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In vitro Evaluation of fluoride uptake from a thixotropic gel

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Abstract

The in vitro fluoride uptake by dental enamel from two conventional acidulated phosphate fluoride gels was compared to a thixotropic acidulated phosphate fluoride gel. The fluoride concentration and enamel biopsy depths were determined using an acid-etch biopsy method based on calcium determinations. A significant fluoride uptake by dental enamel from a thixotropic topical fluoride agent following one minute of application was demonstrated. This trend was also true for the 4-minute topical applications. This study showed that the thixotropic gel was as good as but not superior to conventional acidulated phosphate fluoride gels in terms of promoting fluoride uptake.

Introduction

In the dental office environment, acidulated phosphate fluoride (APF) is the most widely used topical fluoride today. Clinical studies have shown caries reductions following the twice-a-year professional application of APF solutions and gels in nonfluoridated communities to be in the 30–50% range.[1–3] Most APF preparations are available in the gel form which involves the incorporation of a cellulose base or other gelling agents. The gel form has the advantage of being easily applied with a cotton swab and is colored so that the dentist or therapist may visualize the location of the applied fluoride. Gels are more easily utilized when the topical fluoride is applied via a mouth tray.

There is evidence to show that the fluoride uptake by enamel from a gel preparation is comparable to that from a solution with the same chemically active ingredient at the same pH and fluoride concentration.[4] The selection of a solution or gel should, therefore, be based on clinical effectiveness, cost, patient acceptance, and personal preference.

Recently, a thixotropic APF preparation has been marketed commercially.* The term "thixotropic" refers to a solution that sets in a gel-like state (*versus* a solution) but is not a true gel. These compounds are unique in that under stress a thixotropic gel becomes fluid-like and may possibly penetrate into the interproximal areas more easily than a conventional gel. When stress is released, it becomes highly viscous and therefore tends to adhere to tooth surfaces, not being easily swallowed by the patient. However, the clinical effectiveness of these thixotropic fluoride agents has not been tested. As a first step, testing using appropriate laboratory methods should provide an indication of clinical effectiveness in preventing dental caries.

The purpose of this study was to compare the relative fluoride uptake by human dental enamel from two conventional APF gels (A† and B‡) with a thixotropic gel (C*). Specifically it aimed to test the hypothesis that thixotropic gels result in greater fluoride uptake in dental enamel than do conventional APF gels. The study also investigated fluoride uptake as a function of application time.

Materials and methods

Sound, extracted, human third molars were stained with fast green, brushed clean, and stored in a humid atmosphere in the refrigerator.

The teeth were randomly assigned to treatment and control groups of 10 surfaces (buccal or lingual) each. The control (untreated surface) biopsy was immediately adjacent to the treated biopsy site on the same tooth surface in order to minimize intratooth differences in fluoride concentrations. Two complete sets of experiments were performed using 1- and 4-minute application times for each of the three gels. The fluoride uptake was measured using an acid-etch enamel biopsy technique as devised and modified by this laboratory.[5] The acid-etch biopsy consists of dissolu-

* Gel II, Pacemaker Corporation, Portland, Oregon.

† Luride, Hoyt Laboratory, Needham, Massachusetts.

‡ Topical fluoride gel, Pacemaker Corporation, Portland, Oregon.

tion of a microquantity of enamel using 0.5 M $HClO_4$ for 15 seconds. Three consecutive biopsies were taken in order to obtain a profile of the fluoride concentration from the surface into the deeper enamel in order to assess the depth of fluoride penetration.

After the control enamel biopsy was obtained, the site was covered with nail varnish, and the tape was removed to expose the adjacent, sound enamel surface. The teeth were then completely immersed in the test agent for either 1 or 4 minutes. After treatment, the teeth were removed from the gel, rinsed briefly with distilled water to remove the remaining gel, and wiped clean with KimWipe. The teeth were then suspended in a stirred, synthetic saliva for 24 hours after which the surface was rebiopsied for fluoride uptake of the treated site.

The synthetic saliva had a composition of 1 mM calcium, 3 mM phosphate, and 20 mM HCO_3^- and had a pH of approximately 7.0. All biopsies were analyzed for fluoride using a fluoride ion electrode, and the amount of enamel removed was measured by determination of the calcium content of each biopsy. Calcium concentrations were obtained by atomic absorption spectrophotometry.

Results

The mean and standard deviation of the control and treated enamel surfaces are shown in Table 1 for the 1- and 4-minute topical fluoride treatments. The base line fluoride values were consistent with fluoride levels found in enamel from fluoridated areas and were between 843–2953 ppm for the six groups. The biopsy depths ranged from 1.92–3.56 μm. The highest fluoride values (B, 1 minute) corresponded to the shallowest depth, while the low fluoride group (B, 4 minutes) corresponded to the deepest enamel biopsy depths, as one would expect. These fluoride and biopsy depth values are for the first enamel layer removed.

The differences in enamel fluoride concentrations following the application of each gel at both 1- and 4-minute application times compared to their respective controls were found to be statistically significant using a paired *t* test. The treated enamel fluoride levels in the first layer were between 4841–8067 ppm for 1-minute applications and between 6581–8374 ppm for 4-minute applications.

The differences between groups were analyzed with multivariate analysis of variance. Table 2 shows the net fluoride uptake for all three agents for 4 minutes and 1 minute, grouping the three depths together. There was a significantly greater uptake of fluoride after 4 minutes compared to 1 minute with $p = 0.0003$.

