A randomized clinical trial to arrest dentin caries in young children using silver diamine fluoride.

Abstract

Objectives: The study aimed to compare the effectiveness of 38% silver diamine fluoride (SDF) solution, and 5% sodium fluoride (NaF) varnish applied semiannually in arresting dentin caries in young children with high caries risk. **Methods:** Children aged 1-3 years who had at least one active dentin carious lesion were randomly allocated into 2 groups as follows: Group 1 = 38% SDF (Topamine), and Group 2 = 5% NaF varnish (Duraphat). Both agents were applied every 6 months onto the carious surface. Lesion activity was assessed by the visual-tactile examination. Baseline and follow-up examinations were conducted by the same examiner. The children's demographic background, oral health-related habits, and oral hygiene practices, as well as parental satisfaction with children's dental appearance were collected at baseline and the 12-month follow-up. **Results:** At baseline, 153 and 149 children were recruited in Group 1 and Group 2, respectively. The mean dmfs scores in Groups 1 and 2 were 8.89 and 9.79, respectively. After 12 months, 87.1% remained in the study. The caries arrest rate of Group 1 (35.7%) was significantly higher than that of Group 2 (20.9%) ($p < 0.001$). The results of the multilevel logistic regression analysis confirmed that the treatment in Group 1 was more effective in arresting dentin carious lesions than that of Group 2 (OR = 2.04; 95% CI, 1.41-2.96). The presence of plaque on caries lesions, tooth type, tooth surface type, frequency of milk feeding, snack taking, and family income influenced on caries activity. Regardless of the intervention groups, there were no differences in parental satisfaction with on the child's dental appearance before and after receiving the intervention.

Conclusion: Based on the 12-month results, 38% SDF is more effective than 5% NaF varnish in arresting dentin carious lesions in young children. SDF has no negative impact on parental satisfaction with the child's dental appearance.

Clinical significance: To control dentin carious lesions in young children with high caries risk, 38% SDF is more effective than 5% NaF varnish.

Introduction

Early childhood caries (ECC) is a major global health problem, especially in disadvantaged and low socioeconomic groups [1, 2]. ECC is defined as the presence of one or more decayed, missing (due to caries), or filled tooth surfaces in any primary tooth in a child at 71 months of age or younger [3]. The expert panel at the Bangkok Global Summit on ECC 2018 summarized that average worldwide prevalence of ECC in 1 to 5-year-olds was 17%, 36%, 43%, 55%, and 63%, respectively [4]. The prevalence of ECC in 5-year-old children reached 90% in some developing countries [5]. The development and progression of ECC are very typical. The primary teeth of high caries risk children can become carious teeth within 3-6 months after eruption [6]. When initial caries occurs, it can progress to cavitated lesions rapidly [7]. If left untreated, ECC can affect not only children's growth, daily activities, self-esteem, and future dentition but also their family function and distress [8, 9]. In many developing countries, more than 90% of ECC remained untreated [10].

There are many obstacles to managing and preventing the progression of ECC. Limitations on cognitive and psychosocial development make very young children unable to cooperate in

restorative treatment or even routine dental care [11]. The majority of parents are unlikely to bring their children to see a dentist. Restorative management of ECC is generally costly, time-consuming and requires experienced dentists. With a high burden of ECC, preventive and therapeutic modalities that can prevent or delay caries progression with affordable cost and noninvasive procedures should be advocated to manage ECC in young children.

Fluoride in various vehicles has been widely used for caries prevention and control. Sodium fluoride (NaF) varnish has been one of the most widely used topical fluorides for more than 50 years. It can adhere to the tooth surface and release fluoride ion into the oral cavity for several hours. However, a recent systematic review showed that NaF varnish had a modest benefit in preventing new dentin carious lesions [12]. Silver diamine fluoride (SDF) is a topical fluoride solution containing a high concentration of fluoride and silver that has recently drawn much attention from both clinicians and researchers. The caries-arrest effectiveness is promising due to the synergistic effects of silver, which acts as an antimicrobial agent, and fluoride, which promotes remineralization, whereas ammonia helps to stabilize the concentrations of the solution [13]. Several published systematic reviews confirmed the effectiveness of SDF in arresting dentin caries in primary teeth, with high success rates ranging from 65% to 91% [14, 15].

