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Original Article

Effect of biomimetic tooth mousse and toothpaste on the incidence of white spot lesions during fixed appliance orthodontic treatment: A randomized clinical trial

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الملخص

أهداف البحث: يرتبط استخدام الأجهزة الثابتة التقويمية ارتباطا وثيقا بفقدان مينا الأسنان للمعادن. وقد طرحت حلول عديدة إلا أنه لا يوجد اتفاق على تدخل محدد. تم تقييم تأثير منتجات كيراسبيت بيوسمالتو المحاكية للطبيعة (معجون أسنان موس التأثير الاحترافي) على تطور آفات البقع البيضاء خلال الأشهر الستة الأولى من العلاج التقويمي، مقارنةً بمعجون الأسنان التقليدي المفلور.

طريقة البحث: قسم ٧٠ مريضا بتقويم الأسنان، تتراوح أعمارهم بين ١٢ عاما فأكثر، إلى مجموعتين باستخدام مولد أرقام عشوائية حاسوبي. استخدمت المجموعة التقليدية معجون أسنان كولجيت يوميا، بينما استخدمت المجموعة المحاكية للحيوية معجون أسنان كيراسبيت بيوسمالتو المضاد للتسوس والتآكل يوميا مع وضع كيراسبيت بيوسمالتو المضاد للتسوس والتآكل لمعجون موس التأثير الاحترافي على الأسنان الأمامية في كل زيارة. تم تقييم الأفراد شهريا لمدة ستة أشهر. تم قياس تمعدن مينا الأسنان، ومؤشر البلاك المرئي، ومؤشر نزيف اللثة على الأسنان الأمامية العلوية والسفلية. تم تقييم كل سن من حيث تمعدن مينا الأسنان باستخدام قلم دياجنودنت، ونظام الكشف والتقييم الدولي للتسوس، ومؤشر جوريليك.

النتائج: شمل التحليل ٦٢ مشاركا (٣٠ مشاركا تقليديا و ٣٢ مشاركا محاكيا للحيوية). كان لدى كلتا المجموعتين درجات مماثلة لقلم دياجنودنت في جميع الفترات الزمنية. كانت هناك درجات أعلى ذات دلالة إحصائية لقلم دياجنودنت بمرور الوقت في كلتا المجموعتين. لم يتم العثور على فروق ذات دلالة إحصائية بين المجموعتين فيما يتعلق بنظام الكشف والتقييم الدولي للتسوس ومؤشر جوريليك. أظهرت المجموعة التقليدية ارتفاعا ملحوظا في درجات مؤشر البلاك المرئي عند تي ٢ (بعد شهرين)، و تي ٤ (بعد أربعة أشهر)، و تي ٥ (بعد خمسة أشهر)، و تي ٦ (بعد ستة أشهر)، ودرجات مؤشر نزيف اللثة عند تي ٤، و تي ٥، و تي ٦.

الاستنتاجات: لم يُظهر الاستخدام الشهري لمعجون أسنان موس التأثير الاحترافي كيراسبيت بيوسمالتو المعالج للتسوس والتآكل مع الاستخدام اليومي لمعجون كيراسبيت بيوسمالتو المُعالج للتسوس والتآكل فعالية أكبر من معجون الأسنان المفلور في ظهور آفات البقع البيضاء خلال الأشهر الستة الأولى من العلاج التقويمي.

الكلمات الافتتاحية: مواد محاكية للطبيعة؛ إزالة المعادن؛ العلاج التقويمي؛

Abstract

Background: The use of orthodontic fixed appliances is strongly linked to enamel demineralization. Numerous solutions have been presented; however, the best one remains controversial.

Objectives: To evaluate the effect of Biosmalto Impact Action Mousse™ (biomimetic materials) on white spot lesions (WSLs) development during orthodontic treatment.

Trial design: Multicenter, parallel groups, randomized clinical trial.

Methods: A computer random number generator allocated 70 orthodontic patients aged 12 or older to two groups. The control group used Colgate toothpaste daily, whereas the intervention group used Curasept toothpaste daily with the application of Curasept Biosmalto Impact Action Mousse™ to the anterior teeth every visit. The individuals were assessed monthly for six months.

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Enamel mineralization, visible plaque index (VPI), and gingival bleeding index (GBI) were measured on the upper and lower anterior teeth. Each tooth was assessed for enamel mineralization using the DIAGNOdent Pen, International Caries Detection and Assessment System (ICDAS), and Gorelick index (GOI).

Results: The analysis included 62 participants (30 Colgate and 32 Curasept). Both groups had comparable DIAGNOdent pen scores at all time intervals. There was a statistically significant higher DIAGNOdent pen scores over time in both groups. No statistically significant differences were found between groups for ICDAS and GOI. The Colgate group had statistically significantly higher VPI scores at T2 (after 8 weeks), T4 (after 16 weeks), T5 (after 20 weeks), and T6 (after 24 weeks) and GBI scores at T4, T5, and T6.

Limitations: The study findings only demonstrated the effect of biomimetic materials during six months of orthodontic treatment. Long-term effect is worth to be also evaluated.

Conclusions: Monthly application of Biosmalto Impact Action Mousse™ did not seem to be more effective than fluoridated toothpaste on the development of WSLs after six months.

Registration: The study was registered with ClinicalTrials.gov on July 11, 2023 (Registration No. NCT05940701).

