Original Article

Comparison of Drug Regimens (Sofosbuvir and velpatasvir versus Sofosbuvir and Daclatasvir) in Treatment of Chronic Hepatitis C Virus Patients in Terms of Efficacy and Safety

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ABSTRACT

Objective: To compare drug regimens (Sofosbuvir + velpatasvir vs Sofosbuvir + daclatasvir) in treatment of chronic HCV patients in terms of efficacy and safety.

Study Design: A descriptive study,

Place and Duration of Study: This study was conducted at the Gastroenterology Department, Hayatabad Medical Complex, Peshawar from October 2020–June 2021.

Methods: The gastrointestinal department of Hayatabad Medical Complex Peshawar conducted this descriptive research from January to September 2019. Patients were divided into two groups. Both groups A and B included 80 patients. For 12 weeks, group A received sofosbuvir and velpatasvir while group B received daclatasvir. Effectiveness was measured by SVR12 at 12 weeks after treatment. All data analysis was done in SPSS 24.

Results: In group A, 77 (96.25%) individuals had SVR 12, whereas group B had 72 (90%). In group A, 78 (97.5%) achieved ETR, whereas in group B, 74 (92.5%) did. Relapse was detected in 1 (1.25%) patient in group A and 3 (3.75%) in group B. Based on adverse events, group B had 12 (15%), 10 (12.5%), 6 (7.5%), 3 (3.75%), 2 (2.5%), 1 (1.25%), and 1 (1.25%) headache, fatigue, nausea, diarrhea, epigastric discomfort, skin rashes, and oral ulcer, while group A had 9 (11.25%), 8 (8.75%), 5 (6.25%), 1 (1.25%), 1 (1.25%), 00 (00%) and 1 (1.25%).

Conclusion: According to the results of our research, the group treated with sofosbuvir and velpatasvir had a higher sustained viral response than the group treated with sofosbuvir and daclatasvir. Compliance to therapy was comparable in both groups. Furthermore it was found that group treated with sofosbuvir and daclatasvir had a greater role of drug related adverse events.

Key Words: Efficacy; Safety; Sofosbuvir; velpatasvir; daclatasvir; chronic HCV patients

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INTRODUCTION

One of the leading factors contributing to liver abnormalities and hepatocellular carcinoma across the world is chronic hepatitis C infection [(1)]. According to estimates, there are around 71 million individuals worldwide who have hepatitis C, and of them, 3.5 to 5 million die annually [(2)]. The traditional therapy based on interferon, with or without ribavirin, has been tried for years to manage chronic hepatitis C; yet, the method was unsuccessful owing to low effectiveness, an ineffective therapy schedule, poor compliance, and the accompanying side effects. A significant development was the development of directly acting antivirals (DAAs) for the management of chronic hepatitis C. It is presently advised that patients use this therapy method since it addressed all the issues with the standard treatment plan [(3)]. With a sustained virus response of up to 90%, these direct-acting antivirals were previously and are now one of the main sources of treatment for the hepatitis C virus [(4)]. Direct-acting antivirals continue to be the main focus of the current hepatitis C virus care recommendations. The application of sofosbuvir-based

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treatment is recommended by the "national chronic HCV management guidelines" [5]. Current changes to the recommendations called for the inclusion of a daclatasvir-based medication that stops viral replication[6]. In genotype 3 hepatitis C patients, the combination of daclatasvir and sofosbuvir for 12 weeks has been recommended. When daclatasvir and sofosbuvir were evaluated for their efficacy, it was shown that patients' outcomes and compliance both improved[7]. Like sofosbuvir and velpatasvir have been combined into a single medication formulation, velpatasvir has been employed as an HCV inhibitor. Various studies have been conducted so far regarding different regimens for treatment of chronic HCV patients but limited studies done regarding comparasion of 2 regimens in a single study, hence this study was conducted to evaluate the efficacy and safety of Sofosbuvir+ velpatassavir vs Sofosbuvir+ daclatasavir in Chronic HCV patients in our region.

