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Need of genotype determination in HCV treatment in current era

Abstract

Introduction: Hepatitis C virus (HCV) is an important cause of liver disease worldwide and leads to substantial morbidity and mortality. The global prevalence of HCV infection is around 2%, with 170million persons with chronic infection and 3 to 4million persons newly infected each year. The treatment in the era of Pegylated Interferon & Ribavarinwas decided on basis of Genotype but now with the availability of oral pan genotypic Directly acting antiviral (DAA), need of genotypic determination prior to starting treatment is decreasing over period of time.

Aim: To determine difference in Sustained Virological response in HCV Patients treated with oral antiviral in Genotype determined and undetermined groups.

Materials & methods: This was a retrospective study conducted at Medical Gastroenterology Department, PGIMS, Rohtak in which records of HCV treated patients over a span of six years i.e. 01.01.2015 to 31.12.2020 were analyzed. In this study, two groups of 1500 patients each were made. In both groups only those patients who completed treatment and came for Sustained virological response were included. One group was in which pretherapy HCV genotype was determined and in other genotype was not determined.

Observation & results: The complete data pertaining to total 3000 patients were analyzed and two groups of 1500 patients each were made, in one group HCV genotype was determined and in other genotype was not determined.

Conclusion: The availability of pan genotypic oral directly acting antiviral for HCV has made treatment easier with lesser side effects and excellent compliance rates. The higher Sustained virological response (SVR) with DAA has already been proved in many studies. Now with availability of pan genotypic DAA, need of genotype determination for treatment purpose is decreasing and it may lose its relevance in future. This will prove to be helpful in developing countries like India which have not only financial constraints but also HCV has emerged as a major health problem.

Keywords: hepatitis C virus, genotype, sofosbuvir, daclastavir, velpatasvir

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Abbreviations: HCV, hepatitis C virus; DAA, directly acting antiviral; SVR, sustained virological response

Introduction

One of the important causes of hepatic injury is Hepatitis C virus which leads to substantial morbidity and mortality. The complexity and uncertainty related to the geographic distribution of HCV infection and chronic hepatitis C, determination of its associated risk factors, and evaluation of cofactors that accelerate its progression, underscore the difficulties in global prevention and control of HCV.

Although HCV is endemic worldwide but has wide geographic variability in its distribution. The economic burden of chronic hepatitis C might exceed $10billion annually in the United States alone. This disease has a worldwide prevalence of up to 3%, making the global burden of the disease comparably tremendous. The cost of the disease includes direct medical expenses for its hepatic and extra hepatic manifestations, and also indirect costs incurred from impaired quality of life and the loss of work productivity.[1] The impact of this infection is just emerging in India.

The most frequently cited risk factors for HCV transmission worldwide are blood transfusions from unscreened donors, injection drug use, unsafe therapeutic injections, and other health-care related procedures.

The professional blood donation i.e. who donate blood for monetary benefits continues to flourish in India. Another problem in our health system is lack of strict adherence to safe needle practices. Both these factors are potential sources for the spread of hepatitis C in India. Long-term hepatitis has been shown to cause cirrhosis and hepatocellular carcinoma in patients. The disease burden associated with hepatitis B, C, and D appears 10 to 20years after infection. Thus, the prevalence of these infections is important from a public health perspective.[2] The Chronic hepatitis B virus (HBV) infection caused more than half of the deaths due to cirrhosis in Asia-pacific region, followed by alcohol consumption (20·8%), non-alcoholic fatty liver disease (NAFLD; 12·1%), and chronic infection with hepatitis C virus (HCV; 15·7%).[3] The worrying aspect of acute hepatitis C infection is that spontaneous viral clearance is unusual with nearly 54%-86% of the infected individuals progressing to chronic hepatitis. Around a fifth of the patients with chronic hepatitis C progress to cirrhosis over a time spanning nearly a decade. An estimated 27% of cirrhosis and 25% of Hepato cellular carcinoma worldwide occur in HCV infected people.[4]

Aim

To review retrospective data for determining difference in Sustained Virological response in HCV Patients treated with oral antiviral in Genotype determined and undetermined groups.

Material and methods

This was a retrospective study conducted at Medical Gastroenterology Department, PGIMS, Rohtak in which records of HCV treated patients over a span of six years i.e. 01.01.2015 to 31.12.2020 were analyzed. In this study, on basis of available data of HCV patients who achieved SVR, two groups of 1500 patients each were made.

The Sustained virological response was defined as absence of HCV RNA after 12weeks of completion of treatment. One group was in which pretherapy HCV genotype was determined and in other genotype was not determined. In genotype determined group, genotype 1 and 4 patients were treated for 12weeks with Sofosbuvir and Ledipasavir, whereas genotype 3 patients were treated for 12weeks with Sofosbuvir and Daclastavir. In other group, in which genotype was not determined, 12weeks treatment each was given with Sofosbuvir 400mg and Daclastavir 60mg combination for non-cirrhotic and Sofosbuvir 400mgand Velpatasvir 100mg combinationfor cirrhotic respectively.

