ADJUNCTIVE EFFECT OF 0.2% CHLORHEXIDINE-HYALURONIC ACID GEL IN NON-SURGICAL TREATMENT OF POSTERIOR-TEETH PERIODONTITIS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS: A SPLIT-MOUTH STUDY

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Periodontitis is more common and often more severe in patients with type 2 diabetes, especially in posterior teeth, where anatomical complexity may hinder plaque control and treatment. This split-mouth controlled clinical trial evaluated the adjunctive effect of locally delivered 0.2% chlorhexidine-hyaluronic acid gel in patients with type 2 diabetes and periodontitis involving posterior teeth. Thirty-three eligible patients were consecutively recruited at the Dental Clinic of Phu Nhuan District General Hospital, Ho Chi Minh City. All participants received non-surgical periodontal therapy on both sides, while the intervention side additionally received subgingival 0.2% chlorhexidine-hyaluronic acid gel at baseline and day 7. Baseline characteristics included a mean age of 64.1 ± 10.5 years old, diabetes duration of 7.3 ± 4.0 years, and HbA1c of 7.2 ± 1.4%. Periodontal status was comparable between sides at baseline. Both groups showed significant improvement in all periodontal parameters at 1 and 3 months. However, the intervention side demonstrated greater short-term improvement, with lower periodontal pocket count, better clinical periodontal parameters, and a more marked reduction in periodontitis severity. Adjunctive local 0.2% chlorhexidine-hyaluronic acid gel enhanced the short-term effectiveness of non-surgical periodontal therapy in this high-risk population.

Keywords: Type 2 diabetes mellitus, periodontitis, posterior teeth, chlorhexidine-hyaluronic acid gel, non-surgical periodontal therapy.

I. INTRODUCTION

Periodontitis and type 2 diabetes mellitus (T2DM) have a well-established bidirectional relationship, in which diabetes increases periodontal susceptibility through impaired host response, collagen metabolism, oxidative stress, and microvascular dysfunction, while periodontitis may worsen systemic inflammation and glycemic control.[1,2] Posterior teeth are clinically important in this context because multirooted molars have furcation anatomy that favors plaque retention, limits access for instrumentation, and makes daily plaque control more difficult. In patients with T2DM, these local anatomical challenges may further contribute to periodontal destruction, tooth mobility, and functional impairment.[1,3,4]

Although non-surgical periodontal therapy remains the cornerstone of treatment, adjunctive local agents are increasingly used to enhance biofilm control and early periodontal healing. Chlorhexidine is a well-established local antiseptic, whereas hyaluronic acid may support tissue repair and modulate inflammation. Nevertheless, evidence regarding adjunctive local therapy in patients with T2DM

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remains inconsistent, particularly for hyaluronic acid-based approaches.[5-7] Lin et al. found that, in patients with T2DM and periodontitis, the strongest evidence among locally delivered adjuncts favored metformin and statins, whereas evidence for other agents remained less consistent.[6] Dababseh et al. reported additional benefits of topical hyaluronic acid in non-surgical periodontal therapy, but also noted moderate evidence quality and substantial heterogeneity.[8] In T2DM populations, Devina et al. and Al-Abbadi et al. found improvement after periodontal therapy, but the additional benefit of 0.2% hyaluronic acid gel was limited or not consistently significant across CAL, PPD, BOP, biomolecular, and microbiological outcomes.[9,10] Given the anatomical difficulty of posterior teeth and the limited data on repeated subgingival application of combined 0.2% chlorhexidine-hyaluronic acid gel in T2DM patients, further clinical evaluation in this specific setting is warranted.[3] Therefore, in patients with T2DM and posterior-teeth periodontitis, this study primarily aimed to evaluate the short-term efficacy of adjunctive local 0.2% chlorhexidine-hyaluronic acid gel in conjunction with non-surgical periodontal therapy, while also describing the baseline clinical and radiographic characteristics of periodontal lesions in this population.