METHODS

This descriptive study was done by Hayatabad Medical Complex Peshawar's gastrointestinal department. Research covering October 2020–June 2021. The institutional research and ethical review board approved the study. We studied naïve individuals aged 18-60 with compensated cirrhosis and chronic hepatitis C, regardless of gender. Eliminated: cirrhosis, HIV, liver, transplant, and unwilling patients. Simple sampling enrolled patients. WHO determined our 160-person sample. Two patient groups. Both groups A and B included 80 patients. Group A received 400mg Sofosbuvir and 100mg velpatasvir in one pill for 12 weeks, whereas group B received 400mg and 60mg daclatasvir separately. Hospital RT-PCR detected chronic hepatitis C on HCV RNA fragments. RT-PCR HCV RNA levels > 50 copies for six months suggest chronic infection. The liver was evaluated by three factors: Chronic liver disease Physical examination signs include palmar erythema, spider nevi, jaundice, ascites, axillary and pubic hair loss, and contractures. Laboratory testing include serum albumin below 3.5 g/dl, INR above 1.2, and PT over 15 seconds. Every four weeks, they received health and lab testing. Twelve weeks of SVR12 showed therapeutic effectiveness. The HCV viral load was < 50 IU/ml. Twelve weeks following treatment, SVR12 or responders occurred. Non-SVR12 patients did not respond to treatment. No complain, mild to moderate, and moderate to severe side effects. Mild to severe side effects didn't need hospitalization or treatment changes. Anorexia, headaches, nausea, epigastric pain, tiredness, oral ulcer, and rash are moderate to severe side effects. From baseline, "Child-Pugh score, MELD score, liver function tests, and renal profile derangement" were moderate to severe adverse events. SPSS 24 examined demographics, labs, SVR12, and adverse events. Results and gender were established by frequency and percentag.es, whereas age and laboratory data were analyzed using means and standard deviations.

RESULTS

The 160 chronic HCV patients in this study were split into 80 A and 80 B groups. Group A contained 38 (47.5%) male and 42 (53.5%) female patients, whereas group B had 36 (45%) male and 44 (55%). (Figure 1) Group A had a mean age (SD) of 40.1 (4.13) years and group B 39.96 (3.26) years. Table 1 displays demographic and clinical data for both groups. Successful treatment outcomes were 149 (93.13%) SVR 12 and 152 (95%) ETR. Our research included 4 relapses (2.5%). (Figure 2) Sofosbuvir and velpatasvir had a higher SVR 12 rate than daclatasvir. Group A had 77 (96.25%) SVR 12 cases, whereas group B had 72 (90%). ETR was attained by 78 (97.5%) in group A and 74 (92.5%) in group B. One (1.25%) patient in group A stopped therapy, whereas three (3.75%) in group did. Relapse occurred in 1 (1.25%) of group A patients and 3 (3.75%) of group B patients. A had 3 non-responders (3.75%) and B 6 (7.5%). (Table 2) Group B had 12 (15%), 10 (12.5%), 6 (7.5%), 3 (3.75%), 2 (2.5%), 1 (1.25%), and 1 (1.25%) headache, fatigue, nausea, diarrhea, epigastric discomfort, skin rashes, and oral ulcer, while group A had 9 (11.25%), 8 (8.75%), 5 (6.25%), 1 (1.25%), 1 (1.25%), 00 (00%), and 1. Table 2)

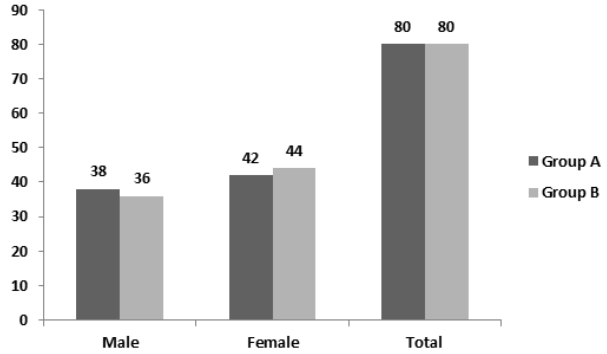

Figure No. 1: Frequency of male and female in both the groups

Table No. 1: Baseline demographic and laboratory parameters of patients in both the group