Although the effectiveness of SDF on caries arrest in children is impressive, most studies were conducted in preschool children. Because ECC is extremely prevalent in Southeast Asia and can progress rapidly with age [2, 16], the adoption of SDF treatment in toddlers in nursery care centers who are at high caries risk would be very beneficial to reduce the severe consequences of untreated caries during the preschool period. To date, there is scarce information regarding the caries-arrest

effectiveness of SDF in children aged 1-3 years. In addition, the safety issues and parental satisfaction with SDF application remain the major concerns for caries management in young children. Therefore, the objective of this study was to compare the effectiveness of 38% SDF solution, and 5% NaF varnish applied semiannually in arresting dentin caries in young children aged 1-3 years. The null hypothesis was that the caries arrest rates of the carious tooth surfaces treated with 2 intervention protocols were the same.

Materials and Methods

This randomized, two-arm, parallel-design, clinical trial was approved by the Institutional Review Board of the Faculty of Dentistry/Faculty of Pharmacy,.....University (No.2018/DT021) and registered in the Thai Clinical Trials Registry (TCTR20180624001).

The study site was conducted in Fang district, Chiang Mai Province, Thailand, where fluoride concentration in drinking water is ≤ 0.3 ppm. In this district, there are 42 registered public child development centers aiming to provide appropriate child care in a day time for young children aged 1-5 years in a safe and educational environment. Consecutive sampling was adopted. Among them, 19 centers were invited, and all of them agreed to join the study. The inclusion criteria were children aged 1-3 years who had at least one active cavitated dentin caries. Children were excluded if they had a history of major systemic diseases, long-term medication, known allergic reaction to fluoride or silver, or colophony agents. The research purposes and procedures, risks and benefits of the study were explained to the parents before they signed informed consent.

A single dentist (S.M.) was trained and calibrated with dental specialists in dental public health (D.D.) and pediatric dentistry (V.J.).

During the calibration, duplicate examinations were conducted in 10 children aged 3 years in a dental clinic until the kappa values of inter and intra-reliability were reached ≥ 0.8. The oral examinations were conducted at the child development centers using World Health Organization CPI periodontal probes (405/WHO probe) with disposable dental mirrors attached to a light-emitting diode (LED) intra-oral light source (MirrorLite, Kudos, Hong Kong) in knee-to-knee position. The oral hygiene status was measured using the visible plaque index (VPI) [17] on the buccal and lingual surfaces of 6 index teeth (55, 51, 63, 71, 75, and 83). The decayed, missing, and filled teeth (dmft) index was used to measure the child's caries experience. The carious lesion activity was evaluated by visual-tactile inspection using a WHO CPI periodontal probe without radiograph examination. A soft tooth surface, when gently drawing the probe, was diagnosed as an active lesion. A smooth and hard tooth surface that could not be penetrated easily was classified as an arrested lesion [18]. Five tooth surfaces (buccal, lingual, mesial, distal and occlusal) were examined in each posterior tooth and 4 tooth surfaces (labial, lingual, mesial and distal) in each anterior tooth.

The estimated sample size was based on the result of the meta-analysis, concluding that the overall percentage of arrested dentin caries was 65.9% [15], and an absolute 10% difference between groups was clinically significant. The power of the study was set at 80% ($\beta = 0.2$), with $\alpha = 0.05$ as the statistical significance level. Thus, at least 343 dentin carious tooth surfaces were required in each arm, as calculated using Sample Power 2.0 (SPSS, Inc.). The mean number of active dentin carious tooth surfaces was anticipated to be 7 [19]. The anticipated intraclass correlation

coefficient (ICC) was 0.3 [20]. Based on the equation of sample size estimation in a multilevel study [21], 960 active carious tooth surfaces in 137 children/group would be required. With an estimated 10% dropout rate, approximately 150 children/group needed to be recruited at baseline.

The participants were randomly assigned to one of the following groups: Group 1 received 38% SDF (Topamine, DentaLife, Australia) and Group 2 received 5% NaF varnish (Duraphat, Colgate Palmolive, USA) via the stratified block randomization method with two strata of the severity of caries experience (dmft = 1-4 and dmft > 4) in a block size of 4. The participant allocation lists were kept in opaque, sealed envelopes and arranged sequentially by a dental assistant, who was not involved in the study. Each envelope was opened after completing an oral examination and right before the application of fluoride treatment. Topical applications of 38% SDF or 5% NaF varnish were carried out by 2 dental nurses who were not involved in the screening and assessing of the lesion activity. Before conducting the study, the 2 dental nurses, who were experienced in the community dental programs, were trained by pediatric dentists (S.M. and V.J.) to apply SDF treatment in an outreach setting. The clinical procedures of the research intervention were followed. All teeth were cleaned and isolated with gauze. No attempt was made to remove carious tissues before fluoride application. In Group 1, each carious lesion was painted and rubbed with 38% SDF using a disposable micro-applicator for 10 seconds. In Group 2, 5% NaF varnish was applied to the lesions. After application, the participants were not allowed to drink or eat for at least 30 minutes. The fluoride applications in both groups were done at baseline and repeated every 6 months.

