Original Article

Sofosbuvir Plus Daclatasvir in Chronic Hepatitis C Genotype 3 Naïve Patients

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ABSTRACT

Objective: To see the response rate of chronic hepatitis C Genotype 3 Naive patients to combination of sofosbuvir and daclatasvir.

Study Design: Prospective observational study

Place and Duration of Study: This study was conducted at the Hepatitis control programme, Medical B unit, Mardan medical complex teaching hospital Mardan from August 2017 to July 2018.

Materials and Methods: Seventy adult eligible both male and female Hepatitis C genotype 3 Naïve patients were included in the study. Sofosbuvir 400mg and Daclatasvir 60mg daily for 12 weeks were given to patients. Patients were tested for absence of detectable HCV RNA by PCR at the end of treatment and 12 weeks after the completion of treatment to look for sustained virological response at 12 weeks.

Results: A total seventy chronic Hepatitis C genotype 3 naive patients received treatment with sofosbuvir 400mg and Daclatasvir 60mg for 12 weeks .All patients completed treatment. Out of seventy patients, thirty nine (55.71%) were female and thirty one (44.29%) were male. The average age of the patients included in the study was 45.6 years. Patients were classified on the basis of APRI score into two categories. In 52 (74.28%) patients the APRI score was <2 and in 18(25.72%) patients the APRI was > 2, which shows cirrhosis. The end of treatment response was 98.57 %(69).Only one patient was non responder. The sustained virological response rate was 97.1 %(67) and only two (2.9%) patients were relapsed. Both patients have APRI score >2 were cirrhotic in relapse group. The overall response rate in cirrhosis liver was 88.8 %(16).

Conclusion: Combination of sofosbuvir plus Daclatasvir for 12 weeks in chronic hepatitis C naive patients was associated with high rates of sustained virological response at 12 weeks.

Key Words: chronic hepatitis C, Sofosbuvir, Daclatasvir

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INTRODUCTION

Chronic Hepatitis C infection affects approximately 130- 150 million people worldwide[1]. It is the major cause of cirrhosis and HCC[2]. Hepatitis C has six major Genotypes designated 1-6[3]. Genotype 3 is the most common genotype in Pakistan[4] and it is the second most abundant genotype in the world[5]. In Pakistan the prevalence rate of chronic hepatitis C is 4.9% in general population[6]. About 79 % patients have genotype 3[7]. The prevalence of chronic HCV infection is 1.1% in KPK.[8] Hepatitis C causes both acute and chronic hepatitis.

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Approximately 15% of patients with acute hepatitis C will spontaneously clear the virus and 85% of patients will develop chronic Hepatitis C[9]. In chronic HCV, the risk of cirrhosis is 15-30% over 20 years[10].The risk of HCC in person with cirrhosis is approximately 2-4% per year[11]. Hepatitis C is the leading indication for liver transplantation[12]. So to prevent these complications and control the disease, there is need for safe and effective treatment. Standard therapy for HCV infection from late 1990s was a combination of peg interferon and ribavirin. A sustained virological response rate to peg interferon plus ribavirin was 70-80% in genotype 3 patients[13]. Treatment with peg interferon based therapy was associated with frequent side effects and high (10-14%)discontinuous rat[14].The recent introduction of oral direct acting antivirals (DAAs) increased the SVR rate to more than 90 %.DAAs recommended for the treatment of HCV is registered in Pakistan at a reasonable price. These drugs with better cure rates and lessor side effects should be considered for the treatment of HCV patients in our country. The sofosbuvir and Daclatasvir are available in our hepatitis control programme OPD free of cost. We observe the response rate of HCV patients to sofosbuvir plus daclatasvir combination therapy.

MATERIALS AND MTHODS

This study was conducted at Mardan medical complex Mardan from August 2017 to July 2018, involving patients attending medical and hepatitis control program opd in Mardan Medical Complex teaching hospital Mardan. Seventy adult eligible both male and female Hepatitis C genotype 3 Naïve patients were included in the study. Sofosbuvir 400mg and Daclatasvir 60mg daily for 12 weeks were given to patients. Patients were tested for absence of detectable HCV RNA by PCR at the end of treatment and 12 weeks after the completion of treatment to look for sustained virological response at 12 weeks.

RESULTS

A total seventy chronic Hepatitis C genotype 3 naive patients received treatment with sofosbuvir 400mg and Daclatasvir 60mg orally for 12 weeks .All patients completed treatment. Out of seventy patients, thirty nine (55.71%) were female and thirty one (44.29%) were male. The median age of the patients included in the study was 45.6 years. Patients were classified on the basis of APRI score into two categories. In 52 (74.28%) patients the APRI score was <2 and in 18(25.72%) patients the APRI was > 2 which shows cirrhosis. Liver biopsy not done because it is an invasive procedure and fibro scan is not available in our set up. The end of treatment response was 98.57 %(69).Only one patient was non responder. The sustained virological response rate was 97.1 %(67) and only two (2.9%) patients were relapsed. Both patients have APRI score >2 were cirrhotic in relapse group. The overall response rate in cirrhosis liver was88.8 %[16].

