

High-fluoride Toothpaste (5000 ppm) in Caries Prevention

Anna Nordström

Department of Cariology
Institute of Odontology at Sahlgrenska Academy
University of Gothenburg



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Abstract

High-fluoride Toothpaste (5,000 ppm) in Caries Prevention

Anna Nordström, Department of Cariology, Institute of Odontology, Sahlgrenska Academy, University of Gothenburg, Box 450, SE-405 30 Göteborg, Sweden.

Dental caries is a common disease in a large number of individuals. Fluoride (F) toothpaste plays an essential role in any programme designed to prevent caries. **Objective:** This thesis focuses on the effect of high-fluoride toothpaste (5,000 ppm) compared with a standard dentifrice (1,450 ppm) in caries prevention. The aims were to investigate: 1) the F retention in proximal plaque and saliva, 2) the effect of post-brushing water rinsing on F retention, 3) the effect on de novo plaque formation, 4) the effect on caries incidence and progression in caries-active adolescents and 5) the effect of a third application of toothpaste on F retention and the pH drop in plaque. **Design:** Papers I, II and IV were randomised, cross-over studies with 12-26 individuals. Paper III was a 2-year, single-blind, longitudinal study of 279 caries-active adolescents. **Results:** High content of F in toothpaste increased the F retention in both plaque and saliva. High-fluoride toothpaste without post-brushing water rinsing increased the fluoride concentration in proximal saliva more than two times, compared with standard toothpaste also without rinsing. Water rinsing immediately after brushing with high-fluoride toothpaste reduced the F concentration in proximal saliva more than two times, which supports the recommendation to refrain from post-brushing water rinsing. Toothpaste slurry with 5,000 ppm F reduced the formation of new dental plaque on tooth surfaces. Caries-active adolescents (14-16-year-olds) using high-fluoride toothpaste during two years had 40% lower progression of caries compared with those using standard toothpaste. Twenty-eight per cent of the adolescents had “poor compliance” and brushed irregularly. Brushing with high-fluoride toothpaste resulted in 42% less new caries lesions among caries-active adolescents with “poor compliance” compared with those with “excellent compliance”. Thus, high-fluoride toothpaste is an excellent home care treatment for individuals with high caries risk. Brushing with high-fluoride toothpaste three times a day resulted in almost four times higher F concentration in saliva compared with standard toothpaste twice a day. The retention of fluoride in plaque increased significantly as well. Brushing with 5,000 and 1,450 ppm toothpastes, twice a day plus the “massage” once a day, resulted in the same F concentration in saliva and plaque as brushing 3 times a day with the same paste. Using toothpaste as a “lotion” to massage the buccal surfaces with the fingertip may be a simple and inexpensive way of delivering F a third time during the day, tentatively at lunch time. **Main Conclusions:** High-fluoride toothpaste has a clear role in prevention of dental caries; targeting those at the greatest risk, reducing and arresting caries lesions and thereby reducing the need for operative treatment in caries-active adolescents.

Key words: Caries-active adolescents, Dental caries, Dental plaque, Dentifrice, de novo plaque formation, Fluoride retention, Frequency of brushing, High-fluoride toothpaste (5,000 ppm), Tooth-brushing, Toothpaste, Water rinsing

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Original Papers

This thesis is based on the following Papers, which will be referred to in the text by their Roman numerals (I-IV):

- I. Nordström A, Birkhed D. Fluoride retention in proximal plaque and saliva using two NaF dentifrices containing 5,000 and 1,450 ppm F with and without water rinsing. *Caries Res* 2009;43:64-69.
- II. Nordström A, Mystikos C, Ramberg P, Birkhed D. Effect on de novo plaque formation of rinsing with toothpaste slurries and water solutions with a high fluoride concentration (5,000 ppm). *Eur J Oral Sci* 2009;117:563-567.
- III. Nordström A, Birkhed D. Preventive effect of a high-fluoride dentifrice (5,000 ppm) in caries-active adolescents – a 2-year clinical trial. *Caries Res* 2010;44:323-333.
- IV. Nordström A, Birkhed D. Effect of a third application of toothpastes (1,450 and 5,000 ppm F), including a “massage” method, on fluoride retention and pH drop in plaque. *Acta Odontol Scand* 2011 (under revision).

Abbreviations and Definitions

The following terminology is used in this thesis.

Caries incidence = Caries-free surfaces that turn into enamel lesions, dentine lesions or fillings in a specific time

Caries prevalence = Caries status = Total caries score at a given time

Caries progression = Enamel lesions that proceed from grade 1 or 2 to grade 3 or 4, or to a filling in a specific time.

Cross-over = Study subjects receive each treatment in a random order

de novo plaque formation = The formation of new dental plaque on tooth surfaces after professional mechanical tooth cleaning

DFS = Number of decayed (dentine caries) and filled surfaces

DFS_a = Number of decayed (dentine caries) and filled proximal surfaces

D_eS_a = Number of proximal tooth surfaces with enamel lesions

DFS_a + D_eS_a = Number of decayed (dentine caries) and filled proximal surfaces plus number of proximal tooth surfaces with enamel lesions

PF = Prevented fraction = Caries reduction = $(I_c - I_e) / I_c = D_eS_a$ in the control group (I_c) (1,450 ppm F) and the incidence in the experimental group (I_e) (5,000 ppm F) divided by the incidence of DFS_a + D_eS_a in the control group (1450 ppm) (Kleinbaum et al., 1982).

Dentine caries (score 3) = Caries lesion with obvious spread in the outer half of the dentine

Dentine caries (score 4) = Caries lesion with obvious spread in the inner half of the dentine

Enamel caries (score 1) = Caries lesion in the outer half of the enamel

Enamel caries (score 2) = Caries lesion more than halfway through the enamel but not passing the enamel-dentine junction. The definition is stated according to the criteria previously set by the Swedish National Board of Health and Welfare (1984)

MFP = Sodium monofluorophosphate

MR = Mouth rinsing

NS = Non-statistical significance

NaF = Sodium fluoride

PMTC = Professional mechanical tooth cleaning

R²/r² = Coefficient of determination

SBU = The Swedish Council on Technology Assessment in Health Care = Statens beredning för medicinsk utvärdering

SD = Standard deviation: in this thesis, it is given as ± SD according to Papers I-IV

Sensitivity = A measure of the probability of correctly diagnosing a condition

Single-blind = Blind to the observer

SLS = Sodium lauryl sulphate

Specificity = A measure of the probability of correctly identifying a nondiseased person

WHO = World Health Organisation

QHI = Quigley & Hein index = Plaque scored at six sites (mesiobuccal, buccal, distobuccal, mesiolingual, lingual and distolingual) on all the teeth, according to the criteria specified in the Turesky modification of the Quigley & Hein Index (QHI) (Turesky et al., 1970; Quigley and Hein, 1962).

QLF = Quantitative light-induced fluorescence

Introduction

Dental Caries in a Global Perspective

Dental caries is one of the most common oral diseases world-wide and remains a problem for society and individuals. It is regarded as a multifactorial disease, caused by the interaction of biological, behavioral and socio-economic factors. Since the middle of the last century, a decline in caries has been observed world-wide among children, adolescents and adults. This reduction is primarily a result of daily use of fluoride toothpastes (Bratthall et al., 1996; Marinho et al., 2003; Twetman et al., 2003). On the other hand, even in the 21st century, caries is a common disease in a large number of individuals and affects almost 50% of children aged 4 (Stecksén-Blicks et al., 2004) and 80% of 15-year-olds in Sweden (Hugoson et al., 2008). In addition, every year, around 20-30% of the adult population develops new caries lesions which require operative treatment (Zickert et al., 2000, Bader et al., 2005).

The WHO (World Health Organisation) collects data from every country in a global health data bank. A mean value of 1.5 decayed and filled teeth (DFT) for 12-year-olds was set as a global goal by 2020. In Sweden, this specific mean value was achieved back in 1995 and it was 0.9 in 2008. Today, the distribution of dental caries is polarised or skewed, implying that those individuals affected by dental caries account for the majority of all caries lesions. In order to make children with poor dental health more visible, Bratthall (2000) introduced the “Significant Caries index” (SiC). This index represents the mean value for the third of the population with poorer dental health and it was stated by the WHO to be a maximum of 3.0 DFT in 2015. The Swedish value was 2.7 in 2001, whereas it increased to 2.9 in 2005, but the value decreased to 2.5 in 2008 (Socialstyrelsen, 2010). The age of 12 years was chosen, because at that age it is possible to obtain data from most countries. However, it would have been more interesting to look at older adolescents, for example 14- to 19-year olds, as these ages are a better reflection of the future need for dental care as adults. Obviously, the efforts to improve dental health among these individuals have so far been ineffective.

Caries-Related Factors

In recent years, caries is recognised as the result of an imbalance between tooth mineral and oral biofilm (plaque). This “ecological caries hypothesis” is described as a disturbance of the homeostatic balance in the biofilm, as members of a resident bacterial flora obtain a selective advantage over other species (Marsh, 2003; Fejerskov, 2004). A triad of factors, i.e. the host, the bacteria and the fermentable carbohydrates, is needed for caries to develop (Keyes and Jordan, 1963; Lingström et al., 2003). The bacterial acid production in the biofilm and the buffering action in saliva result in fluctuations in plaque pH. As the pH falls below a critical point, the demineralisation of enamel, dentine and cementum occurs, while there is an increase in mineral (remineralisation) as the pH increases (Kidd & Fejerskov, 2004). The imbalance and balance between demineralisation and remineralisation take place frequently during the day. Over time, this process leads either to the development or to the reversal of caries lesions (Featherstone, 2004). Consequently, caries lesions are regarded as evidence of the disease rather than the disease itself.

Mutans streptococci (MS) are recognised as the major “criminals” since the late 1970s, according to the “specific plaque hypothesis” (Loesche, 1986). In fact, a systematic review by Tanzer et al. (2001) reported that MS are essential, especially for the initiation of caries on enamel and root surfaces. However, the relationship between MS and caries is not absolute and consequently MS are not considered to be the sole cause of caries development (Bowden, 1997; Aas et al., 2008; Takahashi & Nyvad, 2011). According to the “ecological caries hypothesis”, it is not the presence of certain bacteria that is necessary but bacteria with certain characteristics (Marsh, 2003). Furthermore, ten Cate (2006a) stated that “the arch criminals grow attached to surfaces embedded in a matrix to form a biofilm, and they are living in a complex bacterial society rather than isolated invaders in our oral ecosystem”. It is therefore important to evaluate not only the type or number of bacteria but also their activity in the caries process (Takahashi & Nyvad, 2008).

The high and frequent consumption of fermentable carbohydrates, in particular sucrose, has been known to be associated with caries initiation and development for several decades (Newbrun 1967; Paes Leme et al., 2006). On the other hand, according to a systematic review by Burt & Pai (2001), the connection between sugar consumption and caries experience is not so consistent in combination with frequent fluoride exposure. This is in line with a review by

Lingström et al. (2003), showing that sugar intake alone does not affect caries prevalence. However, for subjects with poor oral hygiene, the frequent consumption of sweets is an important factor and in subgroups without the same fluoride protection, sugar still acts as a potential risk (Zero, 2004). The appearance of early enamel caries lesions should therefore alert the clinician to identify the causal factors driving the local “ecological disturbance” in plaque and deal with both the cause and the effect of the disease.

