Control of White Spot Lesions with Use of Fluoride Varnish or Chlorhexidine Gel During Orthodontic Treatment
A Randomized Clinical Trial

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Objective: *To compare the effectiveness of fluoride varnish and 2% chlorhexidine gel for controlling active white spot lesions (WSLs) adjacent to orthodontic brackets.* ***Study design****: Thirty-five orthodontic patients (17.2 ± 2.3 years old) presenting 60 WSLs adjacent to orthodontic brackets were enrolled in this randomized, blind, 3-armed and controlled clinical trial. The patients were randomly allocated to 1 of 3 arms: (1) two applications of 5% NaF varnish- F, with one-week interval, (2) two applications of 2% chlorhexidine gel-CHX, with one-week interval and (3) usual home care-control (CO). The WSLs were scored by using a DIAGNOdent pen. An independent examiner scored the surfaces using Nyvad criteria for caries assessment.* ***Results:*** *A total of thirty patients presenting 51 lesions completed the study. All treatments reduced the fluorescence values during the experimental period; however, F induced faster remineralization than CHX. After 3 months, 70.58 % were inactive considering all groups. DIAGNOdent pen and Nyvad presented a significant correlation.* ***Conclusion:*** *After 3 months of treatment, F, CHX and CO were capable of controlling the WSLs adjacent to the orthodontic brackets. However, the treatment with F was capable of controlling the progression of the WSLs in a shorter period of time.*

Key words: *Chlorhexidine, Dental Caries, Fluorescence, Fluoride, Orthodontic Appliances, Tooth remineralization.*

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INTRODUCTION

The brackets and accessories used for the orthodontic treatment favor dental biofilm accumulation, increasing the prevalence of cariogenic and peridontopathogenic bacteria and the risk for the development of caries lesions and gingivitis.[1, 2]

Clinically, the demineralization sites are detected as opaque and porous White Spots Lesions (WSLs) that may compromise the final result of the orthodontic treatment. The development of these lesions mainly occurs due to difficulties with oral hygiene. The incidence of WSLs during orthodontic treatment may vary between 15 % and 85 %,[3] thus justifying the need of patient motivation and training to perform tooth cleaning in addition to the use of professional remineralizing treatments, with the purpose of preventing the progression of WSLs in cavities, which would demand operative treatment.

The conservative approaches for WSLs using remineralizing therapies have become a subject of growing interest among clinicians and researchers. Accordingly, the use of fluorides has shown to be a highly effective strategy in the prevention and control of caries lesions, since its presence in the oral cavity reduces demineralization and improves remineralization.[4]

There is a body of scientific evidence that proves the benefits of fluoride varnish in reducing the incidence of WSLs during orthodontic treatment.[5] Fluoride varnish has some advantages as ease of application, safety, prolonged contact time with enamel and good acceptance by patients, which have made it one of the main choices among the remineralizing agents.[6]

On the other hand, some strategies have been adopted for biofilm control with the use of antimicrobial containing pastes, mouthwash solution and varnishes. Chlorhexidine is the most effective antimicrobial agent for the control of periodontal pathologies in orthodontic patient.[7]

The capacity of chlorhexidine to prevent and control caries, by its antimicrobial effect, has been a controversial topic, and the evidence is still inconclusive.[8] Systematic reviews have suggested the need for controlled and longitudinal clinical trials that evaluate the efficacy of chlorhexidine and the possible adoption of antimicrobial therapies with effectiveness similar or superior to fluoride in controlling the progression of WSLs.[9, 10]

Therefore, the aim of this 3-month clinical trial was to compare the effectiveness of fluoride varnish and chlorhexidine gel for controlling active WSLs adjacent to orthodontic brackets.

MATERIALS AND METHOD

This study was previously approved by the Research Ethics Committee of the Araraquara School of Dentistry, Universidade Estadual Paulista- Unesp, under the Protocol Number 29/11, and was conducted in accordance with the principles of medical research involving human subjects described by the Declaration of Helsinki.

