Original Article

Sofosbuvir and Ribavirin in Chronic Hepatitis C Genotype 3 Non Responder Patients

Rahmanuddin, Shah Zeb, Muhammad Abbas and Fazal Rabbi

ABSTRACT

Objective: To evaluate the efficacy of sofosbuvir plus ribavirin in chronic hepatitis C genotype 3 interferon non responder patients.

Study Design: Prospective / observational study

Place and Duration of Study: This study was conducted at the Medical B Unit; Mardan Medical Complex, Mardan from Jan 2016 to December 2017.

Materials and Methods: Forty five adult eligible both male and female Hepatitis C genotype 3 patients non-responder to interferon were included in the study. Sofosbuvir 400mg and ribavirin on weight based daily for 24 weeks were given to patients. Patients were tested for absence of detectable HCV RNA by PCR at the end of treatment and 24 weeks after the completion of treatment to look for sustained virological response at 24 weeks.

Results: A total of forty five chronic Hepatitis C genotype 3 interferon non responder patients received treatment with sofosbuvir 400mg and ribavirin on weight basis for 24 weeks .All patients completed treatment. Out of forty five patients 19 (42.2%) were female and 26 (57.8%) 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. In33 (73.3%) patients, the APRI score was <2 and in 12(26.7%) patients the APRI score was>2.Liver biopsy not done because it is an invasive procedure. The end of treatment response was 80 %(36) while 20 %(9) of the patients were non responder. The sustained virological response rate was 58.33 %(21) while 41.67 % (15) patients were relapsed.

Conclusion: Combination of sofosbuvir and ribavirin for 24 weeks in chronic hepatitis C non responder patients was associated with low rate of sustained virological response at 24 weeks and high rate of relapse. This combination is not a good choice in those patients who has no response to peg interferon or conventional interferon.

Key Words: Chronic Hepatitis C, Sofosbuvir, Ribavirin

Citation of articles: Rahmanuddin, Zeb S, Abbas M, Rabbi F. Sofosbuvir and Ribavirin in Chronic Hepatitis C Genotype 3 Non Responder Patients. Med Forum 2019;30(2):72-74.

INTRODUCTION

Chronic hepatitis C infection is still great challenge in recent era because of its increasing high rate of prevalence and complication.[1] about 3-4 million people are affecting each year. Prevalence is different in different region of the world; it is very high in African countries and Asia while very low in Australia and USA. Now HCV is considered to be leading cause of hepatic lethal complications and mortality.[2] Hepatitis c prevalence is increasing in Pakistan estimated to be 6.8 % among general adult population while active infection found to be 6% of population.[3]

Department of Medicine, Bacha Khan Medical College, Mardan.

Correspondence: Dr. Rahman uddin, Assistant Professor of Medicine, Bacha Khan Medical College, Mardan.
Contact No: 0336-7236551
Email: rehmanmohammad13@gmail.com

Received: September, 2018
Accepted: November, 2018
Printed: February, 2019

Genotype 3 is considered to be the most notorious one, because of its high rate of transformation to hepatoma and development of liver cirrhosis.[4] The prevalence of HCV genotype 3 is very high in Australia and south Asia.[5] Pakistan ranked to be second amongst the countries responsible for global viremia with most common genotype 3 .[6] In Pakistan HCV genotype 3 is very common as compared to other genotypes estimated to be about 69.1 %.[7] Patient with genotype 3 sometime suddenly present with lethal complication because of its rapid progression to fibrosis and rate of steatosis which relates with viral replication level .[8]

Treatment option for HCV genotype 3 has been changed and improved with different types of combination. Sustain viral response with sofosbuvir and ribavirin for 12 week duration is different between non naïve genotype 3 without cirrhosis and naïve genotype 3.[9] The combination of sofosbuvir and ribavirin was considered to be the standard one previously but because of the adverse effects and limitation of ribavirin in certain conditions like child bearing age, haemoglobinopathies and cardiac patients limit the use of this combination.[10] Sofosbuvir a nucleotide analog having activity against all genotypes,

while in combination with ribavirin is more effective against genotype 2 and 3(11,12).This combination is available in our hospital free of cost .We observe the response rate of chronic HCV genotype 3 patients who are non responders to interferon treatment.

MATERIALS AND METHODS

This study was conducted at Mardan medical complex Mardan from Jan 2016 to December 2017, involving patients attending medical and Gastroenterology OPD in Mardan Medical Complex teaching hospital Mardan. Forty five adult eligible both male and female Hepatitis C genotype 3 nonresponder patients were included in the study. Sofosbuvir 400mg and ribavirin on weight base daily for 24 weeks were given to patients. Patients were tested for absence of detectable HCV RNA by PCR at the end of treatment and 24 weeks after the completion of treatment to look for sustained virological response at 24 weeks.

RESULTS

A total of forty five chronic Hepatitis C genotype 3 interferon non responder patients received treatment with sofosbuvir 400mg and ribavirin on weight basis i.e.1000mg for <75kg body weight and 1200mg for >75kg body weight for 24 weeks.