Caries in Adolescents and Risk Assessment

In Sweden, dental caries in 3, 6, 12 and 19 year-olds was reported to the National Board annually from 1985 to 2008. The Swedish 12-year-olds who were “caries-free” in terms of DFT showed an evident improvement from 1985 to 2008, from 22 to 61%. Nevertheless, the value decreased to 58% in 2005 and the subsequent improvement has not been so extensive. The mean DFT for Swedish 19-year-olds was 2.8 in 2008. The corresponding value for proximal surfaces (DFS_a) was 1.2, but, if the “caries-free” individuals were excluded, it increased to 3.1 (Socialstyrelsen, 2010). However, it must be remembered that enamel caries lesions are not included in these data. According to Moberg Sköld et al. (2005a, b), more than 90% of the new proximal lesions are enamel caries lesions at 13 to 16 years of age. This was also confirmed by Alm et al. (2007), showing that two thirds of all Swedish 15-year-olds have proximal caries lesions/fillings and 86% of the total number of proximal caries lesions are enamel lesions. Apparently, these findings confirm the importance of keeping the proximal surfaces caries-free in adolescents.

For the majority of individuals, the progression of caries lesions is a slow process, with a large number of lesions remaining unchanged for a long period of time (Pitts, 1983). The medium survival time for proximal enamel lesions among Swedish adolescents in the 1990s was more than 5 years, while the corresponding figure for dentine lesions was 3.2 years, with a higher progression rate during the period of 14-16 years compared with 16-19 years (Gustavsson et al., 2000). The rate of progression depends on the depth of the lesion, as well as the actual tooth and tooth surface, and is illustrated in the site-specific development of proximal caries by several researchers (Mejäre et al., 1999; 2001; Stenlund et al., 2003). According to Mathisen & Lunder (2000), the risk of progressing old lesions compared with the risk of developing new proximal lesions is four times higher in Norwegian 14- to 18-year-

olds. The recall of caries-active adolescents can be regarded as the assignment to supervise the proximal enamel caries lesions.

Methods for assessing the risk of developing new caries lesions have interested many researchers. Two systematic reviews, one by Powell (1998) and another by the Swedish Council of Technology Assessment in Health Care (SBU, 2007), pointed out that past caries experience is the single best predictor of future caries development among pre-school children, school children and adolescents. Furthermore, Powell (1998) stated that sociodemographic variables are most important in caries prediction models for children. However, there are limited prediction methods for identifying individuals at risk when their teeth are still caries-free and no single test is able accurately to predict an individual's susceptibility to caries (Reich et al., 1999).

Bitewing Radiographs in Caries Diagnostics

The early diagnosis of caries lesions is essential for the optimal treatment of caries and the bitewing radiograph is a useful and necessary diagnostic tool (Clark & Curzon, 2004). In the same way, Kidd & Pitts (1990) reported in a review that bitewing radiographs have been, and continue to be, of great importance in the diagnosis of posterior proximal caries in both deciduous and permanent teeth. As the caries prevalence is decreasing, the disease tends to be more difficult to diagnose clinically. In addition, fluoride therapy makes the outer layer of the enamel harder and the caries lesion more "hidden" in the sub-surface layer.

However, it is not possible to judge from bitewing radiographs whether the caries lesion is active and cavitated or not. The probability of cavitations depends on the depth of the observed radiolucency and it becomes higher deeper in the enamel. Lunder & von der Fehr (1996) showed that the probability of cavitations is higher for adolescents with a high caries risk than for those with a low risk. In addition, the possibility of cavitations in the outer half of the dentine is twice that of lesions in the inner half of the enamel. Furthermore, it is important to remember that the caries lesion seen on the radiograph is histological larger than it looks, as the radiograph underestimates the clinical appearance of tissue changes (Purdell-Lewis et al., 1974; Mejàre & Malmgren, 1986).

The registration of caries diagnosis from a radiograph is associated with many difficulties. There are large discrepancies in caries recording between different dentists and this has been

well known for many years. The level of agreement depends on several factors, including the number of depth codes, whether or not all the radiographs are read in succession and whether the examiner has access to earlier and later radiographs. There are large variations in intra- and inter-reliability and Pliskin and co-workers (1984) showed that the rates varied between 64 and 94%. In addition, a systematic review reported that the sensitivity and specificity values for bitewing radiography in the detection of proximal cavities were 0.66 and 0.95 respectively (Bader et al., 2001).

During the last decade, digital radiographs have been more and more frequently used in dental clinics. In some respects, digital radiographs are more difficult to perform than conventional radiographs, especially in young patients. There are few studies comparing the two techniques; however, Wenzel (2004, 2006) showed only non-significant differences. Recently, some new digital techniques have been introduced and Martignon et al. (2006) showed that digital subtraction radiography appears to be the most sensitive method for assessing the progression of caries lesions.

Fluoride in the Caries Process

The effect of fluoride on caries prevalence, incidence and progression is well documented in the literature and it is primarily a topical action on the tooth surface in the oral cavity (Stephan, 1999; Featherstone, 2000; Marinho, 2008). Several studies show that fluoride exerts its cariostatic effects through the liquid phase surrounding the enamel. Its mechanism of action is based on three principles: 1) inhibiting demineralisation, 2) enhancing remineralisation and 3) inhibiting bacterial metabolism.

Inhibiting demineralisation: fluoride is a highly reactive agent and has a strong affinity for apatite. The formation of fluor-hydroxyapatite and calcium fluoride are two examples of this interaction. Fluor-hydroxyapatite is predominant at low levels of fluoride concentration in a neutral environment, while calcium fluoride is mainly formed at high fluoride concentrations and at low pH levels (Rølla, 1988). Both substances have an important effect on the solubility and dissolution of apatite (Shellis & Duckworth, 1994). In addition, the formation of calcium fluoride acts as a slow-release reservoir at the tooth/biofilm interface and its capacity as a reservoir may last long enough to be of clinical importance (Saxegaard & Rølla 1989; ten Cate, 1997; Øgaard, 2001).

Enhancing remineralisation: the continuous supply of low fluoride concentration in saliva and oral biofilm favours the remineralisation of enamel caries lesions (Lynch et al., 2004). Enamel lesions will partially mineralise more readily than larger dentine lesions. Additionally, ten Cate et al. (2006b) showed that significant differences were observed in the fluoride response between shallow and deep lesions, suggesting that this parameter should be included when testing caries-prevention products.

Inhibiting bacterial metabolism: fluoride in saliva and plaque may also interact with the bacterial metabolism, its acid production and may further reduce the caries progression (Marquis et al., 1995). According to Bradshaw et al. (2002), fluoride exerts dual antimicrobial effects in microbial communities by reducing overall acid production (direct effect) and by reducing the selection of acid-tolerating species such as MS (indirect effect).

Fluoride Toothpaste in Caries Prevention

Fluoride toothpaste plays an essential role in any program designed to prevent dental caries in populations, communities and individuals. From a global perspective, fluoride toothpaste is considered to have had a significant impact on the decline in dental caries (Clarkson et al., 1993; Lewis et al., 1995; Bratthall et al., 1996; Marinho et al., 2003) and there has been a substantial reduction in the prevalence of caries in most industrialised countries. In the era of evidence-based dentistry, the accumulated information on the efficacy of different preventive methods is presented in systematic reviews. A Swedish review of caries prevention methods (SBU, 2002), a Cochrane review by Marinho et al. (2003) and a review by Twetman et al. (2003) reported strong scientific evidence that the daily use of fluoride toothpaste is an effective method for preventing caries in permanent teeth. Walsh et al. (2010) confirmed in a recent Cochrane review that toothpastes containing at least 1,000 ppm fluoride are effective in preventing tooth decay in children and adolescents and the relative caries-preventive effect increases as the fluoride concentration increases. In order to obtain the maximum benefit from fluoride toothpaste, the aim should be to find the most effective products and educate individuals in how to use them in an optimal way.

In addition to “product factors” such as the fluoride concentration in the toothpaste, biological and behavioural factors can modify its anti-caries effectiveness. The following “behavioural factors” should be considered: 1) frequency of brushing, 2) amount of

toothpaste, 3) duration of brushing, 4) post-brushing water rinsing 5) and habits immediately after brushing (Davies et al., 2003; Zero, 2006; Zero et al., 2010). Zero and co-workers stated that “all of these factors interplay in what could be described as the ‘application’ phase (the initial interaction of relatively high concentrations of fluoride with the tooth surface and plaque), and the ‘retention’ phase (the fluoride remaining in the mouth after brushing that is retained in saliva, plaque and plaque fluid, the tooth surface and oral soft tissue reservoirs)” (Zero et al., 1988; Zero et al., 1992a, b).

The concentration of fluoride in the toothpaste is an important factor in caries prevention. The fluoride concentration in dentifrices sold in normal shops varies between 500 and 1,500 ppm. In the European Union, the maximum concentration permissible in an over-the-counter (OTC) product is 1,500 ppm. In Sweden, the most common concentration is 1,450 ppm. During the last decade, there has been a tendency to increase the fluoride concentration in toothpaste for adults and children, as there appears to be a correlation between the fluoride concentrations of dentifrices and caries prevention (see “high-fluoride toothpastes”).

Several studies have shown that the frequency of tooth-brushing has a significant association with caries prevalence, as well as caries incidence in children (Wendt et al., 1994; Stecksén-Blicks et al., 2004; Mattila et al., 2005). In general, fluoridated toothpaste is recommended for brushing twice a day, in the morning, after breakfast, and in the evening, just before bedtime. Julihn et al. (2006) found that irregular brushing in the evening was strongly associated with high caries prevalence in 19-year-olds. The caries increment in subjects who brushed once a day were 20-30% higher than those who brushed twice a day in 3-year clinical trials (O’Mullane et al., 1997; Chester et al., 1992; Chestnutt et al., 1998). Furthermore, Marinho et al. (2003) showed in a Cochrane report that the effect of fluoride toothpaste appears to increase with a higher baseline DMFS level in the subjects, a higher fluoride concentration in the toothpaste and a higher frequency of use and that brushing twice a day or more has a greater preventive effect than once a day. However, there are few studies evaluating the effect of a third application of fluoride toothpaste on fluoride retention.

Another factor of importance is the amount of toothpaste used per application. According to den Besten et al. (1996), the mean salivary fluoride levels after brushing with 0.25 g of toothpaste were approximately one third of those obtained after brushing with 1.0 g of toothpaste. Likewise, Zero et al. (2010) showed an increase in saliva fluoride concentrations

due to the use of 1.5 g dentifrice rather than 0.5 g dentifrice, indicating that more dentifrice is an effective way of increasing fluoride retention in the oral cavity. The application of 1 g (≈ 2 cm) or more of fluoride toothpaste is therefore recommended in adults to increase both the fluoride uptake in the enamel surface and the fluoride concentration in the oral fluid (Koga et al., 2007). In contrast, one clinical trial demonstrated a correlation between plaque fluoride and increasing fluoride concentration in the dentifrice but no correlation between plaque fluoride and the amount of dentifrice used per application (Duckworth et al., 1989).

