Acta Odontologica Scandinavica. 2014; 72: 903–907

informa
healthcare

ORIGINAL ARTICLE

The effect of recommending a CPP-ACPF product on salivary and plaque pH levels in orthodontic patients: A randomized cross-over clinical trial

HALEH HESHMAT[1], SEPIDEH BANAVA[1], EBRAHIM MOHAMMADI[2], MOHAMMAD JAVAD KHARAZIFARD[3] & FARAMARZ MOJTAHEDZADEH[4]

[1]*Department of Restorative Dentistry, Dental Branch, Islamic Azad University, Tehran, Iran,* [2]*Dentist, Private Practice, Tehran, Iran,* [3]*Dental Research Center, Tehran University of Medical Sciences, Tehran, Iran, and* [4]*Orthodontist, Tehran, Iran*

Abstract

Objective. Along with their re-mineralizing capacity, calcium phosphopeptide–amorphous calcium phosphate products combined with fluoride (CPP-ACPF) could also be beneficial by neutralizing acidic salivary and plaque pH. The purpose was to evaluate the effect of CPP-ACPF on salivary and plaque pH in orthodontic patients. ***Materials and methods.*** As a triple-blind, cross-over randomized trial, 30 orthodontic patients with fixed appliances (age range = 15.70 ± 4.08 years) were recruited and randomly assigned to two groups. A CPP-ACPF paste (MI Paste Plus, GC America, Alsip, IL) was used by group 1 ($n = 15$) and a placebo by group 2 ($n = 15$) for 1 month. After a 1 month washout period, patients used the alternative paste for another month. Plaque and salivary pH levels were measured at all before and after periods. ***Results.*** By applying MI Paste Plus, the plaque pH increased from 5.81 ± 0.45 to 6.60 ± 0.38 ($p < 0.05$), whereas the before and after salivary pH recordings, which were 6.72 ± 0.43 and 6.71 ± 0.38, respectively, remained statistically unchanged ($p > 0.05$). ***Conclusion.*** MI Paste Plus can be clinically beneficial in increasing plaque pH levels, but has no effect on the salivary pH.

Key Words: *calcium phosphates/administration & dosage, dental caries prevention, acidity*

Introduction

Although caries itself is a major public health problem, orthodontic patients could be considered as a population which is much more implicated in the issue of dental caries and its prevention. The situation in orthodontic patients is important from the aspect that, due to the configuration of current fixed orthodontic appliances, accumulation of food debris and plaque increases, leading orthodontic patients into a higher caries-prone category [1–3]. Even more, one should remember that the majority of orthodontic patients are adolescents, with a compliance level far from ideal [4].

Along with the increasing demand for orthodontic treatment, seeking solutions to decrease the risk of caries in these patients would be, therefore, highly desirable. Efforts have been made, such as diet control (counseling), mechanical oral hygiene procedures and administration of fluoride supplements [5], only to mention a few and considering that each approach has its own relative level of effectiveness.

Further efforts have led to the development of other products containing casein phosphopeptide–amorphous calcium phosphate (CPP-ACP). These compounds have drawn attention, mostly because of their re-mineralizing capabilities. In this complex, CPP is able to bind with calcium and phosphate ions and transport them in the form of amorphous calcium phosphate (ACP) [6]. CPP has the capability to bind not only with enamel, but also with biofilm and soft tissues. Under oral pH conditions, CPP can transport calcium and phosphate into the tooth structure and enhance enamel regeneration.

The CPP-ACP complex also seems to be even more effective when combined with fluoride (CPP-ACPF). A synergestic effect has been claimed to exist, which in turn leads to an improvement in the synthesis of

Corerspondence: Faramarz Mojtahedzadeh, Apt 3, No 8. 9th Street, Gandhi Ave, Tehran, 1517654114, Iran. Tel: +982188878135. E-mail: mojzad@tums.ac.ir

(Received 6 December 2013; accepted 15 April 2014)

ISSN 0001-6357 print/ISSN 1502-3850 online
DOI: 10.3109/00016357.2014.920515

fluoroapatite crystals [6,7]. A considerable body of literature with a variety in study design exists which has investigated the effect of CPP-ACP products in orthodontic patients in their abilities to eliminate white spot lesions [8–10].