Table 3 shows the increased fluoride uptake in the first layer. There was virtually no increased uptake in the second and third layers as a result of prolonging the treatment time. It may be concluded that, in the first layer of enamel, the surfaces treated for 4 minutes showed significantly greater fluoride uptake as compared to those treated for 1 minute.

Table 4 shows the mean total fluoride uptake by time and treatment. It appears that the thixotropic gel C gave fluoride uptake slightly better than gel A after 4 minutes but was not as high as gel B. In this

Table 2. Mean total F uptake for all three agents as a function of treatment time

Time	F (ppm)
4 min	9462.9 ± 6811.4*
1 min	6720.1 ± 4294.9
$F_{1,54} = 16.8094$	$p = 0.0003$

* Mean ± S.D.

Table 3. Mean F uptake by time and biopsy depth (averaged over agents)

Time	F (ppm) at 3 enamel biopsy depths		
	1	2	3
4 min	6157 ± 4130.7*	2017.6 ± 2209.5*	1288.1 ± 1680.1*
1 min	3964 ± 2695.9	1817.7 ± 1722.1	937.8 ± 1351.8
Diff	2192.6	199.9	350.2
$F_{2,53} = 4.1849$	$p = 0.02$		

* Mean ± S.D.

Table 1. Enamel F concentrations after 1 and 4 min topical application

Time Group		Control (n = 10)		Treated (n = 10)	
		F (ppm)	Depth (μm)	F (ppm)	Depth (μm)
1 min	A	1541 ± 671*	2.10 ± 0.81*	4841 ± 1574*	1.89 ± 0.39*
	B	2953 ± 1002	1.92 ± 0.50	8067 ± 4097	1.74 ± 0.43
	C	2234 ± 824	2.26 ± 0.56	5713 ± 1460	1.76 ± 0.25
4 min	A	1664 ± 637	2.81 ± 0.91	6581 ± 2298	2.48 ± 0.61
	B	843 ± 333	3.56 ± 1.48	7315 ± 5106	2.79 ± 0.88
	C	1291 ± 340	2.88 ± 0.58	8374 ± 4393	2.88 ± 0.63

* Mean ± S.D.

comparison, gel B appears to give the greatest fluoride uptake.

Table 5 shows the differences in fluoride uptake between 4 minutes and 1 minute for the three agents. It may be concluded that the three agents did not increase fluoride uptake by time to the same extent. Agents B and C gave significantly greater total fluoride uptake after 4 minutes than did agent A.

Discussion

The results of this study show that the thixotropic gel C significantly increased enamel fluoride concentrations when compared to its controls, but there was no consistent indication that it was superior to conventional APF gels in that regard. However, a thixotropic gel offers certain practical advantages, such as better physical properties and handling characteristics that may enhance its usefulness in the clinical environment. The thixotropic nature of gel C may allow for better interproximal penetration where fluoride is most effective in the prevention of caries. In addition, once biting forces cease during the topical fluoride application, the viscosity of the gel will increase. This may prevent unwanted ingestion of the fluoride gel and leave the interproximal region with a thin layer of fluoride gel.[6]

This study also confirms the continued fluoride uptake by enamel as a function of time[7] over the application period of 4 minutes. The total fluoride uptake was greater after 4 minutes of application than after only 1 minute of application. This greater fluoride uptake, however, was almost entirely due to a greater uptake in the first enamel layer removed. The second and third enamel layers did not show a significantly greater fluoride uptake with time. It would therefore appear that penetration of fluoride into the deeper layers of enamel was not affected by a change in application time of from 1-4 minutes.

A recent study by Congleton *et al.*[8] has shown that the fluoride release by the same thixotropic gel used in the present study is less than by APF solutions or conventional gels. The authors also state that additives to the gels may have an effect on fluoride release. The fluoride release across a dialysate membrane is a diffusion-controlled process, and therefore the solution showed the greatest release of fluoride in a given time span. Diffusion, however, is dependent on the nature of the gels tested. The clinical relevance of this type of testing has not been demonstrated and needs to be substantiated for use on a wide scale as a screening procedure for possible anticaries agents. The present work does not assure one of clinical effectiveness either, but it does show that the thixotropic gel is comparable to conventional APF gels in regard to fluoride uptake by enamel under laboratory conditions.

If one considers the possible mechanisms of action of fluoride, it is entirely possible that the reduced amount of fluoride released in the study of Congleton *et al.* by the thixotropic agent would be sufficient to produce cariostatic benefits. Enzymatic inhibition, remineralization, and desorption of bacteria will all occur at concentrations much smaller than those used in APF gels. Although the evidence presented here showed a significant fluoride uptake from the thixotropic gel, only a clinical trial of caries reduction will determine the true effectiveness of this fluoride agent.

Table 4. Mean total F uptake by time and treatment (n = 60)

Time	Agents	F (ppm)
4 min	A	6,759.5 ± 4,330.9*
	B	12,066.3 ± 9,719.0
	C	9,562.8 ± 4,540.4
1 min	A	5,819.1 ± 3,132.6
	B	8,585.0 ± 5,638.6
	C	5,756.3 ± 3,468.7

* Mean ± S.D.

Table 5. Difference in F uptake between 4 minutes and 1 minute for the three agents

Agent	F (ppm)
A	940.4
B	3481.3
C	3806.5
$F_{2,54}$ = 6.762	p = 0.0028

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