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Original Research Article

ANALYSIS OF EFFECTIVENESS OF DIRECT ACTING ANTIVIRAL DRUGS IN PATIENTS WITH HCV INFECTION

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ABSTRACT

Background: Hepatitis C virus is a single-stranded RNA virus that can cause both acute and chronic hepatitis. The present study was conducted to analyze effectiveness of direct acting antiviral drugs in patients with HCV infection. **Materials & Methods:** The present prospective study was conducted on 150 patients diagnosed with HCV infection who received full course of anti HCV treatment in the form of direct acting antiviral drugs in the Medical Outpatient Department and ward of Department of Medicine of Government Medical College and Rajindra Hospital, Patiala. This study was carried out over a period of 1 year from March 2019 to February 2020. Patients were followed up at 4 and 8 weeks for clinical assessment, required investigations and to see side effects of direct acting antivirals. **Results:** In the present study, the overall SVR 12 rate achieved was 98 %. SVR12 rate achieved was 99% in non-cirrhotic patients, 97.3% in compensated cirrhotic patients and 90.9% in decompensated cirrhotic patients. SVR12 rate achieved was 94.4% in HIV co-infected patients and was 100% in Hepatitis B co-infected patients. 18.6% of patients experienced a side effect with direct acting antivirals drug use. Fatigue was the most common side effect seen in 10.7% patients. Side effects were seen more in cirrhotic patients. **Conclusion:** The study found that direct-acting antiviral therapy for hepatitis C has a short duration and excellent safety profile. The high SVR12 effectiveness rates demonstrate the real-world efficacy of these regimens, showing they deliver strong clinical outcomes.

INTRODUCTION

The hepatitis C virus (HCV) is a small, enveloped virus with single-stranded, positive-sense RNA. It belongs to the Hepacivirus genus within the Flaviviridae family and was identified in 1989 at.[1] The estimated HCV prevalence in India at present is 1-1.9%. HCV genotypes predominant in India are genotypes 3 and 1, constituting approximately 60 and 30% of the six genotypes, respectively. [2-4] The standard method of diagnosis is by detection of anti-HCV antibody. Both rapid diagnostic tests (RDTs) and Immunoassays are available, with comparable sensitivity and specificity.[5]

The goal of HCV therapy is sustained virological response (SVR), defined as continuously undetectable HCV ribonucleic acid (RNA) levels12 weeks (SVR12) after the end of therapy.[6] Over the past 20-25 years, hepatitis C treatment has evolved from interferon (IFN)-based therapies, often combined with ribavirin (RBV). IFN works by activating the immune system to clear the virus. The treatment regimen typically involved weekly peg interferon injections and daily ribavirin for 48-72 weeks. Furthermore, even eligible patients had SVR rates below 50%, highlighting the need for more effective and tolerable treatments.[6,7]

There was a treatment breakthrough in 2011 when there was the approval of two oral DAAs, boceprevir and telaprevir. These agents were used in combination with PEG-IFN plus RBV for patients with GT 1 and increased SVR rates to as much as 70%; however, cumbersome dosing regimens, strict dietary requirements, and unfavourable adverse effect profiles were also there. A paradigm shift occurred in 2013 with the approval of simeprevir and sofosbuvir. These agents were the first oral once-

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daily treatments that were well tolerated and were able to produce SVR rates greater than 90% either together in combination or with PEG-IFN plus RBV in select genotypes. The newer DAA drugs target various points of the HCV viral replication cycle. Four main classes of DAAs have been developed so far that target three different viral proteins: NS3/4A protease inhibitors, NS5A inhibitors, and two types of NS5Bpolymerase inhibitors.[6,8]

In 2016, the World Health Organization (WHO) recommended shifting from interferon-based regimens to direct-acting antiviral (DAA)-based regimens for treating hepatitis C. Since then, DAA regimens have continued to improve, with several pan-genotypic options emerging that can cure HCV infection in over 85% of treated individuals across all major genotypes.[9]

WHO now recommends pan-genotypic DAA regimens for adults aged 18 and above. Approved regimens include glecaprevir-pibrentasvir (8 weeks) and sofosbuvir-daclatasvir or sofosbuvir-velpatasvir (12 weeks) for non-cirrhotic patients, and sofosbuvir-velpatasvir, sofosbuvir-daclatasvir, or glecaprevir-pibrentasvir (12-24 weeks) for patients with cirrhosis.[10] The present study was conducted to analyze effectiveness of direct acting antiviral drugs in patients with HCV infection.

