Journal of Pharmaceutical Research International

33(24A): 1-8, 2021; Article no.JPRI.66910
ISSN: 2456-9119
(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)

Comparative Study of Compliance between Sofosbuvir and Interferon in the Management of Viral Hepatitis at Tertiary Care Hospital of Gambat, Sindh, Pakistan

Sajid Ali[1], Zuheeb Ahmed[1], Marvi Metlo[1], Tahseen Ahmed[2], Shahzad Ali[1], Arslan Ahmer[2*], Muhammad Murtaza Qureshi[2] and Syed Adeel Ahmed Shah[3]

[1]Department of Pharmacy, Shah Abdul Latif University (SALU), Khairpur, Sindh, Pakistan.
[2]Institute of Pharmaceutical Sciences, People's University of Medical and Health Sciences for Women (PUMHSW), Nawabshah, Sindh, Pakistan.
[3]Department of Pharmaceutics, Faculty of Pharmacy, University of Sindh, Jamshoro, Pakistan.

Authors' contributions

This work was carried out in collaboration among all authors. Author SA designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors ZA, MM, TA, SA, AA, MMQ and SAAS managed the analyses of the study and managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2021/v33i24A31425
Editor(s):
(1) Dr. Mohamed Fawzy Ramadan Hassanien, Zagazig University, Egypt.
Reviewers:
(1) Chidi Ugwuoke, Bayero University Kano, Nigeria.
(2) Alkali Mohammed, Abubakar Tafawa Balewa University, Bauchi, Nigeria.
Complete Peer review History: http://www.sdiarticle4.com/review-history/66910

Original Research Article

Received 28 January 2021
Accepted 04 April 2021
Published 16 April 2021

ABSTRACT

Introduction: Hepatitis can be defined as inflammation of the liver. Hepatitis may be acute or chronic. It is estimated that in 2017, approximately 15 million people suffered from Hepatitis in Pakistan suffering from hepatitis. 150–200 million people, or approximately ~3% of the world's population, are living with chronic Hepatitis C.
Methodology: A descriptive cross-sectional study was conducted on 300 patients selected by purposive sampling who were reported with Hepatitis-C and co infection of Hepatitis-C + Hepatitis-B, at a tertiary care hospital Gambat. A series of questions were asked from reported patients regarding symptoms and compliance.

**Corresponding author: E-mail: arslan.ahmer@gmail.com;*

Results: The results were analyzed by using SPSS-22. Among the 300 patients some were on sofosbuvir (n=150, 50%), which the others were on interferon (n=150, 50%). The findings showed that most of the patients on interferon were non-compliant (n=125,83.3%), and only (n=25, 16.7%) are compliant. Among non-compliant factors, fear from injection was reported in (n=42, 33.6), technique for injection (n=38, 30.4%), prolong duration of action (n=35, 28%), adverse drug reaction (n=26, 20.8%). Better compliance was observed with sofosbuvir (n=93, 62.8%) and non-compliant were (57, 38%).
Conclusion: This study concluded that better compliance was achieved with sofosbuvir as compared to interferon, rate of ADR'S were also less with sofosbuvir.

Keywords: Compliance; hepatitis; interferon; sofosbuvir.

