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High Fluoride Dentifrices for Elderly and Vulnerable Adults: Does It Work and if So, Then Why?

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Key Words
Effectiveness · High fluoride dentifrices · Root caries lesion

Abstract
The primary aim of this work is to present the available evidence that toothpastes containing >1,500 ppm fluoride (2,500–2,800 and 5,000 ppm F) provide an additional caries preventive effect on root caries lesions in elderly patients compared to traditional dentifrices (1,000–1,450 ppm F). The secondary aim of this paper is to discuss why high fluoride dentifrices in general should perform better than traditional F-containing toothpaste. When examining the few studies that have considered the preventive benefits of high fluoride products on root caries the relative risk appears to be around 0.5, and the risk can thus be halved by exchanging traditional F-containing toothpaste for toothpaste containing 5,000 ppm F. There is reasonable evidence that high fluoride dentifrices significantly increase the fluoride concentration in saliva during the day and the fluoride concentration in plaque compared to traditional F toothpaste. Furthermore, the use of toothpaste with 5,000 ppm F significantly reduces the amount of plaque accumulated, decreases the number of mutans streptococci and lactobacilli and possibly promotes calcium fluoride deposits to a higher degree than after the use of traditional F-containing toothpaste.

The effect of topical fluoride on caries is well addressed in the literature. This paper acknowledges that fluoride affects the caries process by reducing demineralization and enhancing remineralization [Fejerskov et al., 1981; Fejerskov, 2004; Twetman and Ekstrand, 2013]. Even with low concentrations of fluoride (<0.1 ppm) in the plaque/saliva interface, it is a supersaturated solution with respect to fluorhydroxyapatite (FHAP) at slightly acidic conditions (pH down to 4.0). Thus, when the pH drops below 5.5, said to be the critical pH for hydroxyapatite (HAP) and HAP is dissolved, FHAP is at the same time precipitated at the surface of the crystals. When the pH rises again (above 5.5), both HAP and FHAP are precipitated at the surface [Twetman and Ekstrand, 2013].

Theoretically, fluoride will also influence microbial metabolism by interfering with enolase, an enzyme that is used by bacteria in the fermentation of carbohydrates. However, studies indicate that it requires a high concentration of fluoride (>10 ppm) [Murray et al., 1991], which is rarely achieved in dental plaque [Larsen and Bruun, 1994].

Fluoride is very reactive and will, when it comes into contact with the dental hard tissue or the plaque/saliva, combine with other elements, such as calcium. When the fluoride concentration in the plaque/saliva interface is above 100 ppm, calcium fluoride is formed; the higher the

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fluoride concentration, the more calcium fluoride is formed [Bruun and Givskov, 1991, 1993; Larsen and Bruun, 1994].

Thus, the significant impact of topical fluoride on caries control is that fluoride is present at the plaque/saliva interface, while the pre-eruptive (systemic) effect of fluoride, previously praised as the benefit of fluoride in caries prevention [Arnold, 1945], seems to play only a minor role, if any [Thylstrup, 1990]. Furthermore, precipitated calcium fluoride products act as a temporary storage of fluoride from which the active ion is gradually released.

With this in mind, methods of applying fluorides to the oral cavity can be performed at community levels (as fluoridated water, milk or salt) or at individualized levels (characterized by professional or self-care applications) [Twetman and Ekstrand, 2013]. Most used among the self-care methods are fluoridated toothpastes, the uses of which have largely been credited for the decrease in caries seen since the 1960s. According to Lippert [2013], tooth powders or toothpastes are known to have been used by ancient Egyptians. In 1914, the first attempt to add fluoride to toothpaste was made, but it was not until the mid-1950s that fluoride-containing toothpastes were first marketed in the USA. The launch of F-containing toothpastes was based on studies performed during the 1940s–1950s. The first study, however, using 500 ppm sodium fluoride, showed no effect on caries [Bibby, 1945], while another study [Muhler et al., 1954] using 1,000 ppm stannous fluoride showed a significant reduction in caries occurrence in children. With regard to the question of how much fluoride toothpaste can contain, there are different regulations in different countries. In the USA, fluoride compounds are regulated as drugs and the maximum permissible fluoride concentration is between 1,000 (MFP) and 1,100 ppm (NaF and SnF), while in the EU fluoride compounds are regulated as cosmetics and the maximum permissible fluoride concentration is 1,500 ppm. Higher fluoride concentration products (such as 2,800 and 5,000 ppm) are available as pharmaceutical products in many countries and require the prescription of a dentist.

