

Comparison of Rapid Virological Response in patient on Treatment with Direct Acting Antivirals (DAA) (Sofosbuvir) Verses DAA Along With Pegylated Interferon for Chronic Hepatitis C Virus Infection Genotype 3

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ABSTRACT

Background: HCV classified in eleven genotypes and the most common is genotype 1, 2 & 3 in USA. The treatment of hepatitis C virus (HCV) infection with the available option is complicated. The rapid virologic responses may lead us to select a better treatment option in genotype 3 patients. New Direct acting antiviral DAA therapies for HCV infections has captured the market since last decade. Hence this study aims to provide a comparison of rapid virologic response over the two treatment options a) DAA and b) DAA plus pegylated interferon for chronic hepatitis C virus infection genotype 3.

Methods: This was a comparative observational study of 50 HCV infection patients with genotype 3. Further divided into two groups based on treatment. Rapid virologic responses were calculated against each treatment therapy.

Results: The RVR rate was 90% in patients with HCV genotype 3 infections who were treated for 24 weeks with DAA plus PEG-IFN and Ribavirin (90% for noncirrhotic patients, 68% for cirrhotic patients), whereas the RVR12 was 68% with the patients who were on treatment with DAA drug only.

Conclusion: We may conclude that the treatment option B that is in a combination produced better virological rates than A, though the treatment duration is long (i.e., upto 24 weeks)

Keywords: Rapid Virologic Response, Direct antiviral Agent, Interferon, Pegylated

INTRODUCTION

Hepatitis C is an infectious liver disease caused by hepatitis C virus (HCV) this virus contains a single strand RNA¹. The infected patients generally undergo for acute hepatitis C that prevail for the lesser time from two weeks to six months. The diagnosis of HCV infection is rare and the yielding disease may be unnoticed until a sever damage in liver appeared². Approximately 3.2 million people in USA with chronic HCV infection^{3,4}. HCV classified in eleven genotypes and the most common is genotype 1, 2 & 3 in USA¹. The treatment of hepatitis C virus (HCV) infection with the available option is complicated. The rapid virological responses may lead us to select a better treatment option in genotype 3 patients. New Direct acting antiviral DAA therapies for HCV infections has captured the market since last decade. Hence this study aims to provide a comparison of rapid virological response over the two treatment options a) DAA and b) DAA plus pegylated interferon for chronic hepatitis C virus infection genotype 3.

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MATERIAL AND METHODS

This was a comparative observational study, conducted in Department of xyz. A total of 50 hepatitis C patients were included in the study through simple random sampling. The exclusion criteria include all the patients with hepatitis B, patients with comorbidities, whereas patients with chronic Hepatitis C virus infections were included in this study. The duration of the study was of one year starting from Aug 2014. The patients were divided into two groups, the 1st group was on treatment with direct acting antiviral drugs like sofosbuvir and the 2nd group patients were on treatment with direct acting antiviral along with pegylated interferon for chronic hepatitis C virus infection genotype 3. Patients of both group detailed medical history; physical examination and demographics were noted, moreover blood samples were taken to measure the viral loads.

Statistical analysis: All the collected information/data was stored electronically & analyzed later by using SPSS version 20. Descriptive statistics were applied to calculate mean and standard deviation. Frequency distribution and percentages were calculated for qualitative variables like gender, treatment used etc. Overall a P values less than 0.05 was considered statistically significant.

RESULTS

In this study, out of 50 patients, 25 patients were on treatment with direct antiviral drug (DAD) named group one patients and 2nd group patients were on treatment with direct antiviral drug along with pegylated interferon. Overall 30 (60%) of the patients were male and 20(40%) were females. The average age of hepatitis C patients was 38.6±9.2. The regimen for HCV genotype 3 infections is given in table 1. *RVR (Rapid Virologic response) PEG-IFN, pegylated interferon; WB, weight-based. WB ribavirin: <75 kg=1000 mg, ≥75 kg=1200 mg.

The RVR rate was 90% in patients with HCV genotype 3 infections who were treated for 24 weeks with DAA plus EG-IFN and Ribavirin (90% for noncirrhotic patients, 68% for cirrhotic patients), whereas the RVR12 was 68% with the patients who were on treatment with DAA drug only.

Table 1: Treatment regimens for genotype 3

Treatment Naïve	Time for RVR12
Sofosbuvir 400mg+WB ribavirin daily	12 weeks
Sofosbuvir 400 mg + WB ribavirin daily for 24 weeks + PEG-IFN weekly for 12 weeks	24/12 weeks
Treatment Failure: PEG-IFN and Ribavirin	
Sofosbuvir 400 mg + WB ribavirin daily	24 weeks
Sofosbuvir 400mg+WB ribavirin daily for 24 weeks+PEG-IFN weekly for 12 weeks	12 weeks

DISCUSSION

The present study demonstrate the difference of rapid/sustained virological response in patients on treatment with DAA (sofosbuvir) with DAA along with pegylated interferon for chronic hepatitis C virus infection genotype 3. In our study we report, 25 Naïve patients, which were given the 12-week sofosbuvir, and ribavirin combination, where the RVR12 rates were less as compared to the patients who were given DAA along with Pegylated interferon for 12 to 24 week, where the RVR is higher than 90%. Similar to this, a recent published study evaluates the same regimen for 12 week with HCV genotype 3 infected patients.^[5-7] The study findings showed good efficacy in both group treatment naïves and treatment experiences patients. It was published and well known that better RVR rates were observed with DAA containing triple or double therapy in comparison to the naïve patients on DAA treatments only with genotype 3 HCV infections^{8,9,10}. In one of the largest study published in 2012, of a cohort of above 7000 treatment Naïve patients of all

genotypes¹¹, patients with Genotype 3 infections were treated with PEG-IFN alpha achieved high RVR rates of those without the earlier mentioned treatment. In another Egyptian study, an association was reported for higher RVR rates and the treatment option 2 (used in group 2 here)¹², while it is less significantly associated with dose reductions. The reason behind may be a confounding factor, where the BMI of patient may act as confounder found consistent in various studies.^[13] The other treatment option of DAA (i.e., Sofosbuvir) is a liver-targeted nucleotide pro drug of the active triphosphate GS-461203, which has been approved for use in HCV genotype 3. It works as an inhibitor of the HCV NS5B RNA-dependent RNA polymerase, which acts as a chain terminator^{14,15}. Its exact mechanism of action is unknown, but one suggested mechanism is its inhibition of hyperphosphorylation of NS5A, which seems to be required for viral production. Oral blend of new DAAs is likely to become the standard of care for chronic HCV in treatment-naïve or treatment-experienced patients. However, till now very less studies of 'easy-to-treat' patients with short post-treatment periods for defining the sustained virologic response. Extension of the number of treated patients and of the post-treatment follow up in a real-life setting could significantly deteriorate the rate of recovery. In these 'difficult-to-treat' patients, the rate of virologic cure with new DAAs could be lower than expected and consequently interferon may be still necessary in combination with the new drugs.

CONCLUSION

We may conclude that the treatment option B that is in a combination produced better virological rates than A, though the treatment duration is long (i.e., upto 24 weeks)

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