Original Article

Painting-on topical fluoride gel markedly reduces the fluoride gel amount compared with tray application

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Kamonwan Sriwongchai D.D.S., Ms.c.[1]
Wacharaporn Tasachan D.D.S.[2]
Kasekarn Kasevayuth D.D.S., Ph.D.[3]
Chutima Trairatvorakul D.D.S.[2]

[1]Department of Pediatric Dentistry, Faculty of Dentistry Chulalongkorn University, Bangkok, Thailand 10330
[2]Instructor, Department of Pediatric Dentistry, Faculty of Dentistry Chulalongkorn University, Bangkok, Thailand 10330
[3]Instructor, Department of Biochemistry, Faculty of Dentistry Chulalongkorn University, Bangkok, Thailand 10330

Abstract

Background/objectives: Professional topical fluoride (F) gel application has been used to prevent dental caries with a concern about safety in young children. The aim of this study is to evaluate a paint-on technique using a No. 8 paint brush for applying professional topical F gel as an alternative method in children at a safer, lower dose compared with a tray.

Materials and Methods: Twenty-one healthy children (12-15-year-old) participated in this clinical crossover study. The amounts of F gel used were 0.4 ml in the paint-on or 5.0 ml in the tray. Saliva and interproximal fluid were collected before, and immediately, 5, 10, 20, 30, and 60 min after application. F retention efficiency was evaluated by salivary flow rate, F concentration, F availability, and time half-life ($t_{½}$).

Results: The salivary flow rate induced by the two methods were similar. The F concentration and availability in the saliva and interproximal fluid in the paint-on technique was significantly higher than those in the tray technique. The $t_{½}$ in the saliva and interproximal fluid in the paint-on technique were shorter than those in the tray.

Conclusion: The novel paint-on technique effectively delivered topical F gel at a safe dose that would allow its use in young children, particularly those with a high caries risk.

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Keywords: clinical studies, fluoride retention, interproximal fluid, saliva, topical fluoride gel

Correspondence: Chutima Trairatvorakul, ctrairat@gmail.com

Introduction

Professionally applied acidulated phosphate fluoride (APF) has been used to effectively prevent dental caries since the 1970s (Marinho et al., 2003). Fluoride (F) gel has the greatest cost/benefit ratio compared with other types of topical F (Øgaard et al., 1994). However, F gel has adverse effects, especially in children under 6-year-old who cannot control their swallowing (Ripa, 1990, Weyant et al., 2013). The probably toxic dose (PTD) of F is 5 mg F/kg body weight (Whitford, 1992). Among dental products containing F 1.23% APF is the most hazardous, with the recommended amount of 5 ml (61.5 mg) exceeding the PTD (60 mg) of 12 kg in children ≤2-year-old (Whitford, 1992). Approximately 0.3-6.1 mg F might be ingested during treatment, which could cause nausea, vomiting, and abdominal pain, depending on the application method (Heath et al., 2001). A lower APF dose would reduce the risk of toxicity and adverse effects, especially in younger children (Whitford, 1992). However, a F gel is recommended for high caries risk patients (Centers for Disease Control and Prevention, 2001).

The American Dental Association (ADA) no longer recommends applying F gel in a tray for children ≤ 6-year-old (Maguire, 2014) due to the high risk of toxicity from swallowed F, and recommends using F varnish instead. However, F varnish is expensive compared with F gel. Thus, the application of a safer dose of F gel requires investigation. The efficacy and safety from the amount of swallowed F were compared between different F gel application methods. Although the application of 2-3 g F gel for 4 min in trays or a brush with 0.6 g F gel for 2 min in adult volunteers resulted in similar salivary F levels, the amount of F swallowed was approximately 10-fold higher in the tray group (Opydo-Szymaczek and Opydo, 2010). Similar results for F ingestion were found when subjects received F gel painted on tooth surfaces with a toothbrush compared with tray application, while the salivary F concentration using a tray was higher compared with the paint-on method (Heath et al., 2001). These studies demonstrated that different F gel delivery methods using the same amount of F gel (0.6 g) generated differences in salivary F retention. We hypothesized that applying a lower dose of F gel using a paint-on method would result in similar salivary F retention compared with typical tray gel application. The objective of this study was to compare salivary F retention in children between using a 0.4 ml (4.9 mg F), 1 min APF gel paint-on technique and traditional tray application with 5 ml (61.5 mg F) of F gel for 4 min.

