

Silver Diamine Fluoride 38%

Scientific Literature Review

August 2016

Silver Diamine Fluoride (SDF) 38% has been receiving a great deal of attention by U.S. dental professionals since it was cleared for use by the Food and Drug Administration in August 2014 under the provisions of the Federal Food, Drug and Cosmetics Act. The Cleared Indications For Use are for the “Treatment of dentinal hypersensitivity. For use in adults over the age of 21.”

In the age of the Internet, access to information that can sometimes be credible and sometimes not, could cause confusion about the history, safety and efficacy of SDF. In addition, a number of local television news programs and social media postings around the U.S. have recently begun communicating information about the use of SDF by both general and pediatric dentists who have begun using it for the treatment of carious lesions in populations of all ages.

While SDF only recently received FDA Clearance it has been used by dental professionals outside the U.S. for both the treatment of dentinal hypersensitivity and as a caries therapy for more than 45 years. This review is intended to provide U.S. medical professionals with an understanding of the history of SDF around the world, including the most current information available regarding its use in the U.S.

Under federal law, the use of a drug or medical device by a licensed medical professional for an indication not Approved or Cleared by the FDA is allowable and not uncommon. This is termed “off-label” use.

As the organization permitted to market the only FDA Cleared SDF product in the United States, (Advantage Arrest™ Silver Diamine Fluoride 38%), it is our intention to provide a review of all scientific literature available to us in order to help insure that medical professionals, and through them, their patients are as well informed as possible about this therapy.

This document is not assumed to contain all published information regarding SDF, as that would be virtually impossible, since SDF has been in use in many countries around the world for decades. It is however meant to provide a fair and balanced view of the benefits and risks of the use of SDF. If, after reading this document, you have any questions please send an email to the address below and we will get back to you promptly.

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Frequently Asked Questions

Since the launch of Advantage Arrest Silver Diamine Fluoride 38% in April, 2015 we have fielded questions from oral health professionals on a range of subjects including Patient Application, Safety, Precautions, Restorative Aspects and Insurance Coding.

Clinical Application

1. Since the FDA cleared Advantage Arrest Silver Diamine Fluoride 38% for the treatment of hypersensitivity, with fluoride varnish as the comparative device, is this clinical application the same as fluoride varnish?

For the site-specific control of hypersensitivity, the technique to apply Advantage Arrest is similar to that of fluoride varnish. It is not for generalized applications. Please read the package insert for full application and precaution instructions.

2. I currently use fluoride varnish off-label as an in-office fluoride treatment for caries prevention or to attempt caries arrest. Can I use Advantage Arrest in this same way?

Yes. However, Advantage Arrest is only applied site-specifically on carious lesions or high-risk sites such as non-sealed occlusal surfaces or interproximal areas where incipient lesions are suspected. Care should be taken to isolate each cleaned application site with cotton rolls. The high pH, metallic taste and propensity to temporarily stain soft tissue/skin and permanently stain demineralization make the application of silver diamine fluoride different than the generalized full-mouth application associated with fluoride varnishes.

The chemical action of the SDF occurs almost immediately in the outer layers of the softened enamel and/or dentin and can be confirmed by changes in the hardness and density of the treated surface, similar to caries that arrests naturally because of positive changes in oral hygiene, diet, or daily application of fluoride in custom trays. The darkening of the lesion occurs over 24 hours and may increase over a week. Reexamination of the lesion at the next regular recall is appropriate and reapplication of SDF may be warranted. Repeat until the lesion has arrested.

3. Does Advantage Arrest prevent caries only at the point of application and adjacent sites?

No. When applied to a carious lesion or at-risk site, Advantage Arrest has demonstrated the ability in studies summarized in this packet to act as a reservoir for silver and fluoride. The silver is bactericidal against cariogenic biofilm not only at the site, but has a halo effect as saliva flows throughout the oral cavity. The same is true for the fluoride, helping to promote remineralization and prevent demineralization on all dentition.

4. Is there a recommended frequency of application of SDF for caries control?

Caries arrest studies were conducted with SDF applications of once and twice annually, with twice annual applications demonstrating the best benefit. Arrested lesions were retreated every six-months.

Clinicians have reported that they will recall their first cohort of SDF patients within 3-6 weeks to evaluate the application and action of the treatment. Once they have a feel for the predictability of the material with their application technique, they will set recall appointments based on the risk level and caries activity of the patient with higher risk patients at 3-month intervals. Moderate to high-risk patients, where it appears that home care and diet counseling has had positive impact, are recalled at 6 months.

5. Does the application of SDF to a lesion cause discoloration?

Darkening of decayed and demineralized sites occurs as the lesion arrests. Non-lesioned tooth structure does *not* stain with the application of silver diamine fluoride.

This process is similar to what is seen when caries arrests due to changes in diet or increased use of other fluorides. A recent study showed that patients see the discoloration as a clear indication that the treatment is working. Similar to the treatment of eroded and hypersensitive dentin, the treated area can be restored using glass ionomer or with a sandwich restoration of both glass ionomer and composite.

38% silver diamine fluoride should not be diluted in an attempt to reduce discoloration. Studies have shown that diluted solutions may not be effective for caries arrest.