Keywords: Biomimetic materials; Demineralization; Orthodontic treatment

Introduction

White spot lesions (WSLs) are characterized by demineralization of the enamel surface and subsurface, often due to plaque accumulation in regions of stagnation. This demineralization process eventually progresses to enamel decay and can eventually lead to formation of a cavity.[1] WSLs are not only an esthetic issue but can also affect the structural integrity of the tooth, since the process of demineralization may increase the enamel pores (with more air and water content).[2] When WSLs are found on smooth surfaces and are visible to the naked eye, they might appear as a chalky white opacity due to the porosities created by this loss of the mineralized layer, which alters the refractive index of the typically transparent enamel.[3]

Modern dentistry is currently focused on preventative care and minimizing invasive treatments. The aim of preventive interception focuses on enhancing oral health while minimizing treatment costs. This approach not only promotes better dental outcomes but also reduces the environmental footprint of dental procedures and lowers the socioeconomic burden on individuals and healthcare systems. The treatment of WSLs should include strategies for both preventing further demineralization and promoting lesion remineralization. Oral hygiene instructions to reduce plaque buildup and the frequency of lesions is the initial and practical method that is usually given to patients.[4] Toothpaste is typically thought to be more readily available and practical for patients.[5] Other methods include using Graphite Fluoride/Bioactive Glass-Containing Orthodontic Primer,[6] graphene oxide/hydroxyapatite-containing orthodontic primer,[7] casein phosphopeptide−amorphous calcium phosphate (CPP-ACP), laser applications, ozone, microabrasion applications, bleaching applications, resin infiltration, and self-assembling peptide P11-4.[8,9]

Fluoride can make tooth minerals less soluble by altering hydroxyl groups and lowering carbonate concentration. By lowering the solubility products of precipitated calcium phosphate, it can aid in mineral precipitation or reprecipitation.[10] It is important to acknowledge that fluoride has beneficial effects on lowering WSLs and caries. Nevertheless, excessive fluoride exposure might have negative consequences like fluorosis. Therefore, alternative materials have also been proposed. ACP and CPP-ACP have been shown to be effective in restoring enamel lesions to their original mineral state.[11] By increasing saliva's buffering ability, ACP may lessen demineralization and boost remineralization.[12] Due to its solubility, ACP sealant may increase calcium and phosphate ion concentrations and stimulate the synthesis of apatite.[13]

Curasept Biosmalto Impact Action Mousse™ contains ACP and fluoride. Fluoride increases the remineralization of enamel and reduces demineralization. Additionally, it inhibits cariogenic bacteria by interfering with their metabolic enzymes.[14–16] On the other hand, ACP is a noncrystalline, highly reactive substance that is rapidly converted into hydroxyapatite; it is the naturally occurring precursor of enamel and dentin. The two functional substances (fluoride and ACP) induce the formation of a new mineral phase that is more resistant to acid attack and mechanical abrasion, thereby increasing resistance to caries and reducing bacterial plaque formation. Iafisco et al.[17] and Ionescu et al.[18] observed the more pronounced buildup of a surface layer of fluor-hydroxyapatite (HAp), which is more resistant to acidic caries invasions than natural HAp. Also, compared to MI Paste Plus™, Curasept Biosmalto Caries, Abrasion and Erosion products were found to be superior at penetrating tooth enamel with their fluoride concentration. Esposti et al.[19] reported in an *in vitro* study that the Curasept Biosmalto Caries, Protection & Abrasion™ toothpastes effectively remineralize the enamel by depositing HAp, which is chemically comparable to biogenic HAp, onto exposed dentinal tubules and deficient enamel prisms. Although *in vitro* studies on Curasept Biosmalto Caries Abrasion and Erosion Products (Impact Action Mousse Pro and toothpaste) have shown that they prevent demineralization and promote remineralization, clinical trials should be conducted to confirm its effectiveness.

Biomimetic materials are novel substances that are intended to replicate the inherent features and activities of living tissues. In dentistry, they are essential for enamel preservation, repair, and remineralization. These materials are designed to interact with tooth structure and saliva,

restoring or replicating enamel natural mineral content and functionality. These substances frequently include fluoride, calcium, and phosphate in forms like those of hydroxyapatite, the primary mineral found in enamel.[20]

Since no study to date has investigated the preventive effect of ACP-containing mousse during orthodontic treatment, this research assessed the effect of Curasept Biosmalto Impact Action Mousse Pro, as a biomimetic material-containing fluoride-ACP, on the development and healing of WSLs during orthodontic treatment compared to conventional preventive regimes. The primary objective was to evaluate the effect of biomimetic system Curasept Biosmalto Caries, Abrasion and Erosion products (Impact Action Mousse Pro and toothpaste) by evaluating the number of WSLs on the labial surfaces of maxillary and mandibular anterior teeth using DIAGNOdent pen scores, International Caries Detection and Assessment System (ICDAS), and Gorelick index (GOI) during 6 months of orthodontic treatment. Secondary objectives were to evaluate the amount of plaque and gingival bleeding by using the visible plaque index (VPI) gingival bleeding index (GBI) at each visit. The null hypothesis was that there is no significant difference in the effectiveness of the Curasept Biosmalto Impact Action Mousse Pro system and conventional fluoridated toothpaste for preventing WSLs during orthodontic treatment'.

Materials and Methods

Trial design and any modifications made thereafter

This research was a multicenter randomized clinical trial using blinded parallel groups, simple nonstratified randomization, and an equal allocation ratio of 1:1. No modifications were made to the procedure after the beginning of the study. The clinical study was registered on ClinicalTrials.gov on July 11.2023 (Registration No. NCT05940701).

Participants, eligibility criteria, and setting

Any patient indicated for fixed orthodontic treatment was eligible to participate in this study, and the inclusion criteria were as follows: 1) No underlying medical conditions requiring medications that may cause dryness of the mouth; and 2) Fully erupted permanent maxillary and mandibular canines and incisors that have not been restored. The exclusion criteria were: 1) Patients receiving professional fluoridation within the last 3 months; 2) Patients with obvious WSL; 3) Patients with anterior teeth missing or considerably rotated (restricting the visibility of facial surfaces), or with untreated cavitated lesions, restorations on the facial surface, enamel hypoplasia, dental fluorosis, tetracycline pigmentation, or dental anomalies related to morphology, anatomy, or development; 4) Patients with pregnancy and xerostomia; 5) Heavy smokers; or 6) Patients with craniofacial syndromes such as clefts.

