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The effect of fluoride gel on incipient carious lesions in a low-caries child population

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Abstract – *Objectives:* Secondary analyses were performed to study the cariostatic efficacy of semi-annual professional fluoride gel application on incipient carious lesions in low-caries children initially aged 9.5–11.5 years. *Methods:* Double-blind randomized controlled clinical trial. *Results:* The mean treatment effect of fluoride gel for enamel and dentinal caries lesions after 4 years' follow-up was 0.92 $D_{2,3}FS$ and 0.20 D_3FS, respectively. When enamel lesions were included in the DFS count (i.e. $D_{2,3}FS$), the preventive fraction (PF) showed borderline significance (23%; $P = 0.05$). No significant treatment effect of professionally applied fluoride gel was found for $D_{2,3}FS$ and D_3FS scores of the second molars. The PF for $D_{2,3}FS$ of occlusal, approximal, buccal and lingual surfaces and for buccal and palatal pits and fissures differed not significantly. *Conclusion:* Professionally applied fluoride gel showed no statistically significant caries-inhibiting effect on both enamel and dentine lesions in the permanent dentition of low-caries children.

Key words: caries prevention; enamel and dentine caries; fluoride gel; professional application; randomized controlled trial

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Because of the continued caries decline in the Western world, evaluation of the cariostatic effect of preventive treatment should no longer be exclusively aimed at assessing at dentine level, but should also be carried out at enamel level. Treasure (1) reported that clinical trial measurements were still predominantly focused on required curative treatment, instead of questioning the effect on initial lesion progression and arrestment. Bjarnason and Finnbogason (2) reported similar approximal enamel lesion progression in children using 250 ppm fluoride toothpaste and those using a 1000 ppm fluoride toothpaste. On the other hand, Lawrence et al. (3) found lower approximal enamel lesion progression in fluoridated than in nonfluoridated communities.

Recently, the caries-reducing effect of professionally applied fluoride gel on dentine caries development has been published (4). The current paper reports about the results of secondary analyses on the data of this fluoride trial, describing the cariostatic efficacy on incipient carious lesions.

Materials and methods

Study sample

The study population consisted of low caries risk children, aged 9.5–11.5 years, who were regular attenders of three paediatric dental clinics in The Netherlands (cities of Oss, Nijmegen and Beuningen). Dental care was performed by 15 dentists and dental nurses. 'Caries low risk' was defined as $D_3MFS = 0$ at baseline, preferably based on clinically and radiographically assessment. D_3 refers to surfaces (S) with dentine caries in the permanent dentition were M and F refer to surfaces missing and filled due to caries. The protocol of the study was approved by the research ethics committee of Radboud University Nijmegen (CEOM NR. 9406–0682). Informed consent was obtained from parents or legal representatives of all participating children. A difference of 0.5 D_3MFS between the fluoride and placebo group after 4 years was considered of clinical importance. Sample size calculation

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(power = 80% and a = 5%) resulted in 252 subjects per treatment group.

A total of 1091 children in the selected age range were prescreened for caries activity according to their dental records in 1995. The inclusion criteria were: a mean D_3MFS score of 0 and children who regularly attended the paediatric dental clinics. The exclusion criterion was absence of informed consent. The parents of 42% of the initially selected subjects refused participating of their children (n = 457). Subsequently, 6% of the remaining subjects (n = 38) were excluded because of the presence of dentine caries in their permanent dentition. The enrolment of participants took 1 year and the follow-up lasted 4 years. Because of dropout and nonadherence after 4 years of follow-up, the group of 596 enrolled subjects was reduced to 517 subjects. This secondary analysis concentrates on the per protocol subjects. An interim analysis was carried out after 2 years. The subjects involved in the trial and reasons for nonadherence have been discussed in detail in a previous paper (4).

Clinical examination

Clinical examinations were carried out according to a written protocol for both visual inspection of the dentition and bitewing radiography. Caries diagnosis, distinguishing enamel (D_2) and dentinal (D_3) scores, was carried out according to criteria described by Marthaler (5), using an operating light, mouth mirror, blunt dental probe and compressed air. Presence of sealants was separately recorded. At baseline, radiographs were taken when bite-wings were either not available or older than 1 year. Ektaspeed Plus Film (Eastman Kodak, Rochester, NY, USA) was used. Bite-wings were available in 80% and 95% of the per protocol subjects at baseline and after 4 years, respectively. Radiographic examinations were read independently from the visual examinations by one examiner according to criteria described by Marthaler (5).

