DOI: https://doi.org/10.53350/pjmhs221641155

ORIGINAL ARTICLE

Comparison of Efficacy of Sofosbuvir & Daclatasvir with Sofosbuvir and Velpatasvir in Achieving SVR in Patients of Chronic Hepatitis C with Genotype 3

TANVEER AHMED[1], OMER HASSAAN AFTAB AHMAD[2], MUHAMMAD BILAL[3], SHER ALAM[4], SHIRJEEL ZAHEER[5], ZAID GUL[6]
[1]*Senior Registrar Gastroenterology, QAMC/ BVH, Bahawalpur*
[2]*Consultant Gastroenterologist, Advance International Hospital, Islamabad*
[3]*Senior Registrar Gastroenterology, Rai Medical College, Sargodha*
[4]*Consultant and Lecturer in Shaikh Zayed University Medical College, Khost*
[5]*Chief Clinical Coordinator, Emergency Medicine, PIMS Hospital, Islamabad*
[6]*Consultant Gastroenterologist, PIMS Hospital, Islamabad*
Corresponding author: Tanveer Ahmed, Email: ahmedtanveer17@yahoo.com, Cell: +92332 7201463

ABSTRACT

Background and Aim: Hepatitis C virus of chronic nature has been appreciated globally to be a major source of hepatic carcinomas and other abnormalities associated with liver function. The epidemiological data on the prevalence of the Hepatitis C virus shows a trend of 71 million people being affected by the disease globally with an annual mortality rate of 3.5 to 5 million death. Pakistan showed a prevalence of up to 8.2% which is among the most common incidents in countries. Since genotype 3 is the most common variant in Pakistan there remains a literature gap that evaluates the effectiveness of velpatasvir plus sofosbuvir and daclatasvir plus sofosbuvir and compares their efficiency. This study will aim to compare the efficiency of sofosbuvir and velpatasvir with sofosbuvir and daclatasvir.

Place and Duration: The study was conducted at the department of Gastroenterology in PIMS Hospital, Islamabad during the period from 21st June 2020 to 20th June 2021.

Methodology: The total number of participants recruited in this study was 1000. Participants were recruited after meeting the inclusion and exclusion criteria. The participants were then divided into two groups of n=500 with group one receiving therapy by Sofosbuvir and Daclatasvir and group two receiving a therapy regimen consisting of Sofosbuvir/Velpatasvir. Both the groups underwent therapy for the same amount of time (12 weeks). Before initiation of regimens, patients underwent baseline testing including blood screens, biochemical screens, fibro scans, genotypes, and PCR. These tests we basis for evaluation before and after the treatment. The goal was to achieve detection of no HCV RNA virus at the end of the management protocol. Due to known complications in patients presenting with cirrhosis, the duration of the drug was extended up to 24 weeks. For the patients who presented with relapse of chronic HCV, the end treatment success was measured by HCV RNA less than or equal to 25 IU/ml after 12 weeks of drug use

Results: Around 98% of the participants receiving sofosbuvir and velpatasvir management retreatment patients reached the end of treatment assessment and showed sustained viral response and at the end of treatment a small amount of 2% of the participants were found to relapse. The number of patients who reached the end of treatment was 96.2% and 3.8% discontinued the treatment which is more than that compared to the sofosbuvir -velpatasvir regimen. The rate of poor response to treatment management in the sofosbuvir -the daclatasvir group was more than that of the sofosbuvir -velpatasvir group in comparison of 4.3% to 5.8%. This group showed a similar rate of relapse which is 2%.

Conclusion: The results of this study showed that sustained viral response was higher in the group managed by sofosbuvir and velpatasvir in comparison to sofosbuvir and daclatasvir. Furthermore, patient compliance to treatment was better in the group treated with sofosbuvir and velpatasvir in comparison to another group. It was also established that the group managed by sofosbuvir and daclatasvir showed a higher incidence of drug adverse events

Keywords: Sofosbuvir and Daclatasvir, Sofosbuvir and Velpatasvir, Chronic Hepatitis C

INTRODUCTION

Hepatitis C virus of chronic nature has been appreciated globally to be a major source of hepatic carcinomas and other abnormalities associated with liver function [1]. The epidemiological data on the prevalence of the Hepatitis C virus shows a trend of 71 million people being affected by the disease globally with an annual mortality rate of 3.5 to 5 million deaths [2]. Unfortunately, the disease has been found to have major prevalence in underdeveloped and developing countries. When assessing the prevalence of hepatitis C among different countries, Pakistan showed a prevalence of up to 8.2% which is among the most common incidents in countries [3]. Owing to the high prevalence of the disease among the population, the source of disease transmission is studied extensively to prevent the progression. Literature shows the hepatitis C virus is transmitted through infected blood and common sources of spread are injections, transmission via infected blood transmission, using infected needles and syringes, spread via hospital and through sharp instruments used in grooming [4]. Hepatitis C virus has various genotypes however the most common genotype seen in the population of Pakistan is genotype 3a [5].

