ORIGINAL ARTICLE

Use of Antiviral Therapy in Patients with Chronic Hepatitis C and its Adverse Effects

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ABSTRACT

Aim: To govern the importance of rapid virological response in predicting adverse side effects in the in patients with chronic hepatitis C treated with sofosbuvir and ribavirin and to determine the importance of antiviral therapy.
Study Design: A Prospective cohort study.
Place and Duration: Gastroenterology Department of Services Hospital Lahore from March 2019 to March 2020.
Methodology: All the cases of chronic hepatitis C treated with sofosbuvir and ribavirin for 24 week were clinically evaluated. The treatment response was inveterate after four and twenty four weeks of treatment called Rapid Virological response (RVR) and also evaluated for End Treatment Response (ETR), respectively. Adverse reactions of treatment was observed every one month for a full 24-week treatment. The main features of the population were observed. A new inception or deteriorating of existing anemia is considered significant while fatigue, headache, coughing, insomnia and itching during treatment was also observed. RVR deficiency was confirmed by statistical dependence on side effects of treatment using SPSS version 20.0.
Results: 52% of 100 patients were women and 48% were men. The patient's age is 45.68 ± 10.71 years to 22 to 70 years old. RVR was 91% (91out of 100) while ETR was 95% (95 out of 100). The baseline anemia was noted in 38% of patients and there was no anemia among 62% of people. The 66% of patients were observed with new onset and worsening of anemia. Other side effects developed during therapy, headache (39%), fatigue (56%), insomnia (14%), itching (5%) and cough (23%). There was a statistically significant relationship with RVR deficiency and headache ($p = 0.002$), fatigue ($p = 0.037$), coughing. ($p = 0.000$) and insomnia ($p = 0.021$).
Conclusion: Response of patients with chronic hepatitis C to sofosbuvir and ribavirin is remarkable in the population of Pakistan. The deficiency of RVR after treatment for four weeks predicts the common adverse effects during entire 24 weeks of treatment.
Keywords: Sofosbuvir, hepatitis C, Ribavirin, rapid virological response, adverse reactions.

INTRODUCTION

Hepatitis C virus (HCV) affects nearly 3-13% of populace in Pakistan. Sofosbuvir plus ribavirin is an excellent treatment option with a higher response rate and low negative effects compared to the popular interferon therapy[1-3]. The interval of ribavirin and sofosbuvir therapy is 24 weeks and the treatment response is determined using real time HCV-RNA polymerase chain reaction (PCR) test[4-5]. At week 4 of treatment; negative HCV-RNA PCR test is indicative of Rapid Virological Response (RVR). The most common side effects seen in the treatment of ribavirin and sofosbuvir (above 20%) are fatigue and headache. Other side effects include anemia, insomnia, itching and dryness[6-8]. If the patient is not being treated, why should he be suffered from side effects of treatment? This question convinced the authors to look for any relationship between the responses of treatment to its adverse effects[9-10]. This study aim was to determine the role of virological response in predicting side effects of sofosbuvir and ribavirin hepatitis C treatment and to determine the importance of antiviral therapy.

MATERIALS AND METHOD

This was a prospective cohort study conducted at the Gastroenterology Department of Services Hospital Lahore for one year duration from March 2019 to March 2020. A total of 110 patients with chronic hepatitis C aged 5 years and older were registered with positive HCV RNA. Exclusion criteria were patients with decompensated liver disease and >12 child pug score, pregnancy, HIV and / or HBV infection, and renal failure with creatinine clearance <50 ml / minute.

Patients selected for the study were treated with a combination of ribavirin and sofosbuvir for 24 weeks. While sofosbuvir is directed at a dosage of 400 mg daily, ribavirin is administered in divided doses of 1000 mg for patients whose weight was less than 70 kg and in divided doses of 1200 mg for subjects having weight above 70 kg.

During the full 24-week treatment, side effects of sofosbuvir and ribavirin therapy such as anemia, fatigue, headache, cough, insomnia and itching were observed every 4 weeks. The main features of the population have been registered. While new onset or worsening is considered important for fatigue, anemia, cough, headache, insomnia and pruritus have also been observed during treatment. Biochemical and hematological tests were performed every 4 weeks for a full 24-week treatment, and serum HCV-RNA tests were performed 4 weeks later and at the end of treatment, respectively, to detect RVR and ETR. When interpreting the data, anemia was distinct as hemoglobin (Hb) below 13.5 g / dl for males and below 12 g / dl for females. While the descriptive analysis of the collected data is done using SPSS version 20.0. The qualitative variables are gender, age groups, RVR, ETR, anemia, fatigue, headache, cough, pruritus and insomnia while the quantitative variable was age only. Research data were interpreted as negative or positive values. The standard deviations and mean for quantitative variables, percentages and frequencies for qualitative variables were calculated. The Chi-square test was used to find a

relationship of factors with a significance level of 5%. Odd ratio with confidence interval (CI) of 95% was also determined for each association.

RESULTS

In total, 110 cases were recorded and treated with sofosbuvir and ribavirin for 24 weeks. 58 cases (53%) were females and 52 (47%) are males. The patients mean age was 45.68 ± 10.71 years. RVR was observed in 98 (89%) and ETR in 102 (93%) of 110 cases. At the commencement of the study, 35% of patients had anemia and 65% had no anemia. 66% of patients developed new or worsening anemia during treatment. Additional adverse effects developed during treatment were headache (43%), fatigue (56%), insomnia (15%), cough (26%) and six percent cases have pruritus. All these side effects are mild and easy to control. Due to serious side effects, none of these patients were excluded from the study (Table 1).

In terms of side effects such as anemia, fatigue, headache, coughing, pruritus and insomnia, two groups of patients were compared (compared with those who achieved RVR and those who could not achieve RVR). Amongst patients who did not attain RVR, 81.8% (8 out of 9) agonized fatigue, 72.7% (8 out of 9) headache, 81.8% (8 out of 9) cough & 45.4% (4 out of 9) suffered insomnia. His association with RVR deficiency was statistically significant at 0.037, 0.002, 0.000 and 0.021 p, respectively. However, the relationship between RVR deficiency and pruritus and anemia was not statistically significant (Table 2).

Table 1: Frequency distribution of qualitative variables (n = 110)

Factors	Category	Frequency	%age
Gender	Male	52	47
	Female	58	53
Age	<45	44	40
	≥45	66	60
RVR	Achieved	98	89
	Not-achieved	12	11
ETR	Achieved	102	93
	Not-achieved	8	7
Anemia (new onset+worsening)	Yes	72	65
	No	38	35
Fatigue	Yes	62	56
	No	48	44
Headache	Yes	43	39
	No	67	61
Cough	Yes	26	24
	No	84	76
Insomnia	Yes	16	15
	No	94	85
Pruritus	Yes	7	6
	No	103	94

Table 2: Statistical correlation between Adverse Effects of Sofosbuvir plus Ribavirin Therapy & RVR (achieved/ not-achieved) (n = 110)

Adverse Effects/Categories		RVR		p-value	Odd ratio with 95% Confidence interval
		Achieved	Not-achieved		
Anemia:	Yes	62 (56.36%)	9 (81.8%)	0.162	0.220 (0.026-1.835)
	No	37 (33.63%)	2 (18%)		
Fatigue:	Yes	53 (48.18%)	9 (81.8%)	0.039	0.410 (0.017-1.162)
	No	47 (42.72%)	1 (10.90%)		
Headache:	Yes	34 (30.9%)	8 (72.7%)	0.005	0.065 (0.008-0.540)
	No	66 (60%)	2 (18.1%)		
Cough:	Yes	18 (16.36%)	9 (81.8%)	0	0.025 (0.003-0.212)
	No	81 (73.63%)	2 (18.1%)		
Insomnia:	Yes	12 (10.9%)	5 (45.4%)	0.023	0.154 (0.035-0.671)
	No	87 (79.09%)	6 (54.5%)		
Pruritus:	Yes	6 (5.45%)	2 (18.1%)	0.386	0.368 (0.037-3.698)
	No	93 (84.54%)	9 (81.8%)		

DISCUSSION

Known side effects of sofosbuvir and ribavirin treatment include headache, fatigue, itching, and insomnia. Cough and anemia with a frequency of 30%, 30%, 27%, 11%, 10% and 6%. However, the most common side effect in our study is anemia in 66% of patients and itching occurs less frequently (5%) [10-11]. This may indicate that further research is needed to see the various negative effects in our society.

International data show that patients receiving sofosbuvir-ribavirin due to discomfort and headache only 1% discontinuation of treatment due to adverse events[12-13]. However, in our study, patient supervision was 100% and all adverse effects were mild and easy to control.

Available data does not show an early assessment of negative effects using existing tools; However, our study shows that RVR deficiency makes the patient vulnerable to most of the negative effects of treatment, such as fatigue, headache, cough and insomnia. In contrast, the effectiveness of the treatment also guaranteed fewer side effects. Possible hypothetical reasons for this difference; bias, drug pharmacokinetics, genetic differences in patients, and pre-existing comorbidities[12-14]. Further studies should be carried out to confirm this benefit of the RVR test in patients with hepatitis C treated with sofosbuvir-ribavirin. Local officials are also advised to review our employees' suggestions based on local data. Other studies may help solve the problem[15].

CONCLUSION

The clinical response was very positive among Pakistani population and side effects of sofosbuvir and ribavirin in our population were mild and easy to control, and compliance was 100%. Anemia was the most common side effect followed by fatigue, headache, coughing, insomnia and itching in the patients studied. RVR deficiency predicts the onset of the most adverse effects of treatment within 24 weeks of treatment.

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