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ORIGINAL ARTICLE

The sofosbuvir plus ribavirin vs sofosbuvir plus daclatasvir in obtaining sustained viral response in chronic Hepatitis C.

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ABSTRACT… Objective: To compare the Sustained viral response (SVR) in patients who had taken Sofosbuvir plus Ribavirin for 24 weeks and Sofosbuvir plus Daclatasvir for 12 weeks to treat hepatitis C. **Study Design:** Randomized Control Trial. **Setting:** Medical Division of Mayo Hospital, Lahore. **Period:** One Year duration, 2021. **Material & Methods:** 130 patients of chronic Hepatitis C were divided into two categories based on whether they met the inclusion requirements. In Group A patients used sofosbuvir plus ribavirin for six months, whereas patients of Group B took sofosbuvir plus daclatasvir for 3 months. In order to determine SVR, PCR for HCV RNA Quantitative was done at week twelve after completion of the course. SPSS 23.0 was applied to enter and analyze the data. **Results:** All cases had an average age of 48.80 + 16.63 years, whereas it was 48.09 +16.43 years for group A and 49.51+ 16.92 years for groups B. In group A, there were 39 cases (60%) of men and 26 cases (40%) of women, while in group B, there were 34 instances (52.3% men and 31 cases (47.7% women). SVR was attained in 34 (52.34%) of group A participants and 54 (83.12%) of group B participants (p-value of 0.001). **Conclusion:** Sof+Dacla group had significantly high SVR than Sof+Riba group especially in non-cirrhotic and treatment-naïve individuals.

Key words: Daclatasvir, HCV, PCR, Ribavirin, Sustained Viral Response, Sofosbuvir.

INTRODUCTION

Viral hepatitis C infection is a serious global health problem, particularly in Asia, Africa, and other developing nations.[1] Hepatitis C prevalence rates in Pakistan range from 4.5% to 8%, ranking second in the world.[2] Hepato-cellular carcinoma (HCC), acute on chronic, or chronic carrier states of hepatitis can all result from HCV. There are six genotypes and numerous subtypes of the hepatitis C.[3] Genotype 3 infection is the most significant predictor of HCC in individuals with cirrhosis and HCV infection. People with chronic HCV genotype 3 cirrhosis had a 5 year HCC incidence rate of 34%, as opposed to 17% for those with other genotypes (P=0.013) in a French population.[4] The Hepatitis C virus is thought to be responsible for the bulk of HCC cases in Pakistan, where chronic liver disease is the outcome of more than half of all HCV infections. There is no HCV vaccine available right now.[5] Prior to the development of direct-acting antivirals (DAAs), the treatment for chronic HCV infection relied on interferon, but there has been a significant improvement in the ability to eradicate the virus with manageable side effects.[6]

Sofosbovir was used first time in humans in 2010. FDA approved combination of sofosbovir and ribavirin in 2013. Daclatasvir was approved by FDA in 2014 in Europe while in India and America in 2015.[7] When used in conjunction with ribavirin, all HCV genotypes can be successfully treated with the oral nucleotide analogue inhibitor sofosbuvir.[8] In a research, individuals with HCV genotype 3 achieved persistent viral response at a rate of 80% to 89%, demonstrating the effectiveness of sofosbuvir-based antiviral therapy.[9]

Patients who received Sofosbuvir and Daclatasvir for 12 weeks while being therapy naive and

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free of cirrhosis saw an SVR12 of 90% to 96%, according to David R. Nelson, et al.'s ALLY-3 phase III trial.[10] Hepatitis C treatment is currently progressing significantly worldwide because introduction of new antiviral drugs.[11] We aimed to assess the SVR in patients with chronic hepatitis C when treated with current regimens because government hospitals in Pakistan continue to use Sofosbuvir/Daclatasvir based antiviral therapy.

MATERIAL & METHODS

It was a randomized control experiment that lasted a year (2021), and it was conducted in the EMW of the Mayo Hospital Lahore after approval from ethical board.(G-2020/ERB/KEMU/525) Two groups of 130 chronic hepatitis C patients that met the inclusion criteria were created. Sofosbuvir and ribavirin were administered to patients in Group A for six months, while sofosbuvir and daclatasvir were administered for three months to those in Group B. The experiment included all patients who were between the ages of 18 and 75, had never received therapy, and had tested positive for HCV RNA for at least three months. Patients, positive for HBsAg or anti-HIVAb were not allowed to participate in the trial. SVR was determined by PCR for HCV RNA Quantitative at week 12 after the end of treatment. The data was entered using SPSS version 23.0, and it was then examined. Age was displayed as a mean + S.D. In terms of frequency and percentages, categorical characteristics including gender and sustained viral response rates were expressed. The chi-square test was utilized in order to compare the two groups. To take effect moderators such as age, gender, and length of hepatitis into consideration, stratification was adopted. Significant was defined as chi-square post-stratification with a p value of 0.05 or lower.

