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Efficacy of a fluoride-releasing orthodontic primer in reducing demineralization around brackets: An in-vivo study

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Introduction: A new, highly filled primer is currently marketed as a fluoride delivery system effective in reducing white spot lesions in orthodontic patients. However, no studies in the literature support this claim. The purpose of this in-vivo study was to investigate the retention and the efficacy of this primer in reducing the formation of white spot lesions. **Methods:** In each patient for whom premolar extractions were planned ($n = 22$), 1 premolar was randomly chosen as the experimental tooth for the application of the fluoride delivery system (Opal Seal; Ultradent Products, South Jordan, Utah), and the contralateral tooth was assigned as the control to receive the standard treatment (Transbond XT; 3M Unitek, Monrovia, Calif). After the bonding procedures, separators were placed around the premolar brackets to encourage plaque retention over 8 weeks. After the extractions, the tooth surfaces were evaluated visually and with microhardness techniques for demineralization. Primer retention was also investigated. **Results:** There were no statistically significant differences in the numbers of white spot lesions between the 2 groups. The primer retention was calculated as 50%. **Conclusions:** The results indicated no significant difference between the efficacies of the fluoride-releasing primer and the control primer in reducing demineralization over the duration of the study. (Am J Orthod Dentofacial Orthop 2014;146:207-14)

During orthodontic treatment, formation of white spot lesions (WSLs) around brackets has long been recognized as a potential risk.[1] WSLs, a clinically detectable manifestation of subsurface enamel demineralization, represent the early stages of caries formation.[1-3] WSLs exhibit up to 50% reduction in enamel mineral loss.[4,5] Because of this mineral loss, there are changes in the hardness and refractive index of the enamel, causing scattering of light and giving the enamel a chalky, opaque appearance.[4]

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WSLs can develop in the gingival areas of teeth in as little as 4 weeks after bracket placement.[5] The high incidence of WSLs is attributed to prolonged plaque retention around brackets, since it is more difficult for orthodontic patients to perform effective oral-hygiene measures with orthodontic attachments.[1,2,5-8] Unfortunately, WSLs often persist and cause esthetic dissatisfaction at the end of orthodontic treatment.[9]

Scientific evidence for the use of fluoride to prevent enamel demineralization is well established.[10-12] Fluoride ions delivered through mouth rinses, varnishes, gels, and fluoride-releasing cements have been reported to reduce the extent and incidence of WSLs during orthodontic treatment with fixed appliances.[10-12] However, regimens to administer fluoride by topical application or home rinse programs are limited because of unpredictable patient compliance.[13]

One approach to minimize demineralization, without a need for patient compliance, is the application of a resin sealant to the enamel surfaces. Although unfilled or lightly filled resin sealants have been shown to be effective in reducing demineralization in vitro, subsequent clinical studies have not supported these results.[14,15] Newer highly filled sealants are reported to resist toothbrush abrasion.[16] Therefore, these materials are effective in reducing enamel demineralization.[17,18]

Recently, a new glass ionomer primer (Opal Seal; Ultradent, South Jordan, Utah) has become commercially available for use in orthodontic patients with poor oral hygiene. Because of its high filler content (38%), this product is claimed to exhibit long-lasting coverage and superior fluoride release and recharge abilities. In a previous study, fluoride ion release from a novel glass ionomer containing polymer was reported.[19] Although it is possible that Opal Seal has a similar profile over a period of time, in the literature there is only 1 study that investigated its release and recharge abilities in vitro at 24 hours.[20] The application of acidulated phosphate fluoride to the Opal Seal disks resulted in recharging the fluoride ions into the primer composition that would be available for subsequent release.[20] Currently, in the literature, no clinical studies have evaluated the efficacy of Opal Seal in the prevention of WSLs in patients undergoing orthodontic treatment with fixed appliances.

The aims of this in vivo study were to (1) compare the efficacy of a new, highly filled fluoride releasing orthodontic primer (Opal Seal) with a conventional nonfluoride orthodontic primer (control, Transbond; 3M Unitek, Monrovia, Calif) in preventing demineralization adjacent to brackets using visual examination and microhardness indentation techniques, and (2) evaluate the retention of Opal Seal on tooth surfaces using black-light detection.

