ORIGINAL RESEARCH

Efficacy of Amorphous Calcium Phosphate (ACP) Containing Adhesive in Preventing Demineralization during Orthodontic Treatment, a Triple Blinded Randomized Clinical Trial (RCT)

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Abstract

Aim: The present study was done to evaluate *in vivo* effects of an amorphous calcium phosphate (ACP) containing adhesive in reducing enamel demineralization during the early stage of fixed orthodontic treatment.

Materials and methods: A triple blinded randomized clinical trial (RCT) was conducted to evaluate enamel demineralization on 255 anterior teeth in 23 patients over a period of 6 months. A split-mouth design was used; half of the anterior teeth were bonded with the ACP containing adhesive and the contralateral teeth received regular adhesive as a control. The enamel demineralization measurements were done at three different time intervals: immediately after bonding (T0), 1 month after bonding (T1), and 6 months after bonding (T2) using the DIAGNOdent device.

Results: Significant enamel demineralization variations were determined among groups ($p < 0.001$). The ACP containing adhesive showed significantly lower enamel demineralization than control adhesive.

Conclusion: The result of this study suggests a positive effect on the reduction of enamel demineralization when using ACP containing adhesives during orthodontic treatment over regular adhesive.

Keywords: Amorphous calcium phosphate, Demineralization, Enamel.

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Introduction

Orthodontic treatment with fixed appliances is usually associated with decalcification of teeth around the brackets.[1,2] Orthodontic treatments may have their own disadvantages especially with fixed appliances, which sometimes act as a nidus for numerous plaque retention sites and thereby increases the patient's risk of developing dental caries and inflammatory reactions of the gingival tissue. In addition, the majority of patients undergoing orthodontic treatment are teenagers. This may also enhance the risk of poor compliance with regard to plaque control and prevention.[3] White spots on enamel (decalcifications) are characterized by loss of opacity due to mineral loss when compared with healthy enamel.

Many studies in the past have shown that white spot lesions (WSLs) can develop in 1 month as a result of prolonged accumulation and retention of bacterial plaque.[4] A clinical study has reported that the incidence of WSLs is as high as 50% in orthodontically treated patients.[5] Lovrov et al.[6] reported that up to 95.3% of orthodontically treated patients develop, at least one new WSL, or there can be an increase in the severity of an existing lesion.

In the process of demineralization, various specific bacteria are retained for long periods on enamel surface.[4,7] Thus, the plaque-retentive properties of fixed appliance predispose the patient to an increased cariogenic risk. Furthermore, the treatment with orthodontic appliances leads to rapid shift in the composition of bacterial flora plaque. It has been reported that in the mouth of orthodontic patients, the levels of acidogenic bacteria, like *S. mutans* and lactobacilli, considerably elevated.[8] If the above-mentioned bacteria receives adequate supply of fermentable carbohydrates, they metabolize the same and acid by-products formed will lower the pH of plaque. Now from here, the process of carious decalcification starts.[9]

It has been observed that in the initial solid phase, amorphous calcium phosphate (ACP) precipitates from a highly super saturated calcium phosphate solution, followed by conversion into further stable crystalline phases such as octacalcium phosphate or apatite products.[10] ACP at a neutral or high pH remains ACP, but at low pH values (at or below 5.8), which occurs during a carious attack, it is converted to HAP and precipitates, thus replacing the HAP lost by acid.[11] Since ACP has the affinity for bone and dental tissues, much of the attention has been purposefully dedicated to the development and the application of ACP-containing products especially in orthopedic and dental fields. An *in vitro* study done by Langhorst et al.[12] observed that experimental ACP composite capably established the process of mineral ion transfer all through the body of the lesions and helped in restoring the

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lost mineral that occurred due to acid attack. Uysal et al.[13] found that the enamel surface hardness of the teeth bonded with ACP containing adhesive resin was significantly higher than that of teeth bonded with conventional adhesive resin. Chow did an *in vitro* study and found that incorporation of ACP into an orthodontic adhesive material results in the decrease of bacterial adhesion and eventually lesion depth formation.[14] The effect of addition of ACP even though was not better than orthodontic adhesive with fluoride, but proved better than the resin control. These results encourage further investigation in the release rate of ACP *in vivo*. Thus, the present study was done to evaluate the "*in vivo*" effects of an ACP containing adhesive in reducing enamel demineralization around orthodontic brackets during a 6-month period.

