Efficacy of Combination Therapy Sofosbuvir Plus Velpatasvir in Treatment of Hepatitis C Virus(HCV)

Shahzad Latif,[1] Wafa Qaisar,[2] Hafiza Qaria Bushra Saleem,[3] Tariq Waseem,[4] Zartasha Hanan Khan[5]

Abstract

Objective: To assess the treatment response and tolerance in HCV patients without doing genotypes.

Method: An interventional study was conducted to evaluate the efficacy and sustained virologic response (SVR) of 200 patients suffering with hepatitis C after an intervention of once-daily Sofosbuvir 400 mg plus Velpatasvir 100 mg for 12 weeks at Akhtar Saeed Trust hospital and Farooq Hospital Lahore between December 2019 to December 2021.The sample size was calculated by using keeping margin of error at 5%, confidence level at 95%, population size 20000 and response rate at 30%. Patients were followed up on weekly basis with CBC, LFTS and RFTS and HCV RNA by PCR at 4th week and six months after completion of 12 weeks treatment. With SPSS 23, Chi square test was applied and p-value of < 0.05 was considered significant.

Results: In this interventional study out of 200 hepatitis C positive patients 139(63.5%) were males and 61(27.9%) were females. A significant association was observed between gender (p=0.000), presenting complaints (p =0.002) abdominal ultrasound findings (0.004), status of patient (p=0.015), comorbidities (p= 0.042) and lab investigations (p=0.000). Various side effects were reported by 69(31.5%) experienced headaches, 60(27.4%) experienced dyspepsia, 57(26%) experienced nausea as a result of this combination therapy.

Conclusion: Twelve weeks of treatment with combination therapy of sofosbuvir and Velpstasvir is well tolerated and has high SVR in HCV patients with all types of genotypes.

Keywords: Combination therapy, Efficacy, Hepatitis C

How to cite: *Latif S, Qaisar W, Saleem HQB, Waseem T, Khan ZH. Efficacy of Combination Therapy Sofosbuvir Plus Velpatasvir in Treatment of HCV. Esculapio - JSIMS 2022;18(03):390-394*

DOI: https://doi.org/10.51273/esc22.2518330

Introduction

The hepatitis C virus (HCV), a single-stranded RNA virus of the family Flaviviridae with six major genotypes, infects more than 200 million people worldwide, representing more than 3% of the world's population.[1,2] According to the World Health Organization (WHO) estimates, Southeast Asia has considered a high-risk region for HCV with a prevalence of 2.15%[3] Chronic HCV infection causes progressive liver fibrosis, which can lead to cirrhosis, hepatic decompensation, and hepatocellular carcinoma.[4] As many as half a million people die annually from liver disease associated with chronic HCV infection.[5] HCV prevalence is highest in Egypt at more than 10% of the general population and China has the most people with HCV (29.8 million) and the ongoing transmission appears to be widespread, occurring in both healthcare and community settings.[6] Understanding HCV epidemiology in Pakistan is critical in developing and targeting cost-effective prevention and treatment interventions against HCV, in order to meet the global target of HCV elimination.[7] Pakistan

1. *Department of Gastroenterology, Akhtar Saeed Medical and Dental College, Lahore.*
2. *Department of Medicine, Rashid Latif Medical and Dental College, Lahore.*
3. *Nawaz Sharif Social Security Hospital, Multan road, Lahore.*
4. *Department of Medicine, Akhtar Saeed Medical and Dental Ccollege, Lahore.*
5. *Department of Community Medicine, Akhtar Saeed Medical and Dental College, Lahore.*

Correspondence:
Dr. Shahzad Latif, *Associate Professor/ HOD, Department of Gastroenterology, Akhtar Saeed Medical and Dental college, Lahore.*

Submission Date: 12-06-2022
1st Revision Date: 29-06-2022
Acceptance Date: 22-07-2022

is enduring an HCV epidemic of historical proportions as one in every 20 Pakistanis has been already infected with this infection playing a major role in the liver disease burden in this country.[8] Since 2014, the United States Food and Drug Administration (FDA) has approved a new wave of direct-acting antiviral (DAA) oral medications that has revolutionized the landscape for hepatitis C virus (HCV) treatment as this therapy is more effective, easier to tolerate, and significantly shorter in duration.[9] In addition, the newer DAA-based therapies are highly effective in traditionally more difficult-to-treat patients, including those with cirrhosis, HIV co-infection, renal failure, or prior HCV treatment experience.[10] The development of a ribavirin-free single-tablet regi-men of short duration that is effective in a broad range of patients with HCV infection would simplify clinical decision-making and reduce the need for pretreatment testing and monitoring during therapy.[11] Sofosbuvir is a nucleotide analogue inhibitor of the HCV NS5B polymerase approved for the treatment of HCV in combination with Velpatasvir is a new pan-genotypic HCV NS5A inhibitor with antiviral activity against HCV replicons in genotypes 1 through 6.[12] Patients being treated with the combination therapy should be monitored and assessed for compliance with therapy and adverse effects.[13] HCV is one of the most common chronic infections in Pakistan and a major burden on the healthcare system. Measures should be taken at the national level to identify its actual burden and to control factors responsible for its spread. This study is aimed to find out the efficacy of combination therapy Sofosbuvir plus Velpatasvir in the treatment of HCV in Pakistan.

