DOI: https://doi.org/10.53350/pjmhs20231710344

ORIGINAL ARTICLE

Comparison of Drug Regimens (Sofosbuvir + Velpatasvir vs Sofosbuvir + Daclatasvir) in Treatment of Chronic HCV Patients in terms of Efficacy and Safety

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ABSTRACT

Background: Hepatitis C is a viral infection that can lead to liver cirrhosis if not treated properly.

Objective: The aim of this study was to compare the drugs regimens (Sofosbuvir + velpatasvir vs Sofosbuvir + daclatasvir) in treatment of chronic HCV patients in terms of efficacy and safety

Material and Method: The present descriptive multicentre study was conducted at KMU-IMS Kohat DHQ Hospital KDA and Khyber Teaching Hospital, Peshawar from January 2023 to June 2023 after taking approval from the research team of the hospital. Sample size was calculated using the WHO calculator. A total of 170 individuals of both genders and different age groups (ranged 18-60) years with compensated liver cirrhosis and chronic hepatitis C were included. The study participants were divided in to groups A and B equally. Group B got 400 mg plus 60 mg of daclatasvir in separate pills, whereas Group A had 400 mg of sofosbuvir plus 100 mg of velpatasvir in a single pill for 12 weeks. On HCV RNA fragments, hospital RT-PCR identified chronic hepatitis C. HCV RNA levels > 50 copies for six months, as determined by RT-PCR, indicated a chronic infection. SVR12 shown therapeutic efficacy after 12 weeks. The viral load of HCV was less than 50 IU/ml. After twelve weeks of treatment, SVR12 or responders appeared. SPSS version 23 was used for data analysis and were presented in frequencies and percentages.

Results: The study participants were divided in to groups A and B and each group had 85 individuals. In A group females were 45(52.9%) and male were 40(47%) and in group B female were 38(44.7%) and male were 47(55.2%). the mean age of the study population in group A was 5.14years and group B was 4.27 years. The sustained virologic response rate was higher for sofosbuvir and velpatasvir than for daclatasvir. The 78 participants (91.7%) in group A had the SVR 12 rate, compared to 73 individuals (85.8%) in group B. Between groups A and B, the end of treatment response (ETR) was attained by 79 (92.9%) and 75 (88.2%), respectively. The major adverse effects in group A were head ache 11(12.9%), Fatigue10 (11.7%) and Nausea 6 (7%) and in group these were oral ulcer 13(15.2%), skin rashes 11(12.9%) and Epigastric discomfort 7(8.2%).

Conclusion: The current study concluded that the group receiving velpatasvir and sofosbuvir had a longer-lasting viral response than the group receiving daclatasvir and sofosbuvir.

Keywords: Drug regimens; Sofosbuvir; Velpatasvir; Sofosbuvir; Daclatasvir; Treatment; HCV

INTRODUCTION

Chronic hepatitis C infection is one of the primary causes of liver abnormalities and hepatocellular cancer.[1] It is estimated that 71 million people worldwide have hepatitis C and out of these individuals 5 million die each year.[2] For many years, the conventional interferon-based therapy, with or without ribavirin, was commonly used to treat chronic hepatitis C. However, the approach has failed due to low efficacy, an inefficient treatment plan, noncompliance, and the associated adverse effects. The creation of directly acting antivirals (DAAs) for the treatment of chronic hepatitis C was a noteworthy advancement. Individuals are currently encouraged to employ this therapeutic approach since it resolved every problem with the conventional treatment strategy.[3] These direct-acting antivirals agents, which have a prolonged virus activity of up to 90%, were previously and at present one of the primary means of treating the hepatitis C virus.[4] The current guidelines for treating the hepatitis C virus still primarily focus on direct-acting antivirals. As per the "national chronic HCV management guidelines," sofosbuvir-based treatment should be used.[5] According to recent revisions to the guidelines, a drug based on daclatasvir that prevents viral reproduction should be included.[6] Combination of daclatasvir & sofosbuvir for a period of twelve weeks has been prescribed for individuals with genotype 3 hepatitis C. When the effectiveness of these antiviral agents were assessed, it was shown that outcomes for patients and compliance both enhanced.[7] Velpatasvir has been used as an HCV inhibitor, similar to the way sofosbuvir & velpatasvir have been combined into a single drug formulation. There have been numerous trials on various treatment regimens for chronic HCV patients to far, but few have compared two regimens in a single research. Therefore the current stuy was carried out to explore the Comparison of drug regimens (Sofosbuvir + velpatasvir vs Sofosbuvir + daclatasvir) in treatment of chronic HCV patients in terms of efficacy and safety.