Previous methods of management of the hepatitis C virus were largely focused on therapy with interferon-based drugs. But some studies show that interferon-based drugs failed to produce sustained virus response in the majority of the population and showed a wide range of serious adverse effects [6]. When assessing the effectiveness of disease management by these drugs, it was seen that only 67% of the participants responded desirably to the drug [7]. Due to the extensive burden of the disease in the country, there have been measures for controlling hepatitis C at provincial levels as well as the federal level. These advisory and regulatory committees have taken substantial steps such as ensuring the availability of direct-acting anti-viral at economical rates [8]. This step has been considered a revolutionary step in the management of hepatitis C in Pakistan and has been considered one of the major drugs in managing hepatitis C throughout the world [9]. These direct-acting antivirals consisted of three subtypes of drugs which were once and still a major source of management of hepatitis C virus with sustainable virus response of up to 90% [10]. The current guidelines for the management of the hepatitis C virus still focus on direct-acting antivirals. The national chronic HCV management guidelines prescribe the use of sofosbuvir-based therapy [10]. Recent amendments within the guidelines showed suggested the addition of daclatasvir-based therapy which targets the replication of the virus [11]. The use of daclatasvir has been suggested in genotype 3 hep C patients along with sofosbuvir with 12 weeks duration. Assessment of the effectivity of daclatasvir with sofosbuvir showed

that improvement was seen in patients in terms of compliance and outcomes [12]. Similarly, velpatasvir has been used as an HCV inhibitor and has been used along with sofosbuvir as a single drug formulation. The use of velpatasvir and sofosbuvir has been approved in Pakistan however the recommendation did not reach authorized levels.

Since genotype 3 is the most common variant in Pakistan there remains a literature gap that evaluates the effectiveness of velpatasvir plus sofosbuvir and daclatasvir plus sofosbuvir and compares their efficiency. This study will aim to compare the efficiency of sofosbuvir and velpatasvir with sofosbuvir and daclatasvir.

METHODOLOGY

Study design and participants: The conducted study is the cohort of observational prospective approach. The study was conducted in Gastroenterology department of PIMS hospital, Islamabad Pakistan after obtaining ethical approval from the relevant body. The study participants were recruited during the period from 21st June 2020 to 20th June 2021 and the number of participants was 1000. All the participants were active cases of HCV. The participants were recruited after meeting the inclusion criteria. The criteria included adult participants aging 18 years or older with a diagnosis of chronic HCV virus. Patients presenting with a coinfection of HCV and HBV were also eligible for research. Other inclusion criteria included patients with complications such as cirrhosis and relapse were also made part of this study. The exclusion criteria of the study included participants who denied consent to the study, patients of were underage, and patients who were undergoing DAA therapy. Before the start of the regimen, patients underwent a fibrosis scan to assess the stage of fibrosis. The recruited participants were then divided into two groups of n=500 with group one receiving therapy by Sofosbuvir and Daclatasvir and group two receiving a therapy regimen consisting of Sofosbuvir/Velpatasvir. Both the groups underwent therapy for the same amount of time (12 weeks). Before initiation of regimens, patients underwent baseline testing including blood screens, biochemical screens, fibro scans, genotypes, and PCR. These tests we basis for evaluation before and after the treatment.

The procedure of drug regimen: Both the groups included in the study were based on sofosbuvir therapy management among chronic HCV patients of genotype 3. The drugs were administered by the combined hospital and patient funding. An everyday dosage of the selected regimen for sofosbuvir was 600mg taken along with food and similarly, the dosage for daclatasvir was 60 mg prescription taken with food. The therapeutic regimen was continued for 12 weeks. An experienced personnel was in charge of overlooking the regimen for recruited participants. When deemed necessary, included physicians who incorporated ribavirin according to patients' mass and age. The other group was on a predetermined dose of sofosbuvir/ velpatasvir dose of 400 mg and 100 mg formulated into a single tablet. This group also received this therapy for 12 weeks.

