ORIGINAL ARTICLE

RESPONSE AND TOLERABILITY OF SOFOSBUVIR PLUS DACLATASVIR IN ELDERLY PATIENTS WITH CHRONIC HEPATITIS-C

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Background: The approval of direct acting anti-viral drugs has expanded the treatment access to all patient populations including elderly patients, who were previously neglected. We evaluated the response and tolerability of sofosbuvir plus daclatasvir in old age patients ≥60 year infected with HCV. **Methods**: In this prospective observational study, 100 patients were enrolled and were divided into two groups: aged 60–69 (group A) and aged 70 and older (group B). All the patients were given sofosbuvir plus daclatasvir. Sustained virologic response at 12 weeks was the primary endpoint. Response and tolerability of treatment were analysed and compared between these patient groups. **Results:** Hundred patients aged ≥60 years were treated with sofosbuvir plus daclatasvir. Sustained virologic response rate was 91% in group A (aged 60– 69 year) and 87.8% in group B (aged 70 year and older). No significant adverse effect was noted in both groups. No treatment discontinuation was encountered. **Conclusions:** Direct acting antiviral drug therapy is highly efficacious and safe for the treatment of HCV in older adults.

Keywords: Chronic hepatitis C; Sofosbuvir; Daclatasvir; Cirrhosis; Sustained virological response; Elderly patients

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INTRODUCTION

Chronic Hepatitis C is a global public health problem, affecting approximately 170 million people worldwide[1] and approximately 350,000 to 500,000 people die each year from HCV related liver diseases[2,3]. Treatment of chronic hepatitis C in old age patients has recently become a hot topic due to lack of safe and effective treatment options in the past. The number of elderly patients visiting the outpatient clinics has increased in the recent time and is expected to increase even more in the near future.[4] According to Center for Disease Control (CDC), the incidence of liver cirrhosis and subsequent hepatocellular carcinoma is expected to rise in the near future in elderly persons.[5] In the era of Interferons, age has been a major limitation to treatment due to comorbidities & poor tolerability. Large-scale studies in the past also showed lower sustained virological response rates and higher withdrawal rates due to side effects of interferons in this particular patient population.[6] The new direct acting antiviral drug treatment seems to be feasible in virtually all the patients with chronic hepatitis C infection regardless of age and comorbidities. Also, the progression of liver cirrhosis is an age- dependent process[7] and studies have shown beneficial effects of SVR on survival even in patients with severe hepatic fibrosis[8,9]. Some authorities do not recommend treatment in patients with multiple co-morbidities and limited life expectancy.[10] Whether this increase frequency of comorbidities & polypharmacy in elderly patients is associated with higher rates of adverse events and/or treatment failure is not known. Therefore, in this study we aimed to assess the clinical effectiveness, safety & tolerability of sofosbuvir plus daclatasvir therapy in old patients aged ≥60 years in a real-world cohort.

MATERIAL AND METHODS

This was a prospective observational study carried out in the department of Gastroenterology, Gujranwala Medical College/ DHQ Teaching Hospital Gujranwala. Consecutive 100 patients who presented between May 2017 to March 2018 to the outpatient department were included in the study. The sample size was calculated using 90% confidence level, 5% margin of error, and taking expected outcome of 90%. Male and female patients aged ≥60 years having positive HCV RNA PCR were included in the study. Both non-cirrhotic and compensated cirrhotic patients were included in the study and those with decompensated liver cirrhosis were excluded from the study. Ultrasonographic features (coarse shrunken liver, splenomegaly, dilated portal vein) and AST to platelet ratio index (APRI) were used as predictors of significant liver fibrosis. An APRI cut-off score of 2.0 was used for detection of cirrhosis.[11] Patients with HIV and HBV co-

infection were excluded from the study. Patients who were previously treated with pegylated interferon or DAA were also excluded. Patients were divided into group A (age 60–69 years) and group B (age ≥70 years). After taking approval from institutional review board, informed written consent was taken from the patients. Demographic parameters, concomitant medications and laboratory findings were recorded. Sofosbuvir plus daclatasvir was given to non-cirrhotic patients for 12 weeks and to cirrhotic patients for 24 weeks. All the patients were followed fortnightly and laboratory parameters as well as adverse effects of the ongoing treatment were recorded. Efficacy of the treatment was assessed by end treatment response (ETR), i.e., negative PCR at the end of treatment and by sustained virologic response (SVR12), i.e., negative PCR after 12 weeks of stopping the treatment. Comparisons were made between these groups of patients in term of efficacy & tolerability.

The data was analysed using the SPSS version 22. Basic descriptive statistics including means and standard deviations were performed. Chi-square test was used for comparison of qualitative data between the two groups. Differences were considered statistically significant if the *p*-value was less than 0.05.

RESULTS

A total of 100 patients received treatment with sofosbuvir and daclatasvir. The mean age was 65 years (SD±2.31) in group A and 74 years (SD±1.63) in group B. Sixty patients (60%) were males and forty patients (40%) were females. Out of 67 patients in group A, 51 patients (76.1%) were non-cirrhotic and 16 patients (23.9%) were cirrhotic. While out of 33 patients in group B, 26 patients (78.7%) were non-cirrhotic and 7 patients (21.2%) were cirrhotic.

