Section A-Research paper
ISSN2063-5346

EFFECT OF SOFOSBUVIR AND DACLATASVIR ON LIPID PROFILE, GLYCEMIC CONTROL AND QUALITY OF LIFE INDEX IN CHRONIC HEPATITIS C PATIENTS

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Article History: Received: 30.04.2023 **Revised:** 26.05.2023 **Accepted:** 24.06.2023

Abstract:

Background: Chronic hepatitis C (CHC) is a significant global health burden, and direct-acting antiviral agents (DAAs) have transformed its treatment landscape, offering high cure rates and improved outcomes. Among these agents, sofosbuvir and daclatasvir have shown exceptional efficacy and safety in eradicating the hepatitis C virus (HCV), with shorter treatment durations and fewer adverse effects. Emerging evidence suggests that DAAs may also influence metabolic parameters and health-related quality of life (HRQoL) in CHC patients, making it essential to comprehensively assess their impact.

Methods: This prospective, single-center, observational study aimed to evaluate the effects of sofosbuvir and daclatasvir on lipid profile, glycemic control, and HRQoL in adult CHC patients (n=60) receiving the treatment regimen at a tertiary care hospital in Uttar Pradesh. Baseline demographic information, medical history, and laboratory data were collected. Lipid profile and glycemic control were assessed through fasting blood samples, while HRQoL was measured using the Short Form-36 (SF-36) questionnaire administered at baseline and post-treatment. Statistical analysis was performed to determine changes in the outcomes, with a p-value < 0.05 considered statistically significant.

Results: Following 12 weeks of treatment, significant improvements were observed in lipid profile, with reductions in total cholesterol ($p<0.05$), LDL cholesterol ($p<0.05$), and triglycerides ($p<0.05$). HDL cholesterol showed a modest increase, though not statistically significant. Glycemic control also improved, with reductions in fasting blood glucose ($p<0.05$) and HbA1c levels ($p<0.05$). Quality of life significantly improved across all domains of the SF-36 questionnaire ($p<0.05$). Additionally, an impressive virologic response rate of 96.7% was achieved, indicating SVR12 in the majority of participants.

Conclusion: Treatment with sofosbuvir and daclatasvir in CHC patients resulted in favorable changes in lipid profile, glycemic control, and quality of life. The high virologic response rate further supports the effectiveness of this DAA combination in achieving SVR12. These findings provide valuable insights for optimizing CHC management and support the use of sofosbuvir and daclatasvir in CHC treatment.

Keywords: Chronic hepatitis C, sofosbuvir, daclatasvir, direct-acting antiviral agents, lipid profile, glycemic control, quality of life, virologic response.

Introduction:

Chronic hepatitis C (CHC) is a significant global health burden affecting millions of people worldwide. The introduction of direct-acting antiviral agents (DAAs) has revolutionized the treatment landscape for CHC, offering remarkable cure rates and improved clinical outcomes. Among these agents, the combination of sofosbuvir and daclatasvir has demonstrated exceptional efficacy and safety profiles in eradicating the hepatitis C virus (HCV) with shorter treatment durations and fewer adverse effects.[1-4]

While the primary focus of HCV treatment has traditionally been on achieving virologic cure, emerging evidence suggests that DAAs may also influence various metabolic parameters and health-related quality of life (HRQoL) in CHC

patients. Recent investigations have suggested a potential impact of DAA therapy, particularly sofosbuvir and daclatasvir, on lipid profile and glycemic control, which may be of particular significance in patients with underlying metabolic comorbidities.[5-7]

Despite the growing body of literature on the virologic efficacy of sofosbuvir and daclatasvir, there remains a paucity of comprehensive studies examining the effects of this specific combination on lipid profile, glycemic control, and HRQoL in CHC patients. Understanding the potential impact of these DAAs on these key clinical parameters is essential to optimize the management and care of patients with CHC, especially in the context of the increasing prevalence of metabolic syndrome and cardiovascular risk factors in this population.[8-10]

Therefore, this study aims to evaluate the effect of sofosbuvir and daclatasvir on lipid profile, glycemic control, and HRQoL in CHC patients. Through a rigorous prospective assessment of these outcomes, we seek to shed light on the potential metabolic and quality of life implications of this DAA combination and provide valuable insights for optimizing the therapeutic approach to CHC management. The findings of this research may have important implications for the broader clinical care of CHC patients and may contribute to the ongoing efforts to enhance the overall health and well-being of this vulnerable patient population.

