DOI: https://doi.org/10.53350/pjmhs22168790

ORIGINAL ARTICLE

Effectiveness of Sofosbuvir and Velpatasvir Combination in Chronic Hapatitis C

AGHA WALI[1], GHULAM HASSAN[2], SOHAIL HUSSAIN[3], MUHAMMAD NAEEM ASLAM[4]
[1]*MD, Sechnov University (aka First Moscow state Medical university), Moscow, Russia*
[2]*Assistant Professor of Psychiatry Sahara Medical College / Sughra Shafi Medical Complex Narowal*
[3]*Consultant Gastroenterologist and Hepatologist, Clinical Coordinator for Postgraduate studies, Ziauddin University Karachi.*
[4]*Consultant Gastroenterologist Mayo Hospital Lahore*
Correspondence to: Muhammad Naeem Aslam

ABSTRACT

Objective: The purpose of this research is to evaluate the efficacy of a combination medication consisting of sofosbuvir and velpatasvir in treating individuals with chronic hepatitis C.

Study Design: Observational/ Prospective study

Place and Duration: Conducted at Department of Gastroenterology Mayo Hospital Lahore, during from the period Feb 2021 to Jan 2022.

Methods: There were 67 participants in this study. The patients' ages ranged from 18 to 70. We gathered demographic information about the patient, such as age, gender, height, and weight, after getting written consent. Hepatitis C patients with known genotypes were shown. A SOF/VLP regimen containing sofosbuvir and velpatasvir was administered to patients for a total of 12 weeks. The entire set of data was examined using SPSS 18.0.

Results: In current study, 42 (62.7%) were males and 25 (37.3%). Included patients had mean age 31.12±15.80 years and mean BMI 24.7±8.34 kg/m^2. We found that efficacy rate was higher and found in 63 (94.03%) cases. As per laboratory findings, aspartate aminotransferase (AST) 37.5± 11.21, alanine aminotransferase (ALT) 26.2±6.44, and haemoglobin level 12.24±10.17 all showed considerable improvement after therapy. Most common adverse outcomes were headache 35 (52.2%), fatigue 22 (32.8%) and nausea 10 (14.9%).

Conclusion: In patients with or without cirrhosis, and regardless of the HCV genotype, the combination of sofosbuvir and velpatasvir has shown to be extremely successful in treating chronic HCV infection. This is true regardless of the HCV genotype.

Keywords:, Hepatitis C, Sofosbuvir, Comorbidities, Velpatasvir,

INTRODUCTION

Pakistan has the world's second-highest hepatitis C prevalence, behind only China. In that nation, 4.8% of people are affected each year. Since there is not a major initiative to test the general population for hepatitis C [1]. Hepatitis C prevalence ranges from 5.46 percent in Punjab to 2.54 percent in Sindh to 6.07 percent in Khyber Pakhtunkhwa to 25.77 percent in Baluchistan to 3.37 percent in federally controlled tribal territories [2]. According to surveys [3], the vast majority of the population have the 3a genotype.

Traditional interferon-based therapy regimens for chronic hepatitis C, with or without ribavirin, have been attempted by many people over the years, but have been met with failure due to low efficacy, insufficient dose schedule, poor compliance, and the unpleasant symptoms that come along with them. Significant progress has been made in the treatment of chronic hepatitis C with the introduction of direct-acting antivirals (DAAs). Due to the fact that this therapy effectively solves all the issues with the conventional treatment plan, it is currently accepted in clinical practise [4,5].

Sofosbuvir is a pan-genotypic antiviral that prevents HCV RNA production by reducing 5B polymerase activity (NS5B). It's trouble-free and resistant [6]. Velpatasvir inhibits HCV protein 5A. (NS5A). It works against every HCV strain [7]. Non-cirrhotic treatment-naive patients had a 99% to 100% (sustained virologic response at 12 weeks [SVR12]) success rate with sofosbuvir and velpatasvir for chronic hepatitis C [8].

