Effect of Regular Fluoride Gel Application on Incipient Carious Lesions

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Objectives: To evaluate the efficacy of weekly supervised tooth-brushing with a toothpaste and a 1.23% acidulated phosphate fluoride gel (APF) gel on white lesion reversal to treat incipient enamel lesions.

Design: A double-blind and randomized controlled trial.

Sample and Methods: Three-hundred seven to 12-year-old Brazilian schoolchildren who presented with white spots on the buccal surfaces of permanent upper incisors were randomly allocated to three groups. In group I, children underwent supervised tooth-brushing and APF gel (1.23%) for one minute once a week. In group II, children were subjected to a weekly supervised tooth-brushing and a topical application of placebo, whereas group III (control) received no intervention. An expert dental examiner performed all intra-oral examinations for dental caries (DMF-s and dmf-s) and oral hygiene (Visible Plaque Index, Gingival Blood Index).

Results: After three months, 258 children and 460 lesions were analyzed. The results of the clinical evaluation of arrested white spots did not differ significantly (p = 0.95) between the two experimental groups (57.9% in group I and 56.8% in group II) but differed significantly between them and the control group (p = 0.022). Logistic regression analysis identified gingival blood index (OR = 1.70, CI = 1.13 – 2.55), DMF – s^2 (OR = 1.61, CI = 1.07 – 2.43) and number of white spot lesions (OR = 1.76, CI = 1.04 to 2.98) as independent 'risk' factors for white spot lesion activities. On the other hand, supervised tooth-brushing with APF (OR = 0.55, CI = 0.34 – 0.91) or without APF (OR = 0.58, CI = 0.35 – 0.94) was a protective factor.

Conclusions: These results suggest that the weekly supervised tooth-brushing was able to arrest enamel white spots and that poor oral hygiene increases the probability of keeping white spots active.

Key words: acidulated phosphate fluoride, dental caries, enamel demineralization, randomized controlled trial

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Several studies have shown that dental caries is a disease that still affects millions of people in Brazil and the world – despite evidence of its decline over the past decades (Marcenes and Bönecker, 2000; Petersson and Bratthall, 1996). According to a national epidemiological survey performed in 1986, the DMFT index of 12-year-old children was 6.7 and was reduced to 3.06 ten years later (1996) (Marcenes and Bönecker, 2000). However, it is important to point out that the level of dental caries continues to be high in low income and low educational level populations (Dini et al, 2000; Gibson and Williams 1999; Gillcrist et al, 2001).

This disease consists of a dynamic and remineralizing process resulting from microbial metabolism on the tooth surface, which may result in a net loss of minerals over time and possibly, but not always, lead to cavities. The clinical features of dental caries may vary from a white spot to a cavity. Regardless of their size or depth, it is important to assess the activity of lesions because active lesions require different treatments and have a different prognosis.

Today, it is known that operative dentistry does not stop the progression of the disease, so that something else needs to be done. Thus, fluoride has emerged as a conservative therapeutic option in order to decrease the speed of tooth decay, preventing the demineralisation process and arresting developed lesions. According to the 'Recommendations for using fluoride to prevent and control dental caries in the United States' (2001), fluoride is needed throughout life to prevent and control dental decay, and the use of fluoride can lead to a reduction of public and private expenditures.

Since the main mechanism of action of tooth decay occurs at the tooth-plaque interface, several topical clinical methods for the prevention of caries have been developed, such as toothpastes (Bartizek et al, 2001), mouth rinses (Petersson et al, 1998) varnishes (Marinho et al, 2003) and gels (Marinho et al, 2003). For preventive purposes, gels have been used at low concentrations and at high frequency or at high concentrations and at low frequency. However, when gels are used for therapeutic purposes, i.e. for the treatment of disease, some authors have recommended topical methods with high concentrations and a higher frequency of use, specifically four to eight weekly or fortnightly sessions (Clarkson and Fejerskov, 1988), or even daily sessions (De Paola, 1993).

