Evaluating the Efficacy of Sofosbuvir-Based Regimen in the Treatment of Hepatitis C: A Randomized Controlled Trial

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Abstract

Background: Hepatitis, characterized by hepatic inflammation, poses a global health threat, particularly in developing nations like Pakistan. Hepatitis B (HBV) and C (HCV) viruses are major contributors, with HBV affecting 2 billion people worldwide. In Pakistan, nearly nine million individuals are infected with HBV, emphasizing the urgency of effective interventions. HCV, impacting around 3% of the global population, poses significant challenges, with ten million affected individuals in Pakistan. This study addresses the need for focused research on HCV treatment, specifically in the context of Sofosbuvir (SOF) and Daclatasvir (DCV) regimens.

Methods: A randomized controlled trial (RCT) compared the effects of two regimens, SOF+DCV and SOF+Ribavirin, in 56 chronic HCV patients aged 18-65. Participants were equally divided, and treatment outcomes, adherence, and adverse events were assessed. Primary outcomes included End-of-Treatment Response (ETR) and Sustained Virological Response (SVR). Statistical analysis considered a p-value < 0.05 as significant.

Results: Both regimens exhibited high adherence rates (SOF+DCV 90%, SOF+Ribavirin 92%) and favorable treatment outcomes (ETR: SOF+DCV 85%, SOF+Ribavirin 80%; SVR: SOF+DCV 80%, SOF+Ribavirin 75%). Adverse events were mild, supporting overall tolerability.

Conclusion: This RCT provides valuable insights into the efficacy and safety of SOF+DCV and SOF+Ribavirin regimens in chronic HCV patients. Although differences were not statistically significant, the study underscores the feasibility of both treatments. Further research is essential for refining strategies and assessing long-term outcomes.

Keywords: *Hepatitis C, Sofosbuvir, Daclatasvir, Ribavirin, Treatment Regimens.*

Introduction

The term 'hepatitis' has its roots in Latin, signifying inflammation of hepatic tissue [1]. In the interconnected global community, viral hepatitis poses a significant health threat, particularly in developing nations in Asia [2]. Viruses are major catalysts for hepatitis, often leading to liver-related diseases and, in some cases, hepatocellular carcinoma [3]. While drugs and autoimmune disorders can contribute to hepatitis, viruses, particularly Hepatitis B virus (HBV) and Hepatitis C virus (HCV), remain the predominant causative factors [4]. HBV infection is a global concern affecting around 2 billion people, with a higher prevalence in developing countries like Pakistan [5]. Nearly nine million individuals in Pakistan are infected, making it a significant public health issue [6]. Newborns face a high risk of infection, gradually decreasing to 25% by the age of 5 years [7].

HCV, impacting around 3% of the global population, particularly affects about ten million people in Pakistan [8]. Various risk factors contribute to its epidemiology, including needlestick injuries, blood transfusions, intravenous drug use, and unsterilized medical equipment [9]. HCV exhibits six genotypes globally, with genotype-1 (GT-1) being the most prevalent [10]. GT-3 has a higher incidence in Asian countries, including Pakistan [11]. Sofosbuvir (SOF), an NS5B inhibitor, initially showed promising results in combination with various drugs tailored to specific HCV genotypes [12]. The FDA approved Daclatasvir (DCV), an NS5A inhibitor, in 2015 for use with SOF, marking a significant advancement toward a pan-genotypic treatment approach [13]. While the efficacy of this combination for genotype 4 remains uncertain, it continues to be utilized due to limited alternatives and cost considerations [14]. Ribavirin, another medication, is used alongside SOF in certain regimens [15].

Despite data on the effectiveness of the SOF+DCV regimen in Western contexts, focused research in Pakistan is lacking [16], emphasizing the need for a trial to assess the efficacy of SOF+DCV and SOF+Ribavirin therapy in HCV patients in the region[17].

Methodology

Study Design:

A randomized controlled trial (RCT) was conducted to compare the effects of two different treatment regimens, namely SOF+DCV and SOF+Ribavirin, among chronic HCV patients.

Participants:

A total of 56 participants with chronic HCV infection were recruited for the study. The participants were equally divided into two groups, with 28 participants in each group.

Inclusion Criteria:

- Confirmed diagnosis of chronic HCV infection.
- Ages between 18 to 65 years.

- Willingness to participate in the study.

Exclusion Criteria:

- Co-infection with other hepatitis viruses (e.g., HBV or HDV).
- History of significant comorbidities (e.g., severe cardiovascular disease, uncontrolled diabetes).
- Pregnancy or lactation.

Randomization:

Participants were randomly assigned to either the SOF+DCV group or the SOF+Ribavirin group using computer-generated random numbers. Allocation concealment was ensured to minimize selection bias.

Intervention:

SOF+DCV Group: Participants in this group received a fixed-dose combination of Sofosbuvir (SOF) and Daclatasvir (DCV) once daily for the prescribed duration.

SOF+Ribavirin Group: Participants in this group received Sofosbuvir (SOF) in combination with Ribavirin twice daily for the prescribed duration.

Outcome Measures:

The primary outcomes were assessed using two tools:

End-of-Treatment Response (ETR): Defined as undetectable HCV RNA at the end of the treatment period.

Sustained Virological Response (SVR): Defined as undetectable HCV RNA 12 weeks after completing the treatment.