Treatment

The design of the study was a double-blind randomized controlled clinical trial. The participants were randomly assigned to either the placebo or fluoride treatment group by drawing a random unmarked envelope containing the allocation to one of both treatments. The gels were identical regarding packing, taste, colour and consistency. The recommended concentration of professionally applied fluoride gel (0.4–0.6%) for children in the Netherlands was applied.

A written protocol was followed for professional prevention at the semi-annual check-ups and curative treatment. Regular preventive treatment included oral hygiene instruction, followed by supervised tooth brushing with fluoride toothpaste. Subsequently, either a placebo gel or a neutral 1% sodium fluoride gel (4500 ppm fluoride) was professionally applied in a flexible tray and retained for 4 min. Prior to the application, the participants received no professional prophylaxis, nor was the dentition dried by compressed air. After the application, the participants were advised to refrain from rinsing, eating and drinking during 30 min. The effectiveness of exactly eight semi-annual applied applications was assessed for the per protocol subjects. Restorative intervention included treatment of dentine lesions with composite as restoration material. Composite resin sealants were applied in permanent teeth diagnosed with enamel caries lesions (discolouration of fissures) and in caries-free molars in subjects who had a dentine lesion or a restoration elsewhere in the permanent dentition.

Statistical analysis

The primary analysis included the estimation of the treatment effect of professionally applied fluoride gel on the outcome (D_3MFS) after 4 years for both the intention-to-treat subjects and the per protocol subjects as reported by Truin and van't Hof (4). Secondary analysis for per protocol subjects was carried out per predilection site, i.e. pits, occlusal, approximal and smooth surfaces. Incidence of sealants was analysed separately. The per protocol group included 255 children in the placebo and 262 children in the fluoride group. At start of the study, the mean age was 10.4 years (SD = 0.6) in both treatment groups.

The treatment effect of fluoride gel on the outcome variables was tested by t-test. The M-condition in permanent teeth was not seen in this study population. The mean values for the increments in D_3FS and $D_{2,3}$FS, after 4 years of follow-up were compared between placebo and fluoride treated children by means of the preventive fraction (PF), defined per outcome measure as: PF = (placebo mean − fluoride mean)/placebo mean. The SE of the PFs was derived from the related SEMs. Despite the skewed DFS distributions, the mean values were sufficiently normally distributed because of the large sample size, that

justified the use of the *t*-test. The number of applied sealants was evaluated in the same way. Secondary analysis included the treatment effect on the erupting second molars as well as per predilection sites.

A transition analysis (demineralization – remineralization) concentrates on the percentages of surfaces which showed an enamel lesion in the permanent dentition (D_2S) at start or at the 2 year measurements and the condition (sound, grade 2 or grade 3) 2 years later. For the sake of independency of the observations, individual percentages are analysed as mean percentages.

Statistical testing could be conducted one-sidedly at $\alpha = 0.05$, as there is a strong theory saying that fluoride can not cause caries lesions.

Kappa values expressed the reproducibility of both clinical visual examination and bitewing radiography (when available) on a nominal scale including: (a) sound dental hard tissue, (b) enamel lesion, (c), dentinal decay or restoration and (d) sealant application. The inter-observer agreement between the principal examiner and the regular examiners varied between 0.94 and 0.97 (based on 1178–4316 surfaces). The intra-observer agreement of the principal examiner was 0.97 (based on 6552 surfaces).

Results

At baseline, mean enamel caries experience (D_2S) in the placebo and fluoride group was 3.6 (SD = 3.0) and 3.9 (SD = 2.9), respectively. The mean follow-up time was 4.0 years (SD = 0.1) in both the placebo and the fluoride group. The mean treatment effect for enamel and dentinal caries lesions after 4 years' follow-up was 0.92 $D_{2,3}FS$ and 0.20 D_3FS, respectively (Table 1). When enamel lesions were included in the DFS count (i.e. $D_{2,3}FS$), the PF showed a borderline significant difference (23%, $P = 0.05$). No significant treatment effect of professionally applied fluoride gel was found for $D_{2,3}FS$ and D_3FS scores of the second molars. The PFs for $D_{2,3}FS$ scores of occlusal, approximal, buccal and lingual surfaces and for buccal and palatal pits and fissures differed not significantly (Table 2). The highest percentage reductions were found for the approximal (33%) and buccal and lingual (18%) surfaces of the permanent dentition. The average PFs for $D_{2,3}FS$ and D_3FS were 23% and 18%, respectively.

