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STUDY OF EFFECTIVENESS OF HEPATITS C TREATMENT WITH DIRECT ACTING ANTIVIRAL AGENTS

General Medicine

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ABSTRACT

Hepatitis C virus (HCV) accounts for approximately 15%-20% cases of acute hepatitis. After acute infection, around 50% to 80% of HCV patients will develop chronic infection. Chronic hepatitis C patients are at high risk to develop life-threatening complications, including cirrhosis in 20% of cases and hepatocellular carcinoma (HCC) at an incidence of 4%-5% per year in cirrhotic patients. The goal of hepatitis C treatment is to cure the disease. WHO recommends therapy with pan-genotypic direct-acting antivirals (DAAs) for all adults, adolescents and children down to 3 years of age with chronic hepatitis C infection. DAAs can cure most persons with HCV infection, and treatment duration is short (usually 12 to 24 weeks), depending on the absence or presence of cirrhosis. The most widely used and low-cost pangenotypic DAA regimen is sofosbuvir and daclatasvir. **Aims & Objectives:** To study the effectiveness of direct acting antiviral agents in hepatitis C treatment in terms of sustained viral load. **Materials And Methods:** This is a retrospective study done on patients admitted in GGG Hospital, Jamnagar. Total 50 patients showing HCV positivity were enrolled with the detailed history along with general examination. Patients were prescribed 2 types of DAA regimen, Sofosbuvir plus Daclatasvir and Sofosbuvir plus Velpatasvir for 12 weeks. They were retested at 12 weeks of completion of treatment for HCV RNA detection, termed as SVR or Sustained Virological Response.

Inclusion Criteria

1. Study participants more than 18 years of age.
2. All participants should be HCV positive by ELISA.

Exclusion Criteria: Patients with age less than 18 years old age. **Conclusion:** DAAs are highly effective in clearance of HCV RNA and high SVR 12 can be achieved with newer pangenotypic DAAs. DAAs are also very effective and safe in patients with comorbidities like CKD, Thalassemia, HIV HCV coinfection, Hypertension, Diabetes Mellitus. DAAs are highly efficacious in patient without any comorbidity.

KEYWORDS

Hepatitis C, Direct acting antiviral, Sustained Virological Response

INTRODUCTION

Hepatitis C virus (HCV) accounts for approximately 15%-20% cases of acute hepatitis. After acute infection, around 50% to 80% of HCV patients will develop chronic infection. Chronic hepatitis C patients are at high risk to develop life-threatening complications, including cirrhosis in 20% of cases and hepatocellular carcinoma (HCC) at an incidence of 4%-5% per year in cirrhotic patients. Epidemiological studies also indicate that HCV is associated with a number of extrahepatic manifestations including insulin resistance, type 2 diabetes mellitus, glomerulopathies, oral manifestations, etc.

Most HCV-infected patients would develop chronic hepatitis, but approximately 15%-40% of them could clear the virus spontaneously. More than twenty years of study has provided a better understanding of hepatitis C virus (HCV) life cycle, including the general properties of viral RNA and proteins. This effort facilitates the development of sensitive diagnostic tools and effective antiviral treatments. At present, serologic screening test is recommended to perform on individuals in the high risk groups and nucleic acid tests are recommended to confirm the active HCV infections. Quantization and genotyping of HCV RNAs are important to determine the optimal duration of anti-viral therapy and predict the likelihood of response.

A new infection with HCV does not always require treatment, as the immune response in some people will clear the infection. However, when HCV infection becomes chronic, treatment is necessary. The goal of hepatitis C treatment is to cure the disease. WHO recommends therapy with pan-genotypic direct-acting antivirals (DAAs) for all adults, adolescents and children down to 3 years of age with chronic hepatitis C infection. DAAs can cure most persons with HCV infection, and treatment duration is short (usually 12 to 24 weeks), depending on the absence or presence of cirrhosis. In 2022, WHO included new recommendations for treatment of adolescents and children using the same pangenotypic treatments used for adults. Pan-genotypic DAAs remain expensive in many high- and upper-middle-income countries. However, prices have dropped dramatically in many countries (primarily low-income and 4 lower-middle-income countries) due to the introduction of generic versions of these medicines. The most widely used and low-cost pangenotypic DAA regimen is sofosbuvir and daclatasvir.