II. METHODS

1. Study population and settings

All patients with T2DM who were diagnosed with periodontitis affecting the posterior teeth and attended the Dental Clinic of Phu Nhuan District General Hospital, Ho Chi Minh City, for examination and treatment from July 2025 to January 2026.

Inclusion criteria were patients who had been diagnosed with and were receiving treatment for T2DM, were concurrently diagnosed with moderate to severe periodontitis in the posterior teeth according to the CDC/AAP case definition, and had periodontal lesions indicated for initial non-surgical periodontal therapy, including supragingival and subgingival debridement, scaling, and root planing. Eligible patients had not used antibiotics continuously within the previous 3 months and agreed to participate in the study.

Exclusion criteria were patients with a history of systemic diseases related to chromosomal abnormalities or conditions affecting periodontal wound healing, such as autoimmune diseases, HIV infection, or leukemia; patients who were pregnant or breastfeeding; individuals with acute oral infections; allergic to chlorhexidine (CHX) or hyaluronic acid (HA); with periodontal lesions associated with endodontic disease or other oral diseases; patients who had received any periodontal treatment within the previous 6 months; or uncooperative, withdrew during the study, or failed to follow the study instructions.

2. Study design and variables

Study design

A split-mouth controlled clinical trial.

Sample size

Sample size was estimated for comparing two means using periodontal pocket depth as the main clinical parameter. The calculation was based on PPD data reported by Rajan et al., in which the mean PPD was 4.09 ± 1.38 mm in the control group and 3.21 ± 0.65 mm in the adjunctive hyaluronic acid group after scaling and root planing.[11] With a two-sided α of 0.05 and 80% power, the minimum required sample size was approximately 25. After allowing for an estimated 20% attrition rate, at least 32 participants were required. A non-probability consecutive sampling approach was used. All patients who met the eligibility criteria and attended the Dental Clinic of Phu Nhuan District

General Hospital during the study period were consecutively recruited until the end of the recruitment period. A total of 35 eligible patients were initially enrolled; however, 2 patients were lost to follow-up during the study period. Therefore, 33 patients completed the study and were included in the final analysis. Given the split-mouth design, each participant contributed one intervention side and one control side for within-patient comparison.

Variables

General characteristics included age, gender, chief complaint, regular dental scaling every 6 months, oral hygiene status, duration of T2DM, history of periodontal disease, tobacco smoking habit, and baseline glycated hemoglobin (HbA1c).

The clinical characteristics of periodontitis were assessed separately for the intervention and control sides and included the number of periodontal pockets, radiographic bone loss percentage, severity of bone loss, pattern of bone loss, periodontal pocket depth (PPD), gingival index (GI), bleeding on probing (BOP), gingival recession (GR), clinical attachment loss (CAL), and severity of periodontitis. The number of periodontal pockets was defined as the total number of periodontal pockets identified on each study side. Radiographic bone loss percentage was defined as the proportion of alveolar bone loss on periapical radiographs, expressed as a percentage. Severity of bone loss was categorized as moderate or severe, whereas the pattern of bone loss was classified as horizontal-angular, vertical-horizontal-angular, or vertical-horizontal. Radiographic bone loss severity was classified based on the percentage of alveolar bone loss relative to root length, including mild bone loss or cervical-third bone loss when bone loss was 1-33%, moderate bone loss or middle-third bone loss when bone loss was 34-66%, and severe bone loss or apical-third bone loss when bone loss was 67-100%. PPD was defined as the distance from the gingival margin to the base of the periodontal pocket and was expressed in millimeters. GI was used to assess gingival inflammation and was recorded as a clinical score, with higher values indicating more severe gingival inflammation. BOP was defined as the percentage of examined sites that bled after gentle periodontal probing. GR was defined as the distance from the cemento-enamel junction to the gingival margin and was expressed in millimeters. CAL was defined as the distance from the cemento-enamel junction to the base of the periodontal pocket and was expressed in millimeters. Severity of periodontitis was classified according to the CDC/AAP case definition as mild, moderate, or severe periodontitis. Mild periodontitis was defined as at least two interproximal sites with CAL of at least 3 mm and at least two interproximal sites with PPD of at least 4 mm on different teeth, or one site with PPD of at least 5 mm. Moderate periodontitis was defined as at least two interproximal sites with CAL of at least 4 mm on different teeth, or at least two interproximal sites with PPD of at least 5 mm on different teeth. Severe periodontitis was defined as at least two interproximal sites with CAL of at least 6 mm on different teeth and at least one interproximal site with PPD of at least 5 mm.[12,13]

