

## Silver Diamine Fluoride for Caries Management in Primary Teeth – A Literature Review

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### Abstract

Global research interest in the efficacy of silver diamine fluoride (SDF) for caries management has rapidly increased in recent years. According to several clinical trials, SDF has had more efficacy for arresting cavitated dentin caries in primary teeth than any comparators. The arresting mechanisms could relate to the unique properties of silver ions and the high concentration of fluoride, including antimicrobial effects, inhibition of demineralization, promotion of remineralization, and inhibition of dentin collagen degradation. Insufficient evidence exists to draw conclusions on the caries prevention effect and non-cavitated caries arrest in primary teeth or the caries prevention and arresting effects in permanent teeth.

The presence of plaque is the most reported factor in reducing caries arrest. Therefore, SDF treatment should be done in conjunction with comprehensive caries preventive measures to achieve maximum efficacy. The black staining from SDF is a barrier to parental acceptance, but the key factors affecting acceptance were the location of the teeth and the child's cooperation. Due to its efficacy and simplicity, SDF is recommended as a potential measure for caries management.

This article highlights the beneficial effects and considerations of SDF treatment in primary teeth based on recent evidence.

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### Introduction

Dental caries is one of the most prevalent diseases in children worldwide.<sup>1</sup> The prevalence of dental caries in pre-schoolers globally ranged from 23% to 90% and was higher than 50% in several countries.<sup>2</sup> Caries in primary teeth negatively affect the quality of life of children and parents, including through weight loss or nutrition problems, increased household expenses, and consequent increased need for extensive treatment under general anesthesia.<sup>3, 4</sup> Previous studies have demonstrated the efficacy of silver diamine fluoride (SDF) for arresting cavitated lesions in both primary and permanent teeth with a high success rate.<sup>5</sup> Therefore, SDF might be a

promising option for caries management at the lesion level, particularly in children with caries susceptibility.

#### Silver diamine fluoride

SDF ( $\text{Ag}(\text{NH}_3)_2\text{F}$ ) is a blue-tinted or colorless alkaline solution containing 24.4–28.8% silver, 5.0–5.9% fluoride, and 8% ammonia.<sup>6</sup> SDF was developed in Japan in the 1960s, and it has been used for arresting caries in preschool children since 1969.<sup>7</sup> SDF is manufactured with different concentrations, such as 10, 12, 30, and 38%.<sup>8</sup> SDF application is a safe, simple, non-invasive, and cost-effective method of caries management comparable to fluoride varnish application.<sup>9</sup>

#### Mechanisms of action

The arresting effects could relate to the properties of the active ingredients in SDF, including the antibacterial effects of 24.4–28.8% silver, the remineralization capability of 5.0–5.9% fluoride, and 8% ammonia as a compound stabilizer, resulting in its high concentration of fluoride components (up to 44,800 ppm) and its alkalinity (pH 10).<sup>10, 11</sup> Several *in vitro* studies have demonstrated that the mechanisms of SDF

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may consist of bactericidal and bacteriostatic activities, inhibition of bacterial adhesion, inhibition of demineralization, promotion of remineralization, and inhibition of dentin collagen degradation.<sup>10</sup> Inhibition of mineral loss may result from the high fluoride concentration in SDF, which can induce the formation of calcium fluoride (CaF<sub>2</sub>) and fluorapatite (Ca<sub>10</sub>(PO<sub>4</sub>)<sub>6</sub>F<sub>2</sub>) on treated lesions.<sup>12</sup> Another typical mechanism of SDF, which directly correlates with the arresting of dentinal caries, is its effect on the dentinal organic content. SDF has shown an inhibitory effect on matrix metalloproteinase (MMP-2, MMP-8, and MMP-9) and cathepsins, which are proteolytic enzymes that contribute to dentin collagen degradation.<sup>13, 14</sup> Therefore, in combination, these mechanisms are likely to promote the caries-arresting effect of SDF over other anticaries agents.<sup>8</sup>

