Original Article

Efficacy of Sofosbuvir and Ribavirin Therapy in Hepatitis C Virus Infection Among Treatment Naïve Cases of South Punjab

Waseem Sarwar Malghani, Anum Khakwani, Shehryar Kanju and Farooq Mohyuddin

ABSTRACT

Objective: This study was done to determine efficacy of Sofobuvir in treatment naïve cases of hepatitis C virus infection in Southern Punjab as there is no such study done in our general population.

Study Design: descriptive / observational study

Place and Duration of Study: This study was conducted at the Department of Gastroenterology, Nishtar Hospital, Multan from 1-7-2016 to 31-3-2017.

Materials and Methods: This study was using non-probability consecutive sampling technique. Patients (n=159) positive for HCV RNA PCR were taken in this study and their baseline investigations were done and treated with Sofosbuvir and ribavirin for 6 months and tested for sustained virological response (SVR) at 12 weeks of therapy. All data was entered in questionnaire and analysis was done using SPSS version 20.

Results: Of these 159 patients, 66 (41.5%) were male patients while 93 (58.5%) were female patients. Mean age of our study cases was 42.70 ± 12.69 years ranging from 19 years to 70 years. Mean age of male patients was 44.77 ± 12.50 years and mean age of the female patients was 41.23 ± 12.68 years which was statistically insignificant (p = 0.082). Eighty three (52.2%) were from rural areas while 76 (47.8%) from urban areas, 86 (54.1%) belonged to poor social background while 73 (45.9%) from middle income social status. Sustained virological response (SVR) at 12 weeks was noted to be in 158 (99.4%).

Conclusion: Sofosbuvirin combination with ribavirin was highly effective in achieving SVR at 12 weeks and it was safe and well tolerated in treatment naïve patients having hepatitis C virus infection. Hence, our study results support treatment of hepatitis C virus infection with Sofosbuvir without significant side effects.

Key Words: Sustained VIrological Response (SVR), HCV infection, efficacy, Sofosbuvir.

Citation of articles: Malghani WS, Khakwani A, Kanju S, Mohyuddin F. Efficacy of Sofosbuvir and Ribavirin Therapy in Hepatitis C Virus Infection Among Treatment Naïve Cases of South Punjab. Med Forum 2017;28(9):

INTRODUCTION

Hepatitis C virus infection remains one of the leading causes of the chronic liver diseases [1, 2] which lead to transplantation of liver and is responsible for increasing social, psychological, financial and health burden globally[3]. It leads to different complications including cirrhosis of liver, decompensated liver diseases and hepatocellular carcinoma (HCC)[4-8]. There are approximately 130-175 million patients who develop chronic infection all over the world with 0.5 million deaths related to HCV infection are being reported annually[9].

The prevalence of HCV infection varies with regards to geographic distribution all over the world, ranging from less than 0.5% in different European countries like Netherlands, Belgium, United kingdom, and Germany which are regarded as low prevalence countries to as high as 10 % in Egypt[10-12]. In Pakistan prevalence of hepatitis C virus infection in general population is 5.9 % which is much higher than our most of the neighboring countries where it is around 0.5 % in Iran, 0.4% in China and around 1 % in India[13]. It is major health problem of Pakistani population with its prevalence is still increasing. In recent years, its prevalence in many developed nations like USA and Scandinavian countries of the Europe has dropped significantly but still incidence is increasing in developing countries where there is low level of awareness regarding spread of the disease, poor screening facilities of the blood, improper sterilization of the surgical instruments and inadequate treatment facilities[14,15].

Six major HCV genotypes have been described owing to their sequence homology with further subtypes with their distribution is variable in different regions as HCV genotype 3a is more common in Pakistan[16].

Significant proportion of the HCV patients are reluctant to undergo interferon based treatment due to weekly subcutaneous injections which included some serious

Department of Gastroenterology, Nishtar Hospital, Multan

Correspondence: Dr. Anum Khakwani, Head of Gastroenterology Unit, Nishtar Hospital, Multan
Contact No: 0300-4120113
Email: malghanidr@gmail.com

Received: June 10, 2017; Accepted: July 14, 2017

side effects such as fatigue, depression, influenza like symptoms and cytopenia[17].