1. INTRODUCTION

Hepatitis can be defined as inflammation of the liver [1]. Hepatitis may be acute or chronic [2]. It is estimated that in 2017, approximately 15 million people suffered from Hepatitis in Pakistan suffering from hepatitis. 150–200 million people, or ~3% of the world's population, are living with chronic hepatitis C [3]. The cases of hepatitis c are also increasing in USA as well [4]. In 2014, approximately 19659 peoples died due to hepatitis C in America [5]. It is caused by the hepatitis C virus (HCV) [6]. The infection is often asymptomatic, but chronic infection can lead to scarring of the liver and ultimately to cirrhosis, which is generally apparent after many years [7]. It can be transferred by intravenous administration of drugs, blood transfusion, Organ Transplant without HCV screening, Sexual/household exposure to anti-HCV-positive contact etc. Hepatitis-C can be treated by using interferon and antiviral agent [8-9]. Compliance can be defined as the degree to which a patient correctly follows medical advice [10]. Most commonly, it refers to medication or drug compliance, but it can also apply to other situations such as medical device use, self care, self-directed exercises, or therapy sessions [11]. Both the patient and the health-care provider affect compliance, and a positive physician-patient relationship is the most important factor in improving compliance, although the high cost of prescription medication also plays a major role [12-13]. Non-compliance can be defined as failure or refusal to comply. In medicine, the term noncompliance is commonly used regarding a patient who does not take a prescribed medication or follow a prescribed course of treatment [14]. The primary factors affecting patient compliance fall into one of two groups: External influencers, or Patient experience [15]. External influencers are all the factors outside of a patient's control that have the potential to impact compliance. All the factors that contribute to a patient's experience using prescriptions are known as patient experience [16-17].

Hepatitis is a chronic and long-term disease, which is influencing the majority of population of Pakistan including Gambat and all over the world. Studies have shown already that onset of hepatitis drug requires prolonged treatment, the therapy may continue from 12-16 weeks sometimes 24 weeks time is needed to show its response. Patients who find the side effects of any hepatitis drug with increased symptoms causes discontinue his/her medicine without informing the prescriber. Some time when patients observed that symptoms are not reduced at initial dose may cause discontinuation of medicines. Sometimes initial dose of interferon may cause anemia, high fever, depression and nausea.

This study will provide best choice or option for the management of hepatitis C that which of the drug either sofosbuvir or interferon has fast and early onset of action to overcome the problem of hepatitis with low symptoms.

2. METHODOLOGY

This study was started by sitting in the hepatitis outdoor patients department and the patients who were suffering with the sign and symptoms of hepatitis C like, Fatigue, dark urine, pale stool, abdominal pain, loss of appetite, unexplained weight loss, yellow skin and eyes, which may be signs of jaundice etc. A predesigned questionnaire for clinical assessment of compliance and non-compliance of patients on sofosbuvir and interferon, during the management of hepatitis C was used to record patient's disease history, habits, medication regimen, complaints and necessary information. 300 patients having hepatitis C participated in the current study. All patients were randomly given Interferon and sofosbuvir. 150 patients were

given sofosbuvir 400mg once a day, 150 patients were prescribed with Interferon alpha 2b, 300 million international units three times a week. Patients were asked, not to change their diet, exercise and medication routine during the study. Study patients were enrolled via purposive sampling (non-probability sampling). The total collected data was analyzed with the help of Statistical Package for Social Science (SSPS) software version 21 for interpreting the data.

2.1 Inclusion Criteria

Patients were selected from the ages of 25-65 years, Patients having co infection of HCV and HBV were included in the study, Patients having co infection of HCV and HIV were included in the study, only those patients were included, who were either on interferon or on sofosbuvir.

2.2 Exclusion Criteria

Children were not included in the study, Study was not only comprising on same gender of patients, Patients whose age was less than 25 years were not included in the study, and patients whose age more than 65 years were excluded from the study. Hepatitis patients who were on drugs other than sofosbuvir or Interferons were not included in study.

3. RESULTS

In Table 1, occupational status of study subjects is described in which indoor job holders were high 101(33.7%).

In Table 2, distribution of hepatitis C and co infection patients were described, which shows that out of 300 study subjects 281 (93.4%) study subjects were suffering from hepatitis c only, 13 (4.3%) patients were of HCV+HBV and 07 (2.3%) study subjects were of HCV+HIV.

In Table 3, management of hepatitis C was described, which shows that out of 300 patients 150 (50%) were on interferons and 150 (50%) were on sofosbuvir.