The study was conducted in two private dental care and two governmental orthodontic specialty centers in Baghdad city. Clinicians were either specialized orthodontists or postgraduate students.

The investigator (S.H.A.) initially determined whether patients were eligible for the research. The study was verbally explained to those who fulfilled the inclusion criteria in order to obtain their consent for participation. Then the patients received the patient information sheet, which explained the purpose of the research. The patients were instructed to thoroughly read the informational material at home and tell the researcher of their intention to participate at the next visit. Participants had to either sign the consent form or obtain their parent's permission (if the participant was under the age of 18 years). The investigator provided the patients with further information or reassurance about the trial if needed.

Interventions

All participants received a standardized treatment protocol. The patients were treated with a straight wire appliance using metal brackets, 37% phosphoric acid etch primer, and white glue adhesive (all from 3B® Orthodontics, Tianjin, China).

The Conventional group received a fluoridated toothpaste (Colgate® MaxFresh toothpaste), whereas the Biomimetic group received Curasept Biosmalto Caries, Abrasion & Erosion toothpaste. Additionally, at each visit, Curasept Biosmalto Impact Action Mousse Pro was applied to the facial surface of the maxillary and mandibular anterior teeth using a tray (the mousse was placed on the labial surface) after good isolation and drying of the teeth surface. After about 3−5 min, the excess mousse was removed, and the patient was asked to refrain from eating or drinking for 30 min according to the manufacturer's instructions.

For each patient recruited, identical toothbrushes and oral care instructions were given. The patients received instructions to brush their teeth for at least 2 min using Charter's method[21] at least three times/day. Additionally, the patients were instructed not to use any additional antimicrobial-containing products (e.g., mouthwash, toothpaste, gel).

Outcome and any modifications after the beginning of the trial

Primary outcome (WSL measures)

With the aid of the DIAGNOdent pen 2190 (KaVo Dental, Biberach an der Riss, Germany), the enamel mineralization score was recorded. In accordance with the guidelines provided by the manufacturer, to obtain readings from the labial/buccal surface of the teeth, four distinct locations were identified: gingival, occlusal, mesial, and distal. The DIAGNOdent pen was calibrated for every patient as recommended by Banks and Richmond.[22] The number 2 pen point was positioned on the labial surface of the tooth under examination, 1 mm from the bracket, and the resultant score was recorded after the tooth surface was dried. The measuring process was carried out pre-treatment (T0), and 1 month (T1), 3 months (T3), and 6 months (T6) after treatment.

Prior to bonding and after teeth polishing with non-fluoridated pumice, the ICDAS scores ranging from 0 to 6[23] were given to the labial surface of each tooth (maxillary and mandibular anterior teeth) (Supplementary Table 1). The GOI[24] was used to determine WSLs on the labial surface as follows: 0, no WSLs; 1, slight WSLs; 2, extended or excessive WSLs; and 3, WSLs with cavitation. Both ICDAS and GOI were recorded pretreatment and at T0, T1, T2, T3, T4, T5, and T6 after treatment.

Secondary outcomes (periodontal health measures)

Every bonded tooth labial surface was dried and the VPI of the labial surfaces of the maxillary and mandibular front teeth were scored as 0 for nonvisible plaque and 1 for visible plaque.

GBI was measured by using a periodontal probe. The gingiva was gently dried with air before the probe was carefully placed into the gingival crevice in a line with the tooth long axis. To avoid damaging the sulcular epithelium, the probe was carefully moved at six separated points (gentle probing) of the labial and palatal/lingual aspects of the maxillary and mandibular canines and incisors. To minimize excessive tissue penetration, the probe was maneuvered in the crevice while gently stretching the epithelium with the least amount of axial force possible and scored as follows: 0, no bleeding; 2, bleeding. No changes in the outcomes occurred in the beginning of the experiment. The data gathering procedure is included in Supplementary Table 2.

Sample size calculation

According to Du et al.,[25] the sample size was set to find a 30% reduction in DIAGNOdent pen mean scores for WSLs in the treated groups relative to the untreated groups. Assuming that the control group's mean score after 6 months would be 13.1 ± 5.19 and using G*Power[26] led to Cohen's D effect size of 0.78. To identify such a difference, using a two-tailed test using a significance level (alpha) of 0.05 and a power of 0.8 power, a sample size of 27 individuals per group (324 teeth) was needed. To accommodate a 15% dropout rate, 31 participants (total of 62 participants) were required per group (372 teeth). This would put the sample within the central limit theorem and solve the issue regarding normality.[27]

Interim analysis and stopping guidelines

If there was a clear sensitivity to the intervention product that the participants were unable to tolerate, it was determined that the trial would be ended.

Randomization

Sequence generation

This process was performed using a computer random number generator (http://www.graphpad.com/quickcalcs/randomn2.cfm) to create a simple nonstratified randomization with an equal allocation ratio of 1:1. Allocation groups were randomly coded by a person who was not part of the study. The trial sample for all centers has been collated into one table (Allocation table) using a centrally managed process. As the Allocation table showed the participants' assigned groups and the study number, it could be used to reveal the groups. Therefore, it was kept sealed and out of the hands of the researchers until the data collection and analysis were completed.

Allocation concealment

Allocation concealment was achieved by using sequentially numbered, sealed, opaque envelopes that were also numbered in accordance with the study numbers. Each envelope contained: 1) Group 1 or 2 treatment allocation card; 2) The related preventive measures products in a sealed and opaque bag; and 3) A set of orthodontic brackets. The envelope was kept closed until the bonding day. At that point, the clinician knew the identity of the allocation group.

Blinding

Since the trial took place at multiple clinics, the investigator (outcome assessor) was able to collect and quantify all data without knowing which patients were in which groups. However, blinding of the operator was impossible during treatment due to the application of Curasept Biosmalto Impact Action Mousse Pro at each visit to the Biomimetic group.