End treatment response in group A was 95.5% (96% in non-cirrhotic patients & 93.7% in cirrhotic patients) and in group B was 93.9% (92.3% in non- cirrhotic patients & 100% in cirrhotic patients). Sustained virologic response (SVR) among the patients receiving sofosbuvir–daclatasvir was 91% in group A (92% in non-cirrhotic patients & 87.5% in cirrhotic patients) and 87.8% in group B (88.5% in non-cirrhotic patients & 85.7% in cirrhotic patients). No serious adverse event was reported in either group. Minor side effects experienced by the patients in both groups were Headache (29%), Fatigue (38%), Nausea/Vomiting (20%), and abdominal discomfort (13%).

Table-1: Clinical & demographic characteristics of the patients (n=100)

	Group A (60-69 yr) n=67	Group B (≥70 yr) n=33
Mean Age±SD	64.75±2.31	73.97±1.63
Gender		
Male (%)	39 (58.2)	21 (63.6)
Female (%)	28 (38.8)	12 (36.4)
Mean Hb (g/dl)±SD	13.1±1.30	12.6±1.39
Mean Platelet Count±SD	168.6±18.06	158.2±18.91
Mean eGFR (ml/min)±SD	96.5±15.5	78.5±18.5
Liver Status		
Non-Cirrhotic (%)	51 (76.1)	26 (78.7)
Cirrhotic (%)	16 (23.9)	07 (21.2)
Mean HVC RNA (log_{10})±SD	6.9±0.8	7.3±0.65

Table-2: Treatment parameters & outcome

	Group A (60–69 year) n=67	Group B (≥70 year) n=33	*p*-value
End Treatment Response (%)			.733
Non-Cirrhotic	64 (95.5)	31 (93.9)	
Cirrhotic	49 (96)	24 (92.3)	
	15 (93.7)	07 (100)	
Non-Responders (%)	3 (4.5)	2 (6.1)	.733
Non-Cirrhotic	2 (3.9)	2 (6.1)	
Cirrhotic	1 (6.3)	0 (0)	
Sustained Virologic Response12 (%)			.620
Non-Cirrhotic	61 (91)	29 (87.8)	
Cirrhotic	47 (92)	23 (88.5)	
	14 (87.5)	06 (85.7)	
Relapse (%)	03 (4.5)	2 (6)	.733
Non-Cirrhotic	2 (3.9)	1 (3.8)	
Cirrhotic	1 (6.3)	1 (14.2)	

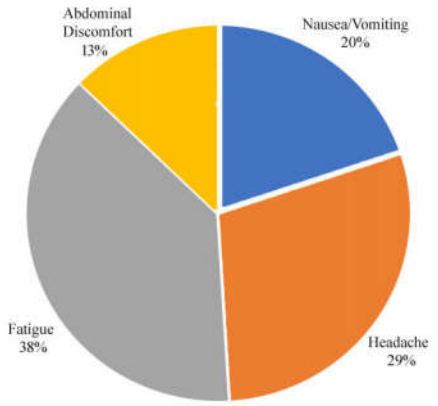

Figure-1: Sustained virological response rate

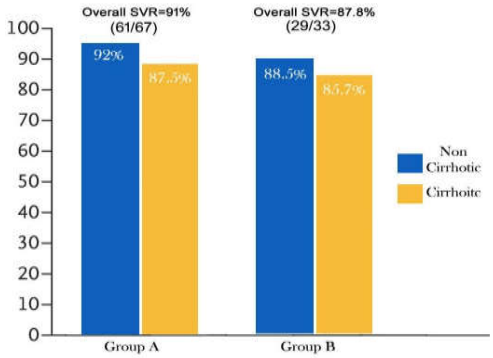

Figure-2: Adverse events during the treatment

DISCUSSION

Until recently, the old age patients suffering from chronic hepatitis C were having very limited treatment options mostly due to contraindications and side effects of the available treatment options. Also, those who tolerated the interferon treatment were having very low sustained virological response.[12] There has been a paradigm shift in the treatment of chronic hepatitis C with the approval of direct acting anti-viral drugs.[13] However, in most of the clinical trials which were conducted initially to assess the efficacy and tolerability of these new DAAs, the representation of the elderly patients was not significant. In our study, we included elderly patients aged ≥60 years having chronic hepatitis C infection and our results showed that combination of sofosbuvir and daclatasvir is safe and effective with overall SVR around 90%. A similar study was conducted at University Hospital Frankfurt, Germany in 2016 by Vermehren *et al*.[14] They evaluated the safety, efficacy and drug interactions of different combinations of direct acting antiviral drugs in 541 elderly patients with chronic hepatitis C and concluded that sustained virological response was 98% in patients with age >65 and 91% in patients with age <65 years. However, side effects of the treatment were similar between two groups (63% vs. 65%). In 2018 Jhaveri *et al* also evaluated the tolerability of commonly prescribed DAA agents in old age population at a Swedish Medical Centre, Seattle, USA and found it safe and efficacious.[15] Our results are further supported by a multicentre study conducted in 2019 at different hospitals of Egypt by Elbaz *et al*.[16] They used sofosbuvir and daclatasvir in elderly patients aged >60 years with chronic hepatitis C and the results showed an overall SVR of 90%. In this study also, the number of adverse events were minimal and were not different between the two age groups.

CONCLUSION

Sofosbuvir plus daclatasvir combination is effective and safe in elderly patients with chronic hepatitis C without any significant adverse effects of the treatment.

Conflict of interest: There were no conflicts of interest.

AUTHORS' CONTRIBUTION

MA & YM: Conceptualized the study. MA, YM, MI: Data collection, interpretation and analysis. MAN, AM: Write-up, proof reading.

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