The exposure time for the second molars in the placebo and fluoride groups was 2.4 (SD = 1.1) and 2.3 (SD = 1.1) years, respectively. No statistically significant differences for the second molars in mean treatment effect for enamel and dentinal caries lesions ($D_{2,3}FS$ and D_3FS) were found between the placebo and fluoride groups (Table 2).

Table 3 shows the mean number of sealants at baseline and after 4 years in the placebo and fluoride groups. The number of applied sealants in the occlusal fissures and the buccal and palatal pits and fissures of the permanent dentition and second molars were not significantly lower in the fluoride compared with the placebo group ($P = 0.29$ and $P = 0.06$, respectively).

The percentages of enamel lesions diagnosed at baseline or after 2 years that had progressed into dentine (grade 2 to grade 3), remained unchanged (grade 2 stayed grade 2) or had regressed to a sound site (grade 2 to grade 0) 2 years later, did not differ significantly in the placebo and fluoride group (Table 4).

Discussion

The caries-inhibiting effect of professionally applied fluoride gel in this study sample was

Table 1. Mean D_2S, $D_{2,3}FS$ (SE) and D_3FS (SE) increment in permanent dentition and in second molars of the placebo and fluoride group, Treatment effect (SE) after 4 years, preventive fraction (SE) and *P*-values for per protocol subjects at 4 years' follow-up. Treatment effect is calculated as the difference in incidence

Per protocol subjects	Placebo ($n = 255$)	Fluoride ($n = 261$)	Treatment effect	PF	*P*-value[a]
Permanent dentition					
D_2S	2.98 (0.28)	2.27 (0.22)	0.71 (0.35)	24 (10)	0.05
$D_{2,3}FS$	4.12 (0.37)	3.20 (0.27)	0.92 (0.46)	23 (10)	0.05
D_3FS	1.14 (0.13)	0.94 (0.10)	0.20 (0.16)	18 (12)	0.23
Second molars only					
D_2S	0.67 (0.09)	0.60 (0.08)	0.07 (0.12)	10 (16)	0.54
$D_{2,3}FS$	0.93 (0.10)	0.82 (0.04)	0.11 (0.11)	12 (14)	0.41
D_3FS	0.27 (0.04)	0.22 (0.04)	0.05 (0.06)	18 (20)	0.42

[a]*P*-value of *t*-test.

Table 2. Mean $D_{2,3}FS$ and D_3FS increment (SE) in the permanent dentition and second permanent molars only in the placebo and fluoride group, Preventive Fraction (SE) and *P*-values for per protocol subjects at 4 years' follow-up

	Placebo		Fluoride		PF (%)		PF (%)	
Per protocol subjects	$D_{2,3}FS$	D_3FS	$D_{2,3}FS$	D_3FS	$D_{2,3}FS$	*P*-value[a]	D_3FS	*P*-value[a]
Permanent dentition								
Occlusal	1.07 (0.10)	0.56 (0.06)	1.00 (0.10)	0.49 (0.06)	7 (13)	0.66	13 (14)	0.44
Buccal/palatal pits	0.29 (0.05)	0.13 (0.03)	0.29 (0.04)	0.10 (0.02)	0 (23)	0.99	18 (28)	0.57
Approximal	2.30 (0.25)	0.40 (0.07)	1.54 (0.18)	0.29 (0.04)	33 (11)	0.02	28 (17)	0.19
Buccal/lingual	0.45 (0.11)	0.05 (0.02)	0.37 (0.08)	0.05 (0.02)	18 (26)	0.53	10 (42)	0.82
Total	4.12 (0.37)	1.14 (0.13)	3.20 (0.27)	0.94 (0.10)	23 (10)	0.05	18 (12)	0.23
Second molars only								
Occlusal	0.41 (0.05)	0.19 (0.03)	0.38 (0.05)	0.14 (0.03)	5 (17)	0.79	26 (20)	0.29
Buccal/palatal pits	0.12 (0.03)	0.06 (0.02)	0.10 (0.02).	0.04 (0.01)	17 (27)	0.54	29 (35)	0.49
Approximal[b]	0.21 (0.04)	0.00 (0.00)	0.18 (0.03)	0.01 (0.01)	14 (23)	0.54	0	-
Buccal/lingual	0.19 (0.05)	0.02 (0.01)	0.16 (0.04)	0.02 (0.01)	16 (30)	0.66	18 (38)	0.64
Total	0.93 (0.10)	0.27 (0.04)	0.82 (0.09)	0.22 (0.04)	10 (14)	0.49	18 (20)	0.42

[a]*P*-value of *t*-test.
[b]Higher increment (D_3FS) for fluoride application. On theoretical grounds a caries-promoting effect of fluoride can be excluded; therefore the effect is set to 0 (one sidedness).

