RESEARCH REPORTS
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Efficacy of Silver Diamine Fluoride for Caries Reduction in Primary Teeth and First Permanent Molars of Schoolchildren: 36-month Clinical Trial

ABSTRACT

We hypothesized that the six-monthly application of silver diamine fluoride (SDF) can arrest the development of caries in the deciduous dentition of six-year-old schoolchildren and prevent caries in their first permanent molars. A prospective controlled clinical trial was conducted on the efficacy of a 38% SDF solution for caries reduction. Four hundred and twenty-five six-year-old children were divided into two groups: One group received SDF solution in primary canines and molars and first permanent molars every 6 mos for 36 mos. The second group served as controls. The 36-month follow-up was completed by 373 children. The mean number of new decayed surfaces appearing in primary teeth during the study was 0.29 in the SDF group *vs.* 1.43 in controls. The mean of new decayed surfaces in first permanent molars was 0.37 in the SDF group *vs.* 1.06 in controls. The SDF solution was found to be effective for caries reduction in primary teeth and first permanent molars in schoolchildren.

KEY WORDS: clinical trial, dental caries, preventive dentistry, silver diamine fluoride.

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INTRODUCTION

The utilization of silver diamine fluoride (SDF) as a cariostatic agent is not novel. Recent reports (Klein *et al.*, 1999; Chu *et al.*, 2002) of its effects in deciduous teeth follow classic studies (Yamaga *et al.*, 1972; Shimizu and Kawagoe, 1976; McDonald and Sheiham, 1994) that had already reported its utility in the treatment and prevention of caries in these teeth. To our best knowledge, no controlled clinical trial has evaluated the effectiveness of SDF in first permanent molars. Fissure sealants are recognized to be the most effective approach for the prevention of caries in fissured surfaces of permanent teeth (Llodra *et al.*, 1993). However, further research on less costly alternatives is warranted, because of their wide use in countries or regions with fewer resources. We hypothesized that the six-monthly application of SDF can arrest the development of caries in the deciduous dentition and prevent caries in first permanent molars.

We conducted a 36-month controlled clinical trial to evaluate whether the six-monthly application of a 38% SDF solution is effective to prevent and arrest caries in deciduous and permanent teeth of a sample of Cuban schoolchildren.

MATERIALS & METHODS

A 36-month controlled clinical trial was conducted from February, 2000, to March, 2003, in a cohort of schoolchildren from Santiago de Cuba (Cuba), a city with a low fluoride content (0.09 ppm F ion) in the drinking water. All children from each school were registered with a government-funded dental health center that they visit annually for dental examination and treatment. All schools in the city run a program for 6- to 15-year-old schoolchildren, which includes toothbrushing instruction, dietary recommendations, and, during term time, mouthrinses every 2 wks with 0.2% sodium fluoride. The population receives no fluoridated water or salt, which, coupled with the extremely limited availability of fluoride toothpastes in this area, meant that all members of the study population shared the same low exposure to fluoride. Moreover, the subjects received no professional fluoride treatments.

The study included 452 schoolchildren of both sexes, none below 6 years of age, and all recruited from the "Colegio 26 de Julio" school. The study was approved by the Ethics Committee of the Institute of Medical Science of the University of Santiago de Cuba. The parents of all participants gave signed informed consent. Two previously calibrated examiners were responsible for all of the dental examinations. Each child underwent 7 examinations, one at baseline and then every 6 mos until the end of the study at 3 yrs. At each examination stage, we re-examined 10% of the schoolchildren to determine the intra-observer agreement. Inter-observer agreement was similarly tested, at baseline and at 1, 2, and 3 yrs. The schoolchildren were assigned on an individual random basis to the SDF or control group by a third researcher,

Table 1. Analysis of Baseline dmfs and Surfaces with Active Caries in the Whole Sample and the Children Completing the 36-month Follow-up (SE in parentheses)

	Whole Sample			Schoolchildren Followed for 36 mos		
Group	No. schoolchildren	dmfs[a]	No. surfaces with active caries	No. children	dmfs	No. surfaces with active caries
SDF	225	3.6 (0.2)	3.0 (0.2)	180	3.7 (0.3)	3.3 (0.3)
Control	227	3.5 (0.3)	2.9 (0.3)	193	3.4 (0.3)	2.9 (0.2)
Significance		$p = 0.74^b$	$p = 0.81^b$	$p = 0.16^c$	$p = 0.40^b$	$p = 0.28^b$

[a] Decayed, missing, and filled surface index of deciduous canines and molars.
[b] Student's *t* test.
[c] χ^2 test.