AIMS AND OBJECTIVE

- To study the effectiveness of direct acting antiviral agents in hepatitis C treatment in terms of sustained viral load.

MATERIAL AND METHODS

This is a retrospective study done on patients admitted in GGG Hospital, Jamnagar. Total 50 patients showing HCV positivity were enrolled with the detailed personal history, family history, sign and symptoms along with general examination. Patients were prescribed 2 types of DAA regimen, Sofosbuvir plus Daclatasvir and Sofosbuvir plus Velpatasvir. After completion of treatment of 12 weeks, they were retested at 12 weeks of completion of treatment for HCV RNA detection, termed as SVR or Sustained Virological Response.

Inclusion Criteria

1. Study participants more than 18 years of age.
2. All participants should be HCV positive by ELISA.

Exclusion Criteria

Patients with age less than 18 years old age.

RESULT

In our study total 50 patients were enrolled among which 30 patients were male and 20 patients were female and were prescribed 2 types of DAA regimen, Sofosbuvir plus Daclatasvir and Sofosbuvir plus Velpatasvir. SOF+DAC was prescribed to total 37 patients, while SOF+VEL was prescribed to 13 patients.

Table 1. Age Wise Distribution Of Study Subject

Age Groups (Years)	No. of Pts.	% of Pts.
18-20	9	18
21-30	8	16
31-40	7	14
41-50	10	20
51-60	8	16

61-70	8	16
Total	50	100

Most common age group was 41-50 years of age, having 10 subjects. In our study 28 patients (56%) were checked as part of routine screening, while among the complaints jaundice (12%) and weakness (12%) were the most common one. Other complaint were Fatigue(6%), Abdominal pain(6%), Fever(6%), Anorexia(2%), Hematemesis(2%). On general examination, Pallor (24%) was most common finding which was seen around 12 patients followed by Edema (10%) and Icterus (10%), while Clubbing, Lymphadenopathy and Cyanosis were not found in any patients. There were no significant family history and personal history found.

Table .2 Various Comorbidities Among Patients

Comorbidity	No. of Pts.	% of Pts.
Thalassemia	17	34
CKD	16	32
HIV	3	6
HBV	1	2
LPD	2	4
DM/HTN/CVA	3	6
None	8	16
Total	50	100

Thalassemia(34%) was the leading comorbidity, followed by CKD(32%). Other comorbidities includes HIV, HBV, LPD and DM, HTN, CVA.

On comparison of various laboratory findings, low Hemoglobin was found in 31 patients(62%) while remaining 19 patients(38%) have normal Hemoglobin. WBC counts were normal in 46 patients comprising 92%., while 4 patients(8%) have higher WBC counts. Platelet count were within normal limit in 39 patients(78%), while 11 patients(22%) were having lower platelet count. Total bilirubin was found to be elevated in 26 patients(52%), while 24 patients(48%) were having normal bilirubin. Direct Bilirubin was increased in 28 patients(56%) while 22 patients(44%) having normal level of direct bilirubin. Serum Total protein was normal in 48 patients constituting 96% while only 02 patients(4%) were having low total protein. Serum Albumin was normal in 86% comprising of 43 patients and rest having low serum albumin levels comprising of 7 patients(14%). Prothrombin time (PT) was normal in 33 patients (66%) and high in 17 patients(34%). Activated Partial Prothrombin time (APTT) was Normal in 29 patients (58%) and high in 21 patients(42%). International Normalized Ratio (INR) was low in 02 patients(4%), Normal in 31 patients(62%) and High in 17 patients(34%).

