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Evidence-Based Dentistry Update on Silver Diamine Fluoride

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INTRODUCTION

The global burden of oral disease and the negative social and economic effect associated with it, are a growing problem worldwide.[1]

The widespread use of water fluoridation and fluoride-containing oral products produced significant decreases in the prevalence and severity of dental caries over the last 70 years.[2,3] However, the benefits of these prevention interventions have not materialized in all segments of society in most countries. Free sugars and processed carbohydrates as a component of diet have increased in many countries, both developed and developing alike. As Thompson and colleagues[4] have shown, lower income groups are particularly vulnerable to high dietary sugar intake. The result has been a disparity in caries experience across socioeconomic groups. In the United States and other high-income countries, untreated dental decay in children is strongly patterned by income and ethnicity, mainly owing to cost and limited availability and/ or access to services.[5] In lower income groups, much of the caries goes untreated, resulting in severe disease levels that leads to pain, expense, and a decreased quality of life for the affected children and their families.[6]

Even when dental services are accessible, traditional restorative treatment can be difficult to deliver to young children with severe disease and those with special management considerations.[7] To address this difficulty, advanced forms of behavior management like sedation and/or general anesthesia are often used, which increase the cost and the risk for the patient and the dentist.[8] Elderly patients often face similar challenges, because increasing rates of untreated decay can severely affect their quality of life, and the difficulties of receiving dental care are accentuated by limitations with mobility and other comorbidities.[9]

When it comes to prevention, epidemiologic studies indicate that when the bacterial challenge is high or the salivary components are lacking, natural remineralization or that

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aided by fluoride products is insufficient to prevent or arrest the caries process. Thus, there is an urgent need to find ways to beneficially modify the biofilm and to enhance the remineralization process to decrease caries experience and attain improved outcomes of oral health.[10] This situation calls for a paradigm change in caries prevention and management. Specifically, we need more effective, affordable, accessible, and safe treatments that are easy to implement in different settings, and are available to the most vulnerable populations.[11]

Silver diamine fluoride (SDF), a clear liquid that combines the antibacterial effects of silver and the remineralizing effects of fluoride, is a promising therapeutic agent for managing caries lesions in young children and those with special care needs that has only recently become available in the United States. Multiple in vitro studies document its effectiveness in reducing specific cariogenic bacteria[12] and its remineralizing potential on enamel and dentin.[13,14] Its in vivo mechanism(s) of action are a subject of ongoing research. What is currently understood is that the fluoride component strengthens the tooth structure under attack by the acid byproducts of bacterial metabolism,[15] decreasing its solubility, but SDF may also interfere with the biofilm, killing bacteria that cause the local environmental imbalance that demineralizes dental tissues.[16] Thus, SDF becomes one of the tools available to address caries by modifying the bacterial actions on the tissue while enhancing remineralization.

Numerous systematic reviews substantiate SDF’s efficacy for caries arrest in primary teeth, and arrest and prevention of new root caries lesions. It meets the US Institute of Medicine’s 6 quality aims of being[7]:

1. Safe—clinical trials that have used it in more than 3800 individuals have reported no serious adverse events[7,17];
2. Effective—arrests approximately 80% of treated lesions[18];
3. Efficient—can be applied by health professionals in different health and community settings with minimal preparation in less than 1 minute;
4. Timely—its ease of application can allow its use as an intervention agent as soon as the problem is diagnosed;
5. Patient centered—is minimally invasive and painless, meeting the immediate needs of a child or adult in 1 treatment session; and
6. Equitable—its application is equally effective and affordable; with the medicament costing less than $1 per application, it is a viable treatment for lower income groups.

The only apparent drawback is that as the caries lesions become arrested, the precipitation of silver byproducts in the dental tissues stain the lesions black, which can be a deterrent for its use in visible areas (Figs. 1–4).

Systematic syntheses of clinical trials’ findings constitute the highest level of evidence and are essential to inform evidence-based guidelines and set the standard of care in all settings of dental practice. This article presents and discusses the findings of systematic reviews and metaanalysis of SDF as a treatment for caries arrest and prevention.

BACKGROUND

Silver compounds, especially silver nitrate, have been used in medicine to control infections for more than a century.[19] In dentistry, reports of use of silver nitrate are well-documented for caries inhibition[20] and, before the twentieth century, silver nitrate was firmly entrenched in the profession as a remedy for “hypersensitivity of dentin, erosion and pyorrhea, and as a sterilizing agent and caries inhibitor in deciduous as well as in permanent teeth.”[21] Howe’s solution (ammoniacal silver nitrate, 1917), was reported to disinfect caries lesions[22] and continued to be used for nearly one-half of a century as a sterilizing and disclosing agent for bacterial invasion of dentin[23,24] to avoid direct pulp exposures, to detect incipient lesions, and to disclose leftover carious dentin.[25]

The relationship of fluorides and caries prevention had been well-established through epidemiologic observations, chemical studies, animal experiments, and clinical trials beginning in the early decades of the twentieth century. It is now well-known that, when fluoride combines with enamel or dentin, it greatly reduces their solubility in acid, promotes remineralization, and results in a reduction of caries.[26]

The use of ammoniacal silver fluoride for the arrest of dental caries was pioneered by Drs Nishino and Yamaga in Japan,[27] who developed it to combine the actions of F^{-} and Ag^{+} and led to the approval of the first SDF product, Saforide (Bee Brand Medico Dental Co, Ltd, Osaka, Japan) in 1970.[28] Each milliliter of product contains 380 mg (38 w/v%) of $Ag(NH_3)_2F$. They described its effects for prevention and arrest of dental caries in children, prevention of secondary caries after restorations, and desensitization of hypersensitive dentin. They reported that it penetrated 20 μm into sound enamel. In dentin, reported penetration of F^{-} was up to 50 to 100 μm and Ag^{+} went deeper than that, getting close to the pulp chamber.[28] They warned that because the agent stains the decalcified soft dentin black, its application should be confined to posterior teeth and gave specific instructions for its application.