However, although the action of acidulated phosphate fluoride (APF) gel has been confirmed in *in vitro* studies (Takagi et al, 2000; Tandon and Mathew, 1997) with respect to the formation of fluoride and its remineralising ability, no reports are available about randomised controlled clinical trials for the determination of how often and for what period of time fluoride should be applied for the remineralisation of early caries lesions (Bader et al, 2001).

The purpose of the present study was to assess the effects of weekly supervised tooth-brushing and a 1.23% APF gel on white lesions reversal after eight weeks and the influence of hygiene oral, caries experience, age and sex on outcome after this period.

MATERIALS AND METHODS

Selection Process

The present clinical trial was conducted in 2001 on seven to 12-year-old children living in Natal in the north west of Brazil, where drinking water contains no fluoride. The children were recruited from 25 schools located in the suburbs and the socioeconomic status of their families was relatively homogeneous and low (an income of approximately US$115 per month). Children eligible for this study were those with good overall health, but with high risk of caries and with white spots on the buccal surfaces of the permanent upper incisors. Children wearing orthodontic bands and using antimicrobial solutions were excluded. The parents received a letter explaining the study with an informed consent form to be signed and returned and the study was approved by the Clinical Research Ethics Committee of the Federal University of Rio Grande do Norte.

Required Sample Sizze

A pre-test was conducted on 90 children with 130 lesions. After seven to eight weeks of supervised tooth-brushing and fluoride application the incidence of active lesions was 55% in the group supervised brushing with a non-fluoridated dentifrice (23/42), 58% in the group supervised brushing with a placebo gel (22/38) and 74% in the control group (37/50). Assuming that the difference in incidence between the experimental and the control groups would be close to 20%, $\alpha = 0.05$ and $\beta = 0.20$, the sample size for each group was 88 children with at least one lesion.

Examination Methods

Personal data of the children were recorded and a calibrated examiner performed an intra-oral examination for dental caries, oral hygiene and gingival condition. The children were assessed by visual-tactile examination by three experienced dentists and were included in the study only when the three examiners agreed about the active white spots. Five percent of the children were re-examined to measure intra-examiner reliability for white spots evaluation (Kappa value). The percentage of agreement for the diagnosis of active and inactive white le-

Fig 1 Active white lesion under plaque.

Fig 2 Active white lesion.

sions was 85% and the Kappa value was 0.62. They were examined in schools under natural daytime light in an open place with the aid of a mouth mirror and a dental and periodontal explorer. Oral hygiene was assessed by recording the visible plaque index (VPI) (Ainamo and Bay, 1975) and gingival blood index (GBI) (Ainamo and Bay, 1975). The percentage of plaque and bleeding sites after probing was calculated for each child. The plaque score was recorded at the beginning and at the end of treatment. The clinical diagnosis of caries was made after cleaning and drying the surface prior to examination. Dental caries were recorded using the criteria described by the World Health Organization (1997) for the classification of tooth surface caries status, as follows: decay, missing-due-to-decay (or extraction advised), or filled permanent and primary surfaces (DMFS and dmfs). An individual DS index was computed using two diagnostic thresholds: D1 for 'caries of enamel and dentin' and D2 for 'white spots' lesions (Kingman and Selwitz, 1997). The length of white spots was recorded. The Cohen Kappa coefficient of agreement for the DMFS scores was 0.82. The effect of the children's diet was not investigated in detail in this study for proper analysis.

Experimental Procedures

Children were randomly allocated to one of three groups by the coordinating centre, which was unaware of subject characteristics. Group I received supervised brushing with a non-fluoridated dentifrice plus seven or eight applications of APF therapy at weekly intervals. After brushing, the teeth were isolated with dry cotton rolls and 1.23% gel was applied to all teeth with a cotton swab. After one minute, the children were instructed to spit out excess gel. Children in group II performed weekly supervised brushing and placebo gel was applied with the same technique as that used in group 1. The gel without fluoride and pH neutral displayed the same characteristics (color, taste, consistency) as those of the fluoridated gel. No intervention was made on group III.