The duration of brushing (application phase) determines how long the relatively high fluoride concentration in the dentifrice slurry stays in contact with the teeth and plaque, allowing fluoride uptake to take place. Zero et al. (2010) showed that both brushing time and the quantity of dentifrice may be important determinants of both fluoride retention in the oral cavity and subsequent enamel remineralisation. These results suggest that the time spent brushing with a dentifrice within the range of common practice can influence fluoride retention in the oral cavity and thereby enamel remineralisation. It is therefore surprising that almost no research has been performed on brushing time in recent years.

Another important determinant of efficacy is the post-brushing behaviour. Post-brushing water rinsing has been routinely advised by the dental profession to remove debris and to avoid swallowing excess fluoride toothpaste, especially in younger children. However, it has been reported that individuals who rinse with large volumes of water have higher caries increment than those using smaller volumes (Chester et al., 1992; Sjögren & Birkhed, 1993; O'Mullane et al., 1997, Chestnutt et al. 1998). The intra-oral levels of fluoride may also differ in subjects with different post-brushing rinsing and spitting habits (Collins et al., 1991; Duckworth et al., 1991; Richards et al., 1992; Attin et al., 1996). Furthermore, a recent study by Duckworth et al. (2009) supports the recommendation that mouth rinsing with water after brushing should be kept to a minimum in order to increase the fluoride retention. In contrast, Machiulskiene et al. (2002) presented limited support for refraining from water rinsing after tooth brushing. The difference between the mean caries increment in children with and without water rinsing was only 0.6 DS and had no statistical significance. However, this study showed relatively large numbers of dropouts (32%) and differences in compliance.

Finally, it should be observed that the “modified fluoride toothpaste technique” (MFTT), in which a slurry rinse with the toothpaste is carried out after brushing, increased the efficacy of fluoride toothpaste and reduced proximal caries in preschool children (Sjögren et al.,

1995). In a recent study by Sonbul et al. (2010), this technique revealed a 66% prevented fraction effect on proximal caries compared with the group with regular oral hygiene habits in an adult Saudi population. Al-Mulla et al. (2010b) showed that the use of the MFTT significantly reduced the incidence of new caries lesions in orthodontic patients. However, it must be remembered that the MFTT contains a package of advice and it is not possible to identify the most important factor. In conclusion, further studies are needed to promote oral health by educating individuals in how to obtain the greatest benefit from fluoride toothpaste.

High-fluoride Toothpaste

One important factor for caries reduction is the fluoride concentration in the toothpaste. The higher concentration, the greater the driving force for fluoride diffusion through plaque towards the tooth surface (Zero et al., 1992a, b). As mentioned earlier, there has been a tendency to increase the fluoride concentration in toothpastes during the last decade. It has been concluded that dentifrices with 1,500 ppm fluoride have a slightly better preventive effect ($\approx 10\%$) compared with those with 1,000 ppm (Twetman et al., 2003, 2009). Several studies indicate that there is a linear dose-response relationship between the fluoride concentration in toothpastes and caries reduction up to 1,500 ppm (Birkeland, 1972; White & Nancollas, 1990). Toothpaste with more than 1,500 ppm fluoride can only be obtained at a pharmacy as an over-the-counter (OTC) product. Dentifrices with 2,800 and 5,000 ppm fluoride have recently been introduced in several countries for patients with a high caries risk. In Sweden, high-fluoride toothpaste containing 5,000 ppm fluoride was introduced in December 2003.

A number of randomised, controlled, clinical trials (duration 1-3 years) have assessed the effectiveness of toothpastes containing up to 2,800 ppm fluoride and these studies are summarised in Table 1. In two old studies, a 2,400 ppm MFP (sodium monofluorophosphate) dentifrice was compared with a placebo, showing caries reduction of 23-43% in children (Hargreaves et al. 1973; Lind et al., 1975). Bisenbrock et al. (2001) reported that 2,200 and 2,800 ppm fluoride dentifrices delivered a statistically significant increase in anticaries protection ($\approx 20\%$) compared with a 1,100 ppm fluoride dentifrice after 1 year. Similar results were reported by Stookey et al. (2004), comparing 2,800 ppm fluoride with 1,100 ppm after 2 years. Other studies have demonstrated a statistically significant dose response for dentifrices

containing 2,500 ppm fluoride (MFP) compared with 1,000 ppm, with a caries reduction of 9-16% (Stephen et al., 1988; Marks et al., 1992; Marks et al., 1994; Chester et al. 2002). These results suggest that, within the range of 1,000-2,800 ppm fluoride, an increase of around 500 ppm in the paste results in an additional 6% reduction in dental caries (Stephen et al., 1988; O`Mullane et al., 1997). However, some of the studies are difficult to evaluate because of the low value of evidence. For example, in a comparison of toothpastes containing 1,250, 2,500 and 5,000 ppm fluoride in children, Cutress et al. (1992) demonstrated that, after 3 years, the 5,000 ppm fluoride toothpaste was significantly more effective in reducing caries than the lower concentrations. The field data were shown to be unusable because of the method of scoring and the children located and re-examined one year later represented only 34% of the original randomised baseline subjects. Only 756 of the original 1,508 children completed the study. Furthermore, studies by Lu et al. (1987) and Ripa et al. (1988) showed large numbers of dropouts (>34%) and poor compliance and these two studies are considered to have a low value of evidence (SBU, 2002). In conclusion, Tavss and co-workers showed, in a review in 2003, that there appears to be a correlation between the fluoride concentration of dentifrices between 0 and 5,000 ppm and caries prevention, but the exact shape of the dose-response curve at the high level of 5,000 ppm is uncertain.

Table 1. Clinical studies (duration 1-3 years) that have assessed the effectiveness of dentifrices containing 1,500-5,000 ppm fluoride compared with 500-1,250 ppm.

	Duration year	Number	Age at baseline	Fluoride formula	Concentr. ppm F	Increment	% diff.	Significance
Hargreaves 1973	3	942	5, 8, 11	MFP	Placebo 2,400	23.0 8.0	23	S
Lind 1975	3	1407	7-12	MFP	Placebo 2,400	2.3 1.3	43	S
Lu 1987	3	2055	7-15	NaF NaF	1,100 2,800	4.4 3.9	12	S
Ripa 1988	3	2500	10-13	NaF/MFP NaF/MFP	1,000 2,500	3.6 3.7		NS
Stephan 1988	3	921 930 466	11-14	MFP MFP MFP	1,000 1,500 2,500	6.8 6.3 5.7	7 16	S S
Marks 1992	3	1120 1116 1076 1112	7-11	MFP MFP MFP MFP	1,000 1,500 2,000 2,500	4.2 4.2 4.1 3.8	11	NS NS S
Marks 1994	3	8027	6-14	MFP MFP MFP MFP NaF	1,000 1,500 2,000 2,500 2,000	4.3 4.3 4.0 3.5 3.5	5 15 15	NS S S
Cutress 1992	3	520	10-15	Not reg.	1,250 2,500 5,000	Not reg.	19 40	S S
Biesenbrock 2001	1	1127 1129 1082 1093	6-15	NaF NaF NaF NaF	1,100 1,700 2,200 2,800	1.7 1.5 1.4 1.4	11 19 20	NS S S
Chesters 2002	2	994 1017	11-14	MFP MFP	1,000 2,500	5.5 5.0	9	S
Stookey 2004	2	955	9-12	NaF NaF NaF	500 1,100 2,800	5.6 4.6	18	NS S

Recently, some short experimental studies (duration <1 year) of high-fluoride toothpaste (2,800-5,000 ppm) have been published and these studies are summarised in Table 2. The reversal of root caries using 5,000 ppm fluoride toothpaste has been documented by Baysan et al. (2001) and Ekstrand et al. (2008). Schirremeister et al., (2007) found that high-fluoride toothpaste reversed non-cavitated fissure caries lesions after two weeks. The group using 5,000 ppm fluoride showed a significantly higher decrease in the laser fluorescence of enamel than the 1,450 ppm fluoride group. In addition, several experimental treatments of demineralised dentine with toothpaste containing 5,000 ppm fluoride reduced mineral loss depth on exposed dentine (Pulido et al., 2008; ten Cate et al., 2008; Bizhang et al., 2009; Diamanti et al., 2010). Furthermore, in an in situ caries model with orthodontic bands, Al-Mulla et al. (2010a) found that the combination of 5,000 ppm fluoride toothpaste and no water rinsing resulted in less QLF average change in fluorescence after 8-9 weeks.

Table 2. Experimental studies (duration <1 year) that have assessed the effectiveness of dentifrice containing 2,800-5,000 ppm fluoride compared with 500-1,450 ppm, including a mouth rinse (MR) with 250 ppm fluoride.

	Duration	Number	Age at baseline	Fluoride formula	Concentr. ppm F	Measurement	Significance
Baysan 2001	6 months	201	>18 years	Not reg. NaF	1,100 5,000	Remineralization of root caries	S
Schirremeister 2007	2 weeks	30	adults	NaF NaF	1,450 5,000	Diagnodent on fissure caries	S
Ekstrand 2008	8 months	28	elderly >75	NaF NaF	1,450 5,000	Progression of root caries	S
Pulido 2008	6 days	21 teeth		NaF NaF	1,100 5,000	Polarized-light-microscopy; digital image analysis	S
ten Cate 2008	15 days	15 bovine teeth		NaF NaF NaF	500 1,500 5,000	Lesion depth with microradiography	S S
Bizhang 2009	3 weeks	15 teeth		Not reg. NaF	250 (MR) 5,000	Lesion depth with microradiography	S
Diamanti 2010	10 days	50 bovine roots		NaF NaF NaF	1,450 2,800 5,000	Surface microhardness (Tukon tester)	S S
Al Mulla 2010	8-9 weeks	24	16 years	NaF NaF	1,450 5,000	QLF	S

High levels of fluoride in the oral cavity may also interact with the bacterial metabolism, its acid production and further reduce the caries process (Marquis et al., 1995). Fluoride reduces the acid production of the bacteria and thereby decreases the cariogenicity of dental plaque by reducing the selection of acid-tolerating species such as MS (Bradshaw et al., 2002). Baysan et al. (2001) found, as a side-effect in a clinical study, significantly lower plaque scores after 3 and 6 months in a group using a dentifrice with 5,000 ppm fluoride compared with a dentifrice with 1,100 ppm. However, the anti-plaque effect of dentifrice slurries with a higher fluoride concentration has so far not been thoroughly investigated. In addition, there are few clinical studies evaluating high-fluoride toothpastes during 2-3 years (Tavss et al. 2003; Davies & Davies, 2008) and further studies are needed.

