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Original Research Article

Case Series of Responders to Sofosbuvir Plus Velpatasvir Based Combination Therapy for Hepatitis C in Chronic Kidney Disease Who are on Maintenance Hemodialysis

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Abstract

Hepatitis C Virus (HCV) infection is a major infection worldwide, with 12.5 million people infected in India alone. In hemodialysis undergoing CKD population in specific, the prevalence of HCV is 4.3 - 45 %. It leads to accelerating decline of renal and liver functions causing higher mortality in hemodialysis patients. WHO recommends use of pan-genotypic, direct-acting anti-virals for the treatment of HCV. Sofosbuvir, in combination with other antivirals, led to a significant paradigm change in the treatment of HCV. Sofosbuvir is metabolized in the liver into an active metabolite which is not detected in circulation and an inactive metabolite that is excreted renally. Sofosbuvir and Velpatasvir combination of drugs was given to 10 HCV positive patients with CKD and on hemodialysis for 12 weeks. Viral load, after the completion of the treatment, were undetectable in all the patients. Sofosbuvir-Velpatasvir combination was demonstrated effective and safe in hemodialysis undergoing HCV patients.

Introduction

HCV causes progressive infection of the liver, leading to cirrhosis is 10-20% population and hepatocellular carcinoma in 1-5% over 20-30 years[3]. HCV is highly prevalent among CKD patients undergoing hemodialysis. Many determinants like use of blood and blood products, nosocomial infections and long dialysis duration increases the risk of this infection in hemodialysis patients.A meta-analysis in 2007 demonstrated that mortality in HCV infected hemodialysis patients was more than that in HCV negative patients[4]. Use of direct-acting anti-viral drugs was a revolutionary change in the treatment of HCV. AASLD recommends Sofosbuvir (400 mg) plus Velpatasvir (100 mg) for a duration of 12 weeks for the treatment of HCV in general population [5]. In November 2019, US FDA permitted use of Sofosbuvir containing regimens in patients with renal disease, including those on dialysis[6]. This case series pertains to use of Sofosbuvir plus Velpatasvir regimen in hemodialysis patients as more information is to be made available to estimate effectiveness and safety of the use of these drugs.

Methods

This case series includes around 10 CKD patients on regular hemodialysis at a tertiary care center of a teaching hospital – S.S.I.M.S and R.C, India, conducted during the time period between Jan 2022 - Dec 2022. In this observational study, the patients were initially subjected to rapid HCV antibody test, followed by ELISA method for HCV antibodies, with titres above 9.95, indicating positive results[7]. Quantitative real time RT-PCR for HCV RNA was performed for confirmation and values were noted. A baseline LFT, ultrasound abdomen were performed before starting the treatment. The treatment, Tab. Sofosbuvir (400 mg) plus Tab. Velpatasvir (100 mg), was given daily for 12 weeks to these patients. Patients were followed up and post-treatment HCV viral load testing by quantitative real time RT-PCR of HCV RNA was done 12 weeks after the completion of the treatment. Post-treatment values were compared with pre-treatment values to see the drug response and thereby, a series of such patients, data was collected and interpreted.

Results

A total of 10 CKD patients undergoing hemodialysis were included in this study, with HCV viremia

detected by quantitative real-time RT-PCR. The laboratory characteristics were baseline prior to the start of the treatment in eight out of ten patients, with two of the patients having increased liver enzyme levels. The patients were given 400 mg of Tab. Sofosbuvir and 100 mg of Tab. Velpatasvir (100 mg) daily for a total of 12 weeks. None of the patients were taking any other protease inhibitors, amiodarone while on treatment. All the patients tolerated the treatment well and adhered to it. One patient developed gastrointestinal symptoms while on treatment and was treated with PPIs. No other significant side effect was noted in the patients while on treatment.

Efficacy outcomes

All the patients completed with treatment.12 weeks after this combination therapy, real time RTPCR testing showed a negative or undetectable viral load of HCV. This indicated a sustained virological response after treatment.

Table 1:

Serial Number	Age	Gender	Baseline USG	Baseline LFT	Pre-treatment viral load (IU/Ml)	Post treatment viral load (IU/Ml)
1	34	Male	Normal study	Normal	25,87,990	<34
2	50	Male	Normal study	Normal	77,88,140	<21
3	67	Male	Normal study	Sgot-155, Sgpt-145	31,85,300	<34
4	42	Male	Normal study	Normal	5,54,890	<34
5	58	Male	Normal study	Normal	86,23,608	<34
6	65	Male	Normal study	Normal	26,36,558	<21
7	66	Female	Normal study	Normal	5,54,257	<34
8	54	Male	Normal study	Sgot-288, Sgpt-167	1,20,655	<34
9	45	Female	Normal study	Normal	3,98,734	<21
10	48	Male	Normal study	Normal	8,89,544	<34

Discussion

In this study, we report the efficacy of Sofosbuvir plus Velpatasvir regimen in treating HCV infected CKD patients on hemodialysis providing more information required to support the previous studies [6]. It also solidifies that the given regimen is effective in Asian ethnic population.

Sofosbuvir is a pan-genotypic, direct-acting nucleotide polymerase inhibitor that has been approved for adequate treatment of HCV virus. However, 80% of it is excreted renally, most of it in the form of its inactive metabolite, GS-331007 [8]. Hence, it's approval for use in CKD patients was given after specific studies by US FDA with no necessity of any dose adjustments [6]. There were no associated significant side effects. Use of Sofosbuvir with amiodarone could cause bradycardia and hence, co-administration was banned by FDA [9].

Velpatasvir is a protease inhibitor and biliary excretion is its major route of elimination [10].

The fixed dose combination of Sofosbuvir 400 mg and Velpatasvir 100 mg, once daily for 12 weeks, has emerged globally as first line regimen in HCV infected CKD patients on maintenance hemodialysis [1].

The primary goal of this therapy is to cure HCV infection, i.e. to achieve sustained virological response (SVR) defined as undetectable HCV RNA after treatment completion. An SVR corresponds to a cure of the HCV infection, as late relapse occurs in less than 0.2% of cases beyond 6 months of followup [3].

The study demonstrated 100% efficacy of this regimen as none of the patients had any relapse after completion of the treatment, unlike a similar study done in 2019, that had 95% efficacy. All the patients completed the treatment and did not experience any major side effects, indicating it to be tolerant and safe. This study, as it was conducted in India, also demonstrated it holds good for Asian ethnicity. While in our experience, Sofosbuvir/Velpatasvir regimen was safe and effective with minimal side effects in patients on hemodialysis, the small number of study group was a limitation in our study.

Conclusion

Sofosbuvir and Velpatasvir based combination regimen is safe and has good efficacy for treatment of Hepatitis C in hemodialysis patients with good patient compliance and adherence.

Sofosbuvir is well tolerated orally, and no patient discontinued the regimen.

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