



Efficacy of velpatasvir and sofosbuvir in treatment of chronic hepatitis C.

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ABSTRACT... Objective: To determine the efficacy of sofosbuvir and velpatasvir in treatment of all genotypes of chronic HCV infection. **Study Design:** Descriptive Case study **Setting:** Department of Medicine Independent University Hospital Faisalabad. **Period:** December 2019 to May 2020. **Material & Methods:** Among patients of chronic hepatitis C presenting in the medical OPD of independent university hospital willing to participate, 80 were included in this study. They were given combination of sofosbuvir and velpatasvir 400/100 mg (FDC) once daily. They were monitored by serum ALT and PCR to HCV quantitative after one month and after three months. End point was undetectable PCR to HCV Quantitative. We observed the number of patients achieving SVR after taking combination of sofosbuvir and velpatasvir. **Results:** In our study, out of 80 cases of chronic hepatitis c 40% (n=32) were male and 60% (n=48) were females, end result revealed 98.8% (n=79) achieved SVR and their PCR remained negative at the end of 03months and 1.3% (n=01) remained positive despite antiviral therapy for 03 months. **Conclusion:** We concluded that using fixed dose combination of sofosbuvir and velpatasvir achieve SVR of 98.8%.

Key words: Chronic Hepatitis C, Sofosbuvir, Serum ALT, Velpatasvir.

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INTRODUCTION

Hepatitis C is an infectious disease of liver caused by hepatitis C virus (HCV). Worldwide 143 million people are infected with (HCV).¹ Pakistan is endemic country for HCV and about 6.8% of general population is infected with this virus with 61.3% of people infected with genotype 3a.²

HCV spreads via blood to blood contact such as intravenous drug abuse, blood transfusion, tattooing, needle stick injuries and surgical procedures.³ Acute infection is rarely symptomatic and usually goes unnoticed. Main symptoms of acute HCV infection, when present are nausea, vomiting, muscle and joint pains, jaundice, dark urine and pale stool. Although acute infection doesn't cause acute liver failure but causes hepatocellular injury and increases liver enzymes.⁴

There is no vaccine for hepatitis C.⁵ About 80 percent of acute infection leads to chronicity

with hepatocellular injury and regeneration. This infection if left untreated may cause cirrhosis of liver and even hepatocellular carcinoma in 30 to 50% of the patients.⁶

Previously hepatitis C was treated with injectible interferon and ribavirin based therapy which had less than 50 percent cure rate and greater side effects⁷ then newer drugs which target nonstructural proteins have been developed.⁸ Sofosbuvir was the first oral drug to be developed for the treatment of chronic HCV.⁹ Sofosbuvir and ribavirin with or without pegylated interferon has been used for twelve weeks in the recent past to treat HCV genotypes 2 and 3.¹⁰

In June 2016 Food and drugs administration (FDA) approved combination of sofosbuvir and velpatasvir for the treatment of chronic HCV with or without cirrhosis for all genotypes.¹¹

Sofosbuvir works by inhibiting viral protein

NS5B.¹² Velpatasvir is NS5A inhibitor which is used along with sofosbuvir for the treatment of all genotypes of chronic HCV.¹³

In 2018 European association for the liver disease (EASL) also recommended the combination of sofosbuvir and velpatasvir for the treatment of all genotypes of chronic HCV in patients without cirrhosis or with compensated cirrhosis.¹⁴

With the introduction of fixed dose combination (FDC) highly efficacious oral antiviral sofosbuvir and velpatasvir, it is claimed to achieve SVR of 91 % to 96% in treatment naïve and experienced patients without cirrhosis with 12 weeks of therapy.¹⁵ With such convenient and efficacious therapy it is now possible to reduce HCV burden and reduce its transmission to healthy persons¹⁶ in endemic countries like Pakistan.

My research will focus on finding the efficacy of (Fixed dose combination) FDC of sofosbuvir and velpatasvir in all genotypes in Pakistan. This is needed because all of research on sofosbuvir and velpatasvir has been done in other countries; Pakistan being endemic country for chronic hepatitis C has not been investigated so extensively.