Material and Methods

This prospective, randomized, triple blinded clinical study was approved by the Research Center at Riyadh Colleges of Dentistry and Pharmacy, Riyadh, Saudi Arabia (Registration no. PGRP/43234003/30). Twenty-six (26) (12 males and 14 females) orthodontic patients aged 12–35 years attending the graduate orthodontic clinics at Riyadh Colleges of Dentistry and Pharmacy (RCsDP), who were scheduled to have fixed appliances for orthodontic treatment, were selected and invited to participate in this study. A signed consent form was obtained before enrolment into the study. Three hundred (*n*) anterior teeth were bonded for the examination in this study. Only 23 patients completed the study, while 255 (*n*) teeth were evaluated for enamel demineralization (6 teeth were debonded and 3 teeth were repositioned that were all excluded from the analysis).

Patients with a full set of permanent fully erupted anterior teeth, patients who were caries free, with healthy periodontal tissue, and medically fit were included. Exclusion criteria were patient with fluorosed teeth, restoration on facial surface, and patients who failed to come at the same or ±1 evaluation day.

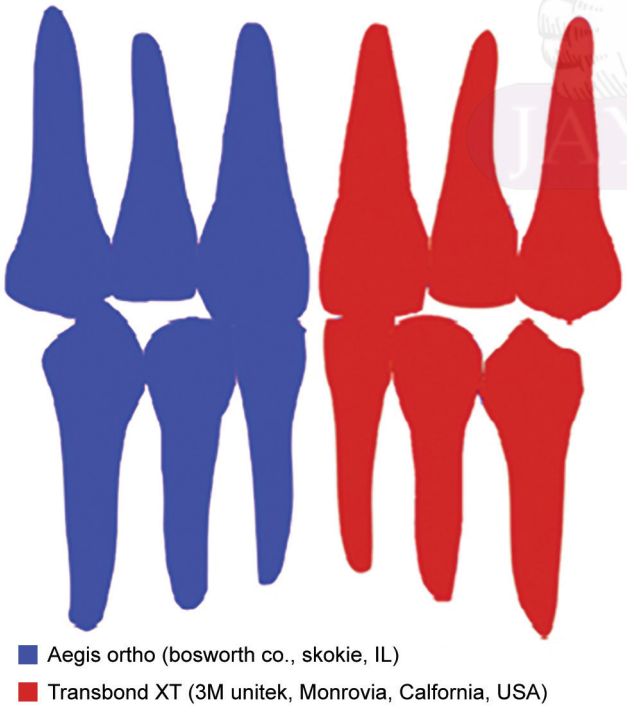
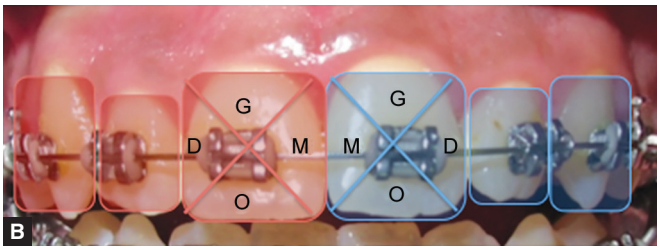


Fig. 1: Split-mouth deign was used in all patients' anterior teeth



Figs 2A and B: (A) Composite tubes were labeled A and B; (B) After application of composite restoration from tubes A and B on teeth

For bracket bonding and adhesive assignment, a split-mouth technique was used (Fig. 1). The assignment of adhesive to a specific side of the mouth was determined with a randomization table.