At the 6- and 12-month follow-ups, the oral health status, and carious lesion activity were assessed by the same examiner who conducted the baseline examination using the same diagnostic criteria stated in the baseline examination and who was blinded to the group assignment. Duplicate examinations of carious lesion activity were randomly conducted on 10% of the participants at baseline and follow-up examinations after 2 week of their first examinations to assess the intraexaminer reliability using Cohen's kappa statistics. Information on participants' demographic background, and children's oral-health related behaviors were administered through a questionnaire completed by the children's parents or caretakers at baseline and 12-month follow-up. Parents' satisfaction with their children's dental appearance was also collected through a self-rated questionnaire with a Likert scale at baseline and 12-month follow-up.

Data were analyzed using the software SPSS 20.0 for Windows (SPSS Inc., Chicago, USA). The level of statistical significance was set at 0.05. The intention-to-treat analysis was undertaken and conducted at the tooth surface level. The caries lesion status at the follow-up visit of the lost participants was replaced with the latest examination status. The carious teeth or surfaces that received operative or surgical treatment between follow-up times were recorded as failures or active lesions. The chi-square test was used to compare the differences between Group 1 and Group 2 in terms of their baseline demographic background, oral health-related behaviors, caries arrest rate and parents' satisfaction. The comparability of age, VPI scores, dmft and dmfs scores between both groups was assessed using an independent samples t-test or Mann-Whitney U test depending on their normality of distribution. A multilevel multivariate logistic regression analysis was performed to analyze the effectiveness of 38% SDF on caries arrest rates at the 12-month examination. The effects of other variables including baseline demographic background, oral

health-related behaviors at baseline, and clinical characteristics on the caries arrest rates were also evaluated.

Results

At baseline, a total of 302 children (57% boys) with 2249 active dentin carious tooth surfaces participated in the study. Their mean (SD) age was 36.8 (6.4) months, ranging from 18 months to 47 months. The overall mean dmft (SD) and dmfs (SD) were 5.3 (3.6) and 9.2 (9.0), respectively. The majority of the study children were on milk feeding (81.1%) and brushed their teeth at least once a day (90.6%) with fluoride toothpaste (91.4%). In Group 1 (38% SDF), the numbers of participants and active dentin carious tooth surfaces were 153 and 1111, respectively, whereas, in Group 2 (5% NaF), there were 149 participants with 1138 active dentin carious tooth surfaces (Fig. 1). At baseline, there were no statistically significant differences between Groups 1 and 2 in terms of demographic background, except family income (Table 1). The baseline oral health related behaviors, caries experiences, and VPI scores of both groups were comparable.

After 12 months, 263 participants (87.1%) remained in the study. The dropout rates in Group 1 and Group 2 were 15.0% and 10.7%, respectively (p = 0.305) (Fig. 1). Intraobserver reproducibility was very good throughout the study. The values of the kappa statistics for the duplicate assessment on dentin carious activity were 0.86, 0.96, and 0.90 at baseline and 6- and 12-month follow-ups, respectively.

As shown in Table 2, the overall proportions of arrested carious surfaces of Groups 1 and 2 were 20.5% and 12.3% at 6 months and 35.7% and 20.9% at 12 months, respectively. There were