Table 2. Analysis of Mean Numbers of New Surfaces with Active Caries, Surfaces with Inactive Caries, and Non-vital Teeth in Deciduous Dentition at 36 Months of Follow-up (SE in parentheses)

Group	No. Schoolchildren	New Surfaces with Active Caries	Surfaces with Inactive Caries	% Surface with Inactive Caries and Black Stain	Non-vital teeth
SDF	180	0.3 (0.1)	2.8 (0.3)	97	0.1 (0.0)
Control	193	1.4 (0.2)	1.8 (0.3)	48	0.1 (0.0)
Significance		$p < 0.001$	$p < 0.05$	$P < 0.001$	$p = 0.65$

ensuring that the examiners were blinded to the group of each child. Examinations were carried out at the school by an examiner using an explorer and flat mirror. In deciduous teeth, data were gathered for the surfaces of only canines and molars. In permanent teeth, data were gathered only on first molars. Each surface was classified as healthy, with active caries (presence of cavity with soft floor/walls), with inactive caries (cavity with hard floor/walls), filled, or absent. In the case of deciduous teeth, only those extracted for caries were considered absent. On healthy surfaces or those with inactive caries, the presence or absence of black stain was recorded. Teeth with an abscess, evidence of pulpal exposure, premature hypermobility, fissure, or abnormal coloring were considered non-vital. The treatment of each tooth (restoration, pulpal treatment, extraction) was also recorded at every examination.

The schoolchildren in the SDF group received, at the beginning of the study and every 6 mos thereafter, an application of 38% SDF solution (Fluoroplat, Laboratorios Naf, Buenos Aires, Argentina) on the decayed surfaces of deciduous teeth and the occlusal surfaces of any first permanent molars that had erupted. No attempt was made to remove decayed tissue from deciduous teeth. In first permanent molars with active caries, the soft surface layer of the decayed dentin was removed with excavators before the SDF solution was applied. The teeth were isolated from saliva with cotton rolls and then painted with the solution for 3 min, with the solution applied to one quadrant at a time. Three min after the application, the teeth were washed with a 30-second water spray.

Statistical Analysis

Sample size estimation was conducted with a 95% confidence interval and statistical power of 80%. Intra-observer and inter-observer agreements were measured with the Kappa test. The comparison of means was studied by the Student's *t* test and multiple linear regression analysis. We used the chi-square (χ^2) test to study the distribution of children lost to follow-up and the distribution of black stain between the two groups. The significance level considered was 0.05. Analyses were performed with use of the SPSS statistical program (version 11.0).

RESULTS

At the beginning of the study, 452 schoolchildren took part, 229 (50.7%) males and 223 (49.3%) females, with an age of 6.29 ± 0.48 yrs (mean ± SD). The entire study period was completed by 373 schoolchildren (82%). Forty-five children (20%) were lost to the follow-up in the SDF group and 34 (15%) in the control group. The Kappa statistic for intra-observer reliability was ≥ 0.93 at all examination stages, and Kappa values for inter-observer reliability were 0.92 at baseline (tested on 38 children), 0.94 at 12 mos (45 children), 0.89 at 24 mos (41 children), and 0.91 at 36 mos (47 children). In the 373 children followed up throughout the study, the mean baseline decayed, missing, and filled surface (dmfs) index scores were 3.68 ± 0.30 and 3.35 ± 0.26 in the SDF and control groups, respectively. The mean number of surfaces with active caries was 3.29 ± 0.28 in the SDF group and 2.91 ± 0.22 in the control group (Table 1). At baseline, there were no statistically significant differences between the groups in dmfs score or number of surfaces with active caries. There were no significant differences in baseline dmfs or number of surfaces with active caries between the children lost to the follow-up and the group that completed the study (results not shown).