With the introduction of highly effective direct acting antiviral (DAA), treatment of hepatitis C virus infection has been revolutionized as it provides interferon free treatment and infact opens a new window for elimination of HCV[18]. Similarly Sofosbuvir is also direct acting nucleotide polymerase inhibitor approved for treatment of HCV infection which is taken orally once daily. It causes RNA replication termination of the viral genome by an active nucleoside triphosphate, within host hepatocyte after phosphorylation, to compete natural nucleotides. The active triphosphate of nucleotide analogues such as Sofosbuvir targets highly conserved NS5B polymerase regions of the HCV[19].

This study was done to document efficacy of Sofosbuvir in our general population of Southern Punjab as there is no such study available to generate evidence of the therapy from this region.

MATERIALS AND METHODS

Our study included a total of 159 patients with chronic hepatitis C virus infection who were treatment naïve. All these patients were included from outpatient department of Department of Gastroenterology, Nishtar Hospital Multan after taking informed consent of participation. Prior permission was taken from Institutional Ethical Review Committee of the Nishtar Hospital Multan to carry out this research work. All the treatment naïve patients who were positive for HCV RNA PCR aged more than 18 years of either sex were included in this study. Patients having hepatocellular carcinoma, co-infection with hepatitis B, having pulmonary TB, brain tumors and those having contraindications to Sofosbuvir were excluded from our study.

Once registered, three ml of venous blood sample was taken and sent to the Nishtar Hospital Laboratory for Hb levels, TLC, platelet counts and serum albumin levels. Sofosbuvir was administered orally (400 mg once daily) plus ribavirin, also administered orally in 2 divided doses as per body weight. The treatment was continued for six months and patients were called for follow up at 12 weeks of therapy to determine sustained virological response (SVR) defined as HCV RNA PCR less than 25 IU/ml which is less than lower limit of quantification at 12 weeks. SPSS version 20 was employed to analyze the data and all the statistical tests were performed at 95 % confidence interval. Two sample t test was used to compare numerical data at the start of therapy with that of after treatment.

RESULTS

A total of 159 patients with hepatitis C virus infection were included in our study. Of these 159 patients, 66 (41.5%) were male patients while 93 (58.5%) were female patients. Mean age of our study cases was 42.70 ± 12.69 years ranging from 19 years to 70 years.

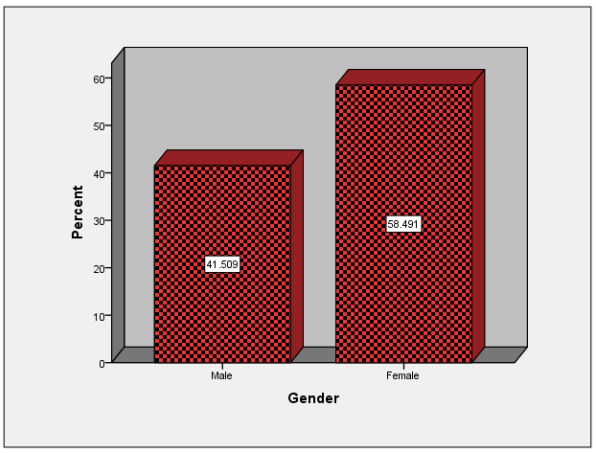

Figure No.1: Gender

Table No. 1. Comparison of clinical characteristics at baseline versus completion of therapy. (n=159)

Characteristics	Baseline values	Post therapy values	P value
	Mean (SD)	Mean (SD)	
Hemoglobin level (g/dL)	12.10± 1.74	12.20± 1.69	0.194
Total leukocyte count (per µl)	8628.95±2530.88	7587.82± 2315.86	<0.001
ALT (IU/L)	26.95 ± 15.75	24.65 ± 15.55	0.112
Platelet count (per µl)	243465.41±86103.12	257610.06± 96697.94	0.023
Serum albumin (g/dL)	4.31 ± 0.47	4.38 ± 0.50	0.119

Table No. 2. Comparison of post therapy clinical characteristics with regards to gender. (n=159)

Characteristics	Gender		Pvalue
	Male Mean (SD)	Female Mean (SD)	
Hemoglobin level (g/dL)	13.18±1.73	11.51±1.28	<0.001
Total leukocyte count (per µl)	7731.21± 2494.60	7486.06± 2188.34	0.512
ALT (IU/L)	27.42± 11.32	22.68±17.76	0.06
Platelet count (per µl)	238651.52 ±91002.71	27106452±98825.91	0.037
Serum albumin (g/dL)	4.48 ±0.55	4.31 ± 0.46	0.037

Mean age of male patients was 44.77 ± 12.50 years and mean age of the female patients was 41.23 ± 12.68 years which was statistically insignificant (p = 0.082). Eighty three (52.2%) were from rural areas while 76 (47.8%) from urban areas, 86 (54.1%) belonged to poor social background while 73 (45.9%) from middle income social status. Sustained virological response at 12 weeks was noted to be in 158 (99.4%).