Ionic silver adsorbs onto almost any protein surface and is especially tenaciously bound to denatured proteins. This accounts for the specificity to carious collagen over normal collagen, but both will stain. The differentiator between these stains is that with SDF use, intrinsic pigmentation of a carious lesion occurs and surface protein staining occurs primarily on healthy tissue. These oxides are bound to the tissue and don't wash or polish away. This is why the blackened lesion retains its dark color, and is most likely the reason the antimicrobial effect is long-lasting.

The functional indicator of effectiveness is when the silver oxide is bound to the diseased collagen. If the surface doesn't turn grey/black, the silver didn't bind and the antimicrobial effect will only be short-lived.

6. Will Advantage Arrest stain composites of crowns?

Surface layer staining is possible if silver diamine fluoride flows past the area of contact onto restorations. The stain can be prevented with careful application and by wiping adjacent restorations following application to lesions or high-risk sites. If staining of restorations occur they can be removed with **standard pumice** or office cleaning devices.

Be aware that existing restorations can present with marginal leakage and associated demineralization. If silver diamine fluoride reaches these compromised margins, it is possible for caries arrest and discoloration to occur.

7. Can I cover a treated and discolored site or excavate on recall appointments?

Yes, if Advantage Arrest is used during a diagnostic appointment to arrest active disease, during the restorative visit the treated site can be evaluated for caries arrest providing you and the patient several options. You could choose to 1) reapply SDF, 2) simply leave the site as is, 3) cover the site without anesthetic or excavation or finally 4) excavate the site and place a restoration.

8. How can I apply Advantage Arrest to interproximal sites where I suspect carious or incipient lesions?

Practitioners have shared success treating interproximal lesions using tufted or sponged floss soaked with silver diamine fluoride, then pulled into the contact point and left for 60 seconds.

9. If a tooth surface does not stain from the application of Advantage Arrest is there no preventative effect of the application?

Studies have shown that there is a protective effect to the site of the application of silver diamine fluoride and a halo effect for the entire mouth.

10. Are there any post appointment instructions for the patient or the caregivers/guardians?

There are no postoperative limitations. Patients may eat or drink immediately. Patients may brush their teeth with fluoridated toothpaste on their regular schedule.

11. What does an arrested lesion treated with SDF look like on radiographs?

Arrested lesions look like a lesion (scar) on radiographs. You will observe only slight increases in radio-opacity as the mineralization of the previously softened dentin increases. Ultimately the best test of arrest is still the color change and tactile hardness of the dentin surface.

It is advised that you educate your referring dentist about your use of Advantage Arrest since the appearance of a treated lesion might be new and confusing for many practitioners.

12. Can SDF be used as a cavity liner?

SDF is cleared in the same FDA category as cavity liners. Although there are no head to head clinical trials comparing SDF as a cavity liner, it has been used successfully in this way.

SDF will not discolor intact enamel or dentin. SDF can discolor demineralized tooth structure brown/black. Some of this discoloration may shadow a restoration and can create less than optimal esthetic restorations.

13. How far into enamel and dentin does SDF penetrate?

Studies have shown that SDF can penetrate approximately 25 microns into enamel and 300 microns into dentin. This will seal off the surface of any lesions and cause the remainder of the lesion to arrest. In a 2002 study by Dr. Chu, 100% of lesions stained black to the outer edge of the lesion were arrested.

14. Who is allowed to apply SDF in clinical practice in my state?

Each State dental practice act is different. Since SDF is a fluoride-containing product indicated for the control of dentinal hypersensitivity, it should fit into the same rules as fluoride varnishes. Please confirm that within your own state's dental practice acts.

Safety

1. What have been the reported adverse events with the use of silver diamine fluoride worldwide?

Where silver diamine fluoride has been used in other countries there are no reports of adverse effects, outside of patients with an allergy to silver.

2. Is SDF safe for use in children?

Regarding the margin of safety for dosing, a study was conducted for FDA review for market clearance in rats and mice to determine the lethal dose by oral and subcutaneous administration. The worst-case scenario is subcutaneous administration and that lethal dose was found to be 380 mg/kg. One drop (25uL) of 38% silver diamine fluoride (SDF) contains 9.5 mg silver diamine fluoride. Thus, one drop of 38% SDF applied to 10 kg (22 lb.) child would equal 0.95 mg/kg, equal to a four hundred fold safety margin.

In setting up protocols for undergraduate application of 38% SDF, the University of California San Francisco set a recommended limit of one drop per 10 kg (22 lb.) per treatment visit, with weekly intervals at most.

3. What are the safety implications for application of SDF for a patient that has more than six sites to be treated?

The Margin of Safety for the volume of product needed to treat six sites is within 130 times the NOAEL (no-observed-adverse-effect-level). Treating more sites in one visit will likely have little practical impact on patient safety. Like protocols for fluoride varnish application, the suspension for several days of fluoride supplements is advised.

4. Is SDF application safe for use with pregnant patients?

The FDA cleared silver diamine fluoride for marketing as a medical device, not a drug, and it has not been studied in pregnant woman. Based on known toxicological and pharmacological information, SDF is not expected to have adverse effects on pregnant patients. This is equivalent to pregnancy category C for drugs.

