Effects of Casein Phosphopeptide Amorphous Calcium Phosphate and Casein Phosphopeptide Amorphous Calcium Phosphate Fluoride on Alterations of Dental Plaque PH Following Sucrose Consumption

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Abstract

Background and Aim: Plaque pH drop after consumption of sugary materials may dissolve enamel minerals. Casein phosphopeptide amorphous calcium phosphate (CPP-ACP) is a paste enriched with calcium and phosphate. The new formulation of this paste, casein phosphopeptide amorphous calcium phosphate fluoride (CPP-ACPF), contains 900 ppm fluoride. This paste can neutralize the low pH of bacterial plaque. This study compares the efficacy of CPP-ACP and CPP-ACPF for neutralizing plaque acidity at different time points.

Materials and Methods: This clinical trial was conducted on 40 students. Plaque pH at the distal of first molar was measured before and 10 minutes after the consumption of 10% sucrose solution. In the next step, CPP-ACP and CPP-ACPF pastes were applied as recommended by the manufacturers to the tooth surface. Plaque pH was measured at 30 minutes, 60 minutes and 24, 48, 72 and 96 hours. Data was recorded and analyzed by repeated measures ANOVA (p<0.05).

Results: Both CPP-ACP and CPP-ACPF increased plaque pH similarly in the first 48 hours. However, the pattern changed from this time point on.

Conclusion: CPP-ACP and CPP-ACPF had similar efficacy for up to 48 hours, but CPP-ACPF was capable of keeping the pH high by up to 96 hours.

Key Words: CPP-ACP, CPP-ACPF, Plaque pH, Demineralization

Introduction

Tooth decay is among the most common infectious diseases worldwide with bacterial origin [1]. Enamel demineralization starts at a pH of ≤5.5 and superficial enamel carious lesions are visible at a pH of 4 or 5 [1]. Thus, dental plaque pH assessment can indicate the risk of dental caries [2]. Many studies have investigated the positive effects of fluoride and calcium and phosphorous ions on enamel remineralization [3-6]. Jensen et al. evaluated the effect of processed cheese on dental plaque pH and showed that consumption of this type of cheese prevented plaque pH reduction following the consumption of sugary foods and made a shift towards remineralization [7]. Casein phosphopeptide is derived from the milk protein casein by tryptic digestion.

Journal of Islamic Dental Association of IRAN (JIDAI) Autumn 2014;26, (4)
Amorphous calcium phosphate provides phosphate and calcium ions in an amorphous soluble form in comparison to calcium and phosphate ions in the saliva. This alkaline compound is super-saturated with phosphate and calcium and thus increases the plaque pH following application [4]. This compound was introduced to the dental market in the form of a crème or paste with the commercial name of GC Tooth Mousse (GC America, Alsip, IL). Fluoride can enhance the efficacy of CPP-ACP. A new formulation of this paste containing 900 ppm fluoride has been recently introduced to the market with the commercial name of MI Paste Plus (GC America, Alsip, IL) [8].

Caruana et al. evaluated the efficacy of CPP-ACP paste for buffering the acidity of dental plaque prior to the consumption of carbohydrates and reported that the magnitude of plaque pH reduction following the consumption of sucrose solution was smaller in the CPP-ACP group compared to the control group [3]. Based on the literature, application of CPP-ACP and CPP-ACPF helps neutralize dental plaque pH [9]. However, no accurate data is available on the efficacy of these two pastes for plaque pH neutralization and the durability of this effect in comparison with one another.

This study aimed to compare the effects of GC Tooth Mousse and MI Paste Plus containing fluoride on plaque pH following sucrose consumption.

Materials and Methods

This double blind, parallel-design clinical trial was conducted on male students in Qom city. The study was approved in the Ethics Committee of Tehran Islamic Azad University, Faculty of Dentistry and registered in the Iranian Registry of Clinical Trials (#IRCT2012113010086N2).

Parents were provided with an information form explaining the methodology and objectives of the study in details and a written informed consent was obtained from them. A total of 40 students in the age range of 12-14 years and moderate plaque index (PI) were enrolled. For PI calculation, the patient chewed a disclosing tablet and number of surfaces with dental plaque was divided by the total number of teeth surfaces and multiplied by 100. Students with moderate PI (minimum of 10%), good oral hygiene and no active caries were selected using non-random sampling [10]. Active carious lesion was defined as a cavitated lesion with soft enamel and dentin on the surface and white appearance, with microbial plaque, opacity and a chalky pattern at the gingival margin and inflammation of the adjacent gingiva [1]. First, dental plaque pH was measured at the distal surface of mandibular first molar. The patients were asked not to brush their teeth or eat for two hours prior to pH measurement [3]. Ten minutes after the consumption of 10% sucrose solution, plaque acidity was measured again at the same spot. The patients were then divided into two groups of 20. In group 1, CPP-ACP was applied to the teeth surfaces according to the manufacturer’s instructions. The teeth were first dried using sterile gauze. Next, the paste was applied to the teeth surfaces for two minutes and the patient was asked to wet the teeth with saliva for three minutes. After rinsing, plaque pH was measured and recorded at 30 and 60 minutes and 24, 48, 72 and 96 hours. In group 2, CPP-ACPF was applied as described above and plaque pH was measured and recorded at the mentioned time points (Table 1).