Statistical analyses

Statistical Package for the Social Sciences (SPSS) for Windows was used for data analyses (version 25.0, SPSS Inc., Chicago, IL, United States). The statistical analyses that were used were listed below.

Descriptive statistics

Descriptive statistics were used to summarize the characteristics of the dataset including: interquartile range, minimum, maximum, mean, median, standard deviation, standard error, and quantities, frequencies, and percentages.

Reliability statistics

The measurement of VPI and GBI were calibrated with a periodontist to achieve adequate inter-examiner calibration. Intraclass correlation coefficient test was used for this assessment.

Inferential statistics

The Levene's test and Shapiro–Wilk test ensured that the group variances were homogeneous and the data were distributed normally. The following tests were employed:

- Two-way analysis of variance (ANOVA) to compare between study groups based on how the DIAGNOdent pen scores changed over time; and
- Mann–Whitney U test to compare the scores of ICDAS, GOI, VPI, and GBI between groups (categorical data).

The level of significance was established at $p < 0.05$, unless a Bonferroni adjustment was used to mitigate type I error. A 95% confidence interval was calculated for the mean difference between the study groups.

Results

Participant flow

Seventy patients were chosen for participation in this study. Of those, 35 were assigned to the Conventional group and 35 to the Biomimetic group. Four patients withdrew from the Conventional group before bonding the appliance. Three patients from the Biomimetic group and one patient from the Conventional group dropped out of the trial before

it was completed due to their inability to attend the scheduled appointments. Fortunately, this did not affect the group balance nor impair the sample size determination (within the anticipated number of dropouts).

The patient enrollment for this study started in December 2022 and concluded in April 2023. The trial concluded in October 2023. Sixty-two subjects who completed the study were included in the analysis (30 in the Conventional group and 32 in the Biomimetic group). Figure 1 illustrates the CONSORT flowchart diagram of the patients in this clinical research.

Baseline data

The participants' ages ranged from 12 to 36 years. The whole trial sample had an average age of 16.47 ± 4.43 years. Although females comprised a larger number of participants in both groups than males (71% of the total sample), there was no statistically significant difference in sex distribution between the two groups. Moreover, other baseline parameters exhibited no statistically significant differences between the groups, as shown in Table 1. The reliability results of the

Table 1: Baseline characteristics of the participants with their comparison between study groups.

Variable	Conventional (n = 30)		Biomimetic (n = 32)		P-value
Continuous data	Mean	SD	Mean	SD	
Age	15.47	2.34	17.41	5.63	0.081#
DIAGNOdent T0	7.97	1.59	7.89	1.55	0.838#
Categorical data (nominal data)	**Count**	**%**	**Count**	**%**	
Female	19	63.3	25	78.1	0.266^
Male	11	36.7	7	21.9	
Categorical data (ordinal data)	**Median**	**IQR**	**Median**	**IQR**	
ICDAS	1.00	4.00	0.00	2.75	0.634"
GOI	0.00	0.00	0.00	0.00	1.000"
VPI	22.92	21.35	22.92	23.96	0.849"
GBI	10.42	12.85	9.03	12.15	0.611"

SD: Standard Deviation; IQR: Interquartile range; T0: pre-treatment; ICDAS: International Caries Detection and Assessment System; GOI: Gorelick index; VPI: visible plaque index; GBI: gingival bleeding index. #: Independent samples *t*-test; ^: Chi square; ": Mann–Whitney U test.