182 statistically significant differences in caries arrest rates between the 2 groups at all follow-up
183 examinations ($p < 0.001$). Regarding the tooth position, the proportions of caries arrest rates of
184 upper and lower anterior teeth and upper posterior teeth in Group 1 were statistically significantly
185 higher than those in Group 2 at the 6- and 12-month follow-ups ($p < 0.001$). However, no
186 differences in caries arrest rates of lower posterior teeth were found between groups at all follow-
187 up examinations ($p > 0.05$). The proportions of arrested tooth surfaces on buccal/lingual, proximal,
188 and occlusal surfaces in Group 1 were significantly higher than those in Group 2 at 12-month
189 follow-up ($p < 0.001$, $p < 0.001$, $p = 0.015$, respectively).
190
191 The results of the multilevel logistic regression analysis are presented in Table 3. The treatment
192 group, presence of plaque on the carious tooth surface, tooth position, tooth surface type, frequency
193 of daily milk feeding, snack taking, and monthly family income influenced on caries activity. The
194 Group 1 treatment was more effective in arresting dentin carious lesions than that of Group 2 (OR
195 = 2.04; 95% CI, 1.41-2.96). The carious surface in a toddler with a higher VPI score had a lower
196 chance of becoming arrested ($p = 0.001$). Regarding the tooth position, the carious tooth surfaces
197 on upper anterior teeth were more likely to become arrested than those on lower posterior teeth
198 (OR = 2.54; 95% CI, 1.51-4.29). The buccal/lingual carious tooth surfaces had a higher chance of
199 becoming arrested compared to occlusal surfaces. The study children who were weaned from milk
200 feeding had an increased chance (2.17 times as likely) of caries arrest, compared to those with milk
201 feeding more than 3 times a day. The chance of caries arrest in a toddler without daily snacking
202 was higher (2.24 times as likely) compared to those taking snacks 3 times or more.
203

Regarding the parents' satisfaction at baseline, 55.6% and 61.7% of parents in Group 1 and Group 2, respectively, were satisfied with their children's dental appearance ($p = 0.383$) (Table 4). At the 12-month follow-up, the parents' satisfaction with their children's dental appearance in both groups remained similar to that reported at baseline (McNemar, $p > 0.05$). No significant difference in parental satisfaction with children's dental appearance between Group 1 (38% SDF) and Group 2 (5% NaF varnish) was found ($p = 0.475$). After the study intervention, no major adverse effects and systematic illnesses, including vomiting or nausea, were reported.

Discussion

Although it has been documented that SDF reduces caries progression significantly when compared with other modalities, most of the published randomized clinical trials were performed in children 3 years old or older [18, 22, 23]. It is uncertain if SDF treatment in younger children would be as effective as that in older children, because of their inability to cooperate during the SDF intervention along with complement with the compromised oral health-related behaviors of young children (e.g., bottle feedings at night and not yet starting tooth brushing). The results of the present study could strengthen the evidence and address the research gap regarding the use of SDF in very young children with high caries risk.

Based on the 12-month results, the use of 38% SDF to arrest dentin caries in young children is supported due to its higher caries-arrest effectiveness compared to 5% NaF varnish when applied semiannually. The null hypothesis assuming no difference in caries arrest rate using 38% SDF and 5% NaF varnish was rejected. The chance of ECC being arrested by SDF treatment was higher (2 times as likely) compared to that of 5% NaF varnish. These findings are in agreement with

previous clinical trials supporting the beneficial effect of SDF in arresting dentin caries in primary teeth [22, 24]. The possible explanation may be that 38% SDF contains a high concentration of both silver (253,870 ppm) and fluoride (44,800 ppm) and has an alkaline property. This altogether could help enhance the dentin remineralization process and inhibit bacterial growth when compared with the comparator (5% NaF varnish), which has a lower concentration of fluoride (22,600 ppm) [25, 26].

Nevertheless, it should be noted that the caries arrest rate with use of 38% SDF in the present study (35.7%) was lower than those reported by Fung et al. (62.6%) and Zhi et al. (53%) at the 12-month examination [22, 24]. The differences in caries arrest rates may be due to theses unfavorable conditions of the study children including younger age group, higher caries experience, compromised oral-health related behaviors, and different demographic background compared to those in the previous studies [18, 24]. Second, the application procedure in very young children is more challenging due to their inability to cooperate compared to older children. ECC management in toddlers with high caries experiences may require more comprehensive preventive measures such as more frequent SDF application and individualized oral hygiene instruction.

As seen in Table 2, the caries arrest rates of both topical fluorides at the 12-month follow-up were higher than those at the 6-month follow-up. This implies that the reapplication of topical fluorides increases the success of caries arrest treatment over time. Thus, if a single application of SDF yields unfavorable outcomes in high caries risk populations, follow-up with reapplication of SDF is required in subsequent visits. Several factors may influence the caries arrest process. In addition, the clustering effect is another concern, because one child may exhibit more than one decayed

tooth surface that can be included in the study. Thus, a multilevel multivariate logistic regression analysis was performed. The final model was adjusted by several significant factors in both levels: patient level and tooth surface level. The results were in line with those of previous studies [18, 24]. Topical fluoride application tends to be more effective in arresting lesions on labial/lingual surfaces and in anterior teeth, compared to other surfaces and posterior teeth [22, 27]. The current study showed that the carious lesions of children who presented with poor oral hygiene and high frequency of milk feeding and snacking were less likely to be controlled by professionally applied topical fluoride alone. In other words, SDF application should not be regarded as a silver bullet to stop ECC. In fact, it is crucial to emphasize children's oral health and encourage parents or caregivers to maintain effective plaque control and adopt healthy child-rearing practices in complement with the follow-up visits with caries risk assessment and SDF reapplication.