RESULTS

All cases had an average age of 48.80 + 16.63 years, compared to 48.09 + 16.4 years for group A and 49.51 + 16.92 years for group B. In group A, there were 39 cases (60%) of men and 26 cases (40%) of women, while in group B, there were 34 instances (52.3% men and 31 cases (47.7% women). (Table-I)

SVR was attained in 34 (52.34%) of group A participants and 54 (83.12%) of group B participants. With a p-value of 0.001, group B considerably outperformed group A in terms of SVR frequency. The incidence of SVR was higher in group B (79.2%) among adults aged 18 to 40 than in group A (48.3%), with a p-value < 0.05. In the age range of 41 to 75 years, group B had a greater SVR frequency (85.5%) than did group A (55.6%), with a p-value of less than 0.05. In instances involving men, group B had a higher frequency of SVR (88.2%) compared to group A (53.8%), with a p-value of less than 0.05. In cases involving females, group B had a higher prevalence of SVR (77.4%) than did group A (50%), with a p-value < 0.05. (Table-II)

	Groups		Total
	Group A	Group B	
Mean Age	48.09±16.43	49.51±16.92	48.80±16.63
Gender			
Men	39(60.0%)	34(52.3%)	73(56.2%)
Women	26(40.0%)	31(47.7%)	57(43.8%)

Table-I. Showing age and gender of both study groups

	SVR	Groups		P-Value
		Group A	Group B	
Total Patients	Yes	34(52.3%)	54(83.1%)	< 0.001
	No	31(47.7%)	11(16.9%)	
Age, years				
18-40	Yes	14(48.3%)	19(79.2%)	0.021
	No	15(51.7%)	5(20.8%)	
41-75	Yes	20(55.6%)	35(85.5%)	0.004
	No	16(44.4%)	6(14.6%)	
Gender				
Male	Yes	21(53.8%)	30(88.2%)	0.001
	No	18(46.2%)	4(11.8%)	
Female	Yes	13(50%)	24(77.4%)	0.031
	No	13(50%)	7(22.6%)	

Table-II. Showing achievement of SVR in both groups (age groups and gender)

DISCUSSION

Studies on the therapeutic outcomes of DAAs for hepatitis C demonstrate enhanced tolerance, increased survival, and fewer problems as compared to prior interferon therapy.[12] Efficacy and tolerability was found more in direct acting antiviral drugs such as Sofosbovir, Daclatasvir and ribavirin in patients with hepatitis C as compared to interferon therapy. In addition side effects of

DAAs were also less.[13]

In the current study, SVR was attained in 54 (83.1%) of group B and 34 (52.3%) of group A participants. With a p-value of 0.001, group B considerably outperformed group A in terms of SVR. The SVR12 rate of 205 patients in another trial was 88.0%, and the following SVR rates were attained. 78.8% after sofosbuvir plus ribavirin, 92.5% after sofosbuvir plus daclatasvir + ribavirin, and 100% after sofosbuvir plus ledipasvir (7 cases). The outcomes confirm our conclusions. Individuals with and without cirrhosis experienced the same rate of SVR when taking a combination of NS5A and NS5B inhibitors (92.2 versus 94.4).[14]

Sulkowski et al found 100% response rate when they used the combination of Daclatasvir and Sofosbovir for 24 weeks for the treatment of chronic hepatitis C in genotype 2 and 3.[15] Similarly, the results of ALLY-3 phase III trial endorsed the use of twelve weeks treatment instead of twenty four weeks in non-cirrhotic patients.[10] Another trial found that SOF + DCV was likely the best oral therapeutic choice, and that RBV did not appear to be required to significantly boost SVR rates.[16]

Similar results were found in a trial that was carried out in Italy, regarding the efficacy of Daclatasvir + Sofosbovir using or excluding ribavirin (RBV). Sustained Virological response (SVR) at 12 weeks was 98.9% (363/366) in patients who finished the research.[17] Kurniawan J et al, conducted a study Of 309 patients, which concluded that, when compared to SOF + RBV, the SOF + DCV regimen demonstrated greater SVR rates (p = 0.034). Nevertheless, despite cirrhosis and HCV genotype, both regimens had outstanding results, with overall SVR12 rates above 90%.[18]

Therefore, it is concluded that combination therapy (Sof + Dac) with or without ribavirin for three months is highly effective and affordable treatment for hepatitis C patients. It reduces Patients' physical and mental stress, as well as hospital visits.

CONCLUSION

Sof+Dacla group had significantly high SVR than Sof+Riba group especially in non-cirrhotic and treatment-naïve individuals.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
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2	Irfan Younus	Acquisition, analysis and interpretation of data.	
3	Muhammad Habib	Drafting the work.	
4	Adnan Qadir	Revising it critically intellectual content.	
5	Shahid Sarwar	Final approval of the version.	
6	Zameer Butt	Drafting the work & revising it critically.	