MATERIAL AND METHODS

Before the study, ethical approval was obtained from the Research Office of Virginia Commonwealth University. Orthodontic patients (10-20 years old) who were scheduled to have at least 2 premolars extracted for orthodontic purposes were identified. The sample size was determined using the data for $\mu 1$, $\mu 2$, and σ from the study by Pascotto et al.[21] A power analysis indicated that 10 patients per group would result in a 90% chance of obtaining significance at the 0.05 level. Because of possible dropouts, 22 patients (11 per group) were enrolled.

At baseline, oral hygiene status was determined using the plaque and bleeding indexes. The presence and absence of WSLs was also evaluated with the visual examination technique. Patients with good overall health and good oral hygiene (with no bleeding after 30 seconds and no plaque, or having a discontinuous band of plaque at the gingival margin) were selected. In addition, the first premolars had to be fully erupted and intact without visible defects on the buccal surfaces. The patients who met all inclusion criteria were enrolled, and informed consent was obtained. A split-mouth study design was used; in each patient, 1 premolar was randomly chosen as the experimental tooth, and the contralateral tooth was assigned as the control.

Before bonding, the tooth surfaces in both groups were cleaned with a rubber prophy cup and fluoride-free pumice, etched for 15 seconds with 37% phosphoric acid gel (3M Unitek), rinsed with water for 5 seconds, and dried with an oil-free air-water syringe. Opal Seal was applied to the experimental teeth according to the manufacturer's instructions. The control teeth received a nonfluoride conventional orthodontic primer (Transbond XT moisture insensitive primer; 3M Unitek). To standardize the amount of adhesive used for bonding of each bracket, precoated premolar brackets were used (APC II Mini Twin Bicuspid; 3M Unitek). After positioning and firmly pressing the bracket on the enamel surface, the excess adhesive was removed with a periodontal probe. The adhesive was then light cured for 3 seconds from the mesial aspect and 3 seconds from the distal aspect using a plasma arc visible light-curing unit (Ortholite; 3M Unitek). All bonding procedures were carried out by the same clinician (D.R.P.). Subsequently, elastomeric spacers were placed around the bracket wings to encourage plaque accumulation so that the ideal environment for the development of WSLs could be provided. At subsequent orthodontic appointments, the accumulation of the plaque was visually confirmed on the teeth around the spacers. The patients were not told which tooth received the experimental orthodontic primer. All patients were instructed to brush twice a day with an over-the-counter fluoride-containing toothpaste. However, they were asked not to use any other fluoride-containing products including antibacterial or fluoride mouth rinse.

The patients were asked to have their teeth extracted approximately 12 weeks after the initial bracket placement and were given bottles containing 1% chloramine T solution for tooth storage. An extraction referral letter asking the dentist to leave the bracket on the tooth surface while performing the extractions, if possible, was also given.

Upon collection from the patients, the teeth were cleaned and placed into bottles filled with fresh 1% chloramine T solution for further disinfection until the visual examinations to evaluate the presence or absence of WSLs.

Visual examination was carried out independently by 2 clinicians (E.T., D.R.P.) who were blinded to the experimental protocol. These evaluators were previously trained and calibrated.

Each tooth was randomly removed from its storage bottle and air dried for 5 seconds, and the buccal surface was examined visually for enamel demineralization with the unaided eye in the portion of the crown gingival to the bracket using the following scale.[22]

0, No visible white spots or surface disruption (no decalcification)
1, Visible white spot without surface disruption (mild decalcification)
2, Visible white spot with a roughened surface but not requiring restoration (moderate decalcification)
3, Visible WSL requiring restoration (severe decalcification)

If the bracket was inadvertently debonded during the extraction procedures, the area gingival to the middle third of the tooth surface was examined for demineralization.

After the visual examination, the teeth were selected in a random order, air dried for 5 seconds, and examined under a hand-held black light. Since Opal Seal has a fluorescing agent in its composition, the tooth surfaces were examined to evaluate primer retention. The tooth surface was divided into mesiogingival, distogingival, mesioclusal, and distoclusal quadrants (Fig 1). The amount of remaining primer was recorded as 100%, 75%, 50%, 25%, or 0%. A score of 100% was assigned if all 4 quadrants fluoresced under the black light, indicating full coverage, whereas a score of 0% indicated the complete absence of the material with no fluorescence in any of the 4 quadrants.