The clinical efficacy of fluoride toothpaste (≤1,500 ppm) has been estimated at approximately 24% compared to placebo [Marinho et al., 2003; Walsh et al., 2010]. Furthermore, the preventive effect of fluoridated toothpaste was found to increase with higher fluoride concentration in the toothpaste, demonstrating a clear dose-response model up to 2,800 ppm. Therefore, it was logical to launch F-containing toothpaste with >1,500 ppm F. Most recognized high fluoride-containing toothpastes comprise 2,500–2,800 or 5,000 ppm F. Davies and Davies [2008] stated that toothpaste containing 2,500 ppm F resulted in an 18% reduction in caries increment in children compared to toothpaste with 1,000 ppm F.

In many countries, the elderly population is increasing as a proportion of the total population, and these individuals are living longer, often maintaining many of their own teeth. In Denmark, for example, a recent survey showed that only 14% of vulnerable elderly people in Copenhagen had full dentures [Christensen et al., 2012]. Another national survey showed that those aged 65 and older in Denmark who had natural teeth had an average of 24 teeth, the mean DMFT was 23 and the decay component made up less than 1 tooth of the DMFT index [Kongstad et al., 2013]. However, a further 7% had 1 or more untreated root caries lesions, while 45% had 1 or more root surface restorations [Christensen et al., 2015]. A German study from 2006 showed that the prevalence of root caries lesions increased from about 16% in 1997 to 45% in 2006 among 65- to 74-year-olds [Michaelis and Schiffner, 2006].

The first aim of this paper is to present the available evidence that toothpaste containing >1,500 ppm fluoride provides an additional caries-preventive effect compared to traditional F-containing toothpaste. As attention is given to elderly and vulnerable adults, this paper will focus on root caries lesions. This is not to ignore the fact that coronal caries in older adults is an issue – indeed their caries increment on coronal surfaces is similar to that of younger children (1 new carious surface per year). However, the available literature on coronal caries in this group is sparse. The second aim of this paper is to discuss why high fluoride dentifrices in general perform better than traditional F-containing toothpaste.

Statistical Considerations

A common way to express the outcome of clinical trials is the preventive fraction, which is the difference in mean caries increment between treatment and control groups, expressed as the percentage of mean caries in the control group. Another measurement commonly reported is the risk ratio (RR), which is the risk of the event in the study group divided by the risk of the event in the control group. To calculate the RR, the number of active lesions at the final examination out of the total number of lesions has to be known in the study group as well as in the control group. Data from Ekstrand et al. [2008] are used in this example (table 1): RR = 57/130 divided by 98/144 = 0.65. Thus, in this study the participants in the study group had a 0.65 lower risk of active root caries lesions compared to the control group.

Table 1. Two-by-two table shows data to exemplify how to calculate the RR

	Events	Total
Study intervention	57	130
Control intervention	98	144

Aims of the Study

Searching for Studies Examining the Effect of High Fluoride Dentifrices on Root Caries Lesions and Results from the Included Papers

