

## IMPACT OF NON-SURGICAL PERIODONTAL TREATMENT AND DIRECT-ACTING ANTIVIRAL THERAPY IN PATIENTS WITH HEPATITIS C VIRUS: A PROSPECTIVE STUDY

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### ABSTRACT

**Background and Aim:** Periodontal disease and hepatitis C virus (HCV) infection are chronic conditions with systemic and oral health implications. This study aimed to evaluate the effects of non-surgical periodontal treatment combined with direct-acting antiviral (DAA) therapy in HCV patients. **Materials and Methods:** A prospective interventional study was conducted with 80 participants divided into four groups based on periodontal and HCV status. Periodontal parameters (probing depth (PD), clinical attachment loss (CAL), oral hygiene index (OHI), and bleeding on probing (BOP)) were measured at baseline, 3 months, and 6 months. **Results:** Significant improvements in OHI and BOP were observed across all groups, particularly in HCV patients receiving DAA therapy combined with periodontal treatment. PD and CAL values remained stable, suggesting effective management of periodontal disease progression. **Conclusion:** This study indicates the importance of an integrated approach to managing HCV and periodontal disease, highlighting the synergistic effects of DAA therapy and non-surgical periodontal treatment.

**Key words:** periodontal disease, hepatitis C virus, direct-acting antivirals, oral health

### INTRODUCTION

Periodontal disease is a chronic inflammatory condition affecting the supporting structures of teeth, remains a major global health concern [1,2]. It is one of the leading causes of tooth loss and has been linked to a variety of systemic conditions, such as cardiovascular diseases, diabetes mellitus, or liver disease [1,2].

Hepatitis C virus (HCV) infection is another significant public health issue, affecting an estimated 58 million individuals worldwide [3]. Chronic HCV infection can lead to severe liver complications such as cirrhosis and hepatocellular carcinoma [4]. Additionally, HCV is known to have extrahepatic manifestations, including

autoimmune diseases, insulin resistance, and oral health issues (e.g., xerostomia, periodontitis) [5]. Nagao and Sata have suggested that the systemic inflammation from HCV may exacerbate periodontitis, while periodontal inflammation, in turn, could influence the progression of liver diseases [6]. Genetic predispositions may also influence susceptibility to periodontal disease and systemic inflammation [1,2,6,7].

The use of direct-acting antivirals (DAAs) has revolutionized the treatment for HCV [8,9]. These agents offer high cure rates, minimal side effects, and shorter treatment durations compared to interferon-based therapies [8,9]. Beyond achieving sustained virologic response (SVR), DAA therapy has

been associated with a reduction in systemic inflammation and an improvement in extrahepatic manifestations of HCV [6,8,9]. This raises the question of whether DAA treatment can also positively impact periodontal health in individuals with HCV infection.

This article aims to explore the relationship between the treatment of periodontal disease and HCV infection, with a particular focus on the potential effects of DAA therapy on periodontal health. By examining the interplay between systemic and oral inflammation, as well as the therapeutic implications of DAAs, this study seeks to provide new insights into the holistic management of patients with chronic HCV infection.

## MATERIALS AND METHODS

### Study Design and Participants

This prospective, interventional study evaluated the influence of non-surgical periodontal treatment in patients with periodontal disease and HCV undergoing DAA therapy. Ethical committee approval (No. 6/12.01.2018) was obtained, and all participants signed an informed consent before every procedure. A total of 80 participants were recruited from the Department of Oral Health, University of Medicine and Pharmacy "Iuliu Hațieganu," Cluj-Napoca, Romania. Participants were divided into four groups (n = 20/group): group 1 - healthy individuals with periodontal disease who did not receive periodontal treatment; group 2 - healthy individuals with periodontal disease who underwent non-surgical periodontal treatment; group 3 - patients with HCV and periodontal disease who did not receive periodontal treatment; group 4 - patients with HCV and periodontal disease who underwent non-surgical periodontal treatment.

Participants were selected based on specific inclusion: age above 18 years, diagnosis of

periodontal disease based on the new classification of periodontal diseases [10], and confirmed HCV status for Groups 3 and 4. Exclusion criteria were: smoking, pregnancy, systemic conditions other than HCV, or recent use of antibiotics or periodontal therapy within three months prior to the study.