Precautions

1. Patient exclusions and inclusions?

Do not use silver diamine fluoride on patients:

- With an allergy to silver
- With ulcerative gingivitis or stomatitis
- Without an informed consent
- With a low caries risk, CDT code D 0601

Do use silver diamine fluoride for patients:

- With any non-symptomatic active caries
- With any incipient watch spot
- With any unsealed, at risk, pits and fissures
- With newly erupted molars

2. Does SDF discolor skin or oral tissue?

Contact to skin is not harmful but is likely to cause temporary tattooing. The effect is not immediate, rather it will be noticed within hours. The speed of discoloration is accelerated with light contact. The staining will be limited to direct areas of contact and will fade over a period of 24-72 hours. Patients should be protected with bibs and safety glasses as in any clinical procedure. If you believe you have touched the applicator to the skin of a patient, it is good to advise them of possible temporary tattooing.

Contact to oral soft tissue is less likely to cause temporary tattooing, but is still possible. Take care to protect soft tissue with petroleum jelly or cocoa butter when an application is adjacent to gingival tissue (root caries, treatment of restoration margins). Light blanching is also possible from prolonged direct contact, but has been reported to be minor and resolves within 1-2 days.

3. Are there any contraindications for the use of SDF for the control of caries?

SDF should not be placed on exposed pulps. Studies have shown that 38% silver diamine fluoride conveys more effective protection against decay in other teeth than fluoride varnish with reduced overall fluoride exposure.

4. Does SDF stain countertops, instruments, clothing etc.?

Yes. When dispensing SDF it is a good idea to use an absorbent material that has a coated bottom like a patient bib under the dappen dish and applicator to avoid contact with metal trays and office countertops. If SDF comes in contact with instruments or countertops wash immediately with water, soap, ammonia or iodine tincture and then rinse thoroughly with water. Sodium hypochlorite (household bleach) can also be used for difficult stains once they set into the surface.

Stains to clothing are permanent. Use an applicator that does not drip the SDF as it passes over the patient to the site of treatment.

Restorative Aspects

1. Can SDF be used on a prepared tooth just prior to restoration cementation?

Yes. Desensitizing agents have been shown to be protective of the pulp when placed on crown preparations to reduce dentin permeability. Advantage Arrest, a desensitizer, has been shown safe to the pulp when placed on exposed dentin. In addition, studies have shown desensitization and efficacy in treating softened dentin before placing direct restorations. Usually the tooth is first treated with silver diamine fluoride 38%. This provides the benefit of sealing tubules plus the antimicrobial benefits of both silver and fluoride.

2. Does an SDF treated site compromise the bond strength of glass ionomer (GI), resin-modified glass ionomer (RMGI) or resin composite restorations?

A recent in vitro study investigated the micro-tensile bonding strength of resin composite to the dentin of primary molars and found that pretreating does not affect the bonding strength. The study concluded: "In the SDF group, the fracture occurred most often within the adhesive layer, suggesting that bonding strength

might be stronger between the adhesive and the dentin pretreated with SDF.” (Pediatric Dentistry, V 38, N 2, Mar/Apr 2016, pgs. 148-153)

SDF treated sites tend to discolor more rapidly with light curing. Care should be taken when bonding translucent restorative materials in anterior teeth. The use of opaquers is recommended when covering extensive anterior treated sites. Self-cured materials may diminish anterior discoloration issues associated with light curing.

Insurance Coding

1. How can Advantage Arrest be coded using CDT?

SDF is indicated and cleared for dentinal hypersensitivity treatment and can be used to treat site-specific locations. That code is: D9910 - Application of a desensitizing medicament, per visit

There is a new CDT code for 2016 specifically for the use of caries arresting medicaments, the off-label use of Advantage Arrest.

The new D1354 code nomenclature reads: Interim caries arresting medicament application. The descriptor reads: Conservative treatment of an active, non-symptomatic carious lesion by topical application of a caries arresting or inhibiting medicament and without mechanical removal of sound tooth structure.

It is common for insurance providers to initially not reimburse for new codes as they are developing usual and customary rates for the procedure. However, it's important the new code is used so the providers can see the volume of use and determine future coverage. There are several providers that have announced coverage in various states.

In the middle of 2016, state Medicaid agencies met and it was announced that several states already had adopted coverage for D1354, or were planning to add coverage shortly. Check with your state Medicaid agency.

For a current list of providers visit:

https://en.wikipedia.org/wiki/Silver_diamine_fluoride.

2. Can I use code D1208 – topical application of fluoride- excluding varnish?

Yes, since Advantage Arrest contains fluoride and studies/articles in this packet demonstrate the ability of silver diamine fluoride to prevent caries, D1208 is an appropriate code when the product is used as a topical application of fluoride. Clinical notes should reflect the reason for the application.

It is also helpful to identify caries risk to justify the reimbursement with a recognized caries risk tool. Codes: D0601 (low), D0602 (moderate) and D0603 (high) codes are especially helpful in adult claims.

Finally, your procedures can always be coded using D1999 - Unspecified preventive procedure by report.

From a third party payer perspective, this allows providers to track the frequency of a procedure and develop usual and customary rates for future coverage.

Advantage Arrest Package Insert

Advantage Arrest

Silver Diamine Fluoride 38%

Professional Tooth Desensitizer

Rx Only

Desensitizing Ingredient: Aqueous Silver Diamine Fluoride, 38.3% to 43.2% w/v

Inactive Ingredients: Purified water

Clinical Pharmacology: Product forms insoluble precipitates with calcium or phosphate in the dentinal tubules to block nerve impulses.

Indication and Usage: Treatment of dentinal hypersensitivity. For use in adults over the age of 21.

Contraindications: This product is contraindicated in patients with ulcerative gingivitis or stomatitis, or known sensitivity to silver or other heavy-metal ions. Patients with more than six affected sites, patients having had full mouth gingivectomies and patients showing abnormal skin sensitization in daily circumstances are recommended for exclusion.