Fig 3 Inactive white lesion.

Trained professional who were unaware of the gel they were applying (with or without fluoride) performed all applications working at the schools. After seven or eight weeks, the evaluation of white spots was performed without the examiners knowing to which group the children belonged. When the buccal surface was white, opaque, rough and frequently with plaque (Fig 1 and 2), it was diagnosed as having active caries. On the other hand, when the surface appeared smooth, hard and glossy (Fig 3), the lesion was diagnosed as inactive caries (Nyvad et al, 1999).

Statistical Analysis

Dichotomous variables were compared at baseline using the chi-square test and one-way ANOVA or the

Table 1 Baseline number of dichotomised variables per group

VARIABLE	CATEGORY	*GROUP*						TOTAL		P*
		I		II		III				
		N	%	N	%	N	%	N	%	
GENDER	M	78	61.9	86	65.2	88	60.3	252	62.4	0.697
	F	48	38.1	46	34.8	58	39.7	152	37.6	
AGE	7–9	62	49.2	64	48.5	82	56.2	208	51.5	0.364
	10–12	64	50.8	68	51.5	64	43.8	196	48.5	
LENGTH	Cervical	107	30.4	122	34.7	123	34.9	352	88.9	0.235
	Beyond cerv.	14	31.8	10	22.7	20	45.5	44	11.1	
N.LESION	2	74	33.6	72	32.7	74	33.6	220	54.5	0.585
	3	24	25.0	32	33.3	40	41.7	96	23.8	
	4	28	31.8	28	31.8	32	36.4	88	21.8	
TOTAL		126	100	132	100	146	100	404	100	

p *: Chi-square test

Kruskal-Wallis test for continuous variables. Two-way ANOVA was used to compare the initial and final plaque index among the groups and multiple comparisons were made using the Tukey honest significant difference test (HSD).

The association between the presence of white lesions after treatment and gender, age, plaque visible index, plaque located on a surface with lesion, gingival blood index, DMFS[1], DMFS[2], dfs, DS, and number and location of white spots was calculated by the chi-square test and by multiple logistic regression analysis. The Hosmer-Lemeshow test was used to verify the goodness-of-fit of the model. The continuous variables were dichotomized using the median value as the cut-off point.

RESULTS

Sample Size after three Months

Of the 300 children studied, 258 were available after 3 months (attrition rate of 14%), with 126 lesions in group I, 132 in group II and 146 in group III (Table 1).

BaselineBalance among Groups

There were no significant differences in baseline characteristics among groups (Tables 1 and 2).

Outcome Variable

Fig 4 shows that group III had the highest percentage of active white lesions after three months' follow-up. Fig 5 shows that there was a significant decrease in plaque index for groups I and II, but not for group III. Groups I and II showed similar results. The number of necessary treatments (NNT) was 6.8.

Multivariate Analysis

Table 3 shows the results of multiple logistic regression analysis. The significant factors associated with the presence of white lesions by the third month were group, gingival bleeding, DMFS[2] and number of white lesions higher than three at the beginning of treatment.

Table 2 Baseline means of continuous variables per group

INDEX	GROUP						P
	I		II		III		
	Mean (sd)	min/max	Mean (sd)	min/max	Mean (sd)	min/max	
VPI	39.2 (19.9)	6–82	43.7 (19.0)	10–91	40.3 (19.4)	2–82	0.160 (A)
GBI	14.3 (11.2)	0–43	16.4 (14.8)	0–70	13.3 (9.9)	0–46	0.829 (K)
DMFdmf	15.2 (11.7)	2–56	14.5 (7.9)	3–38	15.0 (8.3)	3–41	0.357 (K)
DMF1	5.8 (5.3)	0–18	6.9 (7.6)	0–37	6.6 (6.1)	0–26	0.802 (K)
DMFS2	8.8 (5.4)	2–21	10.0 (8.2)	2–39	9.8 (6.2)	2–28	0.649 (K)
Dmfs	1.8 (0.4)	1–2	1.5 (0.5)	1–2	1.5 (0.5)	1–2	0.201 (K)
N. CARIES	11.2 (11.4)	0–56	11.8 (8.3)	0–38	11.0 (8.3)	0–32	0.129 (K)

A: Analysis of Variance (ANOVA one way) or K: Kruskal-Wallis test.

