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Evaluation of the effects of using an interdental brush dipped in 0.2% hyaluronic acid gel on clinical periodontal parameters among patients with periodontitis: a randomized controlled trial

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Abstract

Background The additional use of agents with antibacterial and anti-inflammatory activities, such as hyaluronic acid in treating periodontal disease, has recently become popular. This study aimed to evaluate the effects of using an interdental brush dipped in 0.2% HA gel on clinical periodontal parameters.

Methods This randomized controlled trial was conducted among 60 patients with stages II/III grades A/B periodontitis. After full-mouth scaling root planning and oral hygiene training, the patients were divided into two groups; the test group was asked to use an interdental brush dipped in 0.2% HA, while the control group was asked to use a regular interdental brush. Clinical periodontal parameters [gingival index (GI), plaque index (PI), papillary bleeding index (PBI), pocket depth (PD), and clinical attachment loss (CAL)] were assessed at baseline and in the 1st and 3rd months after treatment.

Results Clinical periodontal parameters were improved in control and test groups at the 1 and 3-month compared to baseline ($p < 0.05$). The 1st- and 3rd-month PBIs were significantly lower in the test group ($p < 0.05$). There was no significant difference between the test and control groups regarding PI, PD, GI, and CAL between the follow-up times.

Conclusions Although the clinical efficacy of the tested methods of interdental brush use was similar, it can be concluded that the use of an interdental brush dipped in HA may contribute to the reduction of gingival bleeding in the early period.

Clinical significance Incorporating HA into the oral hygiene regime after periodontitis treatment using an interdental brush is a useful and practical method.

Name of the registry https://clinicaltrials.gov/

Trial registration number NCT06309797.

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Background

Periodontitis is an inflammatory disease that destroys tooth-supporting structures due to complex interactions between the biofilm and host response [1]. Therefore, the most effective way to prevent and treat periodontitis is to eliminate and prevent the formation of biofilms, especially interdental biofilms [2, 3].

The interproximal areas of the teeth and dental implants are the most difficult areas to clean and maintain. Toothbrushing alone cannot penetrate and clean these areas. Consequently, periodontal disease most commonly develops in interproximal regions [4, 5]. Therefore, interdental cleaning is as important as toothbrushing in effectively removing dental plaques from the teeth [6–8].

Various products can be used for interdental cleaning such as dental flosses, interdental brushes, and plastic and wooden toothpicks [9]. In addition to mechanical cleaning, regenerative biological substances can improve periodontal parameters [10]. Hyaluronic acid (HA) is a disaccharide polymer synthesized by connective tissue cells and is the most predominant glycosaminoglycan in the extracellular matrix [11]. Studies on its chemical and physicochemical properties and physiological role in humans have shown that HA is an ideal biomaterial for cosmetic, medical, and pharmacological purposes. HA contributes to the treatment of periodontal disease as adjunctive, showing anti-inflammatory, anti-edematous, and antibacterial effects [12]. It is routinely used as an adjunct to surgical and non-surgical periodontal treatments [11].

HA is frequently used as a supplement in the treatment of periodontitis. Studies have shown that many clinical periodontal parameters, such as bleeding on probing, the CAL, and the PD, significantly improve in patients treated by local into-pocket application with 0.2% or 0.8% HA gel after scaling and root planning (SRP) [13, 14]. The application of 0.2% HA gel (Gengigel®, Ricerfarma, Milan, Italy) to periodontal pockets following SRP has also been reported to significantly reduce inflammatory infiltration [15].

Since Gengigel is a locally applied agent, it does not enter systemic circulation. No adverse effects of HA application have been demonstrated [16].

Our study aimed to compare the effects of using an interdental brush dipped in 0.2% HA gel with those of using a regular interdental brush on clinical periodontal parameters following Subgingival debridement (SD) among patients with periodontitis.