Other similar products then became commercially available in other regions, like Silver Fluoride 40% in Australia (SCreighton Pharmaceuticals, Sydney),[29] Argentina (SDF 38% several brands), and Brazil (several SDF concentrations and brands).[30]

Since 2002,[31] the search for innovative approaches to address the caries pandemic resulted in the publication of many clinical trials of SDF efficacy (through comparison with no treatment), and its comparative effectiveness with other chemopreventive agents (eg, fluoride varnish [FV]), as well as other treatment interventions (eg, atraumatic restorative treatment [ART]). The results of these studies established the effectiveness of SDF as a caries arresting agent. In 2014, the US Food and Drug Administration approved SDF as a device for dentin desensitization in adults and, in 2015, the first commercial product became available in the United States: Advantage Arrest. Advantage Arrest (Elevate Oral Care, LLC, West Palm Beach, FL) is a 38% SDF solution (Box 1).

Manufacturer’s instructions are limited to its approved use as a dentin desensitizer in adults. However, results from clinical trials conducted in many different countries on more than

3900 children have led investigators to develop recommendations for its use as a caries arrest medicament in children.[7,35]

In 2017, the American Academy of Pediatric Dentistry published a Guideline for the “Use of Silver Diamine Fluoride for Dental Caries Management in Children and Adolescents, Including Those with Special Health Care Needs.”[36] This document encouraged the off-label adoption of this therapy for caries arrest, much as FV is used for caries prevention. In November 2016,[37] the US Food and Drug Administration granted SDF a breakthrough therapy status, which facilitates clinical trials of SDF for caries arrest to be carried out in the United States. Studies are currently underway that may result in the change of its labeling in the near future.[38]

Since 2009,[39] systematic reviews report on SDF’s ability to arrest or prevent caries lesions. For this article, we reviewed systematic reviews reported in English and published or accepted for publication through March 2018. We identified 6 systematic reviews that met most of the PRISMA guidelines.[40] Their details can be found in Table 1. The outcomes reported in these reviews include efficacy (ability to arrest or prevent\ caries lesions) and comparative effectiveness (eg, equivalence or superiority when compared with other modalities such as ART and FV). Included reviews report on the primary and permanent dentitions of children and the permanent teeth on elderly populations. We consider each endpoint separately herein.

CURRENT EVIDENCE ON THE EFFICACY OF SILVER DIAMINE FLUORIDE FOR CARIES ARREST AND PREVENTION

In this section, we evaluate the results for SDF’s efficacy for caries arrest as reported by the systematic reviews and metaanalysis included in Table 1. These systematic reviews used different perspectives to evaluate 17 prospective, parallel design, randomized, controlled clinical trials with a clearly defined outcome. As a result, and apparent from Table 1, many of the systematic reviews included refer to the same body of clinical trials, just updating results as additional studies became available. Details of each of the included clinical trials conducted on children and published in English are included in Table 2.

Taken together, the underlying clinical trials and systematic reviews indicate that SDF arrests caries in primary teeth and root caries in elders. and may prevent formation of new caries. Details on each of the outcomes measured on different dentitions and age groups are described in the following sections.

Caries Arrest on Primary Teeth in Children

All studies reach a similar conclusion supporting SDF’s efficacy in arresting decay in primary teeth compared with no treatment and several other treatment modalities. Based on the Gao 2016 metaanalysis,[18] the proportion of caries arrest on primary teeth treated with different application protocols (1 application, annual, and biannual), and followed from 6 to 30 months, was 81% (95% confidence interval, 68%–89% $p<.001$). Chibinski and colleagues (2017)[51] reported that the caries arrest at 12 months promoted by SDF was 66% higher (41%–91%) than by other active material, but it was 154% higher (67%–85%) than by no treatment. Chibinski and associated[51] also reported a risk ratio of 1.66 (95% confidence interval, 1.41–1.96) when comparing SDF with active treatments, and a risk ratio of 2.54 (95% confidence interval, 1.67–3.85) when comparing SDF with no treatment.

It is apparent that the range of caries arrest is very wide, indicating that a proportion (that varies depending on the study) of the lesions receiving treatment will not become arrested. Several trials have stressed that in their results, anterior teeth have much higher rates of arrest than posterior teeth[41–45] As an example, one of the trials not included in the reviews, because it just published its 30-month results,[42] reports caries arrest by type of primary tooth using SDF 38% semiannually (Box 2).

In addition, this study, as have others,[44,45] found that lesions with visible plaque and large lesions had a lesser likelihood of arrest. The difference in arrest rates in children receiving applications twice per year versus once per year was small between 24 and 30 months in all teeth, but among children who received annual application, those with visible plaque had a lesser likelihood of having their lesions arrested. Fung and colleagues[42] conclude that, for children with poor oral hygiene, caries arrest rate can be increased by increasing the frequency of application from annually to semiannually.

Caries Arrest on Permanent Teeth in Children

The Rosenblatt review is the only one that addresses caries arrest in permanent teeth, and it is based on only 1 trial (Llodra and colleagues [2006][46]). They calculate a preventive fraction of 100% and number needed to treat of 1, basing their calculations on the mean number of arrested lesions was 0.1 in the SDF group and 0.2 in the control group. Llodra and associates (2006)[46] report that around 77% of treated caries that was active at baseline became inactive during the study, both in primary and in first permanent molars. Another small trial (on 22 children) studied caries arrest in permanent molars[47] (see Table 2) and found that SDF was more effective than tooth-brushing or glass ionomer at 3 and 6 months, but they were all equally effective in controlling noncavitated lesions at 30 months No other systematic reviews were able to reach conclusions on caries arrest on permanent teeth in children owing to lack of solid evidence.

Caries Prevention in Children

The review undertaken by Rosenblatt and associates[39] evaluated SDF's potential for prevention using data from 2 trials. The trial from Llodra and colleagues (2006)[46] included primary and permanent molars and found that new caries lesion development (as a marker of caries prevention) in permanent teeth was significantly lower in the SDF group (0.4 new lesions) that in the water control group (1.1 new lesions) over 36 months. In primary teeth, the SDF groups averaged 0.3 new lesions versus 1.4 in the water control group. A trial conducted by Chu and associates (2002)[31] using only maxillary anterior teeth in preschool children found the mean number of new lesions over a period of 30 months in the SDF group was 0.47 versus 0.7 new lesions per year with 4 yearly applications of FV, versus 1.58 new lesions in the water control group. The review concludes that the preventive fraction for SDF was 70.3% (>60% on permanent teeth and >70% on primary teeth). Only 2 other clinical trials have studied caries preventive effect of SDF on permanent teeth. Liu and coworkers (2012)[48] found that proportions of pit/fissure sites with increased dentin caries treated with sealant, VF, and SDF were not significantly different at 24 months and they were all more effective than water control. Monse and associates (2012)[50] found that atraumatic treatment restorations sealants were more effective than a single application of SDF after 18 months. These 4 studies of permanent teeth have not been combined in a metaanalysis because they reported outcomes using different measures (number of teeth with new caries lesions or active lesions, in all surfaces vs only pit and fissure, and provide the data in different units of measurement [means and standard deviation vs number of events]).[51] No solid conclusions can be reached with such a small number of studies on permanent teeth in children.

