Original Article

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Efficacy of Silver Diamine Fluoride for Arresting Non-cavitated Lesions on Approximal Surfaces in Permanent Teeth

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Abstract:

Objective: To evaluate the efficacy of silver diamine fluoride for arresting non-cavitated lesions on approximal surfaces in permanent teeth.

Material and Methods: This randomized controlled trial included 82 participants (396 lesions), aged 6–18 years that had at least one non-cavitated carious lesion on approximal surfaces. They were randomly allocated to either the SDF or sodium fluoride (NaF) group. After tooth separation at baseline (T0), the allocated intervention was applied directly on non-cavitated lesions. Clinical and radiographic examinations were performed to assess caries status at T0 and 6 months (T6).

Results: After 6 months, 77 participants (379 lesions) remained in this study. The caries arrest rates of the SDF group were significantly higher than those in the NaF group. From clinical examination, the proportions of caries arrest rate of the SDF and NaF groups were 100.0% and 80.1%, respectively. These high caries arrest rates were consistently demonstrated from radiographic examination in the SDF and NaF groups at 98.4% and 93.5%, respectively.

Conclusion: At the 6-month follow-up, 38.0% SDF was more effective than 5.0% NaF in arresting non-cavitated carious lesions on approximal surfaces in permanent teeth, and SDF could be a potential treatment option for minimally invasive caries management.

Keywords: caries arresting, caries management, permanent teeth, silver diamine fluoride

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Introduction

Untreated dental caries can adversely impact the oral health-related quality of life[1]. When the tooth structure is destroyed it will usually require restoration and continuing maintenance for the whole of life[2]. According to caries prevalence, approximal surfaces are the second most common sites after pits and fissured surfaces on posterior permanent teeth. The interproximal plaque is more acidogenic than plaque covering on free smooth surfaces, which may be associated with difficulty in cleaning, differences in microbial portion, and saliva access[3]. Approximal initial lesions, which appear limited to the enamel and outer one-third of the dentin on bitewing radiographs, are most likely non-cavitated[4]. Failing to treat these approximal non-cavitated lesions before they progress can lead to the occurrence of cavitated lesions which are difficult to restore directly. This often requires drilling through the marginal ridge, resulting in an unnecessary loss of tooth structure and making treatment more expensive than if the lesions had been arrested earlier. Moreover, these treatments will be even more difficult in uncooperative children. Since these non-cavitated lesions have the potential to be reversed or be arrested by chemical or mechanical interventions[5], the clinician should prioritize the use of non-restorative interventions over drilling. Systematic reviews and network meta-analysis have explored the effectiveness of non-restorative interventions to prevent and arrest approximal carious lesions[6-10]. Their findings demonstrated that flossing had limited efficacy for approximal caries arresting, especially in high-risk of carries populations, because it relies on patient compliance and flossing technique[11]. The more effective measure is 5% sodium fluoride (NaF) varnish application, which is a standard anti-caries agent used to arrest or reverse active non-cavitated lesions. The use of 5% NaF varnish has been found to be effective for caries prevention in permanent and primary teeth at 43 and 37 percent, respectively[6]. However, its efficacy in arresting non-cavitated lesions on approximal surfaces is less remarkable. Among several anti-caries agents, silver diamine fluoride (SDF) has been of interest to both clinicians and researchers. The caries-arresting effect of SDF was suggested to be a consequence of many interactions from the key components[12] :(i) silver ions have antimicrobial activities, including inhibitory effects on the growth, the adherence, and the biofilm formation of cariogenic bacteria (ii) silver can protect dentin degradation by inhibiting matrix metalloproteinases (MMPs) and cathepsins (iii) the high concentration of fluoride can inhibit demineralization and enhance remineralization (iv) The alkalinity of SDF can alter the acidic microenvironment around active carious lesions, promoting their transition to inactive lesions. Several clinical trials have shown that 38% SDF is effective for arresting cavitated lesions and desensitizing tooth hypersensitivity due to these properties[12]. SDF has been demonstrated to be effective in arresting non-cavitated lesions in primary teeth[8,13-16], but in permanent teeth, it remains inconclusive. The caries-arresting effect reported in primary teeth is in accordance with the in vitro results, indicating that SDF can penetrate non-cavitated lesions[17]. The differing characteristics of primary and permanent teeth may affect the caries-arresting effect of SDF application, leading to different outcomes. We designed this randomized clinical trial to evaluate the efficacy of SDF for arresting non-cavitated lesions on approximal surfaces of permanent teeth. If the results of this study reveal that SDF application can effectively arrest non-cavitated lesions, this method will be one of the caries management strategies which can arrest caries, preserve the tooth structures, and be conveniently used in both clinical and community settings.