Materials and methods

Study design and ethical considerations

The clinical research ethics committee of Health Sciences University Gülhane Educational Research Hospital approved the study (2023/86), and all participants signed an informed consent form. The study was conducted in accordance with the Declaration of Helsinki, as revised in 2013. The trial was registered at ClinicalTrials.gov (ID: NCT06309797). This study adopted a single-center, single-blinded, randomized controlled trial design and followed the Consolidated Standards of Reporting Trials Statement.

Patient selection

The study was conducted among patients who visited the Health Sciences University Gülhane Faculty of Dentistry Periodontology Clinic from May 2023 to January 2024. According to the 2017 World Workshop in Periodontics, patients are considered to have periodontitis when either a buccal or oral clinical attachment loss (CAL) of ≥3 mm with pocketing of >3 mm is visible on two or more teeth or an interdental CAL is detectable on two or more nonadjacent teeth, but which cannot be attributed to nonperiodontal sources [17]. Intraoral examination was conducted to screen and diagnose periodontitis, and a classification was then assigned to each patient following the description above.

- Patients who freely consented to participate in the study and received routine dental scaling after being diagnosed with stages II/III, grades A/B, and generalized periodontitis were enrolled (33 female patients and 27 male patients). Patients included were right-handed and had at least 20 natural teeth (at least five evaluable teeth in each quadrant), excluding third molars. Conversely, patients with known systemic diseases, smokers, patients with interface caries and filling, patients using orthodontic appliances or removable prostheses, patients who had undergone periodontal treatment within the previous 6 months, patients with known hypersensitivity to HA, patients who had taken antibiotics within the last three months, and patients who were pregnant or nursing were excluded. Each participant in the study received comprehensive care.

Sample size calculation

This study investigated the differences between two independent groups and within each group at three-time points. Similar studies that could be used as a basis for calculating the sample size of this study were reviewed. The largest sample size was considered according to the statistical methods to be applied in line with the study purpose. The sample size was calculated at a 95% confidence level using G*Power version 3.1.9.2. With an α value of 0.05, a standardized effect size of 1.3968 [^{14}, and a theoretical power of 0.95, the minimum sample size per group was calculated as 15. Considering the possibility of loss of observations over time, 30% of the calculated sample size [15*(30/100) = 5] was added. Thus, the minimum sample size for each group was 20. However, ultimately, 30 patients per group were included. The study flow chart is shown in Fig. 1.

Experimental approach

Each participant underwent a professional supragingival cleaning 2 weeks prior to the start of treatment and received personalized oral hygiene instructions. Baseline periodontal measurements were also recorded. Under local anesthesia, participants underwent a full-mouth SD conducted using ultrasonic (Piezon Master 400 EMS, Electro-Medical Systems, Switzerland) and hand devices (1/2, 3/4, 5/6, 7/8, 9/10, 11/12, 13/14 Gracey curettes, Hu-Friedy, Chicago, USA) 2 weeks later.

All participants received the same toothbrush (TePe Select™, Malmö, Sweden), toothpaste (IPana Pro-Expert®, Gross-Gerau, Germany), and brushing technique instruction (modified Stillman technique). The American Dental Association guidelines for using an interdental brush were explained to participants during oral hygiene promotion. After evaluating the interdental spaces between the incisors and second molars, the diameters of the interdental brushes that fit the embrasure spaces were identified. Additionally, a checklist and written instructions were given to encourage cooperation and guarantee that the device was used correctly. Subsequently, participants were given interdental brushes (TePe Munhygienprodukter AB, Malmö; TePe in diameters between 0.4 and 0.6 mm). Participantsrandomly assigned to the test group also received 20 mL of 0.2% HA gel (Gengigel; Ricerfarma, Milan, Italy). Gengigel is a high-molecular-weight (HMW) exogenous HA-based gel and a biotechnological process generates it without the need for animal experimentation. Xylitol and excipients are present in the gel together with hyaluronan.

In a completely randomized fashion (block randomization method, closed envelope technique), 30 patients were selected for the control group and were asked to brush their teeth and use the interdental brush for oral hygiene. The other 30 patients were included in the test group and were asked to brush their teeth, dip the interdental brush in HA gel, and use the dipped interdental brush. Patients were asked to perform all oral hygiene practices twice a day.