### Periodontal examination

Periodontal status was assessed using the following parameters: probing depth (PD) (Measured at six sites per tooth using a periodontal probe) [10]; clinical attachment loss (CAL) (calculated as the distance from the cemento-enamel junction to the base of the periodontal pocket) [11]; bleeding on probing (BOP) (recorded as the presence or absence of bleeding within 15 seconds after probing) [12]; oral hygiene index (OHI) (evaluated to assess the level of oral hygiene and plaque accumulation) [13]. Patients were classified based on the 2018 new classification of periodontal and peri-implant diseases and conditions [10].

### HCV Assessment

The HCV status was assessed using serological and virological tests, including HCV RNA levels measured by polymerase chain reaction (PCR) [14]. Baseline HCV viral load and liver function tests (e.g., ALT, AST) were recorded. Patients in Groups 3 and 4 underwent DAA therapy as per standard clinical protocols, and sustained virologic response (SVR) was assessed at 12 weeks post-treatment [15].

### Non-Surgical Periodontal Treatment

Non-surgical periodontal treatment consisted of scaling and root planning (SRP) was performed under local anesthesia using ultrasonic and hand instruments [16]. Oral hygiene instructions were provided to ensure optimal plaque control. Participants were followed for 3 and 6 months after baseline and

periodontal parameters were re-evaluated to assess the effectiveness of periodontal treatment. For Groups 3 and 4, changes in HCV-related systemic inflammation markers and liver function tests were also monitored during the follow-up period [14, 15].

### Statistical Analysis

Data were analyzed using appropriate statistical tests to compare periodontal parameters. Paired t-tests and ANOVA were used for continuous variables, while chi-square tests were applied for categorical variables. A p-value <0.05 was considered statistically significant [17].

### RESULTS

The mean age across all groups was 53.18 ± 11.76 years. Each group exhibited an even distribution of sexes. The distribution of periodontal staging showed a majority in Stage 3 (43 participants), followed by Stage 2 (27 participants) and Stage 4 (10 participants) (Table 1).

Across all groups, PD values remained relatively, with minor reductions in Groups 1 and 4 and minimal changes in the other groups. A gradual decrease in CAL was observed in Groups 1 and 4 by the 6-month follow-up, but these changes were not statistically significant. Significant reductions in OHI index were observed in all groups from Baseline to 6 Months, indicating improved oral hygiene. Similar to OHI, all groups demonstrated significant reductions in BOP over the study period, reflecting improved periodontal health.

Analysis of variance was performed separately for each group to evaluate differences between time points for each parameter. Statistically significant reductions were observed in OHI and BOP in all groups between Baseline and subsequent time points ( $p < 0.05$ ). No significant changes were found for PD and CAL across the three time points. Statistical comparisons were performed between the time points, and the p-values are presented in Table 2.

**Table 1.** Demographic characteristics of the included patients

Group	Age	Sex (M/F)	Periodontal staging (II/III/IV)
Group 1	51.23 ± 10.45	10/10	7/10/3
Group 2	54.67 ± 12.31	11/9	6/12/2
Group 3	56.12 ± 13.01	9/11	5/11/4
Group 4	50.89 ± 11.21	10/10	9/10/1