Material and Methods

This randomized controlled trial was conducted in two-arm parallel groups. The participants, aged 6- to 18-year-old, were allocated to one of two intervention groups to compare the efficacy of 38.0% SDF to 5.0% NaF. The outcome was the caries arresting status of non-cavitated

lesions on approximal surfaces in permanent premolars and molars at 6-month follow-up (T6). The 6-month follow-up period was determined based on participants identified as having high caries risk and post-eruptive time, as suggested by previous studies[18-20]. This protocol was approved by the Human Experimentation Committee of the Faculty of Dentistry, Chiang Mai University and was registered at the Thai Clinical Trial Registry (TCTR)[21] (http://www.clinicaltrials.in.th) with the identifier TCTR20210706004. The primary adverse effect of SDF is black staining on tooth surfaces. Therefore, we informed participants of this drawback and obtained informed consent from patients and/or parents before they participated in the study.

Participants

Participants aged 6-18 years, from those coming to the pediatric dental clinic of the Faculty of Dentistry, Chiang Mai University, were recruited according to inclusion/exclusion criteria as follows:

1) Inclusion criteria

Healthy children or adolescents (no systemic diseases/conditions)

Presence of at least one initial carious lesion on intact approximal surfaces of permanent premolars or molars, as indicated by a radiographic score of RA1, RA2, or RA3 according to the International Caries Classification and Management System (ICCMS™)[22], detected through bitewing radiographs.

Presence of at least one active initial carious lesion on intact approximal surfaces of permanent premolars or molars, with a clinical score of 1, 2, or 3 according to the International Caries Detection and Assessment System (ICDAS)[23]. For this purpose, surfaces were evaluated after tooth separation for at least 48 hours. Following the removal of orthodontic separators, approximal surfaces were assessed using visual and tactile examination. All eligible surfaces were included in the study.

2) Exclusion criteria

Children or adolescents who refuse to participate in the study, individuals with allergies to silver, colophony base, or any component of the test products, and those with previously restored surfaces are excluded from the study. Additionally, individuals with Molar-Incisor Hypomineralization teeth (MIH), enamel hypoplasia, or crowded/misaligned teeth that can hinder cleaning are also not eligible for participation.

The researcher collected baseline (T0) data, including factors related to dental caries (age, sex, education level, oral health behavior, and parental status), visible plaque index (VPI), decay, missing, filled surface/tooth (DMFS/DMFT) index, the ICDAS clinical scoring (Table 1), and the ICCMS™ radiographic scoring (Table 2). The calibration of clinical (evaluated by the pediatric dentist, O.W.) and radiographic scoring (evaluated by a radiologist, S.N.) was conducted prior to the commencement of the study, and reliability was assessed using Cohen's kappa coefficient. The values for intra-examiner reliability were 0.91 and 0.86 for the clinical and radiographic evaluations, respectively.

After tooth separation, clinical examination was conducted by direct visual and tactile inspection with light force, using a mouth mirror and a World Health Organization (WHO) probe by an independent experienced pediatric dentist who was blinded to the allocation process. Caries status at tooth surface level (according to ICDAS[23]), lesion activity, and presence of plaque were recorded. If any tooth was found to have a cavitated lesion, it was excluded from the study and referred for appropriate treatment. Bitewing radiographs were taken at T0 and T6 using a dental X-ray unit (Heliodent Plus™, Dentsply Sirona Corp., USA, 70 kV, 10 mA, exposure time 0.1 s). The film holders (Rinn XCP™; Dentsply; USA) or Snap A-Ray, with digital plate size 2 were used for standardization and further processed by a digital dental imaging software 6.13.1 (Carestream Health™, Rochester, New York, USA).

Treatment protocol

SDF group

Soft tissues were protected with petroleum jelly to avoid staining and mucosal irritation. Moisture was controlled using cotton rolls and saliva ejectors. A drop of 38.0% SDF (Topamine™) was used to apply on lesions with a small disposable micro brush for 1 minute. Participants were advised to avoid eating and drinking for 30 minutes.

NaF group

Moisture was controlled using cotton rolls and saliva ejectors. NaF was applied directly on the lesions with a gingival brush. Participants were advised to avoid eating hard food for two hours and brush their teeth the next day.

Patient instruction

Participants were instructed to floss at least once daily.