In 2015, Wierichs and Meyer-Lueckel [2015] reviewed among other preventive topics the effect of high fluoride concentration toothpaste products on root caries in adults. They performed a thorough search and identified 11 studies from 1947 to 2014. Of the 11 studies only 2, dealing with 5,000 ppm toothpaste, passed the inclusion criteria. The RR of 1 of the 2 studies, that of Baysan et al. [2001], was 0.85 (95% Cl, 0.52–0.80). In the other selected study by Ekstrand et al. [2013], the RR was 0.41 (95% CI, 0.33–0.50). When the 2 studies were combined, the total number of lesions in the test and control groups was 315 versus 321, respectively, and the RR was 0.49 (95% CI, 0.42–0.57). The test for overall effect was $p < 0.00001$ and the heterogeneity was $\chi^2 = 9.40$, d.f. = 1 ($p = 0.002$), $I^2 = 89\%$. The latter values indicate that the studies involved ($n = 2$) were comparable on essential parameters, e.g. how to assess whether a lesion is arrested or active. However, the risk of bias of the included study was different as the authors of the review assessed the paper by Baysan et al. [2001] to have a lower risk of bias than the paper by Ekstrand et al. [2013].

The present author found 2 other randomized clinical trials that were not included in the review by Wierichs and Meyer-Lueckel [2015]. The trials showed RR = 0.65 [Ekstrand et al., 2008] (see above) and 0.72 (82/127 divided by 111/124) in the study by Lynch et al. [2000]. The latter study contains the 3-month results of the study of Baysan et al. [2001] already mentioned above. Yet another randomized clinical trial was identified [Srinivasan et al., 2014], but the RR could not be calculated from the study. However, at the end of the study period, ANOVA revealed significantly better surface hardness scores of the lesions in the test groups than in the control groups ($p < 0.0001$). The study concluded that the application of a high fluoride-containing dentifrice (5,000 ppm F) in adults twice daily significantly improves the surface hardness of otherwise untreated root caries lesions compared to the use of regular fluoride-containing toothpastes.

Discussing Why High Fluoride Dentifrices in General Perform Better than Traditional F-Containing Toothpaste

Table 2 provides an overview of studies that have examined the relationship between fluoride in toothpaste and the fluoride concentration in saliva, in plaque and changes in the plaque. Of the identified papers, all were clinical trials where the designs were based on examining the difference between outcome variables after using toothpaste with 5,000 ppm F versus that with 1,150–1,450 ppm F. Authors, publication year, aim(s), designs and main results are presented in the summary table.

Discussion

Studies have revealed that high fluoride toothpaste has a more preventive influence on caries in children, adolescents and young adults than traditional toothpaste with 1,050–1,450 ppm F [Marinho et al., 2003; Davies and Davies, 2008; Wells, 2010]. The first aim of this paper was to look for evidence of high fluoride toothpaste and to assess whether it has a greater potential to prevent caries in the elderly/vulnerable section of the population than traditional toothpaste with 1,050–1,450 ppm F. In the older patient cohort clinical studies have focused on root caries [Michaelis and Schiffner, 2006; Christensen et al., 2015], with no literature identified assessing coronal caries in this group. Root caries is an important clinical entity in the older adult, but coronal and secondary caries continues to be an issue and will require research effort in the future.

Due to the fact that only few randomized clinical trials have been conducted, there is not conclusive evidence at the highest level that high fluoride toothpaste performs better than traditional fluoridate toothpaste in the prevention of root caries. However, data from the few randomized clinical trials in this area indicates at a strong level of evidence that there is a positive influence by using toothpaste with 5,000 ppm F on the prevention or arrest of root caries lesions in the older adult population [Lynch et al., 2000; Baysan et al., 2001], including the elderly frail [Ekstrand et al., 2008] and vulnerable [Ekstrand et al., 2013]. The RR appears to be around 0.5, and thus the risk can be halved by shifting from using traditional F-containing toothpaste to toothpaste containing 5,000 ppm F. No clinical randomized trials have tested the effect of toothpaste with 2,500–2,800 ppm F on elderly people.

Table 2. Overview of selected articles which deal with the influence of high fluoride dentifrices on caries-relevant factors compared to traditional fluoride-containing toothpaste

Authors	Year	Aim	Design	Results
Nordström and Birkhed	2009	Fluoride retention in proximal plaque and saliva and the effect of water rinsing after brushing	Cross-over on 19- to 35-year-olds (n = 26)	High fluoride toothpaste (5,000 ppm) without water rinsing after brushing increased the fluoride concentration in proximal saliva more than 2 times compared to standard toothpaste (1,450 ppm), also without rinsing
Nordström and Birkhed	2009	Fluoride retention in proximal plaque and saliva and the effect of water rinsing after brushing	Cross-over on 19- to 3- year-olds (n = 26)	The difference in F concentration per unit weight of plaque (n = 16) was 2.8 times higher ($p < 0.05$) after using toothpaste with 5,000 ppm F versus 1,450 ppm toothpaste
Nordström and Birkhed	2013	Effect of a third application of toothpaste, including a 'massage' method, on fluoride retention and pH drop in plaque	Cross-over on 23- to 38-year-olds (n = 16)	Brushing with high fluoride toothpaste 3 times a day increased the fluoride concentration in saliva almost 4 times compared to standard toothpaste twice a day. The fluoride retention in plaque increased significantly as well
Ekstrand et al.	2015	To analyze whole saliva fluoride levels and mineral saturation indices during different fluoride toothpaste regimes (TP1–TP4) in home-living elderly; the toothpaste was used 3 times/day	Cross-over on >65-year-olds (n = 30) TP1: 1,450 ppm NaF TP2: 1,450 MFP with addition of calcium TP3: 5,000 ppm F TP4: 5,000 ppm F with additional smearing of toothpaste on teeth twice a day	Use of high fluoride toothpaste resulted in significantly increased fluoride levels in whole saliva during the day
Nordström et al.	2009	Effect on de novo plaque formation	Cross-over on 21- to 43-year-olds (n = 16)	Toothpaste slurry containing 5,000 ppm fluoride reduced the formation of new dental plaque on tooth surfaces
Lynch et al.	2000	To compare the effectiveness of Prevident (5,000 F) and Colgate Winterfresh Gel (1,100 ppm F) to arrest root caries lesions	3 months longitudinally on >18-year-olds (n = 201)	Plaque scores were reduced in those using Prevident 5,000 ($p < 0.001$)
Baysan et al.	2001	To compare the effectiveness of Prevident (5,000 F) and Colgate Winterfresh Gel (1,100 ppm F) to arrest root caries lesions	6 months longitudinally on >18-year-olds (n = 186)	The plaque index in the group with 5,000 F was significantly reduced compared to the group with 1,100 ppm F
Mannaa et al.	2014a	To measure the effects of a toothpaste containing 5,000 ppm F on caries-related factors in dental plaque and saliva	6 weeks longitudinally on mothers with an average age of 38.4 years (n = 17) and 17 teenagers with an average age of 14.5 years (n = 17) Sampling of approximal fluid for fluoride analysis and approximal plaque for organic acid analysis was performed Counts of cariogenic microorganism were performed at each of 4 visits	Six weeks' use of toothpaste containing 5,000 ppm F significantly increased the approximal fluid F concentration ($p < 0.05$) Changes in interproximal plaque acidogenicity were noted, including significant reductions in AUC (5.7 and 6.2, respectively) and maximum pH fall and an increase in minimum pH ($p < 0.05$) A significant increase in the salivary buffer capacity and a reduction in the salivary mutans streptococci were observed ($p < 0.05$)
Mannaa et al.	2014b	To assess the caries risk following 6 weeks' use of toothpaste containing 5,000 ppm F using 'Cariogram' software	6 weeks longitudinally on 17 mothers with an average age of 38.4 years (n = 17) and teenagers with an average age of 14.5 years (n = 17) Mutans streptococci and lactobacilli counts were performed at each of 4 visits	A statistically significant linear trend was observed for mutans streptococci counts ($p < 0.01$) and the number of subjects with a salivary concentration of mutans streptococci $<10^3$ increased at each visit; the same trend was also observed for lactobacilli and buffer capacity scores ($p = 0.04$ and $p = 0.03$, respectively)