However, in addition to the re-mineralizing properties, a preventive role has also been postulated for CPP-ACP, which mostly refers to pH control. There are signs that CPP-ACP products might also be able to improve pH levels in different areas in the oral cavity [11–13]. Although promising, investigations dealing with the effect of CPP-ACP products on plaque and salivary pH levels and in the high risk orthodontic patient appear to be limited and have not been conducted in the form of randomized clinical trials.

Therefore, the purpose of this study was to evaluate the effects of recommending a CPP-ACPF product on salivary and plaque pH levels in patients undergoing orthodontic treatment with fixed appliances as a randomized cross-over clinical trial.

Materials and methods

This study was designed as a triple-blind, single-center and placebo-controlled cross-over randomized clinical trial. The researchers, patients and methodologist were the blinded members of the study. Ethical approval was obtained from the Ethics Committee of the School of Dentistry of Tehran Azad University and informed consent forms were developed in order to be signed by patients or guardians. Sample size was calculated considering expert opinion and similar studies. The Minitab software was used for sample size calculation. Setting the margin of error as $\alpha = 0.05$ and a power of 0.8, a sample size of 24 was calculated. Also adding 20% for any possible loss to follow-up, a sample size of 30 patients was considered for the study. Orthodontic healthy patients of the private practice of one of the authors (FM) older than 12 years undergoing comprehensive orthodontic treatment with fixed appliances for treatment of non-surgical malocclusions (Class I or Class II camouflage treatment) and requiring extraction of four premolars were considered as eligible participants for the study. All patients had previously completed a medical history questionnaire. Other inclusion criteria were: receiving orthodontic treatment for at least 3 months and 12 at most. Exclusion criteria were: history of any systemic disorders, receiving medications that could affect the oral microbial flora, pregnancy, using supplemental fluoride products and loss of first permanent molar.

Thirty patients (nine males, 21 females) were recruited to the study. All patients had previously received similar oral hygiene packages including a toothbrush, toothpaste, dental floss and disclosing tablets at the commencement of orthodontic treatment. The patients were also instructed for oral hygiene procedures both verbally and via written and multimedia material. A randomization sequence for allocating subjects in two cross-over groups of the study was developed by the methodologist (MJK) via block randomization using a block size of 4.

All patients were scheduled for afternoon appointments and were requested not to consume any food or perform any oral hygiene procedure at least 2 h prior to attending the clinic. At the beginning of the study, the baseline pH of both plaque and saliva were measured for each patient. In order to do so, salivary samples were collected using the GC Salivary Buffer Check Kit (GCAmerica, Alsip, IL). Patients were ordered to expectorate into disposable cups provided in the kit and a pH indicator strip was dipped into the sample saliva for 10 s. The color change of the strip was compared with the corresponding color chart, which in turn indicated the acidity level (pH). Supragingival plaque samples were collected from the lower right first permanent molar of all patients and the acidity of the sample was determined using the GC Plaque Indicator Kit (GCAmerica).

Next, and to ensure blinding of the patients, each received similar opaque plastic tubes, which contained either MI Paste Plus (GCAmerica), a product containing CPP-ACPF or a placebo paste (composed of inactive ingredients including silicon dioxide, glycerol, titanium dioxide, water, hydroxybenzoate, flavoring (vanilla),carboxymethylcellulose, propylene glycol, sodium saccharin).