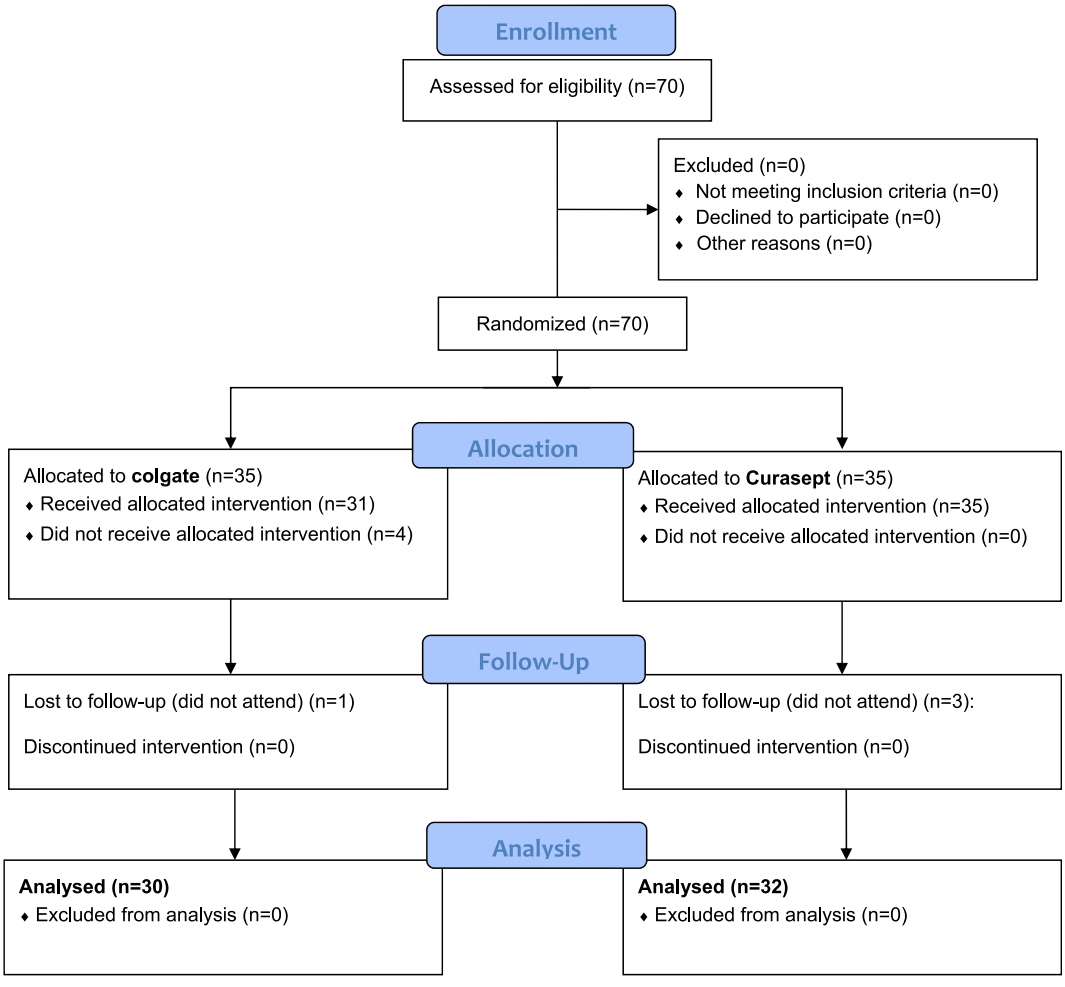

Figure 1: The CONSORT flowchart showing trial participants at each stage.

Table 2: Descriptive statistics for white spot lesion measures.

Variable	Time	Conventional (n = 30)		Biomimetic (n = 32)	
		Mean	SD	Mean	SD
DIAGNOdent	**T0**	7.97(Enamel caries)	1.59	7.89(Enamel caries)	1.55
	T1	9.27(Enamel caries)	1.88	9.75(Enamel caries)	2.47
	T3	8.56(Enamel caries)	1.15	8.78(Enamel caries)	1.58
	T6	8.90(Enamel caries)	0.96	9.03(Enamel caries)	1.15
	(T3−T0)	0.59	1.90	0.90	1.72
	(T6−T0)	0.93	1.57	1.14	1.54
ICDAS		**Median**	**IQR**	**Median**	**IQR**
	T0	1.00	4.00	0.00	2.75
	T1	1.50	4.00	1.50	3.00
	T2	1.50	4.00	1.00	3.00
	T3	2.00	4.00	1.00	3.00
	T4	2.00	4.00	1.50	4.00
	T5	2.00	4.25	2.50	5.00
	T6	3.00	4.25	2.50	5.75
GOI		**Median**	**IQR**	**Median**	**IQR**
	T0	0.00	0.00	0.00	0.00
	T1	0.00	0.00	0.00	0.00
	T2	0.00	0.00	0.00	0.00
	T3	0.00	0.00	0.00	0.00
	T4	0.00	0.00	0.00	0.00
	T5	0.00	0.00	0.00	0.00
	T6	0.00	0.00	0.00	0.00

T0: pre-treatment; T1:1 month; T2: 2 months; T3: 3 months; T4: 4 months; T5: 5 months; T6: 6 months; SD: standard deviation; IQR: interquartile range; ICDAS: International Caries Detection and Assessment System; GOI: Gorelick index.

VPI and GBI indicated high levels of measurement agreement. For the VPI, the intraclass correlation coefficient was 0.908 (95% CI: 0.619−0.977) and that for the GBI was 0.944 (95% CI: 0.782−0.986).

Numbers analyzed for each outcome, estimate, precision, and subgroup analyses

Sixty-two participants were analyzed. Since all patients were recruited in accordance with the predetermined eligibility criteria, there were no obvious qualitative disparities in the patient sample between centers. Similarly, as clinicians adhered strictly to the research protocol, no center effects were seen in the trial.

The descriptive statistics for treatment outcomes of WSL measures (DIAGNOdent pen, ICDAS, GOI) are shown in Table 2. Two-way ANOVA showed that there was no statistically significant difference in the DIAGNOdent pen scores with time × group interaction or between the two groups. However, there was a statistically significant difference between the two groups when the DIAGNOdent pen scores changed over time (Table 3). When pairwise comparisons were used to determine the difference between each two time points (Table 4). T0 showed statistically significantly lower scores than those of T1, T3, and T6. On the other hand, T1 showed a statistically significantly higher score than that of T3. While no statistical difference was observed between T1 and T6 and between T3 with T6. Based on the profile plots for the change in DIAGNOdent pen scores over time for each group (Figure 2), it was shown that at T1, both study groups showed higher values, which decreased at T3 and then slightly increased at T6.

Mann−Whitney U test was used to compare ICDAS and GOI scores between study groups at each follow-up visit (T0−T6). The results showed no statistically significant differences between the study groups. Since six tests in each index were performed addressing the same question, a Bonferroni correction was applied changing the p value from 0.05 to 0.008 (Table 5).

Table 3: Two-way ANOVA test to compare between study groups based on how DIAGNOdent pen score changed with time factor.

Source	df	Mean Square	F	p
Time	2.482	32.574	14.748	**0.000**
Time * group	2.482	1.019	0.461	0.673
Group	1	2.236	0.457	0.502

df: degrees of freedom.

Table 4: Pairwise comparisons between DIAGNOdent scores at different time points.

Time		Mean Difference	p
T0	**T1**	−1.583*	**0.000**
T0	**T3**	−0.741	**0.012**
T0	**T6**	−1.035*	**0.000**
T1	**T3**	0.842*	**0.020**
T1	**T6**	0.548	0.275
T3	**T6**	−0.294	0.637

T0: pre-treatment; T1:1 month; T3: 3 months; T6: 6 months.