Materials and Methods

An interventional study was planned to evaluate the efficacy and sustained virologic response (SVR) of patients suffering with hepatitis C after an intervention of once-daily Sofosbuvir 400 mg plus Velpatasvir 100 mg for 12 weeks at Akhtar Saeed Trust hospital EME Society and Farooq Hospital west-wood branch Lahore. It was conducted between December 2019 to December 2021.

A sample of 200 patients suffering from Hepatitis C was recruited in the study. It included both previously treated and untreated patients, infected with HCV genotype 1, 2, 4, 5, or 6, including those with compensated and decompensated liver cirrhosis. The sample size was calculated by using Raosoft online sample size calculator keeping margin of error at 5%, confidence level at 95%, population size 20000 and response rate at 30%. All those patients who were HCV positive by PCR between age of 18-75 years were included in sample. It included all patients who were newly diagnosed, relapsed, non-responders, treatment left, with compensated or decompensated liver disease. All those patients who were at End stage liver disease, End stage Hepatitis C Cirrhosis, diagnosed with hepatitis other than hepatitis C, had acute Psychiatric illness, end stage kidney disease and Tuberculosis were excluded. All those patients who showed Hypersensitivity for Sofosbuvir & Velpatasvir were also removed from interventional trial. Those who did not give consent to participate in trial or to share their data were also excluded. After recruitment of patients who gave written consent for trial, they were treated and then were followed up for 6 months. This follow up was done on weekly basis with CBC, LFTS and RFTS and HCV RNA by PCR at 4th week and six months after completion of 12 weeks treatment.

Results

In this current study, 200 patients after screening for HCV positive by PCR without doing genotyping were included as open-labeled after written and informed consent, only one patient due to raised s. creatinine was excluded from the safety analysis and so left follow-up. The Bivariate analysis of PCR at 24 week (in Table: 1) showed significant association of gender (p=0.000), presenting complaints (p =0.002) abdominal ultrasound findings (0.004), status of patient (p=0.015), comorbidities (p= 0.042) and lab investigations (p=0.000).

Out of 200 patients, 69(31.5%) experienced headaches, 60(27.4%) experienced dyspepsia, 57(26%) experienced nausea. 14 (6.4%) complained of insomnia after soughing treatment.

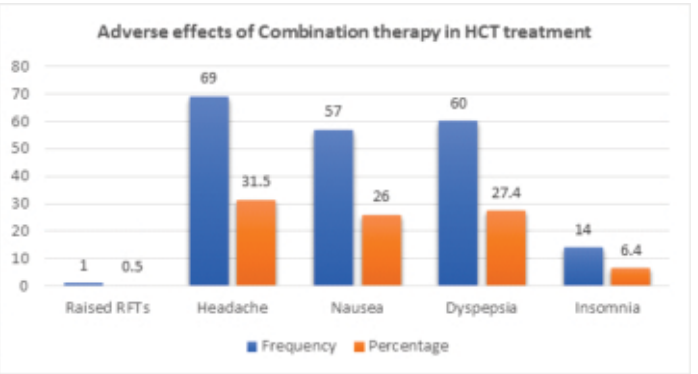

Fig: 1 *Shows the side effects of Sofosbuvir plus Velpatasvir in Treatment of HCV*

Table 1: *Cross tab at PCR 24 weeks:*

Variables	Frequency (n)	Percentage (%)	p-value
Gender			
Male	139	63.5	0.000*
Female	61	27.9	
Presenting complaints			
HCV positive	120	70	0.002*
Lethargy	47	18	
Weakness	33	11.5	
Ultrasound Abdomen findings			
Normal	145	20.7	0.004*
Liver cirrhosis	51	28.7	
Hepatocellular carcinoma	4	44.5	
Status of patients			
Non- cirrhotic	156	71.2	0.000*
Cirrhotic	24	11	
Relapse	14	6.4	
Left treatment	6	2.7	
Comorbidities			
Diabetes Mellitis(DM)	21	9.6	0.001*
Hypertension (HTN)	20	9.1	
Both DM and HTN	19	8.7	
IHD	2	0.9	
No comorbidity	139	63.5	
Hemoglobin			
Less than 10	25	12.5	0.000*
10-13	147	73.5	
More than 13	28	14	
Platelets			
Less than 50	8	4	0.000*
50-100	34	17	
100-150	23	11.5	
More than 150	135	67.5	
Bilirubin			
Normal	200	100	0.000*
raised	0	0	
Albumin			
less than 2	13	6.5	0.000*
2-3	49	24.5	
More than 3	138	69	
Left treatment			
yes	3	1.5	0.901
no	197	98.5	

