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ORIGINAL ARTICLE

Efficacy of Low Dose Sofosbuvir and Daclatasvir in Treatment of Chronic Hepatitis C in Patients with End Stage Renal Disease

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ABSTRACT

Background: Chronic hepatitis C infection is common in patients with end stage renal disease. The management of hepatitis C virus infection has been greatly influenced by the availability of direct acting antivirals.
Aim: To determine the efficacy of low dose Sofosbuvir and Daclatasvir in treatment of chronic hepatitis C in patients with end stage renal disease.
Study design: Descriptive case series.
Place and study duration: The study was conducted in the Department of Nephrology at Shaikh Zayed Hospital, Lahore from 24th March, 2019 to 23rd September, 2019.
Methodology: A total of 180 patients were enrolled in the study. Serum load of HCV was performed by PCR at baseline, and patients were started on low dose of Sofosbuvir (200mg) and Daclatasvir (60mg), once a day orally for 12 weeks and treatment efficacy was re-assessed by PCR after 12 weeks.
Results: A total of 180 patients were enrolled in the study. The mean age of the patients was 40.53±11.210, mean number of dialysis sessions was 13.98±7.96. There were 59.9% males and 41.1% females. Treatment was efficacious in 91.7% of the patients. Side effects associated with treatment were fatigue (23.9%), nausea (12.8%), headache (11.7%) and anemia (5%). No effect was seen of age, gender, number of dialysis sessions and previous history of treatment on efficacy of treatment.
Conclusion: Low dose Sofosbuvir and Daclatasvir were effective in the treatment of hepatitis C infection in patients with end stage renal disease and had a good safety profile.
Keywords: End Stage Renal Disease, Chronic Hepatitis C, Direct Acting Antiviral Agent

INTRODUCTION

Chronic hepatitis C (CHC) infection is highly prevalent in patients with end stage renal disease (ESRD). Previous literature has shown that about 13.5%[1] patients with end stage renal disease who were on dialysis had comorbid hepatitis C. It is suggested that the cause of this high prevalence is nosocomial transmission of hepatitis C infection during hemodialysis.[1]The rate of mortality in chronic kidney disease patients who have comorbid hepatitis C is significantly greater i.e. 34%[1] than those who are uninfected. It is also seen that hepatitis C infection even after transplantation leads to increased mortality and complications such as graft loss and rejection. The use of antiviral treatment in these patients can lead to complications because majority of the agents that are used as anti-HCV therapy can accumulate to such levels that are toxic when there is renal impairment[2,3]. Thus, patients with end stage renal disease who have comorbid chronic HCV infection represent an important population that warrants specific consideration[1-3].

Management of hepatitis C virus infection has been greatly influenced by the availability of direct acting antivirals (DAA)[1-6]. The most important direct acting antiviral drug is Sofosbuvir, which is a nucleotide NS5B inhibitor[5]. It has been found that Sofosbuvir is associated with sustained virological response and has fewer side effects compared to other antivirals currently being used for the treatment of hepatitis C. Sofosbuvir is often used in combination with other antiviral drugs to treat hepatitis C[6]. One such drug is Daclatasvir, which works by inhibiting the HCV proteinNS5A[7]. Taneja et al, conducted a study to evaluate the safety and efficacy of low-dose Sofosbuvir plus full-dose Daclatasvirin chronic hepatitis C patients with chronic kidney disease.[1] They assessed 65 patients and gave them the combination of fixed doses of these drugs for either 12 or 24 weeks. Abad et al, studied the effectiveness of direct-acting antivirals in Hepatitis C virus infection in haemodialysis patients[5]and concluded that these new direct acting antivirals were highly effective with minimal side effects for the treatment.

The objective of the study was to determine the efficacy of low dose Sofosbuvir and Daclatasvir in treatment of chronic hepatitis C in patients with end stage renal disease.