Received on 01-09-2023
Accepted on 27-10-2023

MATERIAL AND METHOD

The present descriptive multicentre study was conducted at KMU-IMS Kohat DHQ Hospital KDA and Khyber Teaching Hospital, Peshawar from January 2023 to June 2023, after taking approval from the research team of the hospitals. A total of 170 individuals of both genders and different age groups (ranged 18-60) years with compensated liver cirrhosis and chronic hepatitis C were included while individuals diagnosed with HIV, underwent liver transplant and were not welling to participate in the study were excluded. The study participants were divided in to groups A and B equally. Group B got 400 mg plus 60 mg of daclatasvir in separate pills, whereas Group A had 400 mg of sofosbuvir plus 100 mg of velpatasvir in a single pill for 12 weeks. On HCV RNA fragments, hospital RT-PCR identified chronic hepatitis C. HCV RNA levels > 50 copies for six months, as determined by RT-PCR, indicated a chronic infection. Three criteria were used to assess the liver: Liver disease that is chronic Signs of a physical examination include contractures, axillary and pubic hair loss, palmar erythema, spider nevi, jaundice, and ascites. Serum albumin levels below 3.5 g/dl, INR levels above 1.2, and PT levels above 15 seconds are all included in laboratory testing. They underwent lab and health testing every four weeks. SVR12 shown therapeutic efficacy after 12 weeks. The viral load of HCV was less than 50 IU/ml. After twelve weeks of treatment, SVR12 or responders appeared. Patients who were not SVR12 did not react to therapy. There are no complaints, mild to moderate side

effects, even moderate to severe ones. Inpatient stays or modifications to treatment were not required for mild to severe adverse effects. Moderate to serious side effects include rash, headaches, nausea, anorexia, fatigue, and epigastric pain. Moderate to severe complications were observed from baseline in the "Child-Pugh score, MELD score, liver function tests, and renal profile derangement. SPSS version 23 was used for data analysis and were presented in frequencies and percentages. Gender and results were determined by frequency and percentages, while means and standard deviations were used to analyze laboratory data and age.

RESULTS

The study participants were divided in to groups A and B and each group had 85 individuals. In A group females were 45(52.9%) and male were 40(47%) and in group B female were 38(44.7%) and male were 47(55.2%). the mean age of the study population in group A was 5.14years and group B was 4.27 years. The demographic and clinical features of the study participants is presented in table 1. Successful treatment results were 162 (95.2) end-of-treatment response and 160 (94.11%) Sustained virologic response at post treatment week 12. The sustained virologic response rate was higher for sofosbuvir and velpatasvir than for daclatasvir. The 78 participants (91.7%) in group A had the SVR 12 rate, compared to 73 individuals (85.8%) in group B. Between groups A and B, the end of treatment response (ETR) was attained by 79 (92.9%) and 75 (88.2%), respectively. 4(4.7%) individuals in group A experienced therapy discontinuation, compared to the two individuals (2.3%) in group A. In group A, two individuals (2.3%) exhibited the rate of relapse, but in group B, 4(4.7%) did. There were three (3.5%) non-respondents in group A while 7 (8.2%) in group B as presented in table 2. The major adverse effects in group A were head ache 11(12.9%), Fatigue10 (11.7%) and Nausea 6 (7%) and in group these were oral ulcer 13(15.2%), skin rashes 11(12.9%) and Epigastric discomfort 7(8.2%) as presented in table 3.

Table 1: Demographic and clinical features of the study population

Demographic Features	Group A N (%)	Group B N(%)
Mean age in years	5.14	4.27
Gender		
Male	40(47%)	47(55.2%).
Female	45(52.9%)	38(44.7%)
Clinical features		
Creatinine	0.7 (0.02)(mg/dl)	1 (0.04)(mg/dl)
Albumin	3.7 (0.20)(g/dL)	3.9 (0.37)(g/dL)
WBC	7.5(1.11) (×109/L)	7.4(1.02)(×109/L)
ALT	44 (3.11) U/L	42 (3.21) U/L
PLT	220 (×109/L	225 (×109/L)

Table 2: Efficacy of Treatment for Individuals in Both Groups

Features	Group A N (%)	Group B N(%)
Sustained virologic response a post treatment Week 12	78(91.7%)	73(85.8%)
End-of-Treatment Response	79(92.9%)	75(88.2%)
Discontinuation of therapy	2(2.3%)	4(4.7%)
Relapse	2(2.3%)	4(4.7%)
Non responders	3(3.5%)	7(8.2%)

Table 3: Adverse Effects Found in Both Groups

Adverse effects	Group A N (%)	Group B N(%)
Oral ulcer	2(2.3%)	13(15.2%)
Rashes of skin	zero	11(12.9%)
Epigastric discomfort	2(2.3%)	7(8.2%)
Diarrhea	2(2.3%)	4(4.7%)
Nausea	6(7%)	3(3.5%)
Fatigue	10(11.7%)	2(2.3%)
Headache	11(12.9%)	2(2.3%)