Previous studies have shown a strong correlation between the hardness values and the mineral content of the enamel.[23-26] Therefore, cross-sectional microhardness testing, an accepted reproducible and reliable analytic method, was used to assess the mineral loss on the enamel surface.

The teeth were embedded in clear epoxy resin (Epoxicure; Buehler, Lake Bluff, Ill) and sectioned parallel to the long axis buccolingually through the brackets using a water-cooled diamond wafering blade on a low-speed rotary saw (Accutom-5; Struers, Westlake, Ohio). If brackets debonded during the sectioning process, these teeth were discarded because it would be difficult to determine distances gingival to the bracket without a reference point. Subsequently, the sections were serially polished through 4000 grit silicon carbide polishing paper.

On each tooth, 42 indentations (Knoop hardness: Duramin-5; Struers) were made at distances of 0, 50, 200, 500, and 1000 μm from the bracket edge and at depths of 25, 50, 75, 100, 125, and 150 μm from the external surface of the enamel (Fig 2). The average value of 3 indentations made in the isolated enamel directly beneath the bracket at the distance of 0 at the depths of 25, 50, 75, 100, 125, and 150 μm was used as the reference Knoop hardness number of the sound enamel at that specific depth. Therefore, the values obtained at 50, 200, 500, and 1000 μm from the bracket at 6 depths were compared with the baseline value (average Knoop hardness number value at distance, 0) to determine the changes in the mineral content of the tooth. Negative differences reflected Knoop hardness number values lower than the reference values.

Statistical analysis

A chi-square test was used to determine whether there were differences between the percentages of visible WSLs observed in the Opal Seal group compared with the Transbond XT group (control). A repeated-measures logistic regression was used to test for the effect of the study variables on the presence of WSLs. Enamel hardness was analyzed using a repeated-measures mixed-model analysis of covariance (ANCOVA) to evaluate the effect of materials, depths from the enamel surface, positions, and their interactions. We used SAS software (version 9.3; SAS Institute, Cary, NC) for all analyses, and the statistical significance was set at $P < 0.05$.

RESULTS

The patients were asked to have their teeth extracted at about 12 weeks (84 days) after the initial bracket-bonding appointment. However, because of a lack of compliance with the instructions, the average length of time that the teeth remained in the oral environment (days in vivo) was 67 ± 28 days.

A total of 72 teeth were evaluated for WSLs by 2 calibrated clinician examiners (E.T., D.R.P.). In 14 subjects, 4 teeth (4 premolar extraction patients with both maxillary and mandibular premolars), and in 8 subjects, 2 teeth (2 premolar extraction patients with either maxillary or mandibular premolars) were observed to have WSLs.

Overall, the results of the visual examination indicated that 46% of the control teeth vs 29% of the experimental teeth exhibited demineralization (Table I). The 2 raters agreed 86% of the time. The chance-corrected kappa coefficient was 0.71, indicating a high level of agreement.[27] Statistical analyses indicated no significant difference in the incidence of WSLs between the experimental and control groups during the study ($P = 0.106$).

Opal Seal remained on an average of 50% of the tooth surfaces at 90 days. Regression analysis indicated no correlation between the percentage of Opal Seal remaining on the tooth surfaces and the number of days the teeth were in the mouth ($r = -0.06$; $P > 0.6$).

The results of the repeated-measures mixed-model ANCOVA showed a statistically significant change in hardness difference across the 6 depths from the enamel surface in both groups (Table II, Fig 3). The hardness