In the deciduous dentition (Table 2), significant differences were observed between the groups in the mean of new decayed surfaces appearing during the study (Student's *t* test, $p < 0.001$). The preventive fraction of SDF in deciduous teeth was 79.7%. The children in the SDF group had significantly more surfaces with inactive caries (Student's *t* test, $p < 0.05$) and a higher percentage of black stains (97%), compared with the control group, in which only 48% of the inactive lesions were black (χ^2 test, $p < 0.001$). There was no significant difference between the groups in mean number of non-vital deciduous teeth (Student's *t* test, $p = 0.65$).

In first permanent molars (Table 3), the control group showed a higher mean number of new decayed surfaces *vs.* the SDF group (Student's *t* test, $p < 0.001$). The preventive fraction of the SDF group was 65% in first permanent molars. Compared with the controls, the SDF-treated children presented more surfaces with inactive caries (Student's *t* test, $p < 0.05$) and a higher proportion of black stains in inactive lesions (χ^2 test, $p < 0.001$). Throughout the study, only 5 first permanent molars with pulpal lesions were observed (2 in the SDF group and 3 in the control group), and no first permanent molar was extracted.

Most of the children studied, 73.9% of the SDF group and 50.2% of the control group, presented no increment or reduction in the DFT-1M index (decayed + filled first permanent molars) at the end of the study. The differences

Table 3. Analysis of Mean Numbers of New Surfaces with Active Caries and Surfaces with Inactive Caries in First Permanent Molars (1M) at 36 Months of Follow-up (SE in parentheses)

	SDF (N = 180)	Control (n = 193)	Comparison, p value
Baseline			
DFS-1M[a]	0.3 (0.0)	0.4 (0.1)	p = 0.66
DS-1M	0.3 (0.0)	0.3 (0.1)	p = 0.87
FS-1M	0.0 (0.0)	0.1 (0.0)	p = 0.02
New with active caries: DFS-1M	0.4 (0.1)	1.1 (0.1)	p < 0.001[c]
DS-1M	0.1 (0.0)	0.2 (0.1)	p = 0.09
FS-1M	0.3 (0.0)	0.9 (0.1)	p < 0.001
Surfaces with inactive caries-1M[b]	0.3 (0.1)	0.1 (0.0)	p < 0.05
% surfaces with inactive caries and black stain-1M	96%	67%	p < 0.001

[a] DFS-1M = Active Decayed (DS)+ filled surfaces (FS) in first permanent molars.
[b] They were arrested, and correspond to baseline surfaces with active caries.
[c] The adjusted difference between groups in DMFT (M1) by linear regression analysis (including the initial value as a potential confounder) arrives at the same conclusion (results not shown).

between the groups were mainly in children showing 3 or 4 new decayed or filled teeth (Table 4).

DISCUSSION

The design of our study is worthy of comment. The validity of the results was strengthened by the use of two previously calibrated examiners and by systematic testing of the intra- and inter-observer agreement. The presence of a cavity was the sole diagnostic criterion for caries, which may be a study limitation, since it excludes incipient caries lesions. It could be argued that black stains, much more frequent in the SDF group, compromised the blinded nature of the analysis. However, numerous black stains also appeared in the control group, making it impossible for the examiner to know the group of the child on this basis. With respect to any possible Hawthorne effect in the SDF group, it should be remembered that all of the schoolchildren continued to receive identical treatments, with the sole exception of the SDF application, regardless of the group to which they were assigned. We chose to conduct our study in Santiago de Cuba for two main reasons: There was an existing school dental health program that had been functioning for more than 40 years, and it was economically impossible in this setting to offer other preventive options, such as fissure sealing, to control caries in first permanent molars.