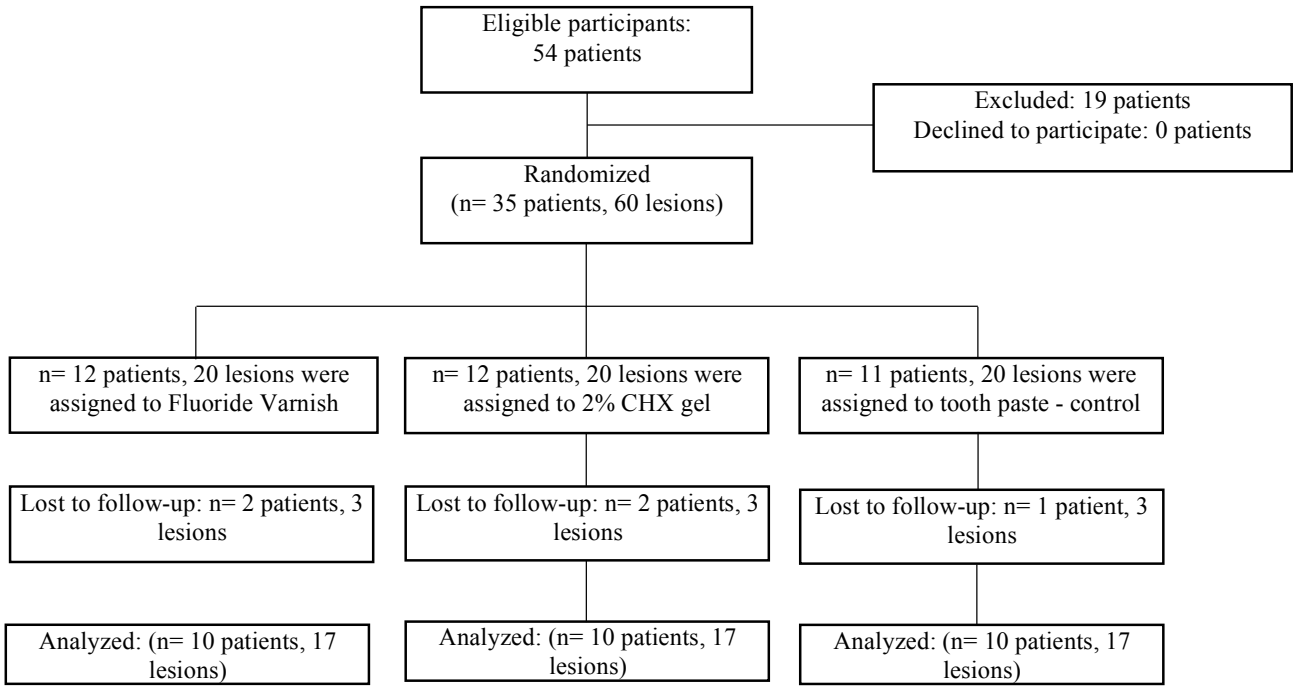
The purpose and procedures were fully explained, and before enrollment in the study, all participants or the guardians of those under 18 years of age signed a term of free and informed consent.

In this randomized, blinded and controlled clinical trial, adolescents who were being under orthodontic treatment at the Araraquara School of Dentistry – Unesp, from March 2011 to January 2013, were enrolled. Sample size calculation was based on detecting a 20 % reduction in DIAGNOdent pen (DDpen) reading, with an assumed significance level of 0.05, standard deviation of 3.0, detectable difference of at least 4.0, and a power of 80 %.[11] It was considered that the values in the readout by the DDPen should not be higher than 20. A sample size of 54 patients was suggested.

From the fifty-four patients selected, thirty-five were eligible (60 lesions in total). They were 13 - 20 years old and from both genders. The inclusion criteria were: age, living in Araraquara city, with fixed appliance in both arches (for a period of 6 - 12 months) using Edgewise technique, treated by a single orthodontist, with at least one active WSL in the buccal surface of anterior teeth and/or pre-molars adjacent to orthodontic bracket. The exclusion criteria were: teeth presenting fillings or enamel defects; patients with periodontal disease, who were under medical treatment or taking any type of medication.

The randomization method and distribution into each group adopted was the simple random method. All patients participated in a meeting, where a draw was held with the aid of computer software, to determine the group to which the patient would be allocated: (1) two applications of 5 % NaF Varnish- F with one-week interval (12 patients, 20 lesions), (2) two applications of 2 % Chlorhexidine gel-CHX with one-week interval (12 patients, 20 lesions) and (3) usual home care control – CO (11 patients, 20 lesions) (Fig. 1).

Figure 1. Flow diagram of participants through the randomized trial.