DISCUSSION

For many years, chronic HCV infection has been treated with interferon-based therapy. In addition to its poor efficacy, the regimen was convoluted and brought up other safety concerns. The development of directly acting antivirals (DAAs) was a major advancement in the treatment of chronic HCV. The second-generation DAAs, which also contained daclatasvir, sofosbuvir, and velpatasvir, addressed every issue with the previous chronic HCV treatment approaches[8-9] in our study the mean age of the study population in group A was 5.14years and group B was 4.27 years and the Successful treatment results were 162 (95.2) end treatment response and 160 (94.11%) sustained virologic response at post treatment week 12. The sustained virologic response rate was higher for sofosbuvir and velpatasvir than for daclatasvir. Another study found that 95.5% of the participants had an overall SVR of 12, and the ultimate treatment response for all patients in both groups was 96.8%, which is nearly identical to our findings. All of these data are consistent with our study.[10] Similar outcomes to our findings were also obtained by another study that was carried out by Ahmed T. et al.[11] In comparison to individuals receiving Sofosbuvir and daclatasvir therapy, patients receiving Sofosbuvir and velpatasvir therapy in our trial showed a significant SVR 12 rate. The 78 participants (91.7%) in group A had the SVR 12 rate, compared to 73 individuals (85.8%) in group B. Between groups A and B, the end of treatment response (ETR) was attained by 79 (92.9%) and 75 (88.2%), respectively. 4(4.7%) individuals in group A experienced therapy discontinuation, compared to the two individuals (2.3%) in group A. In group A, two individuals (2.3%) exhibited the rate of relapse, but in group B, 4(4.7%) did. There were three (3.5%) non-respondents in group A while 7 (8.2%). The major adverse effects in group A were headache 11(12.9%), Fatigue10 (11.7%) and Nausea 6 (7%) and in group these were oral ulcer 13(15.2%), skin rashes 11(12.9%) and Epigastric discomfort 7(8.2%). According to our research, another study found that more of the participants in the Sofosbuvir and Velpatasvir group obtained SVR after 12 weeks than in the Sofosbuvir and Daclatasvir group. There were more non-responders in the Sofosbuvir and Daclatasvir groups in their study. Participants in the Sofosbuvir and Daclatasvir groups also experienced greater relapses, which is consistent with our findings.[10] According to a different study, only two percent of those participating in the Sofosbuvir and Velpatasvir group were found to have relapsed, while 98 percent of individuals reached the end of therapy evaluation and had SVR 12. 96.2 percent of the participants finished their course of treatment, compared to 3.8 per cent who stopped it, when compared to the sofosbavir-velpatasvir combination. The sofosbavir-daclatasvir group experienced a greater rate of poor response to the medication (4.3% compared to 5.8%) than the sofosbavir -velpatasvir group. In this group, a similar relapse rate of 2% was noted. Similar outcomes to our findings were also obtained by another study that carried out by Ahmed T. et al.[11] When compared to the sofosbavir-velpatasvir combination, 96.2% of patients finished their course of treatment, whereas 3.8% stopped it. The sofosbavir-daclatasvir group saw a greater rate of poor response to the medication than the sofosbavir-velpatasvir group. For this group, a similar relapse rate of 3.5% was noted.[13] In a study that was conducted, one group was treated with Sofosbuvir and velpatasvir, while another group was treated with Sofosbuvir and daclatasvir. The antiviral medications were administered to both groups. The study found that the overall sustained viral response was 95.5%. The persistent viral response was assessed after 12 weeks of treatment. The response was 94.4% in the group that received Sofosbuvir and daclatasvir, while it was 94.7% in the group that received Sofosbuvir and velpatasvir.[14] which is consistent with our findings.

In a 2018 study, Omar et al. examined the relationship between the efficacy of daclatasvir and sofosbuvir in individuals with chronic HCV. The trial's results showed a 95.4% SVR 12. This response rate is comparable to the clinical outcome and previously reported research. However, it was discovered that roughly 76 of the participants discontinued their medication after looking into the causes of their restricted reply. These findings are consistent with the clinical study, which showed that patients on daclatasvir and sofosbuvir experienced higher rates of withdrawal.[15] A meta-analysis was conducted to evaluate the effectiveness of Sofosbuvir

and velpatasvir against that of Sofosbuvir plus daclatasvir. Every selected trial adhered to the protocol for a duration of 12 weeks. 16 studies in all, including 4,907 participants, were recruited. According to the metaanalysis's findings, people who received velpatasvir and sofosbuvir had a higher SVR 12 of 98% than those who received sofosbuvir and daclatasvi, which was 95%. [16]

CONCLUSION

The current study concluded that the group receiving velpatasvir and sofosbuvir had a longer-lasting viral response than the group receiving daclatasvir and sofosbuvir. In both groups, therapeutic compliance was same. Moreover, a higher prevalence of drug-related adverse events was observed in the group receiving daclatasvir and sofosbuvir.

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This article may be cited as: Farzand M, Adil K, Iftikhar T, Orakzai SUR, Nazir S, Gul N; Comparison of Drug Regimens (Sofosbuvir + Velpatasvir vs Sofosbuvir + Daclatasvir) in Treatment of Chronic HCV Patients in Terms of Efficacy and Safety. Pak J Med Health Sci, 2023; 17(10): 344-346.