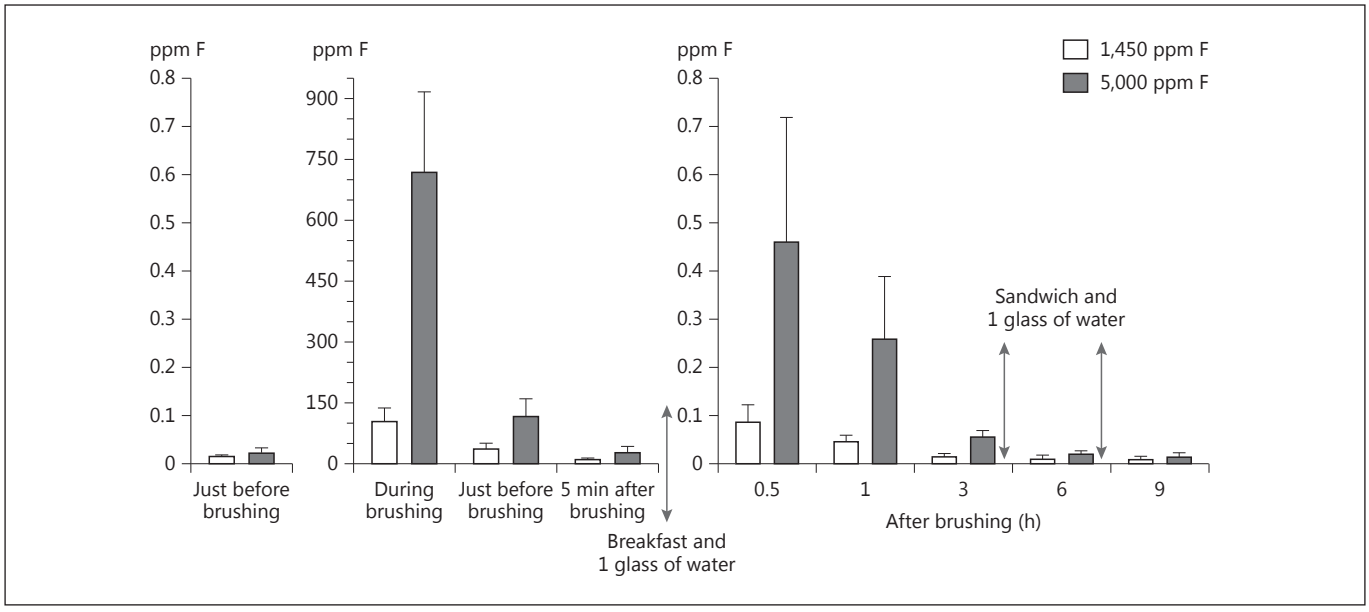

Fig. 1. Fluoride concentrations in whole saliva up to 9 h after brushing for 2 min with 0.6 g of toothpaste containing NaF 1,450 ppm F or NaF 5,000 ppm F. The week up to the measurements the participants had brushed twice a day using toothpaste with either 1,450 or 5,000 ppm F, and just before the measuring started there were no significant differences in the F in saliva whether the participants had used the toothpaste with 1,450 or 5,000 ppm F. Please note that the scale on the y-axis changes.

With this in mind the second aim of this paper was to discuss why high fluoride dentifrices perform better than traditional fluoride dentifrices on both crown and root caries and in all examined age groups. Figure 1 shows the fluoride concentration in saliva in 10 dental students up to 9 h after tooth brushing using toothpaste with either 1,450 or 5,000 ppm F [Ekstrand, 2006]. The fluoride concentration in saliva was significantly higher after the use of toothpaste with 5,000 ppm compared to 1,450 ppm F up to 6 h after tooth brushing. Figure 1 also shows a very high fluoride concentration in saliva during tooth brushing using toothpaste with 5,000 ppm F, at 700 ppm F during tooth brushing and dropping to about 100 ppm F just after brushing. In contrast, using toothpaste with 1,450 ppm F the concentration was only about 100 ppm F during tooth brushing, dropping to less than 50 ppm just after tooth brushing. Thus, and in accordance with our knowledge about the effect of fluoride on caries [Fejerskov, 2004], the following questions can be asked:

– is the fluoride concentration in the tooth/plaque/saliva interface significantly higher after using high versus traditional F-containing toothpaste?
  If so,
– can it influence caries-related factors in the dental plaque and saliva?
– Furthermore, is the fluoride concentration so high after the use of high F-containing toothpaste that it can introduce calcium fluoride products, which can participate in the remineralization process?