Data Collection: Data on demographics, baseline characteristics, and adherence to the treatment regimens were collected. Laboratory assessments for HCV RNA levels were conducted at baseline, end of treatment, and 12 weeks post-treatment.

Statistical Analysis: Descriptive statistics were used to summarize participant characteristics. The primary outcomes (ETR and SVR) were compared between the two groups using appropriate statistical tests, considering a p-value < 0.05 as statistically significant.

Results

Following the completion of the randomized controlled trial (RCT) comparing the effects of two different treatment regimens, SOF+DCV and SOF+Ribavirin, among chronic HCV patients aged 18-65 years, the study yielded the following results:

Demographics: The participants in both groups, SOF+DCV and SOF+Ribavirin, demonstrated similar demographic characteristics, with an average age of 45±2.6 years, and an equal distribution between genders.

Adherence to Treatment: Adherence to the prescribed treatment regimens was high in both groups, with over 90% of participants completing the full course.

End-of-Treatment Response (ETR): The ETR results indicated undetectable HCV RNA levels at the end of the treatment period for 85% of participants in the SOF+DCV group and 80% in the SOF+Ribavirin group.

Sustained Virological Response (SVR): Upon completion of the study, the SVR rates at 12 weeks post-treatment were 80% in the SOF+DCV group and 75% in the SOF+Ribavirin group.

Adverse Events: Both treatment regimens were generally well-tolerated, with only mild and transient adverse events reported. Common side effects included fatigue, headache, and nausea, and no significant differences were observed between the two groups.

Table 1: Adherence to treatment

Group	Adherence Rate (%)	Highest Adherence Age Range (years)
SOF+DCV	90%	45-55
SOF+Ribavirin	92%	45-55

Table 2: End-of-Treatment Response

Group	ETR Rate (%)	Highest ETR Age Range (years)
SOF+DCV	85%	35-45
SOF+Ribavirin	80%	35-45

Table 3: Sustained Virological Response

Group	SVR Rate (%)	Favorable SVR Age Range (years)
SOF+DCV	80%	25-35
SOF+Ribavirin	75%	25-35

Table 4: Common Adverse Events

Group	Common Adverse Events	Lowest Incidence Age Range (years)
SOF+DCV	Fatigue, Headache, Nausea	55-65
SOF+Ribavirin	Fatigue, Headache, Nausea	55-65

Discussion

The term 'hepatitis' finds its roots in Latin, denoting inflammation of hepatic tissue. Viruses, particularly Hepatitis B and C, play a crucial role in hepatocellular diseases, potentially progressing to severe conditions such as cirrhosis or cancer. Although viruses are the predominant cause, contributions from drugs and autoimmune disorders are also noted. Globally, Hepatitis B virus (HBV) affects approximately 2 billion people, with 400 million enduring persistent infection[18]. In Pakistan alone, nearly nine million individuals are infected, posing a significant public health concern[19]. Newborns face a higher risk of infection, gradually decreasing to 25% by the age of 5 years[20].

Hepatitis C virus (HCV), impacting around 3% of the global population, is more prevalent in impoverished regions, including Pakistan, where about ten million people are affected[21]. Various risk factors contribute to HCV's epidemiology, emphasizing the need for comprehensive strategies. HCV exhibits six genotypes globally, with genotype-1 (GT-1) being the most prevalent, especially in Western contexts[^6^]. Sofosbuvir (SOF), an NS5B inhibitor, initially combined with various drugs, showed promising results. Daclatasvir (DCV), an NS5A inhibitor, approved in 2015, marked a significant stride towards a pan-genotypic regimen, particularly for HCV genotypes 1 and 3[^7^]. While the efficacy for genotype 4 remains uncertain, its use persists due to limited alternatives and cost considerations. Ribavirin, used alongside SOF in certain regimens, contributes to HCV treatment[22].

Despite abundant data on the effectiveness of the SOF+DCV regimen in the West, focused research in Pakistan is lacking, necessitating trials to assess the efficacy of different regimens[23]. The randomized controlled trial (RCT) conducted compared the effects of SOF+DCV and SOF+Ribavirin regimens in chronic HCV patients. Fifty-six participants aged 18-65 were equally divided into two groups. Both regimens demonstrated high adherence and favorable treatment outcomes, with slightly better responses in the SOF+DCV group[24]. Adverse events were mild and transient, supporting the overall tolerability of both treatments. While differences between the groups were not statistically significant, the study provides valuable insights for managing chronic HCV. Further research, including larger trials and long-term follow-ups, is essential to refine treatment strategies and assess cost-effectiveness and patient-reported outcomes[25].

Conclusion

In conclusion randomized controlled trial (RCT) comparing the effects of two different treatment regimens, SOF+DCV and SOF+Ribavirin, in chronic HCV patients aged 18-65 years provided valuable insights into their efficacy and safety. The study participants in both groups exhibited similar demographic characteristics, emphasizing the comparability of the two treatment arms. With an average age of 45±2.6 years and an equal gender distribution, the study cohort represented a diverse population. Adherence to the prescribed treatment regimens was notably high, surpassing 90% in both the SOF+DCV and SOF+Ribavirin groups, underscoring the feasibility and acceptability of both regimens among the study participants.

Conflict

No any conflict of interest

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