The teeth were first cleaned using brushing and pumice slurry. Afterwards the teeth were dried and treated with: 5 % NaF varnish (Duraphat®, Colgate Palmolive, Hamburg, Germany) or 2 % chlorhexidine gel (Clorexal gel 2 %, Biodinâmica, Paraná, Brazil). Both agents were applied using a bendable micro applicator brush, two times with an interval of one week between applications. The patients were instructed not to eat anything, or to brush their teeth for at least four hours after the treatment.

In the control group, a saline solution was applied with the aid of a bendable micro applicator brush, in the same way as was done for the groups with F and CHX.

All patients received instructions with respect to oral hygiene and diet. During the study, fluoride toothpaste (Colgate Total with 1.450 ppm F) was used for oral hygiene twice a day. Study participants were also instructed not to use any other fluoride or/and antiplaque agents.

Status of the WSLs were assessed using a DIAGNOdent Pen 2190 – DDpen (KaVo, Biberach, Germany), at the following time intervals: baseline, one week after each application of F or CHX or saline solution, and 1, 2 and 3 months after the treatments. DDpen was previously calibrated using a ceramic standard and regulated by measuring the sound surface of each included tooth ("sound enamel fluorescence"). The measurements were performed after 5 s drying with compressed air using the "tip number 2". The peak reading displayed on the panel of the DDpen was recorded twice for each tooth surface by one blinded and previously calibrated examiner (K value = 0.92).

The progression or regression of the WSLs was also analyzed by visual examination, after prophylaxis, on the facial surfaces of anterior teeth and pre-molars, by one blinded and previously calibrated examiner (k value = 0.89) using the Nyvad criteria- NY (Table 1),[12] at baseline and 3 months after the treatments.

To measure the oral hygiene status the Simplified Oral Hygiene Index (S-OHI) index scores were recorded at the beginning and the end of the study.

The primary outcome was the change in lesions fluorescence measured with the DDPen after 3 months. The fluorescence analysis done 1 week after each application, as well as 1 and 2 months after the treatments, the lesion activity (NY criteria) and the S-OHI after three months were considered the secondary outcomes.

In this study, the patients (and their guardians, when applicable) knew the aim of the study with regard to the control of WSLs, but they were not informed about the products that would be used in the research, or about the group to which the patient belonged. The patients could not identify the products by their smell, texture or appearance. The evaluations using the DDpen were performed by one blinded independent clinician, and the visual exams, using the NY criteria, were performed by another blinded independent clinician. A researcher, who was also blinded in respect to the treatments, performed the statistical analysis.

Statistical analysis

The data were analyzed using R statistical software program (Development Core Team, Vienna, Austria).

The error in the measurements (DDpen readings) was evaluated by the Dahlberg formula and the Interclass Correlation Coefficient (ICC). At baseline and after 3 months the errors of measurements by the Dahlberg formula were 0.29 and 0.28, respectively; and the ICC values were 0.88 and 0.91, respectively.

The normal distribution of data was checked using the Shapiro-Wilk test. The DDpen results were compared using repeated-measures ANOVA and Tukey's tests. Concerning the DDpen data, a mean value of all included sites in each patient was calculated in order to use the patient as a unit. The NY index scores registered at baseline and at the end of the study were compared using repeated-measures ANOVA. To correlate the data obtained from the DDpen and NY criteria, the Spearman correlation was applied. Paired Student's-t test was applied to compare baseline and final S-OHI scores.

RESULTS

No patients reported any side effects during the study. From 35 patients (n= 60 lesions) initially recruited, 5 patients dropped out due to personal reasons: two from F group (3 lesions), two from the CHX group (3 lesions) and one from the CO group (3 lesions). Therefore, 30 patients (18 boys and 12 girls; mean age, 17.2 ± 2.3 years old) with 51 WSLs concluded the study (Figure 1).

Table 1. Indices proposed by Nyvad *et al*, 1999 [12] for the diagnosis of caries lesions, used in this study

Score	Category	Criteria
0	Sound	Normal enamel translucency and texture (slight staining allowed in otherwise sound fissure).
1	Active caries (Intact surface)	Surface of enamel is whitish/yellowish opaque with loss of luster; feels rough when the tip of the probe is moved gently across the surface; generally covered with plaque. No clinically detectable loss of substance. Smooth surface: Caries lesion typically located close to gingival margin.
2	Active caries (Surface discontinuity)	Same criteria as score 1. Localized surface defect (microcavity) in enamel only. No undermined enamel or softened floor detectable with the explorer.
3	Active caries (cavity)	Enamel/dentin cavity easily visible with the naked eye; surface of cavity feels soft or leathery on gentle probing. There may or may not be pulpal involvement.
4	Inactive caries (Intact surface)	Surface of enamel is whitish, brownish or black. Enamel may be shiny and feels hard and smooth when the tip of the probe is moved gently across the surface. No clinically detectable loss of substance. Smooth surface: Caries lesion typically located at some distance from gingival margin.