Oral Fluoride Clearance and Retention

The definition of “clearance” is the ability of the body to eliminate a substance and is dependent on the function of the eliminating organs. The salivary fluoride concentration increases immediately after the intake of fluoride. The increase is determined by the fluoride content and release from the product. However, the salivary fluoride clearance is also the result of a complex interaction between salivary flow rate, swallowing frequency, oral muscular movements, eating and drinking and absorption by the oral mucosa. In addition, the biphasic fluoride clearance model created by Duckworth & Morgan (1991) postulated that brushing with fluoride toothpaste created one reservoir of “unbound” fluoride and a second reservoir of “bound” material that was slowly released into the first reservoir.

Fluoride “retention” is defined as the fluoride remaining in the mouth after brushing that is retained in saliva, plaque and plaque fluid, the tooth surface and oral soft tissue reservoirs (Zero et al., 1988; Zero et al., 1992a, b). The fluoride retention in saliva and plaque has been measured by many authors after a variety of topical fluoride treatments. Duckworth et al. (1992) showed that the fluoride level in saliva decreased in two distinct phases after tooth-brushing, with final values of about 0.02 ppm fluoride, 12-18 hr after brushing. The reported plaque fluoride concentrations vary considerably, but they are significantly higher than salivary values and range from 5-10 ppm fluoride (wet weight) (Tatevossian, 1990). According to Vogel et al. (1992), the higher levels of fluoride in plaque compared with those in saliva were due to the slower removal of fluoride ions from plaque and the release of

fluoride from calcium fluoride in the plaque (Rølla & Saxegaard, 1990). The formation of calcium fluoride acts as a slow-release reservoir at the tooth/biofilm interface (Saxegaard & Rølla 1989; ten Cate, 1997; Øgaard, 2001). Thus, fluoride can be stored in plaque and be released gradually to interact with the underlying tooth surface. Findings from experimental studies (reviewed by ten Cate, 1999; Featherstone, 1999; Lynch et al., 2004) and clinical data (Duckworth et al., 1989, 1992) all suggest that small increases in post-brushing concentrations of fluoride in saliva and plaque can have a marked effect on both experimental caries lesions and caries clinically.

Fluoride Metabolism and Toxicological Aspects

Fluoride enters the human body through the mouth and following ingestion, fluoride is rapidly absorbed into blood plasma, predominantly in the stomach. Furthermore, the content of the stomach and its composition are important for the degree of absorption. Fluoride is then distributed from the plasma to all tissues and organs in the body. It is a highly reactive agent and reacts rapidly with mineralising tissues. The highest proportions of ingested fluoride are deposited during the growth phase of the skeleton through active mineralisation. However, fluoride in the bone is not irreversibly bound to the crystals, as bone constantly undergoes remodelling and fluoride is thus mobilised slowly from the skeleton. The main route for the elimination of fluoride is the kidneys. Fecal fluoride accounts for less than 10% of the amount of ingested fluoride (Ekstrand et al., 1984). Moreover, with age, the mobilisation rate from bone and the efficiency of the kidneys in excreting fluoride change (Ekstrand et al., 1977).

Fluoride ingestion is particularly important in infants and dental fluorosis can only occur when teeth are developing. The prevalence of fluorosis has increased in communities both with and without water fluoridation during the past years. The use of fluoride toothpaste by very young children has been mentioned as a potential risk factor for fluorosis. There is an association with the inability of very young children to spit out and the inevitable swallowing of toothpaste placed in the mouth. The threshold level of fluoride ingested beyond which fluorosis may occur is not known. The amount of toothpaste applied to the brush is particularly important for children under the age of 6. Consequently, parents of young children are advised to supervise their children and apply a pea-sized amount of toothpaste on the brush.

Children under 16 years of age should not use high-fluoride toothpaste, according to the instructions given by the manufacturer. Approximately 5-10% of a dentifrice is swallowed during brushing, when using a minimum amount of water (Sjögren & Birkhed, 1994). The amount of swallowed fluoride is therefore 0.25-0.50 mg when using 1 g of a toothpaste containing 5 mg F/g. This quantity corresponds to the amount of fluoride in 1-2 fluoride tablets containing 0.25 mg or one cup of tea (~ 1dL) and is considered to have no toxic effect in teenagers or adults (Wu & Wei, 2009). Consequently, the age of 12 years would perhaps be a more appropriate age limit, in order to affect the newly erupted premolars and second molars and to avoid new caries lesions during the risk period of 12-16 years.

Aims

The overall aim of this thesis was to study the effect of high-fluoride toothpaste (5,000 ppm) compared with standard toothpaste (1,450 ppm) in caries prevention. The specific aims were to investigate:

- the retention of fluoride in proximal plaque and saliva (Papers I, II & IV),
- the effect of post-brushing water rinsing on fluoride retention in proximal plaque and saliva (Paper I),
- the effect on de novo plaque formation (Paper II),
- the preventive effect on caries incidence and progression in caries-active adolescents (Paper III) and
- the effect of a third application of toothpaste, including a “massage” method, on fluoride retention and pH drop in plaque (Paper IV).

Own Experiments and Results

An outline of the design, population and topics of the four studies is given in Table 3.

Table 3. The four studies and their corresponding design, population and main topic.

Study	Design	Population	Topic
I	Cross-over	26	Fluoride retention in proximal plaque and saliva and the effect of post-brushing water rinsing
II	Cross-over	12-16	Effect on de novo plaque formation
III	Longitudinal	279	Preventive effect on caries incidence and progression in caries-active adolescents
IV	Cross-over	16	Effect of a third application of toothpaste, including a “massage” method, on fluoride retention and pH drop in plaque

Paper I

The aim was to investigate the fluoride retention in proximal plaque and saliva, using a high-fluoride toothpaste (5,000 ppm), compared with a standard toothpaste (1,450 ppm), with and without post-brushing water rinsing.

Design and subjects

A total of 26 subjects participated in a randomised, cross-over study. Sixteen subjects were students at the Dental Hygienist School in Gothenburg, aged 19-35 years (mean 24 years), and 10 subjects were staff from the Public Dental Service Clinic in the city of Varberg Sweden, aged 34-55 years (mean 47 years).

Material and methods

The 4 test periods each lasted for 2 weeks. The subjects brushed twice a day with: 1) 5,000 ppm F; (Duraphat) without water rinsing; 2) 5,000 ppm; 3x10 ml water rinsing (3x10 s), 3) 1,450 ppm F; (Pepsodent Superflour) without water rinsing, 4) 1,450 ppm; as No 2. Prior to each test period, the subjects brushed with F-free dentifrice for one week. Plaque was

collected (2 h after last brushing occasion) with dental floss from all proximal areas and weighed (n=16). The same 26 subjects also participated in an oral F clearance study, directly after each test period. The subjects then brushed with the same toothpaste and the same post-brushing technique as during the 2-week test period. Proximal saliva samples were collected with paper points at 4 sites (16/15, 25/26, 35/36, 45/46) and repeated after 1, 3, 5, 10, 30 and 60 min.



Figure 1. Sampling of proximal saliva samples with small triangular paper points held in a pair of forceps.

Results

The high-fluoride toothpaste without rinsing compared with the standard toothpaste, also without rinsing, produced a fluoride concentration that was 2.5 times higher ($p<0.001$). The high-fluoride toothpaste without post-brushing water rinsing produced the highest fluoride concentration in proximal saliva and the standard toothpaste with water rinsing the lowest. The difference in saliva F concentration (AUC) between the two methods was 4.2 times ($p<0.001$). The corresponding difference per unit weight of plaque (n=16) was 2.8 times ($p<0.05$). The difference between the four methods was most pronounced within the first 30 min. Water rinsing immediately after brushing with high-fluoride dentifrice reduced the fluoride concentration in saliva by 2.4 times ($p<0.001$). The difference between high-fluoride toothpaste with rinsing and ordinary paste without rinsing was therefore small and not statistically significant.

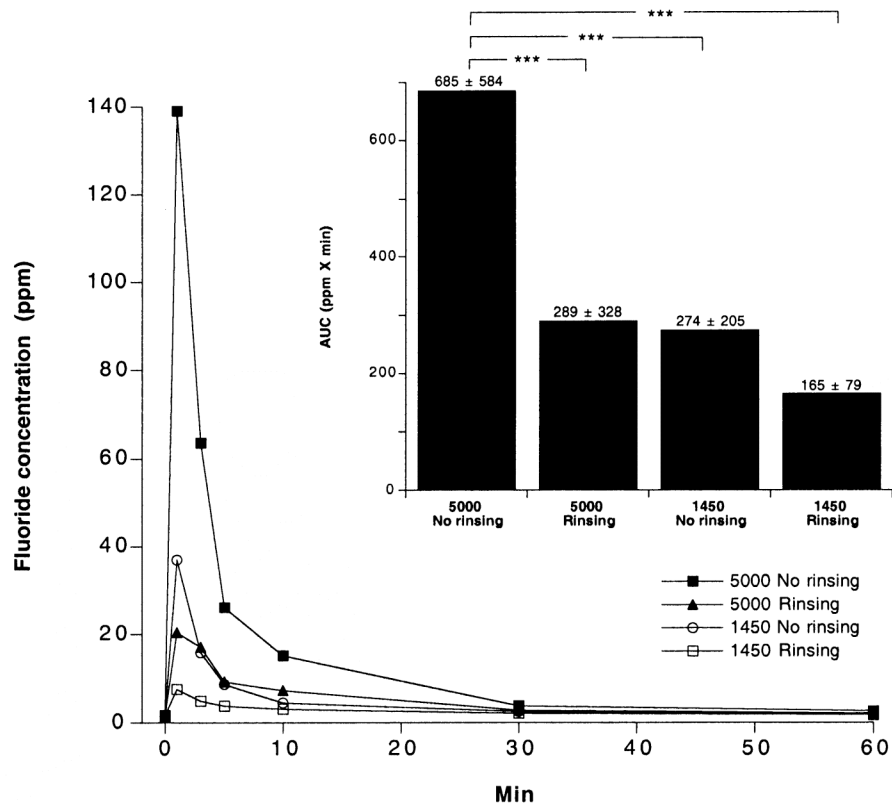


Figure 2. Mean values (n = 26) of F concentration in proximal saliva at various time points up to 60 min after using two NaF dentifrices, with and without post-brushing water rinsing. The bars indicate the statistical significances (*p<0.05) (**p<0.01) (**p<0.001).

Paper II

The aim was to evaluate the effect of rinsing with toothpaste slurries and water solutions with a high fluoride concentration (5,000 ppm) on de novo plaque formation.

Design and subjects

Two test series, here called I and II, were carried out with a randomised, cross-over design. Series I was single blind with 3 cells and Series II was double blind with 5 cells. Sixteen healthy dental students, aged 21-43, were recruited to Series I. Twelve of these 16 subjects also participated in Series II (mean age 24 years).