In their recent systematic review and metaanalysis, Oliveira and colleagues[49] evaluated caries prevention for primary teeth and concluded that, when compared with placebo at 24 months or more, SDF decreased the development of dentin caries lesions in treated and untreated primary teeth with a preventive fraction of 77.5%. Comparisons between SDF and FV concluded that SDF performed significantly better than FV at 18 and 30 months, and comparison between SDF and glass ionomer cements (GIC) showed that GIC was better than SDF at 12 months (not statistically significant). Both of these comparisons are weak because they are based on only 1 trial each.[31,55]

Because the trial from Llodra and associates[46] included only primary posterior teeth and newly erupted first molars, noncavitated lesions in pit and fissures may have been difficult to code and, therefore, may have been missed. In contrast, the trial from Chu and colleagues (2002)[31] studied only maxillary anterior teeth, where detection of new lesions would have been easier. Another problem making statements about the preventive effect of SDF on the whole dentition is that the trials included have reported new caries in only the teeth studied and not the whole dentition. Llodra and associates did not include any data on anterior teeth and the study by Chu and coworkers did not include any data on posterior teeth, even though they report that children had lesions and treatment in teeth not included in their study. Direct comparisons with the preventive effect of other modalities of fluoride applications are problematic, because those trials (on toothpaste of FV as an example) always report new caries in the whole dentition.

Caries Arrest and Prevention in the Elderly

In the only systematic review of SDF on adults, Hendre and colleagues[53] (2017) found no studies on coronal caries, but included 3 studies on root caries arrest and prevention. They found a preventive fraction for SDF of 24% in a 24-month study and 71% over a 36-month study. The preventive fraction for caries progression was 725% greater in a 24-month study and 100% greater than placebo in a 30-month study. From these findings, the investigators recommend the use of SDF for seniors who present increased root caries risk, used alone or in conjunction with oral hygiene education and other treatments. They go on to recommend SDF use to manage dentin sensitivity, based on a 7-day trial conducted on adults that was not included in their review.[52]

Only 1 other systematic review and metaanalysis included SDF in their study of noninvasive treatment of root caries lesions,[56] concluding that weak evidence indicates that SDF varnishes seem to be efficacious to decrease initiation of root caries. They based this conclusion on 2 studies (Tan 2010[67] and Zhang 2013[66]). However, because there seem to be some discrepancies in their methodology for the metaanalysis, we did not include their data in Table 1.

Side Effects and Toxicity

None of the reviews or trials report any acute side effects of the SDF used in the conditions of the individual trials on either children or adults. Minor side effects have been described as transient gingival irritation and metallic taste in a small number of participants. Only 1 published study on adults had an as aim to study gingival erythema 24 hours and 7 days after SDF application and found that, even when there was a very small number of participants who presented mild gingival erythema at 24 hours, there was no difference from baseline at 7 days.[52] This finding suggests that minor gingival irritations heal within a couple of days. A recent report from a clinical trial on young children[17] states that the prevalence of tooth and gum pain reported by parents was 6.6% 1 week after application, whereas gum swelling and gum bleaching were reported by 2.8% and 4.7%, respectively. SDF should not be used on lesions that are suspected of pulpal involvement because it will not prevent further progression of the infection into surrounding tissues[50] (Fig. 5).

The main side effect of the use of SDF is the dark staining of the carious tooth tissue, which has raised concerns of parental satisfaction (see Figs. 3 and 4).[54] This study, which included 799 children in 37 kindergartens in Hong Kong,[17] reported that, although blackening of carious lesions was common with 38% SDF (66% to 76%), parental satisfaction with their children’s dental appearance after 30 months was 71% to 62%. A US web-based survey that used photographs of carious teeth before and after SDF treatment found that parents considered staining on posterior teeth significantly more acceptable than on anterior teeth. However, even among those who found anterior staining unsightly, a significant number of parents would accept SDF treatment to avoid advanced behavioral techniques (like sedation or general anesthesia).[57] Most studies go on to recommend an appropriate informed consent so parents can understand the benefits and compromises of this therapy.[36]

SDF also temporarily stains skin and gingiva, requiring them to be handled so as to avoid contact with these tissues.

Many studies have suggested the use of potassium iodide applied after SDF application to control or reverse the staining. Some commercial products with both products are available (Riva Star, SDI, Baywater, Victoria, Australia). However, one of the trials for adults[58] reported that potassium iodide application had no effect in reducing the black stain on root caries, especially in the long term.

Although there has been no reported acute toxicity with SDF when used as recommended, the high concentration of fluoride has raised some concern,[59] especially with repeated applications on very young children. High concentrations of silver, a heavy metal, have raised similar concerns. Investigators who have conducted many of the clinical trials cited herein[60] have recommended that, although the amount of SDF applied is minute, precautions should be taken and multiple and frequent applications on young children should be avoided. The only study that reported on the pharmacokinetics of SDF after oral application[61] was done on only 6 adults over a period of 4 hours using 6 mL (about one-fifth of a drop) to treat 3 teeth on each subject. Their conclusion was that serum concentrations of fluoride and silver should pose little toxicity risk when used only occasionally in adults.

To date, there are no studies that have evaluated the long-term in vivo effects of silver on the oral microbiome or the total gastrointestinal microbiome. We do not know whether there are measurable traces of silver in saliva or plasma after SDF application and whether there could be long-term cumulative effects of silver in other organs.