Discussion

HCV infection can lead to liver cirrhosis, hepatocellular carcinoma, and death. In this therapeutic interventional study, conducted on hepatitis C-positive patients, the combination therapy of sofosbuvir and velpatasvir was found effective and safe with no major adverse effects.

In this study, the percentage of the male and female population is 63.5% and 27.9% while another study conducted in China showed that HCV positive rates in males and females were 51.66% and 35.93%, respectively.[14] The ultrasound findings in this study reveal that 28.7% of patients developed liver cirrhosis and 44.5% developed hepatocellular carcinoma while another study conducted in Bangkok, Thailand showed that 40% of patients developed cirrhosis and the prevalence of hepatocellular carcinoma is 57% in Northern America.[15,16] The main comorbidities, found in this trial, were hypertension (9.1%) and diabetes mellitus (9.6%) while another study conducted in Brazil reported arterial hypertension in 30.4%, and diabetes mellitus in (24.6%) patients.[17]

Serum albumin and platelet count with (p-value <0.01) were observed in this study, similarly, in a Japanese study, the serum albumin and platelet count were significantly improved with combination therapy of sofosbuvir and velpatasvir (p-value<0.01).[18] In lab investigations, the platelet count ranges from 15-100/µL in 17% of HCV patients whereas a study conducted in Germany showed that 53% of the patients receiving antiviral therapy had platelet counts <90.000/µL.[19]

In the current study, for those who received antiviral therapy, liver function parameters such as serum bilirubin improved significantly in 100% of patients. In contrast, a study conducted in Egypt showed that the majority of patients who received sofosbuvir also showed improvement in bilirubin levels.[20]

In this study, no serious side effects to patients with end-stage renal disease were reported establishing the combination therapy with sofosbuvir and velpatasvir as safe, as well as effective in the management of hepatitis C patients with end-stage renal disease.[21]

In this trial, three patients left treatment while in a prospective open-label interventional trial conducted in Pakistan which investigated the efficacy of sofosbuvir and velpatasvir in hepatitis C patients, only two patients were lost to follow-up.[22]

Conclusion

Once-daily sofosbuvir plus velpatasvir for 12 weeks provided high rates of sustained virologic response (SVR) among both previously treated and untreated

patients infected with HCV genotypes 1, 2,4, 5, or 6, including those with compensated and decompensated liver cirrhosis.

Conflict of Interest *None*

Funing Source *None*

References:

1. Mohd Hanafiah K, Groeger J, Flaxman AD, Wiersma ST. Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. Hepatology 2013; 57: 133342.
2. Messina JP, Humphreys I, Flaxman A, et al. Global distribution and prevalence of hepatitis C virus genotypes. Hepatology 2015; 61: 77-87.
3. Rasheed A, Ullah S, Naeem S, Zubair M, Ahmad W, Hussain Z. Occurrence of HCV genotypes in different age groups of patients from Lahore, Pakistan. Advancements in Life Sciences. 2014 Feb 25;1(2):89-95.
4. Hajarizadeh B, Grebely J, Dore GJ. Epidemiology and natural history of HCV infection. Nat Rev Gastroenterol Hepatol 2013; 10: 553-62.
5. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012; 380: 2095-128.
6. Qureshi H, Bile KM, Jooma R, Alam SE, Afridi HUR. 2010. Prevalence of hepatitis B and C viral infections in Pakistan: findings of a national survey appealing for effective prevention and control measures. East Mediterr. Health J. 16, S15–S23. [PubMed] [Google Scholar]
7. Zaina Al Kanaani,1 Sarwat Mahmud,1 Silva P. Kouyoumjian,1 and Laith J. Abu-Raddad1,2. The epidemiology of hepatitis C virus in Pakistan: systematic review and meta-analyses. R Soc Open Sci. 2018 Apr; 5(4): 180257.
8. Afzal MS, Shah ZH, Ahmed H. Recent HCV genotype changing pattern in the Khyber Pakhtunkhwa province of Pakistan; is it pointing out a forthcoming problem?. Brazilian Journal of Infectious Diseases. 2016 May; 20:312-3.
9. Muir AJ, Naggie S. Hepatitis C virus treatment: is it possible to cure all hepatitis C virus patients? Clin Gastroenterol Hepatol 2015; 13: 2166-72.
10. Galán RJ, Cidoncha EC, Martin MF, Rodriguez CC, Almeida CV, Verdugo RM. Antiviral regimen complexity index as an independent predictor of sustained virologic response in patients with chronic hepatitis C. J Manag Care Pharm. 2013 Jul-Aug;19(6):448-53.
11. Lawitz E, Freilich B, Link J, German P, Mo H, Han L, Brainard DM, McNally J, Marbury T, Rodriguez-Torres M. A phase 1, randomized, dose-ranging study of GS-5816, a once-daily NS 5A inhibitor, in patients with genotype 1–4 hepatitis C virus. Journal of viral hepatitis. 2015 Dec;22(12):1011-9.
12. Foster GR, Afdhal N, Roberts SK, Bräu N, Gane EJ, Pianko S, Lawitz E, Thompson A, Shiffman ML, Cooper C, Towner WJ. Sofosbuvir and velpatasvir for HCV genotype 2 and 3 infection. New England Journal of Medicine. 2015 Dec 31;373(27):2608-17
13. Ferraro M, Painter MS. Hepatitis C–Screening, Diagnosis, Management & Treatment. Osteopathic Family Physician. 2019 Jul 24;11(1):12-9.
14. Li Y, Zhao L, Geng N, Zhu W, Liu H, Bai H. Prevalence and characteristics of hepatitis C virus infection in Shenyang City, Northeast China, and prediction of HCV RNA positivity according to serum anti-HCV level: a retrospective review of hospital data. Virology Journal. 2020; 17:36(1)
15. Bunchorntavakul C, Reddy K. Treat chronic hepatitis C virus infection in decompensated cirrhosis - pre- or post-liver transplantation? the ironic conundrum in the era of effective and well-tolerated therapy. Journal of Viral Hepatitis. 2016;23(6):408-418
16. de Martel C, Maucort-Boulch D, Plummer M, Franceschi S. World-wide relative contribution of hepatitis B and C viruses in hepatocellular carcinoma. Hepatology. 2015; 62(4):1190-1200
17. Boff da Costa R, Boff Costa M, Longo L, Miotto D, Hirata Dellavia G, Trucollo Michalczuk M et al. Direct antiviral agents for hepatitis C and drug interaction risk: A retrospective cohort study with real and simulated data on medication interaction, the prevalence of comorbidities and comedications. PLOS ONE. 2021; 16(2):1-13
18. Takaoka Y, Miura K, Morimoto N, Ikegami T, Khakizaki S, Sato K, Ueno T, Naganuma A, Kosone T, Arai H, Hatanaka T. Real-world efficacy and safety of 12-week sofosbuvir/velpatasvir treatment for patients with decompensated liver cirrhosis caused by hepatitis C virus infection. Hepatology Research. 2021 Jan; 51(1): 51-61.
19. Deterding K, Höner zu Siederdissen C, Port K, Solbach P, Sollik L, Kirschner J et al. Improvement of liver function parameters in advanced HCV-associated liver cirrhosis by IFN-free antiviral therapies. Alimentary Pharmacology & Therapeutics. 2015; 42(7): 889-901.
20. Mohamed M, Hanafy A, Bassiony M, Hussein S. Sofosbuvir and daclatasvir plus ribavirin treatment improve liver function parameters and clinical outcomes in Egyptian chronic hepatitis C patients. European Journal of Gastroenterology, Hepatology. 2017;29(12):1368-1372.

21. Taneja S, Duseja A, Mehta M, De A, Verma N, Premkumar M, Dhiman RK, Singh V, Singh MP, Ratho RK, Ramachandran R. Sofosbuvir and Velpatasvir combination is safe and effective in treating chronic hepatitis C in end-stage renal disease on maintenance hemodialysis. Liver International. 2021;41(4):705-9
22. Butt N, Muhammad I, Abou Bakr A, Akhtar Z, Ali M, Muhammad SS, Maheshwary N. Efficacy and safety of the sofosbuvir-velpatasvir combination in hepatitis C virus-infected Pakistani patients without cirrhosis or with compensated cirrhosis: a prospective, open-label interventional trial. Cureus. 2020 1;12(1)

Authors Contribution

SL: Conceptualization of Project
WQ: Data Collection
HQBS: Literature Search
ZHK: Statistical Analysis
ZHK: Drafting, Revision
TW: Writing of Manuscript