	45 (95.7%)	
ALT flare during therapy:			
Yes	01 (1.9%)	01 (2.1%)	0.722
No	52 (98.1%)	46 (97.9%)	
Minor complaints during therapy:			
Yes	07 (13.2%)	06 (12.8%)	0.593
No	46 (88.8%)	41 (87.2.4%)	

*Chi-square test for independence was used

Discussion

Direct-acting anti-viral drugs (DAAs) are a paradism shift in the management of the patients suffering chronic hepatitis C.[15] In the era of interferons, treatment of the patients with liver cirrhosis due to hepatitis C was problematic because it worsened the misery of the patients. Among DAAs, Sofosbuvir plus Velpatasvir is vastly used in Pakistan. Its efficacy and tolerability is time tested internationally.[16] In 2019, Russian and Swedish authors[17] found SVR-12 of this combination 100% I n cirrhotic and 99% in non-cirrhotic patients. Common adverse events were in 20.1% and included asthenia, headache, and fatigue. In our study, SVR-12 was comparable both in non-cirrhotic and compensated cirrhotic patients (94.3% vs 93.6%, p = 0.605). Similarly, minor complaints of headache, fatigue, nausea, abdominal discomfort were also mild and comparable in both groups of the patients (13.2% vs 12.8%, p = 0.593). With new drugs, it is always a risk of serious or fatal events, as in case of compensated cirrhosis (Child-Pugh A) like flare of ALT more than 15 times ULN, worsening cytopenia, or liver disease decompensation. These events may lead to discontinuation of the treatment regimen. No such adverse event occurred in our study. One patient of compensated liver cirrhosis (group A) suffered increase in ascitic fluid which was easily managed. ALT flare less than 15 times ULN was seen in one patient of each group (p = 0.722). Similarly, worsening cytopenias during treatment was not a problem in our studied population and it was also comparable in both groups of the patients (group A 5.7%, group B 4.3%, p = 0.557). In a similar study from Pakistan,18 SVR-12 was 100% among non-cirrhotic hepatitis C patients who took Sofosbuvir-Velpatasvir combination while it was only 92.1% among compensated cirrhotic hepatitis C patients. This study concluded that cirrhotic patients experienced more side effects of the treatment as compared to non-cirrhotic patients (31.5% vs 20.15%). Samia Pervaiz Khan and her colleagues[19] from Karachi tested Sofosbuvir and Velpatasvir combination showing 100% SVR-12 both in non-cirrhotic and compensated cirrhotic patients suffering chronic viral hepatitis C. Adverse events were negligible. Similar results were published in the studies of Jawad Khan[20] and Arif Qayyum Khan[21]. Hence, Sofosbuvir plus Velpatasvir is doing well in our patients suffering from chronic viral hepatitis C, both non-cirrhotic and compensated cirrhotics in terms of very high response and least negligible adverse effects.

Conclusion

Sofosbuvir plus Velpatasvir combination therapy was highly efficacious and safe in non-cirrhotic and compensated cirrhotic patients with chronic viral hepatitis C. The adverse effects of Velpatasvir plus Sofosbuvir in our population were mild and easily manageable so that treatment compliance was 100%. The response and tolerability of direct acting antiviral drugs was comparable in both studied groups.

Conflict of Interest *None*

Funding Source *None*

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