Conclusions

SDF promises to be a therapy that could benefit many patients. In addition of the guideline for its use published by the American Academy of Pediatric Dentistry, the World Health Organization's 2016 report on Public Health Interventions against Early Childhood Caries, concluded that SDF can arrest dentine caries in primary teeth and prevent recurrence after treatment (very low evidence).[62] It recommends its use as an alternative procedure for tertiary prevention to reduce the negative impact of established disease (cavity) by restoring function and reducing disease-related complications and to improve the quality of life for children with early childhood caries.

Limitations of Current Research

Most of the systematic reviews and metaanalysis included for this article face the obstacles of having to compile data from clinical trials that have substantial differences in treatment protocols (1 application, yearly, or twice a year applications), concentration of SDF used, dentition studied, follow-up time, outcome measured (arrest or prevention), and the way they report their findings. Their reported figures differ depending on the number of studies included and how they group the studies to make their comparisons, which may affect the generalizability of their results.

It is also important to point out that all the clinical trials cited took place in school or community settings. Extrapolating recommendations from their results to clinical practice should take into consideration the availability of the patient for follow-up. Although SDF halts the caries process and desensitizes the decayed teeth, allowing for the implementation of better home care regimes, it does not restore form and function. As patient circumstances change, SDF-treated teeth may be restored as part of a comprehensive caries management plan.[36] SDF seems to be compatible with GIC and its effect on the bond strength of composite to treated dentin is still under study.[53] Laboratory observations report that SDF may also increase resistance of GIC and composite restorations to secondary caries.[63] Long-term clinical studies are required to recommend solid treatment protocols.

Future Research

The current reviews point to the need for studies that address the frequency and intensity of SDF used in conjunction with adjunctive preventive agents (eg, SDF with or without FV), the timing of application (eg, 1–4 times per year), and follow on restorative care (eg, glass ionomer or resin fillings). There may be differences in each of the foregoing strategies when comparing primary and permanent teeth, as well as anterior and posterior teeth. The longevity of arrest and prevention are unknown. Is SDF an agent that can be used, for example, 4 times per year, then terminated? Patient-centered outcomes also need to be addressed. The combination of clinical and patient centered outcomes will facilitate cost–benefit analysis and, thus, payment system improvement. Underlying all of this are generic biological questions, including the following: What is the impact on the oral microbiome? How does the interaction of the oral microbiome, the human genome, and SDF interact to affect caries? And finally, there is a clear need for the continued evolution of well-designed, randomized, clinical trials to produce studies with a low risk of bias during the planning, execution, and reporting of results. Standardization in the presentation of data between studies,[18,51] whether they focus on arrest or prevention, is imperative to be able to combine and translate the data into strong clinical guidelines. As indicated, clinicians need to know how to manage arrested lesions for longer periods, which is important for very young children and imperative for permanent teeth.

CLINICAL APPLICATIONS

From the current evidence available we can summarize that:

- 38% SDF solution is more effective than lower concentrations[18,42];
- Twice a year application is more effective than yearly applications[18,42,45,51];
- Over longer periods (30 months), annual applications of SDF are more effective than 3 weekly applications at baseline[44];
- Application times ranging from 10 seconds[44] to 3 minutes[47,55] achieved various degrees of success that do not seem to be time dependent;
- Anterior teeth have higher rates of arrest than posterior teeth[41,42,44,45];
- Large lesions, occlusal lesions and those with visible plaque have less chances of arrest[41,42,44] (Figs. 6 and 7);
- Its use should be avoided in teeth with suspected pulpal involvement[50] (see Fig. 5); and
- Annual application of SDF seems to be effective for arrest and prevention of root caries on older adults who are capable of self-care. Multiple applications may benefit a more dependent and at-risk older population.[53]

With all age groups, clinicians should use their clinical judgment about application frequency based on individual caries risk factors, fluoride exposure, patient needs, and taking into consideration individual social determinants of health.

Clinical application is simple: the lips are protected with petroleum jelly (Vaseline) or lip balm, the tooth is isolated with cotton rolls, the lesion is cleaned of food debris and dried, and SDF is painted onto the clean lesion and allowed to air dry (Fig. 8 and https://youtu.be/p9Tazwitcao). Rinsing after application does not seem to be necessary.

INDICATIONS

At the tooth level, SDF therapy for caries arrest is indicated for cavitated lesions on coronal or root surfaces that are not suspected to have pulpal involvement, are not symptomatic, and are cleansable. Ideally, these conditions should be verified by radiographic evaluation.

PATIENT SELECTION AND MANAGEMENT

Patients who do not have immediate access to traditional restorative care can benefit from SDF therapy to arrest existing dentin caries lesions. This therapy is contraindicated on patients who report a silver allergy. Patients should be monitored closely to verify arrest of all lesions on a periodic basis based on risk factors; this is especially important when applied to permanent teeth. Follow-up should ideally include radiographic examination and the caries management plan should include plaque control, dietary counseling, combination of other fluoride modalities for caries prevention (like F varnish, fluoride gels, fluoride rinses and fluoride toothpaste) and sealants, depending on patient's age and individual situation. Follow-up on large lesions or lesions in hard-to-clean areas can be combined with the use of glass ionomer restorations or traditional restorative treatment, as patient circumstances allows.

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KEY POINTS

- Silver diamine fluoride incorporates the antibacterial effects of silver and the remineralizing actions of a high-concentration fluoride. It effectively arrests the disease process on most lesions treated.
- Systematic reviews of clinical trials confirm the effectiveness of silver diamine fluoride as a caries-arresting agent for primary teeth and root caries and its ease of use, low cost, and relative safety.
- No caries removal is necessary to arrest the caries process, so the use of silver diamine fluoride is appropriate when other forms of caries control are not available or feasible.
- A sign of arrest is the dark staining of the lesions and affected tooth structures. That could be a deterrent for patients who have esthetic concerns. A thorough informed consent is recommended to ensure high patient satisfaction.
- Silver diamine fluoride use for caries control is recommended as part of a comprehensive caries management program, where individual needs and risks are considered.