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PATIENTS AND METHODS

This is a descriptive case series and was conducted after permission from Ethical Review Board in the Department of Nephrology at Shaikh Zayed Hospital, Lahore from 24th March, 2019 to 23rd September, 2019. A total of 180 patients were enrolled in the study from 18-60 years of age in both genders. Serum load of HCV was performed by PCR at baseline, and patients were started on low dose of Sofosbuvir (200mg) and Daclatasvir (60mg), once a day orally for 12 weeks and treatment efficacy was reassessed by PCR after 12 weeks data was collected through proforma. Patients who fulfilled the inclusion criteria were included in the study. Informed consent was taken from all the patients. Before treatment all patients were subjected to detailed history including history of previous treatment for hepatitis C and any features of decompensated liver disease, and a thorough clinical examination. Quantitative measurement of serum load of hepatitis C (HCV) was performed by PCR at baseline, and patients were started on low dose of Sofosbuvir (200mg) and Daclatasvir (60mg), once daily tablet give orally for 12 weeks. After 12 weeks, PCR test was again performed to see HCV viral load to assess the treatment efficacy (as per operational definition). Quantitative variables such as age and number of dialysis sessions were calculated as mean and standard deviation. Qualitative variables such as gender, efficacy of treatment, previous history of treatment and side effects were presented as frequency and percentages. Data was stratified for age, gender, number of dialysis sessions and previous history of treatment. Post stratification chi square test was applied and a P value of ≤0.05 was considered as significant.

RESULTS

The mean age of the patients was 40.53± 11.210. The mean number of dialysis sessions was 13.98±7.96. There were 59.9% males and 41.1% females (Table 1). Treatment was efficacious in 91.7% of the patients (Table 2). 52.8% patients that were enrolled had already previously taken treatment (Table 3). Side effects associated with treatment were fatigue (23.9%), nausea (12.8%), headache (11.7%) and anemia (5%) (Table 4).

Data was stratified for age, gender, number of dialysis sessions and previous history of treatment. Post-stratification chi square test was applied to see the effect of these effect modifiers and it was found that none of these factors had any significant association with treatment efficacy (Table 5-7).

Table 1: Gender distribution of patients (n=180)

Gender	Frequency	Percent
Male	106	58.9%
Female	74	41.1%

Table 2: Frequency of efficacy of treatment

Efficacy	Frequency	Percent
Yes	165	91.7%
No	15	8.3%

Table 3: Frequency of previous history of treatment

Previous History of Treatment	Frequency	Percent
Yes	95	52.8%
No	85	47.2%

Table 4: Frequency of side effects with treatment

Side effects	Frequency	Percent
No side effects	84	46.7%
Fatigue	43	23.9%
Nausea	23	12.8%
Headache	21	11.7%
Anemia	9	5%

Table 5: Association of age with efficacy of treatment

	Efficacy		P
Age groups	Yes	No	Value
Young age	36(20%)	7(3.9%)	
Early middle age	79(43.9%)	5(2.8%)	
Late middle age	50(27.8%)	3(1.7%)	0.097
Total	165(91.7%)	158.3%)	

Table 6: Association of gender with efficacy of treatment

	Efficacy		P
Gender	Yes	No	Value
Male	95 (52.8%)	11 (6.1%)	
Female	70(38.9%)	4 (2.2%)	0.235

Table 7: Association of number of dialysis session with efficacy of treatment

No. of dialysis sessions	Efficacy	
	Yes	No
Few sessions (1-10)	112 (62.3%)	8 (4.4%)
Large No. of sessions(>10)	53 (29.4%)	7 (3.9%)

