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STUDY TO KNOW THE ADVERSE EFFECTS OF RIBAVIRIN AND SOFOSBUVIR USED FOR TREATMENT OF CHRONIC HEPATITIS C PATIENTS AND ITS CORRELATION TO RAPID VIROLOGICAL RESPONSE

[1]Dr.Fatima munir, [2]Dr.Madiha Waseem, [3]Dr.Muhammad Umair Mazhar

[1]Women Medical Officer Anesthesia uni 1 mayo Hospital, Lahore

[2]Quaid E Azam Medical College, Bahawalpur

[3]King Edward Medical University, Lahore

Abstract:

Objective: *To determine the role of rapid virologic response with chronic hepatitis C patients anticipating the adverse effects of Sofosbuvir and ribavirin treatment.*

Study design: *A prospective cohort study.*

Place and duration of work: *In the Gastroenterology department of Nishter Hospital, Multan for the period of one year from November 2016 to November.*

Methodology: *Patients with chronic hepatitis C were treated with Sofosbuvir plus ribavirin for 24 weeks. The response to treatment was confirmed after 4 and 24 weeks of treatment known as rapid virological response (RVR) and treatment final response (ETR). The adverse effects of treatment were observed at every 4 weeks visit at 24 weeks of treatment. The starting characteristics of the population are noted. For anemia, fatigue, headache, cough, insomnia and pruritus have been reported during treatment, when a new onset or worsening of the current anemia is considered significant. The statistical relationship with the side effects of therapy of RVR deficiency was confirmed by SPSS 15.*

Findings: *In total, 52% of 100 patients were female and 48% were male. The age of the patients ranged from 22 to 70 and ranged from 45.68 ± 10.71 years. The RVR was 91% (91/100) while the ETR was 95% (100/100). At the beginning of the study, 38% of the patients had anemia and 62% had no anemia. During therapy, a new onset or anemia worsens in 66% of patients. Other adverse effects during treatment were fatigue (56%), headache (39%), cough (23%), insomnia (14%) and pruritus (5%). There was a statistically significant relationship between RVR deficiency, p = 0.037 fatigue, headache (.002 P), cough with P=0 and insomnia (p = 0.021).*

Conclusion: *The response of chronic hepatitis C patients to Sofosbuvir plus Ribavirin treatment in the Pakistani population is striking. RVR deficiency at 4 weeks of treatment predicts the onset of the majority of the adverse effects of treatment for the full 24 weeks.*

Key words: *Hepatitis C, Sofosbuvir, Ribavirin, Negative effects, fast virological response.*

Corresponding author:

Dr.Fatima munir,

Women Medical Officer,
Anesthesia uni 1 mayo Hospital,
Lahore

QR code

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INTRODUCTION:

Hepatitis C virus (HCV) is an important health problem affecting 3 to 13% of the population in Pakistan. Sofosbuvir plus ribavirin is an excellent treatment option with a higher response rate and lower efficacy. Adverse effects compared to previous popular interferon treatments. The duration of treatment with Sofosbuvir plus ribavirin was 24 weeks5 and the response of the treatment was confirmed by real-time HCV RNA polymerase chain reaction test. A negative HCV RNA PCR test after 4 Week Treatment is considered as Rapid virologic response (RVR). The most common side effects (≥20%) with Sofosbuvir plus ribavirin treatment are fatigue and headache. Other adverse effects include anemia, insomnia, pruritus and dry cough. Some are treated with treatment, suffer from the negative effects of this treatment? This question convinced the authors to seek any relationship between their responses to the side effects of the treatment. The purpose of the study was to know the rapid virologic response in chronic hepatitis C patients, anticipating the adverse effects of sofosbuvir and ribavirin treatment.

METHODOLOGY:

This is a prospective cohort study carried out in the Gastroenterology department of Nishter Hospital, Multan for the period of one year from November 2016 to November.

100 chronic hepatitis C patients were treated with sofosbuvir and ribavirin for twenty four weeks . Exclusion criteria are creatinine clearance <50 ml / min with decompensated child boxer> 12 liver disease, pregnancy, HIV coinfection and / or HBV and renal dysfunction. Registered patients were treated with a combination of sofosbuvir and ribavirin for 24 weeks. While Sofosuvir was administered at a daily dose of 400 mg, ribavirin received 70 mg for patients who weighed more than 70 kg and 1000 mg for split doses. anemia, fatigue, headache, cough, insomnia and itching. Side effects of treatment with ribavirin sofosbuvir were observed every 4 visits per week for 24 full weeks of treatment. The starting characteristics of the population are noted. For anemia, fatigue, headache, cough, insomnia and pruritus have been reported during treatment, when a new onset or worsening of the current anemia is considered significant. Biochemical and hematologic testing was performed every 4 weeks for full 24-week treatment tests, and serum HCV RNA testing was performed at week 4 at the end of treatment for RVR and ETR, respectively. Descriptive analysis of anemia collected data was performed using SPSS. The age defined for men as at least 12.7 g / dL and at least twelve gram / dL for hemoglobin (Hb) was only quantitative variable for women.10 Gender, age groups, RVR , ETR, anemia, fatigue, headache, cough, insomnia and pruritus were qualitative variables. Research data are interpreted as negative or positive values. For quantitative variables and frequencies standard deviations and Averages were calculated and for qualitative variables percentages were calculated. To find the association of the factors at the 5% significance level Chi-square test was used. An odd ratio was calculated for each relationship with a 95% confidence interval (CI).