Treatment outcomes were defined as the changes in the number of periodontal pockets and the main periodontal parameters, including PPD, GI, BOP, GR, and CAL, at 1 month and 3 months after treatment compared with baseline.

Study protocol

At baseline, all eligible participants underwent demographic and clinical data collection, periodontal examination, and

periapical radiographic assessment. Under the split-mouth design, each patient contributed two study sides with at least one eligible posterior tooth per side. Intervention allocation followed a prespecified enrollment-order sequence: the left half-mouth was assigned to the intervention group in odd-numbered patients and the right half-mouth in even-numbered patients; the contralateral side served as control. Therefore, no random sequence generation or allocation concealment was performed. The allocation sequence was determined before participant recruitment and was applied consecutively according to the order of enrollment. Both sides received standardized non-surgical periodontal therapy in the same treatment session, including supragingival and subgingival debridement with ultrasonic and hand instruments, root planing, and irrigation with 0.12% chlorhexidine. All procedures were performed by the same treating dentist following a standardized protocol. On the intervention side, 0.2% chlorhexidine-hyaluronic acid gel was delivered subgingivally into each eligible periodontal pocketuntil adequately filled using a sterile single-use 1-mL syringe, followed by placement of a resorbable periodontal dressing. On the control side, no adjunctive gel was applied, and the same periodontal dressing was placed after irrigation to ensure that both sides received comparable post-treatment coverage except for the adjunctive gel. Because the treating dentist had to apply the adjunctive gel only on the intervention side, operator blinding was not feasible. Oral hygiene instructions were provided to all participants. At day 7, treated sites were re-evaluated and irrigated; gel application was repeated once on the intervention side, whereas the control side received chlorhexidine irrigation alone. Follow-up periodontal assessments were performed at 1 and 3 months post-treatment. The same periodontal assessment procedure was used for both sides at all follow-up visits to minimize measurement variability. Periodontal outcome assessments were performed by an independent examiner who was not involved in the intervention procedure.

Data analysis and processing

All statistical analyses were performed using R version 4.5.0 (R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were summarized as mean and standard deviation (SD), whereas categorical variables were presented as frequencies and percentages. Baseline comparisons between the intervention and control sides were performed using the paired-samples t test for continuous variables and the McNemar test or marginal homogeneity test for paired categorical variables, as appropriate. Changes in periodontal outcomes over time, including baseline, 1 month, and 3 months after treatment, were analyzed using repeated-measures analysis of variance (repeated-measures ANOVA). When indicated, post hoc pairwise comparisons were performed to identify differences between time points. A two-sided p value of less than 0.05 was considered statistically significant.

3. Ethics approval

The study was approved by the Scientific Research Council and the Biomedical Research Ethics Committee of Can Tho University of Medicine and Pharmacy on June 30, 2025, under Approval No. 25.527.HV/PCT-HĐĐĐ.

III. RESULTS

A total of 33 eligible patients were enrolled during the study period, and their baseline characteristics are presented in Table 1.