The orthodontist, which was also blinded to the contents and generated sequence of tubes, delivered them to patients as provided by the other researcher (EM), who in turn had sorted the tubes according to the previously generated randomized sequence and blind to the patients receiving the tubes. All patients were instructed to use the paste every night before sleep and after performing their routine oral hygiene procedures. A pea-sized amount of paste was administered and rubbed with the index fingertip to the surfaces of the entire teeth. They were informed to expectorate after 10 min but avoid rinsing, eating or drinking thereafter. Printed instructions were also given to each participant. In the following orthodontic appointment which was scheduled for 4 weeks later, the salivary and plaque pH levels were once again measured, as previously mentioned, and, from that point, all participants experienced a 4-week washout period. At the following appointment pH levels were once again measured and the alternative paste was given to all patients, who were instructed to use the paste in the previous manner. Again, after 1 month of using pastes the pH measurements were repeated. One researcher (HH) made all measurements and was blind to other components of the study. Consequently, the duration of the intervention for all patients was a total of 12 weeks.

Table I. Descriptive data of participants' gender and age distribution.

	n	Mean age	SD	Minimum	Maximum	*p*-value
Male	9	15.57	4.31	12	22	0.45*
Female	21	15.76	4.11	12	23	
Total	30	15.70	4.08	12	23	

**p*-value based on one-tailed independent sample *t*-test.

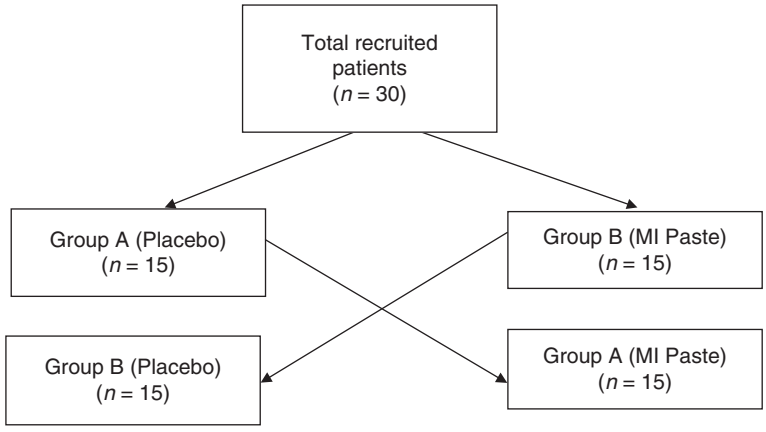

Figure 1. Schematic diagram of the study design.

All collected data and scores were compiled and tabulated by the other researcher (SB) to remove identifiers so that the methodologist responsible for statistical analysis remained blind to the data associated with each study group. In addition to determining descriptive data, the salivary and plaque pH results were analyzed with paired *t*-tests for investigating period effects, independent *t*-tests for possibility of carryover effects and two-way repeated measure ANOVA tests for treatment effects, all with the aid of SPSS software version 16 (SPSS, Chicago, IL). The level of significance for all tests were set at $p = 0.05$.

Results

The descriptive data of participants recruited in this study are presented in Table I. The mean and standard deviations of both groups in each period of time are displayed in Figure 1. As patients were undergoing orthodontic treatment, all patients continued to participate and no loss to follow-up was observed in this study.

Plaque pH

The mean values for plaque pH of both groups are shown in Table II. The results of the paired *t*-tests for determining the period effect between the baseline findings showed no significant difference ($p > 0.05$), hence ruling out the period effect. The results of the independent *t*-test also showed no significant difference ($p > 0.05$) and, in turn, the possibility of a carryover effect was also set aside. Results of two-way repeated measure ANOVA, considering time and type of intervention as the variables, showed a significant difference in plaque pH changes ($p = 0.002$). In addition, paired *t*-test findings between before and after results of each treatment regimen protocol showed that MI Paste Plus significantly increased in plaque pH ($p < 0.001$), while this finding in the placebo group remained statistically unchanged ($p = 0.48$).

Salivary pH

Table II also shows the mean salivary pH results. The same statistical approach was used for salivary pH

Table II. Total salivary and plaque pH results based on type of paste.

