RESEARCH REPORTS
Clinical

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Efficacy of Silver Diamine Fluoride for Arresting Caries Treatment

ABSTRACT

Arresting Caries Treatment (ACT) has been proposed to manage untreated dental caries in children. This prospective randomized clinical trial investigated the caries-arresting effectiveness of a single spot application of: (1) 38% silver diamine fluoride (SDF) with tannic acid as a reducing agent; (2) 38% SDF alone; (3) 12% SDF alone; and (4) no SDF application in primary teeth of 976 Nepalese schoolchildren. The *a priori* null hypothesis was that the different treatments have no effect in arresting active cavitated caries. Only the single application of 38% SDF with or without tannic acid was effective in arresting caries after 6 months (4.5 and 4.2 mean number of arrested surfaces; $p < 0.001$), after 1 year (4.1 and 3.4; $p < 0.001$), and after 2 years (2.2 and 2.1; $p < 0.01$). Tannic acid conferred no additional benefit. ACT with 38% SDF provides an alternative when restorative treatment for primary teeth is not an option.

KEY WORDS: fluorides, silver diamine fluoride, clinical trial, arresting caries treatment.

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INTRODUCTION

Untreated dental caries is a global pandemic (Edelstein, 2006). Due to limited financial resources, poor access to basic oral care, and the high cost of restorative treatment, children of low-income nations have their general health, social well-being, and education opportunities affected by untreated dental caries (Baelum *et al*., 2007). Arresting Caries Treatment (ACT) has been proposed to manage untreated dental caries in children of disadvantaged communities (Bedi and Sardo-Infirri, 1999). Silver diamine fluoride (SDF), $Ag(NH_3)_2F$, has been used to arrest caries since 1969 (Nishino *et al*., 1969; Nishino and Yoshido, 1969; Yamaga and Yokomizo, 1969). Yearly applications of 38% SDF (44,800 ppm F) to decayed primary anterior teeth of Chinese preschool children have been shown to be significantly more effective in arresting caries and preventing new caries than three-monthly applications of sodium fluoride varnish (22,600 ppm F) (Lo *et al*., 2001; Chu *et al*., 2002). In a Cuban study, 38% SDF applied every 6 mos demonstrated clinical effectiveness in arresting caries and preventing new caries in the dentition of 6- to 15-year-old schoolchildren over a three-year period (Llodra *et al*., 2005).

Currently, the optimal frequency of application of SDF is unknown, but in resource-limited situations, repeated applications of SDF are unlikely to be either practical or affordable to local communities, even when applied by trained primary-health-care workers.

Therefore, this current study compares the effectiveness of a single spot application of two concentrations of SDF, 38% or 12%, in arresting caries, with or without the use of tannic acid from tea as a reducing agent. The *a priori* null hypothesis is that the different treatments have no effect in arresting active cavitated caries.

MATERIALS & METHODS

This prospective randomized clinical trial on a cohort of 976 kindergarten and primary schoolchildren, 545 males (56%) and 431 females (44%), with ages ranging from 3-9 yrs and a mean age of 5.2 (SD = 1.2) yrs at time of enrollment, was conducted in Kathmandu, Nepal, a city with low-fluoride-content drinking water (0.03 ppm). Fluoridated toothpaste is available from retailers, but the children received neither professionally applied fluorides nor fluoride supplements. Treatment was provided between May and August, 2005, and the children were re-examined after 6 mos, 1 yr, and 2 yrs. The study was approved by the Ethics Committee of the Nepal Health Research Council. Written information explaining the study was sent to the parents. As well as obtaining a written consent from the parents, verbal consent was obtained from the children prior to commencement of the study. The children were at liberty to withdraw from the study at any time during the study, and the same freedom was afforded to the parents to withdraw their children from the study.

The SPSS statistical program (version 10.0) was used for random allocation of the children to one of the treatment groups/ protocols:

- Group 1: One application of 38% SDF for 2 min without a reducing agent.
- Group 2: One application of 38% SDF for 2 min, with tea as a reducing agent.
- Group 3: One application of 12% SDF for 2 min, without a reducing agent.
- Group 4: No treatment for carious teeth. This was the control group.