Calculating the efficacy of the regimen: After implementation of the drug regimen in both groups evaluation of efficacy was planned at the end of the procedure. The goal was to achieve detection of no HCV RNA virus at the end of the management protocol. Due to known complications in patients presenting with cirrhosis, the duration of the drug was extended up to 24 weeks. For the patients who presented with relapse of chronic HCV, the end treatment success was measured by HCV RNA less than or equal to 25 IU/ml after 12 weeks of drug use.

Assessing the safety of patients: The adverse incidents were made part of the safety assessment as all the patients were included in the safety assessment. It was made sure that safety assessments for each participant were carried out according to prescribed guidelines by the hospital. The safety assessment via hematological, and biochemical were performed at the start of the treatment, at the end of the treatment, and after 12 weeks of the treatment.

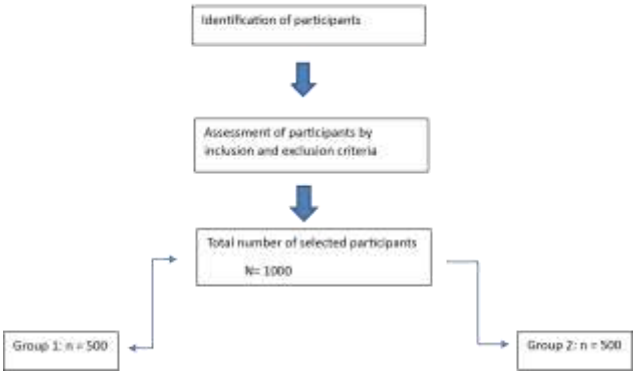
Pretreatment data of participants:

Social and demographic data: Participants of all age groups and BMI were included in the study. Another pretreatment variable was if patients were previously treated or untreated for their HCV. Other comorbidities were assessed as pretreatment variables. These included systemic conditions like hyperglycemia, hypertension, and overweight BMI. The risk factors that were studied in the participants were habits of smoking, history of blood transfusion, and surgery.

Assessment of liver function and severity of disease by non-invasive testing: The hematological assessment of participants included a complete blood picture and INR. To assess the liver function, a liver function test was performed which included a screening of AST, ALT, albumin, bilirubin, and levels of creatinine within the blood. HCV RNA was subjected to a quantitative assessment of viral load and participants were divided into high and low viral loads with a cut-off value of 80,000 IU/ml PCR value. Patients were also tested for the surface antigen of HBV. Furthermore, genotyping was carried out for the hepatitis virus. Cirrhosis diagnosis was made by using a fibro scan or biopsy.

RESULTS

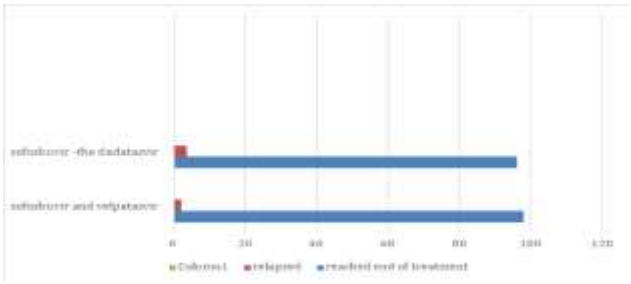
The results were generated from all 1000 participants that were recruited for the study. The participants in group one received sofosbuvir and daclatasvir whereas group 2 participants received therapy with sofosbuvir and velpatasvir.



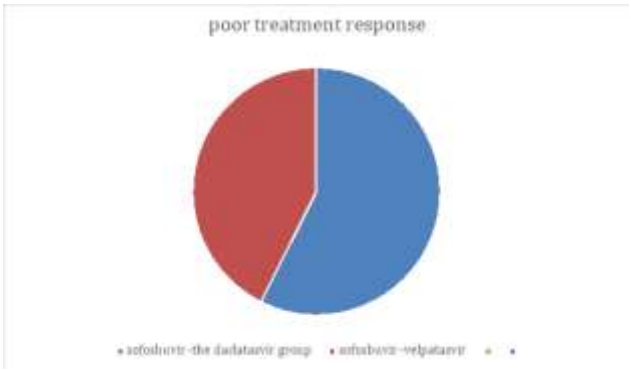
The mean age of recruited participants was 40.2 years ± 11.7 years. The gender breakdown of the recruited participants showed a female predilection with 53.1% and patients who were undergoing management of HCV for the first time at 81.4%. Diagnosis of liver cirrhosis was made only in 4.9% of participants and these participants additionally received management by ribavirin. The study assessed the efficacy of treatment in group one with group two after 12 weeks of drug therapy in tertiary care hospital of Islamabad, Pakistan.