Parameter	Group A	Group B
Age	40.1 (4.13) years	39.96 (3.26) years
WBCs	7.4(1.12) ($\times 10^9$/L)	7.3(1.01)($\times 10^9$/L)
HB	13 (1.96) (g/dL)	12.6(2.1) (g/dL)
PLT	222 ($\times 10^9$/L)	227 ($\times 10^9$/L)
ALT	45 (3.11) U/L	43 (3.21) U/L
Albumin	3.8 (0.21)(g/dL)	4 (0.36)(g/dL)
Creatinine	0.8 (0.01)(mg/dl)	1 (0.05)(mg/dl)

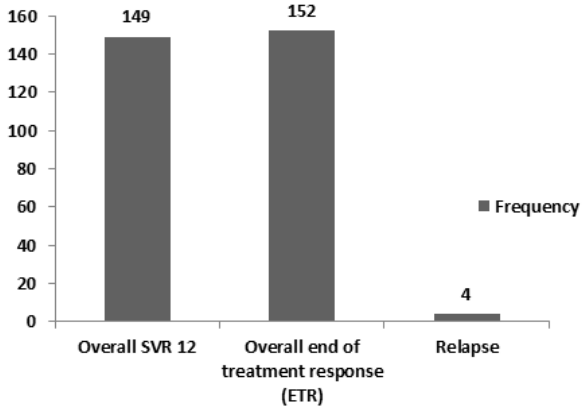

Figure No. 2: Overall SVR 12 and end of treatment response

Table No. 2: Treatment efficacy amongst patients of both the groups

Parameter	Group A N (%)	Group B N (%)
SVR 12	77 (96.25%)	72 (90%)
ETR	78 (97.5%)	74 (92.5%)
Discontinuation of therapy	1 (1.25%)	3 (3.75%)
Relapse	1 (1.25%)	3 (3.75%)
Non responders	3 (3.75%)	6 (7.5%)

Table No. 3: Adverse events observed in both the groups

Parameter	Group A N (%)	Group B N (%)
Headache	9 (11.25%)	12 (15%)
Fatigue	8 (8.75%)	10 (12.5%)
Nausea	5 (6.25%)	6 (7.5%)
Diarrhea	1 (1.25%)	3 (3.75%)
Epigastric discomfort	1 (1.25%)	2 (2.5%)
Skin rashes	00 (00%)	1 (1.25%)
oral ulcer	1 (1.25%)	1 (1.25%)