#### **The effectiveness of SDF for caries arrest in primary teeth**

The evidence from all systematic reviews, despite methodological heterogeneity across studies, has demonstrated that SDF had more efficacy for arresting caries than any comparators (placebo, sodium fluoride [NaF] varnish, glass ionomer cement [GIC], and atraumatic restorative treatment [ART]).<sup>5</sup> Several clinical trials have shown the most evidence of caries arrest from SDF application to cavitated dentin caries in primary teeth (Table 1). The overall success rate in dentin caries arrest ranges from 65 to 91%, which is very high compared to those of other fluoride products.<sup>5</sup> The comparative analysis, separated by type of controls (placebo or active comparators), profoundly demonstrated the performance of SDF.<sup>8</sup> The use of SDF was 154% more effective in caries arrest than placebo or no treatment, as indicated by the risk ratio of 2.54 (95% CI: 1.67–3.85). While the use of SDF is 66% more effective than the active comparators (NaF varnish and ART), as indicated by the risk ratio of 1.66 (95% CI: 1.41–1.96). In the comparison of caries arrest between SDF and NaF varnish, all clinical trials had consistently reported that SDF was superior to NaF varnish, despite different application protocols.<sup>15, 16</sup> In addition, SDF arrested carious lesions faster and with a lower application frequency than NaF varnish. The researchers speculated that the higher caries arrest effect of annual SDF application may be a result of the booster effect of reapplication at 12 and 24

months. Therefore, reapplying SDF at least yearly was recommended to maintain and enhance the caries arrest effect.<sup>16</sup> Although most clinical studies have reported high caries arrest rates, a 12-month follow-up study conducted in children aged 1–3 years reported the superiority of semiannual 38% SDF, with a relatively low caries arrest rate (35.7%).<sup>17</sup> The authors suggested that the differences in caries arrest rates may be attributed to many unfavorable factors found among very young participants with high caries risk; caries experience, compromised oral health-related behaviors, different demographic backgrounds, and inability to cooperate during the application procedure.

Moreover, ART has proven to be an effective caries management technique that is more comfortable and well-accepted by children than the drilling technique.<sup>18</sup> Based on the findings of several clinical trials, SDF and ART are equally effective for caries arrest in primary teeth.<sup>19-21</sup> However, SDF treatment has many advantages over ART, including less chair time, less cost, and less dependence on operator skill. Therefore, SDF treatment was suggested to be a superior option to ART, especially for underserved populations in public health settings.<sup>20-22</sup> ART may be selected in some circumstances because of its advantages, such as restoring occlusal surfaces for mastication, reducing food stagnation, and providing greater esthetics with tooth-colored restoration. The important limitation of ART restorations is the relatively low retention rate.<sup>22</sup> In addition to the agents that have been widely used in clinical studies as mentioned above, propolis fluoride is another agent that has been revealed antibacterial and remineralization abilities from the *in vitro* study.<sup>23</sup> These properties were also found from SDF, which correlated with its effectiveness in caries arresting. The clinical trial revealed that SDF was more effective than propolis fluoride in caries arresting (88.68% versus 55.78%), but propolis fluoride did not cause black staining on carious lesions.<sup>24</sup>

#### **The effectiveness of SDF for enamel caries arrest**

A 30-month clinical trial revealed that the superiority of SDF found with application on cavitated lesions was not observed in the case of non-cavitated lesions.<sup>16</sup> Whereas the caries arrest rate of cavitated lesions (ICDAS code of 5 or 6) treated with SDF was significantly greater

than for those treated with NaF varnish, no significant differences were found in moderate caries lesions (ICDAS code of 3 or 4) treated with these fluoride types. Regardless of the types or protocols of fluoride used, no progression to cavitation was observed in half of non-cavitated lesions. Exposure to other sources of topical fluoride, such as fluoride toothpaste, may be a contributing factor to significantly slowing the progression of enamel caries in a high proportion of these lesions. Additionally, enamel resistance may depend more on the calcium and phosphorus content than the fluorine or magnesium content.<sup>25</sup> Therefore, exposure to any source of calcium and phosphorus may be considered another contributing factor to remineralizing enamel caries. To draw conclusions from these statements, further investigations are needed.

#### **The effectiveness of SDF for caries prevention in primary teeth**

Insufficient evidence exists to draw conclusions on the effectiveness of SDF for caries prevention in primary teeth.<sup>5, 26</sup> The findings from the systematic reviews including only two clinical trials revealed that SDF may effectively prevent the development of new carious lesions.<sup>15, 27-29</sup> When compared to placebo, the prevented fraction of 38% SDF ranged from 70.3% to 79.7%, whereas the prevented fraction of NaF varnish was 55.7% for caries prevention in primary teeth.<sup>15</sup> Although these studies showed promising efficacy of SDF for caries prevention, they had more than one research domain with an unclear or high risk of bias.<sup>27</sup> The possible mechanisms of SDF for caries prevention remain unclear. An insoluble protective layer of silver chloride and silver phosphate, formed on tooth surfaces after SDF application, may help to decrease demineralization.<sup>10</sup> Although several *in vitro* studies have shown results that may correlate with a preventive effect, Li et al. reported that a small amount of silver particles could be detected on the sound enamel surface, which could explain why SDF application does not cause black staining on caries-free surfaces.<sup>30</sup> These findings suggest that the use of SDF as a potential caries-preventive agent requires further study.

