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Comparative Analysis of Adverse Drug Reactions between Interferon Alpha 2B and Sofosbuvir in the Treatment of Hepatits C at GIMHS, Sindh, Pakistan

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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 MM, ZA, TA, AA, MAA, SS and SAAS managed the analyses of the study and managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

A descriptive cross-sectional study was conducted on 300 patients selected by random sampling who were reported with Hepatitis-C at GIMHS. Questions were asked from patients regarding symptoms and adverse drug reactions (ADR'S). Results were analyzed by using SPSS-22. Out of total patients (n=300) the frequency of male gender was (n=192) as compared to females (n=108). Among 300 patients some patients were on sofosbuvir (n=150), patients on interferon (n=150). Rate of ADR'S observed with interferon as fever (n=28), anemia (n=27), hair loss (n=21), headache (n=19), insomnia (n= 11), nausea (n=13), depression (n=14, 09), malaise (n=25), vomiting (n=06), ulcer (n=13), pain and redness at site of injection (n=17). While rate of ADR'S in patients who were on sofosbuvir, fever (n=33), chill (n=17), nausea (n=28), anemia (n=06), headache (n=14), insomnia (n=13), loss of appetite (n=5), diarrhea (n=1). This study concluded that as compared to Interferon, rate of ADR'S were less with Sofosbuvir.

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Keywords: Hepatitis; interferon; sofosbuvir; compliance.

1. INTRODUCTION

When the inflammation of the liver occurs due to the Hepatitis C Virus (HCV), family Flavivirdae then the condition is known as hepatitis C. It may be mild, moderate or severe. Its cure may require few days, few weeks, few months, or even years are required to cure it [1,2]. The causative agent of this disease is present in the blood of a hepatitis c +ve patients, so if a normal healthy person is exposed even to a small quantity of that blood then the virus may be transferred to healthy person where it grow and multiply and causes infection [3,4]. Sofosbuvir is the drug which is used in the management of hepatitis C virus either alone or some other drugs may be added [5,6]. Sofosbuvir acting on the virus directly, therefore this drug is also called as directly acting antiviral drug. These type of drugs are the group of medications which shows their effects by making the virus to be unable to multiply and to produce its offspring. Sofosbuvir effects on nucleotide polymerase (genetic material of the virus), therefore by affecting on it the virus becomes unable to grow and multiply, to produce new baby viruses, so by doing this they kill the viruses and cure a patient from disease. If the cured person again exposed to such virus then he will again need the treatment [7-9]. The recommended dose of sofosbuvir for healthy individual is 400mg once a day, for 12 weeks in some cases given for 16 or upto 24 weeks for better results it should be given along with ribavirin [10]. When sofosbuvir is prescribe along with ribavirin, then most common side effects of this combination may include: Trouble resting, Exhaustion, Migraine, Deficiency of platelets, Deficiency of RBCs, Decreased in the WBC count, Feeling discomfort [11]. Interferon alfa-2b infusion is utilized to treat hepatitis B and C, lymphoma (lymph hub tumor), harmful melanoma (skin malignancy), genital warts, bushy cell leukemia (platelet malignancy), and Kaposi sarcoma (AIDS-related tumor). Interferons are substances created by cells in the body to help battle contaminations and tumors. Interferon alfa-2b is an engineered (man-made) adaptation of these substances [12,13]. The correct instrument of activity is obscure. Intron A has been appeared to have intracellular, antiviral immunomodulatory, and antiproliferative impacts, in-vitro and in-vivo. These incorporate consequences for intracellular oncogene articulation, incitement of common executioner and cytotoxic T-cells, microphage initiation, and acceptance of cytokine generation. Antiproliferative impacts indicated incorporate moderating of cell division and inversion of tumor cells to a typical phenotype [14,15]. Side effects may include diminished white platelet checks, fever, myalgia, anorexia, heaving /queasiness, expanded liver protein level, cerebral pain, chills, and sorrow. Symptoms were normal and controllable through dosage alterations [16]. The suggested dosage of interferon alpha 2 b for the management of unending hepatitis C is 3 million IU three times in a week, directed subcutaneously for 12 weeks is some cases it is given for 24 or up to 36 weeks. In patients enduring treatment with standardization of ALT at four months of treatment, Interferon treatment ought to be stretched out to 18 to two years (72 to 96 weeks) at 3 million IU administered subcutaneously for three times in a week to enhance the maintained reaction rate. Patients who don't standardize their ALTs or have perseveringly elevated amounts of HCV RNA following four months of treatment once in a while accomplish a managed reaction with augmentation of treatment. Thought ought to be given to suspending these patients from treatment [17].