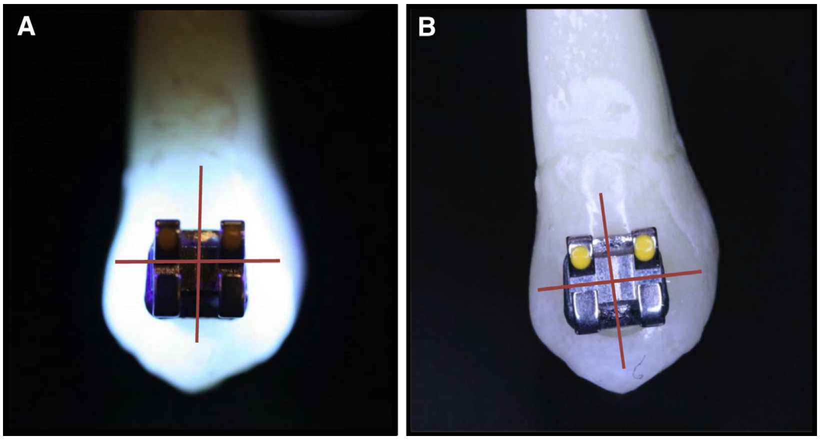

Fig 1. 100% Opal Seal remaining viewed under **A,** black light, and **B,** ambient light. *Red lines* show the 4 quadrants (mesiogingival, distogingival, mesioclusal, distoclusal) used to determine the percentage of sealant on the tooth surface.

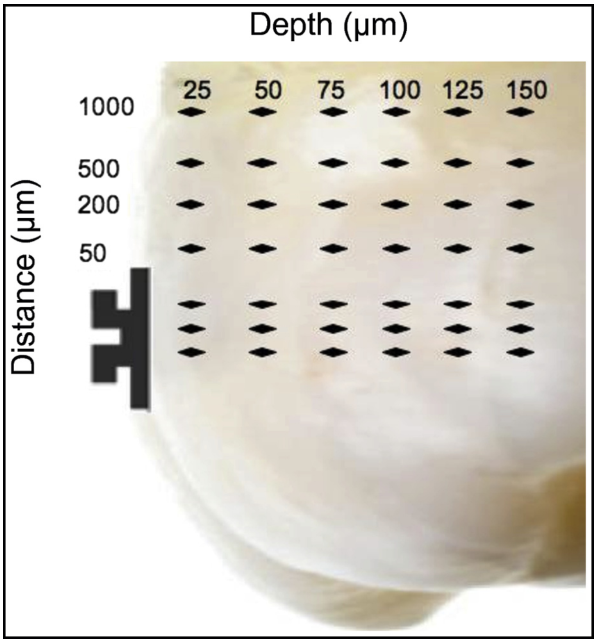

Fig 2. Location of indentations (distances, 0, 50, 200, 500, and 1000 μm from the bracket edge; depths, 25, 50, 75, 100, 125, and 150 μm into the enamel).

values were low at the depths of 25 and 50 μm, and they increased as the depth increased for both the control and experimental groups ($P < 0.001$). When compared with the hardness values directly under the bracket (0-mm distance), a significant decrease in the hardness value was observed for the indentations at 50, 200, 500, and 1000 μm from the bracket base toward the cervical portion in both the experimental and control teeth ($P < 0.001$). There were no statistically significant differences overall between the 2 groups across the indentation locations ($P > 0.8$).

Table I. Prevalence of WSLs in the Transbond XT and the Opal Seal groups

	WSLs			
	No	*Yes*	*% yes*	P *value*
Pairs				0.106
Transbond XT	39	33	46	
Opal Seal	51	21	29	

P value from repeated-measures logistic regression (chi-square = 2.62; df = 1).

DISCUSSION

Early detection of WSL development and implementation of fluoride regimens to control demineralization during orthodontic treatment are especially important because of the high incidence and rapid onset of WSLs. In this split-mouth study, a highly filled fluoride-releasing orthodontic primer, Opal Seal, was used for fluoride delivery, and its potential to reduce or prevent enamel demineralization was evaluated. Specifically, the enamel surfaces were examined visually, and microhardness indentation techniques were used to evaluate demineralization in the sample after the premolars were extracted.

The overall incidence of WSLs in this study was 38% of all teeth examined visually. The control teeth and the experimental teeth had incidences of 46% and 29%, respectively. In this study, the incidence appeared to be high after such a short period of time. Chapman et al[28] reported an incidence of at least 1 tooth having