Due to the high concentrations of fluoride and silver, the toxicity of 38% SDF remains a concern when applying in very young children. In the present study, we used one drop of 38% SDF (25 μL) per child. Thus, it contained approximately 1.12 mg of fluoride and 6.34 mg of silver. Based on the probably toxic dose of fluoride at 5 mg/kg [28] and the median lethal dose of silver by oral administration suggested to be 380-520 mg/kg [29], the amount of fluoride and silver would be far below the toxic doses. As a result, no systemic adverse events were reported by parents or caregivers in the child development centers during the whole study period. The results of this study could provide and strengthen clinical evidence regarding the safety of using one drop (25 μL) or less when applying 38% SDF semiannually in toddlers.

The known side effect of SDF in blackening carious lesions was commonly reported in previous studies. In the United States, the most frequently reported barrier to adopting SDF was the parental acceptance of black staining [31]. In our study, after the parents were informed about the application procedures and SDF's effectiveness, most parents (93.5%) accepted this drawback and agreed to join the study. After 12 months, parental satisfaction with the children's dental appearance in both groups remained unaltered, compared to that at baseline. Put differently, parents' satisfaction with children's dental appearance did not deteriorate after caries arrest treatment. The results are in accordance with a previous study in Hong Kong [30]. Nevertheless, in many cultures where dental esthetics is a concern, the unavoidable side effect of SDF (black staining) should be described and discussed with parents before applying SDF. Caution should be exercised when transferring these findings to other countries where child-nurturing practices and cultures are different.

The present study has several strengths, such as high participation rate, sufficient sample size, and good intraexamination reliability. Some study limitations should also be addressed. First, this study assessed caries activity using the visual-tactile examination [32] because radiography was infeasible and impractical in the community setting. Second, detection bias could have occurred due to the black staining of SDF. Nonetheless, a trained examiner who was not involved in the treatment protocol was blinded throughout the study period. In addition, the 12-month study period was relatively short for confirming caries progression and activity. A future study with a longer follow-up period is required to verify or refute the clinical effectiveness of SDF in very young children with high caries risk.

Our results concur with those of Chu et al. [33] that ECC management with 38% SDF is more effective than the use of NaF varnish for controlling existing cavitated lesions. However, the effectiveness of SDF in children with severe ECC in the present study was much lower than that reported in a previous study [33]. The possible explanation is that our study applied the treatment on both anterior and posterior teeth in children aged 1-3 years, whereas the previous study applied SDF on anterior primary teeth in older children. Further study (e.g., with more frequent application per year) is needed to investigate if the caries-arrest effectiveness of SDF could be enhanced when applying in very young children with severe ECC.

Based on the results of the present study, SDF is safe for toddlers who are normally unable to cooperate with traditional caries management. SDF treatment is simple and practical to implement in a community setting because it requires less time and fewer resources. No special equipment and no dental specialist are needed. It is likely that SDF treatment can be delivered by trained primary dental care providers or allied health care professionals to improve access to dental care in remote areas or disadvantaged communities where untreated ECC and early loss of primary teeth are prevailing.

Conclusion

Semiannual application of 38% SDF is more effective than that of 5% NaF varnish in arresting dentin carious lesions in young children with high caries risk. Both topical fluoride agents have no significant side effects and no impact on parental satisfaction with children's dental appearance.

References

[1] J. Pinilla, M.A. Negrín-Hernández, I. Abásolo, Time trends in socioeconomic inequalities in the lack of access to dental services among children in Spain 1987–2011, Int J Equity Health 14(9) (2015). https://doi.org/ 10.1186/s12939-015-0132-8.

[2] D. Duangthip, S.S. Gao, E.C. Lo, C.H. Chu, Early childhood caries among 5- to 6-year-old children in Southeast Asia, Int Dent J 67(2) (2017) 98-106.

[3] Policy on Early Childhood Caries (ECC): Classifications, consequences, and preventive strategies, Pediatr Dent 38(6) (2016) 52-54.