#### **Confounding factors affecting SDF effectiveness**

Among the various concentrations of SDF,

previous studies have consistently revealed a concentration of 38% yielded the best effectiveness for caries arrest and prevention in primary teeth.<sup>31-33</sup> Regarding the frequency of SDF application, the American Academy of Pediatric Dentistry (AAPD) has suggested that the effectiveness of caries arrest decreases over time. After a single application, half of the arrested lesions at 6 months had returned to be active lesions at 24 months.<sup>31</sup> Therefore, patients should be followed up and evaluated for reapplication to maintain an inactive caries status and increase the caries-arresting effect in every recall visit.<sup>16, 34</sup> Biannual application resulted in higher caries arrest rates compared to annual application.<sup>32</sup> Clinical trials have demonstrated that several confounding factors could influence SDF efficacy, including the quantity of plaque stagnation, tooth location, tooth surface, cavity size, fluoride exposure, baseline caries experience, age, oral health-related behaviors, diet, socioeconomic status, and application procedure (Table 1). The presence of plaque is the most mentioned factor in reducing the caries arrest rate.<sup>16, 17, 19, 32</sup> Notably, some of these confounding factors are related to the presence of plaque, including tooth location, tooth surface, and oral health-related behaviors (especially brushing and flossing). SDF application on lower anterior teeth yielded the highest success rate, followed by upper anterior teeth, lower posterior teeth, and upper posterior teeth.<sup>32</sup> In addition, SDF treatment seems to be more effective on buccal and lingual surfaces, which are easier to clean.<sup>19</sup> Biannual application is recommended in children with a high visible plaque index because this may increase the caries arrest rate better than annual application.<sup>32, 33</sup> These findings emphasize that caries management by fluoride treatment should be done in conjunction with meticulous plaque control to achieve maximum effectiveness.

#### **Disadvantages and adverse effects**

A major disadvantage of SDF is the black staining caused by silver phosphate ( $\text{Ag}_3\text{PO}_4$ ), which is a photosensitive substance. Silver oxide ( $\text{Ag}_2\text{O}$ ) and silver sulfide ( $\text{Ag}_2\text{S}$ ) from the combination of oxygen or sulfur with silver can also contribute to the black staining.<sup>35</sup> Sound enamel and dentin will not stain; however, sound cementum on the root surface has been found to stain because cementum is a relatively porous tissue.<sup>36</sup> Cavitated or non-cavitated lesions,

superficial enamel defects, and hypomineralized enamel will stain black if they are sufficiently porous to allow penetration of significant amounts of silver phosphate.<sup>11</sup> Potassium iodide (KI) has been used to minimize the black staining by use as a second step immediately after SDF application. SDF with KI treatment has reduced secondary caries formation on GIC restoration, but it was not as effective as SDF treatment alone. Moreover, staining on the restoration margin was observed, but the intensity of staining was less than that with SDF treatment alone.<sup>10</sup> Currently, no agent or technique eliminates SDF staining completely.<sup>37</sup> Although the black stain is considered an undesirable effect, its clinical

observation has been suggested as an indication of arrested caries.<sup>14</sup> There are several concerns regarding the high fluoride concentration in SDF. The previous study has demonstrated that the low fluoride concentrations were found in the urine of adult subjects after applying one drop of SDF on enamel.<sup>38</sup> There was a reduction of urinary fluoride concentration from the baseline to 30 minutes, then the elevated fluoride concentration was detected after two and three hours of application. Further studies are needed to draw the conclusions. There are currently no reports of acute symptoms or serious side effects, such as allergic reactions or toxicity.