Materials and Methods

Ethics and clinical trial consideration

The study protocols were approved by the Human Research Ethics Committee of Chulalongkorn University (HREC-DCU 2017-001) and The Thai Clinical Trials Registry, Thailand (TCTR20180710004).

Subjects

The sample size was calculated to be 16 volunteers ($\alpha = 0.05$, $\beta = 0.2$ and 95% confidence level) (Rattanawiboon et al., 2016). Thus, 21 subjects were recruited to compensate for the drop out, comprising 11 boys and 10 girls aged 12-15 years old who resided in Bangkok, where the municipal water fluoridation is less than 0.3 ppm. The inclusion criteria were (1) good general and dental health, (2) 28 permanent teeth, and (3) not wearing fixed orthodontic appliances or removable denture. The parents of each child read and signed an informed consent form in which all procedures, possible discomforts or risks, and benefits were fully explained.

Procedures

This was a randomized crossover design study. The subjects performed a standardized brushing routine with 1,000-ppm F dentifrice (Colgate Cavity Protection Great Regular Flavor, Colgate-Palmolive Company, Thailand) for 2 min and then rinsed with 10 ml water for 5 sec, twice a day for 1 week before and

during the experimental period. The subjects were randomly allocated into 2 different APF gel application method groups. After a 7-day washout period (Williams et al., 2004), each group of subjects received the other application method. The subjects were instructed not to eat/drink/rinse for 60 min after gel application. The APF gel application methods were:

1. *Tray application*

The subjects received a 4-min F gel application using commercial trays. The procedure was performed per the manufacturer's instruction, 5 ml and F gel was used (2.5 ml/tray) (Pascal, Pascal Co., WA, USA). The APF 1.23% contains 12,300 ppm which equals to 12.3 mg F/ml. The amount of F in 5 ml APF was 61.5 mg F (12.3×5). The subjects sat with their head tilted forward and were instructed not to swallow the gel or saliva during the procedure, a saliva ejector was used throughout the procedure and high-power suction was used to remove excess F gel after 4 min. The subject expectorated for 60 sec after the procedure then subject started to collect saliva and interproximal fluid samples.

2. *Paint-on application*

The amount of F gel used in the paint-on technique was based on LeCompte's study where F retention was 9% in the oral cavity after tray application in 8-12 years old children (Lecompte, 1987). In our