We used 38% SDF (44,800 ppm F) (Bee Brand Medical Dental Company Ltd., Osaka, Japan) and 12% SDF (PROBEM - Lab. Prod. Farmacêuticos e Odontológicos LTDA, São Paulo, Brazil) to treat the teeth. We prepared tannic acid by slowly boiling 2 teabags (Mechhi Tea; grown and manufactured in Nepal) in 300 mL of water for 10 min.

Primary-health-care workers were trained to carry out the treatment and collect information on the children's oral health behavior, quality of life, and socio-economic status. Treatment assignment appeared on the children's treatment plans, and treatment was supervised by a dentist (RY). Prior to treatment, the children brushed their teeth with a toothbrush without toothpaste and rinsed with water. The carious primary teeth were isolated and kept dry with cotton rolls, and any debris was removed with cotton pellets. No caries was removed. One drop of SDF was placed in a plastic dappen dish, and a Vivabrush #533664 type (Ivoclar Vivadent, Schaan, Liechtenstein) was used to apply the SDF to carious surfaces of the primary teeth for 2 min. If the protocol required the application of a reducing agent, this was applied to the SDF-treated surface by means of a cotton pellet until the surface turned dark brown. The excess was removed by gentle blotting with another cotton pellet. After treatment, the children were asked not to eat or drink for 1 hr. At the start of the study, all children received a free tube of fluoridated toothpaste and a toothbrush. Children with painful or abscessed teeth were offered free extraction.

The dentist (RY) and a dental therapist (DL) performed the baseline examinations prior to treatment, while follow-up examinations were carried out at 6, 12, and 24 mos by the dental therapist (DL), blind to the children's treatment group assignment. All examinations were carried out in the school courtyard or in a well-lit classroom. The children were positioned supine on a bench or table and examined by the dental examiners using LED headlamps and mouth mirrors. Cotton pellets were used to dry the teeth and wipe away gross debris. A sharp sickle probe was used, with the tip gently passed over the entire surface of the cavity to detect and confirm visual evidence of caries. Pits and fissures were not probed, to prevent the risk of fissure damage. Ten percent of the schoolchildren were re-examined to determine examiner reproducibility. Each surface of the tooth was classified according to the criteria given in Table 1. For the follow-up evaluation, surfaces with arrested caries were defined as surfaces with active cavitated caries (d2) at baseline that changed into surfaces with arrested cavitated caries. Surfaces with new caries were defined as sound or 'initial caries' surfaces at baseline that changed into surfaces with active or arrested cavitated caries or restored surfaces.

Table 1. Diagnostic Criteria for the Classification of the Tooth Surface

Caries Criteria	Description
Sound	Surfaces not soft to the touch with a sharp sickle probe, but they may be discolored.
Initial caries	Localized enamel breakdown (microcavity) in opaque or discolored enamel.
Arrested cavitated caries	As d2, but the wall and floor of the cavity were hard and could not be penetrated by the sharp sickle probe.
Filled surface with no decay	A permanent restoration is present, and there is no caries anywhere on the surface.
Non-vital tooth	Abscessed/pulpally involved teeth with abnormal coloring.
Missing due to caries	Teeth extracted due to caries. Included in this category were teeth having more than two-thirds (2/3) of the crown destroyed by caries and the root remaining.

Statistical Analysis

Estimation of the sample size was based on the expected number of arrested caries surfaces. Power of the study was fixed at 80% ($\beta = 0.20$), with $\alpha = 0.05$ as the significance level. On the basis of a difference of 1 in mean number of arrested caries surfaces between groups, and a standard deviation of 3.5 (Llodra *et al*., 2005), the sample size was estimated to be around 160. When the expected dropout rate over a 2-year period was taken into account, the sample size was increased to 240 *per* group.

The data were entered into a computer and analyzed with SAS 9.1 software. Chi-square tests were applied to determine differences in the distribution of children's ethnic background, parents' education and occupation, report of oral pain, brushing habits, and use of fluoridated toothpaste among the four groups. Chi-square tests were also used to determine differences in number of dropouts among the four groups. Differences found in the data of the four groups regarding mean age, dmft, ds, d2s, mean number of non-vital teeth, and mean number of surfaces with arrested caries were tested with analysis of variance (ANOVA). In case of a significant ANOVA test, differences between groups were tested with Student's *t* test. Inter-examiner reproducibility at the tooth-surface level at baseline and intra-examiner reproducibility at follow-up examinations were measured by the Kappa statistic.