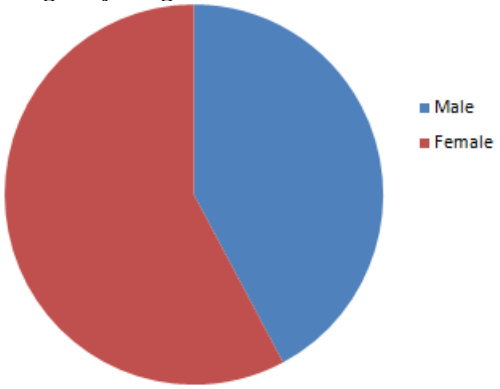

Figure No.1: Sex distribution

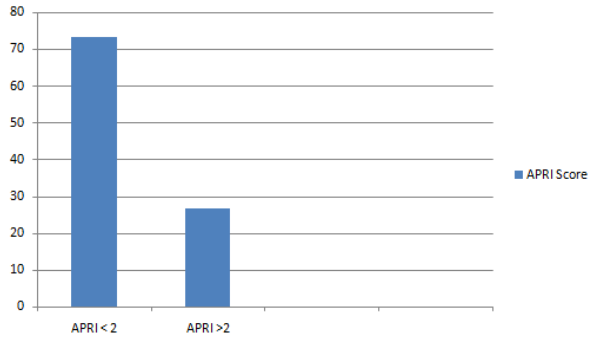

Figure No.2: APRI score in patients

All patients completed treatment. Out of forty five patients 19 (42.2%) were female and 26 (57.8%) 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 33 (73.3%) patients the APRI score was <2 and in 12(26.7%) patients the APRI score was >2.Liver biopsy not done because it is an invasive procedure. The end of treatment response was 80 %(36) while20%(9) of the patients were non responder. The sustained virological response rate was 58.33 %(21) while 41.67%[15] patients were relapsed.

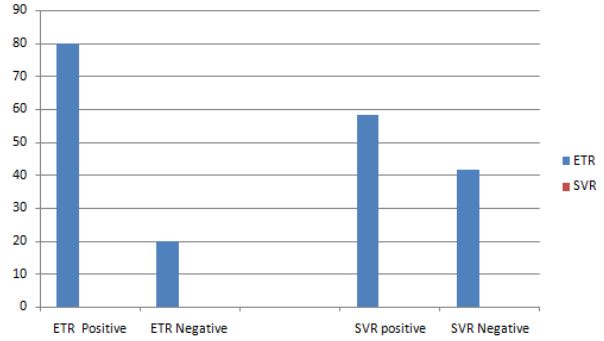

Figure No.3: ETR and SVR ratio in patients

DISCUSSION

Pakistan` is facing an epidemic of Hepatitis C virus. About 8 million people in Pakistan have `HCV infection[13]. Incidence of HCV isvery high in Pakistan and it is increasing day by day due to lack of awareness 14. We observe the response rate of sofosbuvir plus ribavirin in chronic hepatitis C genotype 3 nonresponder patients. The goal of treatment is to cure HCV infection in order to prevent complication and prevent further transmission of HCV. The endpoint of treatment was an (SVR24) sustained virological response at 24 weeks after the completion of treatment. SVR 24 is defined by undetectable HCV RNA in the serum at 24 weeks after the end of therapy[15]. 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[16]. 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 aminotransferase to platelet ratio index (APRI). It in simple, cheap and noninvasive and the information it give is reliable. 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.Recent introduction of direct acting antivirals increased the SVR rate to more than 90%.Sofosbuvir is recommended for the treatment of HCV is registered in Pakistan at a reasonable price and available in our hospital free of cost. We used Sofosbuvir 400mg daily and ribavirin on weight basis i.e. 1000mg a day for <75 kg body weight and 1200mg a day for >75kg body weight for 24 week. Sofosbuvir is a nucleotide analogue HCV NS5B polymerase inhibitor, while ribavirin is a synthetic guano sineanalogue; both of them have potent antiviral activity and are administered orally. The SVR varies in different populations and

pathological conditions[17]; it is also lower in cirrhotic patient as compared to non-cirrhotic[18], in our study the end of treatment response was 80%(36), while 20 %(09) of the patient were nonresponder. The sustained virological response rate was 58.33% (21) at 24 weeksand 41.67%[15] of patients were relapsed. It is almost comparable with other studies like In FISSION trial the SVR 12 rate in genotype 3 patients were only 56%[19]. Similarly in POSITRON trial the SVR after 24 weeks were 61%[20] and in FUSSION trial similar results were achieved showing poor SVR rates of 62% in genotype 3 patients. Compared with above studies, the sustain virological response found to be lower with Sofosbuvir and ribavirin combinations.