In Table 4, distribution of gender of patients who were on interferon was described, which shows that out of 150 patients 90 (64.7%) were male and 53 (53.7%) were females. Among study subjects who were on interferon male patients were more as compared to female.

In Table 5, compliance and non-compliance among study subjects who were on interferon was described, which shows that out of 150 patients 125 (83.3%) study subjects were non compliant with interferon where as 25 (16.7%) study subjects were compliant with interferon. This study shows that majority of study subjects were non-compliant with interferon.

Table 1. On the basis of occupation patients were divided into 4 groups

S.No	Occupation	Frequency	Percentage
1	Indoor job	101	33.7%
2	Outdoor job	70	23.3%
3	Jobless	43	14.3%
4	Housewives	86	28.7%
	Total	300	100%

Table 2. Hepatitis c and co infection study subjects

S.No	Disease	Frequency	Percentage
1	HCV Only	280	93.4
2	HCV+HBV	13	4.3
3	HCV+HIV	07	2.3
Total		300	100%

Table 1. Management of Hepatitis-C

Name of drug	Frequency	Percent
Interferon	150	50.0
Sofosbuvir	150	50.0
Total	300	100.0

Table 4. Gender wise distribution of study subjects who were on interferon

Gender	Frequency	Percent
Female	53	35.3
Male	97	64.7
Total	150	100

Table 5. Patient compliance and non-compliance

Type of Patient	Frequency	Percent
Compliant	25	16.7
Noncompliant	125	83.3
Total	150	100.0

In Table 6, non-compliant factor fear from injection was dominant, which shows that out of 125 non-compliant study subjects 42 (33.6%) study subjects were non compliant because having fear from injection.

In Table 7, non-compliant factor duration of therapy among non compliant study subjects was

described, which shows that out of 125 non compliant study subjects 35 (28%) patients were non compliant due to prolong therapy of interferon.

In Table 8, non-compliant factor technique by which interferon was injected among non compliant study subjects who were on interferon was described, which shows that out of 125 non compliant study subjects 38 (30.4%) study subjects were non compliant with interferon due to technique of injection.

In Table 9, non-compliant factor adverse drug reaction which were reported among non compliant study subjects who were on interferon was described, which shows that out of 125 non compliant study subjects 26 (20.8%) study subjects were non compliant with interferon due to appearance of adverse drug reactions.

In Table 10, distribution of gender of patients who were on sofosbuvir was described, which shows that out of 150 patients 95 (63.4%) were male and 55 (36.7%) were females. Among study subjects who were on sofosbuvir male patients were more as compared to female.

In Table 11, compliance and noncompliance among study subjects who were on sofosbuvir was described, which shows that out of 150 patients 57 (38%) study subjects were noncompliant with sofosbuvir where as 93 (62%) study subjects were compliant with sofosbuvir. This study shows that majority of study subjects were compliant with sofosbuvir.

In Table 12, non-compliant factor taste of sofosbuvir was described, which shows that out of 57 non compliant study subjects 32 (56.2%) study subjects were non compliant because taste of sofosbuvir.

Table 6. Noncompliance factor (Fear from injection) from injection (interferon)

Non Compliance factor	Frequency	Percent
Fear from injection	83	66.4
Others	42	33.6
Total	125	100

Table 7. Noncompliance factor (Prolong duration of therapy) (interferon)

Non compliance factor	Frequency	Percent
Prolong duration of therapy	90	72.0
Others	35	28.0
Total	125	100.0

Table 8. Noncompliance factor (Technique for injection) (interferon)

Noncompliance factor	Frequency	Percent
Technique for injection	38	69.6
Others	87	30.4
Total	125	100.0

Table 9. Noncompliance factor (Adverse drug reactions) (interferon)

Noncompliance factor	Frequency	Percent
Adverse drug reaction	26	79.2
Others	99	20.8
Total	125	100.0

Table 10. Gender wise distribution of study subjects who were on sofosbuvir

Gender	Frequency	Percent
Male	95	63.3
Female	55	36.7
Total	150	100.0

In Table 13, non-compliant factor adverse drug reaction of sofosbuvir was described, which shows that out of 57 non-compliant study subjects 12 (21.1%) study subjects were non compliant adverse drug reaction of sofosbuvir.