Participants were evaluated at baseline and in the 1st and 3rd months after treatment. The gingival index (GI; Loe and Silness GI) [19], plaque index (PI; Turesky–Gilmore–Glickman modification of the Quigley–Hein PI) [20], papillary bleeding index (PBI) [21], PD, and CAL were recorded [17]. With the use of a Williams periodontal probe(122-006, Hu-Friedy), the GI, PD, and CAL were measured at six sites for each tooth (apart from the third molar), three sites for the buccal area (disto-buccal/labial, mesio-buccal/labial, and mid-buccal/labial), and three sites for the lingual area (disto-lingual/palatal, mesio-lingual/palatal, and mid-lingual/palatal). In the measurement of the PBI, the mesial and distal regions of the papillae were probed, and bleeding was recorded after 15 s (0: no bleeding, 1: one bleeding point, 2: thin bloodline, 3: blood filling the interdental triangle, 4: intense bleeding). The PBI was calculated by dividing the total sum by the number of the papillae. In measuring the PI, a plaque staining agent (Tri Plaque ID Gel™, GC Dental, USA) was applied to all tooth surfaces using a fine-tipped brush. The pink-, purple-, or blue-colored areas on the tooth surfaces were scored from 0 to 5 (0: no plaque, 1: independent plaque islands on the gingival margins, 2: plaque in the form of thin bands on the gingival margins, 3: plaque not exceeding 1/3 of the tooth surface, 4: plaque not exceeding 2/3 of the tooth surface, 5: plaque exceeding 2/3 of the tooth surface). The whole mouth was divided into six different areas, and the average PI was calculated by taking the mathematical proportion of the values obtained from the mesial, distal, lingual, and vestibular surfaces of specific teeth in each sextant.

Since individual differences in probing technique and force may affect the results, all clinical measurements and the initial periodontal treatment were performed by the same experienced periodontist (OSA). A different investigator (SCS) conducted the randomization. The investigator carrying out the measurements was unaware of which patients were assigned to the test group. Five patients with periodontitis who were not part of the study underwent intra-examiner calibrations. Re-examinations were performed 3 days later to eliminate the possibility of the examiner remembering the previous scores and to get rid of the misleading effect of the plaque staining agent left on the teeth in plaque scoring. Cohen's κ values for the PBI (0.84), PI (0.86), and GI (0.84) were obtained.

Participants were advised not to use any antiseptic mouthwash and dental floss during the study.