Warnings: This product is intended for local application only. Not for ingestion. Protect the patient's eyes. Use caution to avoid contact with skin or clothing. In the event of exposure to eyes or skin, flush the area copiously with water and immediately seek medical consultation. This product yielded positive cytotoxicity in standard testing.

Precautions for Use:

- 1) Advantage Arrest does not normally stain enamel or burnished dentin. Advise patients that soft dentin or margins of composite restorations may be stained. Staining may be reversed by gentle polishing with tincture of iodine (weak iodine solution).
- 2) Advise patients that air-drying and product application can cause momentary transient pain to hypersensitive areas. Advantage Arrest has not been shown to cause pulpal necrosis even when soft dentin is treated.
- 3) Minimize product contact with gingiva and mucous membrane by using recommended amounts and careful application. Advantage Arrest may cause reversible short-term irritation. When applying Advantage Arrest to areas near the gingiva, apply petroleum jelly or cocoa butter and use cotton rolls to protect the gingival tissues. Alternatively, a rubber dam can be used to isolate the area.
- 4) If accidental contact occurs, thoroughly wash the area with water, saline solution or ~3% hydrogen peroxide. This includes contact with skin, clothes, floors and cabinets. Because Advantage Arrest is clear and thus

may be difficult to see, use caution to avoid transferring the material from gloved hands to other surfaces.

Precautions for Handling:

1. Storage Precautions

- 1) Store in original packaging in a cool, dark place.
- 2) Replace cap immediately after use.
- 3) Use as soon as dispensed.

2. Advantage Arrest will stain skin, clothes, counter tops, floors and instruments brown or black. Refer to the following for stain removal:

- 1) Skin; wash immediately with water, soap, ammonia or iodine tincture and then rinse thoroughly with water. Do not use excessive methods in an attempt to remove difficult stains from skin as the stains will eventually fade.
- 2) Clothing/Countertops/Floors/Instruments; use the same procedures as with stained skin. Difficult stains may be treated with sodium hypochlorite.

3. If Advantage Arrest is dispensed into a separate container, be sure to wash or thoroughly wipe the container clean immediately after use.

Adverse Reactions: Transient irritation of the gingiva has rarely been reported.

Dosage and Administration:

1. Isolate the affected area of the tooth with cotton rolls or protect the gingival tissue of the affected tooth with petroleum jelly. Alternatively, a rubber dam can be used to isolate the area.
2. Clean and dry the affected tooth surface.
3. For up to 5 treated sites per patient, dispense 1-2 drops of solution into a disposable dappen dish. Transfer material directly to the tooth surface with an applicator.
4. Air-dry.

If needed, one or two reapplications may be administered at intervals of one week.

How Supplied: Single 10 mL dropper-bottle containing 8 mL of product. Not sterile.

Storage: Do not freeze or expose to extreme heat. Keep in an air-tight container in a dark place.

Caution: Federal law restricts this device to sale by or on the order of a dentist or physician.

Distributed by:

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ELE137-0315

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J Dent Res 90(2):203-208, 2011

ABSTRACT

Tooth sensitivity is a common clinical problem. This multi-center randomized clinical trial assessed the effectiveness and safety of topical diammine silver fluoride. From two sites (Lima and Cusco, Peru), 126 adults with at least one tooth sensitive to compressed air were randomly assigned to either the experimental treatment or sterile water, and pain was assessed by means of a 100-mm visual analogue scale at 24 hours and 7 days. The diammine silver fluoride reduced pain at 7 days at both sites. At the Lima site, the average change in pain scores between baseline and day 7 for the silver fluoride group was -35.8 (SD = 27.7) mm vs. 0.4 (SD = 16.2) mm for the control group ($P < 0.001$). In Cusco, the average change in pain scores for the silver fluoride group was -23.4 (SD = 21.0) mm and -5.5 (18.1) mm for the control group ($P = 0.002$). No tissue ulceration, white changes, or argyria was observed. A small number of participants in the silver fluoride group experienced a mild but transient increase in erythema in the gingiva near the tooth. No changes were observed in the Gingival Index. We concluded that diammine silver fluoride is a clinically effective and safe tooth desensitizer.

KEY WORDS: tooth sensitivity, silver diamine fluoride, diammine silver fluoride, silver diamine fluoride, fluorides, topical.

DOI: 10.1177/0022034510388516

Received August 13, 2010; Revised September 3, 2010;
Accepted September 3, 2010

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The Short-term Effects of Diammine Silver Fluoride on Tooth Sensitivity: a Randomized Controlled Trial

INTRODUCTION

Tooth sensitivity to various stimuli, including cold air, has been explained by hydrodynamic changes within the dentinal tubules that activate intradental nerves (Markowitz and Pashley, 2008). Incidence is thought to be increasing. The etiology can be tooth wear, aggressive oral hygiene, and diet. Successful treatments physically block dentinal tubules (Arends *et al.*, 1997).

Sodium fluoride varnish and fluoride solutions and gels have been shown to reduce sensitivity (Thrash *et al.*, 1992; Ritter *et al.*, 2006). However, there is continuing interest in finding effective treatments. Nevertheless, recent studies have designs that are weak or statistically underpowered (Erdemir *et al.*, 2010; Jalali and Lindh, 2010).