Box 1

Manufacturer production description of silver-diamine fluoride 38%

Silver-Diamine Fluoride 38% Desensitizing ingredient[32]	Professional tooth desensitizer Aqueous silver diamine fluoride, 38.3%–43.2% w/v
Presentation[32,33]	Light-sensitive liquid with ammonia odor and blue coloring 8 mL dropper-vials contain: approximately 250 drops; enough to treat 125 sites; a site is defined as up to 5 teeth; the unit-dose ampule contains 0.1 mL per ampule
Specific gravity[34]	1.25
Composition[34]	24%–27% silver 7.5%–11.0% ammonia 5%–6% fluoride (approximately 44,800 ppm) <1% blue coloring ≤62.5% deionized water

Data from Refs.[32–34]

Box 2

Caries arrest by type of primary tooth using SDF 38% semiannually

Overall arrest at 30 mo all teeth	75.0%
Lower anterior teeth	91.7%
Upper anterior teeth	85.6%
Lower posterior teeth	62.4%
Upper posterior teeth	57.0%

Data from Fung MHT, Duangthip D, Wong MCM, et al. Randomized clinical trial of 12% and 38% silver diamine fluoride treatment. J Dent Res 2018;97(2):171–8.

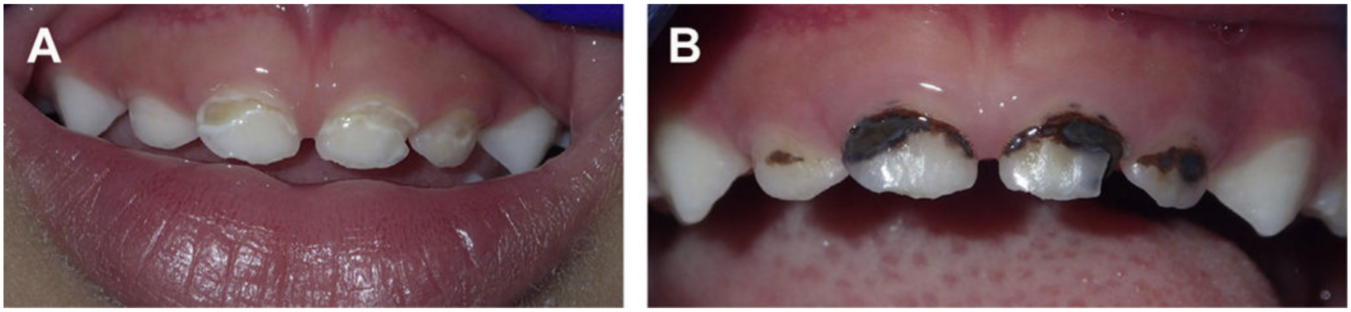

Fig. 1.
(*A*) Enamel and dentin caries lesions in primary anterior teeth. (*B*) Same lesions showing staining after SDF treatment.

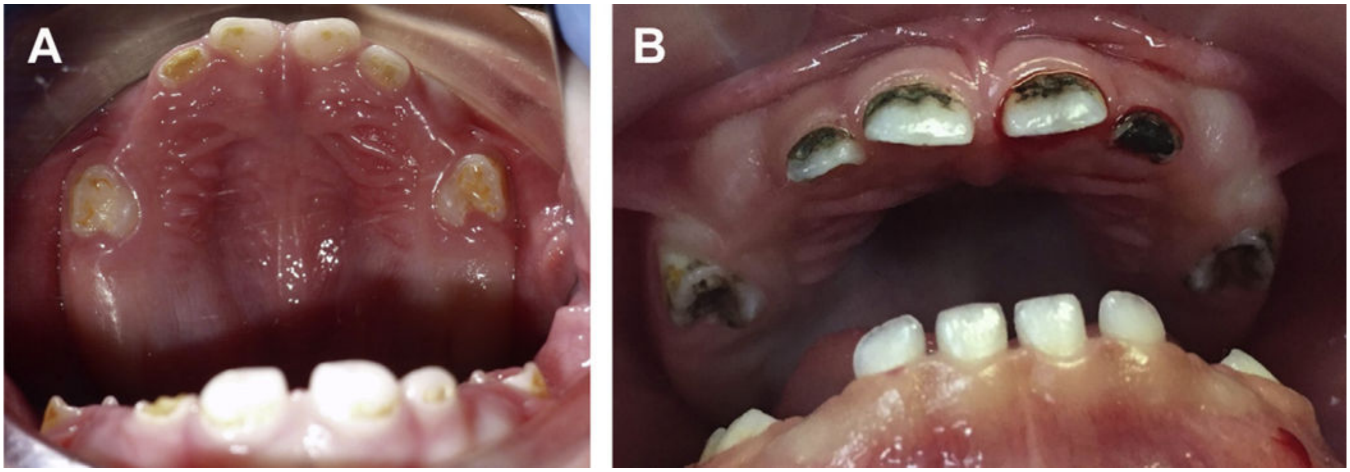

Fig. 2.
(*A*) Caries lesions on enamel and dentin on young primary teeth. (*B*) Same lesions showing staining after SDF treatment.

Fig. 3.
Stained arrested caries lesions on primary anterior teeth.

Fig. 4.
Staining on non-cavitated and partially-cavitated enamel lesions.

Fig. 5.
Large lesion with cellulitis.

Fig. 6.
Posterior arrest.