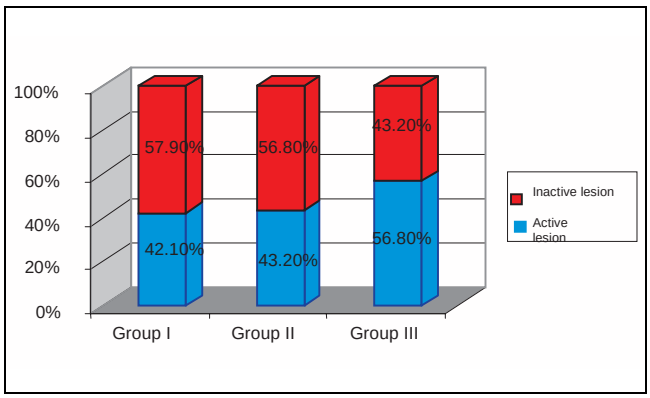

Fig 4 Percentage of active and inactive white lesions at month 3 in each group.

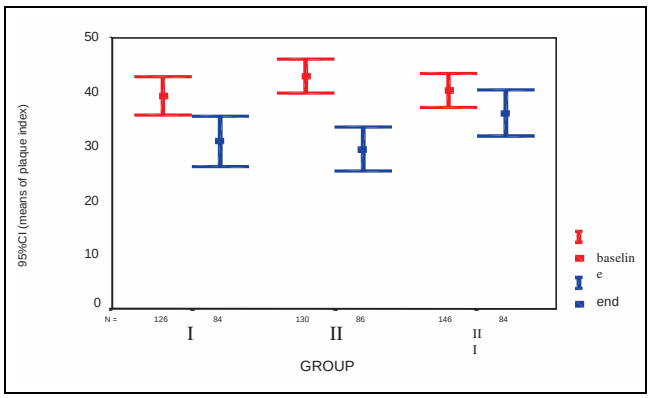

Fig 5 Means of plaque index between baseline and the end of treatment.

DISCUSSION

The weekly supervised tooth-brushing treatment trial led to an important reduction of active white spots (14%) after 8 weeks. In this study, no additional benefit was observed after treating the buccal enamel white spots with APF, which means that tooth-brushing was likely to be a major determining factor of the arrest of the white spots. Although many factors are involved in this process, the reduction of local microbial activity was probably the most important one regarding the results observed.

These results agree with reports (Artun and Thylstrup, 1986; Holmen et al, 1987, 1987) that confirmed that the simple mechanical removal performed by daily brushing over a period of one month was enough to arrest the enamel demineralization produced by the biofilm accumulated on orthodontic brackets. During the clinical examinations it was possible to verify the arrest of white spots, since at that point they were glossy and hard, leading them to conclude that such an appearance was rather due to the abrasion caused by brushing than to mineral re-aggregation.

It is important to point out that the children investigated in this study had a high decay index (DMF – s = 9.5) and poor oral hygiene (IPV = 41.0%, ISG = 14.6) which may have contributed to the low rate of white spot reversals (around 50%). It would also be expected that a longer time of treatment might have led to a larger number of inactive lesions since the plaque index was declining. In addition, a longer time of fluoride treatment might have induced additional benefits.