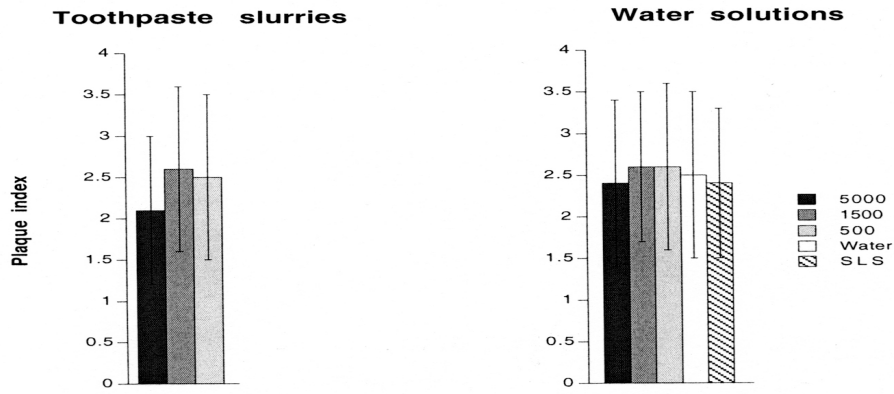
Material and methods

Series I: 16 subjects rinsed 3 times a day for 4 days with the following dentifrice slurries: 5,000, 1,500 and 500 ppm F. Series II: 12 subjects rinsed with water solutions: 5,000, 1,500, 500, 0 ppm F and 1.5% SLS (sodium lauryl sulphate). Plaque was scored after each 4-day period, on all teeth at six sites, according to the Quigley & Hein Index (QHI). Plaque samples for F analysis were collected in Series I.

Results

High fluoride concentration in toothpaste slurry reduced the formation of new plaque on tooth surfaces. Significantly ($p<0.05$) less plaque was scored for dentifrice slurry with 5,000 ppm F (buccal and all surfaces) and for water solution with 1.5% SLS (buccal surfaces). The difference in plaque scores between the 5,000 and the 1,500 ppm slurry was 19% for all surfaces and 33% for buccal surfaces. The difference between a water solution with 1.5% SLS and the 1,500 ppm F for buccal surfaces was 23%; the corresponding difference for the 5,000 ppm F was 17% ($p<0.05$). The 5,000 ppm dentifrice slurry accumulated 56% more fluoride in plaque ($p<0.05$).

All surfaces



Buccal surfaces

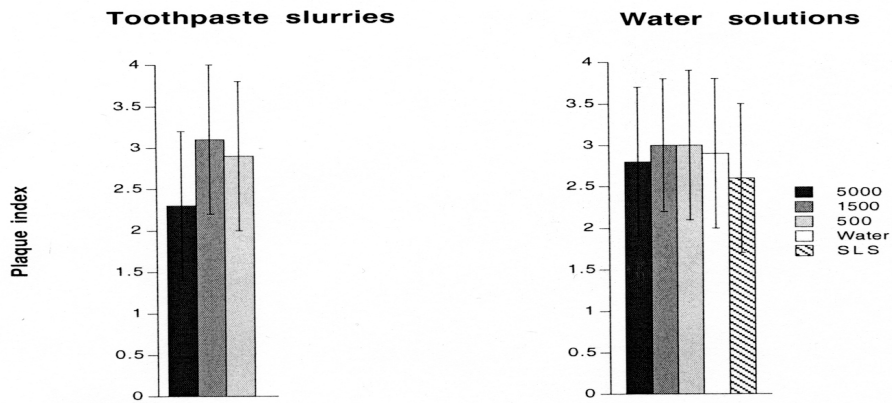


Figure 3. The mean plaque index (QHI) scores \pm SD for buccal and all surfaces, representing each experimental 4-day period in Series I (toothpaste slurries; n = 16) and Series II (water solutions; n = 12).

Paper III

The aim was to evaluate high-fluoride toothpaste (5,000 ppm) compared with standard toothpaste (1,450 ppm), in caries-active adolescents.

Design and subjects

The design was a 2-year, single-blind clinical trial and 211 adolescents of 279 (76%) completed the trial. The subjects were caries-active adolescents (146 boys and 133 girls), aged between 14 and 16 years at the start. They were recruited at the Public Dental Service Clinic in the city of Varberg, Sweden.

Material and methods

The subjects were randomly selected into two groups and were given one of the assigned toothpastes for daily unsupervised brushing: 1) 5,000 ppm F (Duraphat) and 2) 1,450 ppm F; (Pepsodent Superfluor) both as NaF. The outcome variables were caries incidence and progression of proximal and occlusal caries. At the last appointment, the subjects were asked to fill in a questionnaire to evaluate their compliance and they were divided into two subgroups: A) “excellent” and B) “poor” compliance. The latter group comprised subjects with irregular brushing habits.



Figure 4. An example of radiographs from adolescents included in the study.

Results

Subjects using high-fluoride toothpaste had significantly lower progression of caries compared with those using standard toothpaste in both compliance groups (A: $p < 0.01$, B: $p < 0.001$), with a prevented fraction (PF) of 40%. Twenty-eight per cent of the adolescents had “poor” compliance (compliance B) and brushed irregularly. Twice as many boys as girls were included in this group. Brushing with high-fluoride toothpaste resulted in significantly less new caries lesions among adolescents in compliance B ($p < 0.05$; PF 42%) compared with compliance group A (“excellent” compliance). The data indicate that high-fluoride toothpaste has a greater impact on individuals with irregular brushing habits.

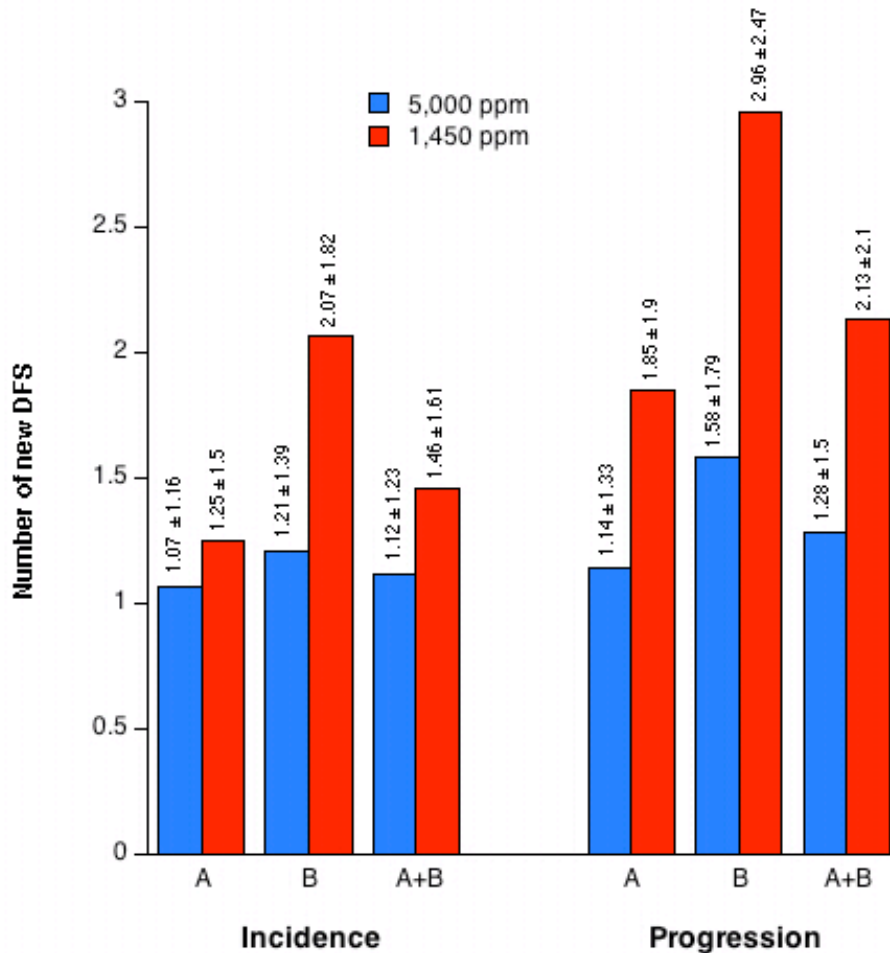


Figure 5. Caries incidence and progression after 2 years (mean ± SD for the two compliance groups (A = excellent, B = poor) and for all subjects (A +B)).

Paper IV

The aim was to study the effect of a third application of two NaF toothpastes (5,000 and 1,450 ppm F) on fluoride retention and pH drop in plaque.

Design and subjects

The investigation was a randomised, cross-over, single-blinded study and 16 subjects, aged 23-38 years (mean 26 years) participated. The outcome measures were retention of fluoride in plaque and saliva and the plaque-pH change in situ after a sucrose rinse was used as an indicator of the microbiological activity. In addition, a special toothpaste “massage” method was evaluated in the same way.

Material and methods

The subjects used 6 different tooth-brushing methods, each for 2 weeks, followed by a wash-out period of one week, i.e. a total of 18 weeks. The toothpastes were: (1) 5,000 ppm F (Duraphat) for brushing twice a day, (2) 5,000 for brushing 3 times a day, (3) 5,000 for brushing twice a day, plus the “massage” once a day, (4) 1,450 ppm F (Pepsodent Super Fluor) for brushing twice a day, (5) 1,450 for brushing 3 times a day and (6) 1,450 for brushing twice a day, plus the “massage” once a day. A method using F toothpaste as a “lotion” to massage the buccal surfaces was also evaluated (Fig. 6).



Figure 6. The toothpaste “massage” method; using toothpaste as a “lotion” and massaging the buccal surfaces with the fingertip.

The subjects were instructed to apply at least 1 cm of toothpaste on the fingertip and to “massage” the buccal surfaces, in both the upper and lower jaw, at the same time. The toothpaste should be kept in the mouth for 2 min, followed by spitting out the slurry carefully and no further water rinsing afterwards.

Results

The highest mean peak saliva fluoride concentration were found after using toothpaste with 5,000 ppm (No 1-3) and differed significantly from those with 1,450 ppm (No 4-6). Brushing with high fluoride toothpaste 3 times/day (No 2) resulted in 3.6 times higher fluoride concentration in saliva compared to a standard paste twice a day (No 4) (1036/288; $p < 0.001$). The corresponding difference in plaque was 2.2 times (13.7/6.2; NS). In order to increase the power, fluoride application 3 times a day (No 2; No 5) and twice a day + “massage” once a day (No 3; No 6) were pooled for the toothpastes (No 2+3 and No 5+6). Increasing the frequency of fluoride application, from twice to 3 times a day, increased the fluoride retention in plaque 1.6 times in this analysis (13.5/8.5 and 9.9/6.2; $p < 0.05$). There was also a suggestion of a positive association between the fluoride accumulation in proximal plaque and the fluoride concentration in the 1,450 vs. 5,000 ppm toothpaste ($p = 0.088$). Brushing with 5,000 and 1,450 ppm toothpastes, twice a day plus the “massage” once a day, resulted in the same fluoride concentration in saliva and plaque as brushing 3 times a day with the same paste (Fig. 7).