At the baseline, 49 lesions (96.07 %) were classified as active with intact surface (NY, score 1) and 2 lesions (3.93 %) as active with surface discontinuity (NY, score 2). With respect to both NY score and DDpen readings, the baseline values were similar among the groups ($p > 0.05$) (Table 2).

Generally, the fluorescence values diminished during the course of the study (Figure 2). The WSLs had a mean DDpen reading at baseline of 17.2 ± 2.3 in F group, 16.8 ± 1.8 in CHX group and 17.0 ± 1.7 in CO group, which decreased to 7.2, 9.2 and 10.5, respectively, at the end of the study (3 months) (Table 3).

One week after the first application, the fluorescence values were significantly lower than those at the baseline for F ($p < 0.01$) and CHX ($p < 0.01$) (intragroup comparison); significant differences from the baseline values were found for the control only one week after the second application ($p < 0.01$). The fluorescence values for F remained constant from the 1st to the 3rd month and significantly differed from the baselines values ($p < 0.05$). At the third month, the fluorescence values of F were similar to CHX ($p > 0.05$), but significantly differed from CO ($p < 0.05$). However, the CHX values were similar to the values of CO ($p > 0.05$).

At the end of the study, 70.58 % of WSLs were classified as inactive with intact surface (NY, score 4) and 29.42 % as active with intact surface (NY, score 1). There was no significant difference among the groups at the end of the study; however, the percentages of scores differed significantly at the end of the study in comparison with the baseline for all treatments (Table 2).

DDpen and NY presented a significant correlation ($r^2 = 0.67$, $p = 0.043$). There was a statistically significant difference in S-OHI scores between the baseline (1.67 ± 0.54) and the final (0.81 ± 0.47) evaluation for all groups ($p < 0.05$).

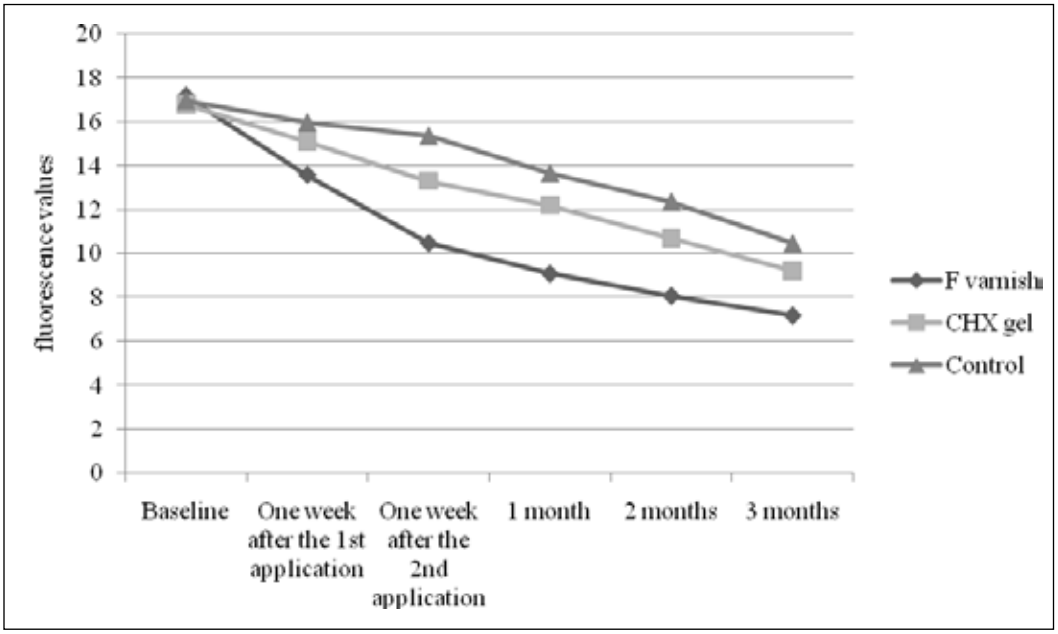
DISCUSSION

In this study, WSLs adjacent to the orthodontic bracket were treated and monitored for a period of 3 months in adolescents who were undergoing active orthodontic treatment between 6 - 12 months. Factors such as material, surface, location, roughness and bracket configuration are related to the increase of biofilm accumulation. Hadler-Olsen *et al* reported that 50 % of the patients with fixed appliances developed at least one WSL during treatment.[13] Another study found that 72.9 % of patients, undergoing orthodontic treatment, developed at least one caries lesion, of which 2.3 % presented cavitation.[14] Using Quantitative Light-Induced Fluorescence - QLF, Boersma *et al* observed that 30 % of the orthodontic patients developed WSLs during the course of treatment.[15] These data emphasize the high susceptibility of enamel surface adjacent to the orthodontic bracket for developing initial caries lesions. Thus, this is a relevant clinical problem that may compromise the aesthetic result of treatment and require restorative treatment either. Therefore, early diagnosis enables the clinician to implement remineralizing therapies with the goal of paralyzing lesion progression.[16]

In this study, the most affected tooth by WSLs was the maxillary lateral incisor (20 %), possibly due to the short distance between the bracket base and gingiva, which makes it difficult for patients to perform cleaning, and favors biofilm accumulation. A high incidence of WSLs in the maxillary canines and lateral incisors has been reported in other studies.[5, 17] In the present study, it was also observed that 45 % and 11.5 % of the patients presented 2 and 3 active WSLs, respectively after 6 - 12 months of the beginning of the treatment. The study of Tufekci *et al* showed a considerable increase in the number of WSLs during the first 6 months of treatment.[16] These findings reinforce the importance of evaluating the oral hygiene condition of the patient before and during treatment, and if necessary, the inclusion of remineralizing therapies.

The clinical quantification of changes resulting from caries lesions may be performed by using different methods as laser fluorescence devices. The DDpen is able to capture, analyze and quantify the fluorescence emitted from porphyrins and other chromophores. Studies have shown a good performance in detecting initial caries lesions [18, 19] and in monitoring the remineralization process.[11, 20]

Figure 2. Alterations in the fluorescence values (DDpen) of F, CHX and CO during the time of follow-up



The visual clinical exam was performed in accordance with the Nyvad criteria,[12] which presented a moderate and significant correlation with the DDpen readouts. This result indicates that WSLs may be moderately correlated with microbial activity, since the DDPen is capable of quantifying the products of bacterial metabolism, such as porphyrins.[21] DDPen is a non-invasive option for monitoring caries lesions, which allows quantitative follow-up of the progression of WSLs treated using different protocols.[22] The DDpen, as an outcome measure, may have a limitation for the difficulty of interpret clinically the values of the readings. Similarly to other authors, we did not interpret the results obtained with the DDPen based on cut-off points used to determine health/disease; i.e., healthy/carious, but as a quantitative indicator of the improvement of WSL after the treatments. [23] Furthermore, the use of DDPen is a good appeal for improving patients' motivation, because it quantitatively shows the lesion regression/ progression. However, we must consider its high cost, time consume and the possibility of false-positive results.[24] On the other hand, the correct use of visual criteria provides an easier, more economical and fast method, which allows the diagnosis and the treatment decision, however, it presents limitations as subjectivity and it is less informative to the patient.

The anticaries and remineralizing effect of fluoride varnish is well established.[25] However, the appropriate intervals for fluoride varnish application in orthodontics patients remain undetermined. There is a very clear need of further studies on this subject. In the present study, lesions treated with F varnish responded faster than the other treatments, showing remineralization after the first and second application, which was maintained over the course of three months. This demonstrated that two applications of F varnish associated with good oral hygiene and use of fluoridated toothpaste were sufficient to arrest lesion progression.

It has been previously demonstrated a reduction in caries prevalence by the application of F varnish twice per year,[26] but for orthodontic patients with active WSLs, the clinical protocol has not been established. With regard to chlorhexidine, there is a lack of scientific evidence with respect to its efficacy against dental caries as well as the best concentration and the clinical protocol of application.[27] Therefore, the capacity of chlorhexidine to prevent the progression of initial caries lesions must be considered as done in the present study. The clinical protocol applied in this study was based on previous works aiming to establish a treatment protocol for short periods of time with a good cost-benefit ratio.[26, 28]

A benefit of F varnish application is the precipitation of a CaF_2-like layer on the enamel, which acts as a reservoir, releasing fluoride during cariogenic challenges. Is important to note that the inhibition of enamel demineralization and the enhancement of remineralization are positively but not linearly related to the concentration of fluoride .[29] However, we believe that since brackets favor biofilm accumulation, they could also favor the retention of varnish, thereby increasing its contact time with enamel. Therefore, it is expected a high reactivity between NaF and tooth surface,[30] which justifies the use of F varnish in orthodontic patients with active WSL.