Paste application and measurement of plaque pH were done at the Hygiene Room of the center by a trained dental student. This study had a double blind design and both the operator and students were blinded to the composition and difference of the two pastes. The pH indicator kit (Dental SUZHO GC, China) was used for plaque pH measurement.

The trend of alterations of plaque acidity following the consumption of sucrose at the mentioned time points was evaluated using repeated measures ANOVA by considering type of paste as the between subject factor and time of measurement after the consumption of sucrose as the repeated factor. The efficacy of the two pastes was compared using Bonferroni test. Level of significance was set at 0.05.

Results

The mean pH reached 5.7 in all subjects after the consumption of sucrose solution. Application of both CPP-ACP and CPP-ACPF gradually increased the pH. The ascending trend of pH was
Table 1. The mean, standard deviation (SD), and descriptive statistics of plaque pH after the application of pastes

<table>
<thead>
<tr>
<th>Paste</th>
<th>Time</th>
<th>Before the consumption of sucrose solution Mean± SD</th>
<th>10 min after the consumption of sucrose</th>
<th>30 min after the application of paste</th>
<th>60 min after the application of paste</th>
<th>24 h after the application of paste</th>
<th>48 h after the application of paste</th>
<th>72 h after the application of paste</th>
<th>96 h after the application of paste</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPP-ACP</td>
<td>5.8±1.15</td>
<td>5.72±0.07</td>
<td>5.88±0.17</td>
<td>6.21±0.12</td>
<td>6.38±0.17</td>
<td>6.25±0.14</td>
<td>6.11±0.15</td>
<td>5.87±0.12</td>
<td></td>
</tr>
<tr>
<td>CPP-ACPF</td>
<td>6.04±0.14</td>
<td>5.65±0.12</td>
<td>5.95±0.14</td>
<td>6.16±0.15</td>
<td>6.29±0.19</td>
<td>6.34±0.2</td>
<td>6.32±0.17</td>
<td>6.23±0.18</td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>0.632</td>
<td>0.381</td>
<td>0.225</td>
<td>0.17</td>
<td>0.077</td>
<td>0.051</td>
<td>0.000</td>
<td>0.000</td>
<td></td>
</tr>
</tbody>
</table>
similar in both groups by up to 48 hours and was not significantly different. In other words, the effect of the two pastes on increasing the plaque pH was not significantly different in the first 48 hours. At 48 hours and after that, the two pastes started to show differences and at 72 hours, a significant difference was observed in the efficacy of the two pastes (Table 1). Statistical analysis revealed that the effect of CPP-ACPF lasted longer than that of CPP-ACP and that the CPP-ACPF maintained the pH over 6.2 by up to 96 hours (Diagram 1).

![Diagram 1](image.png)

**Diagram 1.** Changes of plaque pH before and after the application of 10% sucrose solution at the mentioned time points

**Discussion**

This study was a double blind, parallel-design clinical trial aiming to compare the effects of CPP-ACP and CPP-ACPF on dental plaque pH and its neutralization. The results revealed that both CPP-ACP and CPP-ACPF significantly increased plaque pH after the consumption of sucrose solution. The effects of the two pastes were similar by up to 48 hours but CPP-ACPF maintained a high plaque pH by up to 96 hours. It means that 900 ppm fluoride in conjunction with CPP-ACP is more efficient for neutralization of plaque pH and has a long-lasting effect.

Tooth decay is due to the effect of plaque pH changes on the tooth surface [2]. The pH of the saliva and plaque is measured in many studies to evaluate its effects on tooth caries. In other words, plaque pH measurement at different time points shows changes in the acidity of dental plaque and activity of white spot lesions (WSL) over time [2]. The highest drop in pH occurs within the first 10 minutes following the consumption of sucrose solution [11]. However, one problem of plaque pH measurement is that patients often brush their teeth before presenting to dental office [2]. In the current study, the subjects were asked to refrain from brushing their teeth or eating prior to the first plaque pH measurement; and plaque pH was measured again 10 minutes after the consumption of sucrose solution.

Plaque pH drop is more severe after the consumption of sucrose solution in subjects with active caries and also in plaques containing a higher percentage of acidogenic bacteria [1,12]. Studies have demonstrated that the highest number of mutans Streptococci accumulate on the proximal surfaces of molars and second premolars [12]. Thus, plaque sampling was done at the distal surface of the first molar tooth.