2. MATERIALS AND METHODS

2.1 Study Design

A descriptive hospital based study was conducted by collecting the patient's feedback on predesigned questionnaire. Management of Hepatitis C was assessed clinically through a series of questions were asked from patients. The rate of ADRs with sofosbuvir and interferon were observed. Data were analyzed using SPSS version 23.

2.2 Sampling

A total of 300 patients were involved in the study, which were diagnosed with hepatitis C and co infections. via random sampling. Out of 300 patients 150 patients were received Interferon α 2b 3 million IU three times in a week, subcutaneously, while 150 patients were given Sofosbuvir 400mg once daily.

3. RESULTS

In Table 1, age of patients were discussed, according to age of patients, patients were divided in four groups.

Table 1. Distribution of age among study subjects

Age groups	Frequency	Percent
25-35 years	81	27.0
36-45 years	124	41.5
46-55 years	70	23.4
56-65 years	25	8.1
Total	300	100

In Table 2, gender of patients were described which shows that out of 300 patients 192 (64%) were male whereas 108 (36%) were females. In this majority of study subjects were male.

In Table 3, locality of patients was described, which shows that out of 300 patients 171 (57%) were belongs to rural areas and 129 (43%) were from urban areas. In this study majority of patients were belong to rural areas.

In Table 4, distribution of hepatitis c patients were described, which shows that out of 300 study subjects 281 (93.7%) study subjects were suffering from hepatitis c only.

In Table 5, description of co infected study subjects having hepatitis c along with hepatitis b was given, which shows that 13(4.3%) study subjects were suffering from co infection of hepatitis c and hepatitis b.

In Table 6, the description of co infected study subjects who were suffering from hepatitis c along with HIV were given, which shows that 7 (2.3%) study subjects were suffering from co infection of HCV + HIV.

In Table 7, 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 8, Adverse drug reactions which were reported among study subjects who were on interferon was described, which shows that out of 150 study subjects who were on interferon adverse drug reaction were reported in 129 (86%) patients whereas adverse drug reaction were not reported in 21 (14%) study subjects. In this study ADRS were reported in majority of patients.

In Table 9, types of adverse drug reactions among study subjects who were on interferon were described which shows that out of 150 study subjects, mild ADRS were reported in 58(38.7%) study subjects, moderate ADRS were reported in 71(47.3%) study subjects, no any sever ADR was reported. In this study moderate ADRs were reported in study subjects.

In Table 10, types of adverse drug reactions among study subjects who were on interferon were described which shows that out of 150 study subjects, mild ADRS were reported in 58(38.7%) study subjects, moderate ADRS were reported in 71(47.3%) study subjects, no any sever ADR was reported. In this study moderate ADRs were reported in study subjects.

In Table 11, comparison of adverse drug reaction between sofosbuvir and interferon was described. In this study, more adverse drug reactions were reported with interferon as compared to sofosbuvir.

Table 2. Distribution of gender among study subjects

Gender	Frequency	Percent
Male	192	64.0
Female	108	36.0
Total	300	100.0

Table 3. Locality wise distribution study subjects

Location	Frequency	Percent
Rural	171	57.0
Urban	129	43.0
Total	300	100.0

Table 4. Distribution of Hepatitis C study subjects

Hepatitis C	Frequency	Percent
Hepatitis C Patients	281	93.7
Hepatitis C+ Coinfection	19	6.3
Total	300	100.0

Table 5. Distribution of Co-infection of HCV + HBV

Hepatitis C + Hepatitis B	Frequency	Percent
HCV+HBV Patients	13	4.3
Others	287	95.7
Total	300	100.0