[4] N. Tinanoff, R.J. Baez, C. Diaz Guillory, K.J. Donly, C.A. Feldens, C. McGrath, P. Phantumvanit, N.B. Pitts, W.K. Seow, N. Sharkov, Y. Songpaisan, S. Twetman, Early childhood caries epidemiology, aetiology, risk assessment, societal burden, management, education, and policy: Global perspective, Int J Paediatr Dent 29(3) (2019) 238-248.

[5] K.J. Chen, S.S. Gao, D. Duangthip, E.C.M. Lo, C.H. Chu, Prevalence of early childhood caries among 5-year-old children: A systematic review, J Investig Clin Dent 10(1) (2019) e12376.

[6] S. Thitasomakul, A. Thearmontree, S. Piwat, O. Chankanka, W. Pithpornchaiyakul, R. Teanpaisan, S. Madyusoh, A longitudinal study of early childhood caries in 9- to 18-month-old Thai infants, Community Dent Oral Epidemiol 34(6) (2006) 429-36.

[7] M. Grindefjord, G. Dahllöf, T. Modéer, Caries development in children from 2.5 to 3.5 years of age: a longitudinal study, Caries Res 29(6) (1995) 449-54.

[8] B.T. Pahel, R.G. Rozier, G.D. Slade, Parental perceptions of children's oral health: the Early Childhood Oral Health Impact Scale (ECOHIS), Health Qual Life Outcomes 5 (2007) 6.

[9] H. Ayhan, E. Suskan, S. Yildirim, The effect of nursing or rampant caries on height, body weight and head circumference, J Clin Pediatr Dent 20(3) (1996) 209-12.

[10] N.J. Kassebaum, E. Bernabé, M. Dahiya, B. Bhandari, C.J. Murray, W. Marcenes, Global burden of untreated caries: a systematic review and metaregression, J Dent Res 94(5) (2015) 650-8.

[11] C.M. Pine, P.M. Adair, G. Burnside, A.D. Nicoll, A. Gillett, S.A. Borges-Yáñez, Z. Broukal, J. Brown, D. Declerck, F.X. Ping, T. Gugushe, J. Hunsrisakhun, E.C. Lo, S. Naidoo, U. Nyandindi, V.J. Poulsen, N. Razanamihaja, C. Splieth, B.K. Sutton, T.C. Soo, H. Whelton, Barriers to the treatment of childhood caries perceived by dentists working in different countries, Community Dent health 21(1 Suppl) (2004) 112-20.

[12] F.S.O. de Sousa, A.P.P. Dos Santos, P. Nadanovsky, P. Hujoel, J. Cunha-Cruz, B.H. de Oliveira, Fluoride varnish and dental caries in preschoolers: a systematic review and meta-analysis, Caries Res 53(5) (2019) 502-513.

[13] A. Rosenblatt, T.C. Stamford, R. Niederman, Silver diamine fluoride: a caries "silver-fluoride bullet", J Dent Res 88(2) (2009) 116-25.

[14] N. Seifo, H. Cassie, J.R. Radford, N.P.T. Innes, Silver diamine fluoride for managing carious lesions: an umbrella review, BMC Oral Health 19(1) (2019) 145.

[15] S.S. Gao, S. Zhang, M.L. Mei, E.C. Lo, C.H. Chu, Caries remineralisation and arresting effect in children by professionally applied fluoride treatment - a systematic review, BMC Oral Health 16 (2016) 12.

[16] D. Duangthip, K.J. Chen, S.S. Gao, E.C.M. Lo, C.H. Chu, Early childhood caries among 3- to 5-year-old children in Hong Kong, Int Dent J 69(3) (2019) 230-236.

[17] J. Ainamo, I. Bay, Problems and proposals for recording gingivitis and plaque, Int Dent J 25(4) (1975) 229-35.

[18] D. Duangthip, M.C.M. Wong, C.H. Chu, E.C.M. Lo, Caries arrest by topical fluorides in preschool children: 30-month results, J Dent 70 (2018) 74-79.

[19] S. Sutthavong, S. Taebanpakul, C. Kuruchitkosol, T.I. Ayudhya, T. Chantveerawong, S. Fuangroong, S. Cae-Ngow, R. Rangsin, Oral health status, dental caries risk factors of the children of public kindergarten and schools in Phranakornsriayudhya, Thailand, J Med Assoc Thai 93(6 Suppl) (2010) S71-78.

[20] M. Masood, Y. Masood, J.T. Newton, The clustering effects of surfaces within the tooth and teeth within individuals, J Dent Res 94(2) (2015) 281–288.