Follow-up

Participants were scheduled for follow-up the presence of biofilm and clinical caries activity every 3 months (T3), aligning with the appropriate interval for patients at high caries risk. If any tooth was found to have a cavitated lesion, it would be restored and excluded from the study. At T6, bitewing radiographs were taken, and a direct clinical examination was conducted after tooth separation.

Table 1 Clinical features and definition of the international caries detection and assessment system (ICDAS)[23]

Code	Description
0 Sound surface	Sound tooth surfaces: no evidence of visible caries (no or questionable change in enamel translucency) when viewed clean and after prolonged air-drying (5 seconds)
1 Initial stage caries	First visual change in enamel: a carious opacity or discoloration when viewed clean and after prolonged air-drying (5 seconds)
2 Initial stage caries	Distinct visual change in enamel: a carious opacity or discoloration that can be seen when the tooth is wet
3 Moderate stage caries	A white or brown spot lesion with localized enamel breakdown due to caries with no visible dentin
4 Moderate stage caries	Underlying dentin shadow (with or without enamel breakdown)
5 Extensive stage caries	Distinct cavity with visible dentin in opaque or discolored enamel with visible dentin
6 Extensive stage caries	Extensive distinct cavity with visible dentin

Table 2 Radiographic scoring system in the international caries classification and management system (ICCMS™)[22]

Code		Description
0: Sound surface		No radiolucency
RA: Initial stages	RA1	Radiolucency in the outer ½ of the enamel
	RA2	Radiolucency in the inner ½ of the enamel +/- DEJ (dentin-enamel junction)
	RA3	Radiolucency limited to the outer 1/3 of dentin
RB: Moderate stages	RB4	Radiolucency reaching the middle 1/3 of dentin
RC: Extensive stages	RC5	Radiolucency reaching the inner 1/3 of dentin, clinically cavitated
	RC6	Radiolucency into the pulp clinically cavitated

Outcome assessment

The criteria for assessing caries arresting through clinical and radiographic examination are either the absence of progression (no change in score) or a decrease in ICDAS or ICCMS radiographic scores. The patient variables were analyzed by the Mann-Whitney U test, Chi-square test, Fisher's exact test, or independent t-test using Statistical Package for Social Sciences (SPSS) 19.0 (SPSS Science, Chicago, Illinois, USA) and STATA 16.0 (Stata Corp, College Station, Texas, USA). The significant differences of caries arresting rates between both groups were tested using the test in proportions and Fisher's exact test with a 95% confidence level.

Results

A total of 82 patients were eligible (Figure 1). After screening, 396 lesions were included: 198 lesions from the NaF group and 198 lesions from the SDF group. At T6, 77 participants, or 93.9%, completed this clinical trial. The dropout rates in the NaF group and the SDF group were 7.0% and 5.1%, respectively. Three participants in the NaF group and two in the SDF group dropped out due to relocation and declined further participation, which is unrelated to caries progression.

The demographic characteristics of participants at baseline are presented in Table 3. According to factors that related to caries arrest rate, 78.0% of participants had exposure to between-meal sugar-containing snacks or beverages 1-2 times per day. For oral hygiene care, all participants brushed at least twice a day with fluoride toothpaste. However, most of them had never used dental floss (93.9%). Regarding clinical characteristics, the mean DMFT index and VPI score of all participants were 4.6±2.1 and 1.5±0.4, respectively. No significant differences in almost any of the factors, except baseline radiographic depths of the collected lesions. Demographic characteristics