RESULTS

Since inter-examiner consistency in scoring 'initial caries' at baseline was only 47%, the 'initial caries' scores were collapsed

Table 2. Mean Age, Mean dmft, Mean Number of Decayed, Missing and Filled Teeth, Mean Number of Cavitated Active and Arrested Caries Surfaces, Mean Number of Cavitated Active Caries (d2) Surfaces, and Mean Number of Non-vital Teeth of Children at Baseline According to the Different Groups

Groups	n	Mean Age (yrs, SD)	dmft (SD)	ds* (SD)	d2s (SD)	Non-vital Teeth (SD)
38% SDF	243	5.0 (1.2)[a]	4.5 (3.1)	7.9 (7.6)	6.6 (6.4)	0.3 (1.5)
38% SDF + tea	249	5.3 (1.2)[b]	4.7 (4.7)	8.3 (8.5)	7.2 (7.6)	0.3 (1.6)
12% SDF	243	5.3 (1.2)[b]	4.5 (4.6)	8.0 (7.9)	6.8 (7.0)	0.3 (1.5)
Control	241	5.3 (1.2)[b]	4.6 (4.7)	8.0 (8.5)	6.6 (7.3)	0.3 (1.6)
All groups	976	5.2 (1.2)[b]	4.6 (4.3)	8.0 (8.1)	6.8 (7.1)	0.3 (1.6)

a<b $P < 0.01$.
*ds = Surfaces with cavitated active (d2) + arrested caries.

into the 'sound' score category prior to the analysis of the data. After this adjustment, the unweighted inter-examiner Kappa at baseline examination was 0.81, and intra-examiner Kappas were 0.80 (RY) and 0.81 (DL), while intra-examiner unweighted Kappas at six-month, one-year, and two-year follow-up examinations were 0.85, 0.86, and 0.93, respectively.

Although the children were randomized over the four groups, the mean age of the children treated with 38% SDF only was significantly lower than the mean age of children in the other groups (Table 2). At baseline, 66% of the children reported brushing once a day with fluoride toothpaste. The children's ethnic background, parents' education and occupation, report of oral pain, brushing habits, and use of fluoridated toothpaste were similarly distributed in the 4 groups (X^2 test, $p > 0.05$). The caries data and the mean number of non-vital teeth of the four groups at baseline are shown in Table 2. Since the numbers of missing teeth due to caries and filled teeth were very low, the dmft was almost exclusively formed by the 'd' component. No statistically significant differences were found in the caries data among the four groups at baseline (ANOVA $p > 0.05$).

The numbers of children who were examined at 6, 12, and 24 mos were 908, 768, and 634, respectively, resulting in dropout rates of 7%, 21%, and 35%. The dropout rates in the four groups did not differ statistically significantly (X^2 test, $p > 0.05$). The parents' educational level, ethnicity, brushing habits, and use of fluoride toothpaste did not differ for the dropouts and for the children remaining in the study at 24 mos (X^2 test, $p > 0.05$). There were also no differences in baseline caries parameters between children lost to the follow-up and those remaining in the study at 24 mos (ANOVA $p > 0.05$).

At 6, 12, and 24 mos, the mean number of arrested carious surfaces was significantly higher in the two groups treated with 38% SDF than in the 12% SDF and control groups (Table 3). The difference observed at 6 mos decreased over 24 mos, but remained statistically significant. There was no significant difference in the mean number of arrested carious surfaces between the 38% SDF and the 38% SDF + tannic acid groups, or between the 12% SDF and the control groups throughout the 24-month study period. There was also no significant difference between the groups in the mean number of non-vital teeth and the mean number of exfoliated surfaces at any time.

DISCUSSION

This is the first clinical trial to evaluate the effectiveness of a one-time application of SDF with 2 different concentrations of SDF and the effect of a reducing agent. The use of a reducing agent such as 10% stannous fluoride (Craig *et al.,* 1981) has been advocated to accelerate the deposition of silver phosphate, which results in the instantaneous black discoloration of the area. This indicates that a successful reaction has occurred and minimizes the risk of SDF being washed away or contaminated by saliva. However, stannous fluoride is difficult to obtain in low-income countries, and tannic acid from boiled tea has been suggested as an inexpensive substitute.