Kitasako compared the plaque pH over sound enamel and enamel around a WSL. Plaque pH was 6.7±0.2 over the sound enamel and 5.94±0.17 around the WSL. This difference was statistically significant. In their study, the mean plaque pH one hour after the consumption of sucrose solution was 5.88±0.37 in subjects with at least one carious lesion. The plaque pH values obtained in our study were similar to those obtained by Kitasako, although they used a pH meter for plaque pH measurement. Saliva and dental plaque pH in subjects with active caries is usually much lower than the normal threshold [6, 13]. Saliva is the first protective barrier against caries [1]. Despite the presence of saliva and its buffering capacity, plaque pH after the consumption of sucrose solution drops rapidly to a level below the critical pH threshold. On the other hand, pH returns to its neutral state around 7 very slowly within 20 to 50 minutes [1]. The higher the number of active caries and bacterial count in the oral cavity, the more time is required for plaque pH to return to its neutral state [1, 14]. Such slow return of plaque acidity to neutral state is due to the fact that plaque itself acts as a protective barrier against the diffusion of saliva [14]. On the other hand, saliva does not play an equal role in different parts of the...
oral cavity depending on the oral anatomy, path of secretion of saliva and its flow towards the pharynx [15].

Another characteristic of the saliva is that it can be maintained in a supersaturated state with calcium and phosphate ions in the oral cavity, protecting the hydroxyapatite crystals and enhancing the remineralization of enamel. In a physiologic state, the buffering capacity of the saliva and its content of ions maintain the pH of oral environment at a level close to saturation state [14]. However, for various reasons, this balance may shift towards demineralization of tooth structure. In the study by Srinivasan, no remineralization occurred in demineralized enamel immersed in the saliva compared to groups that received one time application of CPP-ACP and CPP-ACPF. It can be concluded that in many cases, due to the presence of active caries or mature bacterial plaques [1], application of remineralizing agents is necessary to make a shift towards remineralization [16]. Thus, although saliva has calcium and phosphate ions, it cannot make a shift towards remineralization by itself.

Many studies have discussed that CPP-ACP paste is mixed with the saliva, pellicle and dental plaque following its application and acts as a calcium reservoir with remineralizing potential [3, 17]. This paste stabilizes calcium and phosphate ions on the tooth surface. Deposition of active, soluble derivatives onto the WSL enhances remineralization. Also, it has been demonstrated that CPP-ACP buffers dental plaque acidity and is capable of gradually changing its composition.

On the other hand, deposition and accumulation of CPP-ACP in dental plaque neutralizes its acidic pH and makes a shift towards remineralization [2, 9]. Remineralization and demineralization are dynamic processes depending on the calcium and phosphate content of the tooth surface. On the other hand, pH at the time of remineralization and demineralization depends on the concentration of calcium and phosphate ions in the saliva and dental plaque. When enamel surface pH drops, plaque loses its saturation and demineralization occurs. When pH increases, plaque becomes super-saturated with ions and these ions are absorbed into the enamel [4]. The critical pH is below 5.5 for enamel demineralization and below 6.2 for demineralization of dentin and root surface [1, 18].

Thus, changes in plaque acidity due to the application of CPP-ACPF can prevent caries in dentin and root surfaces. On the other hand, fluoride is necessary for treatment of WSL and prevention of caries and has a synergistic effect with many anticaries compounds and methods [1]. As described earlier, calcium and phosphorous ions must be available to enhance remineralization and in order for the fluorapatite and fluorohydroxyapatite crystals to form in presence of calcium, phosphorous and flour ions. Some researchers believe that fluoride deposition in dental plaque depends on the presence of calcium ions [19]. In a study by Ogata et al, remineralization depth was measured and compared following the application of CPP-ACP alone, in conjunction with different concentrations of fluoride and fluoride alone using micrography and it was observed that remineralization in presence of CPP-ACP in conjunction with fluoride was more favorable compared to their separate application. Thus, CPP-ACP provides a buffering effect and fluoride promotes remineralization [20].

Despite various investigations on the effect of CPP-ACP on tooth structure, the exact duration of the effect of CPP-ACP and CPP-ACPF on pH and the durability of the enamel remineralizing potential of these materials have not been mentioned in articles or even in the manufacturers’ instructions. Thus, GC Tooth Mousse must be used at least every 48 hours and MI Paste Plus twice a week. On the other hand, due to ethical considerations, we did not have a control group to clinically assess the trend of increase in plaque pH following the consumption of sucrose solution with no intervention and only in presence of saliva.

**Conclusion**

Within the limitations of this study, it may be concluded that application of CPP-ACP and CPP-ACPF can make a shift towards remineralization for up to 48 and 96 hours, respectively.

**References**