Table II. Microhardness values Knoop hardness numbers

Depth (μm)	Transbond XT control Hardness	Transbond XT control 95% CI	Opal Seal experimental Hardness	Opal Seal experimental 95% CI
Distance = 0 μm				
25	302.2	294.3-310.2	303.1	295.8-310.4
50	302.2	294.2-310.2	303.6	296.2-310.9
75	303.1	295.1-311.0	304.1	296.8-311.4
100	303.9	296.0-311.9	305.7	298.3-313.1
125	305.5	297.5-313.6	305.8	298.4-313.2
150	305.6	297.6-313.6	308.5	301.0-316.0
Distance = 50 μm				
25	287.1	274.1-300.2	276.9	264.9-288.9
50	284.6	271.5-297.6	283.1	271.1-295.1
75	298.9	285.9-312.0	299.1	287.1-311.1
100	301.5	288.5-314.6	295.7	283.7-307.7
125	293.0	280.0-306.1	299.3	287.2-311.3
150	302.6	289.5-315.6	304.3	292.2-316.4
Distance = 200 μm				
25	279.9	266.8-292.9	285.1	273.1-297.1
50	279.9	266.9-293.0	295.7	283.7-307.6
75	288.2	275.2-301.2	292.7	280.7-304.7
100	294.1	281.0-307.1	299.1	287.1-311.1
125	301.8	288.7-314.8	308.8	296.8-320.8
150	296.1	283.1-309.2	293.3	281.2-305.4
Distance = 500 μm				
25	282.0	269.0-295.1	274.1	262.1-286.1
50	299.4	286.4-312.4	281.9	269.9-293.9
75	293.6	280.6-306.6	299.5	287.5-311.5
100	305.5	292.5-318.6	299.8	287.8-311.8
125	302.8	289.7-315.8	309.7	297.7-321.7
150	304.4	291.4-317.5	303.5	291.4-315.6
Distance = 1000 μm				
25	284.6	271.6-297.6	284.7	272.7-296.7
50	287.4	274.4-300.5	288.0	276.0-299.9
75	301.0	288.0-314.1	296.6	284.6-308.6
100	303.5	290.5-316.6	302.8	290.8-314.8
125	302.8	289.7-315.8	308.8	296.7-320.8
150	304.7	291.6-317.7	298.1	286.0-310.2

Estimated hardness from repeated-measures mixed-model ANCOVA.

a WSL to be 36% on examining intraoral photos after orthodontic treatment. Gorelick et al[2] reported at least 1 WSL in 50% of patients examined after removal of the orthodontic appliances. The higher incidence in this study was most likely due to the placement of an elastomeric spacer around the wings of the bracket to help facilitate the retention of plaque and create a favorable environment for WSL development. A similar technique was used by Farhadian et al[29] with T-loops to increase plaque retention. In that study, although WSL incidence was not investigated, significant demineralization was reported in both the experimental and control teeth within a similar time period. Additionally, in our study, the presence of WSLs was evaluated after the teeth were extracted. It is likely that any areas of decalcification would be more easily identified with this technique, since there was no gingiva or saliva to interfere with direct visualization of the gingival portion of the tooth.

The interrater reliability for this study showed good agreement, with a Cohen kappa value of 0.71 (high level of agreement). Interestingly, both examiners stated that identifying WSLs was more challenging in teeth with intact brackets compared with teeth without a bracket as a result of dislodgement during the extraction procedure. The difficulty of accurately diagnosing WSLs in orthodontic patients could lead to underestimation of the incidence while brackets are still present during treatment. Therefore, it is likely that WSLs might be missed clinically and not noted until the removal of the appliances.

Over the course of the study, there was no significant difference in the incidence of WSLs between the experimental and control groups ($P = 0.106$). However, the statistical analyses indicated a significant interaction between the groups and the number of days the teeth were in the oral environment (days in vivo). The incidence of WSLs was significantly lower in the Opal Seal group compared with the Transbond XT group when the teeth were in the oral environment less than 90 days ($P = 0.009$; Table III).

The time-dependent protective effect of Opal Seal might be explained by decreased fluoride release from the primer or removal of the primer from the tooth surface over time. In a previous study, Basdra et al[30] reported an initial burst of fluoride ions within the first 24 hours, and noted that the amount of fluoride released decreased significantly with time. At the end of 90 days, no fluoride ions were detectable in the surrounding medium.