CONCLUSION

Combination of sofosbuvir and ribavirin for 24 weeks in chronic hepatitis C non responder patients was associated with low rate of sustained virological response at 24 weeks and high rate of relapse. This combination is not a good choice in those patients who has no response to peg interferon or conventional interferon. We therefore not recommend this regimen in chronic hepatitis C genotype 3 nonresponder patients

Author's Contribution:

Concept & Design of Study:	Rahmanuddin
Drafting:	Shah Zeb
Data Analysis:	Muhammad Abbas, Fazal Rabbi
Revisiting Critically:	Rahmanuddin, Shah Zeb
Final Approval of version:	Rahmanuddin

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

REFERENCES

1. Sarwar S, Khan AA, Tarique S. Response Guided interferon therapy for genotype 3 of chronic hepatitis C and outcome. Pak J Med Sci 2015, 843-847.
2. Qureshi MS, Iqbal M, Nomani AZ, Rasheed K, Time for Change: Conventional Interferon Regimes Should Not Be the Standard of Care for Management of Pakistani Genotype-3 in Chronic Hepatitis C, J Coll Physicians Surgeons Pak 2014; 24(1):70-72.
3. Kanwal F, Kramer JR, Ilyas J, et al. HCV genotype 3 is associated with an increased Risk of Cirrhosis and Hepatocellular Cancer in a National Sample of US. Veterans with HCV. Hepatol 2014;60(1): 98-105.
4. Umer M, Iqbal M. Hpatitis C virus Prevalence and genotype distribution in Pakistan. World J Gastroenterol 2016;22(4):1684-1700.
5. Baig S, Masood N, Shaikh IA. Distribution frequency of hepatitis C virus genotypes in patients attending Liaquat University Hospital Jamshoro/ Hyderabad. J Post Med Inst 2014;28(4): 367-71.
6. Akhter TS, Umar M, Khawar HTB. Sofosbuvir for the treatment of hepatitis C genotype 3 infected patients in Pakistan Tayyab. J Ayub Med Coll Abbottabad 2017;28(4 Suppl 1):884–89.
7. Capileno1 YA, den Bergh RV, et al. Management of chronic Hepatitis C at a primary health clinic in the high-burden context of Karachi, Pakistan https://doi.org/10.1371/journal.pone.0175562 April 27, 2017.
8. Leroy V, Angus P, Bronowicki JP, et al. Daclatasvir, Sofosbuvir, and Ribavirin for Hepatitis C Virus Genotype 3 and Advanced Liver Disease, Hepatol 2016;63(5):1430-41.
9. Poll S, Pichard AV, Mariocorouqe. Treatment of Hepatitis C virus genotype 3-infection. Liver Int 2014;18-23.
10. Foster GR, Afdhal N, Roberts SK, et al. Sofosbuvir and Velpatasvir for HCV Genotype 2 and 3 Infection. N Engl J Med 2015;373:2608-17.
11. Lawitz E, Mangia A, Wyles D, et al. Sofosbuvir for Previously Untreated Chronic hepatitis C Infec J Med 2013;368:1878-87.
12. Zeuzem S, Dusheiko GM, et al. Sofosbuvir and Ribavirin in HCV Genotypes 2 and 3. N Engl J Med;370;21 nejm.org may 22, 2014 1993-2001.
13. National survey on prevalence of Hepatitis B and Clin General population of Pakistan. 2008(http://www.pmrc.org.pk/hepatitisbc.htm) accessed on 25-08-2015.
14. Qureshi SR, Memon NH, et al. Pegylated Interferon (PEG-INF) Plus Ribavirin Response in Patients with HCV Genotype-3 in Hyderabad, Sindh.CPQ Microbiol 2018;1(6):110.
15. Nahon P, Bourcier V, Layese R, Audureau E, Cagnot C, Marcellin P, et al. Eradication of Hepatitis C virus infection in patients with cirrhosis reduces risk of liver and non-liver complication. Gastroenterol 2017;152:142-156.
16. Castera L, Sebastiani G, Le Bail B, De Ledinghen V, Couzigou P, Alberti A. Prospective comparison of two algorithms combining noninvasive methods for staging liver fibrosis in chronic hepatitis C. J Hepatol 2010;52:191-198.
17. Khaliq S, Raza SM. Current Status of Direct Acting Antiviral Agents against Hepatitis C Virus Infection in Pakistan. Medicina 2018;54:80.
18. Jacobson IM, Gordon SC, et al. Sofosbuvir for Hepatitis C Genotype 2 or in Patients without Treatment Options. N Engl J Med 2013;368;20 nejm.org.1867-77.
19. Lawitz E, Mangia A, Wyles D, Rodriguez-Torres M, Haddanien T, Gordon SC, et al. Sofosbuvir for previously untreated chronic hepatitis C infection. N Engl J Med 2013;368(20):1878-87.
20. Jacobson IM, Gordon SC, Kowdley KV, Yosshida EM, Rodriguez-Torres M, Sulkowski MS, et al. Sofosbuvir for hepatitis C genotype 2 or 3 in patients without treatment option. N Engl Med 2013;386(20):1867-77.