The main aim of our study was to test the anti-caries efficacy of a six-monthly application of a 38% SDF solution in both deciduous teeth and first permanent molars. Both the preventive and therapeutic (possibility to arrest or reverse active caries) effects of this technique were analyzed. With respect to the prevention of new caries lesions, our SDF treatments showed a greater percentage of efficacy in deciduous teeth (around 80%) than in first permanent molar (65%) teeth. A recent Chinese study of deciduous incisors (Chu *et al.*, 2002) reported a percentage of efficacy of 70-83%, depending on the clinical application protocol, similar to our

Table 4. Percentage Distribution of DFT-1M[a] Increment over 36 Months in the Children Completing the Follow-up Study

DFT Increment	SDF (n = 180)	Control (n = 193)
-1	12 (6.7%)	5 (2.6%)
0	121 (67.2%)	92 (47.6%)
1	25 (13.9%)	33 (17.1%)
2	15 (8.3%)	26 (13.5%)
3	4 (2.2%)	21 (10.9%)
4	3 (1.7%)	16 (8.3%)

[a] Permanent first molars with caries or filling.

results. In the present study, the baseline level of caries was much higher in deciduous teeth (mean of > 3 surfaces with caries) than in first permanent molars (0.3 surfaces with caries), which may explain the greater efficacy of the SDF solution in the deciduous dentition.

The application of fissure sealants is the most widespread model for the prevention of caries in first permanent molars. Llodra *et al.* (1993) published a meta-analysis that demonstrated a preventive fraction of 70% at 36 mos of follow-up. Our search of the literature disclosed no controlled clinical study based on the use of SDF in permanent teeth, although some clinical studies with small sample sizes have been published. Green (1989) reported that a solution of SDF + SnF_2 was more effective in reducing caries in first permanent molars, compared with the application of SnF_2 alone. Yamaga *et al.* (1972) studied 25 schoolchildren and found an 8% incidence of caries in SDF-treated first permanent molars, compared with 32% in controls, after a nine-month follow-up.

With respect to the therapeutic effect of SDF (arrest of caries), around 77% of treated caries that was active at baseline became inactive during the study, both in deciduous teeth and in first permanent molars. In the SDF group, practically all (97%) of inactive lesions presented black stain at the end of the follow-up. Yamaga *et al.* (1972) suggested that deposits of silver phosphate are the main action mechanism of SDF, responsible for the increased hardness and black staining. In relation to the desirability of removal of decayed dentin before the application, Chu *et al.* (2002) found no differences between SDF groups with or without prior excavation in deciduous teeth. No study has been published on the effects of the prior removal of decayed dentin in permanent teeth.

A hypothetical risk attributed to SDF is its possible toxicity to the pulp (Russo *et al.*, 1989; Gotjamanos, 1996). This concern was not supported by the present results. On the contrary, there was a similar incidence of pulpal lesions between the groups, in both deciduous and permanent teeth. Some authors (Yamaga *et al.*, 1972) have predicted reversible lesions in oral mucosa through inadvertent contact with SDF solution. This occurred in three patients in our study, with the appearance of a small, mildly painful white lesion in the mucosa, which disappeared at 48 hrs without treatment. The possibility of acute toxicity or the induction of fluorosis through the use of 38% SDF has been widely debated in the literature (Gotjamanos, 1997; Neesham, 1997). We applied the minimal amounts (4 mL to treat a mean of 80 quadrants), and special care was taken in the application, including abundant

washing with water. Another proposed drawback of SDF treatment is the appearance of black stains, although in our view this is far outweighed by the caries-preventive benefits of SDF treatment.

There are no published recommendations for the frequency of SDF applications. Some authors applied the solution annually and others six-monthly. There is no documented evidence that starting treatment with multiple applications in a short period is preferable to starting with a single initial application. The application of a 38% SDF solution is a simple and low-cost method that does not require the cooperation of the patient or the complex training of the health professional. This approach may be of great utility as an alternative to more costly preventive methods in communities with limited resources. Its mechanism of action means that it can be useful to prevent and arrest caries in all teeth and surfaces. Wider studies of this treatment are required to investigate alternative protocols, different age groups, and high-risk groups, to evaluate longer-term outcomes, and to evaluate the efficiency of this approach, using more sensitive criteria for caries diagnosis.

The outcomes at 36 mos showed that the six-monthly application of a 38% SDF solution is efficacious to control caries in deciduous teeth. Our findings indicate that this approach is also efficacious to control caries in first permanent molars.

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