ACP a light cured containing adhesive Aegis Ortho (Bosworth Co., Skokie, IL), with 38% ACP fillers, was used on 128 of the teeth and Transbond XT (3M Unitek, Monrovia, California, USA) a light cured adhesive composite was used as the control adhesive 127 teeth (Fig. 2A). The application of adhesive was done in a triple blinded manner, by asking an independent orthodontic resident to identify the adhesive tubes by refilling its content into new empty identical tubes. The new tubes were then labeled A and B. The assignment of each letter and which adhesive material it pertained to was noted on a piece of paper, and kept in a sealed envelope and was not revealed to the researcher until the study was over. After accomplishing the study and analyzing the results, the envelope was then opened to identify each group. The statistician had no knowledge of group assignment during the analysis.

The bonding procedure was performed by four different clinicians following the manufacturer's recommendation. All teeth underwent a fluoride-free prophylaxis and were rinsed with de-ionized water and air-dried. The teeth were etched according to the recommendations from the manufacturer for 15 seconds using 37% ortho-phosphoric acid gel (3M Dental Products, St Paul, Minnesota USA). Then rinsed with water for 15 seconds and dried with oil-free air for 10 seconds. The manufacturer's recommendations were followed to apply the adhesive and the composite. Excessive composite adhesive around the bracket was removed with a clinical probe and then light cured with (Henry Schein® LED 1200) curing light from the mesial, distal, incisal, and gingival to the bracket for 10 seconds each. On the experimental teeth, the same primer and technique were used as on the control. Then the Aegis ortho adhesive applied to the bracket and excess was removed and light cured using the same protocol on the control teeth (Fig. 2B). Detection of enamel demineralization was measured by DIAGNOdent® which was calibrated according to the manufacturer's instructions

before and after taking the readings for each patient. Prior to the start of this study, the blinded examiner was introduced to the measurement protocol, and the use of the DIAGNOdent® and its calibration for laser fluorescence. Intra-examiner reliabilities were assessed by selecting 20 surfaces measuring by device in a patient without orthodontic appliances. The same 20 surfaces were remeasured 1 week later and the intraclass correlation coefficient (ICC) was calculated and found to be 0.91. The same device and tip were used for all the readings throughout the study. Each tooth was pumiced with a fluoride-free paste and then dried using the dental unit air water syringe. Then, the DIAGNOdent® tip was placed on the measurement site, slightly tilted with a circular movement on all sides around the bracket until it reached the maximum reading for each side (mesial, distal, incisal, and gingival). The measurements were done at three different time intervals: immediately after bonding (T0), 1 month after bonding (T1), and then 6 months after bonding (T2). For each group, the demineralization variation (ΔD) was determined as the change from baseline demineralization (T0) score to the highest score (T1) or (T2).

Data Analysis

Data entry and analysis were done using the IBM SPSS version 22 for Mac OS.

Results

A two-way analysis of variance was used to test the effect of adhesive materials (ACP and control) and time intervals, base line (T0), 1 month (T1), and 6 months (T2), show that there was a significant interaction between the adhesive materials and the times (p value = 0.000) (Table 1).

Table 1: Interaction between the adhesive materials and times

Tests of between-subjects effects			
Dependent variable: demineralization			
Source	*Mean square*	*F*	*Sig.*
Intercept	30137.503	13587.48	0.000*
Group	222.779	100.440	0.000*
Interval	447.900	201.936	0.000*
Group* interval	81.137	36.581	0.000*