Table 3 Logistic regression model for status of white lesions at the third month of examination

Variable	Category	OR overall	IC (OR overall)	Adjusted OR	IC (adjusted OR)	*p*
Group	I	0.55	0.33–0.92	0.55	0.34–0.91	0.020
	II	0.58	0.35–0.95	0.58	0.35–0.94	0.028
	III	1.00				
Gingival bleeding (GBI)	High	1.71	1.13–2.60	1.70	1.13–2.55	0.010
	Low	1.00				
DMFS[2]	High	1.80	1.18–2.73	1.61	1.07–2.43	0.022
	Low	1.00				
No. of white lesions	2	1.00				
	3	1.16	0.70–1.93	1.04	0.63–1.71	0.874
	4	1.99	1.17–3.40	1.76	1.04–2.98	0.033
Hosmer-Lemeshow test: $p = 0.5263$						

Biesbrock, Faller, Bartizec, Court and McClanahan (1998) compared two different dentifrices (sodium- and stannous fluoride-based) with a control group (brushing with a fluoride-free dentifrice). After a two-year follow-up, they observed a significant difference in the reversal of initial lesions between the experimental group and the control group, even though the latter showed a high level of reversal. These results indicated that fluoride at low concentrations and at a high frequency can be an important factor in reversing caries in combination with daily brushing.

Concerning the therapeutic effects of fluoride at high concentrations and low frequency, such as the APF gel, Johnston and Lewis (1995) and Mainwaring and Naylor (1978) and conducted studies on children that had been receiving semi-annual fluoride applications for three years. These authors were unable to identify a significant effect on the average reversal of dental caries. According to them, reversals of diagnosis were low and accounted for less than 5% of the observed increments. Despite the long period of treatment, the low frequency of intervention and the high prevalence of baseline caries (DMFS = 8) seem to explain the ineffectiveness of the method in reversing the pre-existing caries lesions.

In the present study, the effect of dental plaque on white spots was clearly demonstrated by the strong association found between the variables 'plaque visible index' ($p < 0.001$), 'located plaque' ($p < 0.001$), 'gingival blood index' ($p = 0.009$) and active enamel caries activity in the groups with two lesions. This implies that better oral hygiene – i.e., a lower plaque index and fewer tooth surfaces harboring plaque – are rather more related to inactive than active lesions.

According to similar results obtained by Ravald and Birkhed (1991), the plaque score was significantly correlated with active root caries activity when analyzing the relationship between root carious lesions deemed either clinically active or inactive and a number of variables believed to be related to root caries in patients referred for treatment of periodontal disease. Similarly, Backer Dirks (1966) and Carvalho (1992) considered the altered environmental conditions to be mainly the result of better usage of the fully erupted teeth, thereby promoting natural removal of bacterial deposits.

It should be noted that in the present study the children were instructed to maintain oral hygiene as usual, i.e. tooth-brushing with a fluoride toothpaste. However, this should not be regarded as a 'bias', since all groups followed the same procedure.

The improvement in oral hygiene during follow-up was verified in all groups ($p < 0.05$). The experimental groups (I and II) showed better results com-

pared to control (III). This might have been the key point for the decline in the control group. It is important to state that of the children who continued to show active white spots, only 27% had a low plaque index at the end of the treatment, against 73% who had inactive white spots. The results showed that the children with higher plaque levels had three times the chance to continue with their active lesions.

Although several studies have previously investigated the caries-poor oral hygiene relationship, the findings are still inconclusive. There are some reports suggesting that poor oral hygiene does not increase an individual's risk to develop caries (Etty et al, 1994; Klock et al, 1989) while others express a completely different opinion (Mascarenhas, 1998; Russel et al, 1991; Tubert-Jeannin et al, 1994). In some of these studies, gingival bleeding, tooth-brushing frequency and some plaque index were used to assess oral hygiene instead of the visible plaque index. Some shortcomings were detected in the design of such studies and the subjects studied were not appropriate because the prevalence and incidence of caries were very low (Etty et al, 1994; Klock et al, 1989). It should also be pointed out that the cited studies assessed the relationship between hygiene and dental caries rates, without observing their relationship with caries activity at the time of investigation.