MATERIAL & METHODS

This study was conducted in department of Medicine Independent University Hospital Faisalabad, No IUH/IRB/00009. Total duration of study was 06 months from December 2019 to May 2020. Patients were selected by using convenience sampling. Study design was descriptive case study. Sample size was calculated by using sample size calculator.

By using sample size calculator

Margin of Error = 5%

Confidence interval = 95%

Prevalence of HCV = 5.46%

Sample Size = 80

Inclusion criteria

All the patients of chronic hepatitis C

Both genders will be included

Age >20 years and < 80 years

Exclusion Criteria

Patient with decompensated cirrhosis

Patient with documented HCC

After taking approval from hospital ethical review committee, patients fulfilling the selection criteria were enrolled in the study and informed consent was taken from patients/caregivers. Detailed history was recorded in each case. Detailed physical examination with special emphasis on abdomen and relevant was conducted in all patients. Serum ALT levels and PCR to HCV RNA advised on first visit after one month and after 3 months in all patients through hospital pathology laboratory. Collected data was recorded in a structured Performa by me.

All the data was analyzed by using SPSS 22. Mean and standard deviation was calculated for all the quantitative variables like age, serum ALT. Frequency and percentage was calculated for all the qualitative variables like gender.

RESULTS

In our study, out of 80 cases of chronic hepatitis C 40% (n=32) were male and 60% (n=48) were females (Table-I). Age distribution reveals 26.3% (n=21) of patients belongs to age range of 24-35 years, 25% (n=20) of patients belong to age range of 35-45 years, 36.3% (n=29) of patients belong to age range 45-55 years, 12.5% (n=10) patients were older than 55 years (Figure-1). Regarding serum ALT 23.8% (n=19) of patients were having Serum ALT between 25-45mg/dl, 42.5% (n=34) of patients were having Serum ALT between 45-65mg/dl, 32.5% (n=26) of patients were having serum ALT between 65-85mg/dl and 1.3% (n=01) of the patients was having serum ALT > 85mg/dl (Figure-2). Regarding PCR 98.8% (n=79) were having undetectable viral load after one month (Table-IV) and three months and 1.3% (n=01) was having detectable viral load after one month and virus remained detectable even after 03 months of antiviral therapy (Table-V).

End result revealed 98.8% (n=79) get cured and their PCR remained negative at the end of 03 months and 1.3% (n=01) remained positive despite antiviral therapy for 03 months (Table-VI).

	N	Minimum	Maximum	Mean	Std. Deviation
Serum_ALT	80	22.00	89.00	57.3500	16.07664
Age	80	27.00	65.00	43.4125	9.74185
Valid N (listwise)	80				

Table-I. Descriptive Statistics.