MATERIALS AND METHODS

The present prospective study was conducted on 150 patients diagnosed with HCV infection who received full course of anti HCV treatment in the form of direct acting antiviral drugs as per National Viral Hepatitis Control Programme in Medical Outpatient Department and ward of Department of Medicine of Government Medical College and Rajindra Hospital, Patiala. This study was carried out over a period of 1 year from March 2019 to February 2020. Patients of 18 years and above having hepatitis C i.e patients with positive HCV antibodies and detectable HCV RNA in the serum were included in the study. Patients of chemotherapy with deranged liver enzymes, patients with impaired renal function, patients with hepatocellular carcinoma, pediatric patients, thalassemic patients, treatment experienced patients, patients with pregnancy were excluded from the study. Cases were selected on the basis of presence of anti HCV antibodies (by Elisa method) and detectable HCV RNA viral load in the serum. Quantitative HCV RNA viral load assessment was done by using Real-Time Polymerase Chain. Reaction (RT-PCR) methodology by Core diagnostics under NVHCP. Baseline investigations were obtained in all selected cases in the form of: HCV RNA viral load, CBC, RBS, LFTs, RFTs, PTI/INR, HBsAg, HIV. Clinical profile of all 150 HCV positive patients with detectable HCV RNA viral load was studied in form of age, gender, risk factors, occupation, residence, clinical presentation. Patients were divided into non-cirrhotic and cirrhotic. Cirrhotic patients were further divided into compensated cirrhotic and decompensated cirrhotic based on signs of decompensation like jaundice, ascites, variceal bleed and hepatic encephalopathy. Patients were put on different treatment regimens as per National Viral Hepatitis Control Programme based on cirrhosis of liver. Patients were followed up at 4 and 8 weeks for clinical assessment, required investigations and to see side effects of direct acting antivirals. Effectiveness of direct acting antiviral drugs is measured in the form of Sustained virologic response (SVR) rate, which is percentage of patients achieving the SVR after 12 weeks of end of treatment. SVR is defined as undetectable HCV RNA viral load or HCV RNA viral load below the limit of detection after 12 weeks of end of treatment.

RESULTS

The maximum number of patients was between 41-50 years. The mean age in this study was 42.9 years. 70% patients were males and 30% were females. 49.3% of patients were asymptomatic. Most common symptom seen was fatigue in 48(32%) patients.

Mean HCV RNA viral load at start of treatment in non-cirrhotic patients was 1342887.72, in compensated cirrhotic patients was 1480992.08 and in decompensated cirrhotic patients was 725227.27 respectively. Statistically it was insignificant as p value is >0.05.

All 102 Non cirrhotic patients were given regimen A (Sofosbuvir + Daclatasvir) for 12 weeks. In 37 compensated cirrhotic patients, 30 were given regimen B (Sofosbuvir + Velpatasvir) for 12 weeks while 7 who were on ART were given modified regimen A (Sofosbuvir + Daclatasvir + Ribavirin) for 12 weeks. In 11 decompensated cirrhotic patients, 8 were given regimen C (Sofosbuvir + Velpatasvir + Ribavirin) for 12 weeks while 3 anaemic patients who were ineligible for Ribavirin were given regimen B (Sofosbuvir + Velpatasvir) for 24 weeks.

Out of 150 HCV patients who took full treatment and came for HCV RNA detection after 12 weeks of end of treatment, target (i.e. HCV RNA viral load) was detected in 3 (2%) patients, while in 147 (98%) patients no target (HCV RNA viral load) was detected. So the overall SVR12 rate in this study came out to be 98%.