DISCUSSION

Interferon-based therapy has been used for treating chronic HCV infection for many years. The regimen was complicated and raised a number of safety issues in addition to its low effectiveness. Directly acting antivirals (DAAs) was a significant development in the management of chronic HCV. All of the drawbacks of the earlier chronic HCV therapy modalities were resolved by the second-generation DAAs, which also included daclatasvir, Sofosbuvir and velpatasvir [8,9]. In our study, the mean age (SD) in group A was 40.1 (4.13) years while in group B, the mean age (SD) was 39.96 (3.26) years. Based on treatment efficacy, the overall, SVR 12 in our study population was achieved by 149 (93.13%) participants while the end of treatment response (ETR) was achieved by 152 (95%) patients. The overall relapse in our study was 4 (2.5%). In accordance with our study, another study reported comparable results to our findings they reported the overall SVR 12 in 95.5% of the patients while the end treatment response in over all patients of both the group was 96.8%. The overall relapse in their study was 1.5% which is almost similar with our findings [10]. Another study piloted by Ahmed T et al. also reported comparable results to our findings [11]. In our study, the patients on Sofosbuvir and velpatasvir therapy were observed with high SVR 12 rate as compared to patients on Sofosbuvir and daclatasvir therapy. The SVR 12 rate in group A was observed in 77 (96.25%) patients while in group B it was 72 (90%). The end of treatment response (ETR) was achieved by 78 (97.5%) in group A while in group B it was achieved by 74 (92.5%). Discontinuation of therapy was observed in 1 (1.25%) patient in group A while in group it was noticed in 3 (3.75%) patients. The rate of relapse in group A patients was shown by 1 (1.25%) patient while in group B it was observed in 3 (3.75%) patients. The non responders in group A were 3 (3.75%) while in group B they were 6 (7.5%). (Table 1) Based on adverse events, in group B the headache, fatigue, nausea, diarrhea, epigastric discomfort, skin rashes and oral ulcer was observed in 12 (15%), 10 (12.5%), 6 (7.5%), 3 (3.75%), 2 (2.5%), 1 (1.25%) and 1 (1.25%) respectively whereas in group A, headache, fatigue, nausea, diarrhea, epigastric discomfort, skin rashes and oral ulcer was observed in 9 (11.25%), 8 (8.75%), 5 (6.25%), 1 (1.25%), 1 (1.25%), 00 (00%) and 1 (1.25%) respectively. In accordance with our study another study reported consistent results to our findings they reported the more patients in Sofosbuvirand velpatasvir group achieved SVR after 12 weeks as compared to Sofosbuvirand daclatasvir group. In their study, non responders were more in Sofosbuvir and daclatasvir group. Relapse was also more in patients of Sofosbuvir and daclatasvir group which is similar with our results[10]. Another study reported that 98% of individuals in the Sofosbuvir and velpatasvir group reached the end of treatment evaluation and shown SVR 12, and only 2% of the patients were revealed to have relapse. In comparison to the sofosbavir-velpatasvir combination, 96.2% of patients completed their course of therapy, while 3.8% of them discontinued it. In compared to the sofosbavir-velpatasvir group, there was a higher incidence of poor response to the therapy in the sofosbavir-daclatasvir group (4.3% vs. 5.8%). A comparable relapse rate of 2% was observed in this group. Another study piloted by Ahmed T et al also reported comparable results to our findings[11]. In comparison to the sofosbavir-velpatasvir combination, 96.2% of patients completed their course of therapy, while 3.8% of them discontinued it. In compared to the sofosbavir-velpatasvir group, there was a higher incidence of poor response to the therapy in the sofosbavir-daclatasvir

group (4.3% vs. 5.8%). A comparable relapse rate of 2% was observed in this group [13]. In a research that was carried out in which one group received therapy with Sofosbuvir and velpatasvir, whereas a separate group underwent therapy with Sofosbuvir and daclatasvir. Both groups were given the antiviral drugs. The research revealed a 95.5% overall sustained viral response. After 12 weeks of therapy, the sustained viral response was evaluated. In the group controlled by Sofosbuvir and daclatasvir, the response was 94.4%, but in the group provided with Sofosbuvir and velpatasvir, the response was 94.7% which is comparable with our results [14]. In a 2018 research, Omar et al. investigated the link between Sofosbuvir and daclatasvir effectiveness in chronic HCV patients. Results of the trial indicated a SVR 12 of 95.4%. This response rate is similar to the clinical result and earlier research that was described. But upon investigating the reasons for the participants' limited reaction, it was found that about 76 of them stopped their treatment. These results are in line with those of the clinical research, which revealed that patients with Sofosbuvir and daclatasvir had greater rates of withdrawal [15]. To compare the efficacy of Sofosbuvir and velpatasvir to that of Sofosbuvir and daclatasvir, a meta-analysis was done. All of the chosen trials followed the regimen for 12 weeks. 4,907 people were included in a total of 16 studies, which were recruited. The results of the meta-analysis revealed that individuals receiving Sofosbuvir and velpatasvir had higher SVR 12 of 98% as opposed to 95% with Sofosbuvir and daclatasvi. The limitation of the current research was low sample size and single centre nature. Moreover the genotype of the virus was not determined before the treatment [16].

CONCLUSION

According to the results of our research, the group treated with Sofosbuvir and velpatasvir had a higher sustained viral response than the group treated with Sofosbuvir and daclatasvir. Compliance to therapy was comparable in both groups. Furthermore it was found that group treated with Sofosbuvir and daclatasvir had a greater role of drug related adverse events.

Author's Contribution:

Concept & Design of Study:	Umair Latif
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Revisiting Critically:	Umair Latif, Fahad Shaheen
Final Approval of version:	Umair Latif

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