It is possible that the split-mouth design of this study affected the results. Although the key advantage of a split-mouth design over the parallel-group design is the elimination of intersubject variations, a carry-across effect is possible. As described by Benson,[31] any fluoride released from the fluoride-containing material can be carried across from 1 site to another. In this case, the teeth that received the nonfluoride material (control) might show a false preventive effect. Therefore, randomized controlled trials with larger samples are still needed to study the effectiveness of fluoride-containing materials in reducing demineralization.[31,32]

Currently, Opal Seal is marketed as a new product with superior fluoride release and recharge abilities. Furthermore, the manufacturer claims that it is effective in preventing the formation of WSLs. Therefore, if this claim is true, the use of this sealant would be a valuable adjunct to orthodontic therapy. However, in the literature only 1 study has analyzed the fluoride release and

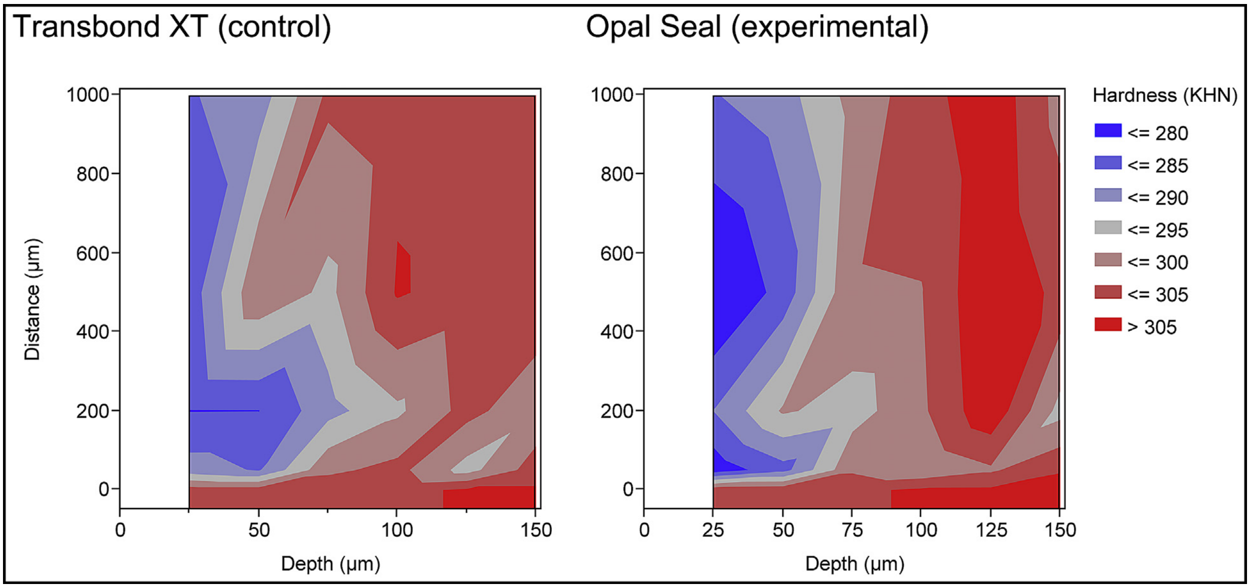

Fig 3. Color-coded map showing the variations in the hardness values as a function of depth into enamel toward dentin (x-axis) and distance from the bracket edge (y-axis). For example, point "25,0" represents the indentation at the depth of 25 μm and distance of 0 μm from the bracket edge (under the bracket), and point "50,400" represents the indentation at 50 μm depth and 400 μm from the bracket edge. The color transition from *red* to *blue* indicates softening of the enamel.

Table III. Visual examination results when a "pairs by days in vivo" interaction is incorporated into the statistical analyses

	Presence of WSLs						
	Transbond XT (control)			*Opal Seal (experimental)*			
Days in vivo	*No*	*Yes*	*%*	*No*	*Yes*	*%*	*P value*
<90 days	27	21	44	41	7	15	0.0178
>90 days	12	12	50	10	14	58	>0.09

Logistic regression indicated that the control vs the experimental difference depended on days in vivo ($P = 0.009$). The P values in the table compare the pairs within each of the days in vivo groups.

reuptake property of Opal Seal.[20] In that study, the amount of fluoride ions released from the Opal Seal disks increased from 1.20 to 7.79 ppm 24 hours after the application of 1.23% acidulated phosphate fluoride, indicating the effect of fluoride reuptake. However, a rapid decrease in the amount of fluoride release was observed subsequently. In an in-vitro study with an over-the-counter fluoride-containing toothpaste, limited fluoride reuptake was shown with Pro Seal, a fluoride-containing sealant similar to Opal Seal.[33] In our study, the patients were asked to carry out their routine oral-hygiene measures. However, their compliance with the oral-hygiene protocols was not evaluated specifically. Therefore, it would be difficult to determine whether the fluoride recharge ability of Opal Seal played any role in the prevention of demineralization in these patients.