Out of 150 HCV patients who took full treatment and came for HCV RNA viral load detection after 12 weeks of end of treatment, SVR12 rate achieved was 99% in non-cirrhotic patients, 97.3% in compensated cirrhotic patients and 90.9% in decompensated cirrhotic patients respectively.

Out of 18 HIV patients who took full treatment for HCV, target (HCV RNA viral load) was detected in 1 patient. So, SVR 12 rate achieved was 94.4% in this population.

SVR12 was achieved in all HCV and HBV co-infected patients, so SVR12 rate achieved was 100% in this group of patients.

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Out of total 150 patients, 122(81.3%) patients did not experience any side effects. Fatigue was seen in 16(10.7%) patients, nausea in 6(4%) patients, headache in 5(3.3%) patients, anaemia in 3(2 %) patients and diarrhoea in 3(2%) patients. Few patients had more than one side effects.

Result for fatigue, anaemia was highly significant for non-cirrhotic, compensated cirrhotic and decompensated cirrhotic patients as p value was < 0.001. Result for Diarrhoea, Nausea, Headache was significant for non-cirrhotic, compensated cirrhotic and decompensated cirrhotic patients as p value was < 0.05.

Table 1: HCV RNA viral load in study population

		Mean	S.D	P value	Significance
HCV RNA TITRE (IU/ml)	Compensated Cirrhotic	1480992.08	2656763.65	0.642	NS
	Decompensated Cirrhotic	725227.27	989173.87		
	Non-Cirrhotic	1342887.72	2317739.75		

Table 2: Regimens for treatment of HCV patients

Regimen	Compensated Cirrhotic		Decompensated Cirrhotic		Non-Cirrhotic	
	n	%	n	%	n	%
Sofosbuvir + Daclatasvir	0	0	0	0.0	102	100.0
Sofosbuvir + Velpatasvir	30	81	3	27.3	0	0.0
Sofosbuvir + Daclatasvir + Ribavirin	7	19	0	0	0	0
Sofosbuvir + Velpatasvir + Ribavirin	0	0.0	8	72.7	0	0.0
Total	37	100.0	11	100.0	102	100.0

Table 3: SVR12 rate in overall study population

SVR12	Number	Percentage
Target (HCV RNA viral load) Detected	3	2
Target (HCV RNA viral load) not Detected	147	98
Total	150	100.0

Table 4: SVR12 rate according to severity of disease.

SVR12	Compensated Cirrhotic		Decompensated Cirrhotic		Non-Cirrhotic	
	n	%	n	%	n	%
Target (HCVRNA viral load) Detected	1	2.7	1	9.1	1	1
Target (HCVRNA Viral load) Not Detected	36	97.3	10	90.9	101	99.01
Total	37	100.0	11	100.0	102	100.0
Chi square	3.456					
P value	0.117					
Significance	NS					

Table 5: SVR12 rate in HIV/HCV co-infected patients.

SVR12	Number	Percentage
Target (HCV RNA viral load) Detected	1	5.6
Target (HCV RNA viral load) not Detected	17	94.4
Total	18	100.0

Table 6: SVR12 rate in HBV/HCV coinfected patients.

SVR12	Number	Percentage
Target (HCV RNA viral load) Detected	0	0
Target (HCV RNA viral load) not Detected	3	100
Total	3	100.0

Table 7: Side effects seen in study population.

Side Effects	Number	Percentage
Fatigue	16	10.7
Nausea	6	4
Headache	5	3.3
Anaemia	3	2
Diarrhoea	3	2

Table 8: Side effects according to disease severity.