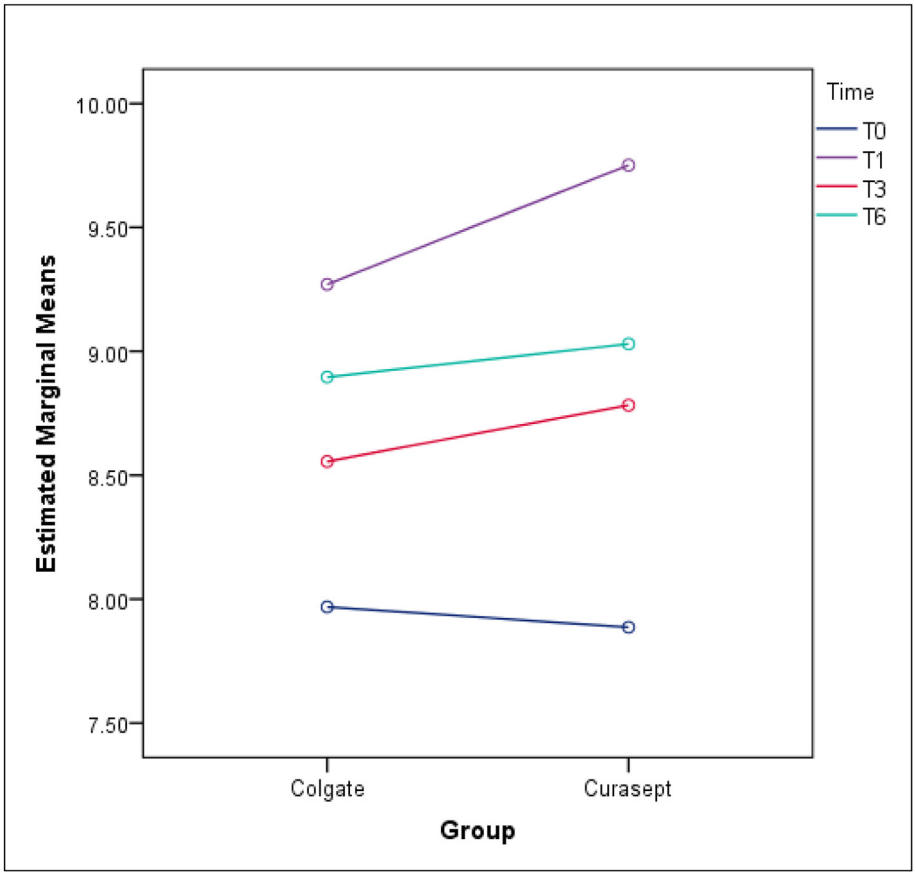

Figure 2: Profile plots for the change in DIAGNOdent pen scores over time for each group.

Table 5: Mann–Whitney U test to compare ICDAS and GOI scores between study groups at different time points.

Variable	Time	Conventional (n = 30)		Biomimetic (n = 32)		p
		Mean Rank	Sum of Ranks	Mean Rank	Sum of Ranks	
ICDAS	**T1**	32.50	975.00	30.56	978.00	0.656
	T2	33.02	990.50	30.08	962.50	0.500
	T3	33.53	1006.00	29.59	947.00	0.370
	T4	31.70	951.00	31.31	1002.00	0.930
	T5	31.40	942.00	31.59	1011.00	0.966
	T6	31.53	946.00	31.47	1007.00	0.989
GOI	**T1**	31.50	945.00	31.50	1008.00	1.000
	T2	31.50	945.00	31.50	1008.00	1.000
	T3	32.03	961.00	31.00	992.00	0.302
	T4	32.03	961.00	31.00	992.00	0.302
	T5	32.03	961.00	31.00	992.00	0.302
	T6	31.52	945.50	31.48	1007.50	0.982

$P < 0.008$.
T1:1 month; T2: 2 months; T3: 3 months; T4: 4 months; T5: 5 months; T6: 6 months; ICDAS: International Caries Detection and Assessment System; GOI: Gorelick index.

Table 6: Descriptive statistics for periodontal health measures.

Variable	Time	Median	IQR	Median	IQR
VPI	**T0**	22.92	21.35	22.92	23.96
	T1	53.13	32.29	38.54	18.75
	T2	51.04	24.48	34.38	30.21
	T3	50.00	40.10	45.83	44.27
	T4	42.71	26.04	22.92	24.48
	T5	46.88	24.48	21.88	32.29
	T6	50.00	25.00	20.83	16.67
GBI		**Median**	**IQR**	**Median**	**IQR**
	T0	10.42	12.85	9.03	12.15
	T1	16.67	20.83	12.50	12.15
	T2	18.06	11.46	13.19	13.89
	T3	14.58	12.15	9.03	14.58
	T4	15.28	9.72	8.33	6.25
	T5	15.28	15.97	5.56	11.11
	T6	16.67	12.85	6.94	8.33

T0: pre-treatment; T1:1 month; T2: 2 months; T3: 3 months; T4: 4 months; T5: 5 months; T6: 6 months; IQR: interquartile range; VPI: visible plaque index; GBI: gingival bleeding index.

According to the median scores, the Conventional group showed higher plaque scores than the Biomimetic group at all time points, except T0. Regarding the GBI, the Conventional group generally showed higher scores, which were more obvious in the later appointments (Table 6). The Mann–Whitney U test was used to evaluate disparities between the study group regarding periodontal health measures. For the VPI, statistically significant higher scores in the Conventional group were found at the successive time points of T2, T4, T5, and T6. Whereas for the GBI, there

Table 7: Mann–Whitney U test to compare VPI and GBI scores between study groups at different time points.

Variable	Time	Conventional (n = 30)		Biomimetic (n = 32)		p
		Mean Rank	Sum of Ranks	Mean Rank	Sum of Ranks	
VPI	**T1**	35.50	1065.00	27.75	888.00	0.091
	T2	36.42	1092.50	26.89	860.50	**0.038**
	T3	33.37	1001.00	29.75	952.00	0.430
	T4	37.98	1139.50	25.42	813.50	**0.006**
	T5	39.93	1198.00	23.59	755.00	**0.000**
	T6	42.80	1284.00	20.91	669.00	**0.000**
GBI	**T1**	34.97	1049.00	28.25	904.00	0.142
	T2	34.25	1027.50	28.92	925.50	0.244
	T3	34.70	1041.00	28.50	912.00	0.176
	T4	38.33	1150.00	25.09	803.00	**0.004**
	T5	38.12	1143.50	25.30	809.50	**0.005**
	T6	40.82	1224.50	22.77	728.50	**0.000**

$P < 0.008$.
T1:1 month; T2: 2 months; T3: 3 months; T4: 4 months; T5: 5 months; T6: 6 months. VPI: visible plaque index; GBI: gingival bleeding index.

were statistically significantly higher scores in the Conventional group at T4, T5, and T6. Since six tests in each index were performed addressing the same question, a Bonferroni correction was applied, changing the p value from 0.05 to 0.008. Subsequently, the difference of VPI at T2 could not be considered statistically significant after this correction (Table 7).