Table 11. Patient compliance and noncompliance with sofosbuvir

Type of patient	Frequency	Percent
Compliant	93	62.0
Noncompliant	57	38.0
Total	150	100.0

Table 22. Taste of drug among study subjects who were on sofosbuvir

Noncompliant factor	Frequency	Percent
Taste of drug	25	43.8
Others	32	56.2
Total	57	100.0

In Table 14, non-compliant factor prolong duration of therapy with sofosbuvir was described, which shows that out of 57 non-compliant study subjects 24 (42.1%) study subjects were non compliant due to prolong duration of therapy with sofosbuvir.

In Table 15, comparison of compliance and noncompliance was described. In this study, patients were more compliant with sofosbuvir as compared to interferon.

In Table 16, statistical analysis of compliance with gender of those patients who were on interferon was done. On applying Chi-Square Test result shows both variables are independent on each other.

In Table 17, statistical analysis of compliance versus gender among study subjects who were on sofosbuvir was done. On applying Chi-Square Test result shows that both variables are independent on each other.

4. DISCUSSION

Abdel-Razek W *et al*, 2020, conducted a study at Tropical Medicine Department, of National Hepatology & Tropical Medicine Research Institute in Cairo, Egypt. The aim of the study was to assess and compare PEG-IFN α 2a with PEG-IFN α 2b in Optimizing the management for those patients who have Hepatitis C Virus genotype 4. This study was published in Clinical Liver Disease. The study concluded that an increased SVR results were observed in a large proportion of patients with Hepatitis C Virus with Pegylated interferon. The researchers has observed that the two forms of PEG-IFN have been proved to be a key element in creating a competition resulting in lower prices. Thus, a careful analysis must be made when trying to decide which PEG-IFN provides best results, and in our opinion, the debate is still ongoing to manage the HCV patient in a better way so that the patient get maximum efficacy, less toxicity and it must be cost effective or available in reasonable price [18]. Our study providing insight that sofosbuvir is best choice to treat patients who are suffering from chronic as well as acute hepatitis C has better patients acceptability for infections of hepatitis C plus hepatitis b, because in the current study which compared interferon and sofosbuvir, it was observed that sofosbuvir got more compliance among study subjects than interferon with less adverse drug reactions were reported with sofosbuvir as compared with interferon. Vincent Leroy et al, 2016, conducted a study to assess the response of oral anti viral agents such as daclatasvir along with sofosbuvir and ribavirin, they concluded that the oral antivirals were well tolerated and their

Table 13. Study subjects who were non-compliant with sofosbuvir due to ADRS

Noncompliant factor	Frequency	Percent
Adverse drug reaction	12	12.1
Others	45	78.9
Total	57	100.0

Table 14. Non compliance with sofosbuvir due to prolong duration of therapy

Noncompliant factor	Frequency	Percent
Prolong duration of therapy	24	42.1
Others	33	57.9
Total	57	100.0

Table 15. Comparison of compliance between sofosbuvir and interferon

Name of drug	Compliance frequency	Compliance Percent	Noncompliance frequency	Noncompliance Percent	Total
Sofosbuvir	93	62	57	38	150
Interferon	25	16.7	125	83.3	150
Grand total				100.0	300

Chi-Square Tests

Table 16. Statistical analysis of compliance with gender (interferon)

	Value	Df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	3.647[a]	1	.056		
Continuity Correction[b]	2.824	1	.093		
Likelihood Ratio	3.511	1	.061		
Fisher's Exact Test				.068	.048
N of Valid Cases	150				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 8.83.
b. Computed only for a 2x2 table