Variable	Group	Before, *M* (SD)	After, *M* (SD)	*p*-value
Plaque	Placebo	5.77 (0.46)	5.72 (0.46)	0.002
pH	MI Paste plus	5.81 (0.45)	6.60 (0.38)	
Salivary	Placebo	6.84 (0.35)	6.79 (0.32)	0.484
pH	MI Paste plus	6.72 (0.43)	6.71 (0.38)	

results. Similar to plaque pH findings, the results of paired *t*-tests and independent *t*-tests again showed no significant difference ($p > 0.05$). However, in contrast to plaque pH results, repeated measure ANOVA test of salivary pH changes showed no significant difference either ($p = 0.658$). This was also the same for pre- and post-treatment salivary pH changes, where paired *t*-test results showed no significant change over time ($p = 0.714$).

Discussion

The results of the current study showed that applying MI Paste Plus once a day in patients undergoing fixed orthodontic treatment caused a significant increase in plaque pH levels when compared to a placebo, while the salivary pH levels remained almost unchanged.

Irrespective of the difficulty and limitations, this randomized clinical trial was designed and launched with the hope to draw conclusions with a higher level of evidence. Therefore, every effort was made to design the study as carefully as possible and exclude any item that could adversely affect the outcomes of the study.

The incident of increased or even extreme salivary flow usually observed after the insertion of orthodontic appliances is a familiar issue. Changes in salivary flow rate, buffer capacity, plaque and cariogenic micro-organism levels show an increase after 1 month of appliance insertion [14]. The most intensive changes appear to be between 6–12 weeks [15], where, beyond that point, the changes are assumed to decline and reach a relatively steady state [16]. That was the reason for selecting participants who had started their orthodontic treatment for at least 3 months. Comparison of the first and second baseline pH values which were analyzed by the paired *t*-test can be in agreement with this assumption, showing that the pH changes beyond 3 months of appliance insertion do not seem to rise and fall significantly.

Obtaining proper salivary and plaque samples could be disrupted if patients performed oral hygiene procedures immediately or shortly prior to the sampling process [12], which is why patients in the current study were strictly advised to refrain from eating or brushing 2 h prior to the sampling procedure.

The possibility of carry-over effects in cross-over clinical trials is an issue that requires proper consideration. A minimum washout period of 2 weeks has been suggested for caries assessment studies [17]. The 4-week period considered in this study was selected both with the intention to exceed the suggested baseline and to eliminate the need for an extra appointment, hence increasing the chance of completing the study and reducing the possibility of dropouts. The results of the *t*-tests for baseline values confirm the adequacy of the washout time span.

The short-term effect of CPP-ACP in buffering the pH of plaque has been previously observed in a group of non-orthodontic individuals; showing that CPP-ACP was capable of controlling the drop in plaque pH which is usually seen after exposure of the oral cavity to fermentable carbohydrates [13].

In contrast to previous findings which state that CPP-ACP may cause changes in salivary pH levels [11], this variable remained relatively constant throughout the present study. Salivary pH levels are believed to be mostly influenced by flow rate, which in turn affects the composition [18]. Therefore, it would be unlikely to observe a cause persistent change; only transient changes can be assumed to be possible.

Other possible reasons for the difference in results observed in comparison to other studies can be related to the difference in study designs. For example, the results of before–after designs seen in other studies [11] could be under the influence of confounding factors such as increased patient awareness towards oral hygiene maintenance once recruited in the study.

In order to obtain even more clinically useful findings, further research is suggested to determine both the longevity of the pH changes seen in dental plaque following the use of MI Paste Plus and also the contribution of CPP-ACP in increasing plaque pH independent from fluoride.

Conclusion

The results of the current study show that, along with the re-mineralizing properties attributed to MI Paste Plus as a CPP-ACPF compound, this product can also play a preventive role by neutralizing the pH of plaque accumulated around fixed orthodontic appliances. No significant changes in salivary pH levels were observed under the influence of this product.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

[1] Derks A, Kuijpers-Jagtman AM, Frencken JE, Van't Hof MA, Katsaros C. Caries preventive measures used in orthodontic practices: an evidence-based decision? Am J Orthod Dentofacial Orthop 2007;132:165–70.