Authors, Year Subjects (% dropout)	Age (years), Follow-up (months), Settings	Intervention groups and application protocols	Outcomes	Confounding factors affected on the outcomes
<b>SDF versus No treatment</b>				
Llodra et al., 2005 n=452 (18%)	6-15, 36, Schools	(1) 38% SDF: Biannually (2) No treatment	(1) Mean number of new decayed surfaces in primary teeth: Group 1=0.29, Group 2=1.43 (2) Mean number of new decayed surfaces in first permanent teeth: Group 1=0.37, Group 2=1.06	- Fluoride exposure
<b>SDF versus NaF varnish</b>				
Chu et al., 2002 n=375 (18%)	3-5, 30, kindergartens	(1) 38% SDF + excavation: Annually (2) 38% SDF: Annually (3) 5% NaF + excavation: every 3 months (4) 5% NaF: every 3 months (5) Water: single application at baseline	(1) Children who received an annual application of SDF had more arrested caries lesions in their upper anterior teeth than did the children in other groups. (2) Caries excavation before SDF application had no significant beneficial effect.	- Toothbrushing - Baseline dmfs of anterior teeth
Duangthip et al., 2018 n=371 (17%)	3-4, 30, kindergartens	(1) 30% SDF: Annually (2) 30% SDF: 3 times at weekly intervals (3) 5% NaF: 3 times at weekly intervals	(1) For cavitated lesions, the caries arrest rate in Group 1 (48%) was higher than those in Group 2 (33%) and Group 3 (34%). (2) For non-cavitated lesions, the caries arrest rates were 45%, 51% and 44% in Group 1, 2, and 3, respectively. (3) Annual application is more beneficial than three weekly applications or NaF varnish.	- Tooth brushing with fluoride toothpaste - Tooth type - Surface type - Plaque accumulation
Mabangkhu et al., 2020 n=302 (13%)	1-3, 12, child centers	(1) 38% SDF: Biannually (2) 5% NaF: Biannually	(1) The caries arrest rate of Group 1 (35.7%) was higher than Group 2 (20.9%). (2) Application of 38% SDF had superior efficacy in arresting dentin caries compared to 5% NaF.	- Oral-health behaviors - Caries experience - Plaque accumulation - Application procedure
<b>SDF versus ART/GIC/IRT</b>				
Zhi et al., 2012 n=212 (15%)	3-4, 24, kindergartens	(1) 38% SDF + excavation: Annually (2) 38% SDF + excavation: Biannually (3) Excavation + GIC	(1) Annual application of SDF and GIC are equally effective. (2) Increasing frequency of SDF application increases caries arrest rate. (3) Anterior teeth and buccal/ lingual surfaces are more likely to become arrested.	- Toothbrushing - Fluoride toothpaste - Tooth site - Surface type
Dos santos et al., 2012 n=91 (N/A)	5-6, 12, primary schools	(1) 30% SDF: Annually (2) IRT (excavation + GIC)	(1) 30% SDF was more effective for caries arresting than IRT (Arrested lesions in SDF group=67%, IRT group=39%)	- Toothbrushing with fluoride toothpaste - Diet - Fluoridated water
Vollu et al., 2019 n=68 (17%)	2-5, 12, pediatric dental clinic	(1) 30% SDF: Biannually (2) ART (excavation + GIC)	(1) The caries arrest rates in both groups were similar. (2) No differences regarding anxiety, adverse events and oral health related to quality of life between SDF and ART were found	- Toothbrushing with fluoride toothpaste - Tooth site - ICDAS
Abdellatif et al., 2021 n=79 (33%)	3-8, 12, pediatric dental clinic	(1) 38% SDF: Biannually (2) ART (excavation + GIC)	(1) Caries arresting rate at 12 months were very high and similar in the two treatment groups without any statistically significant differences. (2) The overall rate of failures from the baseline in the ART group was 9.68% compared to 1.09% in the SDF group.	- Lesion location - ICDAS

**Table 1.** A summary of clinical studies investigating the efficacy of silver diamine fluoride for caries management in primary teeth.

SDF, silver diamine fluoride; NaF, sodium fluoride; dmfs, decayed, missing, and filled surfaces of primary teeth; ART, atraumatic restorative treatment; GIC, glass ionomer cement; IRT, interim restorative treatment.

### Acceptance of SDF treatment

The black staining from SDF affects the esthetic appearance of a child, which can be a reason for parents to reject the treatment or dentists to be reluctant to recommend it.<sup>39, 40</sup> This issue is consistent with findings from several studies in which the most frequently reported barrier to SDF treatment was parental acceptance.<sup>41, 42</sup> Although many factors may affect parental acceptance (e.g., parental

education, family income, ethnicity, dental workplace), the key factors affecting parental acceptance were the location of the teeth and the child's cooperation.<sup>42, 43</sup> Staining on posterior teeth was more acceptable than staining on anterior teeth under all circumstances. Although staining on anterior teeth was undesirable, most parents preferred this option to advanced behavioral techniques such as sedation or general anesthesia.<sup>42</sup>

## Conclusion

SDF has the potential to be a good option for caries management, particularly in children with high caries risk, because it has greater efficacy than any comparators. Among several confounding factors affecting the efficacy of SDF, the presence of plaque is the most mentioned factor in reducing the caries arrest rate. Caries management by SDF treatment should be done in conjunction with comprehensive caries preventive measures to achieve maximum efficacy.

## Declaration of Interest

The authors report no conflict of interest.

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