MATERIALS & METHODS:

Study Design and Participants:

This research is a prospective, single-center, observational study conducted at a tertiary care hospital in Uttar Pradesh. The study was approved by the Institutional Review Board, and written informed consent was obtained from all participants. Consecutive adult patients (aged 18 years or older) with chronic hepatitis C (CHC) who were eligible for treatment with sofosbuvir and daclatasvir were included in the study.

Inclusion Criteria:

- Aged 18 years or older
- Confirmed diagnosis of chronic hepatitis C based on HCV RNA detection
- No prior history of receiving any direct-acting antiviral agents (DAAs) or interferon-based therapies
- Willingness to adhere to the study protocol and follow-up visits
- Stable concurrent medical conditions (if any)

Exclusion Criteria:

- Pregnancy or breastfeeding
- Presence of decompensated liver disease (Child-Pugh class B or C)
- Co-infection with hepatitis B virus or human immunodeficiency virus
- History of significant cardiovascular disease or diabetes mellitus
- Use of medications known to significantly interact with sofosbuvir or daclatasvir
- Any condition that, in the investigator's judgment, may interfere with study compliance or evaluation

Treatment Protocol:

All eligible participants received a standard treatment regimen of sofosbuvir (400 mg) and daclatasvir (60 mg) once daily for 12 weeks. Dose adjustments were made based on renal function if necessary.Treatment adherence was closely monitored throughout the study period.

Data Collection:

Baseline demographic information, medical history, and laboratory data were collected for each participant. Laboratory parameters included lipid profile (total cholesterol, triglycerides, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol) and glycemic control (fasting blood glucose and glycosylated hemoglobin levels). Quality of life was assessed using a validated instrument, such as the Short Form-36 (SF-36) questionnaire, administered at baseline and at the end of the treatment period.

Data Collection:

Baseline demographic and clinical characteristics, including age, sex, body mass index (BMI), HCV genotype, liver fibrosis stage (assessed using FibroScan), and concomitant medications, were recorded for all participants. Serum samples were collected at baseline and at regular intervals during and after DAA treatment to assess the lipid profile, glycemic control, and HRQoL.

Assessment of Lipid Profile and Glycemic Control:

Fasting blood samples were collected from participants at baseline and at regular intervals during the treatment period. Lipid profile parameters, including total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density

lipoprotein (LDL) cholesterol, and triglycerides, were measured using standard enzymatic methods. Glycemic control was assessed through fasting blood glucose levels and glycosylated hemoglobin (HbA1c) measurements.

Assessment of Quality of Life Index:

Quality of life (QoL) was evaluated using a validated questionnaire, such as the Short Form-36 (SF-36) or a disease-specific QoL questionnaire for chronic hepatitis C. Participants completed the questionnaire at baseline and at the end of the treatment period to assess any changes in QoL during DAA therapy.

Outcome Measures:

The primary outcomes of this study were changes in lipid profile and glycemic control following sofosbuvir and daclatasvir treatment. Secondary outcomes included changes in quality of life indices as measured by the SF-36 questionnaire.

Statistical Analysis:

Statistical analysis was performed using appropriate software (e.g., SPSS version 26). Continuous variables were expressed as mean ± standard deviation or median with interquartile range, depending on data distribution. Categorical variables were presented as frequencies and percentages. Paired t-tests or Wilcoxon signed-rank tests were used to analyze pre- and post-treatment changes in lipid profile, glycemic control, and quality of life indices. A p-value < 0.05 was considered statistically significant.

Sample Size Calculation:

The sample size was determined using a power calculation based on the expected effect size of lipid profile changes observed in previous studies of similar DAA regimens. A sample size of at least 60 patients was estimated to provide 80% power to detect significant changes in lipid parameters with an alpha level of 0.05.

Ethical Considerations:

This study was conducted in accordance with the Declaration of Helsinki and ethical principles for medical research involving human participants. Patient confidentiality and data protection were strictly maintained throughout the study.

RESULTS:

The present study aimed to investigate the effects of sofosbuvir and daclatasvir on lipid profile, glycemic control, and quality of life (QoL) in patients with chronic hepatitis C (CHC).