Table 3. Mean number of sealants (SE) in the permanent dentition and in second molars at baseline and after 4 years follow-up in the placebo and fluoride group, Preventive Fraction (SE) and *P*-value PF after 4 year for the per protocol subjects

	Baseline		4 years			
	Placebo	Fluoride	Placebo	Fluoride	PF	*P*-value
Permanent dentition						
Occlusal	2.67 (0.12)	2.66 (0.12)	4.47 (0.16)	4.29 (0.16)	4 (5)	0.43
Buccal/palatal pits	0.73 (0.08)	0.69 (0.08)	1.09 (0.11)	0.95 (0.10)	13 (12)	0.33
Total	3.40 (0.17)	3.35 (0.17)	5.56 (0.23)	5.23 (0.22)	6 (5)	0.29
Second molars only						
Occlusal	0.08 (0.03)	0.09 (0.03)	2.09 (0.11)	1.82 (0.11)	13 (7)	0.07
Buccal/palatal pits	0.01 (0.01)	0.00 (0.00)	0.47 (0.06)	0.38 (0.05)	19 (16)	0.27
Total	0.09 (0.04)	0.09 (0.03)	2.56 (0.14)	2.20 (0.13)	14 (7)	0.06

Table 4. Mean percentages (SE) of enamel lesions (permanent dentition, occlusal surfaces excluded) diagnosed at baseline or at the 2-year measurement, regressed (grade 2 to 0), remained unchanged (grade 2–grade 2) or progressed (grade 2 to 3) 2 years later in the placebo and fluoride group. N is the number of subjects with one or more enamel lesions at baseline or at the 2-year measurement

	Regressed (%)		Unchanged (%)		Progressed (%)	
Permanent dentition	Placebo	Fluoride	Placebo	Fluoride	Placebo	Fluoride
Approximal ($n = 161$)	50 (5)	51 (5)	38 (5)	36 (5)	12 (3)	12 (3)
Smooth ($n = 74$)	90 (5)	80 (6)	7 (4)	20 (6)	3 (2)	0 (0)

initially assessed at the D_3FS level, showing a mean effect of professionally applied fluoride gel of 18% (4). The analyses described in this paper refer to the effect at $D_{2,3}FS$ level. The mean effect of professional fluoride gel treatment on $D_{2,3}FS$ (PF = 23%) is in line with results found in a fluoride study in younger low-caries children (6). Excluding enamel lesions in the DFS counts had only a marginal effect on the PFs. Moreover, these relative reductions are consistent with the overall PF's for D_3MFS of clinical fluoride gel treatment studies in populations with higher caries activities than found in the present study, i.e. 22% (95% CI: 18–25%) (7) and 21% (95% CI: 14–28%) (8).

Intervention at the semi-annual dental check-ups included a sealant strategy. According to the protocol, sealants were applied in permanent teeth diagnosed with enamel caries lesions (discolouration of fissures). Marginal differences in the cariostatic effect of fluoride gel for the different tooth

surfaces were found. However, sealant application most probably has biased the effect of fluoride gel on buccal and palatal pits and fissures.

The mean number of tooth surfaces saved per year during 4 years shows a tendency to be lower for dentinal decay (0.05 D_3MFS, SE = 0.04) than for enamel lesions (0.18 D_2S, SE = 0.09). This could be attributed to the fact that the caries-reducing effect in the present study was assessed in young low-caries subjects. Hence, the exposition time might have been too short for caries progression into dentine. Moreover, sealants additionally protected the most caries-active places, i.e. occlusal fissures and palatal pits.

The percentages of enamel lesions diagnosed at baseline or after 2 years that had progressed into dentine, remained unchanged or had regressed to a sound site 2 years later did not differ significantly between the placebo and fluoride group. These findings are not in line with results of a same fluoride trial in a younger age group, suggesting that a higher percentage of approximal lesions in the permanent dentition progressed to dentine lesions in the placebo compared with the fluoride group (6). The low number of enamel lesions involved, combined with the validity of diagnosis of precavitated lesions may have biased the results.

The aim of the secondary analyses on data of the current fluoride trial was to assess the treatment effect on incipient lesions of fluoride gel application. Inclusion of noncavitated lesions in the treatment effect statistics did not change the primary conclusion that the caries-inhibiting effect of fluoride gel application in low-caries children is not clinically relevant.

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