Since visual examination is somewhat subjective, Knoop microindentation was also used as a quantitative measurement technique to compare the efficacy of fluoride-releasing primer with the nonfluoride primer. There were no statistically significant differences in the mineral content between the experimental and control groups across indentation locations. In the study by Pascotto et al,[21] depths were recorded in increments of 10 μm, starting at 10 μm up to 90 μm. In that study, significant differences were found between the experimental and control samples at depths of 10 and 20 μm, but there were no differences beyond 30 μm. In our study, there were no significant differences between the experimental and control teeth for any depth, but the first indentation was performed at 25 μm. If a shallow lesion were present at a depth of less than 25 μm, it would not have been detected with our protocol. Therefore, it is possible that the lesions were too shallow (<25 μm) to detect with the hardness test but visible enough to detect clinically.

An interesting finding of the hardness test was that the enamel at all locations from the bracket edge (50, 200, 500, and 1000 μm) at the depths of 25 and

50 μm from the tooth surface was approximately 9% softer when compared with sound enamel. This trend was true for both the experimental and control teeth, and it could be attributed to the acid-etching technique used during the bonding procedures. This agrees with previous studies that reported that initial acid etching significantly reduced the hardness of the enamel.[34,35] Therefore, it is highly recommended to etch only the portion of the tooth surface where the bracket will be exactly bonded so that the enamel is not predisposed to future demineralization.

Since average orthodontic treatment time is approximately 24 to 28 months, the retention of the primer on the tooth surface throughout treatment is important to be effective in preventing demineralization.[36] Previous in-vivo studies where orthodontic sealants were used to protect enamel surfaces showed a lack of sealant retention most likely due to its inability to resist mechanical abrasion from toothbrushing and mastication.[37,38] In-vitro studies have found that highly filled sealants can withstand simulated wear and decrease the number and intensity of WSLs.[14,18] Since Opal Seal is a highly filled primer, its wear resistance is expected to be superior to that of unfilled resins.[20] In addition, it is claimed to exhibit a fluoride recharging property and the ability to penetrate deeply into fissures of teeth resulting in superb retention.[20] In this study, Opal Seal remained on over 50% of applied tooth surfaces at 90 days. There was no correlation between the amount of primer remaining on the teeth and the number of days in vivo ($r = -0.06$; $P > 0.6$). However, it was not the purpose of this study to investigate primer retention longitudinally. Future studies on the retention of Opal Seal are needed to determine whether and when reapplication is necessary.

A limitation of this study was the short duration that the teeth remained in the oral cavity, but it would have been unethical to prolong treatment time by delaying the premolar extractions that were required. Nevertheless, it is well supported in the literature that enamel demineralization can occur within 4 weeks of bracket placement.[2] In addition, it would be ideal to control the duration of the study by having the teeth extracted at the predetermined end of the study (eg, 30 or 60 days) to minimize the effect of subjecting these teeth to varying experimental conditions. However, because of the scheduling variations of the patients by their dentists, this was a difficult task to achieve. Therefore, future randomized controlled trials with a larger sample size, a longer observation period of controlled duration, and smaller microhardness indentation increments are needed to determine the efficacy of fluoride-releasing sealants in the prevention of WSLs.

CONCLUSIONS

The results indicated no significant difference in the numbers of WSLs observed in teeth treated with Opal Seal compared with teeth treated with Transbond XT ($P = 0.106$) over the duration of the study. However, there was a significant reduction in the number of WSLs in teeth treated with Opal Seal if they were observed before 90 days in vivo. This finding suggests that Opal Seal has some efficacy in preventing demineralization, but this protective effect might diminish after 3 months. At the end of the study, only 50% of the primer was still present on the tooth surfaces. Therefore, multiple applications might be needed during the orthodontic treatment.

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