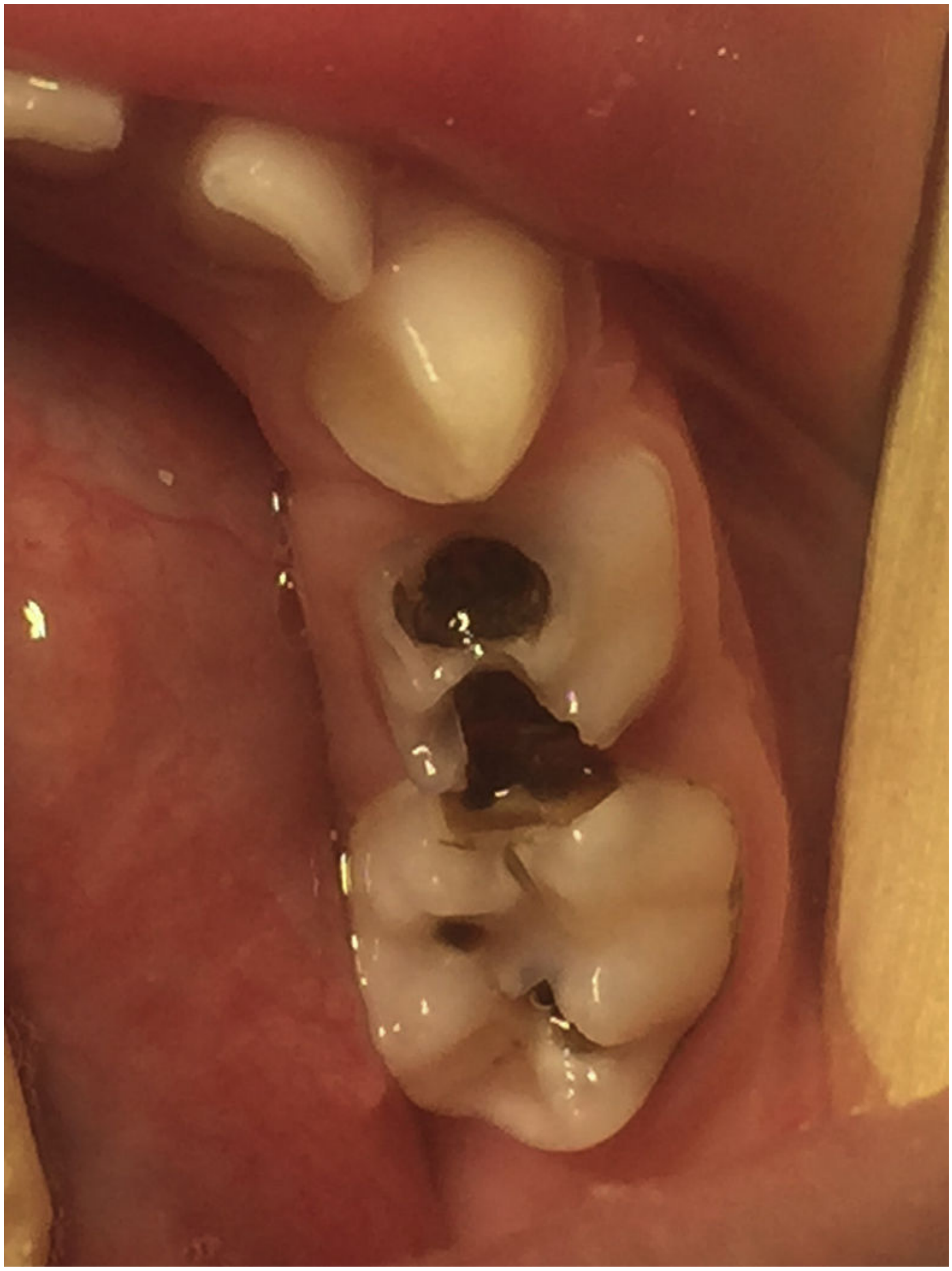

Fig. 7.
Posterior partial arrest.

Fig. 8.
Silver diamine fluoride application.

Table 1

Systematic reviews/metaanalysis on silver diamine fluoride trials

Author, Year	Outcome Measures	Studies Included and Max Follow-up Time Analyzed[a]		Dentitions Included/ Frequency of SDF Application[b]	Results
Rosenblatt et al,[39] 2009	Caries arrest and caries prevention	Systematic review Chu,[31] 2002 30 Llodra,[46] 2005	30 mo 36 mo	Primary max ant/q 12 mo Primary post teeth and First permanent molars/q 6 mo	SDF prevented fraction: caries arrest 5 96.1%; caries prevention 5 70.3%
Horst et al,[35] 2016	Caries arrest and/or prevention	Systematic review Chu,[31] 2002 30 Llodra,[46] 2005	30 mo 36 mo	Primary max ant/q 12 mo Primary post teeth and First permanent molars/q 6 mo	Descriptive for each of the studies
		Zhi,[45] 2012	24 mo	Primary ant and post/q 6 and q 12 mo	
		Yee,[64] 2009	24 mo	Primary ant and post/1 app only	
		Liu,[48] 2012	24 mo	Permanent first molars/q 12 mo	
		Monse,[50] 2012	18 mo	Permanent first molars/1 app only	
		Dos Santos,[65] 2014	12 mo	Primary ant and post/1 app only	
		Zhang,[66] 2013	24 mo	Root caries on elders/q 12 and q 24 mo	
		Tan,[67] 2010	36 mo	Root caries on elders/q 12 mo	
Gao et al,[18] 2016	Caries arrest in children	Metaanalysis included only SDF 38% at different time periods			Caries arrest rate of SDF 38% was
		Chu,[31] 2002	30 mo	Primary max ant/q 12 mo	
		Llodra,[46] 2005	36 mo	Primary post teeth and First permanent molars/q 6 mo	86% at 6 mo 81% at 12 mo
		Zhi,[45] 2012	24 mo	Primary ant and post/q 6 and q 12 mo	78% at 18 mo 71% at 30 mo or >
		Yee,[64] 2009	24 mo	Primary ant and post/1 app only	
		Wang, 1964 Chinese	18 mo	Primary ant and post/q 3 and q 4 mo	Overall arrest was 81% (95% CI, 68%–89%; P<.001)
		Yang, 2002 Chinese	6 mo	Primary teeth/1 app only	
		Ye, 1994 Chinese	12 mo	Primary teeth/1 app only	
		Fukumoto, 1997 Japanese	48 mo	Primary teeth/1app only	
Chibinski et al,[51] 2017	Control of caries progression in children after 12 mo follow-up	Metaanalysis included only studies with “low risk” of bias Evaluated at 12 mo results only (regardless of follow-up time) SDF vs control materials			Caries arrest was 89% higher than using active materials/placebo at 12 mo
		Duangthip,[43] 2016	12 mo	Primary ant and post/1 app/year or 3 app weekly at baseline	