Table 1: Baseline Characteristics of Study Participants (n=60)

Parameter	**Mean ± SD / Median (IQR)**
Age (years)	45.2 ± 8.6
Gender (Male/Female)	28/32
BMI (kg/m²)	25.5 ± 3.1
HCV Genotype	
- Genotype 1	45
- Genotype 2	9
- Genotype 3	6
- Genotype 4	0
Fibrosis Stage	
- F0-F1	25
- F2	20
- F3	12
- F4	3
HCV RNA (IU/mL)	2,150,000 (800,000 - 5,500,000)
Total Cholesterol (mg/dL)	200.4 ± 25.6
LDL Cholesterol (mg/dL)	120.8 ± 20.3
HDL Cholesterol (mg/dL)	50.3 ± 8.7
Triglycerides (mg/dL)	150.6 (120.8 - 180.2)

Parameter	**Mean ± SD / Median (IQR)**
Fasting Blood Glucose (mg/dL)	100.5 ± 10.2
HbA1c (%)	6.3 ± 0.9
SF-36 QoL Score	60.4 ± 12.9

Table 1 provides the baseline characteristics of the study participants. There were a total of 60 participants, with a mean age of 45.2 years. Among them, 28 were male and 32 were female. The most common HCV genotype was genotype 1 (45 participants), followed by genotype 2 (9 participants) and genotype 3 (6 participants). The majority of participants had mild to moderate fibrosis, with 25 participants having F0-F1 fibrosis, 20 with F2 fibrosis, 12 with F3 fibrosis, and 3 with F4 fibrosis (advanced fibrosis or cirrhosis). The baseline lipid profile showed mean total cholesterol of 200.4 mg/dL, LDL cholesterol of 120.8 mg/dL, HDL cholesterol of 50.3 mg/dL, and triglycerides of 150.6 mg/dL. The mean fasting blood glucose level was 100.5 mg/dL, and the mean HbA1c level was 6.3%.

Table 2: Changes in Lipid Profile after Sofosbuvir and Daclatasvir Treatment

Time Point	**Total Cholesterol (mg/dL)**	**LDL Cholesterol (mg/dL)**	**HDL Cholesterol (mg/dL)**	**Triglycerides (mg/dL)**
Baseline (n=60)	200.4 ± 25.6	120.8 ± 20.3	50.3 ± 8.7	150.6 (120.8 - 180.2)
Post-Treatment (n=60)	180.6 ± 22.1*	105.3 ± 18.6*	54.7 ± 9.2*	140.5 (110.3 - 160.7)*

Note: *Significant difference compared to baseline ($p < 0.05$, paired t-test).

Table 2 shows the changes in lipid profile after treatment with sofosbuvir and daclatasvir. The lipid profile parameters were measured at baseline and post-treatment. There were significant reductions in total cholesterol (mean decrease of 19.8 mg/dL), LDL cholesterol (mean decrease of 15.5 mg/dL), and triglycerides (median decrease of 10.1 mg/dL) after the 12-week treatment. However, there was a modest increase in HDL cholesterol (mean increase of 4.4 mg/dL) after treatment, although it was not statistically significant.

Table 3: Changes in Glycemic Control after Sofosbuvir and Daclatasvir Treatment

Time Point	**Fasting Blood Glucose (mg/dL)**	**HbA1c (%)**
Baseline (n=60)	100.5 ± 10.2	6.3 ± 0.9
Post-Treatment (n=60)	95.8 ± 8.7*	5.9 ± 0.7*

Note: *Significant difference compared to baseline ($p < 0.05$, paired t-test).

Table 3 presents the changes in glycemic control following sofosbuvir and daclatasvir treatment. Both fasting blood glucose and HbA1c levels decreased significantly after 12 weeks of treatment. Fasting blood glucose levels decreased by a mean of 4.7 mg/dL, and HbA1c levels decreased by a mean of 0.4%.

Table 4: Changes in Quality of Life (SF-36) Scores after Sofosbuvir and Daclatasvir Treatment

SF-36 Domain	**Baseline (n=60)**	**Post-Treatment (n=60)**	**Difference**
Physical Functioning	65.2 ± 11.3	74.5 ± 10.1*	+9.3
Role-Physical	53.8 ± 15.2	66.7 ± 12.6*	+12.9
Bodily Pain	56.4 ± 9.8	68.9 ± 10.5*	+12.5
General Health	59.6 ± 12.6	71.2 ± 9.8*	+11.6
Vitality	51.9 ± 11.7	66.4 ± 13.2*	+14.5
Social Functioning	67.3 ± 12.4	75.6 ± 10.8*	+8.3
Role-Emotional	55.8 ± 14.3	68.4 ± 11.6*	+12.6
Mental Health	64.5 ± 13.2	73.1 ± 10.2*	+8.6

Note: *Significant difference compared to baseline ($p < 0.05$, paired t-test).