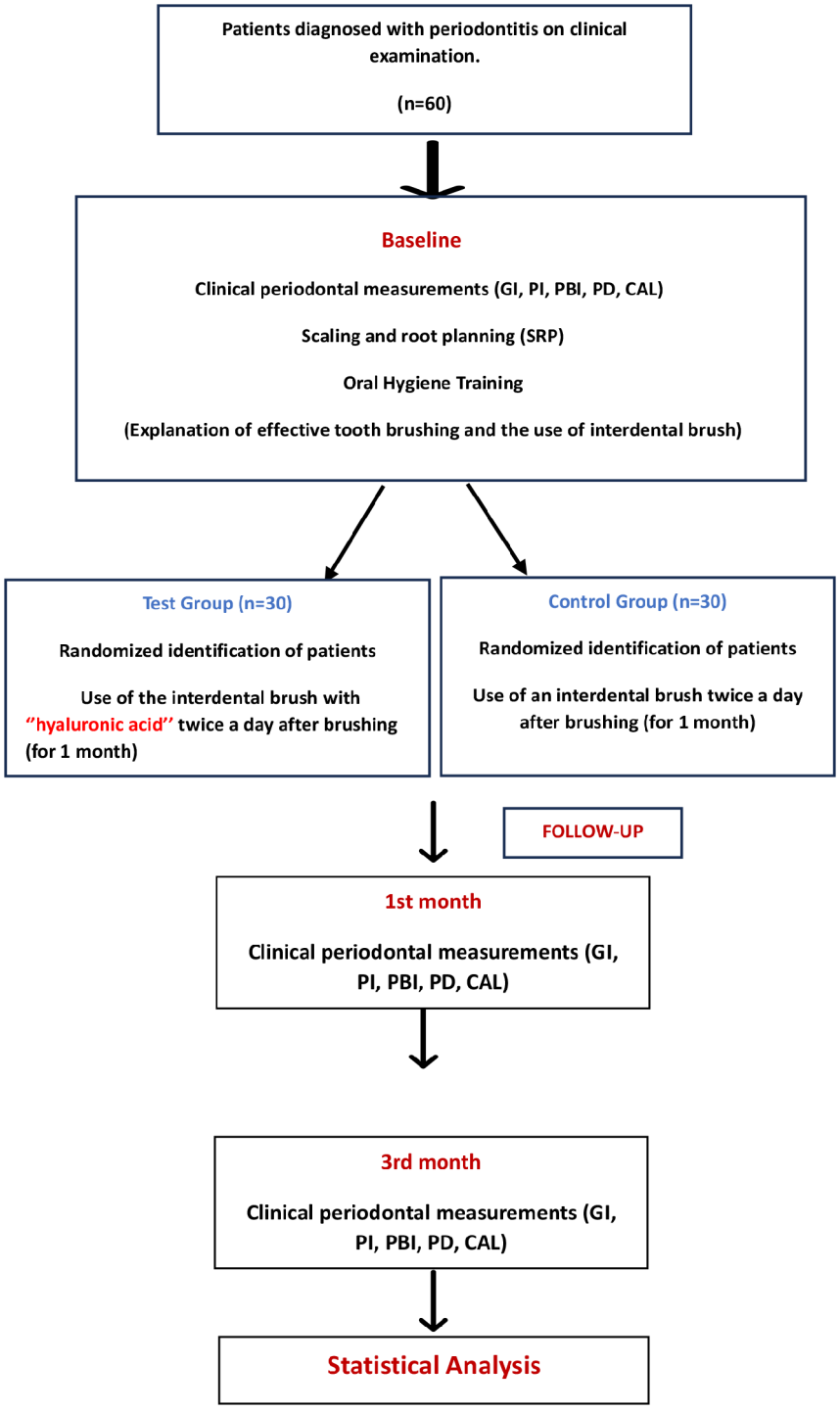

Fig. 1 Flow chart of the study

Statistical analysis

Descriptive statistics, including numbers, percentages, means, standard deviations, and medians, were used to present the data. As the first step of the statistical analysis, the normality assumption was checked using the Shapiro–Wilk test. An independent sample t-test and the Mann–Whitney U test were used to compare two independent variables with normal and non-normal distributions, respectively. The Friedman test was used to compare three or more repeated measures that are not normally distributed. The post hoc Bonferroni correction test was used to determine which group/s contributed to any observed difference. All analyses were performed using IBM SPSS version 25 (IBM Corp., Armonk, NY).

Table 1 Distribution and comparison of demographic characteristics according to study groups

	Test Group		Control Group					
Sex	**n**	**%**	**n**	**%**	**p**	**Age**	**Average ± S.D. (M.)**	**p**
Female	17	56.7	16	53.3	1.000	Test Group	42.87 ± 8.9(42.5)	0.081
Male	13	43.3	14	46.7		Control Group	39.17 ± 7.12(35.5)	

