Original Article

Efficacy and Safety of Sofosbuvir/ Daclatasvir VS Sofosbuvir/Velpatasvir in Chronic Hepatitis C Patients

Noman Kareem Qureshi[1], Syed Rizwan Hussain[2], Mehreen Toufique[1], Syeda Mariam Batul Bukhari[2], Shafaq Shafique Abbasi[2] and Zarnab Munir[2]

ABSTRACT

Objective: The present study aims to compare the efficacy and safety of SOF/DCV and SOF/VEL in treating chronic hepatitis C patients.

Study Design: Randomized controlled trial study.

Place and Duration of Study: This study was conducted at the SKBZ hospital CMH Muzaffarabad from 1st July 2023 to 30th June 2024.

Methods: Through non probability consecutive sampling, 200 patients aged above 18 years, either gender, diagnosed with Chronic HCV (Viral titer >10, 000 IU/mL) were included in the present study. Co-infection with hepatitis B virus (HBV) or human immunodeficiency virus (HIV), decompensated liver disease, significant renal impairment, pregnant patients were excluded from the present study. Patients were randomized in a 1:1 ratio to receive either SOF/DCV (400 mg Sofosbuvir and 60 mg Daclatasvir daily) (n=100) or SOF/VEL (400 mg Sofosbuvir and 100 mg Velpatasvir daily) (n=100), with treatment extending for 12 weeks

Results: The baseline HCV viral titer in the patients of both study groups were 6.84±0.5 and 7.1±0.9 g/dL ($p<0.0001$). Sustained virological response (SVR) at 12- week was achieved in 92% patients in SOF/DCV group and 95% in SOF/VEL group. Mild adverse effects were observed in both the study groups

Conclusion: In conclusion, the efficacy in achieving sustained viral response (SVR) in the group managed by Sofosbuvir and velpatasvir was higher (95%) against Sofosbuvir and Daclatasvir (92%).

Key Words: SVR, Sofosbuvir, Daclatasvir, Velpatasvir, HCV

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INTRODUCTION

Hepatitis C is an infection caused by the hepatitis C virus and mainly affects the liver. It's an important public health concern, with an approximate 71 million people living with chronic Hepatitis C infection worldwide[1]. This infection ranges from mild illness, usually lasting a few weeks, to a serious lifelong chronic condition. Long-term issues associated with chronic hepatitis C infection include severe complications such as cirrhosis, liver failure, and hepatocellular carcinoma; it is thus one of the main causes of morbidity and mortality worldwide. Direct acting antivirals (DAAs) inhibit certain steps of the HCV life cycle, as such, viral replication is inhibited, leading to effective clearance of the virus from the bloodstream[2]. These agents have recently been classified into several classes according to their mechanism of action: NS3/4A protease inhibitors, NS5A inhibitors, and NS5B polymerase inhibitors. Combination of different classes of DAAs significantly improved treatment outcomes across various HCV genotypes[3]. Sofosbuvir is the most critical NS5B polymerase inhibitor in the treatment regimens for HCV, and it must be combined with other DAAs against different HCV genotypes to attain significant cure rates[4]. Two essential combinations that have been created are Sofosbuvir/Daclatasvir and Sofosbuvir/ Velpatasvir. The efficacy and safety profiles of these regimens are so high that they take precedence over other combinations in treating HCV. Several HCV genotypes have been evaluated for SOF/DCV, which has demonstrated high efficacy. In a landmark study, Wehmeyer et al. examined the effectiveness of SOF/DCV in 200 patients with various HCV genotypes.

[1.] Department of Gastroenterology / Medicine[2], CMH/Shaikh Khalifa Bin Zayad Hospital Muzaffarabad AJK,

Correspondence: Dr. Noman Kareem Qureshi, Assistant Professor Gastroenterology, CMH/Shaikh Khalifa Bin Zayad Hospital, Muzaffarabad, AJK
Contact No: 0333-4404054
Email: naumanqureshigvig@gmail.com