DISCUSSION

Hepatitis C virus infection remains one of the leading causes of the chronic liver diseases which lead to transplantation of liver and is responsible for increasing social, psychological, financial and health burden globally. It leads to different complications including cirrhosis of liver, decompensated liver diseases and hepatocellular carcinoma (HCC). There are approximately 130-150 million patients who develop chronic infection all over the world with 0.5 million deaths related to HCV infection are being reported annually.

A total of 159 patients with hepatitis C virus infection were included in our study. Of these 159 patients, 66 (41.5%) were male patients while 93 (58.5%) were female patients. Our study results are in compliance with that of AKhter et al [20] from Rawalpindi who also reported female gender predominance with 56.4% which is close to our results. Sarwar et al [21] from Lahore reported almost equal distribution of male to female gender. However other studies have shown male gender preponderance in patients with HCV infection, Zaigham et al [22] from Karachi reported 56.4 % male patients with HCV infection undergoing same therapy which is different from our study results, similarly others have also reported high proportion of male patients.

Mean age of our study cases was 42.70 ± 12.69 years ranging from 19 years to 70 years. Mean age of male patients was 44.77 ± 12.50 years and mean age of the female patients was 41.23 ± 12.68 years which was statistically insignificant (p = 0.082). Akhter et al [20]from Rawalpindi also reported 46.84 ± 10.49 years mean age of the patients undergoing same therapy, which is close to our findings. Zaigham et al [22] from Karachi reported mean age was 46.6 years ranging from 20 – 72 years which is similar to our findings. Sarwar et al [21]from Lahore also reported 49.4 ± 12.1 years which is close to our study results.

Eighty three (52.2%) were from rural areas while 76 (47.8%) from urban areas, 86 (54.1%) belonged to poor social background while 73 (45.9%) from middle income social status.

Different local and international studies have documented efficacy of Sofosbuvir among relapsers, patients with and without interferon therapy, relating it with disease severity, patients with or without cirrhosis; however limited data regarding its efficacy in treatment naïve. Sustained virologicalresponse at 12 weeks was noted to be in 158 (99.4%). Akhter et al from Rawalpindi[20] also reported 96.5 % SVR which is comparable to our study results. Foster et al [23] also reported 88 % SVR at 12 weeks of therapy which is comparable to our study results. Zaigham et al [22] from Karachi reported 81.7 % SVR which is slightly lower than that being reported in our study. Sarwar et al [21]from Lahore also reported 83.18 % SVR at 12 weeks of therapy showing efficacy Sofosbuvir.

CONCLUSION

Sofosbuvir in combination with ribavirin was highly effective in achieving SVR at 12 weeks and it was safe and well tolerated in treatment naïve patients having hepatitis C virus infection. Hence, our study results support treatment of hepatitis C virus infection with Sofosbuvir without significant side effects.

Author's Contribution:

Concept & Design of Study:	Waseem Sarwar Malghani
Drafting:	Anum Khakwani
Data Analysis:	Shehryar Kanju
Revisiting Critically:	Farooq Mohyuddin
Final Approval of version:	Waseem Sarwar Malghani

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

REFERENCES

1. Khullar V, Firpi RJ. Hepatitis C cirrhosis: New perspectives for diagnosis and treatment. World J Hepatol 2015;7(14):1843-55.
2. Razavi H[1], Elkhoury AC, Elbasha E, Estes C, Pasini K, Poynard T, et al. Chronic hepatitis C virus (HCV) disease burden and cost in the United States. Hepatol 2013;57(6):2164-70.
3. Duberg AS, Blach S, Falconer K, Kåberg M, Razavi H, Aleman S. The future disease burden of hepatitis C virus infection in Sweden and the impact of different treatment strategies. Scand J Gastroenterol 2015;50(2):233-44.
4. Myers RP, Krajden M, Bilodeau M, Kaita K, Marotta P, Peltekian K, et al. Burden of disease and cost of chronic hepatitis C infection in Canada. Can J Gastroenterol Hepatol 2014;28(5):243-50.
5. Cramp ME, Rosenberg WM, Ryder SD, Blach S, Parkes J. Modeling the impact of improving screening and treatment of chronic hepatitis C virus infection on future hepatocellular carcinoma rates and liver-related mortality. BMC Gastroenterol 2014;14:137.
6. Ferreira PR, Brandão-Mello CE, Estes C, GonçalesJúnior FL, Coelho HS, Razavi H, et al.