Author, Year	Outcome Measures	Studies Included and Max Follow-up Time Analyzed[a]		Dentitions Included/ Frequency of SDF Application[b]	Results
		Zhi,[45] 2012	24 mo	Primary ant and post/q 6 and q 12 mo	
		NSP or SDF vs placebo Dos Santos,[65] 2014		Primary ant and post/1 app only	
		NSP	12 mo		
		Seberol and Okte,[68] 2013		Primary max ants only/1 app only	
		SDF (unpublished)	12 mo		
Oliveira et al,[49] 2018	Prevention of new caries lesions in primary teeth	Metaanalysis included comparable studies evaluated at _24 mo SDF vs placebo			SDF applications reduce
		Chu,[31] 2002	30 mo	Primary max ant/q 12 mo	development of dentin lesions in treated and untreated primary teeth
		Llodra,[46] 2005	36 mo	Primary post teeth and First permanent molars/q 6 mo	PF: 77.5%; 95% CI, 67.8%–87.2%
		SDF vs GIC Dos Santos,[55] 2012	12 mo	Primary ant and post/1 app only	
Hendre et al,[53] 2017	Caries arrest and prevention in older adults	Systematic review only			Prevention:
		Tan,[67] 2010 n = 203	36 mo	Root caries on elders/q 12 mo	PF of SDF vs placebo 5 71% in 36-mo study
		Zhang,[66] 2013 n = 227	24 mo	Root caries on elders/q 12 and q 24 mo	21% in a 24-mo study
		Li,[58] 2016 n =67	30 mo	Root caries on elders/q 12 and q 24 mo	Arrest: PF of SDF vs placebo 5 725% greater in 24-mo study 100% greater in 30 mo study

Abbreviations: ant, anterior; app, reapplication; CI, confidence interval; NSP, nano-silver particles; PF, preventive fraction; post, posterior; SDF, silver-diamine fluoride.

[a]Number of subjects in published studies for SDF in children are included in Table 2 n 5 listed in this table corresponds with the number of subjects in the study quoted not included in Table 2.

[b]q × mos refers to frequency of reapplication in months.

Table 2

Description and clinical details of randomized control trials on children

	Chu et al,[31] 2002	Yee et al,[64] 2009	Zhi et al,[45] 2012	Dos Santos et al,[55] 2012	Duangthip et al,[44]2018	Fung et al,[42] 2018	Llodra et al,[46]2005	Braga et al,[47] 2009	Liu et al,[48]2012	Monse et al,[50]2012
Location	**China**	**Nepal**	**China**	**Brazil**	**Hong Kong**	**China**	**Cuba**	**Brazil**	**China**	**Philippines**
Dentition studied	Primary anterior only	Primary	Primary anterior And posterior	Primary	Primary anterior And posterior	Primary anterior and posterior	Primary cuspids, Molars and permanent first molars	Permanent first molars	Permanent First molars	Permanent first molars
Caries effect studied	Arrest	Arrest	Arrest	Arrest	Arrest	Arrest	Arrest and prevention	Arrest	Prevention	Prevention
Groups compared	1. SDF (38%) 1 × /y with caries removal	1. SDF (38%) 1 × followed by tannic acid as reducing agent	1. SDF (38%) 1 × /y	1. SDF(30%) 1 ×	1. SDF (30%) 1 × /y	1. SDF (38%) 2 × /y	1. SDF (38%) 2 × /y	1. SDF (10%) 3 × at 1-wkinterval	1. SDF (38%) 1 × /y	1. SDF 38%) 1 × on Sound and cavitated molars
	2. SDF (38%) 1_ × /y without caries removal	2. SDF (38%) 1 × alone	2. SDF (38%) 2 × /y	2. ITR (Fuji IX) w/ conditioner 1 ×	2. SDF (30%) 1_/week for 3 wk at baseline	2. SDF (38%) 1 × /y	2. No treatment	2. GI (Fuji III) sealant 1 ×	2. Resin sealant	2. ART (highviscosity Ketac molar) on sound And cavitated molars
	3. FV 5% 4 × y with caries removal	3. SDF (12%) 1 × alone	3. GI (Fuji VII) w/ conditioner 1 × /y		3. FV (5% 1 × /wk for 3 wk at baseline	3. SDF (12%) 2 × /y		3. Cross Toothbrushing Noncavitated Caries lesions On each child 1 molar was assigned to each group	3. 5% NaF varnish 2 × y	3. NT Some Schools had Tooth brushing programs And some did not
	4. FV 5% 4 × y without caries removal	4. No treatment				4. SDF (12%) 1 × /y			4. Yearly placebo Deep fissures or noncavitated early lesions Each child got same treatment in all molars	
	5. Water control									
Main findings	1. SDF was more Effective than FV or control (65% arrested lesions for SDF groups vs 41% for FV groups vs 34% for control)	1. SDF was more effective than controls (31% arrested lesions for SDF groups vs 22% for SDF 12% vs 15% for control)	1. SDF and GI are equally effective (91% Arrested lesions for SDF 2× _/y vs 79% SDF 1× /y, vs82% GI 1× /y)	1. SDF was More effective than ITR (67% arrested lesions in SDF group vs 39% in control)	1. SDF 1 × /y was more effective than SDF or FV 3 weekly applications at baseline (arrest of cavitated lesions: 48% SDF 1x/y vs 33% in group 2% and 34% with FV; for arrest of moderate lesions the 3 protocols were equally effective: 45% SDF 1 × /y vs44% in group 2% and 51% with FV)[c]	1. SDF 38% 2 × /y was more effective than SDF 38% 1 × /y, SDF 12% 2_/y or 1 × /y (77% arrested lesions vs 67%, 59% and 55%, respectively)	1. SDF 2 × /y was more effective for caries arrest Than controls (85% arrested lesions with SDF vs 62% in control)	1. SDF was more effective Than toothbrushing or GI at 3 and 6 mo	1. The 3 active Treatments are effective in caries prevention (progression of caries into dentin was 2.2% for SDF, 1.6% for sealant, 2.4% for FV vs 4.6% for control)	1. ART sealants were more Effective than a single Application of SDF (caries Increment in the brushing group was: 0.08 for NT; 0.09 for SDF; 0.01 For sealants. In nonbrushing group: 0.17 for NT; 0.12 for SDF; 0.06 for sealants)
	2. Caries removal had no effect	2. Tannic acid had no effect	2. Increasing frequency of SDF (2 × /y) increases caries arrest			2. SDF was Effective for caries reduction in both Primary and permanent Teeth (0.29 surfaces with		2. All equally effective in controlling initial (noncavitated) occlusal caries at 30 mo	2. Control group Developed more Dentin caries than treatment groups	2. Caries increment was lower in toothbrushing group