*$p < 0.05$

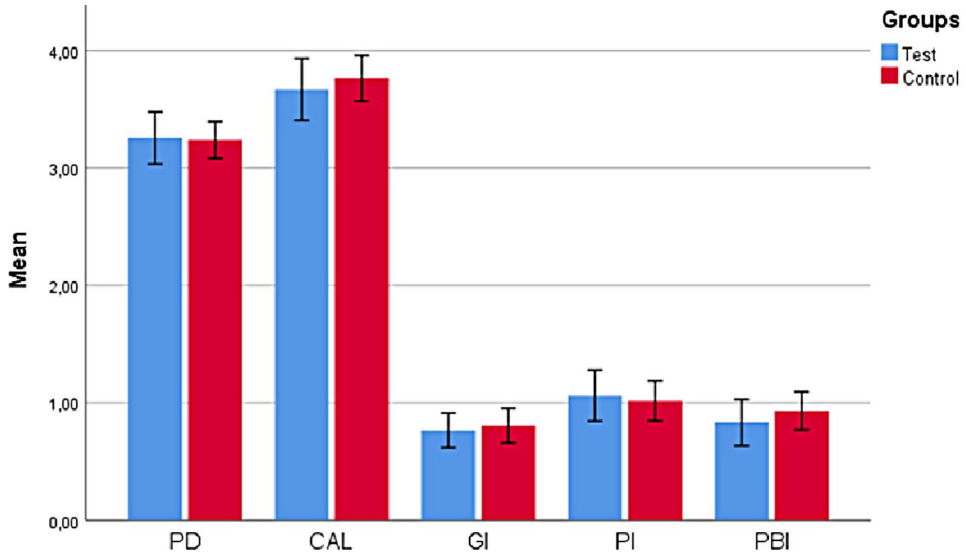

Fig. 2 Graph of the distribution of clinical measurements according to the study groups

Results

The Pearson chi-square test and independent sample t-test were performed to compare sex and age between the groups. The mean age was slightly higher in the test group (42.87 ± 1.63 SE) compared to the control group (39.17 ± 1.30 SE), although this difference did not reach statistical significance ($p = 0.081$). Similarly, sex did not significantly differ between the groups ($p = 1.000$), indicating that sex was homogeneously distributed (Table 1).

There was no statistically significant difference between baseline clinical periodontal parameters (Fig. 2).

The Mann–Whitney U test was used to compare the clinical parameters between the groups and the Friedman test between the measurement time points. Significant differences were observed between the 1st- and 3rd-month PBIs in both groups ($p < 0.05$). At the first month, the test group showed significantly lower PBI scores (0.23 ± 0.051 SE) compared to the control group (0.48 ± 0.062 SE) ($p = 0.002$). At the third month, the difference remained significant, with the test group scoring 0.23 ± 0.055 SE and the control group 0.47 ± 0.062 SE ($p = 0.001$) (Table 2). Significant differences were also found in the PD, CAL, GI, PI, and PBI between the measurement time points in both groups ($p < 0.05$). In the test group, the Bonferroni test showed that the baseline, 1-month, and 3-month measurements of PD, CAL, GI, PI, and PBI were significantly different from each other ($p = 0.000$). The baseline measurements for all parameters were higher than the 1st- and 3rd-month measurements ($p = 0.000$). In the control group, the Bonferroni test showed that the baseline and 1st- and 3rd-month PDs, CALs, GIs, PIs, and PBIs also significantly differed (both $p = 0.000$). The baseline measurements for all parameters were higher than the 1st- and 3rd-month measurements ($p = 0.000$).

Discussion

The treatment for periodontal disease aims to decrease symptoms and repair lost tissues by combining various periodontal treatment approaches [22]. The primary method of preventing periodontitis is strict oral hygiene, including cleaning the teeth using an electric toothbrush and interdental brush, flossing, fluoride toothpaste, and mouthwash [23]. In this study, patients were asked to use an interdental brush for interdental cleaning.

In the literature, a limited number of studies investigating the effectiveness of interdental brushes containing different active ingredients [24]. Studies have revealed noticeably greater reductions in the GI with the use of cetylpyridinium chloride gel [25] and chlorhexidine gel [26] than control treatments, proving the superiority of active components when utilized with interdental brushes. According to the results of a recent comprehensive analysis, there is insufficient evidence to support the

Table 2 Distribution and comparison of clinical measurements according to study groups