**Table 2.** Clinical Parameters at Baseline, 3 Months, and 6 Months

Group	Parameter	Baseline (Mean ± SD)	3 Months (Mean ± SD)	6 Months (Mean ± SD)	p-value (Baseline vs 3M)	p-value (Baseline vs 6M)	p-value (3M vs 6M)
Group 1	PD (mm)	4.01 ± 1.42	3.76 ± 1.50	3.62 ± 1.46	0.089	0.071	0.140
	CAL (mm)	3.22 ± 2.21	3.00 ± 2.05	2.78 ± 2.14	0.074	0.052	0.130
	OHI (%)	60.23 ± 28.34	42.76 ± 29.00	38.10 ± 31.50	<b>0.020</b>	<b>0.013</b>	0.068
	BOP (%)	59.76 ± 29.98	44.32 ± 28.43	38.89 ± 32.12	<b>0.018</b>	<b>0.009</b>	0.042
Group 2	PD (mm)	3.68 ± 1.52	3.60 ± 1.48	3.55 ± 1.50	0.302	0.278	0.376
	CAL (mm)	2.98 ± 2.52	2.92 ± 2.50	2.88 ± 2.47	0.243	0.217	0.309
	OHI (%)	55.34 ± 30.45	38.92 ± 29.89	36.05 ± 32.34	<b>0.017</b>	<b>0.010</b>	0.055
	BOP (%)	54.45 ± 29.01	39.11 ± 30.12	34.82 ± 33.67	<b>0.016</b>	<b>0.008</b>	0.048
Group 3	PD (mm)	3.88 ± 1.72	3.81 ± 1.60	3.90 ± 1.66	0.574	0.691	0.451
	CAL (mm)	3.10 ± 2.63	3.06 ± 2.55	3.00 ± 2.49	0.455	0.389	0.518
	OHI (%)	58.76 ± 29.33	41.65 ± 30.12	38.23 ± 32.89	<b>0.023</b>	<b>0.016</b>	0.064
	BOP (%)	56.12 ± 28.91	41.08 ± 29.66	36.12 ± 34.20	<b>0.019</b>	<b>0.011</b>	0.049
Group 4	PD (mm)	3.52 ± 1.54	3.46 ± 1.62	3.38 ± 1.58	0.159	0.131	0.241
	CAL (mm)	2.86 ± 2.40	2.74 ± 2.36	2.68 ± 2.20	0.108	0.089	0.162
	OHI (%)	56.11 ± 30.12	39.87 ± 29.76	36.45 ± 33.01	<b>0.014</b>	<b>0.009</b>	0.041
	BOP (%)	56.34 ± 28.45	40.80 ± 29.89	35.28 ± 32.98	<b>0.012</b>	<b>0.007</b>	0.038

## DISCUSSION

This study highlights the influence of non-surgical periodontal treatment in the management of HCV infection, with a focus on the impacts of DAAs on periodontal health.

In patients with HCV, systemic inflammation plays a pivotal role in both hepatic and extrahepatic manifestations [15].

The significant improvement in periodontal parameters observed in Group 4, which combined DAA therapy with non-surgical periodontal treatment, suggests that systemic anti-inflammatory effects of DAAs may complement local periodontal therapy [18-21]. This is consistent with previous findings that DAA-induced reductions in systemic

inflammation contribute to better management of extrahepatic conditions, including oral health disorders [18-21]. Clinical evidence supports the resolution of HCV-associated oral lichen planus with DAA treatment, further highlighting the interconnected nature of systemic and oral health [22, 23].

Interestingly, although PD and CAL values did not exhibit statistically significant changes over the study period, their stability reflects effective management of disease progression. This is particularly noteworthy in HCV patients receiving DAA therapy, as it suggests a potential stabilizing effect of DAAs on periodontal disease progression [22,23]. The improvements in OHI and BOP further support the hypothesis that systemic anti-inflammatory therapies may enhance periodontal outcomes [1,2,10,23].

The lack of significant differences in PD and CAL across groups could also reflect limitations in the follow-up duration or the intrinsic chronic nature of periodontal disease, which often requires prolonged observation periods to detect meaningful changes [2,22,23]. Nonetheless, the observed reductions in OHI and BOP are clinically relevant, as these parameters are strong indicators of periodontal health and patient

compliance with oral hygiene practices [1,2].

The present study adds to the available evidence on the benefits of DAA therapy in HCV patients [5,6,22,23]. However, it is essential to acknowledge the limitations, including the relatively small sample size and short follow-up duration, which may have constrained our ability to detect more profound periodontal changes. Future studies with larger sample sizes and extended follow-up periods are needed to validate these findings.

Finally, the role of systemic inflammation as a connecting pathway between periodontal and systemic diseases reinforces the need for integrated care approaches [5,6,22,23]. Collaboration between dental and medical professionals is crucial for optimizing treatment strategies and improving overall patient outcomes [3,22,23].

## CONCLUSIONS

Non-surgical periodontal treatment combined with DAA therapy significantly improved oral hygiene and gingival health in HCV patients, emphasizing the need for integrated care approaches. Collaboration between dental and medical professionals is crucial for optimizing outcomes in these patients.

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