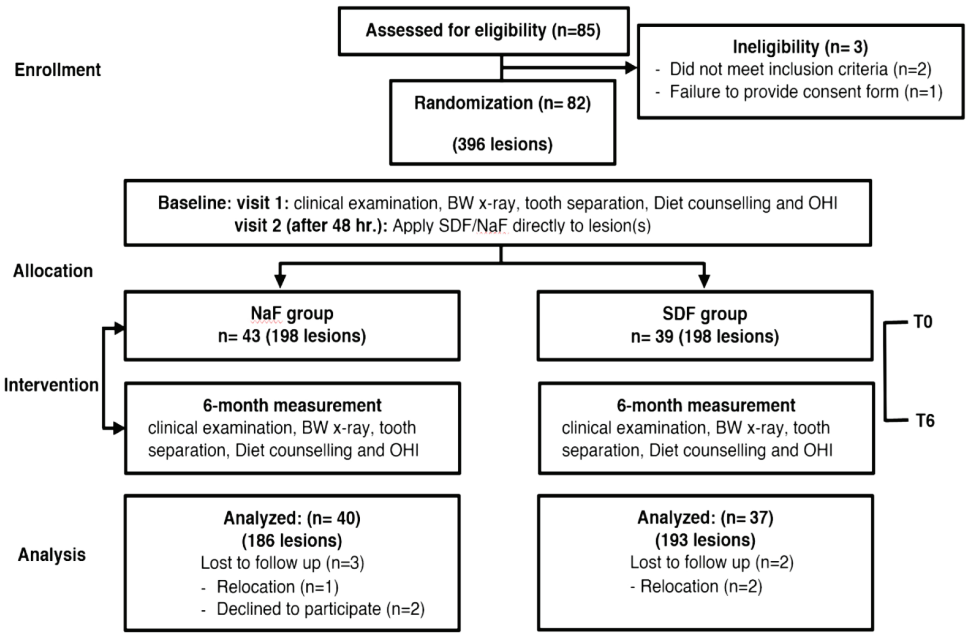

Figure 1 Consort flow of this study (Thai Clinical Trial Registry: TCIR20210706004)

of the 77 (93.9%) participants with 379 lesions who completed this trial were re-evaluated at 6-month follow-up. The NaF and SDF groups were balanced in all aspects. Likewise, there were no significant differences between the participants who remained in the study and those who dropped out of the study.

The caries arrest rates of the SDF group in clinical and radiographic assessments were significantly higher than those of the NaF group (Table 4). From clinical examination, the proportions of the caries arrest rates of the SDF and the NaF groups were 100.0% and 80.1%, respectively. These high caries arrest rates were consistently demonstrated from radiographic examination in the SDF and the NaF groups by 98.4% and 93.5%, respectively.

Table 3 Demographic characteristics of participants at baseline

Variables	Total (N=82)	Intervention group		p-value
		5% NaF (n=43)	38% SDF (n=39)	
Mean age ± S.D., years	10.9±2.7	10.6±2.7	11.1±2.8	0.473[a]
Gender, n (%)				0.280[b]
Male	28 (34.1)	17 (39.5)	11 (28.2)	
Female	54 (65.9)	26 (60.5)	28 (71.8)	
Daily snack taking, n (%)				0.749[c]
No	3 (3.7)	2 (4.7)	1 (2.6)	
1-2 times	64 (78.0)	32 (74.4)	32 (82.0)	
≥3 times	15 (18.3)	9 (20.9)	6 (15.4)	
Oral care products, n (%)				0.495[c]
Yes	2 (2.4)	2 (4.7)	0 (0)	
No	80 (97.6)	41 (95.3)	39 (100)	
Flossing, n (%)				0.665[c]
Regularly	0 (0)	0 (0)	0 (0)	
Sometimes	5 (6.1)	2 (4.7)	3 (7.7)	
No	77 (93.9)	41 (95.3)	36 (92.3)	
Clinical characteristics				
DMFT index, mean ± S.D.	4.7±2.1	4.7±2.0	4.6±2.3	0.783[d]
VPI score, mean ± S.D.	1.6±0.5	1.5±0.5	1.6±0.5	0.622[d]
ICDAS score				0.149[b]
1	17 (4.3)	7 (3.5)	10 (5.1)	
2	334 (84.3)	174 (87.9)	160 (80.8)	
3	45 (11.4)	17 (8.6)	28 (14.1)	
ICCMS™ score				0.024[c]
0	3 (0.7)	1 (0.5)	2 (1.0)	
RA1	321 (81.1)	155 (78.3)	166 (83.8)	
RA2	65 (16.4)	35 (17.7)	30 (15.2)	
RA3	7 (1.8)	7 (3.5)	0 (0)	

S.D.=Standard deviation, DMFT index=the number of decayed (cavitated), missing, and filled permanent teeth, VPI score=the score of visual plaque index, SDF=silver diamine fluoride, ICDAS scores demonstrate clinical characteristic of carious lesions, the score 1 represents the first visual change in enamel, the score 2 represents distinct visual change in enamel, and the score 3 represents localized enamel breakdown, ICCMS™ scores demonstrate the radiographic depth of lesions, the score 0 represents sound surfaces, the score RA1 represents radiolucency in the outer half of the enamel, the score RA2 represents radiolucency in the inner half of the enamel, and the score RA3 represents radiolucency in the outer third of the dentin. The significant differences were tested using [a]Mann-Whitney U test, [b]Chi-square test, [c]Fisher's exact test, or [d]independent t-test