Sofosbuvir, a pan-genotypic antiviral, inhibits 5B polymerase activity, therefore blocking the generation of HCV RNA (NS5B). No maintenance is required, and it's sturdy [6]. The hepatitis C virus protein 5A is inhibited by velpatasvir (NS5A). Against all known HCV subtypes, it is effective [7]. Sofosbuvir and velpatasvir for chronic hepatitis C showed a 99% to 100% (sustained virologic response at 12 weeks [SVR12]) success rate in treatment-naive individuals without cirrhosis [8].

In a comprehensive real-world examination of 5552 patients from 12 clinical practise cohorts across Europe and North America, just 1% of patients did not achieve SVR, with liver cirrhosis being the only disease linked with a higher risk of not obtaining SVR [10]. A phase 3 clinical research including 375 HCV patients in Asia showed an SVR rate of 97%, with cirrhotic patients faring less well [11]. However, 2,821 people with cirrhosis were included in a second Canadian cohort study, which revealed no correlation between the two. [12].

The National Chronic Hepatitis C Infection Treatment Guidelines have updated their recommendations for the treatment of HCV to include SOF-based DAAs. Recently, daclatasvir (DCV), an inhibitor of the HCV NS5A replication complex, was introduced to the National Hepatitis Control Program and is now approved for use in the treatment of GT3 when combined with SOF during a 12-week period. Government-run treatment programmes that include daclatasvir have seen enhanced adherence and success rates (Cavalcante and Lyra, 2015; Capileno et al., 2017). [13,14] Treatments using the NS5A inhibitor velpatasvir (VEL, Epclusa®) have shown success in the management of hepatitis C virus (HCV) (Link et al., 2019). [15] Although the sofosbuvir and velpatasvir (SOF/VEL) combination has been commercially available in Pakistan since March 2018, it is not currently included in the country's national hepatitis control initiatives. When it comes to DAAs, the government has no role to play. As a result, generic producers compete fiercely with brand-name drugmakers (in 2017, SOF faced 14 generic rivals, DCV faced 4, and SOF/VEL faced 1 generic business file for US$ 180). As stated by the group itself (Organization, 2018). [16]

We did this study to examine the effectiveness of sofosbuvir and velpatasvir combined therapy in hepatitis C patients.

MATERIAL AND METHODS

This prospective/observational study was conducted at Department of Gastroenterology Mayo Hospital Lahore, during from the period Feb 2021 to Jan 2022 and comprised of 67 patients. Patients' signed consent was obtained before collecting any personal data. Patients with life-threatening illnesses and those who refused to sign a consent form were excluded from the study.

The age range of the patients was from 18 to 70. Patients with hepatitis C were evaluated if they were between the ages of 20 and 60. The standard treatment for all patients was the

administration of 400 mg of sofosbuvir and 100 mg of velpatasvir in fixed-dose combination tablets twice daily by mouth for 15 weeks. Patients with liver cirrhosis were also administered ribavirin with sofosbuvir and velpatasvir. It was prescribed to cirrhotic patients whose haemoglobin levels remained suboptimal after the addition of supplements and the start of daily 600 mg ribavirin treatment. The presence of HCV RNA fragments was confirmed by RT-PCR (reverse transcription-polymerase chain reaction) at the hospital laboratory, confirming the presence of chronic hepatitis C. Using RT-PCR, we determined that the presence of an HCV RNA level more than 50 for longer than six months constitutes chronic HCV infection. When determining a person's liver health, the following criteria were taken into account: Check for palmar erythema and jaundice, both of which are signs of chronic liver disease; order lab tests, such as an albumin level below normal or an INR over 1.2; and do imaging procedures, such as ultraxial computed tomography.