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The rates of SVR12 reported in this study were 97% for genotype 1, 93% for genotype 2, and 94% for genotype 3 patients[5]. Subsequent studies—including a 2019 study by Alonso et al.—pointed out the makers of remarkable efficacy of SOF/DCV against HCV infection, especially against genotypes 1 and 3[6]. SOF/VEL is a pangenotypic regimen that has been demonstrated to have activity against all major HCV genotypes[7]. In the landmark trial ASTRAL-1, published in 2018, it was able to show SVR-12 rates of more than 98% across all genotypes 1-6. This study had a very diverse patient population, underlining that the efficacy of this regimen applies to an extremely wide range of patients[8]. Subsequent studies, such as ASTRAL-2 and ASTRAL-3, also reproduce these superb results, demonstrating that SOF/VEL performs well across all HCV genotypes[9]. Several comparative studies and meta-analyses compared the relative efficacy and safety of SOF/DCV versus SOF/VEL. In a meta-analysis by conducted by a researcher, evaluating both regimens in various patient populations, it was shown that both combinations achieved high rates of SVR12 and differed slightly between genotypes and patients. The pangenotypic coverage of SOF/VEL was better, as was its good and comparable safety profile to that of SOF/DCV. In a large sample of CHC patients, a cohort study by a researcher, compared the real-world effectiveness of SOF/DCV versus SOF/VEL. In the said research, SVR12 rates were 96% for SOF/VEL and 94% for SOF/DCV, hence showing comparable efficacy. Both regimens had comparable safety profiles, with no significant difference in the incidence of serious adverse events. The present study aims to compare the efficacy and safety of SOF/DCV and SOF/VEL in treating chronic hepatitis C patients.

METHODS

After the ethical approval from the institutional review, this randomized controlled trial was conducted at at SKBZ hospital CMH Muzaffarabad from 1st July 2023 to 30th June 2024 Through non probability consecutive sampling, 200 patients aged above 18 years, either gender, diagnosed with Chronic HCV (Viral titer >10, 000 IU/mL) were included in the present study. Co-infection with hepatitis B virus (HBV) or human immunodeficiency virus (HIV), decompensated liver disease, significant renal impairment, pregnant patients were excluded from the present study. Patients were randomized in a 1:1 ratio to receive either SOF/DCV (400 mg Sofosbuvir and 60 mg Daclatasvir daily) (n=100) or SOF/VEL (400 mg Sofosbuvir and 100 mg Velpatasvir daily) (n=100), with treatment extending for 12 weeks. The primary outcome measured was the sustained virological response at 12-weeks post-treatment (SVR12) determined by viral titer through RT-PCR, defined by undetectable HCV RNA levels. Secondary outcomes included SVR24, adverse event incidence, virological failure rates, and liver function test results. Baseline assessments collected demographic data, medical history, and laboratory tests, while follow-up assessments at weeks 4, 8, 12, and 24 monitored HCV RNA levels, and adverse events. SPSS version 21 was utilized to analyse the data. Categorical variables were presented as frequency and percentages and continuous variables were represented as Mean and standard deviation. Primary outcomes were compared between the study groups by t-test. P value ≤ 0.05 were considered to be significant.

RESULTS

Table 1 shows the demographic and clinical parameters of the recruited participants in both study groups. The average age of the patients in both the study groups were 47.99±11.3 and 49.8±12.3 years. (p=0.106). The female to male ratio in both the study groups was 2:1 and 1.17:1 respectively (p=0.045). in SOF/DCV group 14% of the patients had cirrhosis, while in 19% in SOF/VEL group (p=0.025). The baseline HCV viral titer in the patients of both study groups were 6.84±0.5 and 7.1±0.9 g/dL (p<0.0001). Table 2 shows the efficacy of the DAAs in the HCV patients. Sustained virological response (SVR) at 12- week was achieved in 92% patients in SOF/DCV group and 95% in SOF/VEL group. Table 3 shows the adverse effects of the drugs observed in patients of both groups. Mild adverse effects were observed in both the study groups. In SOF/DCV majority of the patients 15% observed fatigue as an adverse effect, while in SOF/VEL majority of the patients 20% experienced nausea.

Table No.1: Demographic and clinical parameters

Variables	SOF/DCV Group (n=100)	SOF/VEL group (n=100)	P Value
Age (years)	47.99±11.3	49.8±12.3	0.106
Male gender n (%)	42 (42%)	46 (46%)	0.045
Cirrhosis n (%)	14 (14%)	19 (19%)	0.025
Hemoglobin (g/dL)	11.5±0.90	11.45±0.95	0.350
WBCs ($\times 10^9$/L)	7.56±0.6	7.4±0.7	0.012
Platelets ($\times 10^9$/L)	246.78±20.45	243.5±30.2	0.280
AST (ULN: 40 U/L)	81.78±10.3	81.68±10.4	0.847
ALT (ULN: 40 U/L)	60.46±7.9	59.09±8.8	0.069
Albumin (mg/dL)	39.53±1.66	43.3±3.5	0.300