As seen from table 2 an increasing fluoride concentration in saliva was also noted by Nordström and Birkhed [2009, 2013] (young adults), Ekstrand et al. [2015] (adults aged 65 years and older) and Mannaa et al. [2014] (teenagers/mothers after use of toothpaste with 5,000 compared to 1,450 ppm F). Actually, in the extreme, the data from the study by Ekstrand et al. [2015] showed an average fluoride concentration of around 1 ppm in the saliva during the whole day when 5,000 ppm of fluoridated toothpaste was used 3 times/day (1 g) and the teeth were smeared with a little drop of the 5,000 ppm toothpaste twice a day. According to the findings by ten Cate and Duijsters [1983] and ten Cate [2013], such values make it quite difficult for caries to develop and progress.

It is stated that if the fluoride concentration in plaque is higher than 10 ppm, then an influence on the plaque metabolism can be expected [Murray et al., 1991]. Nordström and Birkhed [2009, 2013] showed that the fluoride accumulation in proximal plaque was borderline significantly higher after the use of toothpaste containing 5,000 ppm F than that with 1,450 ppm F (table 2). The fluoride

concentration in plaque after the use of 5,000 ppm toothpaste reached the level of around 14 ppm F, while the corresponding value after the use of toothpaste with 1,450 ppm F was around 10 ppm. Mannaa et al. [2014a, b] even found that the pH dropped less after rinsing with 10% sucrose solution when tooth brushing was performed using 5,000 ppm toothpaste compared to toothpaste with 1,450 ppm F. Thus, even though the fluoride concentration in plaque does not reach 10 ppm for a longer period, it seems that the higher concentration of fluoride changes the cariogenic potential in the plaque, perhaps by decreasing the number of lactate-forming microorganisms [Mannaa et al. 2014b], which then results in the pH not dropping so low after a cariogenic rinsing in 10% sucrose. This may also explain that Lynch et al. [2000], Baysan et al. [2001] and Nordström et al. [2009] found lower plaque scores after the use of 5,000 ppm toothpaste compared to toothpaste with 1,450 ppm F (table 2). Tenuta et al. [2009] even suggested that the F uptake by dental plaque not removed by brushing may be the main reason of the anticaries effect of dentifrices.

It has been acknowledged that calcium fluoride is formed when the fluoride concentration is higher than 100 ppm F [Larsen and Bruun, 1994; ten Cate, 1997] and that traditional F-containing toothpaste does not create a significant amount of calcium fluoride [Tenuta and Cury, 2013]. To the best knowledge of the author, no studies have investigated the amount of calcium fluoride formed on the teeth after the use of high fluoride toothpaste. As seen in figure 1 the fluoride concentration in saliva reaches about 700 ppm during tooth brushing with toothpaste containing 5,000 ppm F and stays around 100 ppm just after tooth brushing. This indicates that during the period of 2 min it is possible that calcium fluoride can precipitate, particularly in the accessible root caries lesions.

In summary, the available data from the few clinical trials suggest that high-concentration fluoridated toothpaste provides better caries prevention on root caries lesions in the elderly population than traditional F-containing toothpaste. Similar results are seen with coronal caries in younger populations. The mechanism of action is likely to be enhanced F concentration in both saliva and plaque after the use of high F-containing toothpaste compared to traditional F-containing toothpaste. Theoretically, high fluoride toothpaste should also perform better than traditional F-containing toothpaste in the formation of calcium fluoride products. Initial data suggest that by using high fluoride toothpaste concentrations, about 800 ppm F is noted in the saliva within the period of 2 min that tooth brushing takes, which is about 7 times higher than the 100 ppm required to create calcium fluoride. However, this particular area requires further research.

Disclosure Statement

The author has no conflicts of interest to declare.

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