First 12 weeks, participants had weekly physicals and bloodwork. The medication's effectiveness was measured 12 weeks after therapy. At 12 weeks post-treatment, patients had SVR12 if their HCV viral load was undetectable or less than 50 IU/ml. SVR12 failures are non-responders. No complaints, mild, moderate, and severe adverse occurrences were categorised. Mild adverse effects were non-life threatening, lasted less than a week, and did not need hospitalisation or a dose adjustment. The manufacturer said anorexia, headaches, and epigastric discomfort were the worst side effects. Child-Pugh, MELD, liver function tests, and renal profile alterations were moderate. The death was ruled a serious adverse response after all other causes were ruled out. After collecting data, we used SPSS 20.0 to analyse SVR12, adverse events, and demographics.

RESULTS

In current study, 42 (62.7%) were males and 25 (37.3%). Included patients had mean age 31.12±15.80 years and mean BMI 24.7±8.34 kg/m^2. Majority of the patients were naïve 50 (74.6%) and 17 (25.4%) were treatment experienced. (table 1)

Table 1: Details of patients that have been enrolled

Variables	Frequency	Percentage
Gender		
Male	42	62.7
Female	25	37.3
Mean age (years)	31.12±15.80	
Mean BMI (kg/m^2)	24.7±8.34	
Type of Patients		
Naïve	50	74.6
Treatment Exp.	17	25.4

Comorbidities were hypertension found in 37 (55.2%) cases, diabetes in 15 (22.4%), ischemic heart disease in 10 (14.9%) cases and 5 (7.5%) patients.(figure 1)

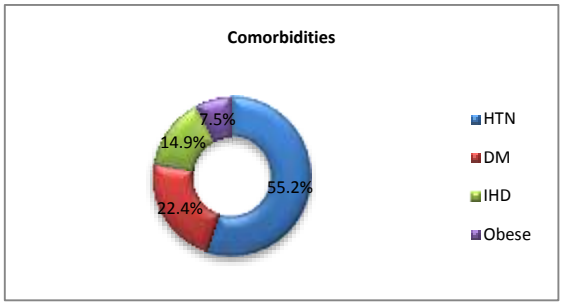

Figure-1: Frequency of other diseases among all cases

We found that efficacy rate was higher and found in 63 (94.03%) cases. As per laboratory findings, aspartate aminotransferase (AST) 37.5± 11.21, alanine aminotransferase (ALT) 26.2±6.44, and haemoglobin level 12.24±10.17 all showed considerable improvement after therapy.(table 2)

Table-2: Post-treatment efficacy among all cases

Variables	Frequency	Percentage
Effectiveness		
Yes	63	94.03
No	4	5.97
Laboratory Results		
Aminotransferase U/L	37.5± 11.21	
alanine aminotransferase U/L	26.2±6.44	
Haemoglobin g/dl	12.24±10.17	
Bilirubin mg/dl	0.3±3.28	

Most common adverse outcomes were headache 35 (52.2%), fatigue 22 (32.8%) and nausea 10 (14.9%).(figure 2)

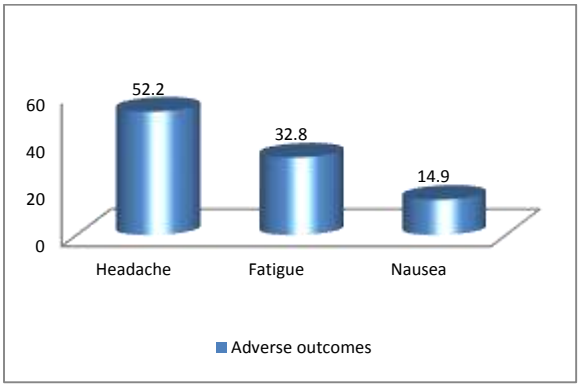

Figure-2: Post-treatment frequency of adverse events

DISCUSSION

Since 2014, the usual treatment for HCV has evolved from long-term, interferon-based regimens with average performance and many adverse events (AEs) to short-term, well-tolerated, all-oral DAA therapy [17]. This success encouraged the WHO to establish the goal of eradicating HCV infection by 2030 [18] and to change its recommendations for screening, care, and treatment in 2017. By removing the need for expensive genotyping and frequent lab monitoring, pan-genotypic DAAs may speed up HCV eradication and simplify treatment algorithms [19].