	Chu et al,[31] 2002	Yee et al,[64] 2009	Zhi et al,[45] 2012	Dos Santos et al,[55] 2012	Duangthip et al,[44]2018	Fung et al,[42] 2018	Llodra et al,[46]2005	Braga et al,[47] 2009	Liu et al,[48]2012	Monse et al,[50]2012
Location	**China**	**Nepal**	**China**	**Brazil**	**Hong Kong**	**China**	**Cuba**	**Brazil**	**China**	**Philippines**
						new caries in SDF group vs 1.43 in control in primary teeth and 0.37 vs 1.06 in permanent molars)				
	3. Control group developed more new caries than treatment groups	3. Arrest benefit decreases over time	3. Anterior teeth and buccal/ lingual surfaces are more likely to become arrested							
Additional findings	1. Arrested lesions Looked black Without changing Parental satisfaction (93% of Parents did not mention a difference)	1. Single SDF Application prevented one-half of arrested surfaces at 6 mo from reverting to active lesions Again over 24 mo	1. GI provides a more esthetic outcome	1. 43% of GIC fillings were lost a 6 mo and dentin was soft.	1. Lesions in anterior teeth, buccal/ Lingual surfaces and Lesions with no plaque had a Higher chance to become arrested	1. Lesion site was significant with lower anteriors having the Highest rates of arrest Followed by upper anteriors, lower posterior, and upper posterior	1. SDF showed more Efficacy to arrest decay in deciduous teeth than permanent teeth	1. Retention rates for GI sealants were 32% at 6 mo and 9% at 30 mo	1. Teeth with Early caries at baseline were More likely to develop dentin caries after 24 mo	1. Retention rate for sealants was 58% after 18 mo
		2. No complaints From parents or children to SDF	2. Only 3.5% Retention of GI after 24 mo still Provides caries arrest	2. Higher rate of failure when GIC Involved multiple surfaces.		2. Lesions with visible plaque and large lesions had lower chance of becoming arrested		2. GI sealants were more Time consuming that SDF application	2. 46% sealant retention	
			3. 45% of parents in all groups were Satisfied with appearance							
SDF Clinical Application Protocol	[a]Two treated groups had caries removal and 2 did not	[a]No caries removal	[a]Minor excavation	[a]No caries removal	[a] No caries removal	[a] Does not specify SDF amount used, time of exposure, or kind of isolation	[a]Minor decay excavation on permanent molars only	[a] No caries removal	[a] Does not specify SDF amount used, time of exposure, or whether it was rinsed or not	[a] Does not specify SDF amount used, SDF rubbed for 1 min followed by tannic acid, dried with cotton pellet, and coveredwith petroleum jelly
	[a]Does not specify SDF amount used or time of exposure	[a]One drop of SDF applied for 2 min to carious surfaces and dried with cotton pellet	[a]Does not specify SDF amount used or time of exposure	[a]Does not specify SDF amount used	[a]Does not specify SDF amount used or kind of isolation		[a] Does not specify SDF amount used	[a]Does not specify SDF amount used	[a] Cotton roll isolation	[a] Cotton roll isolation

	Chu et al,[31] 2002	Yee et al,[64] 2009	Zhi et al,[45] 2012	Dos Santos et al,[55] 2012	Duangthip et al,[44]2018	Fung et al,[42] 2018	Llodra et al,[46]2005	Braga et al,[47] 2009	Liu et al,[48]2012	Monse et al,[50]2012
Location	**China**	**Nepal**	**China**	**Brazil**	**Hong Kong**	**China**	**Cuba**	**Brazil**	**China**	**Philippines**
		[a]No food or drink for 1 h after	[a]No food or drink for 30 min after	[a]Cotton roll isolation, petroleum jelly on gingiva, SDF applied for 3 min and rinse and spit [a]No food or drink for 1 h	[a] SDF rubbed for 10 s _ No food or drink for 30 min		[a] Cotton roll isolation, SDF applied for 3 min and wash for 30 s	[a] Cotton roll isolation and petroleum jelly on gingiva, SDF applied for 3 min, and wash for 30 s [a] No food or drink for 1 h	[a] No food or drink for 30 min	
Adverse effects	None	None	None	None	None	None	0.1% Gingival irritation	None	None	None
Duration of study (mo)	30	24	24	12	30	30	36	30	24	18
Baseline caries	3.92 dmfs (active Anterior lesions)	6.8 dmfs (active lesions)	5.1 dmft (3 random teeth/child)	3.8 dmft	4.4 dmft 6.7 dmfs	3.84 dmft 5.15 dmfs	3.2 dmft	Noncavitated Molar occlusal	No cavitated lesions	At least 1 sound permanent molar
Background F exposure	Low F exposure reported use of F toothpaste	Low F exposure Provided F toothpaste	Low F exposure low access to F toothpaste	Low F Exposure access to F toothpaste	F water F toothpaste	Low F exposure F toothpaste	Low F exposure 1 0.2% NaF rinse in school every other week	Low F Exposure Provided F toothpaste	Low F Exposure Provided F toothpaste	Low F exposure Provided F toothpaste
No. of subjects at baseline	375	976	212	91	371[b]	888	425	22 children, 66 molars	501	1016
No. of subjects at endpoint	308	634	181	?	309[b]	799	373	?	485	704
Examinations after baseline	× 6 mo	1, 12, and 24 mo	× 6 mo	× 6 mo	× 6 mo	× 6 mo	× 6 mo	3, 6, 12, 18 and 30 mo plus radiographs at 6, 12 and 30 mo	× 6 mo	18 mo

Abbreviations: ART, atraumatic restorative treatment; dmfs, decayed/missing/filled surface; dmft, decayed/missing/filled teeth; FV, fluoride varnish; GI, glass ionomer; GIC, glass ionomer cements; NT, no treatment; SDF, silver diamine fluoride.

[a]Low F exposure = low F in the water, no other professionally applied fluorides or fluoride supplements.

[b]Number of subjects at baseline and endpoint reported on 30-mo results is different that numbers reported on 18-mo results.

[c]Cavitated lesions were International Caries Detection and Assessment System (ICDAS) 5 or 6; moderate lesions had no visible dentine and were ICDAS 3 or 4.

Modified from Crystal YO, Niederman R. Silver diamine fluoride treatment considerations in children's caries management. Pediatr Dent 2016;38(7):467–8; with permission.