Harms

The results did not reveal any adverse effects.

Discussion

This study was designed as a multicenter randomized clinical trial, which is the gold standard for evaluating the effectiveness of such an intervention. Since the results of this study revealed no statistically or clinically significant differences between both groups on WSL avoidance, providing inadequate evidence to reject the null hypothesis.

The total sample size of this trial was comparable to other previous research comparing preventative agents, as their sample size ranged between 50 and 65 participants.[28,29] The age range of the participants (12–36 years) ensured that the permanent anterior teeth had erupted, allowing accurate WSL scores to be obtained on the labial surface without any difficulty. On the other hand, the greater number of female participants supports the typical finding that females are more conscious about their appearance, and thus have a greater probability of having their teeth treated.[30]

Several clinical studies consider the DIAGNOdent pen a reliable and noninvasive option to monitor initial caries lesions,[31–34] and have adequate specificity and excellent sensitivity.[35–37] Other studies, however, found that the device specificity was low,[38,39] there was no correlation between DIAGNOdent pen scores and visual examination,[40] or that the device was invalid in detecting initial carious lesions.[41] Those latter findings may be because the device was used in an *in vitro* setting that was not compatible with its method of action, which relies on bacterial byproduct rather than the structural breakdown of enamel tissue. In another study, the DIAGNOdent pen was unable to identify minor WSLs that could be detected by visual examination. This might, however, be the result of persistent discoloration of the underlying layer and partial remineralization of the enamel outer surface. Because plaque, stains, calculus, and tooth biofilm frequently alter DIAGNOdent pen scores, it is important to analyze these scores cautiously.[42,43] The teeth in the current study were carefully polished to reduce the chance of false-positive findings. Furthermore, teeth that had morphological abnormalities were mostly excluded from the study. In addition to the DIAGNOdent pen scores, the ICDAS and Gorelick index were employed in this study to ensure higher levels of evaluation of the WSLs.

In this study, the findings showed a significant difference in the DIAGNOdent pen scores over time. This could be attributed to difficulty in maintaining a normal balance between the demineralization and remineralization processes following bracket bonding, as well as food impaction around the fixed appliance assembly, which increases acid attacks and causes dissolution of the enamel outer surface. During the first month of bracket bonding, this became evident, when both groups showed a significant change in DIAGNOdent values. This was in line with the findings of Fejerskov et al.[44] and Al Tuma and Yassir,[45] who showed that demineralization surrounding orthodontic brackets develops more rapidly than with conventional caries due to the accumulation of unaltered plaques on the surface of the enamel. This may result in mineral depletion on the external enamel surface within a period of 3–4 weeks. Furthermore, the findings of the current study agreed with those of previous research demonstrating that WSLs might form within 1 month following bracket bonding.[46,47]

The scores gradually decreased (improved) after the first month compared to the first month's scores, although they were still higher than the baseline. The reason for this is that the initial acid attacks led to a significant degree of demineralization, which was then somewhat balanced by remineralization of the outer enamel surface, potentially strengthening the outer enamel surface. Additionally, after the first month, patients' experiences with keeping the area around the bracket cleaner could be enhanced. This decrease in DIAGNOdent pen scores over the course of the treatment was agreed with the findings of Restrepo et al.[31]

According to this study, the Curasept Biosmalto Impact Action Mousse Pro could be useful for remineralizing subsurface lesions on the long-term use, but it had no superiority in improving the surface activity or severity compared to regular fluoridated toothpaste at 6 months after use. Compared to the Conventional group, the WSL appearance did not improve as much in the Biomimetic group. Karabekiroğlu et al.[37] found that using CPP-ACP paste did not improve the appearance of WSLs any more than standard care. Other studies comparing the effect of CPP-ACP with fluoridated agent (toothpaste and varnish) at different observation intervals, also discovered that their effectiveness was equivalent to the remineralization efficacy of a fluoridated agent.[37,48–50] Moreover, Farzanegan et al.[51] concluded

that ACP is as effective as fluoride. In an *in vitro* study, Ionescu et al.[18] showed that every toothpaste and mousse had a remineralizing effect on human enamel and that the evaluated hydroxyapatite and ACP formulations had the ability to regenerate biomimetically. On the other hand, Robertson et al.[28] found that MI Paste Plus (CPP-ACP) assisted in preventing the formation of WSLs during orthodontic treatment compared to placebo paste. Similarly, other studies have shown that CPP-ACP caused a significant reduction in WSLs in orthodontic patients.[29,52,53] The variation in results throughout studies could be attributed to comparator groups, which could contain fluoride or placebo, as fluoride more likely shows an effect and could mask the difference with other intervention. Additionally, the methods and the standardizations of examinations and duration of study follow-up may also affect the results.