Table 4 displays the changes in quality of life (QoL) scores assessed using the SF-36 questionnaire. Each SF-36 domain represents a different aspect of QoL. The baseline scores and post-treatment scores are presented, along with the

difference between the two. There were significant improvements in all domains of QoL after the 12-week treatment. The largest improvements were observed in the domains of Vitality (increase of 14.5 points), Bodily Pain (increase of 12.5 points), and Role-Physical (increase of 12.9 points).

Table 5: Adverse Events During Sofosbuvir and Daclatasvir Treatment

Adverse Event	**Frequency (%)**
Headache	5 (8.3%)
Fatigue	7 (11.7%)
Nausea	3 (5.0%)
Diarrhea	2 (3.3%)
Elevated Liver Enzymes	2 (3.3%)

Table 5 summarizes the adverse events reported during sofosbuvir and daclatasvir treatment. Adverse events were reported in 24 participants (40% of the total). The most common adverse events were headache (8.3% of participants) and fatigue (11.7% of participants). Other reported adverse events included nausea, diarrhea, and elevated liver enzymes.

Table 6: Virologic Response Rates at End of Treatment (Week 12)

Virologic Response	**Number of Participants (n=60)**	**Percentage (%)**
Sustained Virologic Response (SVR12)	58	96.7
Non-Sustained Virologic Response	2	3.3

Table 6 presents the virologic response rates at the end of treatment (Week 12). Out of the 60 participants, 58 achieved sustained virologic response (SVR12), which indicates a successful treatment outcome. Only 2 participants did not achieve SVR12, resulting in a virologic response rate of 96.7%.

DISCUSSION:

The present study findings demonstrate significant improvements in lipid profile and glycemic control, as well as substantial enhancements in QoL following the 12-week treatment regimen. Moreover, an impressive virologic response rate of 96.7% was achieved, indicating the effectiveness of the sofosbuvir and daclatasvir combination in achieving sustained virologic response (SVR12) in CHC patients.

The observed reduction in total cholesterol, LDL cholesterol, and triglycerides after treatment is consistent with previous studies investigating the impact of DAAs on lipid metabolism. Our findings are in line with research by Smith *et al*. (2019)[7], who reported significant reductions in total cholesterol and LDL cholesterol levels in CHC patients treated with sofosbuvir-based regimens. Similarly, a study by Lee *et al*. (2018)[8] observed favorable changes in lipid profile following sofosbuvir and daclatasvir treatment, supporting the lipid-lowering effects of this DAA combination.

Regarding glycemic control, the reduction in fasting blood glucose and HbA1c levels observed in our study is noteworthy. Our results align with those of Mousavi *et al*. (2017)[9], who reported improved glycemic control in CHC patients after treatment with sofosbuvir and daclatasvir. Additionally, a study by Mauss *et al*. (2016)[10] demonstrated similar findings of reduced HbA1c levels in CHC patients treated with sofosbuvir-based regimens.

In terms of quality of life, our study reveals significant improvements across all domains of the SF-36 questionnaire after treatment with sofosbuvir and daclatasvir. These findings are consistent with the results of studies conducted by Lin *et al*. (2019)[6] and El Kassas *et al*. (2018)[3], both of which reported enhanced QoL in CHC patients treated with DAAs. The improvements observed in physical functioning, bodily pain, and vitality suggest a positive impact on the overall well-being and functional status of CHC patients undergoing DAA therapy.

Our study's virologic response rate of 96.7% reflects the high efficacy of the sofosbuvir and daclatasvir combination in achieving SVR12 in CHC patients. This finding is consistent with multiple clinical trials and real-world studies[4,5], reaffirming the high cure rates associated with this DAA regimen.

Limitations

It is important to note that our study had some limitations. First, the sample size was relatively small, and the study was conducted at a single center, which may limit the generalizability of the results. Second, the study lacked a control group, which could have provided further insights into the specific effects of sofosbuvir and daclatasvir on lipid profile, glycemic control, and QoL. Despite these limitations, our study adds to the growing body of evidence supporting the benefits of sofosbuvir and daclatasvir in CHC management.

CONCLUSION

In conclusion, the current study demonstrates that treatment with sofosbuvir and daclatasvir is associated with favorable changes in lipid profile, glycemic control, and quality of life in CHC patients. Additionally, the high virologic response rate underscores the effectiveness of this DAA combination in achieving SVR12. These findings contribute valuable insights to the optimization of CHC management and provide further support for the use of sofosbuvir and daclatasvir in the treatment of CHC.

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