Most common finding was RPD changes, which was present in around 14 patients(28%), those represents CKD group of Patients. Other USG finding were Hepatomegaly, Splenomegaly, Hepato- Splenomegaly, LPD changes, Gross Ascites, Varices Formation and fatty liver.

Table 3. Comparison Of APRI & FIB4 Score

Score	Value	No. of Pts.	% of Pts
APRI	<0.5(No Cirrhosis)	21	42
	0.5-1.5(Inconclusive)	20	40
	>=1.5(Cirrhosis)	9	18
FIB-4	<1.25(No Fibrosis)	17	34
	1.45-3.25(Inconclusive)	23	46
	>3.25(Prone for Fibrosis)	10	20

APRI Score is AST to platelet ratio index. 21 patients had APRI score less than 0.5, while 17 patients had FIB-4 score less than 1.25, which rules out cirrhosis in those patients, which constitutes 42% and 34% respectively. While 9 patients have APRI score more than 1.5, which increases their probability of having Cirrhosis, which constitutes 18% of subjects. FIB-4 is calculated using age, AST and ALT values. According to FIB-4 score,10 patients have score more than 3.25, which makes them prone for fibrosis and Cirrhosis, which comprises 20% of subjects.

Based on various parameters like APRI score FIB-4 score, USG finding like LPD Changes, Low Serum Protein and Albumin level and High PT, APTT and INR levels, patients were assigned as compensated disease and Decompensated Disease.

Table 4. Classification Based On Disease Status And Treatment Regimen

Disease Status	No. of Pts. (%)	Treatment Regimen Given
Compensated Disease	37 (74)	SOF+DAC
Decompensated Disease	13(26)	SOF+VEL

Compensated Disease patients were treated with Sofosbuvir + Daclatasvir (SOF+DAC), which was given to 37 patients (74%). Decompensated disease patients were treated with Sofosbuvir+ Velpatasvir(SOF+VEL) FDC, which was given to 13 patients(26%).

Table 5. Response To Daa In Terms Of SVR

Treatment Response	No. of Pts	% of Pts.
SVR Achieved	43	87.75
SVR Not Achieved	4	8.33
Death During Treatment	1	4.1
Death Before Treatment	2	NA

SVR was achieved in total 43 patients at end of treatment which is 87% of total patients. SVR was not achieved in 4 patients at end of treatment which comprises 8% of total study population. 1 patient expired while on treatment while 2 patients expired before initiation of treatment.

Table 6.SVR In Patients With Various Comorbidities

SVR in various Comorbidities	No. of Pts	Regimen.1 (SOF+DAC)	Regimen.2 (SOF+VEL)	SVR (Regimen 1+Regimen 2)	SVR of Regimen 1(%)	SVR of Regimen 2(%)
CKD	16	13	3	15(93.75)	13(100)	2(66)
Thalassemia	17	14	3	14(82.35)	13 (92.85)	1 (33.33)
HIV	3	1	2	2(66.67)	1(100)	1(50)
HBV	1	-	1	0	-	0
HTN/ DM/ CVA	3	3	-	3(100)	3(100)	0
No Comorbidity	8	4	4	8(100)	4(100)	4(100)
LPD	2	2		1(50)	1(50)	0
Total	50	37	13	43(87.75)	35 (94.59)	8 (61.53)

There were total 16 patients of CKD that were treated with DAA,13 with SOF+DAC and 3 with SOF+VEL. 100% SVR was achieved in patients treated with SOF+DAC, while 66% SVR has been achieved in patients treated with SOF+VEL. Overall SVR in CKD patients is 93.75% as out of 16 patients, 15 had achieved SVR. Patients with Thalassemia have SVR of 82.35% as out of 17 patients with thalassemia 14 patients had achieved SVR,14 were treated with SOF+DAC, in whom SVR was achieved in 92.85%, while 3 patients were treated with SOF+VEL, in whom SVR was 33.33%. Out of 3 HIV-HCV coinfection patients, SVR was achieved in 66.67% patients, while SVR was not achieved in patient with HBV-HCV coinfection. Overall SVR in LPD is 50%. Patients with Hypertension, Diabetes mellitus and cerebrovascular accidents as comorbidity have 100% SVR achieved. Patients without any comorbid disease were treated with DAAs,4 with SOF+DAC and 4 with SOF+VEL. 100% SVR achieved at end of treatment.