Table 1. Baseline characteristics of 33 participants

Characteristics (n = 33)		Frequency (n)	Percentage (%)
Age (years), mean (SD) [Min - Max]		64.1 (10.5) [40 - 86]	
Gender, n (%)	Male	13	39.4
	Female	20	60.6
Chief complaint, n (%)	Gingival bleeding + tooth mobility	5	15.2
	Tooth sensitivity + tooth mobility	3	9.1
	Tooth mobility	18	55.5
	Routine dental check-up	7	21.2
Regular dental scaling every 6 months		6	18.2
Oral hygiene	Poor	21	63.6
	Needs improvement	12	36.4
Duration of T2DM (years), mean (SD) [Min - Max]		7.3 (4.0) [3 - 20]	
History of periodontal disease		31	93.9
Tobacco smoking habit		14	42.4
HbA1c, mean (SD) [Min - Max]		7.2 (1.4) [6.1 - 12.4]	

As shown in Table 1, the mean age of the participants was 64.1 ± 10.5 years old, and females accounted for a higher proportion than males (60.6% vs. 39.4%). Tooth mobility was the most common chief complaint (55.5%), while poor oral hygiene was observed in 63.6% of patients. The mean duration of T2DM was 7.3 ± 4.0 years, most participants had a history of periodontal disease (93.9%), 42.4% had a smoking habit, and the mean HbA1c was 7.2 ± 1.4%.

Table 2. Periodontal characteristics of the intervention and control sides

Characteristics	Intervention group	Control group	p
Number of periodontal pockets	16.88 (5.57)	17.15 (5.40)	0.393[a]
Radiographic bone loss percentage	44.06 (9.40)	44.36 (9.09)	0.535[a]
Severity of bone loss			0.999[b]
Moderate	7 (21.2)	6 (18.2)	

Characteristics	Intervention group	Control group	p
Severe	26 (78.8)	27 (81.8)	
Pattern of bone loss			0.317[c]
Horizontal, angular	28 (84.8)	27 (81.9)	
Vertical, horizontal, angular	4 (12.1)	4 (12.1)	
Vertical, horizontal	1 (3.0)	2 (6.1)	
Periodontal pocket depth (PPD)	3.40 (0.31)	3.41 (0.22)	0.862[a]
Gingival index (GI)	2.15 (0.38)	2.15 (0.38)	-
Percentage of BOP-positive sites (%BOP)	43.01 (8.31)	44.82 (10.80)	0.148[a]
Gingival recession (GR)	2.77 (0.31)	2.81 (0.36)	0.196[a]
Clinical attachment loss (CAL)	6.18 (0.49)	6.23 (0.44)	0.442[a]
Severity of periodontitis			0.999[b]
Moderate	31 (93.9)	31 (93.9)	
Severe	2 (6.1)	2 (6.1)	

[a]Paired Sample T test, [b]McNemar test, [c]Marginal Homogeneity test

Table 2 shows the baseline periodontal characteristics were comparable between the intervention and control sides, with no statistically significant difference in the number of periodontal pockets, radiographic bone loss percentage, severity and pattern of bone loss, PPD, GI, BOP, GR, CAL, or periodontitis severity (all $p > 0.05$). Severe bone loss was observed in most sites in both groups, whereas moderate periodontitis was the predominant clinical severity.

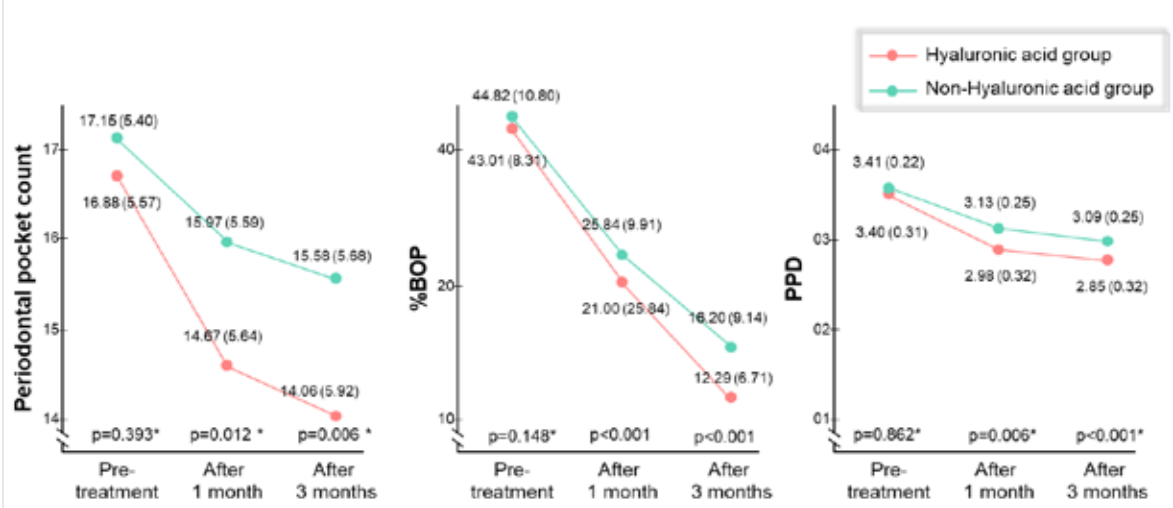

Figure 1a. Changes in periodontal pocket count and periodontal parameters before treatment and at 1 and 3 months after treatment

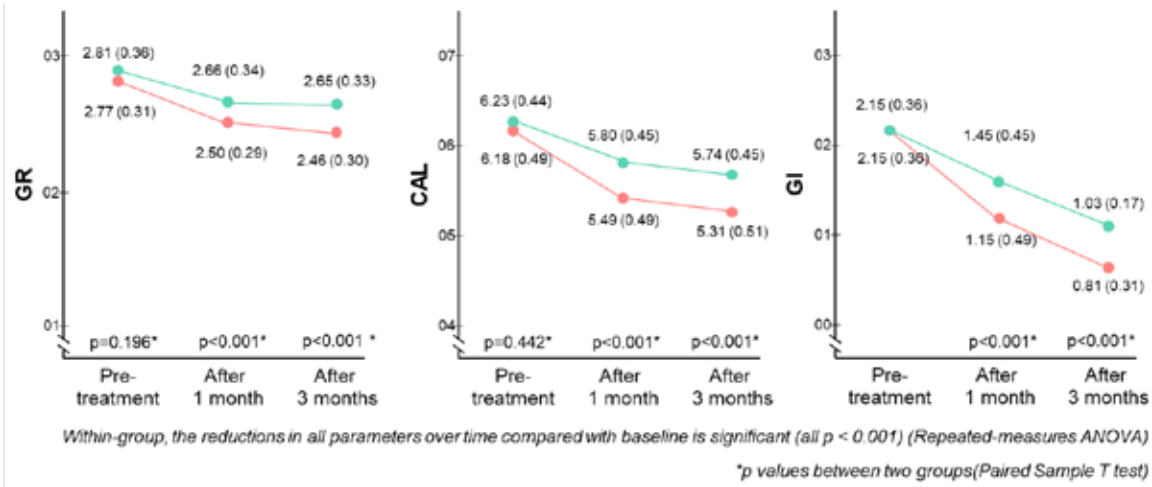

Figure 1b. Changes in periodontal pocket count and periodontal parameters before treatment and at 1 and 3 months after treatment

Figure 1 shows that all periodontal parameters improved over time in both groups, with significant reductions from baseline to 1 month and 3 months (all within-group p < 0.001). At baseline, no significant between-group differences were observed in the number of periodontal pockets, %BOP, PPD, GR, or CAL. However, at 1 month and 3 months, the hyaluronic acid group showed significantly greater improvements than the non-hyaluronic acid group, as reflected by lower periodontal pocket count, %BOP, PPD, GR, CAL, and GI values. Overall, the adjunctive use of hyaluronic acid was associated with superior short-term periodontal outcomes compared with control treatment alone.

Table 3. Changes in periodontal parameters from baseline to 3 months

Characteristic	Difference in change between 2 group, mean (95% CI)	p
Periodontal pocket count	1.24 (0.54 - 1.95)	0.001
%BOP, percentage points	2.10 (-0.28 - 4.49)	0.082
PPD, mm	0.23 (0.15 - 0.32)	<0.001
GR, mm	0.14 (0.09 - 0.19)	<0.001
CAL, mm	0.37 (0.26 - 0.49)	<0.001

At 3 months, the intervention group showed significantly greater reductions in periodontal pocket count, PPD, GR, and CAL than the control side, whereas the between-side difference in %BOP reduction was not statistically significant.

Table 4. Distribution of periodontitis severity at 1 and 3 months after treatment

Characteristics	Intervention group	Control group	p
	After 1 month		**0.046**
Mild	9 (27.3)	3 (9.1)	
Moderate	22 (66.7)	28 (84.8)	
Severe	2 (6.1)	2 (6.1)	
	After 3 months		**0.032**
Mild	15 (45.5)	10 (30.3)	
Moderate	18 (54.4)	22 (66.7)	
Severe	0 (0.0)	1 (3.0)	
	Marginal Homogeneity test		

As shown in Table 4, the distribution of periodontitis severity differed significantly between the two groups at both follow-up time points. At 1 month, the intervention group had a higher proportion of mild periodontitis than the control group (27.3% vs. 9.1%, p = 0.046). At 3 months, this difference became more pronounced, with mild periodontitis observed in 45.5% of the intervention group compared with 30.3% of the control group, while no severe case remained in the intervention group (p = 0.032). These findings suggest that adjunctive hyaluronic acid was associated with a more favorable improvement in periodontitis severity over time.

IV. DISCUSSION

This split-mouth controlled clinical trial showed that, in patients with T2DM and periodontitis affecting the posterior teeth, adjunctive subgingival chlorhexidine-hyaluronic acid gel used together with standardized non-surgical periodontal therapy was associated with a more favorable short-term clinical response than control treatment alone. Beyond improvement in individual periodontal indices, the intervention side also demonstrated a more favorable shift in periodontitis severity over follow-up. The additional benefit was most evident in the reduction of periodontal pocket count, PPD, GR, and CAL at 3 months, suggesting that the adjunctive gel mainly enhanced local periodontal stabilization rather than merely changing the overall severity category. From a clinical perspective, these findings suggest that a locally delivered chlorhexidine-hyaluronic acid gel may represent a practical chairside adjunct for posterior periodontal pockets in medically compromised patients, especially when early inflammation control and tissue stabilization are desirable and surgical therapy is not the first-line approach. Because the study used a split-mouth design, these findings should be interpreted primarily as local periodontal effects at the treated sides, rather than as patient-level systemic benefits.

The baseline periodontal profile observed in this study is biologically plausible and broadly consistent with previous literature on diabetes-associated periodontitis.[1] Singh et al. reported that more than 95% of patients with T2DM exhibited some degree of periodontal

destruction, highlighting the high periodontal burden in this population.[4] These findings support the notion that diabetes is not merely a background comorbidity but a major modifier of periodontal phenotype. Mechanistically, chronic hyperglycemia enhances advanced glycation end product signaling, impairs neutrophil function, alters collagen metabolism, and sustains a pro-inflammatory environment that accelerates connective tissue breakdown and bone loss.[1] The decision to focus on posterior teeth is also supported by furcation anatomy itself, since nearly half of molar furcations in one morphometric study did not allow appropriate engagement with standard area-specific curettes, emphasizing why posterior periodontal lesions can be particularly persistent and difficult to instrument. In the present study, the average HbA1c was elevated but not markedly uncontrolled, which may partly explain why the disease profile appeared clinically substantial yet not uniformly at the most destructive end of the spectrum.

The superior short-term outcomes associated with adjunctive chlorhexidine-hyaluronic acid gel are broadly in line with the evolving literature on hyaluronic acid in periodontal therapy, although the magnitude of benefit varies across studies and populations.[6,14] In the 2019 meta-analysis by Eliezer et al., hyaluronic acid used as an adjunct to non-surgical and surgical periodontal therapy was associated with additional clinical benefit.[15] More recently, Dababseh et al. reported pooled improvements in probing depth reduction and clinical attachment gain with topical hyaluronic acid adjunctive to non-surgical periodontal therapy, while also emphasizing the moderate quality and heterogeneity of the available evidence.[8] In contrast, Devina et al., in a double-blind randomized trial involving patients with periodontitis and T2DM, found that most groups improved after treatment but that between-group differences were generally not significant, except for clinical attachment loss.[10] Likewise, Al-Abbadi et al. studied 26 patients with controlled T2DM, HbA1c below 7%, and stage II periodontitis, and found significant improvements in both arms but no significant between-group differences in CAL, PPD, or BOP, whereas HbA1c decreased only in the HA group.[9] The stronger clinical separation seen in the present study may therefore relate to differences in disease phenotype and intervention design, including the focus on posterior teeth, the likelihood of deeper and anatomically more complex periodontal sites, and the repeated subgingival application of a chlorhexidine-containing gel rather than hyaluronic acid alone. This distinction is important because previous T2DM trials mainly evaluated hyaluronic acid alone, whereas the present intervention combined an antiseptic component with a wound-healing adjunct, which may be more relevant in posterior pockets where mechanical debridement is technically limited. This interpretation is biologically plausible because hyaluronic acid contributes hydration, cell migration, tissue repair, and inflammatory modulation, whereas chlorhexidine provides local antiseptic pressure against periodontal biofilm. In vitro, both hyaluronic acid and 0.2% chlorhexidine have demonstrated activity against Porphyromonas gingivalis, supporting the rationale for a dual-mechanism local approach.[5] At the same time, recent evidence indicates that local adjunctive therapies in T2DM remain heterogeneous across agents and outcomes, and not all adjuncts appear to yield the same magnitude of benefit. Therefore, the present findings should be viewed as supportive short-term clinical evidence rather than definitive proof of long-term superiority.

Several limitations should be acknowledged. First, the study included a relatively small

number of consecutively recruited patients from a single center, which may limit generalizability. Although 35 patients were initially enrolled, 2 were lost to follow-up, and the final analysis was based on 33 complete cases rather than a full intention-to-treat population. Second, the follow-up period was short and therefore does not allow conclusions regarding long-term stability, recurrence, retreatment needs, or tooth survival. Third, because the intervention combined chlorhexidine and hyaluronic acid in the same gel, the independent contribution of each component cannot be fully separated. In addition, microbiological or biomolecular outcomes were not assessed, so the potential mechanisms underlying the observed clinical improvement could not be directly evaluated. Fourth, although the split-mouth design reduced inter-individual confounding, side allocation followed a pre-specified enrollment-order rule rather than concealed randomization, and cross-over behavioral or biological influences within the same oral cavity cannot be fully excluded. Finally, the cohort represented patients with T2DM whose baseline HbA1c was, on average, only moderately elevated, so the findings should be extrapolated cautiously to individuals with poorer metabolic control or more generalized periodontal destruction. Because systemic inflammatory markers and longitudinal glycemic outcomes were not primary endpoints, the findings should be interpreted mainly as short-term local periodontal effects.

V. CONCLUSION

In patients with type 2 diabetes and periodontitis affecting the posterior teeth, adjunctive local 0.2% chlorhexidine-hyaluronic acid gel combined with non-surgical periodontal therapy was associated with greater short-term improvement in clinical periodontal parameters and a more favorable shift in periodontitis severity distribution compared with non-surgical periodontal therapy alone. Given the non-randomized split-mouth controlled design, relatively small sample size, and 3-month follow-up period, these findings should be interpreted as short-term clinical evidence and validated in larger randomized clinical trials with longer follow-up.

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