Despite the controversial nature of this question, it is important to remember that classical and well-designed studies, such as those carried out by Axelsson and Lindhe, (1973–1981), had already pointed out the importance of the control of dental biofilm for the reduction of dental caries. However, the results obtained were also attributable to fluoride since the treatment for the control of dental biofilm was always associated with fluoride-containing substances such as toothpastes and other methods of topical fluoride application.

One of the difficulties found in the present study was how to diagnose the activity of the white spots. The Kappa coefficient obtained, only 0.62, confirmed the limitation of the clinical diagnosis. The concept of caries reversal has been somewhat controversial, with the majority of reversals observed in clinical studies often being attributed to examiner's error as opposed to biological remineralisation of compromised enamel. There is no doubt that a diagnosis of caries reversal can be made as a consequence of examiner's error. However, clinical examination remains the basic system for the detection of dental caries in spite of its low accuracy (Ismail, 1997; Nyvad et al, 1999).

Nyvad et al (1999) described a new set of clinical caries diagnostic criteria that differentiate between active and inactive caries lesions at both the cavitated and non-cavitated levels and evaluated the reliability of these criteria in a population with high caries experience. According to the cited authors, there is a need to define new standards for in vivo evaluation of caries through diagnostic systems.

With respect to the size and location of the white spots, there was a statistically significant difference ($p = 0.001$) in number between those located at the cervical base and those extending around the buccal surface. This means that, the smaller the lesion, the greater the probability to determine its inactivity (OR = 0.30). Similarly, when three white spots are diagnosed, the chances that such lesions will remain active are doubled. Although the above results imply a protective effect according to characteristics and number of lesions, the presence of a localized biofilm seems to be the main cause of ongoing activity.

No significant association was found for the variables DMF-s^1 ($p = 0.404$), dmfs ($p = 0.541$), DMF-dmf ($p = 0.855$) and number of lesions ($p = 0.985$). This implies that baseline caries prevalence did not influence the final condition of white lesions. In contrast, Klock et al (1989), Russel (1991) and Wilson and Ashley (1989) found that higher caries prevalence is a predictor of the development of new caries lesions. However, when white spots were considered in the DMF-s^2, a significant difference ($p = 0.004$) was found between it and the activity of lesions, showing that the high numbers of active lesions may represent a 'risk' to maintain white spots active.

Concerning the variables sex and age, no statistical significance was found with white spots activity, despite the better results obtained in the female group (57.9% inactive lesions) and in the 10 to 12-year-old age group (56.1%). These findings were expected, since older children have greater manual ability when it comes to tooth-brushing and girls seem to take better care of their oral hygiene (Lo et al, 1998).

Finally, multiple regression analysis showed that supervised tooth-brushing both with (OR = 0.55, 95% CI = 0.34 to 0.91) and without (OR = 0.58, 95% CI = 0.35 to 0.94) APF acted as a protective factor in the present study. These results seem to contradict established clinical conduct since the

APF gel has been routinely used to treat white spots. It is important to remember that no concrete information has been obtained in any previous randomised clinical trial proving that this type of therapy is efficient. Niederman and Badovina (1999) believe that many therapeutic dental interventions are being used without a scientific basis. APF gel application is part of normal routine and a typical example of tradition taking the place of scientific evidence.

CONCLUSIONS

The findings of this randomised clinical trial indicated that weekly supervised tooth-brushing resulted in a statistically significant reduction of active white spots. It is possible that the use of the APF gel for only three months was not sufficient to provide further benefits in terms of the inactivation of initial tooth enamel caries. The results of this study also support the view that poor oral hygiene increases the probability of keeping white spots active.

LIMITATIONS OF THE STUDY AND PROPOSALS FOR FUTURE STUDIES

This trial tested only one fluoride method, 1.23% APF gel, in children with a low level of oral hygiene and a high index of caries. The results do not necessarily apply to other methods, especially those based on a lower fluoride concentration, on a higher frequency of application, and on longer periods of time. Studies on larger samples and on a broader range of children for the treatment of early caries lesions should be stimulated.

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