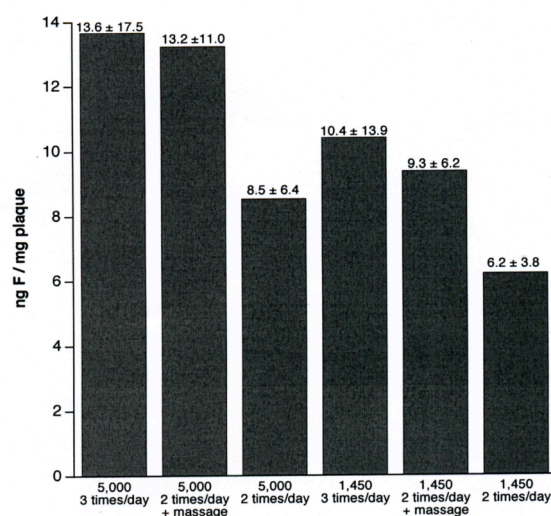


Fig 7. Fluoride accumulation in proximal plaque, expressed as ng F/mg plaque wet weight.

Fluoride Analysis

The saliva and plaque samples were analysed blindly with regard to subjects and methods. A volume of 200 µl of liquid consisting of distilled water and TISAB III (10:1) (Thermo Electron Corp., Waltham, USA) was added to the plaque and saliva samples. The plaque suspension was homogenised by sonification for 20 s (Branson W185D, Dansbury, Connecticut, USA) in order to disperse the plaque. The samples were kept in a refrigerator at +4°C over night. The tubes were then vibrated in a Minishaker MS1 (IKA, Wilmington, USA) for 20 s. One hundred microliters of the solution was placed as a drop on a Petri dish. The fluoride concentration was measured by an ion-specific electrode (model 96-09, Orion Research Inc.) by carefully lowering the electrode into the fluid. The surface tension of the drop ensured that the liquid enclosed the entire membrane surface of the electrode. In order to calibrate the electrode in saliva, three standard solutions were used (0.1, 1.0 and 10 ppm F). The fluoride concentration was expressed as both ppm in the suspension and ng F/mg plaque. The method for analysing the fluoride concentrations using 100 µl was evaluated in 50 samples from 1-100 ppm fluoride and the r^2 value was calculated as > 0.95 . The salivary fluoride concentrations (both as ppm and log ppm) were plotted vs. time (in min) and the area under the curve ($AUC_{0-60min}$) was calculated for each individual and each brushing method using a computer program (KaleidaGraph 3.01, Synergy Software, Reading, PA, USA).

De Novo Plaque Formation

On a given day (Day 0), dental plaque was disclosed with erythrosine (Diaplac, LIC AB, Enköping, Sweden) and all the participants received PMTC (professional mechanical tooth cleaning). They were asked to refrain from tooth-brushing and proximal cleaning for 4 days. New plaque was registered at the end of the 4-day period in two quadrants by one of the authors (C.M.). After disclosing with erythrosine (Diaplac®, LIC AB, Enköping, Sweden), plaque was scored on all teeth at six sites (mesiobuccal, buccal, distobuccal, mesiolingual, lingual and distolingual), according to the criteria specified in the Turesky modification of the Quigley & Hein Index (QHI) (Turesky et al., 1970; Quigley and Hein, 1962).

Plaque-pH Measurements

Plaque pH was measured with the microtouch method at baseline and at various time points during 45 min. Plaque pH was registered by inserting an iridium microelectrode (Beetrode® MEPH-1; W.P. Instrument, New Haven, Conn., USA) into 3 proximal sites (16/15, 11/21 and 25/26) according to Lingström et al. (1993). For each individual, the same sites were used throughout the entire study, i.e. for all six test periods and all time points. The electrode was connected to an Orion SA 720 pH/ISE Meter (Orion Research, Boston, Mass., USA), equipped with a porous glass reference electrode (MERE 1; W.P. Instruments). A salt bridge was created in a 3 M KCL (potassium chloride) solution between the reference electrode and one of the subject's fingers. After measuring resting pH (0 min), a mouth rinse with 10 ml of 10% sucrose was carried out for 1 min. Plaque pH was then measured at 7 different time points (1, 3, 5, 10, 15, 30 and 45 min) after the rinse.

Questionnaire

A questionnaire was used in Paper III (see appendix). At the last appointment, the subjects were asked to fill in a questionnaire in order to evaluate their compliance. The adolescents were then divided into two subgroups according to their compliance: A) "excellent" compliance and B) "poor" compliance. The latter group comprises subjects with irregular brushing habits; i.e. subjects who did not use the toothpaste regularly, or did not brush twice a day.

Ethical Considerations

Three studies (I, III & IV) were approved by the Ethics Committee at the University of Gothenburg (S 188-05, S 289-04, S 568-09). The design in Paper II, studying 4-day de novo plaque formation, has previously been approved by the ethical review board at the University of Gothenburg. Both verbal and written information about each study was given to the subjects and written informed consent was obtained. All studies were conducted in accordance with the Helsinki Declaration. All subjects were coded and statistical analyses were performed with unidentifiable data.

Statistical Methods

Analysis of variance, two-way ANOVA followed by Scheffe's test were used in Papers I and IV to compare the 4 and 6 brushing methods regarding the fluoride accumulation in proximal plaque, the fluoride retention in proximal saliva based on the area under the curve (AUC), and the mean plaque pH \pm SD. The calculation was made for each subject and each brushing method. The power analyses in Paper I and IV were based on our experience of similar designs and 12-16 subjects were considered to be enough. In some of the analyses in Paper IV, the groups were pooled in order to increase the power and p-values below 0.05 were considered statistically significant.

In Paper II, analysis of variance, two-way ANOVA followed by Student-Neumann-Keul's (SNK) test, were applied to evaluate the mean QHI scores (Series I & II) and the mean fluoride concentration in plaque (Series I). Power analyses were based on a difference of 0.8 QHI score units. There was an 80% power to detect a 20% difference in mean plaque reduction, including 12 subjects and p-values below 0.05 were considered statistically significant.

In Paper III, a power analysis with the assumption significance level of 5%, standard deviation 1.3, least detectable difference in incidence 0.6 and a power for that detection of 90% was performed and a sample size of approximately 100 subjects in each group was suggested. Descriptive statistics including means, standard deviations and frequency distributions were calculated for the two dentifrice groups. The comparisons between the two dentifrices were tested using an unpaired two-sample t-test.

Discussion

This thesis is based on the concept that, even in the 21st century, dental caries is a common disease in a large number of individuals. The prevention of caries should be based on frequent fluoride administration, a reduction in total sugar intake and frequency, and improved oral hygiene. Fluoride toothpaste plays an essential role in any programme designed to prevent dental caries and Marinho et al. (2003) stated in a Cochrane report that “in the case of self-administrated care, fluoride toothpaste is the most powerful intervention for caries prevention because of its high clinical effectiveness and social acceptability”. Consequently, in order to obtain the maximum benefit from fluoride toothpaste, the aim should be to find the most effective products and educate individuals in how to use them in an optimal way. The current thesis focuses on high-fluoride toothpaste (5,000 ppm) compared with a standard toothpaste (1,450 ppm) and investigates: the fluoride retention in plaque and saliva, the effect of post-brushing water rinsing, the effect on de novo plaque formation, the preventive effect on caries incidence and progression in caries-active adolescents and the effect of a third application, including a “massage” method, on fluoride retention and pH drop in plaque.

The retention of fluoride in proximal plaque and saliva

The fluoride remaining in the mouth after tooth-brushing is retained in saliva, plaque and plaque fluid, tooth surfaces and oral soft-tissue reservoirs. The main result in Paper I was that high fluoride concentration in toothpaste increased the fluoride retention in the proximal area. The high-fluoride toothpaste, without post-brushing water rinsing, compared with standard toothpaste, also without rinsing, produced fluoride retention that was 2.5 times higher in proximal saliva. The combination of high-fluoride toothpaste and no post-brushing water rinsing resulted in saliva fluoride retention that was 4.2 times higher compared with an ordinary toothpaste with 3 times post-brushing water rinsing. The corresponding difference in plaque per unit weight was 2.8 times. These values should be compared with the actual difference in fluoride levels of the two toothpastes (5,000 vs. 1,450 ppm = 3.5 times). One explanation for the discrepancy, especially in plaque, could be that fluoride does not continue to accumulate over time and Heijnsbroek et al. (2006) found no fluoride accumulation in

plaque after 6 hr using an AmF/SnF₂ dentifrice. However, another explanation could be that fluoride continues to accumulate over time. It has been suggested that intra-oral fluoride reservoirs may take weeks to “fill”, possibly due to the time taken for the establishment of steady-state fluoride concentrations in plaque (Duckworth & Morgan, 1991). In the present study, the number of subjects was quite small and the experimental period was relatively short to reveal significant differences in plaque fluoride levels. In fact, the use of fluoride dentifrices maintains increased fluoride levels in the whole plaque (Duckworth et al., 1992; Paes Leme et al., 2004; Pessan et al., 2008) and in the plaque fluid (Cenci et al., 2008) even 10 hr or more after brushing. Similarly, Lynch et al. (2004) showed that the fluoride concentration in plaque after brushing was still increasing four weeks after starting to use the fluoride toothpaste and a further elevation was seen after eight weeks. Tenuta et al. (2009) even suggested that “fluoride uptake by dental plaque not removed by brushing may be the main cause of the anticaries effect of dentifrices”. Fluoride is also distributed into plaque by diffusion and it is well established that fluoride can be stored in plaque for some time before it is released gradually (Tatevossian, 1990; Ekstrand & Oliveby, 1999). Zero et al. (1992) found that “the higher fluoride concentration, the greater the driving force for fluoride diffusion through plaque towards the tooth surface”.

The salivary fluoride concentration increases immediately after the intake of fluoride. The increase is dependent on the content and release of fluoride from the product. The salivary fluoride clearance is also the result of a complex interaction between flow rate, swallowing frequency, oral muscular movements, eating and drinking and absorption by the oral mucosa. In Paper I, the difference in saliva fluoride concentration between the four methods was most pronounced within the first 30 min, but it also differed after 60 min. Moreover, Duckworth et al. (1992) showed that the fluoride level in saliva decreased in two distinct phases after tooth-brushing, with final values 12-18 hr after brushing. Several experimental studies (ten Cate, 1999; Featherstone, 1999; Lynch et al., 2004) and clinical data (Duckworth et al., 1989, 1992) all suggest that even small increases in post-brushing concentrations of fluoride in saliva and plaque can have a marked effect on both experimental caries lesions and caries clinically. In conclusion, the high-fluoride toothpaste in Paper I increased the fluoride concentration in proximal saliva immediately after brushing and the accumulation of fluoride in proximal plaque. These findings could be of clinical importance for the prevention of proximal caries.