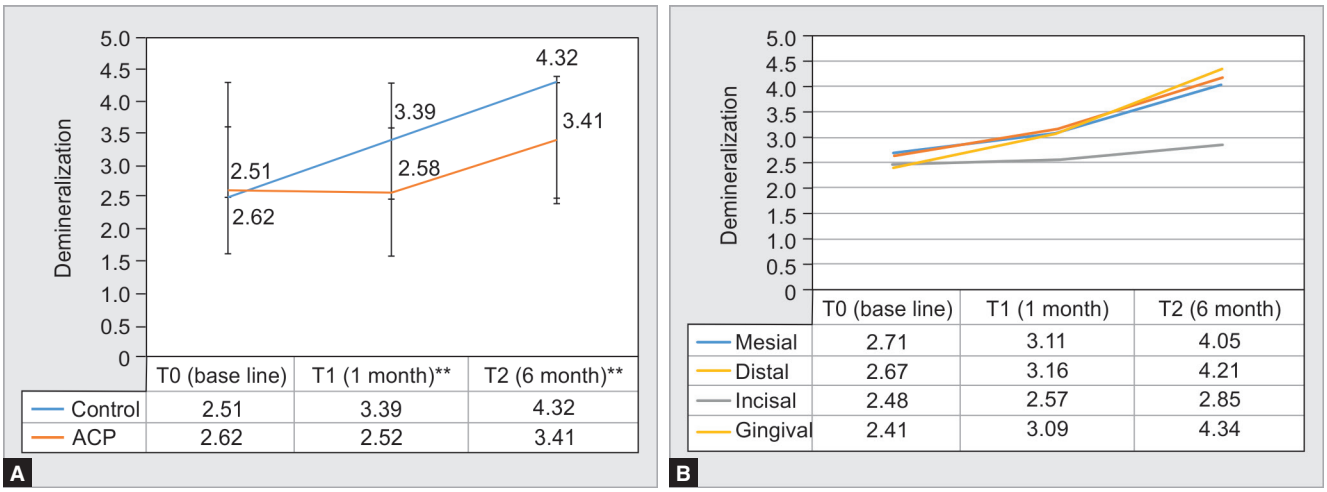
**$p < 0.01$ (highly significant)

Figure 3A shows that there was no significant difference (p = 0.208) between control 2.51 (±1.21) and ACP 2.62 (±1.54) groups at the base line (T0). At 1 month (T1), there was a significant difference between control 3.39 (±1.29) and ACP 2.58 (±1.11) groups (p = 0.000). Furthermore, at six months (T2), there was a significant difference between control 4.32 (±2.32) and ACP 3.41 (±1.11) groups (p = 0.000).

In both control and ACP groups, one-way ANOVA repeated measurements show that there was a significant difference in the demineralization between different time intervals. To further analyze the interaction between different time points, a paired t test was performed and there was a significant difference (p = 0.000) between all three-time intervals within the control group of 6 months (T2) significantly higher than 1 month (T1) and 1 month (T1) was significantly higher than base line (T0). Similarly, for the ACP group, a paired t test show that there was no significant difference between means of demineralization at T0 and T1 (p = 0.321) but the means of demineralization at both base line (T0) and 1 month (T1) were significantly lower than the mean of demineralization at 6 months (T2) (p = 0.000) individually (Tables 2 and 3).

In the control group, the correlation coefficient between the time intervals and demineralization showed a significant positive moderate relationship (p value = 0.000). While in the ACP group, the correlation coefficient between the time intervals and demineralization was r = 0.243, showing a significant positive weak relationship (p value = 0.000) (Table 4).

In Table 5 and Figure 3B, it was observed that at T0 (base line), the one-way ANOVA shows that there was a significant difference between surfaces demineralization (p = 0.041); however, Games–Howell multiple comparison refuses this result and shows that there was no significant difference between surfaces demineralization around the brackets. At 1 month (T1), the one-way ANOVA shows that there was a significant difference between surfaces demineralization (p = 0.00). Furthermore, the Games–Howell multiple comparison shows the incisal surface to have significantly lower deminiralization than other surfaces around the brackets (mesial, distal, and gingival to the brackets) (p = 0.00). At 6 months (T2), there was a significant difference between surfaces demineralization (p = 0.00). The incisal surface to the bracket was significantly lower than other surfaces around the brackets (mesial, distal, and gingival to the brackets) (p = 0.00).