	Baseline		1st month		3rd month		By time‡
	Average ± S.D. (M.)	p	Average ± S.D. (M.)	p	Average ± S.D. (M.)	p	p
PD							
Test Group	4.05 ± 0.86(4.06)	0.280	3.00 ± 0.97(2.75)	0.530	2.72 ± 0.87(2.48)	0.246	**0.000***
Control Group	3.84 ± 0.59(3.71)		3.03 ± 0.66(3.15)		2.85 ± 0.59(2.82)		**0.000***
CAL							
Test Group	4.53 ± 1.07(4.34)	0.894	3.40 ± 1.14(3.13)	0.367	3.09 ± 1.11(2.76)	0.070	**0.000***
Control Group	4.39 ± 0.8(4.33)		3.50 ± 0.85(3.38)		3.41 ± 0.84(3.37)		**0.000***
GI							
Test Group	1.63 ± 0.44(1.59)	0.515	0.36 ± 0.3(0.3)	0.395	0.31 ± 0.26(0.26)	0.859	**0.000***
Control Group	1.69 ± 0.36(1.63)		0.4 ± 0.3(0.37)		0.33 ± 0.28(0.24)		**0.000***
PI							
Test Group	2.19 ± 1.05(1.94)	0.865	0.53 ± 0.40(0.39)	0.433	0.47 ± 0.34(0.4)	0.935	**0.000***
Control Group	2.06 ± 0.44(2.05)		0.54 ± 0.33(0.45)		0.46 ± 0.28(0.4)		**0.000***
PBI							
Test Group	2.04 ± 0.52(2.07)	0.160	0.23 ± 0.28(0.17)	**0.002***	0.23 ± 0.30(0.14)	**0.001***	**0.000***
Control Group	1.85 ± 0.57(1.76)		0.48 ± 0.34(0.39)		0.47 ± 0.34(0.43)		**0.000***

*$p < 0.05$ ve ‡: Friedman Test

increased clinical effectiveness of interdental cleaning tools that include active ingredients in terms of their ability to prevent gingivitis and plaque [24]. Our study used HA as an adjuvant to interdental brushes and observed a significant difference in the PBI in favor of the test group.

HA has shown potential benefits in periodontal disease management. It possesses anti-inflammatory properties, aiding in the reduction of gingival inflammation associated with periodontitis [27]. HA can also contribute to tissue repair and regeneration by promoting the healing of damaged periodontal tissues [28]. Additionally, its ability to retain water helps maintain tissue hydration, supporting overall gum health [29]. In our study, we sought to combine the mechanical effect of an interdental brush with the chemical activity of HA. Our analysis showed that HA yielded additional benefits in treating periodontitis based on thepapillary bleeding index. Although numerous clinical studies have reported additional benefits of HA use in the treatment of periodontitis [11], our study is the first to provide an easy and sustainable application method for patients.

In the treatment of residual periodontal pockets, applying HMW HAformulations in addition to SRP has been reported to improve clinical and microbiological parameters compared with controls, although the difference is not significant [30]. Subgingival application of 0.8% HA gel has also been shown to cause more significant decreases in *Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis* levels [31]. Similarly, intra-pocket Hyadent application after SRP significantly improves clinical parameters results regarding reduction in inflammation, measured by bleeding on probing and gain in periodontal attachment, while it had no effect on probing depth reduction compared with controls [32]. In a recent study, subgingival application of sodium hypochlorite/amino acid gel and HA in addition to SRP yielded significantly greater improvements than SRP alone [33]. In another split-mouth study, Ariel et al. reported that the subgingival application of a thermosensitive gel with an active HA ingredient and a preservation system of octenidine HCl 0.625% in conjunction with SRP provided higher CAL gains and bleeding on probing (BOP) reductions in residual pockets of stage 3 periodontitis patients at 3 and 6 months. BOP changes between groups were not statistically significant at the 3-month follow-up but reached a statistically significant difference in favor of the test group at the 6-month follow-up [34]. The findings of our study support the literature. However, the follow-up period is three months and longer follow-up is necessary to ensure that the difference in PBI is maintained over the 6-month period.