The effect of post-brushing water rinsing on fluoride retention in plaque and saliva

Another interesting observation in Paper I was that post-brushing water rinsing had a negative effect on fluoride retention in the proximal area. Water rinsing immediately after brushing with high-fluoride toothpaste reduced the fluoride concentration in proximal saliva by 2.4 times. The difference between high-fluoride toothpaste with water rinsing and standard toothpaste without rinsing, in terms of the fluoride concentration in saliva, was therefore small and not statistically significant. Several earlier studies have shown that intra-oral levels of fluoride in saliva may differ in subjects with different post-brushing rinsing and spitting habits (Collins et al., 1991; Duckworth et al., 1991; Richards et al., 1992; Sjögren & Birkhed, 1994; Attin et al., 1996; Sjögren & Melin, 2001). Similarly, Issa & Toumba (2004) found that, by avoiding water rinsing, particularly in adults, the salivary fluoride level can remain high up to 2 h post-brushing. In addition, a recent study by Duckworth et al. (2009) supports the recommendation that mouth rinsing with water after brushing should be kept to a minimum in order to increase fluoride retention. Post-brushing water rinsing may also affect caries increment. As a result, individuals who rinse with large volumes of water have higher caries increment than those using smaller volumes (Chester et al., 1992; O'Mullane et al., 1997; Chestnutt et al. 1998). On the other hand, Machiulskiene et al. (2002) found no significant benefit from refraining from water rinsing after tooth-brushing in their 3-year clinical study. However, this study showed relatively large numbers of dropouts (32%) and differences in compliance. The combination of high-fluoride toothpaste and no post-brushing water rinsing in Paper I produced the highest fluoride concentration in plaque and saliva. This combination was recently evaluated in relation to enamel demineralisation, in an in situ caries model with orthodontic bands, and resulted in less QLF average change in fluorescence after 8-9 weeks (Al-Mulla et al., 2010a). In Study III, 74% of the adolescents rinsed with water after tooth-brushing. There was a difference in caries increment between those who rinsed and not rinsed with water after brushing, but the difference was not statistically significant. Nevertheless, the post-brushing water rinsing was not the primary outcome in this Paper. The evidence from studies mentioned above and clinical data from Paper I suggest that post-brushing water rinsing tends to have a negative effect on fluoride concentration in proximal plaque and saliva. These findings support the recommendation to refrain from post-brushing

water rinsing in order to increase oral fluoride retention. High fluoride toothpaste is not available in every country and, as a compromise, standard toothpaste could be used but without post-brushing water rinsing to optimise the effect of fluoride in caries prevention.

The effect on de novo plaque formation

The main result in Paper II was that high levels of fluoride in toothpaste slurries reduced the formation of new dental plaque on tooth surfaces. Significantly less plaque was scored for toothpaste slurry with 5,000 ppm fluoride and for water solutions with 1.5% SLS. This is in line with Baysan et al. (2001) who observed that the plaque index after 3 and 6 months was significantly lower in a 5,000 ppm fluoride group compared with a 1,100 ppm fluoride group. In contrast, van Loveren et al. (1995) found that fluoride dentifrice does not affect plaque composition, or fluoride tolerance, or the acidogenicity of MS. Similarly, Lynch et al. (2004) concluded that the fluoride level in 1,500 ppm toothpaste is insufficient to interfere with bacterial growth and metabolism. Both fluoride and SLS in dentifrices are usually regarded as weak plaque inhibitors. Bacteria attached to surfaces are embedded in a matrix and grow to form biofilm. In this mode of growth, bacteria often show reduced susceptibility to antimicrobials and a higher concentration of these compounds is needed (ten Cate, 2006a). In Study II, the fluoride concentration was 5,000 ppm, 3.5 times higher than that in a standard dentifrice, and the rinsing procedure was extended from 2 to 3 times a day. Furthermore, it has been reported that the penetration of fluoride into plaque biofilm increases with the duration of fluoride exposure (Watson et al., 2005).

An experimental period of 4 days may initially be regarded as too short to detect major differences in de novo plaque formation for weak plaque inhibitors. The plaque-inhibiting effect of a high-fluoride dentifrice observed by Byasan et al. (2001) was actually detected after a period of 3 and 6 months. It has been suggested that intra-oral fluoride reservoirs may take weeks to “fill”, possibly due to the time taken for the establishment of a steady-state fluoride concentration in plaque (Duckworth et al., 1991). On the other hand, according to Furuichi et al. (1996), and Ramberg et al. (1996), no major difference was observed in plaque formation after 4 or 14 days with no mechanical cleaning. Similarly, Claydon & Addy (1995) reported that even a 24-hr plaque re-growth study design using conventional measurements of plaque accumulation could be useful as a rapid method of screening potential inhibitory

agents. From an ethical point of view, it is preferable to use a short experimental period since the subjects had to refrain from all oral hygiene.

Fluoride in saliva and plaque may also interact with the bacterial metabolism. According to Bradshaw et al. (2002), fluoride exerts dual antimicrobial effects in microbial communities by reducing overall acid production and by reducing the selection of acid-tolerating species such as MS. In addition, Fernanda et al. (2006) reported that SLS alone and in combination with NaF reduces bacterial viability, lactate formation and extracellular polysaccharide formation both in vitro and in vivo. It was also reported that SLS and NaF in combination had additive effects. The viability of bacteria in newly formed plaque may therefore be of some interest. Dental plaque bacteria form complex, robust cell aggregates which cannot be counted accurately using epifluorescence microscopy and this causes a problem when quantifying their viability. Welin-Neilands & Svensäter (2007) tested the acid tolerance of MS by exposing biofilm cells to pH 3.5 for 2 hr and then counting the number of survivors by plating on blood agar. The result showed that the presence of NaF (0.5 M) inhibited the acid tolerance, with 77% fewer viable cells as a consequence. However, 0.5 M NaF corresponds to 9,500 ppm fluoride, almost twice as high a concentration as in high-fluoride toothpaste. Consequently, further studies evaluating the viability of bacteria in newly formed plaque after using high-fluoride dentifrice are needed.

The preventive effect on caries incidence and progression in caries-active adolescents

The main result in Paper III was that caries-active adolescents using high-fluoride toothpaste showed 40% less caries progression compared with those using standard toothpaste. Twenty-eight per cent of the adolescents had “poor compliance” and brushed irregularly. The high-fluoride toothpaste resulted in 42% less new caries lesions among caries-active adolescents with “poor compliance” compared with those with “excellent compliance”. The data indicate that high-fluoride toothpaste has a greater impact on individuals who do not use toothpaste regularly or do not brush twice a day. Thus, high-fluoride toothpaste is an excellent home care treatment for adolescents with irregular brushing habits and high caries risk.

Another interesting observation was that adolescents with a high caries risk did not brush their teeth every day and especially not twice a day. This result is in accordance with earlier findings. Two independent studies by Klock et al. (1989) and Koivusilta et al. (2003) found

that 25% of 14-year-old adolescents do not use toothpaste regularly. Hugoson et al. (1995) reported that the percentage of 15-year-olds who brushed their teeth twice a day had decreased from 89% to 78% between 1983 and 1993. During the same period, the percentage of 15-year-olds who brushed just “now and then” had increased from 1% to 5%. The caries increment in subjects who brushed once a day was 20-30% higher than in those who brushed twice a day, in three separate 3-year clinical trials (O’Mullane et al., 1997; Chester et al., 1992; Chestnutt et al., 1986). In Study III, we found that 60 subjects (28%) had “poor compliance”. In addition, there were twice as many boys as girls in this group and the adolescents most commonly “forgot to brush their teeth in the evening” (49%).

In a systematic review, Pitts (1983) reported that, for the majority of individuals, the progression of small proximal caries lesions is a slow process, with a large number of lesions remaining unchanged for long periods. This was also confirmed by Mejäre et al. (1999). The medium survival time for proximal enamel lesions among Swedish adolescents in the 1990s was more than 5 years, while the corresponding figure for dentine lesions was 3.2 years (Gustavsson et al., 2000). As a result of this slow progression rate of proximal caries among Swedish adolescents, it is possible to question the experimental period of 2 years. However, from a practical point of view, it is preferable to use a short study period. At this time point, adolescents are graduating from school and they are moving from the city of Varberg in order to study elsewhere. Another year of observation might have increased the dropouts. According to Chester et al. (2002), the length of clinical studies could be reduced from the conventional 3 years to 2 years. In addition, Stookey et al. (2004) reported a difference in caries increment between toothpaste containing 1,100 and 2,500 ppm fluoride after 2 years.

In some respects, digital radiographs are more difficult to perform compared with conventional radiographs, especially in young patients. The film holders are harder and thicker and it is easy to miss the distal surfaces of the canines in the upper jaw and especially in the lower jaw. In the present study, we therefore decided to exclude the distal surfaces of the canines. Few studies have compared digital and conventional radiographs. However, Wenzel (2004; 2006) reported only non-significant differences between the two methods. Recently, a new digital technique has been introduced and Martignon et al. (2006) reported that digital subtraction radiography appears to be the most sensitive method for assessing the progression of caries lesions. This method could have been used in the present study if we had been familiar with the technique in 2003.

The effect of a third application of toothpaste, including a “massage” method, on fluoride retention and pH drop in plaque

In overall terms, Paper IV confirmed the result found in Paper I that a high content of fluoride in the toothpaste increased the fluoride retention in both saliva and plaque. The highest mean peak saliva fluoride concentration were found using toothpaste with 5,000 ppm fluoride and differed significantly from those with 1,450 ppm. Brushing with high-fluoride toothpaste 3 times a day resulted in 3.6 times higher fluoride concentration in saliva compared to a standard paste twice a day. The corresponding difference in plaque was 2.2 times (NS) and one explanation could be that fluoride continues to accumulate over time. In the present study, the number of subjects was small and the experimental period was relatively short to reveal significant differences in plaque fluoride levels. According to Duckworth & Morgan (1991), the intra-oral fluoride reservoirs in plaque may take several weeks to “fill”. This view was also supported by Lynch et al. (2004); showing that the fluoride concentration in plaque after brushing was still increasing four weeks after commencing the use of the fluoride toothpaste and a further elevation was seen after eight weeks. Tenuta et al. (2009) even suggested that “fluoride uptake by dental plaque not removed by brushing may be the main cause of the anticaries effect of dentifrices”. In conclusion, it is generally agreed that even small increases in post-brushing concentrations of fluoride in saliva and plaque can have a marked effect on both experimental caries lesions and caries clinically (Duckworth et al., 1989; ten Cate, 1999; Duckworth et al., 1992; Lynch et al., 2004).

On the other hand, increasing the frequency of fluoride application, from twice a day to 3 times a day, increased the fluoride retention in plaque significantly, when the two methods for application 3 times a day were pooled. This finding is consistent with Watson et al. (2005), who found that the penetration of fluoride into plaque appears to increase with the duration of fluoride exposure. Moreover, there was a suggestion of a positive association between the accumulation of fluoride in proximal plaque and the fluoride concentration in the toothpaste in the “pooled analysis”. Similarly, Duckworth et al. (1989) showed that plaque fluoride increased with increasing fluoride content in the dentifrice and an increasing frequency of dentifrice use. In general, fluoride toothpaste is recommended for brushing twice a day; in the morning, after breakfast, and in the evening, before bedtime. From a cariological point of view, it is interesting to evaluate the effect of a third application of fluoride dentifrice,

especially as the manufacturer recommends the 5,000 ppm toothpaste (Duraphat) for brushing “3+3+3”, i.e. 3 min, 3 times a day, for 3 months. As mentioned earlier, the frequency of brushing has a significant association with caries prevalence, according to a number of researchers (Chester et al., 1992; O’Mullane et al., 1997; Chestnutt et al., 1998; Marinho et al., 2003). However, most studies deal with the difference between brushing once a day vs. twice a day and not twice a day vs. 3 times a day, as in the present study. On the other hand, individuals who need extra fluoride therapy may not be motivated to brush their teeth up to 3 times per day.