RESULTS:

A total of 100 cases were treated with sofosbuvir and ribavirin for 24 hours and treated. Forty-eight cases (48%) were male and 52 (52%) were female. The mean age of the patients was 45.68 ± 10.71. ETR was seen in 91 (91%) and 95 (95%) of 100 cases. At the beginning of the study, 38% of the patients had anemia and 62% had no anemia. During treatment, 66% of patients had a new onset or worsening anemia. Other adverse effects. During treatment, fatigue (56%), headache (39%), cough (23%), insomnia (14%) and pruritus (5%) were common. All these adverse effects are of light intensity and can be managed easily. There were no significant side effects and none of these patients stopped working (Table 1).

Table 1: *Frequency distribution of qualitative variables (n = 100).*

Factors	Category	Frequency	Percentage
Gender	Male Female	48 52	48.0 52.0
Age	<45 ≥45	40 60	40.0 60.0
RVR	Achieved Not-achieved	91 09	91.0 09.0
ETR	Achieved Not-achieved	95 05	95.0 05.0
Anemia (new onset + worsening)	Yes No	66 34	66.0 34.0
Fatigue	Yes No	56 44	56.0 44.0
Headache	Yes No	39 61	39.0 61.0
Cough	Yes No	23 77	23.0 77.0
Insomnia	Yes No	14 86	14.0 86.0
Pruritis	Yes No	5 95	5.0 95.0

RVR = Rapid Virological response; ETR= End Treatment Response

Two groups of patients (who obtained RVR versus those who could not reach RVR) were compared in terms of side effects such as anesthesia, fatigue, headache, cough, insomnia and pruritus. 88.9% (8 of 8 patients) had fatigue, 88.9% (9 of 9) had headache, 88.9% (9 of 8) had cough and 44.4%) They have had insomnia. Their association with RVR deficit was statistically significant with 0.037, 0.002, 0.000, and 0.021 p values, respectively. However, the association of RVR deficiency with anemia and pruritus was not statistically significant (Table 2).

Table 2: *Statistical correlation between Adverse Effects of Sofosbuvir plus Ribavirin Therapy & RVR (achieved/ not-achieved) (n = 100).*

Adverse Effects/Categories		RVR		p-value	Odd ratio with 95% Confidence interval
		Achieved	Not-achieved		
Anemia:	Yes No	58 (63.7%) 33 (36.3%)	8 (88.9%) 1 (11.1%)	0.161	0.220 (0.026-1.835)
Fatigue:	Yes No	48 (52.7%) 43 (47.3%)	8 (88.9%) 1 (11.1%)	0.037	0.410 (0.017-1.162)
Headache:	Yes No	31 (34.1%) 60 (65.9%)	8 (88.9%) 1 (11.1%)	0.002	0.065 (0.008-0.540)
Cough:	Yes No	15 (16.5%) 76 (83.5%)	8 (88.9%) 1 (11.1%)	0.000	0.025 (0.003-0.212)
Insomnia:	Yes No	10 (11.0%) 81 (89.0%)	4 (44.4%) 5 (55.6%)	0.021	0.154 (0.035-0.671)
Pruritus:	Yes No	04 (04.4%) 87 (95.6%)	1 (11.1%) 8 (88.9%)	0.382	0.368 (0.037-3.698)

RVR = Rapid Virological response

DISCUSSION:

Known side effects of treatment with Sofosuvir plus ribavirin are headache, fatigue, pruritus, insomnia, cough and anemia; 30%, 27%, 11%, 10% and 6%, respectively. The most common side effect in our study was anemia observed in 66% of patients and less frequent occurrence of pruritus (5%). This may indicate that greater work is needed to see the diversity of adverse effects in our population. International data suggests that cessation of adverse events is only 1% of patients on treatment with sofosbuvir-ribavirin due to weakness and headache. However, in our study the follow-up was 100% and all the negative effects could be managed lightly and easily. The present data are insufficient to provide early estimates of adverse effects through the use of available tools; However, our study suggests that the lack of RVR is prone to the adverse effects of treatment such as fatigue, headache, cough, and insomnia in the patient. On the contrary, the efficacy of the treatment is also guaranteed to be less adverse. Possible hypothetical reasons for this difference may be prejudice, pharmacokinetics of the drug, genetic differences of the patient, and pre-existing co-morbidities. Further studies should be conducted to confirm this benefit of RVR tests in patients with hepatitis C treated with Sofosuvur-ribavirin. Local authorities are also advised to re-examine our people's recommendations based on local evidence. Other work may make it easier to solve the problem.

CONCLUSION:

Adherence to treatment was 100% since the adverse effects of sofosbuvir plus ribavirin in our population were mild and easy to manage. Anemia is the most common side effect and this has been followed by fatigue, headache, cough, insomnia and pruritus. RVR deficiency predicts that most of the adverse effects of treatment will occur during the 24-week treatment period.

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