Hyaluronan, an extracellular matrix glycosaminoglycan, exhibits different biological functions depending on its molecular weight [35]. Low-molecular-weight HA (LMW-HA) shows pro-inflammatory and immunostimulatory properties, while HMW HA has anti-inflammatory and immunosuppressive effects [36]. Like the majority of HA-based medical products used in periodontal therapy, the patented medication employed in this investigation contains HMW-HA and is extremely pure [32]. In this study, we utilized HMW-HA and observed its positive impact on gingival bleeding.

In a previous study, a 2% chlorhexidine-impregnated floss was noted to be more effective in addressing supragingival biofilm accumulation than a regular floss but did not provide any additional benefit on marginal gingival bleeding [37]. A recent clinical study showed that waterjet irrigation systems used as an adjunct to oral hygiene

outperformed dental flosses in terms of clinical parameters, but the difference in microbiome diversity was not significant [38].

In our study, different interdental cleaning products were not compared because we believe that an interdental brush is superior in terms of both ease of use and financial accessibility. The fact that chemical activity can be easily added to the physical activity of an interdental brush is another important advantage. In a recent pilot study, microbial sampling of interdental brushes was found to be at least as effective as paper points in detecting periodontal pathogens [39]. This finding supports that the use of an interdental brush is the most convenient and easy way for HA to reach the interdental space and provide efficacy.

Although some studies have reported that the greater the number of cleaning cycles, the greater the cleaning effect [40], a recent study investigating the effectiveness of interdental brushes using 3D modeling concluded that repeated cleaning of more than five cycles is not necessary and may create a risk of interdental gingival (papillary) bleeding [41]. In this context, it becomes even more important to coat interdental brushes with a substance with antibacterial and anti-inflammatory properties to achieve maximum effectiveness with fewer cycles.

Patients have found interdental brushing more comfortable than flossing [42]. However, a recent study among individuals with periodontal disease reported that the rate of often or always using an interdental brush was only 14.6% [43]. In this respect, for patients who do not believe in the effectiveness of using only interdental brushes, the thought that they are also using medication may be motivating for regular use.

We would like to point out that one of the most important limitations of our study is 'performance bias' according to the Cochrane Handbook and risk of bias tool [44] as we did not use a placebo in the control group due to budget constraints. We acknowledge that patients who were aware that they were in the test group often exhibited slight changes in behavior, which may have contributed to a slightly better outcome. Patient compliance and ability are factors that cannot be ignored in the effective use of oral appliances [45]. Therefore, the most important limitation of this study is interindividual differences. Furthermore, it should be noted that the present study included only systemically healthy and non-smoking individuals, which may limit the generalizability of the findings to the broader population. Another limitation is the short follow-up time of 3 months, it is of interest if the anti-inflammatory effect will persist for at least 6 months. The fact that we limited our analysis to clinical periodontal parameters is another significant drawback. Additional research using microbiological and biochemical analyses could bolster our findings.

Conclusions

According to the results of this study, both the use of an interdental brush alone and the use of an interdental brush dipped in HA in addition to tooth brushing in oral hygiene practices following initial periodontal treatment provided significant improvements in clinical periodontal parameters in the early period. However, using an interdental brush dipped in HA may be considered more effective in reducing gingival bleeding. Although further research is needed, incorporating HA into periodontal treatments may be a promising approach for improving oral health.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12903-025-06038-7.

Supplementary Material 1

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None.

Author contributions
OSA and GU conceived the idea; OSA and SCS identified suitable patients; OSA performed the first periodontal treatment and clinical measurements; SCS conducted the randomization, EO and OSA analyzed the data; and OSA, SCS, and GU led the writing. All authors reviewed the manuscript.

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Data availability
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study was approved by the Health Sciences University Gülhane Training and Research Hospital Clinical Research Ethics Committee (2023/86). The study was conducted in accordance with the Declaration of Helsinki revised in 2013. All participants were informed about the study and signed an informed consent form.

Consent for publication
Written informed consent was obtained from all individual participants included in the study.

Competing interests
The authors declare no competing interests.

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