All the recruited participants were genotype 3. The majority of participants managed by group 2 were relatively older and with a higher BMI in comparison to their group 1 counterparts. Participants of group two had relatively poor liver function profiles with elevated levels of AST and ALT. patients of this group furthermore showed poor levels of hemoglobin and platelets and higher levels of hyperglycemia and obesity.

Around 98% of the participants receiving sofosbuvir and velpatasvir management retreatment patients reached the end of treatment assessment and showed sustained viral response and at the end of treatment a small amount of 2% of the participants we found to relapse. The number of patients who reached the end of treatment was 96.2% and 3.8% discontinued the treatment which is more than that compared to the sofosbuvir -velpatasvir regimen.



The rate of poor response to treatment management in the sofosbuvir -the daclatasvir group was more than that of the sofosbuvir -velpatasvir group in comparison of 4.3% to 5.8%. this group showed a similar rate of relapse which is 2%.



When assessing the demographics of participants who did not show sustainable viral response (n= 101) were considerably older and presented with higher levels of ALT and pretreatment high viral loads. When analyzing the associated variables that may result in not sustained viral response showed that age and liver cirrhosis significantly influence the end of treatment outcomes of the patients. When assessing the safety of individuals in response to treatment with sofosbuvir -daclatasvir it was appreciated that patients showed common adverse effects of skin rash and oral ulcerations more than groups undergoing sofosbuvir -velpatasvir therapy.

DISCUSSION

The results of this study showed that sustained viral response was higher in the group managed by sofosbuvir and velpatasvir in comparison to sofosbuvir and daclatasvir. Furthermore, patient compliance to treatment was better in the group treated with sofosbuvir and velpatasvir in comparison to another group. It was also established that the group managed by sofosbuvir and daclatasvir showed a higher incidence of drug adverse events. This portion of literature will assess the findings of this study to those pre-existing in literary shreds of evidence.

A study conducted by Falade-Nwulia et al. 2017 studied two groups treated with sofosbuvir and vel while another group was treated with sofosbuvir and daclatasvir. The study showed a generalized sustainer viral response of 95.5%. when assessing the sustained viral response after 12 weeks at the end of treatment the sustained viral response of the group managed by sofosbuvir and daclatasvir showed a 94.4% response whereas that of the group treated with sofosbuvir and velpatasvir showed the response of 94.7% [8]. The outcomes of this study are comparable to the outcomes of our clinical study showing that groups treated with sofosbuvir -velpatasvir are associated with better outcomes. However, the discussed study shows comparable outcomes among both groups but sofosbuvir and velpatasvir are at the leading edge in comparison to sofosbuvir and daclatasvir. When studying and exploring the causes of poor sustained viral response among patients being treated with sofosbuvir with daclatasvir. A study conducted by Omar et al. 2017 studied the relationship of efficacy in chronic HCV patients managed by sofosbuvir and daclatasvir. The study used a regimen for 12 weeks and used sofosbuvir 400 mg and daclatasvir 60 mg. the study outcomes showed a sustained viral response of 95.4%. this response rate is comparable with this clinical outcome and previously discussed study. However, when exploring the cause of limitation of response among the participants it was found that almost 76 participants discontinued therapy these findings are also in accordance with findings of this clinical study that the group treated with sofosbuvir and daclatasvir is found to have higher rates of patient withdrawals. The reason for such withdrawal must be focused on for further discussion. Another study conducted by Belperio et al. 2019 assessed the effectiveness of sofosbuvir with velpatasvir or daclatasvir. The study population included 5,400 participants. the recruited participants were of genotype 2 and genotype 3. The outcomes of the study showed the comparable sustained viral response of sofosbuvir and daclatasvir and sofosbuvir/ velpatasvir. For genotype 3, the sustained viral response in sofosbuvir and velpatasvir participants showed a sustainable response of around 92% whereas the response in participants managed by sofosbuvir and daclatasvir was recorded to be around 90% [9]. A meta-analysis was conducted to assess the effectivity of sofosbuvir and velpatasvir in comparison to sofosbuvir and daclatasvir. The regimen was conducted for 12 weeks in all the selected studies. A total number of 16 studies were recruited with a total number of 4,907 participants. The outcomes of the meta-analysis showed that sustained viral responses among participants treated with sofosbuvir and velpatasvir showed more sustained responses of 98% in comparison to sofosbuvir and daclatasvir 95% [10].