Both the effectiveness and safety of SOF/VEL have been shown in clinical studies and real-world scenarios, making it the first pan-genotypic DAA to be approved [20]. The PI-free SOF/VEL regimen has several advantages over PI-containing DAA regimens, including a decreased pill load, fewer probable drug interactions, and the capacity to treat decompensated cirrhosis and renal failure [21]. SOF/VEL treatment also improves health-related quality of life [22].

In our research 67 patients of both genders with ages 18-70 years had hepatitis C were included. 42 (62.7%) were males and 25 (37.3%). Included patients had mean age 31.12±15.80 years and mean BMI 24.7±8.34 kg/m^2. Majority of the patients were naïve 50 (74.6%) and 17 (25.4%) were treatment experienced. Results of our study was comparable to the studies conducted in past.[23,24] Comorbidities were hypertension found in 37 (55.2%) cases, diabetes in 15 (22.4%), ischemic heart disease in 10 (14.9%) cases and 5 (7.5%) patients.[21-24]

Our research demonstrated sofosbuvir and velpatasvir to be extremely efficient against chronic HCV in 94.03%. In a study by Wong et al. in Asia, individuals with chronic hepatitis C had a 99.5% SVR rate with sofosbuvir and velpatasvir with or without ribavirin. Patients with decompensated cirrhosis had an 88% SVR rate. We detected similar SVR trends [25]. The SVR rate for sofosbuvir with velpatasvir was 94.7, whereas for cirrhotics it was 88%. A prospective observational study in Pakistan with 1,388 chronic HCV patients, 30% of whom got sofosbuvir and

velpatasvir, discovered this. Our results are supported by this research [26]. Since Southeast Asia is the only location where HCV genotype 6 is common, Western treatment research have given it less attention. The results cannot be extended to the broader population in endemic locations with this genotype. In our sample of 166 genotype 6 patients, SVR rates were high with DAC + SOF, LDV/SOF, and SOF/VEL [27].

It is sometimes challenging to accurately determine the amount of hepatic fibrosis, which is necessary for the evaluation and therapy of patients with chronic liver disease. However, there are limitations to each technique used to evaluate liver fibrosis, and it is difficult to compare data from multiple methods [28]. We employed the FIB-4 index to determine the cutoff for advanced fibrosis, as opposed to the more expensive and less widely available FibroTest, FibroScan, or liver biopsy used by Asselah et al. Fast and inexpensive determination of the FIB-4 score is possible by employing age, AST, ALT, and platelet count [29]. The diagnostic performance of this score [30] was shown when it was used to the evaluation of liver fibrosis in patients from Asia who were suffering from chronic viral hepatitis B and C. It has been shown that the FIB-4 score is more accurate than the CPT class and the MELD score in predicting the long-term prognosis of HCV patients [31].

Most common adverse outcomes were headache 35 (52.2%), fatigue 22 (32.8%) and nausea 10 (14.9%). When Mei et al. looked at the side effects of sofosbuvir and velpatasvir, they found an incidence of 44.4%. However, fatigue was the study's most prevalent side effect. [32]

CONCLUSION

In patients with or without cirrhosis, and regardless of the HCV genotype, the combination of sofosbuvir and velpatasvir has shown to be extremely successful in treating chronic HCV infection. This is true regardless of the HCV genotype.

REFERENCES

1 The cost of eliminating hepatitis C in Pakistan. Abbas Z, Abbas M. Lancet Glob Health. 2020;8:0–4.

2 Epidemiology of hepatitis C infection in Pakistan: current estimate and major risk factors. Arshad A, Ashfaq UA. Crit Rev Eukaryot Gene Expr. 2017;27:63–77.

3 Prevalence of hepatitis C virus genotypes in Pakistan: current scenario and review of literature. Haqqi A, Munir R, Khalid M, et al. Viral Immunol. 2019;32:402–413.