The purpose of this study was to assess the clinical effectiveness and safety of topical diammine silver fluoride as a tooth desensitizer in adults.

METHODS

Design

This is a randomized clinical trial with two groups (Fig. 1). The study tested application of diammine silver fluoride in a single visit, because previous unpublished work had shown that a single application forms insoluble precipitates with calcium and phosphate that physically block dentinal tubules. The International Clinical Trials Registry number is NCT01063530.

Study Sites

The study was conducted in two sites, Lima and Cusco, Peru.

Participants

To be included, a participant must have at least one vital cuspid or premolar with a buccal cervical defect and clinical hypersensitivity in response to compressed air with a score ≥ 15 on a visual analogue scale (VAS) for pain. The individual will have had generally healthy gum tissue surrounding this tooth and no ulceration and no leukoplakia in this gingival tissue.

Candidates were excluded if they were using any type of tooth desensitizer, had received a fluoride varnish treatment within the preceding month, or were taking prescription medications, aspirin, or non-steroidal anti-inflammatory drugs; women who were pregnant were also excluded. Individuals using smokeless tobacco or chewing coca leaves were excluded. Individuals with known sensitivity to silver or other heavy-metal ions were excluded.

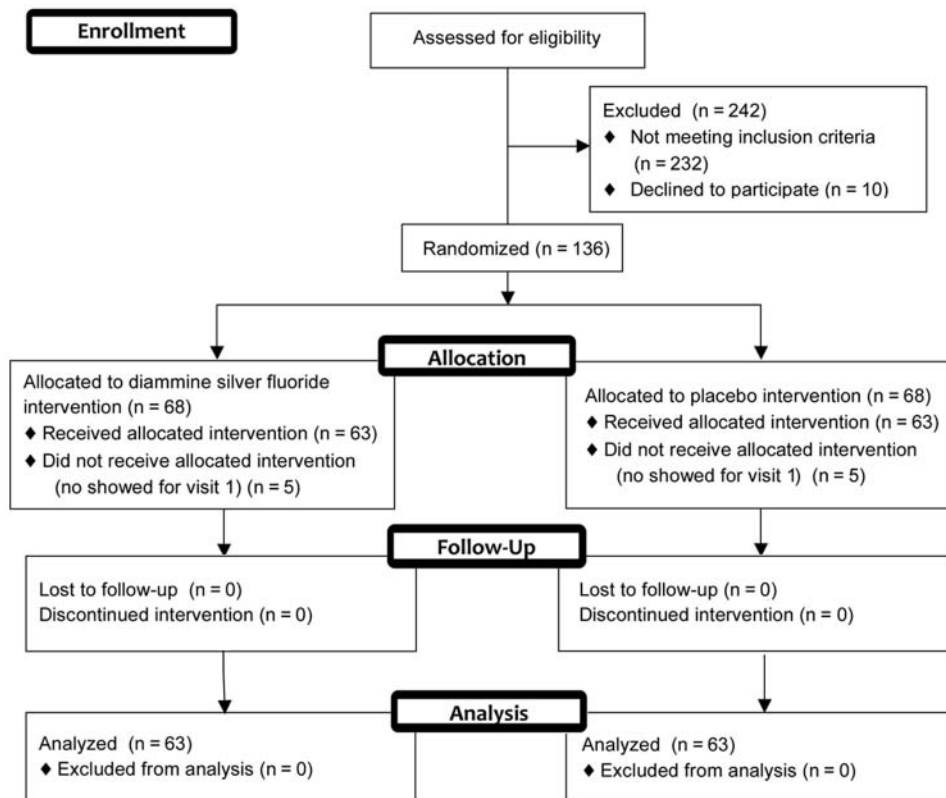


Figure 1. Flow chart for clinical trial sites combined.

Participants were recruited from the patient populations of Cayetano University School of Dentistry and the private dental practices of the investigators in Lima and Cusco between January and June, 2010, and were offered a small financial incentive for participation.

The Institutional Review Board of Universidad Peruana Cayetano Heredia approved the protocol, and the informed consent of all participants was obtained.

Treatment Conditions

Diammine silver fluoride [$\text{Ag}(\text{NH}_3)_2\text{F}$, CAS RN 33040–28–7, Saforide, Toyo Seiyaku Kasei Co. Ltd. Osaka, Japan] was used. It is clear and colorless, with a weak odor of ammonia. According to the manufacturer, the solution includes not less than 24.4 w/v% and not more than 26.8 w/v% of silver (Ag), not less than 5.0 w/v% and not more than 5.9 w/v% of fluorine (F). Diammine silver fluoride is also referred to as silver diammine fluoride, silver diamine fluoride, or silver fluoride.

Assignment to Conditions

Participants were randomly assigned to treatment with diammine silver fluoride or sterile water. The randomization was stratified on study site and baseline tooth sensitivity score (< 37 and ≥ 37) to a five-second blast of pressurized air at 2 cm distance from the tooth, and blocking was used to ensure that the

two groups would be balanced across the study period and within each stratum. The stratification at 37 was chosen from the literature (Ritter *et al.*, 2006). A pre-test of the VAS with 10 individuals confirmed the mean response in this range. Block sizes were equal to 2 or 4, and were chosen randomly with 2/3 and 1/3 probability, respectively. The assignments were generated by the project statistician, using the “sample” function of R statistical software (Version 2.7.1, The R Foundation for Statistical Computing, 2008). The assignments were recorded on slips of paper numbered consecutively within each stratum and then placed inside sealed envelopes sequentially numbered by stratum. The statistician retained the master list until all the data were analyzed. The clinician would open the envelope and apply the agent. The agents (active or control) were packaged in identical dark glass bottles labeled as A or B. The packaging was done at Cayetano University.