The above-mentioned discussion shows similar results in accordance with those of the outcomes of this clinical research. Therefore, it can be appreciated that sustained viral responses are more sustainable among sofosbuvir and velpatasvir. The group further shows improved patient compliance and lesser adverse effects than a group of the sofosbuvir and daclatasvir groups.

CONCLUSION

This study aimed to evaluate the comparison of effectivity of sofosbuvir and vel in comparison to sofosbuvir and daclatasvir. This study aimed to fill the literature gap that exists inefficient management of genotype 3. This study aims to provide a means of improving the clinical management of patients. This study will also provide a prototype for other studies to further explore the physiology and outcomes of the management of the patient.

REFERENCES

1 T. F. B. T. L. J. K. N. D. R. Baumert, "Status of direct-acting antiviral therapy for hepatitis C virus infection and remaining challenges," Gastroenterology, vol. 156, no. 2, pp. 341-445, 2019.
2 G. Q. H. M. H. H. S. D. C. F. T. A. e. a. Lim, "Curbing the hepatitis C virus epidemic in Pakistan: the impact of scaling up treatment and prevention for achieving elimination," Int. J. Epidemiol, vol. 47, no. 2, pp. 550-560, 2018.
3 M. I. M. Umer, "Hepatitis C virus prevalence and genotype distribution in Pakistan: Comprehensive review of recent data," World J. Gastroenterol, vol. 22, no. 4, p. 1684, 2016.
4 Z. M. S. K. S. P. A.-R. L. J. Al Kanaani, " The epidemiology of hepatitis C virus in Pakistan: systematic review and meta-analyses.," R. Soc. Open Sci., vol. 5, no. 4, p. 180257, 2018.
5 S. A. I. B. M. K. Q. M. H. Z. N. A. S. e. a. Khan, "Molecular Epidemiology of Hepatitis C Virus Genotypes Among Chronically Infected Patients in Pakistan.," Jundishapur J. Microbiol, vol. 12, no. 3, pp. 1-7, 2019.
6 M. P. M. J. G. G. S. C. R. V. K. S. M. R. R. e. a. Manns, "Peginterferon alfa-2b plus ribavirin compared with interferon alfa-2b plus ribavirin for initial treatment of chronic hepatitis C: a randomised trial," the Lancet, pp. 958-9965, 2001.
7 S. A. B. A. I. M. N. A. N. S. I. e. a. Ali, "Virological response to conventional interferon therapy combined with ribavirin against various HCV genotypes in Khyber Pakhtunkhwa, Pakistan.," Asian Pacific J. Cancer Prev, vol. 17, no. 5, pp. 2407-2410, 2016.

8 H. M. B. K. A. S. E. A. A. A. W. Qureshi, " Treatment of hepatitis B and C through national programme-an audit," J. Pak Med. Assoc, vol. 63, no. 220, p. e4, 2013.
9 World Health Organization, "Progress report on access to hepatitis C treatment: focus on overcoming barriers in low-and middle-income countries.," World Health Organ, 2018.
10 U. Spengler, "Direct antiviral agents (DAAs)-A new age in the treatment of hepatitis C virus infection," Pharmacol. Ther, vol. 183, p. 118–126, 2018.
11 L. N. L. A. C. Cavalcante, "Predictive factors associated with hepatitis C antiviral therapy response," World J. Hepatol, vol. 7, no. 12, p. 1617, 2015.
12 J. O. T. J. G. T.-M. A. K. D. K. A. A. K. E. S. e. a. Link, "Discovery of velpatasvir (GS-5816): A potent pan-genotypic HCV NS5A inhibitor in the single-tablet regimens Vosevi® and Epclusa®," Bioorg. Med. Chem. Lett., vol. 29, no. 16, p. 2415–2427, 2019.
13 O. S.-C. C. N. D. R. F. M. W. S. J. B. S. M. S. Falade-Nwulia, "Oral direct-acting agent therapy for hepatitis C virus infection: a systematic review," Ann. Internal Med, vol. 166, no. 9, pp. 637-648, 2017.
14 P. S. S. T. A. L. T. P. M. L. A. B. L. I. Belperio, "Real-world effectiveness of daclatasvir plus sofosbuvir and velpatasvir/sofosbuvir in hepatitis C genotype 2 and 3.," J. Hepatol, vol. 76, no. 1, pp. 15-23, 2019.
15 P. A. R. L. O. N. C. Mariantonietta, " Efficacy of 12-weeks velpatasvir plus sofosbuvir-based regimen in HCV-naive subjects with mild fibrosis: a meta-analysis.," Acta Bio Med.: Atenei Parmensis, vol. 90, no. 2, p. 187, 2019.