Chi-Square Tests

Table 37. Statistical analysis of compliance versus gender with sofosbuvir

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.537[a]	1	.464		
Continuity Correction[b]	.312	1	.576		
Likelihood Ratio	.535	1	.465		
Fisher's Exact Test				.489	.287
N of Valid Cases	150				

0 cells (0.0%) have expected count less than 5. The minimum expected count is 20.90. b. Computed only for a 2x2 table

results in high and similar SVR12 after giving regimen for 12 or 16 weeks of treatment among genotype 3-infected patients along with advanced liver disease [19]. There study is similar to current study because current study also proves that the sofosbuvir is well tolerated their compliance rate is more than interferons and less adverse drug effects reported with sofosbuvir hence it could be safe as well.

Surakit Pungpapong et al, 2015, a multicenter study for the assessment of effectiveness, tolerance and safety profile of Sofosbuvir was conducted along with or without ribavirin in the management of hepatitis C genotype 1 virus, after liver transplantation, they summarized their findings which was conducted on multiple centers as all-oral without interferon or interferon free antiviral regimen using simeprevir and sofosbuvir along with or without RBV for 12 weeks. They were very well tolerated and resulted in excellent SVR12 rates in LT recipients who were diagnosed with HCV genotype 1 infection [20]. As compared to above studies in the current study the safety and compliance of 300 patients were assessed and divided into two groups of 150 patients. Sofosbuvir is appears to be safe as compared to interferon and compliance rate of sofosbuvir was more than interferon. However, a more elaborate my study revealed the extent of the findings.

Younossi *et al* 2016, conducted a study to assess the adherence to treatment of chronic hepatitis c with different interferon and interferon free anti HCV regimen [21]. Their findings were similar with the current study because in that study patients who were on interferon therapy their adherence and compliance score was smaller as compared with sofosbuvir based therapy, similarly in current study rate of compliance was better achieved with sofosbuvir.

5. CONCLUSION

It was revealed that out of 300 study subjects, 100 patients were doing indoor job, 70 were outdoor job, 43 jobless and 86 house wives. Out of 300 patients, 280 patients were having hepatitis C virus infection only, 13 Hepatitis C+B and 7 have HCV+HIV. The compliance rate among study subjects was better with sofosbuvir i.e. 62% as compared to interferon alpha 2b where the rate of compliance among study subjects was only 16.7%. This study concluded that compliance rate of sofosbuvir was 45.3% more than interferon and 26% less adverse drug reaction reported with sofosbuvir, means sofosbuvir is safer than interferon.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors Have Declared That No Competing Interests Exist.

REFERENCES

1. Anthony SJ, St. Leger JA, Liang E, Hicks AL, Sanchez-Leon MD, Jain K, et al. Discovery of a Novel Hepatovirus (Phopivirus of Seals) Related to Human Hepatitis A Virus. mBio. 2015;6(4):e01180-15.
2. Antonello VS, Antonello ICF, Herrmann S, Tovo CV. Proteinuria is common among HIV patients: what are we missing? Clinics (Sao Paulo, Brazil). 2015;70(10):691–5.
3. Aqel BA, Pungpapong S, Leise M, Werner KT, Chervenak AE, Watt KD, Vargas HE. Multicenter experience using simeprevir and sofosbuvir with or without ribavirin to treat hepatitis C genotype 1 in patients with cirrhosis. Hepatology (Baltimore, Md.). 2015;62(4):1004–12.
4. Edlin BR, Eckhardt BJ, Shu MA, et al. Toward a more accurate estimate of the prevalence of hepatitis C in the United States. Hepatology. 2015;62:1353–1363.
5. Ly KN, Hughes EM, Jiles RB, et al. Rising mortality associated with Hepatitis C Virus in the United States, 2003–2013. Clin Infect Dis. 2016;62:1287–1288.
6. Aspinall E, Fraser A, Goldberg D, Hawkins G, Hutchinson S. Hepatitis B prevention, diagnosis, treatment and care: a review. Occupational Medicine. 2011;61(8):531–40.
7. Allen AM, Kim WR, Larson J, Loftus EV. Efficacy and safety of treatment of hepatitis C in patients with inflammatory bowel disease. Clinical Gastroenterology and