Clinical Procedure

The clinical procedure was that a disposable microbrush was dipped into a drop of the diammine silver fluoride or the control and then applied to the surface for 1 sec. Then the surface was gently air-dried and the procedure repeated.

Measures

Primary Outcome-Clinical

Reduction of pain (tooth sensitivity)—The teeth were isolated with gauze, and participants were asked to report tooth pain on a 100-mm visual analogue scale (VAS; Ritter *et al.*, 2006) before treatment and after treatment with a five-second blast of pressurized air at 2 cm distance from the tooth. The VAS was anchored with “no pain” and “intolerable pain”. The follow-up test was repeated at 24 hrs and 7 days later. A single person in each site conducted the assessment in Spanish. The scale was pre-tested to ensure that the descriptors were translated properly.

Safety

Damage to gingiva—Tissues were photographed before treatment to establish the normal baseline condition. A single examiner examined gingival tissues surrounding each treated tooth immediately after treatment, and at 24 hrs and 7 days later. The primary safety measure is erythema. It was assessed visually

Table 1. Tooth Sensitivity by Study Site and Condition

Study Site	Time	Condition		
Lima		Silver Fluoride (N = 37)	Control (N = 34)	
		Mean VAS (SD) [Range]	Mean VAS (SD) [Range]	P-value*
	Baseline	57.3 (26.7) [17, 99]	49.3 (19.3) [15, 84]	0.16
	24 hrs	28.2 (22.1) [2, 75]	52.1 (22.8) [16, 89]	
	Change from baseline	-29.1 (27.5) [-94, 10]	2.6 (15.3) [-44, 32]	< 0.0001
	7 days	21.5 (23.0) [1, 78]	49.9 (21.2) [9, 85]	
	Change from baseline	-35.8 (27.7) [-97, 12]	0.4 (16.2) [-38, 33]	< 0.0001
Cusco		Silver Fluoride (N = 26)	Control (N = 29)	
		Mean VAS (SD) [Range]	Mean VAS (SD) [Range]	P-value
	Baseline	51.7 (20.5) [22, 92]	51.6 (22.4) [16, 99]	0.98
	24 hrs	45.2 (24.1) [11, 87]	50.6 (22.0) [15, 95]	
	Change from baseline	-6.5 (13.1) [-34, 22]	-1.0 (11.7) [-37, 20]	0.11
	7 days	28.3 (21.8) [2, 94]	46.1 (24.4) [3, 92]	
	Change from baseline	-23.4 (21.0) [-56, 24]	-5.5 (18.1) [-77, 18]	0.0015

*Two-sample *t* test (unequal variances).

with the use of a standard dental light. Erythema (red changes) was rated on a 1 to 3 scale, where 1 is no redness, 2 is redness with bleeding on probing, and 3 is a severe change. The Gingival Index (Löe, 1967) was used to measure gingival inflammation in the mouth overall. White changes, ulceration, and staining were secondary measures. Changes were rated as present or absent. Examiners were trained to criteria using photographs and clinical cases. Intra- and inter-examiner reliability was established in 15 cases, and intraclass correlation was used to assess reliability. All intraclass correlations exceeded 0.8.

Data Analysis Plan

The data from the two sites were analyzed. To confirm reduction in pain, we calculated average difference scores between pre- and post-treatment VAS scores for each individual for each time-point (24 hrs and 7 days after treatment), and *t* tests were used to compare changes. The primary end point was at 7 days. Generalized estimating equations (GEE) linear regression was used in a secondary analysis to compare the reduction in pain across the 3 time-points, where the outcome is pain at the 3 time-points, the baseline pain is a covariate, and robust standard errors are used to account for multiple observations *per* participant and heteroscedasticity (Hardin and Hilbe, 2002). In addition, separate analyses of covariance were done at each time-point to compare the reduction in pain due to the active treatment between the two study sites, where the outcome is the pain at a particular time-point, baseline pain was entered as a covariate, and treatment and site, as well as a treatment-group-by-site interaction, were entered as factors.

We used Fisher’s Exact Test to assess whether there were more participants with erythema score > 1 in the silver fluoride group *vs.* the control group at 24 hrs and 7 days post-treatment. The primary end-point was assessed at 24 hrs. A *t* test assessed any differences in Gingival Index. Any white changes, ulceration, and staining (argyria) were reported.

Power Analysis

The data from the two sites were analyzed separately, and power is described below for the separate site analyses.

Reduction in tooth sensitivity—The primary end-point was assessed at 7 days post-treatment. In a similar desensitization study comparing fluoride varnishes (Ritter *et al.*, 2006), pain in response to air dropped from 36.9 (SD = 26.2) at baseline to 20.8 (SD = 4.3) at 2 wks post-treatment. We expected a similar or larger drop after 7 days with diammine silver fluoride, based on unpublished work from the University of Hong Kong, and little or no drop from the water. Thus, having 31 individuals in a group will allow for detection of effect size from 0.64 upwards, with an alpha of 0.05 and power of 0.8.