Figs 3A and B: (A) Demineralization between groups in different time intervals (**p = 0.000); (B) The mean surface demineralization around the orthodontic brackets at different time intervals (control or ACP or pooled)

Table 2: Comparison of demineralization within each group at different time intervals by one-way ANOVA repeated measurements' test

Group	*Time intervals*	*Mean*	*Std. deviation*	*Sig.*
Control	T0 (baseline)	2.51	1.215	0.000*
	T1 (1 month)	3.39	1.288	
	T2 (6 months)	4.32	2.315	
ACP	T0 (baseline)	2.62	1.539	0.000*
	T1 (1 month)	2.58	1.106	
	T2 (6 months)	3.41	1.112	

Table 3: Paired *t* test comparing time intervals within each group

Group	*Time intervals*	*Time intervals*	*Mean difference*	*Sig.*
Control	T0 (baseline)	T1 (1 month)	−0.880*	0.000*
	T0 (baseline)	T2 (6 months)	−1.809*	0.000*
	T1 (1 month)	T2 (6 months)	−0.929*	0.000*
ACP	T0 (baseline)	T1 (1 month)	0.045	0.321
	T0 (baseline)	T2 (6 months)	−0.787*	0.000*
	T1 (1 month)	T2 (6 months)	−0.832*	0.000*

Table 4: Correlation between time and demineralization within each group

Demineralization in		*Time intervals*
Control	Pearson correlation	0.402
	Sig. (2-tailed)	0.000**
	N	1524
ACP	Pearson correlation	0.243
	Sig. (2-tailed)	0.000**
	N	1536

Table 5: Comparison of difference between orthodontic surfaces demineralization at different time intervals

		ANOVA				
		Sum of squares	*Df*	*Mean square*	*F*	*Sig.*
Baseline	Between groups	15.878	3	5.293	2.763	0.041
	Within groups	1946.588	1016	1.916		
	Total	1962.467	1019			
1 month	Between groups	58.780	3	19.593	12.624	0.000
	Within groups	1576.902	1016	1.552		
	Total	1635.682	1019			
6 months	Between groups	360.957	3	120.319	38.203	0.000
	Within groups	3199.827	1016	3.149		
	Total	3560.784	1019			

Games–Howell multiple comparison between each surface demineralization

Dependent variable	*Surface*	*Surface*	*Mean difference*	*Sig.*
Baseline (T0)	Mesial	Distal	0.04314	0.985
		Incisal	0.23137	0.320
		Gingival	0.29804	0.054
	Distal	Incisal	0.18824	0.457
		Gingival	0.25490	0.088
	Incisal	Gingival	0.06667	0.947
1 month (T1)	Mesial	Distal	−0.04314	0.982
		Incisal	0.54510*	0.000**
		Gingival	0.02353	0.997
	Distal	Incisal	0.58824*	0.000**
		Gingival	0.06667	0.935
	Incisal	Gingival	−0.52157*	0.000**
6 months (T2)	Mesial	Distal	−0.15686	0.813
		Incisal	1.20784*	0.000**
		Gingival	−0.28235	0.351
	Distal	Incisal	1.36471*	0.000**
		Gingival	−0.12549	0.896
	Incisal	Gingival	−1.49020*	0.000**

Discussion

Demineralization of enamel is an expected side effect associated with fixed orthodontic treatment, especially with poor oral hygiene patients.[15] In the orthodontic database, the role of ACP, the bioactive material, capable of reducing the new increments of dental caries, has been investigated in various studies.[16,17] The present clinical study evaluated the *in vivo* effect of orthodontic ACP containing adhesive compared with the conventional orthodontic adhesive material on enamel demineralization around orthodontic brackets by using the DIAGNOdent device. The added advantage associated with ACP is the disordered structure, making the material exceedingly reactive with body fluids. On the evidence-based hierarchy, it has been found in the literature that osteo-conductivity of ACP was slightly better than hydro apatite when used *in vivo*. External factors like plaque, calculus, stains, and certain other fluorescent materials could be a hindrance to the penetrating ability of laser used by the DIAGNOdent device. To overcome such obstructions, facial surfaces of all the teeth were cleaned using a rotating brush and water jet, which may reduce any false positive results. The subjects were randomly selected and each subject underwent split-mouth design as it eliminates variables pertaining to difference in patient's cooperation and diet. WSLs have the potential of formation within 4 weeks from the beginning of fixed orthodontic treatment.[4] A 6-month measurement was done to evaluate the alteration in effect of the experimental adhesive containing ACP over a long period of time.