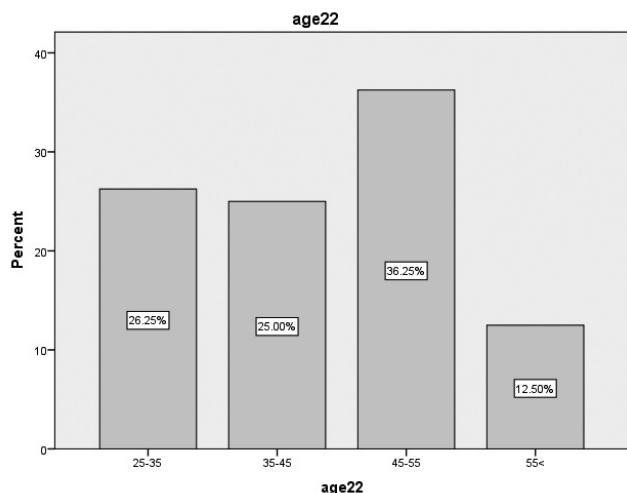


Figure-1

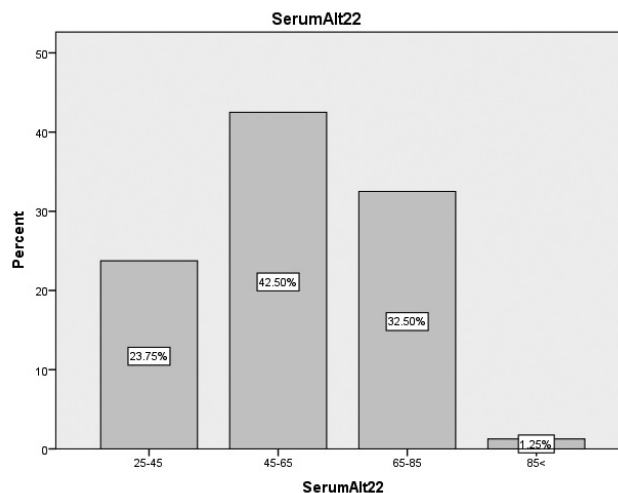


Figure-2

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Positive	1	1.3	1.3	1.3
	Negative	79	98.8	98.8	100.0
	Total	80	100.0	100.0	

Table-II. PCR after one Month.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Positive	1	1.3	1.3	1.3
	Negative	79	98.8	98.8	100.0
	Total	80	100.0	100.0	

Table-III. PCR after 03 Months.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Achieved SVR	79	98.8	98.8	98.8
	Not Achieved SVR	1	1.3	1.3	100.0
	Total	80	100.0	100.0	

Table-IV. End Result.

DISCUSSION

With the approval of fixed dose oral antiviral therapy, safe and effective combination regimens are now available for the majority of chronically infected patients with HCV. Cure rates greater than 90% can be achieved in most patients, regardless of genotype, treatment experience, or the presence of cirrhosis. A fixed dose

combination of antiviral drugs which is effective in all genotypes of HCV will eliminate the need for expensive pretesting and will reduce the cost burden for developing countries.¹⁷ Although the proportion of patients who do not achieve SVR with currently approved regimens is small, the absolute number of treatment failures will increase as the rate of treatment taken increases.

Direct acting oral antiviral failures has no medical alternative available at this time. However those patients who failed to achieved SVR on Sofosbuvir and velpatasvir. The addition of voxilaprevir for 12 weeks increases SVR rate to 98% (POLARIS -1 and POLARIS-4).¹⁸

In this study, the combination of sofosbuvir and velpatasvir for 12 weeks was shown to be safe and highly effective for treatment naive patients with HCV infection irrespective of genotype. The result of our study is comparable with the studies done abroad (ASTRAL-1) and published in New England journal of medicine.¹⁹

Currently approved treatment regimens have durations of 12 to 24 weeks, depending on the choice of treatment regimen and the patient's baseline characteristics, such as HCV genotype, treatment history, and presence or absence of cirrhosis.

The efficacy of sofosbuvir and velpatasvir in decompensated cirrhosis is reduced to 83% (SVR) for twelve week treatment, but with the addition of ribavirin to sofosbuvir and velpatasvir increases the SVR rate from 83% to 94%.²⁰

The possibility of shortening the duration of treatment has been a research objective, in particular for treatment regimens without ribavirin. Several clinical trials have studied various combinations of direct acting oral antiviral for 4 weeks, but with uniformly disappointing results.²¹ In addition, the high levels of SVR across all genotypes suggest pangenotypic use of sofosbuvir and velpatasvir.

This study was limited by its small sample size. Only 80 treatment naïve patients were included in this study out of which 79 people get cured and 01 patient remained positive despite antiviral. Secondly genotyping was not done in our patients because of pangenotypic regime was given to the patients covering all genotypes.

CONCLUSION

We concluded that fixed dose combination of velpatasvir and sofosbuvir is highly efficacious

and having SVR of 98.8% in treatment native patients without cirrhosis.



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AUTHORSHIP AND CONTRIBUTION DECLARATION

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2	Hafiz Bilal Bashir	Data collection, Write up.	
3	Mahpara Munir	Proof reading.	