Disease burden of chronic hepatitis C in Brazil. Braz J Infect Dis 2015;19(4):363-8.
7. Flisiak R, Halota W, Tomasiewicz K, Kostrzewska K, Razavi HA, Gower EE. Forecasting the disease burden of chronic hepatitis C virus in Poland. Eur J Gastroenterol Hepatol 2015;27(1):70-6.
8. Yu ML, Chuang WL. Treatment of chronic hepatitis C in Asia: when East meets West. J Gastroenterol Hepatol 2009;24(3):336-45.
9. Mohamed AA, Elbedewy TA, El-Serafy M, El-Toukhy N, Ahmed W, Ali El Din Z. Hepatitis C virus: A global view. World J Hepatol 2015; 7(26):2676-80.
10. Hatzakis A, Chulanov V, Gadano AC, Bergin C, Ben-Ari Z, Mossong J, et al. The present and future disease burden of hepatitis C virus (HCV) infections with today's treatment paradigm - volume 2. J Viral Hepat 2015;22Suppl 1:26-45.
11. Sibley A, Han KH, Abourached A, Lesmana LA, Makara M, Jafri W, et al. The present and future disease burden of hepatitis C virus infections with today's treatment paradigm - volume 3. J Viral Hepat 2015;22Suppl 4:21-41.
12. Mühlberger N, Schwarzer R, Lettmeier B, Sroczynski G, Zeuzem S, Siebert U. HCV-related burden of disease in Europe: a systematic assessment of incidence, prevalence, morbidity, and mortality. BMC Public Health 2009;9:34.
13. Taseer IH, Ishaq F, Hussain L, Safdar S, Mirbahar AM, Faiz SA. Frequency of anti – HCV, HBs Ag and related risk factors in pregnant women at Nishtar Hospital, Multan. J Ayub Med Coll Abbottabad 2010;22(1):13-16.
14. Williams IT, Bell BP, Kuhnert W, Alter MJ. Incidence and transmission patterns of acute hepatitis C in the United States 1982-2006. Arch Int Med 2011;171(3):242–248.
15. Ueno Y[1], Sollano JD, Farrell GC. Prevention of hepatocellular carcinoma complicating chronic hepatitis C. J Gastroenterol Hepatol 2009;24(4): 531-6.
16. Waheed Y, Shafi T, Safi SZ, Qadri I. Hepatitis C virus in Pakistan: a systematic review of prevalence, genotypes and risk factors. World J Gastroenterol 2009;15(45):5647–5653
17. Chung RT. A watershed moment in the treatment of hepatitis C. N Engl J Med 2012;366(3):273–275.
18. Alfaleh FZ, Nugrahini N, Matičič M, Tolmane I, Alzaabi M, Hajarizadeh B, et al. Strategies to manage hepatitis C virus infection disease burden - volume 3. J Viral Hepat 2015;22Suppl 4:42-65.
19. Azam Z, Shoaib M, Javed M, Sarwar MA, Shaikh H, Khokhar N. Initial results of efficacy and safety of Sofosbuvir among Pakistani Population: A real life trial - Hepatitis Eradication Accuracy Trial of Sofosbuvir (HEATS). Pak J Med Sci 2017; 33(1):48-52.
20. Akhter TS, Umar M, Khaar H, Aslam F, Nisar G, Naseer A, et al. Sofosbuvir for the treatment of hepatitis c genotype 3 infected patients in Pakistan. J Ayub Med Coll Abbottabad 2016;28(4):884-89.
21. Sarwar S, Khan AA. Sofosbuvir based therapy in hepatitis C patients with or without cirrhosis: is there difference. Pak J Med Sci 2017;33(1):37-41.
22. Zaigham A, Saad M, Nadeem R, Jawed F, Abbas M. Sofosbuvir and ribavirin with or without pegylated interferon for hepatitis C genotype 3: a real world experience. Hepat Mont 2017; e45525.
23. Foster GR, Pianko S, Brown A, Forton D, Nahass RG, George J, et al. Efficacy of sofosbuvir plus ribavirin with or without peginterferon-alfa in patients with hepatitis C virus genotype 3 infection and treatment-experienced patients with cirrhosis and hepatitis C virus genotype 2 infection. Gastroenterol 2015;149(6):1462-70.