The present findings showed that ACP containing adhesive had a preventive effect on enamel demineralization in the four surfaces around the orthodontic brackets. This was in agreement with the study done by Uysal et al.[7] who demonstrated a positive effect of ACP containing adhesive on enamel demineralization after the first 30 days *in vitro* and in other *in vivo* studies.[18] Another study evaluated the potential of ACP containing adhesive, fluoride varnish, resin sealer, and MI Paste under *in vitro* conditions to prevent enamel demineralization around orthodontic brackets, the finding observed a positive, though not significant effect of both ACP containing adhesive and MI Paste.[19]

In all previous studies, the experimental period was just 30 days or less while in the present study, the duration of follow up ended at 6 months which may help evaluate the material performance over an extended period of time. During the follow up for 6 months, the ACP containing adhesive maintained its advantage over the control adhesive but both groups exhibited an increase in enamel demineralization which could be attributed to the initial release of calcium and phosphate ions into the tooth surface within first 30 days. A study done by Richards et al.[20] reported that ACP containing adhesive lose their chemical release potential after 56 days. Currently,

there is no study evaluating the chemical effect of ACP containing adhesive over prolonged periods and whether their ions releasing capacity could replenish by any means.

In this study, all surfaces around orthodontic brackets were evaluated. The gingival, mesial, and distal surfaces around the brackets had the highest enamel demineralization value and they were statistically higher than the incisal surface, this might be due to the difficulty in cleaning of these areas, which was in agreement with the study done by Sukontapatipark et al.[21] It was reported that those sites had the highest rate of WSL formation.[5,22–23] Incorporation of ACP into an orthodontic adhesive material decreases the bacterial adhesion and lesion depth formation better than the resin control.[14] Another advantage of ACP is that it gives higher enamel microhardness than those bonded with conventional composite resin.[13]

The results of the study should be viewed in the light of limitations; first of all, the demineralization of enamel is a continuous process with periods of remineralization and demineralization and the brackets are placed for a 1 year and above, but the study lasted for 6 months only. The oral hygiene practices, cultural factors, dietary patterns, availability of food items, caries activity of the oral cavity, and many more risk factors should be taken into consideration before coming to a conclusion, hence, the results of the present study cannot be generalized to the society. Further multicentric studies from different parts of the world with more multicentric robust sample size and longer follow up periods will be required to give more reliable conclusions. Nevertheless, the present study gives a platform to use ACP as an adhesive for brackets' placements in orthodontics so that the enamel demineralization can be reduced and the prognosis can be further improved. This study also opens the avenue for further research worldwide. Greater strides in the development of tissue engineering technology and techniques and day-to-day enrichment in applied dental material sciences, it is thought that ACP will be used comprehensively in the coming future. It is a promising material, which can stop demineralization and can prevent dental caries due to placement of orthodontic brackets.

Conclusions

It is believed that proper oral hygiene and diet are the first steps toward the prevention of WSL. Other measures to control plaque accumulation could be recommended to those patients who exhibit high caries prevalence. ACP containing adhesive shows a promising effect on reducing the incidence of WSL irrespective of oral hygiene. Follow up clinical studies with longer duration are recommended as no previous study evaluated prolonged effect of using ACP containing adhesive in orthodontic treatment.

Clinical Significance

Preserving morphology of the tooth is always a prime importance in dentistry. Demineralization of enamel can lead to many problems in the tooth and, hence, can be a limiting factor in the prognosis of the orthodontic treatment; ACP can be a promising agent in preventing enamel demineralization.

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