Table 4 Caries arrest rates of non-cavitated lesions at 6-month measurement

Outcome	Arrested lesions, n (%)			Difference (95% CI)	p-value
	Total (n=379)	5.0% NaF (n=186)	38.0% SDF (n=193)		
Clinical examination	342 (90.2)	149 (80.1)	193 (100.0)	19.9 (14.1, 25.6)	<0.001
Radiographic examination	364 (96.0)	174 (93.5)	190 (98.4)	4.4 (0.5-8.2)	0.017

The significant differences were tested using the test of proportions and Fisher's exact test. NaF=sodium fluoride, SDF=silver diamine fluoride, 95% CI=confidence interval

Discussion

Regarding clinical trials in primary teeth, the results demonstrated that participants who received SDF application had more arrested dentin carious lesions than those who received fluoride varnish application[24-26]. Although most of the studies demonstrating SDF efficacy were conducted in primary teeth, the expert panel convened by the American Dental Association Council did not expect SDF to have a substantially different effect when applied on coronal surfaces of permanent teeth[27]. Therefore, this study was designed to evaluate SDF efficacy for caries arresting in permanent teeth. Our outcomes revealed that 38.0% SDF application was more effective for arresting approximal non-cavitated caries than 5.0% NaF varnish application at 6-month measurement. This finding is consistent with the results from previous studies which have demonstrated the superior caries-arresting effect of SDF compared to other interventions[16,28-30]. The study of Llodra and co-authors[29] demonstrated that biannual application of 38.0% SDF was effective in preventing and arresting caries on occlusal surfaces in first permanent molars by 96.0%. Moreover, the study of Braga and coworkers[31] revealed that SDF had a faster ability to arrest or inactivate initial occlusal carious lesions in erupting permanent first molars when compared to cross tooth-brushing with fluoride toothpaste and glass ionomer fissure sealant.

Despite a small number of clinical studies demonstrating SDF efficacy for non-cavitated caries arresting in permanent teeth, the findings from the *in vitro* study on the effects of 38.0% SDF on the demineralized enamel have revealed the possibility[32-34]. This laboratory study has demonstrated that silver penetration was observed on the demineralized enamel that was intact and passed through the dentino-enamel junction[17]. Silver particles can precipitate and mechanically seal the demineralized enamel and dentinal tubules, leading to the blockade of bacterial and acid penetration to dentin. In addition, some studies[35,36] found that SDF could prevent biofilm growth and reduce bacterial adhesion on demineralized and sound tooth surfaces.

This study evaluated caries' outcomes through direct clinical assessment and bitewing radiograph. Most previous studies of caries detection on approximal surfaces used bitewing radiographs as a gold standard for evaluating carious lesions, however, improper angulation or poor image quality can also result in misinterpretation. Therefore, tooth separation was performed to provide a more accurate direct evaluation of approximal caries[37]. Due to significant differences in the baseline radiographic depth (ICCMS™ score) of the collected lesions, seven lesions in the NaF group were classified as RA3 (3.5%), while none were found in the SDF group. We considered the lesion

changes in detail, it was revealed that the most common radiographic progression was from RA1 to RA2 (3.4%), followed by changes from sound surface to RA1 (0.3%) and from RA2 to RA3 (0.3%). However, all RA3 lesions were arrested. Therefore, it can be speculated that the significant differences in baseline radiographic depth are unlikely to affect the results of the study.

A systematic review[14] reported the arresting rates of SDF for dentinal caries in primary teeth at 6, 12, 18, and 30 months as 86.0%, 81.0%, 79.0%, and 71.0%, respectively. It was found that the caries arresting rate of SDF in this study was much higher than in these studies. The authors speculated that this was due to three issues. First, the slow rate of caries progression in permanent teeth may be attributed to the higher mineral content of the enamel surface. Second, this study focuses on enamel-level caries, which progress more slowly than dentin caries. Microstructurally, primary enamel has a thicker, more pronounced, and less mineralized prismatic layer. Hollender and Koch[18] reported that 40-50% of enamel caries in 10-year-old children progressed into dentin or became filled during a three-year follow-up period. Consequently, a longer follow-up period for enamel caries progression in permanent teeth may be required[18]. Third, monitoring caries progression in permanent teeth over six months may be insufficient. A long-term clinical study is needed to gather more information and draw definitive conclusions.

Conclusion

Our study showed that 38.0% SDF was more effective than 5.0% NaF in arresting non-cavitated carious lesions on approximal surfaces in permanent premolars and molars at 6-month follow-up time, and SDF could be a potential treatment option for minimally invasive caries management.

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Conflict of interest

There are no potential conflicts of interest to declare.

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