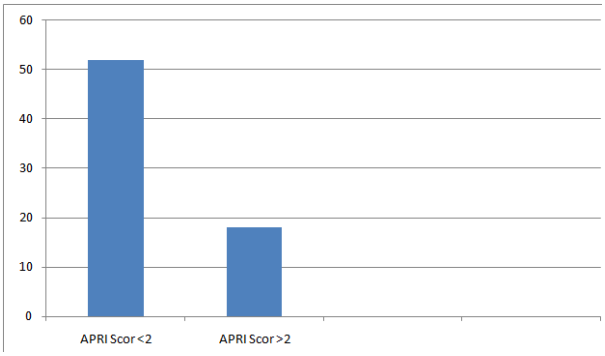

Figure No,1: Age distribution

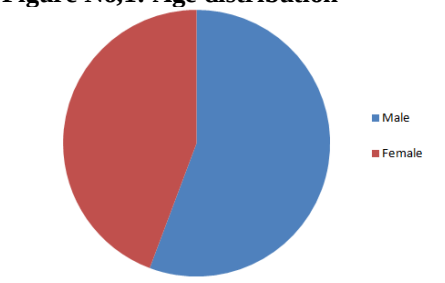

Figure No.2: Sex distribution

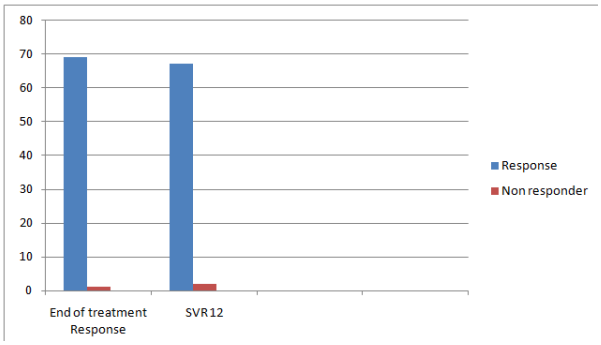

Figure No.3: treatment response.

DISCUSSION

We observe the response rate of sofosbuvir plus Daclatasvir in Chronic hepatitis C genotype 3 naive patients. The goal of treatment is to cure HCV infection in order to prevent complications like cirrhosis, decompensation and HCC and improve quality of life and also prevent further transmission of HCV. The endpoint of treatment was an (SVR12) sustained virological response at 12 weeks after the completion of treatment. SVR 12 is defined by undetectable HCV RNA in the serum at 12 weeks after the end of therapy (16). An SVR corresponds to cure of HCV infection and it reduces the rate of decompensation and will also reduce but not abolish the rate of HCC. Assessment of liver disease severity is necessary prior to treatment, it will identify patients with cirrhosis. We used noninvasive methods instead of liver biopsy to assess liver disease severity. We use aspartate amino transferase to platelet ratio index (APRI).It in simple, cheap and noninvasive and the information it give is reliable[17,18]. On the basis of APRI score patients were divided into two groups, one with APRI score less than <2 and the other group with APRI score >2, shows cirrhosis. We used Sofosbuvir 400mg and Daclatasvir 60mg orally for 12 weeks Sofosbuvir is a nucleotide analogue HCV NS5B polymerase inhibitor while Daclatasvir is HCV NS5A replication complex inhibitor[19], both of them have potent antiviral activity and pan genotypic coverage and are administered orally once daily. In our study the end of treatment response was 98.57 %(69).It was almost similar to ALLY-3 study by Nelson DR et al which shows 99% response rate at the end of treatment[20].Only one patient was non responder. The sustained virological response rate was 97.1 % (67) and only two (2.9%) patients were relapsed. Both patients were cirrhotic in relapse group. The overall response rate in cirrhosis liver is 88.8 % (16) as compared to ALLY-3 study which shows 63% SVR at 12 weeks, it may be because of small number of patients. The combination of sofosbuvir plus Daclatasvir was well tolerated with minimal side effects and associated with a favorable safety profile. The most common side effects were body aches, headache and easy fatigability. There was no severe side effect which can lead to discontinuation of the drugs. The response rate was higher in patients without cirrhosis (97.1%) as

compared to cirrhotic (88.8%).Adding ribavirin and or extending treatment in cirrhosis will improve the durability of response.

CONCLUSION

Combination of sofosbuvir plus Daclatasvir for 12 weeks in chronic hepatitis C naive patients was associated with high rates of sustained virological response. It is well tolerated, efficacious, treatment option in genotype 3 naïve patients

Author's Contribution:

Concept & Design of Study:	Rahman ud Din
Drafting:	Shah Zeb
Data Analysis:	Muhammad Arshad
Revisiting Critically:	Rahman ud Din, Shah Zeb
Final Approval of version:	Rahman ud Din

Conflict of Interest: The study has no conflict of interest to declare by any author.

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