Table 6. Distribution of Co-infection of HCV + HIV

Hepatitis C + HIV	Frequency	Percent
Hepatitis C + HIV patients	7	2.3
Others	293	97.7
Total	300	100.0

Table 7. Management of hepatitis C study subjects

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

Table 8. Adverse drug reactions reported with interferon

Adverse drug reaction	Frequency	Percent
Reported	129	86.0
Not reported	21	14.0
Total	150	100.0

Table 9. Types of Adverse drug reactions reported with interferon

S.No	Name of Adverse Drug Reaction	Frequency	Percentage
1	Anemia	24	18.6%
2	Fever	27	21%
3	Headache	17	13.1%
4	Insomnia	06	4.6%
5	Hair loss	14	10.8%
6	Nausea	12	9.3%
7	Vomiting	08	6.2%
8	Ulcer	03	2.3%
9	Depression	04	3.1%
10	Malaise	09	6.9%
11	Pain and redness at site of injection	05	3.8%
Total		129	100%

In Table 12, Statistical analysis on compliance with gender of those patients who were on interferon was done. On applying Chi-Square Test, result shows that both variables are independent on each other.

In Table 13, statistical analysis of adverse drug reaction reported with interferon versus gender was done. On applying Chi-Square Test result shows that both variables are independent on each other.

In Table 14, statistical analysis of adverse drug reactions versus age among study subjects who were on sofosbuvir was done. On applying Chi-Square Test result shows that both variables are independent on each other.

In Table 15, statistical analysis of adverse drug reactions 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

Hepatitis C is a burning issue in Pakistan. It was surveyed in 2017 that approximately 15 million of Pakistani peoples are suffering from hepatitis C and hepatitis B.

An observational study was conducted in Peshawar during 2001 to 2004 to assess the effects in chronic hepatitis C patients which were managed by interferon + ribavirin, in patients the common side effects 92.5% (n=370) in hematological , 91% (n=364) in flu like symptoms, 88.5% (n=354) in gastrointestinal, 81.5% (n=326) in dermatological, 71.25%(n=285) in neuropsychiatric, 14% (n=57) in respiratory symptoms, 4% (n=16) in thyroid function abnormalities, 1% (n=4) in major depression and 0.5% (n=2) in suicide attempts and moderate and mild side effects were also observed. The severe adverse effects were noted in 50 (12.5%) patients after reduction/ withdrawal in dose or treatment. He summarized that combination therapy is harmful in the Hepatitis C treatment. The side effects mostly were attributed to interferon and several to ribavirin [18].Compared with our study some side effects were similar such as hematological side effects, gastrointestinal effects and depression. Vincent Leroy et al, 2016, conducted a study to assess the response of oral anti viral agents such as daclatasavir along with sofosbuvir and ribavirin, they concluded that the oral anti virals were well tolerated and their 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]. This 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 safe as well.

Table 10. Types of Adverse drug reactions reported with sofosbuvir

S.No	Name of ADR	Frequency	Percentage
1	Chill	05	8.5%
2	Fever	04	6.7%
3	Nausea	22	37.3%
4	Headache	12	20.3%
5	Anemia	4	6.7%
6	Insomnia	5	8.5%
7	Loss of appetite	4	6.7%
8	Diarrhea	3	5.0%
Total		59	100%

Table 11. Comparison of ADRS between sofosbuvir and interferon

Name of drug	ADRS Reported frequency	ADRS Reported percent	Without ADRS Frequency	Without ADRS Percent	Total
Sofosbuvir	91	60.2	59	39.3	150
Interferon	129	86	21	14	150
Grand total				100.0	300

Table 12. Statistical analysis on compliance with gender

Chi-Square Tests			
	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	11.453[a]	3	.010
Likelihood Ratio	11.757	3	.008
N of Valid Cases	150		

a. 2 cells (25.0%) have expected count less than 5. The minimum expected count is .84.