4 Sofosbuvir for previously untreated chronic hepatitis C infection. Lawitz E, Mangia A, Wyles D, et al. N Engl J Med. 2013;368:1878–1887

5 Safety and efficacy of sofosbuvir plus velpatasvir with or without ribavirin for chronic hepatitis C virus infection: a systematic review and meta-analysis. Ahmed H, Abushouk AI, Attia A, Gadelkarim M, Gabr M, Negida A, Abdel-Daim MM. J Infect Public Health. 2018;11:156–164.

6 Inhibitors of the hepatitis C virus RNA-dependent RNA polymerase NS5B. Powdrill MH, Bernatchez JA, Götte M. Viruses. 2010;2:2169–2195.

7 A phase 1, randomized, dose-ranging study of GS-5816, a once-daily NS5A inhibitor, in patients with genotype 1-4 hepatitis C virus. Lawitz E, Freilich B, Link J, et al. J Viral Hepat. 2015;22:1011–1019.

8 Sofosbuvir/velpatasvir: a promising combination. Bonaventura A, Montecucco F. World J Hepatol. 2016;8:785–789.

9 Chahine EB, Sucher AJ, Hemstreet BA. Sofosbuvir/velpatasvir: the first pangenotypic direct-acting antiviral combination for hepatitis C. Ann Pharmacother. 2017;51:44–53.

10 Mangia A, Milligan S, Khalili M, Fagiuoli S, Shafran SD, Carrat F, et al. Global real-world evidence of sofosbuvir/velpatasvir as simple, effective HCV treatment: analysis of 5552 patients from 12 cohorts. Liver Int. 2020;40:1841–52.

11 Wei L, Lim SG, Xie Q, Van KN, Piratvisuth T, Huang Y, et al. ofosbuvir–velpatasvir for treatment of chronic hepatitis C virus infection in Asia: a single-arm, open-label, phase 3 trial. Lancet Gastrenterol Hepatol. 2019;4:127–34.

12 Wilton J, Wong S, Yu A, Ramji A, Cook D, Butt ZA, et al. Real-world effectiveness of sofosbuvir/velpatasvir for treatment of chronic hepatitis C in British Columbia, Canada: a population-based cohort study. Open Forum Infect Dis. 2020;7(3):ofaa055.

13 Cavalcante, L. N., Lyra, A. C. (2015). Predictive factors associated with hepatitis C antiviral therapy response. World J. Hepatol. 7 (12), 1617.

14 Capileno, Y. A., Van den Bergh, R., Donchunk, D., Hinderaker, S. G., Hamid, S., Auat, R., et al. (2017). Management of chronic Hepatitis C at a primary health clinic in the high-burden context of Karachi, Pakistan. PloS One 12 (4), e0175562. doi: 10.1371/journal.pone.0175562

15 Link, J. O., Taylor, J. G., Trejo-Martin, A., Kato, D., Katana, A. A., Krygowski, E. S., et al. (2019). Discovery of velpatasvir (GS-5816): A potent pan-genotypic HCV NS5A inhibitor in the single-tablet regimens Vosevi® and Epclusa®. Bioorg. Med. Chem. Lett. 29 (16), 2415–2427.

16 Organization, W. H. (2017). Regional action plan for the implementation of the global health sector strategy on viral hepatitis 2017–2021 (World Health Organization. Regional Office for the Eastern Mediterranean).

17 Lam BP, Jeffers T, Younoszai Z, Fazel Y, Younossi ZM. The changing landscape of hepatitis C virus therapy: focus on interferon-free treatment. Ther Adv Gastroenterol. 2015;8:298–312.

18 Global Hepatitis Report 2017. Geneva: World Health Organization; 2017. Licence: CC BY-NC-SA 3.0 IGO. http://www.who.int/hepatitis/publications/global-hepatitis-report2017/en/. Accessed 20 Feb 2021.

19 Zoratti MJ, Siddiqua A, Morassut RE, Zeraatkar D, Chou R, van Holten J, et al. Pangenotypic direct acting antivirals for the treatment of chronic hepatitis C virus infection: a systematic literature review and meta-analysis. EClinicalMedicine. 2020;18:100237.