HCV Titer (g/dL)	6.84±0.5	7.1±0.9	<0.0001
Comorbidity n(%)			0.765
Diabetes	26 (26%)	20 (20%)	
Obesity	43 (43%)	54 (54%)	
Hypertension	31 (31%)	26 (26%)	

Table No.2: Efficacy of drugs in both study group

Variables	SOF/DCV Group (n=100)	SOF/VEL group (n=100)	P value
SVR-12			0.083
Yes	92 (92%)	95 (95%)	
No	8 (8%)	5 (5%)	
Relapses			0.158
Yes	5 (5%)	3 (3%)	
No	95 (95%)	97 (97%)	
Non-responders			0.320
Yes	3 (3%)	2 (2%)	
No	97 (97%)	98 (98%)	

Table No.3: Adverse effects of the drugs in both study group

Adverse Effects n (%)	SOF/DCV	SOF/VEL	P value
Headache	15	12	0.596
Nausea	14	20	
Anemia	13	10	
Fatigue	19	15	
Abdominal pain	10	9	
Fever	9	12	
Rash	7	9	
Diarrhea	5	2	
Myalgia	3	2	
Dizziness	2	3	

DISCUSSION

The development of DAAS has had a profound and transformative impact on the treatment of HCV. These treatment plans result in greater rates of sustained virologic response (SVR) and restrict the advancement of liver cirrhosis. The use of IFN for the treatment of HCV has been discontinued worldwide, and therapy based on DAAs is increasingly becoming the preferred approach[10]. The availability of generic versions of DAAs in 101 developing countries has led to a significant decrease in their prices (Hill et al., 2016). However, it is necessary to conduct scientific evaluation and validation in order to confirm the effectiveness and safety of these generic products. To effectively treat HCV infection on a wide scale, it is advisable to thoroughly examine the existing real-world data on the effectiveness of these treatment plans across all categories of HCV patients[11].

This study reported that the efficacy in achieving sustained viral response (SVR) in the group managed by sofosbuvir and velpatasvir was higher against sofosbuvir and daclatasvir. In a 2017 research, Falade-Nwulia et al. compared the effects of two different combinations of sofosbuvir and vel, as well as sofosbuvir and daclatasvir. A viral response rate of 95.5% was observed in the research. 94.4% of patients in the group treated with sofosbuvir and daclatasvir shown a sustained viral response after 12 weeks of therapy, whereas 94.7% of patients in the group treated with sofosbuvir and velpatasvir demonstrated a response[12]. In 2022, Ahmed et al. investigated the effectiveness of sofosbuvir and daclatasvir in the treatment of chronic HCV patients. Sofosbuvir 400 mg and daclatasvir 60 mg were the prescribed medications in the 12-week trial. The results of the investigation demonstrated that 95.4% of the viral load was maintained[13]. In 2019, Belperio et al. evaluated the efficacy of sofosbuvir in combination with velpatasvir or daclatasvir. Five thousand four hundred people were a member of the research population. The people who were recruited belonged to genotypes 2 and 3. Both sofosbuvir and daclatasvir, as well as sofosbuvir and velpatasvir, exhibited similar persistent viral responses, according to the study's results. The sustained viral response for genotype 3 was around 92% in individuals treated with velpatasvir and sofosbuvir, and nearly 90% in persons managed with daclatasvir and Sofosbuvir[14]. The efficacy of Sofosbuvir/daclatasvir, and sofosbuvir/velpatasvir was evaluated in a meta-analysis. All the studies that were chosen followed the regimen for a duration of 12 weeks. A grand total of 4,907 individuals

were enrolled across 16 different investigations. The results of the meta-analysis demonstrated that the combination of sofosbuvir and velpatasvir resulted in a higher rate of persistent viral responses (98% vs. 95%) in the patients treated with these two drugs[15].

CONCLUSION

In conclusion, the efficacy in achieving sustained viral response (SVR) in the group managed by Sofosbuvir and velpatasvir was higher (95%) against Sofosbuvir and Daclatasvir (92%).

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Noman Kareem Qureshi, Syed Rizwan Hussain, Mehreen Toufique
Drafting or Revising Critically:	Syeda Mariam Batul Bukhari, Shafaq Shafique Abbasi, Zarnab Munir
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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