[21] J.W.R. Twisk, Applied multilevel analysis: practical guides to biostatistics and epidemiology, Cambridge University Press, Cambridge, 2006.

[22] Q.H. Zhi, E.C. Lo, H.C. Lin, Randomized clinical trial on effectiveness of silver diamine fluoride and glass ionomer in arresting dentine caries in preschool children, J Dent 40(11) (2012) 962-967.

[23] J.C. Llodra, A. Rodriguez, B. Ferrer, V. Menardia, T. Ramos, M. Morato, Efficacy of silver diamine fluoride for caries reduction in primary teeth and first permanent molars of schoolchildren: 36-month clinical trial, J Dent Res 84(8) (2005) 721-4.

[24] M.H.T. Fung, D. Duangthip, M.C.M. Wong, E.C.M. Lo, C.H. Chu, Randomized clinical trial of 12% and 38% silver diamine fluoride treatment, J Dent Res 97(2) (2018) 171-178.

[25] O.Y. Yu, I.S. Zhao, M.L. Mei, E.C.M. Lo, C.H. Chu, Caries-arresting effects of silver diamine fluoride and sodium fluoride on dentine caries lesions, J Dent 78 (2018) 65-71.

[26] M.L. Mei, E.C.M. Lo, C.H. Chu, Arresting Dentine Caries with Silver Diamine Fluoride: What's Behind It?, J Dent Res 97(7) (2018) 751-758.

[27] D. Duangthip, C.H. Chu, E.C. Lo, A randomized clinical trial on arresting dentine caries in preschool children by topical fluorides--18 month results, J Dent 44 (2016) 57-63.

[28] G.M. Whitford, Fluoride in dental products: safety considerations, J Dent Res 66(5) (1987) 1056-60.

[29] J.A. Horst, H. Ellenikiotis, P.L. Milgrom, UCSF Protocol for caries arrest using silver diamine fluoride: rationale, indications and consent, J Calif Dent Assoc 44(1) (2016) 16-28.

[30] D. Duangthip, M.H.T. Fung, M.C.M. Wong, C.H. Chu, E.C.M. Lo, Adverse effects of silver diamine fluoride treatment among preschool Children, J Dent Res 97(4) (2018) 395-401.

[31] T. Nelson, J.M. Scott, Y.O. Crystal, J.H.Berg, P. Milgrom, Silver diamine fluoride in pediatric dentistry training programs: survey of graduate program directors, Pediatr Dent 38(3) (2016) 212-217.

[32] M.M. Braga, S. Martignon, K.R. Ekstrand, D.N. Ricketts, J.C. Imparato, F.M. Mendes, Parameters associated with active caries lesions assessed by two different visual scoring systems on occlusal surfaces of primary molars - a multilevel approach, Community Dent Oral Epidemiol 38(6) (2010) 549-58.

[33] C.H. Chu, E.C. Lo, H.C. Lin, Effectiveness of silver diamine fluoride and sodium fluoride varnish in arresting dentin caries in Chinese pre-school children, J Dental Res 81(11) (2002) 767-70.

407

408

409 **Table 1.** Demographic background, oral health–related habits, and clinical characteristics of
410 participants at baseline.

	Group 1: 38% SDF (N=153)	Group 2: 5% NaF (N=149)	P-value
Demographic background	Mean (SD)	Mean (SD)	
Age	36.6(6.7)	37.0(6.1)	0.558[#]
	n (%)	n (%)	
Gender			0.369
Male	91(59.5)	81(54.4)	
Female	62(40.5)	68(45.6)	
Mother's education level			0.089
Primary school or lower	79(51.6)	93 (62.4)	
Secondary school	58 (37.9)	39 (26.2)	
College or university	16 (10.5)	17 (11.4)	
Monthly family income			0.020
< 10,000 Baht	98 (64.1)	75 (50.3)	
≥ 10,000 Baht	55 (35.9)	74 (49.7)	
Oral health related habits	n (%)	n (%)	
Daily milk feeding			0.393
None	27(17.6)	30(20.1)	
1-3 times	75(49.0)	80(53.7)	
> 3 times	51 (33.3)	39 (26.2)	
Daily snack taking			0.382
< 1 time	12(7.8)	15(10.1)	
1-2 times	108(70.6)	94(63.1)	
≥ 3 times	33(21.6)	40(26.8)	
Daily tooth brushing			0.904
< 2 time	15(9.8)	14 (9.4)	
≥ 2 times	138 (90.2)	135(90.6)	
Brushing with fluoride tooth paste			0.631
Yes	141 (92.2)	135 (90.6)	
No	12 (7.8)	14 (9.4)	
Clinical characteristics	Mean (SD)	Mean (SD)	
dmft	5.01 (3.1)	5.54 (3.9)	0.515[*]
dmfs	8.89 (7.4)	9.79 (10.4)	0.910[*]
Visible plaque index	0.69 (0.24)	0.71(0.23)	0.624[#]