RESULTS

Participants

One hundred twenty-six adults (71 in Lima and 55 in Cusco) participated. About 378 candidates were screened between January and June 2010. The main reason (95%) for exclusion was lack of tooth sensitivity. The remainder were excluded because of the use of medications. No individuals were excluded because of tobacco use or coca. All of those eligible agreed to participate, but 10 were excluded because they failed to appear for the first visit. The proportion of women enrolled was 86% in Lima and 80% in Cusco. The average age of participants was 44 yrs and 43 yrs, respectively. There were no dropouts.

Participants and clinicians were blind to treatment assignment. Odor was not a threat to blinding, because the smell is not detectable clinically when such small quantities are used. Taste was not a threat in this study, because only minute amounts of material were applied and the tooth was air-dried after application.

Table 2. Numbers and Percentages of Participants with Erythema Score of 2 by Study Site and Condition

Study Site	Time	Condition		
Lima		Silver Fluoride (N = 37)	Control (N = 34)	
		n (%)	n (%)	P-value*
	Baseline	3 (8.1)	2 (5.9)	1.0
	24 hrs	3 (8.1)	2 (5.9)	1.0
	7 days	3 (8.1)	1 (2.9)	0.61
Cusco		Silver Fluoride (N = 26)	Control (N = 29)	
		n (%)	n (%)	P-value*
	Baseline	6 (23.1)	7 (24.1)	1.0
	24 hrs	10 (38.5)	2 (6.9)	0.0076
	7 days	3 (11.5)	3 (10.3)	1.0
Sites combined		Silver Fluoride (N = 63)	Control (N = 63)	
		n (%)	n (%)	P-value*
	Baseline	9 (14.3)	9 (14.3)	1.0
	24 hrs	13 (20.6)	4 (6.3)	0.035
	7 days	6 (9.5)	4 (6.3)	0.74

*Fisher's exact test

Clinical Effectiveness

The average pain scores before and after treatment, by site, are given in Table 1. At the Lima site, the silver fluoride group had slightly higher baseline scores (average = 57.3) than the control (average = 49.3; $P = 0.16$). At the Cusco site, the baseline scores were similar between the silver fluoride group (average = 51.7) and control (average = 51.6; $P = 0.98$). The primary study endpoint was the change from baseline to 7 days. In Lima, the average change in pain score between baseline and day 7 for the silver fluoride group was -35.8 (SD = 27.7) mm vs. 0.4 (SD = 16.2) for the controls ($P < 0.0001$). In Cusco, the average change in pain score between baseline and day 7 for the silver fluoride group was -23.4 (SD = 21.0) mm vs. -5.5 (SD = 18.1) mm ($P = 0.0015$) for water.

Comparison of tooth sensitivity at 24 hrs and 7 days between study groups by analysis covariance, adjusted for the baseline sensitivity level, gave similar results.

There was no significant three-way interaction among study site, time, and study group (GEE linear regression; $P = 0.20$), but all two-way interactions were significant: study site by time ($P = 0.043$), study site by study group ($P = 0.0006$), and study group by time ($P = 0.0076$). Hence, an analysis of time effect was done separately by study site. In Lima, there was no significant time-by-study-group interaction ($P = 0.21$). The overall study group difference in tooth sensitivity (over both time-points), adjusted for baseline sensitivity, was 29.9 ($P < 0.001$). The overall difference in sensitivity between 24 hrs and 7 days was 4.5 ($P = 0.014$). In Cusco, there was a significant study-group-by-time interaction ($P = 0.015$), so the overall study group difference is not reported. The differences in sensitivity between 24 hrs and 7 days were 16.9 ($P = 0.005$) for silver fluoride and 4.5 ($P = 0.097$) in the control group, respectively.

Safety

The number and percent of participants with a erythema score of 2 for the gingival tissue of the tooth treated for each treatment condition by site and time are given in Table 2. Scores were low; no individual had score 3, severe erythema, either before or after the application of silver fluoride. There was no difference in the proportion of participants with erythema score > 1 between the silver fluoride group and the placebo (Fisher's Exact Test, $P = 1.0$) at any time-point in the Lima population. There was a small but significant increase in the proportion of participants at the Cusco site who experienced an erythema score > 1 at 24 hrs ($P = 0.0076$). There was no difference in the proportion of participants with an erythema score > 1 between the groups in Cusco after 7 days ($P = 1.0$). No white or dark changes were noted in gingiva in any participant at any time in any condition at either site. An independent examiner, who was blind to treatment condition and time, examined the photographs and confirmed this lack of change.

The Gingival Index scores for each treatment condition and site are listed in Table 3. The mean (SD) Gingival Index scores for the mouth for treatment and control groups at baseline were: (Lima) silver fluoride, 0.29 (0.24), control 0.33 (0.35) ($P = 0.59$); and (Cusco) silver fluoride, 0.47 (0.24), control 0.38 (0.27) ($P = 0.19$). At 7 days, the mean (SD) changes in GI scores were: (Lima) silver fluoride, -0.02 (0.09), control 0.03 (0.13) ($P = 0.076$); and (Cusco) silver fluoride, -0.16 (0.27), control -0.03 (0.09) ($P = 0.023$). Similar results were observed after 24 hrs.

Photographs of the teeth suggest that the silver fluoride did not stain most exposed root surfaces (see Fig. 2 for an example). This result was found only when surfaces had untreated decay.