It has been hypothesized that the precipitation of ions on the superficial layer may obliterate the pores and prevent the diffusion of ions into the body of the lesion. However, a study has shown that after the application of F, the pores are not totally obliterated and remineralization of the lesion body may also occur.[29] ten Cate and collaborators affirmed that F- deposition during treatment depends not only on F concentration, but on lesion depth either.[31] WSLs usually have a large crystallite surface area for F-adsorption allowing the formation of fluoridated hydroxyapatite crystals within the lesion, favoring remineralization.[31]

It should be considered that biofilm accumulation is also associated with gingival inflammation during orthodontic treatment. An increase in the number of periodontopathogenic bacteria has been demonstrated in this group of patients.[2] The benefits of using antimicrobial agents for the control of gingivitis have been widely discussed in the literature, and at the present, CHX is considered the most effective agent for this purpose.[7] CHX has capacity to inhibit biofilm formation, which is one of the main etiological factors of caries disease.

Table 2. Number of WSLs by group classified according to Nyvad *et al*, 1999[12] at baseline and after 3 months

Nyvad	Baseline*		3 months*		Intragroup
Group	Active caries (intact surface)	Active caries (surface discontinuity)	Active caries (intact surface)	Inactive caries (intact surface)	*p-value*
F varnish	15	2	2	15	*p < 0.001*
CHX gel	17	-	7	10	*p < 0.001*
Control	17	-	6	11	*p < 0.001*

* For intergroup comparison, no significant differences were detected ($p > 0.05$)

Table 3. Fluorescence values at Baseline and at the end of the intervention (3 months). Values denote mean, standard deviation (SD) and 95 % confidence intervals (CI)

	F varnish (n= 10 patients, 17 lesions)			CHX gel (n= 10 patients, 17 lesions)			Control (n= 10 patients, 17 lesions)		
	Mean	SD	CI	Mean	SD	CI	Mean	SD	CI
Baseline	17.2	2.3	16 - 18.4	16.8	1.8	15.9 – 17.8	17	1.7	16.1 – 17.9
3 months	7.2*	1.6	6.4 - 8	9.2*	1.6	8.4 – 10.1	10.5*	2	9.5 – 11.6

* Statistically significant difference compared with baseline ($p < 0.05$)

However, its effect on the prevention and control of WSLs has not yet been confirmed.[32]

The results of this study suggest no additional effect of the application of 2 % CHX gel for the purpose of remineralizing WSLs in orthodontic patients. Similar results were also reported by Øgaard *et al*,[33] showing that the association of fluoride and CHX did not result in significant reduction in the development of WSLs on the buccal surface, in comparison with fluoride only. However, the use of antimicrobial agents cannot be discarded in other situations for the control of biofilm and gingivitis, which are also frequently present during orthodontic treatment.

All the patients received oral hygiene instructions and used fluoridated dentifrices throughout the entire experiment. The interpretation of the null findings should not be considered unfavorable results, but highlight the relevance of the patients' motivation to take care of oral health. However, this type of approach is 100 % acceptable, justifying the relevance of the findings showing the F varnish was able to accelerate the regression of active WSLs, and it could be indicated for patients unmotivated or with difficulties in performing adequate oral hygiene.

Although this study attained its objectives, some limitations were found. The sample size may have been very small; thus, studies with a larger sample size are necessary to confirm our results. Furthermore, future studies with a longer follow-up time, as well as with the inclusion of more clinically relevant outcomes, besides DDpen that presents some limitations, must be conducted to verify whether any significant difference can be observed between the treatments. Other criteria such as the type of bracket, orthodontic technique and the association between fluoride and antimicrobial agents, as well the use of products containing Casein Phosphopeptide-Amorphous Calcium Phosphate (CPP-ACP) [34, 35] should also be considered in the future.

CONCLUSION

After 3 months, F, CHX or CO was capable of controlling the WSLs adjacent to the orthodontic bracket. However, the treatment with F varnish was capable of controlling the progression of the lesion in a shorter period of time.

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