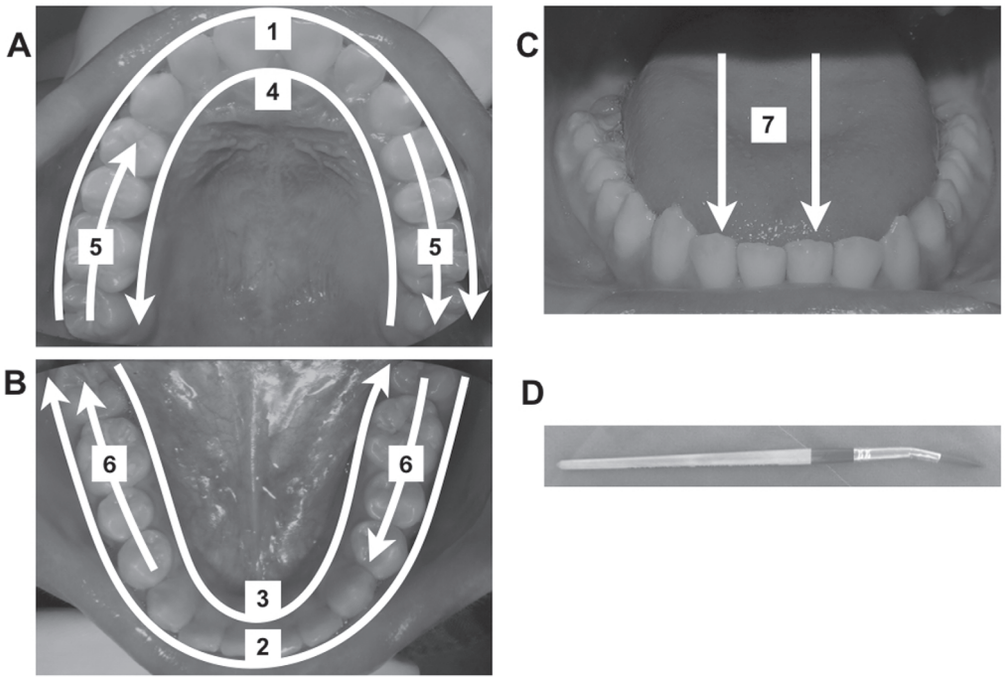

Figure 1: Application method of the paint on technique. Fluoride gel was applied on teeth and oral soft tissue with angled paint brush No. 8 (D). The application of tooth surfaces, upper and lower arches were systematically applied in numerical order: buccal surface of upper arch from right to left side (A-1), then buccal surface of lower arch from left to right side (B-2), lingual surface of lower arch from right to left side (B-3), then lingual surface of upper arch from left to right side (A-4), occlusal surface of the teeth on upper arch (A-5) and lower arch (B-6). Lastly, the F gel was applied to the tongue (C-7). The angled paint brush No. 8 (D) was squeezed against the oral soft tissue and teeth during application.

study 5 ml of fluoride gel was used in tray application technique. The amount of F gel used in paint on technique was (9×5)/100 = 0.4 ml. The amount of F in 0.4 ml APF was 4.9 mg F (12.3×0.4). A No. 8 paint brush was bent at an angle (Figure 1D) to facilitate painting. The APF gel was applied on the teeth and oral soft tissue as indicated in Figure 1 with the angled No. 8 brush for 1 min without expectorating or using a saliva ejector or high-power suction.

Sample collection

Unstimulated whole saliva and interproximal fluid were collected before each APF gel application as baseline and immediately, 5, 10, 20, 30, and 60 min after each application as previously described (Navazesh et al., 2008). The saliva was spat out every 1 min for 5 min into a plastic tube. The unstimulated whole saliva was kept at 4°C until used (≤2 weeks).

Interproximal fluid samples were obtained from 4 interproximal sites (Kashani et al., 1998) using a triangle paper point (base: 1.5 mm, length: 5 mm). The samples were collected from locations in the following order: 11/21, 25/26, 31/41, and 45/46. Triangle paper points were placed into the gingival crevice. The paper point was left for 20 sec to absorb the interproximal fluid (average 2.0±0.2 µl fluid/paper point). The cheek was retracted with a mouth mirror to avoid moisture from the oral mucosa absorbing into the paper point. The paper points were removed and transferred to plastic tubes containing 220 µl buffer solution. The paper point in buffer solution was kept at 4°C until used (≤2 weeks).

Salivary flow rate measurement

The salivary flow rate was measured as previously described (Navazesh et al., 2008). Unstimulated whole saliva was collected in a pre-weighed plastic container for 5 min. After collection, the container with saliva was weighed. The weight of the saliva was the difference in container weight after and before saliva collection. Saliva is mostly composed of water, thus 1 g saliva equals 1 ml. The salivary flow rate (ml/min) was calculated by weight difference divided by time.

Fluoride concentration analysis

Each 300 µl saliva sample was mixed with 30 µl total ionic strength adjustment buffer III at a 10:1 ratio (TISAB III, Thermo Fisher Scientific Inc., Beverly, USA). The approximately 4 µl interproximal samples were mixed with 200 µl de-ionized water and 20 µl TISAB III. The salivary F level (ppm) of each sample was measured twice using a calibrated ion selective electrode (ORION EA940, Orion Research Inc., MA, USA) by a blinded investigator and reported as mean and standard deviation. The results were used to plot F concentration and half-life over time curves. The Kaleidagraph program (version 4.1.3, Synergy Software Inc., PA, USA) was used for curve-fitting the F concentration curve. An exponential decay equation was used for curve-fitting.

Area under the curve calculation

The area under the curve (AUC) represented F bioavailability, which is the amount of free ionized F that can interact with dental hard tissue during remineralization. The AUC of the F concentration curve was calculated by an integration of the curve-fitting equation (Zero et al., 2012).

Half-life ($t_{½}$) calculation

The half-life ($t_{½}$) is the amount of time required for the F concentration to decline to half of the initial concentration. The slope from the F concentration over time curve of saliva and interproximal fluid was the elimination rate (K_e), which was the decrease in F concentration over time. The $t_{½}$ of each elimination phase was calculated using the equation; $t_{½} = 0.693/K_e$. The longer the $t_{½}$, the longer the F is present in the oral cavity.

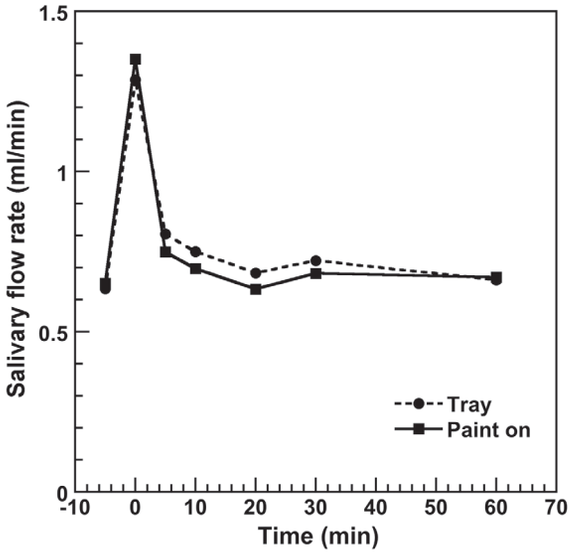

Figure 2: The salivary flow rate of two F gel applications in various times.

Statistical analysis

Repeated measures ANOVA was used to analyze salivary flow rate and salivary and interproximal F concentration at different time points. The $t_{½}$ and AUC were analyzed with the paired-samples t-test. The F concentration was reported as mean and standard deviation. A *P*-value of 0.05 was used to indicate significance. The effect size for the analysis of salivary and interproximal F concentration was calculated as partial Eta Square (η^2_p), while the analysis of $t_{½}$ and AUC was Cohen's *d* (Lakens, 2013). The average values from all interproximal sites were used for statistical analysis. The results were analyzed with IBM SPSS Statistics version 22.0 (IBM Corporation, Armonk, USA).

Results

The amount of F gel used with the paint-on method (0.4 ml) was 12.5-fold less than used in the tray. The saliva and interproximal fluid baseline F concentration between the application methods were not significantly different ($P = 0.232$ and 0.136, respectively). Thus, there were no carryover effects including period, intervention, and sequence effects from the previous procedure.

Salivary flow rate

The salivary flow rate in the two method groups had similar profiles, which increased immediately after F gel application and then decreased to their rest level within 20 min. There was no significant difference in salivary flow rate between the groups ($P = 0.694$).

Fluoride Concentration

Both F gel application methods resulted in an elevated F concentration in saliva (Figure 3A) and interproximal fluid (Figure 3B-F) that then decreased over time. The F concentration decreased in a biphasic exponential manner. The highest F concentration was seen immediately after F gel application in both method groups. The F level quickly decreased within 10 min after application (initial phase) and then slowly decreased close to the baseline F level (late phase). Repeated measures ANOVA revealed that the salivary F concentration in the paint-on group was significantly higher compared with the tray group ($P < 0.001$). The average interproximal fluid F concentration from all sites in the paint-on group were also significantly higher compared with the tray group ($P < 0.001$) (Figure 3B). Moreover, the F concentration in the interproximal fluid collected from each specific site in

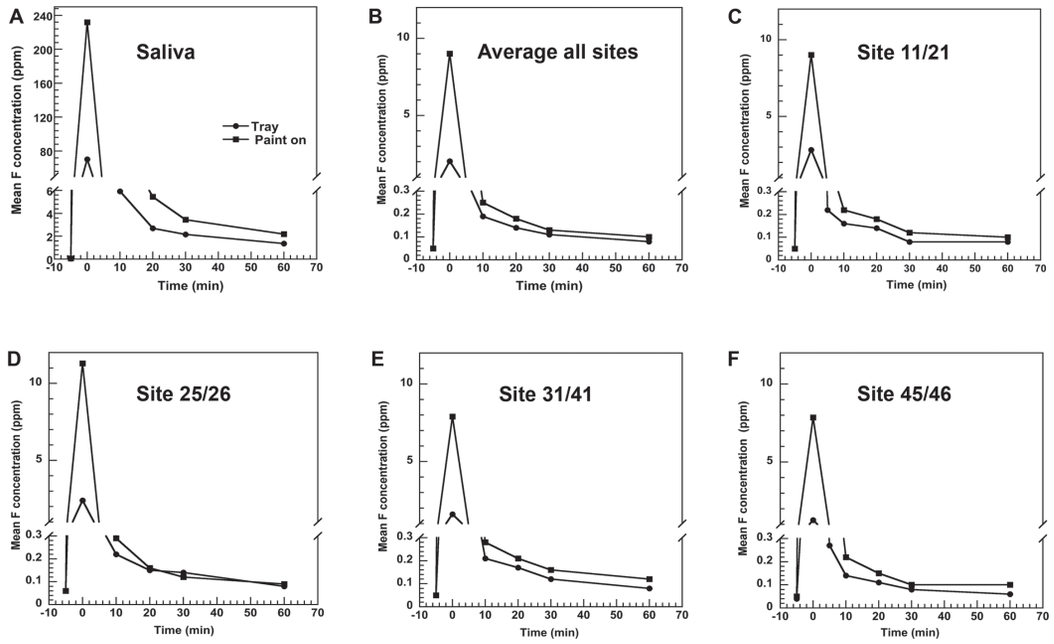

Figure 3: Comparison of the F concentration by two methods in saliva (A), interproximal fluid (average values from all sites, B) and various site of interproximal fluids (C-F). F concentrations of paint on method were statistically higher than those of tray method in both saliva and interproximal fluids at $P < 0.01$.

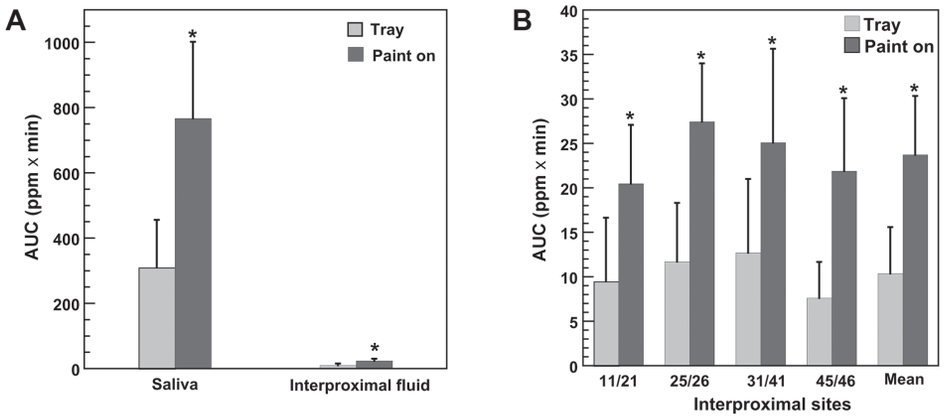

Figure 4: The comparison of AUC of oral fluids. Mean AUC in saliva and interproximal fluid average values from all sites were shown in A. The AUC of separate interproximal sites were shown in B. The asterisks showed statistical differences between two application methods at $P < 0.001$.

the paint-on group was similarly significantly higher than that in the tray group ($P<0.01$) (Figure 3 C-F).

Fluoride bioavailability

The AUC represents F bioavailability in the mouth. In the saliva samples, the AUC in the paint-on group was 767.02±34.72 and 310.33±145.29 in the tray group. For the interproximal fluid, the AUC in the paint-on and tray groups was 23.74±6.61 and 10.38±5.23, respectively. Similar to the F concentration results, the saliva ($P<0.001$) and interproximal fluid ($P<0.001$) AUC in the paint-on group were significantly two-fold higher compared with the tray group (Figure 4A). The AUC of the interproximal fluid using the paint-on method was similarly significantly higher compared with using as tray at all interproximal sites (Figure 4B).

Half-Life of Fluoride in the oral cavity

The $t_{½}$ was calculated from slope of the F concentration over time curve. The $t_{½}$ occurred in two phases; an initial phase where F rapidly decreased from 0-10 min and a late phase where F slowly decreased from 10-60 min. The initial phase $t_{½}$ of the F concentration in the saliva samples in the paint-on group was 2.22±0.27 min and 3.06±1.05 min in the tray group (Table 1). Moreover, the initial phase $t_{½}$ in the interproximal fluid using the paint-on application was 2.02±0.39 min and 5.03±1.92 min using a tray. The initial $t_{½}$ in the tray groups were significantly longer compared with the paint-on group in the saliva ($P=0.003$) and in the interproximal fluid ($P<0.001$) (Table 1). The late phase $t_{½}$ in the paint-on and tray groups in the saliva were 36.55±14.28 and 49.68±23.72 min, respectively. The late $t_{½}$ in the tray group was also significantly longer than those in the paint-on group ($P=0.008$). The late $t_{½}$ of the interproximal fluid could not be calculated because K_e was very low (Table 1).

Discussion

The present study evaluated the salivary F retention in children when applying an APF gel using a paint-on technique compared with the standard tray

Table 1: F concentration half-lives in the oral cavity from the F gel application methods.

Oral Fluid	Application methods	$t_{½}$(min) (mean±SD)	t	*P*-value	Effect size (*d*)
Initial phase					
Saliva	Paint-on	2.22±0.27	3.51	0.003	0.83
	Tray	3.06±1.05			
Interproximal fluid*	Paint-on	1.97±0.41	7.34	<0.001	1.6
	Tray	4.61±2.10			
Late phase					
Saliva	Paint-on	36.55±14.28	3.01	0.008	0.71
	Tray	49.68±23.72			
Interproximal fluid*	Paint-on	N/A	N/A	N/A	N/A
	Tray	N/A			

N/A: not available, *Average all sites

application. Despite applying approximately 12-fold less gel for 25% of the time typically used with tray application, the paint-on method resulted in significantly higher F concentration and F availability in the saliva and interproximal fluid. These findings confirmed our hypothesis that the paint-on technique using less F gel would result in effective salivary F levels. Interestingly, the F concentration $t_{1/2}$ in the saliva and interproximal in the paint-on group was shorter, despite both groups having similar salivary flow rates. The F retention also depends on swallowing rate (Dawes and Weatherell, 1990). The paint-on technique of APF gel on oral mucosa and tongue stimulated sensory nerves which initiated swallowing (Dodds, 1989). This occurred especially in paint-on technique, not in tray technique. The higher frequency of swallowing results in the shorter $t_{1/2}$.

F is an anti-caries agent that inhibits demineralization, promotes remineralization, and inhibits bacterial acid production (Buzalaf et al., 2011). Topical F is effective in tooth remineralization when at least a 0.1 ppm concentration of F is maintained in saliva (Toumba and Curzon, 2005). Therefore, we aimed to raise the salivary F level above this baseline for as long as possible to promote remineralization. One hour after the tray and paint-on application, the F concentration in the saliva and interproximal fluid was above 1.0 ppm and 0.1 ppm, respectively.

Our fluoride concentration results reflected that the F level in saliva after using topical F is divided into two phases. After an immediate increase in F level, the F concentration decreases dramatically through F clearance from swallowing, salivary flow, and adsorption into oral soft tissue. Next, oral F reservoirs slowly release F into the saliva. Higher residual salivary F levels promote tooth remineralization (Zero et al., 1992). Notably, our results showed that the saliva and interproximal fluid F concentration from the paint-on technique were significantly higher compared with the tray technique ($P < 0.001$). The F could adsorb on the oral tissue such as oral mucosa, lip and tongue, resulted in increasing F retention (Dawes and Weatherell, 1990). In our study we applied APF gel by paint-on technique on tongue and when we applied on buccal surface of teeth the APF gel also applied to oral mucosa of upper and lower lips. This might increase F retention of paint-on technique higher than tray technique during the late phase. Using a No. 8 brush to paint the fluoride gel on the tooth surface, compared with immersing the tooth in the gel as occurs with a tray may explain our findings. Indeed, applying F gel using a cotton bud resulted in the highest net F retained in the mouth (LeCompte and Doyle, 1982).

Applying a high concentration of F leads to the formation of a CaF_2 layer on the enamel surface that serves as a F reservoir (LeCompte and Rubenstein, 1984). This layer dissolves rapidly and releases bioavailable F (LeCompte and Rubenstein, 1984). The F concentration and AUC of the interproximal fluid from the paint-on technique was higher than using the tray technique. This demonstrates that more F was retained in the interproximal area after F application using the paint-on technique compared with a tray. The use of the brush may more efficiently force the gel into the restricted interproximal space compared with tray delivery This is an advantage of the paint-on method because interproximal tooth surfaces are at a higher risk for dental caries and where early lesion development is not easily visualized (Burt et al., 1988, Sundin et al., 1992).

The clearance rate of F from the oral fluids is shown by the $t_{1/2}$. F clearance from the mouth is affected by an individual's salivary flow rate, and factors that aid in retaining F in the mouth, such as spaces between the teeth and soft tissue, tooth structure, and surface coatings of hard and soft oral tissue (Ekstrand and Koch, 1980, Ekstrand et al., 1981,

LeCompte and Doyle, 1982, Wei and Chik, 1990). We controlled for all these factors. Our $t_{½}$ results corresponded with the F concentration results. The rapid decrease in F concentration and short $t_{½}$ in the first 10 min can be explained by the salivary flow (Dawes and Weatherell, 1990) results where the flow rate rapidly increased immediately after F gel application and subsequently returned to rest state after 20 min. The return of the salivary flow to the resting level also explains the gradual decease in F concentration and extended $t_{½}$ we observed post-10 min. Interestingly, despite the higher F concentration and AUC in the paint-on group, the $t_{½}$ in the paint-on group was shorter compared with those in the tray group. The amount of F use in tray is 12.5 times of paint-on technique contributing to longer clearance, more swallowing thus resulting in longer $t_{½}$ (Duckworth and Morgan, 1991). In contrast, this may be beneficial for young children since $t_{½}$ in saliva is correlated to $t_{½}$ in plasma (Ekstrand, 1977). Moreover, our results showed there was no significant difference in salivary flow, which is an important factor in F clearance, between the two methods. This indicates that salivary flow may not have influenced F retention. We hypothesize that the close application of the F gel using a No. 8 brush may have, in some fashion, allowed for more F to react with the tooth surface, removing it from the saliva. This concept requires further investigation.

Importantly, the paint-on technique applies F gel using a much lower amount of F gel for less time compared with traditional tray application. Traditionally, APF in tray method was used to apply for 4 min. Garcia-Godoy and et al., found that the application times of APF 1 min and 4 min were no significant difference of the reduction in lesion depth of sound enamel (Garcia-Godoy et al., 1995). These had an advantage to use APF for shorter time to reduce risk of children to swallow. Our results have several meaningful clinical implications. The paint-on method is safer, expands the use of F gel to younger children, economical, and can be used in a community setting.

The dosage of F used in the paint-on technique is much less than the recommended dosage of F varnish for children under 6 year-old (0.25 ml), which is 5.6 mg F, while our dosage is 4.9 mg F. The PTD for 1-2 year-old children is 50-60 mg F, and for 3-6 year-old children is 70-100 mg F, which are 10-20-fold higher than our dose. The nausea and vomiting dose (1 mg F/kg body weight), in 1-, 2-, 3-, and 6-year-old children is 2-4 folds higher than the dose we used. Thus, this method can be used to apply F gel to children < 6-year-old. The paint-on technique could be used to prevent fluorosis and reduce the risk of excessive F ingestion in children. This technique would greatly reduce the risk of F toxicity, including in 3 year-old children. Furthermore, the paint-on technique reduces the gel application time from 4 min to 1 min. The 0.4 ml F gel was easily applied with a No. 8 paint brush within 1 min, which may result in better compliance in younger patients. This technique might benefit high caries risk preschoolers in public health care programs.

The paint-on approach is cost effective by eliminating the need for trays, high-speed suction, saliva ejector, and amount of F gel due to no excess F gel to be eliminated. The reduction in using single-application products makes this method eco-friendly. The markedly reduced cost of this procedure and not requiring specialized equipment makes the pain-on method applicable in a community setting, allowing for the application of F gel to high caries risk patients of all ages.

We performed this study in teenage children because they had a full dentition. Children ≥ 6 year-old with a transitional dentition may have edentulous areas due to primary tooth exfoliation that could result in less F stored between the interdental spaces. This study was not performed in 3-5 year-old children with a primary dentition, because they might not be cooperative over the course of the study.

A study (Bretz et al., 2001) found a lower salivary flow rate in children compared with our subjects, thus, the F retention in saliva in children could be longer which would increase remineralization and inhibit demineralization. Another study demonstrated that an elevated salivary F level (0.11 ppm) in saliva was related to a lower caries incidence in children compared with control level (0.03 ppm) (Toumba and Curzon, 2005). This study focused on the presentation of F around tooth surface in term of saliva and interproximal fluid which has only one indicator. The other indicator might investigate on increasing remineralization and/or decreasing demineralization on enamel surface to see effective use of APF of these two methods. Further study is needed to compare the remineralizing effect and enamel fluoride uptake of the two techniques on enamel caries.

Conclusions

The paint-on 0.4 ml F gel technique could be an alternative to tray application, including in young children due to its lower dosage and application time, which may induce better cooperation. Our results suggest that applying F gel using the paint-on technique was effective as an alternative method to apply professional topical F gel. This technique might be useful for high caries risk children and patients who either cannot control their swallowing or have impaired swallowing. Moreover, this technique is safe, economical, environmentally friendly, easy to perform, and could be used in a community setting for patients of all ages.

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Conflict of interest

The authors declare that they have no potential conflict of interest with respect to the authorship and/or publication of this article.

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