A new concept of using fluoride toothpaste was introduced in this thesis. Brushing with 5,000 and 1,450 ppm toothpastes, twice a day plus the “massage” once a day, resulted in the same fluoride concentration in saliva and plaque as brushing 3 times a day with the same paste. Using toothpaste as a “lotion” to massage the buccal surfaces with the fingertip may be a simple and inexpensive way of delivering fluoride a third time during the day, tentatively at lunchtime. It is easy to carry a small package of dentifrice, apply toothpaste on the fingertip, massaging the buccal surfaces and then spitting out the slurry. The basic idea is also consistent with Seppä et al. (1997), who showed that “just rinsing with a toothpaste water mixture (without using a toothbrush) appears as a good alternative for adults who need extra fluoride therapy”. Nevertheless, it should be pointed out that the “massage” method should not replace brushing the teeth morning and evening.

The pH falls after rinsing with 10% sucrose were found to be somewhat more pronounced for the standard dentifrice (No 4-6) compared with the high-fluoride toothpaste (No 1-3), but no statistically significant differences were found. The presented method of measuring plaque pH with the microtouch method has been evaluated by Lingström et al. (1993). The volunteers in the latter study were asked to avoid tooth-brushing and all oral hygiene measures for 3 days. However, the subjects in the present study were participating in six different brushing regimens and they could therefore only avoid cleaning their teeth proximally by no flossing. Moreover, the volunteers were dental students and the amount of visible proximal plaque was not so extensive. All these factors may have influenced the plaque-pH values and they showed a considerable variation within individuals but also between individuals. In conclusion, further long-term studies are needed to evaluate the effect of a third application of high-F toothpaste and the “massage” method on dental caries clinically.

Methodological and Ethical Considerations

It should be noted that, in Paper I, no plaque weight data were available for 10 subjects of 26 and the accumulated fluoride in the extracted plaque suspension was measured and expressed only as ppm fluoride. In addition, the toothpaste slurries in Paper II could not be provided without SLS and it was therefore impossible to identify the separate effects of high-fluoride and SLS on de novo plaque formation. Furthermore, the toothpaste slurries in Paper II (Series I) and the dentifrices in Paper III could not be provided in blind packages and these studies were consequently only single-blind (blind to the observer).

The clinical routine in Paper III was to provide adolescents with fluoride varnish (Duraphat, 22,500 ppm F) once a year at the yearly examination. Subjects with extremely high caries progression ($\approx 10\%$) were recalled after 6 months for new radiographs and were then given a second fluoride varnish application. Subjects with “poor” compliance then had a significantly lower caries incidence and it could be argued that these subjects were the same as the 10% that were treated with fluoride varnish a second time. Consequently, the effect on caries incidence in this group might have been due to the second treatment with fluoride varnish. However, this fact was re-checked afterwards and no such connection was found. In actual fact, 19 subjects of 60 with “poor compliance” were treated with fluoride varnish a second time and 41 subjects were not.

In Paper III, 68 adolescents (24%) were regarded as dropouts. The most common reasons for not completing the clinical study were orthodontic treatment, no wish to participate, or moved from the area. Adolescents with a high caries risk are not easy to manage, as they miss their appointments more frequently and 11 subjects were excluded for this reason.

From an ethical point of view, it was necessary to provide caries-prevention strategies for patients with a high caries risk in Paper III. Nowadays, fluoride varnish treatment (Duraphat) is a common preventive method and, applied at school or at the dental clinic, it is the only fluoride therapy that is independent of the patient’s co-operation. As mentioned earlier, the clinical routine was to provide adolescents with fluoride varnish once a year at the yearly examination. Subjects with extremely high caries progression ($\approx 10\%$) were recalled after 6 months and were then given a second fluoride varnish application. The prevented fraction, for 5,000 ppm toothpaste, might have been larger if the application of fluoride varnish once or

twice a year could have been excluded. However, this was impossible from an ethical point of view.

Clinical Implications

Adults and adolescents aged 16 years, with a high incidence and progression of coronal/root caries as a result of behavioural and/or medical/physical disabilities should be advised to brush twice a day or preferably three times a day with high-fluoride toothpaste as part of a preventive programme. Adolescents in particular run a certain caries risk when their teeth just have erupted and it is especially important to avoid new caries lesions during this risk period. Thus, high-fluoride toothpaste is an excellent home care treatment for adolescents with high caries risk. High-fluoride toothpaste has also been recommended for optimal caries prevention strategies during orthodontic treatment (Derks et al., 2004). However, the high-fluoride toothpaste and the presented alternative method of application are also interesting for the elderly. Whether living at home, or in residential care homes, elderly people run an increased risk of developing coronal/root caries, owing to functional dependence and cognitive impairment. One recommendation could be to encourage carers to assist in tooth-brushing and to use high-fluoride toothpaste. The “massage” method, using toothpaste as a “lotion” and massaging the buccal surfaces with the fingertip, may be another simple and inexpensive way of delivering fluoride a third time during the day, especially in residential care homes.

Standard fluoride toothpastes are insufficient for some individuals. High-fluoride toothpaste has a clear role in prevention of dental caries; targeting those at the greatest risk, reducing and arresting caries lesions and thereby reducing the need for operative treatment in caries-active adolescents. Methods for caries prevention should be easy to manage. Changing dentifrice and refraining from post-brushing water rinsing are examples of easy actions of this kind. Furthermore, using toothpaste as a “lotion” to massage the buccal surfaces with the fingertip may be a simple way of delivering fluoride a third during the day, tentatively at lunch time. On the other hand, it should be pointed out that the “massage” method should not replace brushing the teeth in the morning and evening.

Conclusions

- High-fluoride toothpaste (5,000 ppm) without post-brushing water rinsing increased the fluoride concentration in proximal saliva more than two times, compared with standard toothpaste (1,450 ppm), also without rinsing (Paper I).
- Water rinsing immediately after brushing with high-fluoride toothpaste reduced the fluoride concentration in proximal saliva more than two times, which supports the recommendation to refrain from post-brushing water rinsing (Paper I).
- Toothpaste slurry containing 5,000 ppm fluoride reduced the formation of new dental plaque on tooth surfaces (Paper II).
- Caries-active adolescents (14-16-year-olds) using high-fluoride toothpaste had 40% lower progression of caries compared with those using standard toothpaste (Paper III).
- Brushing with high-fluoride toothpaste resulted in 42% less new caries lesions among caries-active adolescents with “poor compliance” compared with those with “excellent compliance”. Thus, high-fluoride toothpaste is an excellent home care treatment for adolescents with irregular brushing habits and high caries risk (Paper III).
- Brushing with high-fluoride toothpaste three times a day increased the fluoride concentration in saliva almost four times compared with standard toothpaste twice a day. The fluoride retention in plaque increased significantly as well (Paper IV).
- Using toothpaste as a “lotion” to massage the buccal surfaces with the fingertip may be a simple and inexpensive way of delivering fluoride a third time during the day, tentatively at lunch time (Paper IV).

Clinical Advices

- Make sure that fluoride toothpaste is used at least twice a day, after breakfast and just before bedtime.
- Select toothpaste with a fluoride concentration corresponding to the needs and use it in an optimal way.
- Refrain or minimize the post-brushing water rinsing for optimal fluoride retention.
- Increase the brushing to three times a day or use the toothpaste as a “lotion” to massage the buccal surfaces with the fingertip as the third application.

Svensk Sammanfattning

- Högfluortandkräm (5,000 ppm) utan vattensköljning ökade fluorhalten i approximal-saliv mer än två gånger jämfört med vanlig tandkräm (1,450 ppm) utan sköljning (Studie I).
- Vattensköljning efter tandborstning med högfluortandkräm reducerade fluor-koncentrationen i saliv mer än två gånger, vilket stöder rekommendationen att undvika vattensköljning efter tandborstning (Studie I).
- ”Tandkrämsslurry” med 5,000 ppm fluor minskade nybildningen av dentalt plack (Studie II).
- Kariesaktiva ungdomar (14-16 år) som borstade tänderna med högfluortandkräm hade 40% lägre kariesprogression jämfört med dem som borstade med vanlig tandkräm (Studie III).
- Högfluortandkrämen gav 42% färre nya kariesskador hos ungdomar med dålig följsamhet, jämfört med de med god följsamhet. Resultatet indikerar att tandkrämen fungerar bättre för kariesaktiva ungdomar som inte ”sköter sig” och borstar tänderna oregelbundet (Studie III).
- Högfluortandkräm tre gånger per dag gav nästan fyra gånger högre fluorkoncentration i saliv jämfört med vanlig tandkräm två gånger per dag. Fluorretentionen i plack ökade också signifikant (Studie IV).
- Att använda tandkräm som en ”salva” och massera tändernas framsidor med fingret kan vara ett enkelt sätt att tillföra fluor en tredje gång per dag, förslagsvis efter lunch (Studie IV).

Kliniska Råd

- Använd fluortandkräm minst två gånger varje dag, efter frukost och före sänggåendet. Fuska inte!
- Välj tandkräm med en fluorkoncentration som motsvarar behovet och använd den på rätt sätt för optimalt effekt.
- Undvik eller minimera vattensköljning efter tandborstning för ökad fluorretention.
- Borsta tänderna en tredje gång per dag eller använd tandkrämen som en ”salva” och massera tändernas framsidor med fingret som den tredje applikationen.

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Tandkrämsenkät

Patientnummer _____

• Kön: Tjej Kille

• **Varför tycker du att man ska borsta tänderna? Du kan kryssa i flera rutor**

Undvika ”hål” Undvika blödande tandkött Vet inte
 Fräsch andedräkt Rena tänder Det är inte så viktigt

Kommentar:

• **Hur ofta borstar du tänderna?**

Aldrig Flera gånger/månad Flera gånger/vecka
 Varannan dag Varje dag (se nästa fråga)

Kommentar:

• **Du som borstar tänderna ”Varje dag” Hur många gånger per dag borstar du?**

Mer än två gånger Två gånger En gång

Kommentar:

• **Ibland glömmar man att borsta tänderna. När glömmar du?**

på morgonen på kvällen jag glömmar sällan

Kommentar:

• **Använder du din ”studietandkräm” när du borstar tänderna?**

Ja Nej Ibland

Kommentar:

• **Hur mycket tandkräm lägger du på tandborsten?**

Två cm En cm En halv cm

Kommentar:

• **Hur länge borstar du tänderna?**

- 10sek 30sek 1min 2min mer än 2min

Kommentar:

• **Sköljer du munnen med vatten efter tandborstning?**

- Ja Nej

Kommentar:

• **Hur många gånger sköljer du munnen med vatten efter tandborstning?**

- Flera gånger Två gånger En gång Sköljer inte

Kommentar:

• **Använder du mugg eller handen för att skölja munnen med vatten efter tandborstning?**

- Ja Nej

Kommentar:

• **Hur tycker du tandkrämen smakar?**

- Mycket bra Bra Godkänt Mindre bra Äckligt

Kommentar:
