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EFFICACY OF SOFOSBUVIR IN COMBINATION WITH DACLATASVIR FOR THE TREATMENT OF HEPATITIS C GENOTYPE 3A PATIENTS IN A TERTIARY CARE CENTER IN PAKISTAN

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Abstract:
Patients with recurring illnesses of the hepatitis C virus frequently develop chronic liver disease, which causes tissue destruction ranging from cirrhosis to hepatocellular carcinoma (HCC). Hepatic-linked deceases are a result of this, both locally and globally. The efficacy of Sofosbuvir (SOF) and Daclatasvir (DCV) for treating individuals per enduring hepatitis C virus genotype 3a infection in either treatment-experienced or treatment-naive patients was examined in the study that was described below. At the Ziauddin Hospital North campus, a retrospective cohort research was carried out over 24 months, from January 2016 to December 2018. Regardless of the history of liver cirrhosis or behavior, patients with Genotype 3a HCV were treated for 12 weeks with Daclatasvir and Sofosbuvir.. Real-time PCR was cast-off to estimate the Sustained Virological Response (SVR12) 12 weeks following therapy. To do the statistical analysis, using SPSS version 20.0. In the study, there were 119 patients total, of which 79 (41.36%) were male, and 112 (58.63%) were girlish. The patient's normal age stood 43.72 13.05. One hundred eighty-two patients (95.28%) had SVR12. Forty patients reported minimal side effects (18.32%). In conclusion, SOF with DCV is an excellent regimen for the genotype 3a virus and highly successful treatment for chronic HCV.

Keywords: Hepatitis C, Genotype 3a, Daclatasvir, Sofosbuvir.

Introduction

Hepatic tissue is destroyed to varied degrees as a result of lasting liver disease, single of the record severe results usually observed in patients infected with chronic hepatitis C virus (HCV). Cirrhosis and hepatocellular carcinoma (HCC) are examples of the structural and functional tissue damage that results, which is a factor in the increase in liver-related mortality cases found globally (1).

Pakistan has experienced a sharp rise in Hepatitis C cases over the years, with Genotype 3a being the most often found variant in the country's population. Pakistan, regrettably, is one of the most Hepatitis C-prevalent nations in the world with a current prevalence rate of 8.64% of individuals who are infected, up from a prior figure of 6.7%. (2, 3). Recent developments in the management of Hepatitis C using direct-acting antivirals (DAA) have showed favourable effects in terms of increased sustained virological response and shorter treatment time. Sofosbuvir (SOF) and

daclatasvir are two of the most widely used DAA medications, and they are the subject of this study (DAC). In accordance with the severity of the condition, prior treatment history, and comorbidities, doctors can make certain adjustments to the regimens. Before these developments, Interferon was used to treat HCV, but it was ineffective and had little toxicity. DAAs essentially suppress the replication of HCV. Daclatasvir inhibits HCV nonstructural protein 5 (NS5A), whereas sofosbuvir inhibits HCV nonstructural protein 5B (NS5B), according to the unique mechanism of action (4).
Sofosbuvir has played a significant role in providing outstanding effectiveness and safety profile in numerous combination medication regimes for the treatment of chronic HCV. Additionally, throughout clinical studies, sofosbuvir-NS5A inhibitor combinations, notably daclatasvir (DAC), ledipasvir (LDV), and velpatasvir (VEL), have shown outstanding performance with a Post-treatment SVR rate well over 95%, as observed at week 12. (5).

An excellent virological response was also seen in the 2016 ALLY-3 Phase III trial, which compared SOF-DAC combination therapy in HCV Genotype 3 patients who took never acknowledged handling before to persons who spent. The study concluded that SVR is higher in non-cirrhotic patients, with excellent SVR at 96% for treatment-naive patients and 86% for treatment-experienced patients. Additionally, the ALLY3+ research found that individuals with advanced liver disease who received SOF-DAC in combination with weight-based ribavirin increased the SVR rate in HCV genotype three infected patients (6, 7). Additionally, individuals with HCV genotype three should take the grouping regimen of sofosbuvir and daclatasvir under the American Association for the Study of Liver Disease (AASLD) Guidelines (2017). Furthermore, the recommendations suggest that weight-based RBV must be further to the protocol unrelatedly of a patient's prior experience receiving ribavirin (RBV) and pegylated interferon treatments (8). The SOF+DAC combination medication regimen with or without RBV is a game-changer in trials and other clinical settings, according to the research described above and their outstanding results.
Hepatitis C virus genotype 3a, found in the public of patients with chronic HCV contagion, is the most prevalent genotype in Pakistan. In previous research based on DAA evaluation, HCV Genotype 3a harboring patients were not commonly analyzed aside from local prevalence. As a result, there are questions about the efficacy of DAA combination regimens in Pakistan due to the circumstances and the dearth of evidence on Genotype 3a-positive HCV patients.
The goal line of this learning was gather sufficient data to evaluate the worth of the amalgamation (Daclatasvir + Sofosbuvir) regimen in treating HCV Genotype 3a patients in Pakistan, nonetheless of past dealing practice or disease severity. This cohort analysis also yields the examined combination regime's safety profile.

Material and Methods

This Reviewing Cohort Study evaluated the effectiveness of Direct Acting Antivirals (DAA) given to 191 HCV-positive patients over 24 months (Jan. 2016–Dec. 2018). Age, gender, abdominal ultrasound, previous treatment status, anti-HCV antibody status, HCV RNA status by real-time PCR and HCV genotype stayed all included in the data documentation for the patient, which what collected from the gastroenterology department. Using PCR, we identified the hepatitis C infection. Patients were enrolled in the trial regardless of their history of liver cirrhosis or treatment with ribavirin or interferon if they had Genotype 3a HCV, which was diagnosed by Genotype Testing. Females who are pregnant and those who have a renal impairment (probable glomerular separation rate 30 ml/min/1.73 m2 and serum creatinine >2.5 mg/dl). It was possible to receive an ERC exemption from Ziauddin University's ERC. Patients chosen at random received a 12-week prescription for daclatasvir 60 mg and sofosbuvir 100 mg. Real-time PCR was used to evaluate sustained virological responses (SVR12) after treatment and 12 weeks afterward. To do the statistical analysis, we used SPSS version 20.0. The data analysis uses SPSS version 20.

Results

In the study, there were 119 patients total, of which 79 (41.36%) were male, and 112 (58.63%) remained lady. The patient's usual oldness was 43.72 + 13.13. One hundred sixty-six individuals (86.91%) had never received therapy before and were treatment-naive. 25 (13.08%) had received treatment before but had not improved after interferon therapy. Table 1 shows that 32 (16.75%) patients were cirrhotic while 159 (83.24%) patients were not.

Variables		**Number (191)**	**%**
Age (years)	Mean±SD	43.72 ± 13.05	
Gender	Male	79	41.36%
	Female	112	58.63%
Liver status	non-cirrhotic	159	83.24%
	Cirrhotic	32	16.75%
Treatment status	Treatment Naïve	166	86.91%
	Treatment experienced	25	13.08%

Table-1: Baseline demographic data of the HCV genotype 3a patients

The primary outcome of the sofosbuvir plus daclatasvir was detected by SVR_{12}. SVR_{12} was shown by 182 (95.28%) in all 191 patients, as shown in figure-1.

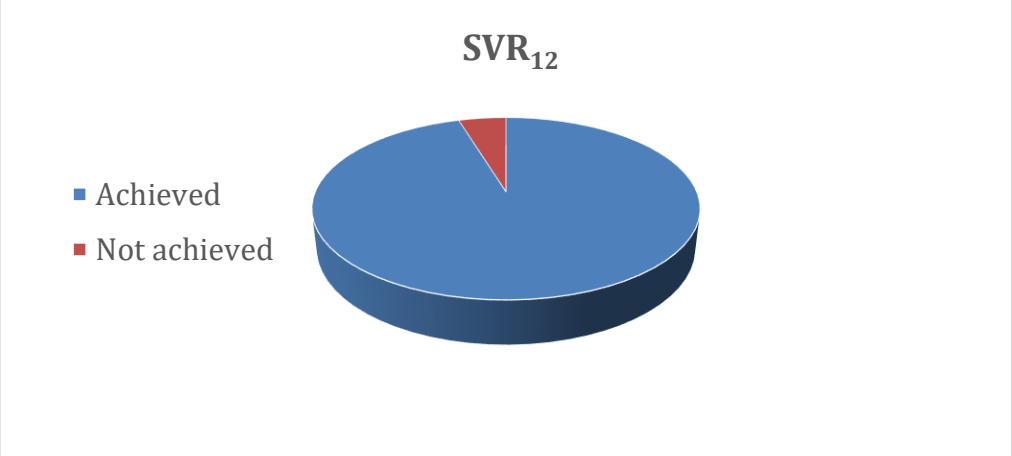

Figure-1: Pie chart showing the SVR_{12} response in combination regimen treated patients infected with HCV genotype 3a.

There were 40 patients who reported minimal side effects (18.32%). According to Table 2, the adverse events included body aches in 5 patients (2.61%), fever in 12 patients (6.28%), headache in 15 patients (7.85%), and exhaustion in 17 patients (8.9%).

Side effects	**Number (191)**	**%**
No side effects	151	79.05
Had side effects	40	18.32
Fatigue	15 patients	7.85
headache	in 17 patients	8.9
Fever	in 12 patients	6.28
Body ache	Five patients	2.61

Table-2: Adverse effects of the treatment in the patient population

Discussion

The treatment environment has dramatically changed due to the development of anti-HCV DAA. These treatment combinations have significantly improved SVR and slowed the spread of the illness to the cirrhotic liver. Interferon-based traditional therapy for the treatment of HCV has shown widespread declines, and DAA-based therapy is on the rise. Due to the availability of generic versions in more than 100 countries, the price of DAA has significantly decreased (9). However, scientific validation and assessment are required to define important parameters, such as the drug's efficacy and safety. Furthermore, it would make sense to assess the history of current antiviral medication regimens in contexts including patient populations infected with various HCV genotypes.

Lesser SVR rates in HCV genotype 3a patients through advanced disease have been demonstrated, even though existing treatment procedures for numerous HCV genotypes are successful in various contexts. Hepatocellular carcinoma development, cirrhosis, and steatosis are typical manifestations of genotype 3. According to evidence from hospital registries and real-world situations, HCV genotype 3a is often difficult to treat (9, 10, 11). Improving the treatment success in these infected patients is essential since the undetectable viral load is linked to lower liver morbidity.

Regardless of the patient's prior medical history or liver cirrhosis, our investigation has demonstrated that they have positive therapeutic responses. In genotype 3a infected patients, prior DAA regimens based on sofosbuvir and ribavirin had lower SVR12 independent of previous treatment history.. Patients receiving a 24-week weight-based dosage of SOF/RBV were shown to have a decreased SVR12 (12). In addition, Feld et al. demonstrated decreased SVR12 in cirrhotic patients who customary the same medication programme regardless of prior treatment (13). In patients with cirrhosis who have hepatitis C genotype 3a, combining SOF with RBV is not advised.

As a result, experiments using alternative antiviral combination regimens, like SOF and DCV, were examined. Patients with advanced hepatic fibrosis in a trial received a regimen of DCV, SOF for 24 weeks, either with or without weight-based RBV. SVR12 was demonstrated in 89% of patients who had the DCV/SOF combination and in 88% of those who had the DCV/SOF/RBV combination (14). Although the duration was prolonged to 24 weeks, there was no additional efficacy with RBV when administered with the DCV/SOF regimen, according to the response rates, which were not significantly different between the two groups. In line with this, another study found that after 24 weeks of treatment with DCV + SOF or DCV/SOF/RBV, patients with cirrhosis had SVR12 values of 86% and 82%, respectively (15).

The patients' follow-up is a crucial component of HCV treatment. Particularly in genotype 3, those who have received both DAA treatment and Interferon treatment in the past are more vulnerable to recurrent illness. In patients with HCV Genotype 3, disease severity, prior RBV treatment, and nucleotide changes linked to resistance are risk factors for relapse that contribute to non-responder patients (16). There is consensus in a clinical and real-world environment regarding the ability of a combined DAA regimen to produce almost 100% SVR, regardless of a patient's treatment experience or if they are non-cirrhotic; nevertheless, minor geographical variances may exist (17).

Conclusion

Patients per hepatitis C genotype 3a have shown success with the blend of sofosbuvir and daclatasvi r, regardless of prior usage or cirrhosis.

Acknowledgments

Conflict of interest

No encounter of curiosity was found in the study.

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