P value 0.253

DISCUSSION

Hepatitis C infection is commonly seen and is a cause of mortality in chronic kidney disease patients.[1,2]Previously the guidelines by EASL had recommended that pegylatedinterferon must be used along with ribavirin which was dose adjusted in patients with chronic kidney disease who were infected with HCV of genotype 3, but these medicines had poor tolerability and were less efficacious.[4]Sofosbuvir, which is a NS5B inhibitor is excreted renally.[1,3]In patients with renal insufficiency, the plasma levels of its metabolites is increased too. So issue remains regarding its efficacy and safety profile in patients whose GFR is <30 mL/min/1.73m^2. Previous studies used full dose, alternate day's full dose and even half doses of Sofosbuvir in patients who are difficult to treat, the data is still limited and has yielded no clear recommendations[2]. The current study is the first study conducted in Pakistan on the use of low dose Sofosbuvir alongwith Daclatasvirin patients who had end stage renal disease and had superimposed hepatitis C infection. The current study revealed that this treatment combination was effective in 91.7% of the patients and had a good safety profile with the most common symptoms that were encountered were fatigue, nausea, headache and anemia. No serious side effects were noted with this combination of treatment.

Taneja et al, evaluated the efficacy and safety of low dose Sofosbuvir and Daclatasvirin full dose in patients with chronic hepatitis C and chronic kidney disease.[1] 65 patients whose glomerular filtration rate was <30 mL/min/1.73 m^2. All patients were treated with 200mg of Sofosbuvir (half dose) and full dose of Daclatasvir60mg that was given daily irrespective of genotype of hepatitis C virus. The treatment was given for 12 weeks. After 12 weeks of treatment efficacy was assessed by sustained virological response and negative hepatitis C virus RNA. The results showed that 32% patients had cirrhosis and 15.4% already had a history of previous treatment. 98.5% of the patients achieved end of treatment response and 100% attained sustained virological response. The drug acting antiviral agents were well tolerated by all the patients and none of the patient reported any serious side effects. The side effects that were commonly seen were nausea, headache, pruritus and insomnia. So the authors concluded that low dose Sofosbuvir and full dose Daclatasvir are efficacious and have good safety profile when used for the treatment of chronic hepatitis C patients with chronic kidney disease whose eGFR is <30mL/min/1.73 m^2. The results were similar to current study results which also revealed that combination of low dose Sofosbuvir and full dose Daclatasvir was effective in treating hepatitis C virus in patients with end stage renal disease and had a good safety profile. The effects related to treatment as current study reported that the most common side effects were fatigue, nausea, headache and anemia, whereas the study by Taneja et al reported that nausea, headache, insomnia and pruritus were seen commonly[1].

Hepatitis C virus infection is frequently seen in patients who are on hemodialysis and is associated with poor prognosis as compared to those patients who do not have this infection. As interferon and ribavirin are tolerated poorly and limited data is available on direct acting antivirals, therefore, another study was carried out by Abad who analyzed retrospectively the prevalence of hepatitis C virus infection and the effectiveness and safety profile of direct acting antivirals different regimens in the patients who were on hemodialysis.[5] It was an observational study conducted at various centers. Hepatitis C virus antibodies were assessed in 465 patients and 11.6% i.e. 54 patients were found to be positive for the antibodies. Among these 54 patients, 29 were with genotype 1 and 4. These were treated with different regimens of direct acting antivirals such as combinations of paritaprevir/ ritonavir, ombitasvir, dasabuvir, Sofosbuvir, Simeprevir, Daclatasvir and Ledipasvir, with/without ribavirin. Majority of the patients around 72.4% were male and the most common cause of chronic kidney disease in the patients was glomerular in origin. After 24 weeks, sustained virological response was seen in all patients i.e. treatment was efficacious in 100% of the cases regardless of the direct acting antiviral regimen. There were no significant adverse effects and the treatments were tolerated well by all patients. In 15 cases, where ribavirin was combined with direct acting antiviral drugs, the most common side effect was anemia, although no patient required transfusion. The current study also showed similar results of good efficacy and safety profile of direct acting antivirals i.e. Sofosbuvir and Daclatasvir.

CONCLUSION

Low dose Sofosbuvir and Daclatasvir were effective in the treatment of hepatitis C infection in patients with end stage renal

disease and had a good safety profile. The results of this study are reassuring and can guide in formulating further guidelines for the management of hepatitis C infection.

Conflict of interest: Nil

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