20 Lee R, Kottilil S, Wilson E. Sofosbuvir/velpatasvir: a pangenotypic drug to simplify HCV therapy. Hepatol Int. 2017;11:161–70.

21 Borgia SM, Dearden J, Yoshida EM, Shafran SD, Brown A, Ben-Ari Z, et al. Sofosbuvir/velpatasvir for 12 weeks in hepatitis C virus-infected patients with end-stage renal disease undergoing dialysis. J Hepatol. 2019;71:660–5.

22 Chugh Y, Dhiman RK, Premkumar M, Prinja S, Grover GS, Bahuguna P. Real-world cost-effectiveness of pangenotypic sofosbuvir-velpatasvir combination versus genotype dependent directly acting anti-viral drugs for treatment of hepatitis C patients in the universal coverage scheme of Punjab state in India. PLoS ONE. 2019;14(8):e0221769.

23 Shah I, Ahmad W, Qadir A, Muhammad I, Islam M, Shah M, Jan N, Anjum S. Efficacy and Safety of Sofosbuvir and Velpatasvir Combination for the Treatment of Chronic Hepatitis C in Patients With or Without Cirrhosis. Cureus. 2021 Nov 20;13(11):e19768.

24 Huang, YT., Hsieh, YY., Chen, WM. et al. Sofosbuvir/velpatasvir is an effective treatment for patients with hepatitis C and advanced fibrosis or cirrhosis in a real-world setting in Taiwan. BMC Gastroenterol 21, 259 (2021).

25 Efficacy and safety of sofosbuvir/velpatasvir in a real-world chronic hepatitis C genotype 3 cohort. Wong YJ, Thurairajah PH, Kumar R, et al. J Gastroenterol Hepatol. 2021;36:1300–1308

26 Efficacy and safety of generic sofosbuvir plus daclatasvir and sofosbuvir/velpatasvir in HCV genotype 3-infected patients: real-world outcomes from Pakistan. Mushtaq S, Akhter TS, Khan A, Sohail A, Khan A, Manzoor S. Front Pharmacol. 2020;11:550205

27 Hlaing NKT, Nangia G, Tun KT, Lin S, Maung MZ, Myint KT, Kyaw AMM, Maung ST, Sein Win S, Bwa AH, et al. High sustained virologic response in genotypes 3 and 6 with generic NS5A inhibitor and sofosbuvir regimens in chronic HCV in Myanmar. J Viral Hepat. 2019;26(10):1186–99.

28 Shiha G, Ibrahim A, Helmy A, Sarin SK, Omata M, Kumar A, et al. Asian-Pacific Association for the Study of the Liver (APASL) consensus guidelines on invasive and non-invasive assessment of hepatic fibrosis: a 2016 update. Hepatol Int. 2017;11:1–30.

29 Vallet-Pichard A, Mallet V, Nalpas B, Verkarre V, Nalpas A, Dhalluin-Venier V, et al. FIB-4: an inexpensive and accurate marker of fibrosis in HCV infection. Comparison with liver biopsy and FibroTest. Hepatology. 2007;46:32–6.

30 Wang HW, Peng CY, Lai HC, Su WP, Lin CH, Chuang PH, et al. New noninvasive index for predicting liver fibrosis in Asian patients with chronic viral hepatitis. Sci Rep. 2017;7:3259.

31 Butt AA, Ren Y, Lo Re V III, Taddei TH, Kaplan DE. Comparing Child–Pugh, MELD, and FIB-4 to predict clinical outcomes in hepatitis C virus-infected persons: results from ERCHIVES. Clin Inf Dis. 2017;65:64–72.

32 Efficacy and safety of sofosbuvir-based direct-acting antiviral agents treatment for patients with genotype 3/6 hepatitis C virus infection. Mei YY, Chen YM, Wu YK, Zhang XH, Xu WX. Can J Gastroenterol Hepatol. 2020;2020:8872120