Hepatology : The Official Clinical Practice Journal of the American Gastroenterological Association. 2013;11 (12):1655–60.
8. Afdhal N, Reddy KR, Nelson DR, Lawitz E, Gordon SC, Schiff E, Kwo P. Ledipasvir and Sofosbuvir for Previously Treated HCV Genotype 1 Infection. New England Journal of Medicine. 2014;370(16):1483–1493.
9. Brillanti S, Garson J, Foli M, et al. A pilot study of combination therapy with ribavirin plus interferon alfa for interferon alfa-resistant chronic hepatitis C. Gastroe-nterology. 2016;107:812-817.
10. Chemello L, Cavalletto L, Bernardinello E, Guido M, Pontisso P, Alberti A. The effect of interferon alfa and ribavirin combination therapy in naive patients with chronic hepatitis C. J Hepatol. 2014;23 (2):8-12.
11. Davis GL, Lau JYN. Factors predictive of a beneficial response to therapy of hepatitis C. Hepatology. 2001;26(1):122-127.
12. Knodell RG, Ishak KG, Black WC, et al. Formulation and application of a numerical scoring system for assessing histological activity in asymptomatic chronic active hepatitis. Hepatology. 2015;1:431-435.
13. Bedossa P, Poynard T. An algorithm for the grading of activity in chronic hepatitis C: the METAVIR Cooperative Study Group. Hepatology. 2005;24:289-293.
14. Shindo M, Arai K, Sokawa Y, Okuno T. Hepatic hepatitis C virus RNA as a predictor of a long-term response to interferon-α therapy. Ann Intern Med. 2015;122:586-591.
15. Picciotti A, Brizzolara R, Campo N, et al. Two year interferon retreatment may induce a sustained response in relapsing patients with chronic hepatitis C. Hepatology. 1996;24(1):273.
16. Keeffe EB, Hollinger FB, Consensus Interferon Study Group. Therapy of hepatitis C: consensus interferon trials. Hepatology. 1997;26(1):101-07.
17. Le X, Zhou X, Dai X. Evaluation of interferon-α-2b for the treatment of relapsed hepatitis-C. Hepatology. 2008;24(l):536.
18. Abdel-Razek W, Hassany M, El-Sayed MH, et al. Hepatitis C Virus in Egypt: Interim Report From the World's Largest National Program. Clin Liver Dis (Hoboken). 2020;14(6):203-206.
19. Vincent Leroy, Peter Angus, Jean-Pierre Bronowicki, Gregory J. Dore, Christophe Hezode, Stephen Pianko, Stanislas Pol, Katherine Stuart, Edmund Tse, Fiona McPhee,.Daclatasvir, Sofosbuvir, and Ribavirin for Hepatitis C Virus Genotype 3 and Advanced Liver Disease: A Randomized Phase III Study (ALLY-31). Hepatology. 2016;63(5):2043-47.
20. Surakit Pungpapong, Bashar Aqel, Michael Leise, K. Tuesday Werner, Jennifer L. Murphy, Tanisha M. Henry, Kristen Ryland,.Multicenter experience using simeprevir and sofosbuvir with or without ribavirin to treat hepatitis C genotype 1 after liver transplant. Hepatology. 2015; 34:42-48.
21. Younossi ZM, Stepanova M, Henry L, Nader F, Younossi Y, Hunt S. Adherence to treatment of chronic hepatitis C: from interferon containing regimens to interferon and ribavirin free regimens. Medicine (Baltimore). 2016;95(28):e4151.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/66910