[2] Tufekci E, Dixon JS, Gunsolley JC, Lindauer SJ. Prevalence of white spot lesions during orthodontic treatment with fixed appliances. Angle Orthod 2011;81:206–10.

[3] Boersma JG, van der Veen MH, Lagerweij MD, Bokhout B, Prahl-Andersen B. Caries prevalence measured with QLF after treatment with fixed orthodontic appliances: influencing factors. Caries Res 2005;39:41–7.

[4] Kukleva MP, Shetkova DG, Beev VH. Comparative age study of the risk of demineralization during orthodontic treatment with brackets. Folia Med 2002;44:56–9.

[5] Noble J, Cassolato S, Karaikos N, Wiltshire WA. Point of care. Preventive and interceptive measures for improving and maintaining good oral hygiene and cariogenic control in orthodontic patients. J Can Dent Assoc 2009;75:441–3.
[6] Reynolds EC, Cai F, Cochrane NJ, Shen P, Walker GD, Morgan MV, et al. Fluoride and casein phosphopeptide-amorphous calcium phosphate. J Dent Res 2008;87:344–8.
[7] Lennon ÁM, Pfeiffer M, Buchalla W, Becker K, Lennon S, Attin T. Effect of a casein/calcium phosphate-containing tooth cream and fluoride on enamel erosion in vitro. Caries Res 2006;40:154–7.
[8] Robertson MA, Kau CH, English JD, Lee RP, Powers J, Nguyen JT. MI Paste Plus to prevent demineralization in orthodontic patients: a prospective randomized controlled trial. Am J Orthod Dentofacial Orthop 2011;140:660–8.
[9] Sudjalim TR, Woods MG, Manton DJ, Reynolds EC. Prevention of demineralization around orthodontic brackets in vitro. Am J Orthod Dentofacial Orthop 2007;131:705.e1–9.
[10] Chen H, Liu X, Dai J, Jiang Z, Guo T, Ding Y. Effect of remineralizing agents on white spot lesions after orthodontic treatment: a systematic review. Am J Orthod Dentofacial Orthop 2013;143:376–82.
[11] Marchisio O, Esposito MR, Genovesi A. Salivary pH level and bacterial plaque evaluation in orthodontic patients treated with Recaldent products. Int J Dent Hygiene 2010;8:232–6.
[12] Kitasako Y, Cochrane NJ, Khairul M, Shida K, Adams GG, Burrow MF, et al. The clinical application of surface pH measurements to longitudinally assess white spot enamel lesions. J Dent 2010;38:584–90.
[13] Caruana PC, Mulaify SA, Moazzez R, Bartlett D. The effect of casein and calcium containing paste on plaque pH following a subsequent carbohydrate challenge. J Dent 2009;37:522–6.
[14] Lara-Carrillo E, Montiel-Bastida NM, Sánchez-Pérez L, Alanís-Tavira J. Effect of orthodontic treatment on saliva, plaque and the levels of Streptococcus mutans and Lactobacillus. Med Oral Patol Oral Cir Bucal 2010;15:e924–9.
[15] Chang HS, Walsh LJ, Freer TJ. The effect of orthodontic treatment on salivary flow, pH, buffer capacity, and levels of mutans streptococci and lactobacilli. Aust Orthod J 1999;15:229–34.
[16] Peros K, Mestrovic S, Anic-Milosevic S, Slaj M. Salivary microbial and nonmicrobial parameters in children with fixed orthodontic appliances. Angle Orthod 2011;81:901–6.
[17] Curzon ME, Hefferren JJ. Modern methods for assessing the cariogenic and erosive potential of foods. Br Dent J 2001;191:41–6.
[18] Nederfors T. Xerostomia and hyposalivation. Adv Dent Res 2000;14:48–56.