Hadler-Olsen et al.[54] found that patients receiving orthodontic treatment had a markedly increased chance of acquiring WSLs during treatment, and that there may be an association between WSL development and patient compliance. In this study, patients who developed WSLs had poorer oral hygiene (according to VPI and GBI). Even though there were no differences between groups at T0, over time, the Biomimetic group practiced superior dental hygiene compared to the Conventional group, which may help explain why the ICDAS scores of Conventional group were slightly higher (yet still not significant). It has been proven that poor oral hygiene poses a significant risk for the development of WSLs.[54–56]

Visual examination using ICDAS scores has been introduced as an efficient method to evaluate enamel demineralization and formation on the tooth surface.[57] Consistent with the results of this study, several other investigations have reported no significant difference in regard to enamel demineralization between remineralizing agent groups and fluoride-containing material groups based on visual examination.[37,49,58]

The use of GOI to detect WSLs was in line with several studies.[37,49,54,59] Gorelick and a co-worker used a photographic approach to assess WSLs, which may be regarded as less precise than the direct clinical examination that was used in this study. They found a prevalence of WSLs of 50% among fixed orthodontic patients.[24] The findings of the present study revealed a statistically nonsignificant difference between the two groups during the 6-month course of treatment.

In this study, the VPI showed an increase in both groups after 1 month of bonding, in line with a study by Naveed et al.[60] which reported that the bacterial ecology of the plaque changes significantly when orthodontic fixed appliances are inserted into the mouth. Acidogenic bacteria are more concentrated in plaque, with *Lactobacilli* and *Streptococcus mutans* being the most prominent. Thus, during orthodontic treatment, stressing the enhancement of adequate oral hygiene is advantageous to reduce the amounts of these germs.

According to VPI, there were superior results of Biomimetic group compared with the Conventional group at time points T4, T5, and T6, whereas the Biomimetic group scores were comparable to those of the baseline scores. Although this finding could be attributed to the cooperation of the patient, it can also be due to the mechanism of action of Curasept. Despite the active components of Curasept Biosmalto Impact Action Mousse Pro, their effectiveness was comparable with the fluoride toothpaste remineralization efficacy alone. This may be related to the duration of the study (6 months only) or frequency of using mousse, as both might be increased to reflect greater impact of ACP-containing mousse.

In the current study, the mean GBI increased in both groups during the 2 months after the brackets were bonded. This supports the fact that fixed appliances can make brushing more difficult, and when plaque builds up at the gingival edge, gingival irritation, and bleeding have been reported.[61,62] However, from the third month until the end of the trial, the mean GBI in the Biomimetic group significantly decreased and reached the baseline level. This was a consequence to the drop in the VPI in the same group in the second half of the trial.

This study outcomes in terms of VPI and GBI in addition to the above-mentioned mechanism of action of Curaspet Biosmalto Caries, Abrasion and Erosion products (Impact Action Mousse Pro and toothpaste) suggest that these products may have a potential advantage in the remineralization of WSLs regarding long-term effects. Daily use of the toothpaste may lead to more pronounced effects over time, but this was not apparent within the time frame of this study. The current results may be related to the effect of fluoride, which is present in both groups, whereas other ingredients such as carbonate, magnesium, and strontium salts (which are present in the Curasept Biosmalto Caries, Abrasion & Erosion toothpaste) and ACP (which is present in the Curasept Biosmalto Mousse Pro) did not seem to have an effective impact within this period.

Based on this study, the Curasept Biosmalto Caries, Abrasion and Erosion products (Impact Action Mousse Pro and toothpaste) and Colgate fluoridated toothpaste have nearly similar effects on preserving enamel from WSLs. Therefore, a suggestion to clinicians is to emphasize the use of a preventive protocol, either a fluoride-containing toothpaste or professional mousse.

Limitations of the study

The main problem faced with the DIAGNOdent pen was the false-positive scores. Therefore, DIAGNOdent pen scores must be assessed judiciously, as they may be influenced by plaque, bacterial metabolites, staining, calculus, dental biofilm, and sticky substances, potentially leading to false-positive results if not adequately eliminated. In this research, meticulous and sometimes repeated tooth cleaning was performed at each visit before scoring to address this problem. Moreover, during bonding of the brackets, they were checked with great care so that no obvious extra adhesive has remained on the tooth surface around the brackets.

Additionally, since there are concerns about the results of the DIAGNOdent pen, this study did not rely solely on Diagnodent results to identify the WSLs. It was used in adjunct to the ICDAS and Gorelick indices to detect the WSLs to provide a more comprehensive and robust assessment.

Despite efforts to address the compliance barriers, such as providing patients with brushing technique instructions, similar toothbrushes, and standardizing brushing duration and frequency, patients' cooperation could not be fully controlled.

The study findings only demonstrated the effect of Curasept Biosmalto Impact Action Mousse Pro during the 6 months of orthodontic treatment. It is worth evaluating the long-term effects. A future research direction could involve evaluating the effectiveness of Curasept Biosmalto Impact Action Mousse Pro in the remineralization of post-orthodontic WSLs. In addition, it may be worth re-testing these biomimetic products using individual scores for teeth to identify the frequency of teeth presenting one or more WSL per group/time point.

Future studies are recommended to compare the effectiveness of the mousse with other methods such as ICON in managing WSLs. Such comparisons could provide valuable insights into their relative efficacy in remineralizing enamel and improving the aesthetic appearance of lesions, helping clinicians choose the most appropriate treatment approach.

Conclusions

Monthly application of Curasept Biosmalto Impact Action Mousse Pro with daily use of Curasept Biosmalto Caries, Abrasion & Erosion toothpaste did not seem to be more effective than regular daily use of fluoridated toothpaste in preventing the development of WSLs during the first 6 months of orthodontic treatment.

Regular daily use of Curaspet Biosmalto Caries, Abrasion and Erosion products (Impact Action Mousse Pro and toothpaste) particularly the toothpaste could result in improved gingival health and reduced plaque accumulation over time.

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The study was self-funded.

Conflict of interest

None to declare.

Ethical approval

Ethical approval was provided by The University of Baghdad's College of Dentistry's Ethics Committee on February 19, 2023 (Reference No. 775423).

Authors contribution

SHA Writing - preparation of the original document, writing - review and editing, software, validation, research, resources, methodology, and visualization. YAY Administration of project, supervision, formal analysis, validation, conceptualization, resources, data curation and visualization. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

Data availability statement

Data are available upon request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jtumed.2025.06.004.

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Further reading

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