Statistical analysis

Statistical analysis was performed by the SPSS program version 25.0. The chi square test was used and p value less than 0.05 were taken to indicate a significant difference.

Observations and results

The complete data pertaining to total 3000 patients were analyzed. Two groups were made of 1500 patients each who completed their treatment and reported for SVR testing. The utmost care was taken that age, sex, geographical, cirrhosis vs. non cirrhosis status matched in both the groups. In first group A, genotype determination has been done and patients were treated with 12weeks each with combination of Sofosbuvir 400mg and Ledipasavir 90mg for genotype 1 & 4 and Sofosbuvir 400mg & Daclastavir 60mg combination for genotype 3 for non cirrhotic and 24weeks for cirrhotic. In second group B, where genotype was not determined, all non-cirrhotic patients were treated with 12weeks combination of Sofosbuvir 400 mg and Daclastavir 60mg and all cirrhotic were treated with 12weeks combination of Sofosbuvir 400 mg and Velpatasvir 100mg. In both the groups A & B, male predominance was seen i.e. 1005 (67%) patients& 990 (66%) patients respectively while females were only 495 (33%) & 510 (34%). There was predominance of patients belonging to poor socio economic status having rural background i.e. 975 patients (65%) in group A and 990 (66%) in group B. The maximum number of patients belonged to younger age group i.e. from 20-40yrs of age group i.e. 825 patients (55%) in group A & 810 patients (54%) in group B with minimal representation at extreme of age group. In group A, 225 patients (15%) were cirrhotic whereas in group B 240 patients (16%) were cirrhotic. The sustained virological response (SVR) in Group A was 95% & 92 % in non-cirrhotic and cirrhotic respectively whereas in Group B it was 93% & 91% in non-cirrhotic and cirrhotic respectively (Tables 1 & 2).

Table 1 Showing Epidemiological Distribution in Two Groups

Total Patients	Sex	Rural/ Urban	Age	Cirrhotic
Genotype Determined (1500)	Males (67%) Females (33%)	Rural (65%)	20-40 yrs (55%)	Cirrhotic (15%) Non-cirrhotic (85%)
Genotype Not Determined (1500)	Males (66%) Females (34%)	Rural (66%)	20-40 yrs (54%)	Cirrhotic (16%) Non-cirrhotic (15%)

Table 2 Showing Sustained Virological Response in Two Groups

Total Patients (3000)	Sustained Virological Response (SVR)	
Genotype Determined (1500) (Group A)	Non-cirrhotic-95%	Cirrhotic-92%
Genotype Not Determined (1500) (Group B)	Non-cirrhotic-93%	Cirrhotic-91%

Discussion

The availability of pan genotypic oral directly acting antiviral for HCV has made treatment easier with lesser side effects and excellent compliance rates. The Sustained virological response (SVR) with DAA is very good and has already been proved in many studies.[6] Now with use of pan genotypic DAA, need of genotype determination before starting therapy is decreasing and it may lose its relevance in future. The HCV treatment has seen paradigm shift from simple Interferon to combination of Pegylated Interferon & ribavarin combination followed by availability of orally acting DAA's, which has now further been elaborated by use of pan genotypic effective drugs. Hence before availability of these pan genotypic DAA, the type and duration of treatment was based on genotype. In the current era of therapy with DAAs, SVR is achievable in the vast majority of hepatitis C-infected patients.[5] Other studies conducted in the interferon (IFN) era have established that achievement of SVR is associated with significant clinical benefits, including reduced risk of fibrosis progression.[6,7] liver-related complications, extra hepatic manifestations of HCV,[8] as well as improved quality of life.[9] Collectively, these SVR benefits translate into reductions in hepatic and non-hepatic morbidity and mortality.[10] In India, under National Viral Hepatitis Control Program (NVHCP) in view of treatment with these pan genotypic drugs, genotype determination. All non-cirrhotic were to be treated with 12weeks combination of Sofosbuvir 400mg and Daclastavir 60mg whereas all cirrhotic were to be treated with 12weeks combination of Sofosbuvir 400mg and Velpatasvir. Collectively, multiple studies have shown results with DAA therapy which suggest SVR12 has a positive predictive value for SVR24 of >97%.[11] Our study is in concordance with them, depicting high and almost equal SVR in both genotype determined and non-determined group**.** The difference in SVR in genotype determined and undetermined group was not statistically significant, as p value was greater than 0.05.

Conclusion

In view of high and comparable SVR in absence of pre-therapy genotype determination, our study hints that importance of genotype determination in HCV treatment may decrease in future but more large scale studies are required before reaching any definitive conclusion. The strength of our study is that, analysis is based upon a significant number of HCV treated patients i.e. 3000 and if same results are proven in other large scale studies, then it will prove to be very beneficial in developing countries like India where HCV has emerged as a major health problem in background of financial constraints. The limitation of study is that it is based on one geographical area of Northeren India, hence it has to be seen that whether same results are seen in studies done in different countries.

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None.

Conflicts of interest

We declare there is no conflict of interest.

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