Table 13. Statistical analysis of ADRs with gender on study subjects who were on Interferon

Chi-Square Tests					
	Value	**Df**	**Asymp. Sig. (2-sided)**	**Exact Sig. (2-sided)**	**Exact Sig. (1-sided)**
Pearson Chi-Square	1.419[a]	1	.234		
Continuity Correction[b]	.893	1	.345		
Likelihood Ratio	1.497	1	.221		
Fisher's Exact Test				.326	.173
N of Valid Cases	150				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 7.42; b. Computed only for a 2x2 table

Table 14. Statistical analysis of ADRs versus age among study subjects who were on sofosbuvir

Chi-Square Tests			
	Value	**Df**	**Asymp. Sig. (2-sided)**
Pearson Chi-Square	5.621[a]	3	.132
Likelihood Ratio	5.775	3	.123
N of Valid Cases	150		

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 7.47.

Table 15. Statistical analysis of ADRs versus gender among study subjects who were on sofosbuvir

Chi-Square Tests					
	Value	**Df**	**Asymp. Sig. (2-sided)**	**Exact Sig. (2-sided)**	**Exact Sig. (1-sided)**
Pearson Chi-Square	.834[a]	1	.361		
Continuity Correction[b]	.548	1	.459		
Likelihood Ratio	.841	1	.359		
Fisher's Exact Test				.390	.230
N of Valid Cases	150				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 21.63; b. Computed only for a 2x2 table

Naglaa F. A. Youssef et al, 2017, a prospective observational study was conducted in Egypt, the aim of the study was to assess the quality of life in patients who were diagnosed with chronic hepatitis C while receiving Sofosbuvir-based regimen, along with interferon and without Interferon, that was published in journal of BMC Gastroenterology, according to their assessment it was found a significant change in Health Related Quality of Life of those reported patients who were on drugs that have direct effect on virus. Health related quality of life were measure during 3 different time intervals. It was observed that, depression was the main factor that may change the Health Related Quality of Life prior to therapy [20]. As compared with our study in which sofosbuvir directly compared with interferon in the management of hepatitis c, compliance and adverse drug reaction were measured, it was observed that depression was reported only in those patients who were on interferon, it means that health related quality of life is better with sofosbuvir as compared to interferons. Peter J.Ruane et al, 2015, assessed the safety and efficacy of sofosbuvir which is a polymerase inhibitor along with ribavirin in an open labeled study which was carried out in Egypt on those patients who were diagnosed with genotype4 of hepatitis virus. Two groups of 30 patients were made, one group comprises of naïve patients and other group comprises of previously treated patients, 12 weeks and 24 weeks treatment were given to them, among reported patients, diabetic patients were of 38%, and cirrhotic patients were of 23%, whereas among naïve treated patients 14% were of interferon ineligible patients, among previously treated patients 63% were experienced non respondent, SVR was achieved by 68% in 12 weeks group and 93% of patients in 24 weeks group. The common ADRs observed during study were pain in head, loss of sleep, tiredness, no any reported patient had discontinue his or her treatment due to experience of ADRs.

Therefore on basis of above mentioned findings study concludes that in 24 weeks treatment sofosbuvir along with ribavirin were efficacious and safer against genotype4 virus [21]. 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 genotype1virus, after transplantation of liver patients, they summarized their study 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 was very well tolerated and resulted in excellent SVR12 rates in LT recipients who were diagnosed with HCV genotype 1 infection [22]. As compared to above studies in current study the safety of 300 patients were assessed, all the 300 study subjects were divided into two groups of 150 patients. In current study sofosbuvir is proved to be safe as compared to interferon.

5. CONCLUSION

It was concluded that out of 300 study subjects, 192 patients were male and 108 were females. Mostly reported patient were aged from 36-45 years. 171 reported patient belongs to a rural area where as 129 patients were from urban areas. Out of 300 patients, 281 patients were having an only hepatitis C, 13 Hepatitis C+B, 7 have HCV+HIV. It was concluded that majority of Adverse drug reaction were reported with interferon i.e. 86%, as compared to sofosbuvir where only 60% adverse drug reaction were reported. This study concluded that 26% less adverse drug reaction reported with Sofosbuvir.

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.

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