Side Effects	Statistic	Fatigue	Diarrhoea	Nausea	Headache	Anaemia
Noncirrhosis (N=102)	N	4	1	1	1	0
	%	3.9	0.9	0.9	0.9	0
Compensated Cirrhosis (N=37)	N	4	0	2	2	0
	%	10.8	0	5.4	5.4	0
Decompensated Cirrhosis (N=11)	N	8	2	2	2	3
	%	72.7	18.2	18.2	18.2	27.3

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Chi square		55.99	15.99	9.77	9.77	36.68
P value		<0.001	0.014	0.012	0.012	<0.001
Significance		HS	S	S	S	HS

DISCUSSION

The present study was conducted on 150 patients diagnosed with HCV infection who received full course of anti HCV treatment in the form of Direct acting antiviral drugs under National Viral Hepatitis Control Programme and were called for follow up after 12 weeks of end of treatment in Medical Outpatient Department and ward of Government Medical College and Rajindra Hospital, Patiala. The maximum number of patients was between 41-50 years. The mean age in this study was 42.9 years. 70% patients were males and 30% were females. 49.3% of patients were asymptomatic. Most common symptom seen was fatigue in 48(32%) patients.

The mean HCV RNA viral load at start of treatment in non-cirrhotic, compensated cirrhotic and decompensated cirrhotic patients was 1342887.72 IU/ml, 1480992.08 IU/ml and 725227.27 IU/ml respectively. Statistically these results were insignificant. So, no correlation was seen between HCV RNA titre and severity of disease.

In this study, out of 150 HCV positive patients, 147 patients achieved sustained virological response after 12 weeks of end of treatment i.e. HCV RNA viral load was undetectable. So SVR12 rate achieved was 98% in overall population. The 3 patients who did not achieve SVR12 were -one was 52 year compensated cirrhotic male with HIV co-infection, second was 63-year-old female with decompensated cirrhosis and third was 45 year non cirrhotic male who was obese and diabetic. In this study, SVR 12 rate achieved was 99% in non-cirrhotic patients, 97.3% in compensated cirrhotic patients and 90.9% in decompensated cirrhotic patients. SVR 12 rate achieved was 94.4% in HIV co-infected patients and was 100% in Hepatitis B co-infected patients. So, in this study SVR12 rate achieved was above 90% in all group of patients ie non cirrhotic, compensated cirrhotic, decompensated cirrhotic, HIV coinfected and HBV coinfected. SVR 12 rate achieved was maximum in HBV coinfected and non-cirrhotic patients. Charatcharoenwitthaya et al. (2020) in their study achieved SVR 12 rate of 97.9% in overall population of 1021 patients. SVR 12 rate achieved in compensated cirrhosis patients was 98.5 % and in decompensated cirrhosis patients was 91 %. These results are comparable to present study.[11] Similarly, in a study by Gupta et al. (2018) on 499 HCV positive patients, SVR 12 rate achieved was 97 % in overall population.[12] Kim et al. (2019) in their study achieved SVR12 rate of 96.5% in HIV and HCV co-infected patients which is comparable to present study.[13] Charatcharoenwitthaya et al. (2020) studied that all 25 HBV and HCV co- infected patients achieved SVR 12, So SVR 12 rate was 100% in this population group. This is comparable with present study.[11]

In this study, out of total 150 patients, 28 (18.6%) patients experienced side effects with direct acting antivirals drug use. Fatigue was seen in 16(10.7%) patients, nausea in 6(4%), headache in 5(3.3%), anaemia in 3(2%) and diarrhoea in 3(2%) patients. These side effects were seen more in cirrhotic patients as compared to non- cirrhotic patients. Similar findings were seen by Curry et al. (2015) in their study on 267 HCV positive patients, where they observed that most common adverse events of direct acting antiviral drugs were fatigue, nausea and headache.[14]

Charatcharoenwitthaya et al. (2020) in their study, observed that most common adverse events of direct acting antiviral drugs were non-specific, such as fatigue (11%), insomnia (2.7%), headache (2.5%), gastrointestinal events (1.8%), rash (1%) and arthralgia (0.7%). These results are comparable with present study.[11]

CONCLUSION

The study found that direct-acting antiviral therapy for hepatitis C has a short duration and excellent safety profile. The high SVR12 effectiveness rates demonstrate the real-world efficacy of these regimens, showing they deliver strong clinical outcomes.

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