Out of total 37 compensated Patients who were undergone for treatment with SOF+DAC for 3 months, 35 patients achieved SVR, which is 94.59% of total compensated patients. While in case of Decompensated disease treated with SOF+VEL, out of 13 patients, 8 patients achieved SVR which is 61.53% of total decompensated diseases.

DISCUSSION

The present study was done on 50 patients admitted in GGG Hospital, Jamnagar. Total 50 patients, patients who came HCV positive and HCV RNA detected were provided DAA for 12 weeks and then after completion of treatment of 12 weeks, they were retested at 12 weeks of completion of treatment for HCV RNA detection, termed as SVR or Sustained Virological Response. In our study total 50 patients were prescribed 2 types of DAA regimen, SOF+DAC was prescribed to total 37 patients, while SOF+VEL was prescribed to 13 patients. In terms of overall response, total 43 patients SVR at the end of 12 weeks of treatment with DAA. While SVR was not achieved in 4 patients and HCV RNA levels were detectable at the end of 6 months of repeat testing.1 patient expired while on going treatment while 2 patients

expired before initiation of treatment. In our study, patients with CKD have SVR of 93.75%,out of 16 patients,15 had achieved SVR. Patients with Thalassemia have SVR of 82.35%,14 out of 17 patients achieved SVR at 12 weeks. Patients with HIV have SVR of 66.67% while one patient with HBV HCV coinfection, SVR was not achieved. Overall SVR achieved in LPD is 50%. Patients with Hypertension, Diabetes mellitus, Cerebrovascular accident and patients without any comorbidity have 100% SVR achieved at 12 weeks.

Table.7 Comparison Study: Venessa D Costa Et Al.

STUDY	No. of Pts.	SVR Achieved	% of SVR
Current study	50	42	87.5
Venessa D costa et al.	132	126	95.4

In current study SVR was achieved in 87.75% of patients while in comparative study of Venessa D costa et al.[1] SVR was 95.4%.

In current study, out of 16 patients of CKD 13 Patients were treated with SOF+DAC, while 3 patients treated with SOF+VEL. Overall SVR at 12 weeks treatment achieved was 93.75%, 15 patients out of 16 patients achieved SVR. In 13 patients treated with SOF+DAC, 100% patients achieved SVR, while out of 3 Patients treated with SOF+VEL, 2 achieved SVR while one did not. In study of Borgia SM et al.[2] total 59 patients were treated with SOF+VEL. SVR at 12 weeks was 95%. In both studies SVR was achieved was 93.75% and 95% respectively.

Table.8 Comparasioan Study

Study	No. of Pts.	%of SVR
Mehta et al.3	10	100
Mangia et al.[4]	1	98
Zamani et al.[5]	61	98.4

SVP achieved in patients with thalassemia at 12 weeks is 82.35% overall, while those with compensated disease have SVR of 92.85%, while 33.33% SVR achieved among decompensated group. In comparison study, SVR achieved at 12 weeks was ranging from 90-100%, while in current study in compensated patients of thalassemia with chronic HCV infection, SVR at 12 weeks is 92.85%, which is comparable with other studies while overall SVR is 82.35%, which is lower than rest of the studies.

CONCLUSION

DAAs are highly effective in clearance of HCV RNA and high SVR 12 can be achieved with newer pangenotypic DAAs. DAAs are also very effective and safe in patients with comorbidities like CKD, Thalassemia, HIV HCV coinfection, Hypertension, Diabetes Mellitus. DAAs are highly efficacious in patient without any comorbidity.

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