The large proportion of dropouts from the study (35%) at 24 mos was due to a school closing and to the mobility of the parents. This did not have any effect on the results, since the 4 groups, as well as the dropouts and those remaining in the study, were similar in all other respects.

The results of this study support the null hypothesis for the application of 12% SDF, in that this agent had no significant effect on arresting caries. For a single application of 38% SDF, the hypothesis was rejected. A single application of 38% SDF, with or without the use of tea as a reducing agent, was significantly more effective in arresting dental caries in both the anterior and posterior primary dentitions of young children than 12% SDF or no application (control). The arresting caries effect of 38% SDF decreases slowly over time. A single application of 38% SDF was sufficient to prevent only 50% of the arrested surfaces at 6 mos from reverting to active lesions again over 24 mos. The tannic acid from boiled tea does not appear to have any significant additional effect on arresting caries compared with 38% SDF alone.

The advantages and disadvantages of this ACT approach have been elucidated in previous studies (Chu *et al.,* 2002; Llodra *et al*., 2005). The black discoloration of the carious dentin after SDF treatment is probably the most notable undesirable side-effect. This staining may be eliminated by the application of potassium iodide (KI) after the SDF application (Knight *et al.*, 2005); however, the clinical effectiveness of SDF/KI remains to be evaluated. Some concerns have also been raised over dental fluorosis and accidental toxic overdose from the routine use of 40% silver fluoride, which has the same mode of action as SDF (Gotjamanos and Afonso, 1997; Gotjamanos, 1997). Although these concerns have been refuted (Neesham, 1997), the less-frequent application of lower concentrations of SDF might help to alleviate such concerns. In this current study, there were no adverse effects observed or complaints from either parents or the children concerning the SDF treatment.

The outcomes of this 24-month SDF study on both anterior and posterior primary teeth show that: a single spot application of 38% SDF is effective in arresting caries lesions, but the effectiveness decreases over time; tannic acid from tea confers no additional benefit; and 12% SDF is not effective.

Table 3. Mean Number of Active Cavitated Surfaces at Baseline that Changed at Follow-up Examination into Surfaces with Arrested Cavitated Caries and Into Mean Number of Surfaces Lost Due to Exfoliation and Mean Number of Non-vital Teeth at 6-, 12-, and 24-month Follow-up Examinations

	6 Mos				12 Mos				24 Mos			
Groups	n	Arrested Caries (SE)	Non-vital Teeth (SE)	Lost Surfaces (SE)	n	Arrested Caries (SE)	Non-vital Teeth (SE)	Lost Surfaces (SE)	N	Arrested Caries (SE)	Non-vital Teeth (SE)	Lost Surfaces (SE)
38% SDF	223	4.2(0.3)[a]	0.4(0.1)	0.0(0.0)	189	3.4(0.3)[a]	0.6(0.1)	0.0(0.0)	157	2.1(0.3)[a]	0.4(0.1)	0.4(0.1)
38% SDF + tea	233	4.5(0.4)[a]	0.4(0.1)	0.0(0.0)	189	4.1(0.4)[a]	0.6(0.1)	0.0(0.0)	156	2.2(0.3)[a]	0.4(0.1)	0.4(0.1)
12% SDF	228	2.3(0.2)[b]	0.4(0.1)	0.0(0.0)	188	1.7(0.3)[b]	0.6(0.1)	0.1(0.0)	156	1.5(0.3)	0.3(0.1)	0.4(0.1)
Control	223	1.6(0.2)[b]	0.5(0.1)	0.0(0.0)	187	1.3(0.2)[b]	0.7(0.1)	0.1(0.0)	155	1.0(0.2)[b]	0.5(0.1)	0.4(0.1)
		a>b $P < 0.001$				a>b $P < 0.001$				a>b $P < 0.01$		

Arresting Caries Treatment (ACT) with a single spot application of 38% SDF provides an alternative where restorative treatment for primary teeth is not an option.

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