[#]independent samples t-test
[*]Mann-Whitney U test

Table 2. Caries arrest rates of active dentine carious tooth surfaces at 6 and 12-month follow-up examinations

	Group 1: 38% SDF % (n/N)	Group 2: 5%NaF % (n/N)	P-value
Overall			
6 months	20.5 (228/1,111)	12.3 (140/1,138)	<0.001
12 months	35.7 (397/1,111)	20.9 (238/1,138)	<0.001
Tooth position			
Upper anterior teeth			
6 months	21.0 (157/746)	14.6 (97/666)	0.002
12 months	39.1 (292/746)	27.0 (180/666)	<0.001
Upper posterior teeth			
6 months	17.8 (26/146)	8.0 (14/176)	0.008
12 months	30.8 (45/146)	10.8 (19/176)	<0.001
Lower anterior teeth			
6 months	26.7 (23/86)	6.7 (7/105)	<0.001
12 months	45.3 (39/86)	9.5 (10/105)	<0.001
Lower posterior teeth			
6 months	16.5 (22/133)	11.5 (22/191)	0.194
12 months	15.8 (21/133)	15.2 (29/191)	0.882
Tooth surface type			
Buccal / Lingual surface			
6 months	29.3 (112/382)	15.8 (69/438)	<0.001
12 months	42.9 (164/382)	25.8 (113/438)	<0.001
Proximal surface			
6 months	15.5 (83/537)	9.6 (46/479)	0.006
12 months	35.9 (193/537)	20.7 (99/479)	<0.001
Occlusal surface			
6 months	17.2 (33/192)	11.3 (25/221)	0.091
12 months	20.8 (40/192)	11.8 (26/221)	0.015

Table 3. Multilevel logistic regression model of the caries arrest rate of dentin carious tooth surfaces at the 12-month follow-up

Explanatory variables	Adjusted Odds ratio[b]	95% CI	P-value
Group			
38% SDF	2.04	1.41 – 2.96	<0.001
5% NaF[a]			
Tooth position			
Upper anterior	2.54	1.51 - 4.29	0.001
Lower anterior	1.94	0.90 – 4.18	0.091
Upper posterior	1.53	0.96 – 2.43	0.074
Lower posterior[a]			
Tooth surface type			
Buccal / lingual	1.70	1.18– 2.43	0.004
Proximal	1.13	0.75 – 1.71	0.596
Occlusal[a]			
Daily milk feeding			
None	2.17	1.24-3.77	0.006
1-3 times	1.63	1.06 - 2.51	0.027
> 3 times[a]			
Daily snack taking			
None	2.24	1.12-4.46	0.022
1-2 times	1.08	0.69-1.69	0.745
≥ 3 times[a]			
Monthly family income			
< 10,000 Baht	1.73	1.17- 2.56	0.006
≥ 10,000 Baht[a]			
Visible plaque index	0.23	0.10-0.54	0.001

[a] reference category

[b] excluded non-significant variables: sex, dmfs at baseline, parental status, education level of parents, main caretaker, who brushed the children's teeth, method of milk feeding, sleep with bottle, frequency of tooth brushing, and use of fluoride toothpaste.

Table 4. Parental satisfaction on participant's dental appearance at baseline and the 12-month follow-up.

	Group 1: 38% SDF	Group 2: 5%NaF	P-value*
Baseline	n=153	n=149	0.383
Very satisfied	2.0 (3/153)	4.0 (6/149)	
Satisfied	55.6 (85/153)	61.7 (92/149)	
Unsatisfied	41.2 (63/153)	33.6 (50/149)	
Very unsatisfied	1.3 (2/153)	0.7 (1/149)	
12-month	n=130	n=133	0.475
Very satisfied	1.5 (2/130)	2.3 (3/133)	
Satisfied	54.6 (71/130)	63.2 (84/133)	
Unsatisfied	41.5 (54/130)	32.3 (43/133)	
Very unsatisfied	2.3 (3/130)	2.3 (3/133)	
P-value**	0.227	0.474	

*Chi-square test; ** McNemar-Bowker Test