Table 3. Overall Gingival Index Score by Study Site and Condition

Study Site	Time	Condition		
Lima		Silver Fluoride (N = 37)	Control (N = 34)	
		Mean (SD) [Range]	Mean (SD) [Range]	P-value*
	Baseline	0.29 (0.24) [0.0, 1.2]	0.33 (0.35) [0.0, 1.5]	0.59
	24 hrs	0.28 (0.24) [0.0, 1.2]	0.35 (0.36) [0.0, 1.7]	
	Change from baseline	-0.01 (0.05) [-0.2, 0.1]	0.02 (0.07) [-0.2, 0.2]	0.076
	7 days	0.27 (0.23) [0.0, 1.2]	0.36 (0.39) [0.1, 1.8]	
	Change from baseline	-0.02 (0.09) [0.2, 0]	0.03 (0.13) [-0.5, 0.3]	0.076
Cusco		Silver Fluoride (N = 26)	Control (N = 29)	
		Mean (SD) [Range]	Mean (SD) [Range]	P-value*
	Baseline	0.47 (0.24) [0.1, 0.9]	0.38 (0.27) [0.0, 1.2]	0.19
	24 hrs	0.36 (0.21) [0.1, 0.8]	0.36 (0.24) [0.0, 1.2]	
	Change from baseline	-0.11 (0.16) [-0.6, 0.1]	-0.02 (0.12) [-0.3, 0.3]	0.020
	7 days	0.31 (0.19) [0.0, 0.8]	0.35 (0.26) [0.1, 1.2]	
	Change from baseline	-0.16 (0.27) [-0.8, 0.7]	-0.03 (0.09) [-0.3, 0.2]	0.023
Sites Combined		Silver Fluoride (N = 63)	Control (N = 63)	
		Mean (SD) [Range]	Mean (SD) [Range]	P-value**
	Baseline	0.36 (0.26) [0.0, 1.2]	0.35 (0.32) [0.0, 1.5]	0.72
	24 hrs	0.31 (0.23) [0.0, 1.2]	0.35 (0.31) [0.0, 1.7]	
	Change from baseline	-0.05 (0.12) [-0.6, 0.1]	0.00 (0.10) [-0.3, 0.3]	0.0023
	7 days	0.28 (0.22) [0.0, 1.2]	0.35 (0.33) [0.1, 1.8]	
	Change from baseline	-0.08 (0.20) [-0.8, 0.7]	0.00 (0.12) [-0.5, 0.3]	0.0028

*Two-sample test (unequal variances).

**Analysis of covariance, adjusted for study site, with heteroscedasticity-consistent standard errors.

DISCUSSION

In a population with teeth sensitive to air, this trial demonstrated that a topical solution of diammine silver fluoride was more effective than a placebo in reducing tooth pain. Reductions grew larger between 24 hrs and 7 days post-treatment. The study was conducted in two sites by different investigators to increase generalizability and had sufficient statistical power to detect clinically meaningful differences in pain. The study involved many more individuals than the typical study (Ritter *et al.*, 2006).

The results, however, are consistent with those from similar studies of other desensitizers, such as self-administered 0.717% fluoride solution (Thrash *et al.*, 1992) or fluoride varnish (Ritter *et al.*, 2006). In the fluoride solution study, the authors concluded that two one-minute applications reduced sensitivity to cold. Participants in the varnish study experienced a pain reduction in response to ice, but not to air, at 2 wks. The current study reported significant pain reductions in response to air in 24 hrs that were maintained at 7 days. The magnitude of reduction was considerably greater than in the other studies. The current study did not use ice as a stimulus.

There were no unintended effects on the gingiva, and any inflammation resulting from the treatment was minor and transient. No staining of the gingival tissues was observed.



Figure 2. Root caries at baseline (left panel), 24 hrs after treatment (middle panel), and 7 days after treatment with diammine silver fluoride (right panel).

Staining of teeth was found only when surfaces had untreated decay. The staining of carious dentin can be minimized by the application of potassium iodide solution after treatment without reducing the effect (Knight *et al.*, 2006).

Diammine silver fluoride has been shown to arrest caries in animal models (Tanzer *et al.*, 2010) and to be more effective than sodium fluoride varnish in human trials (Chu *et al.*, 2002; Llodra *et al.*, 2005; Rosenblatt *et al.*, 2009; Tan *et al.*, 2010). It did not cause abscesses in teeth with open cavities that were treated. The mechanism of action for caries arrest may be antimicrobial (Knight *et al.*, 2009). Studies have also shown that diammine silver fluoride is free of adverse effects (Chu *et al.*, 2002; Llodra *et al.*, 2005; Tan *et al.*, 2010). This suggests that diammine fluoride may be particularly effective in individuals in whom sensitivity is associated with demineralization and caries.

Diammine silver fluoride has been demonstrated to be a clinically effective and safe tooth desensitizer after 24 hrs and 7 days. Clinical trials are warranted to examine effectiveness over a longer period of time and in comparison with other agents.

ACKNOWLEDGMENTS

The authors acknowledge the contributions of Silvia Navarro in recruitment of participants. ADP Silver Dental Arrest, LLC, Redmond, OR, USA, was the study sponsor.

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UCSF Protocol for Caries Arrest Using Silver Diamine Fluoride: Rationale, Indications and Consent

Jeremy A. Horst, DDS, PhD; Hellene Ellenikiotis, DDS; and Peter L. Milgrom, DDS

ABSTRACT The Food and Drug Administration recently cleared silver diamine fluoride for reducing tooth sensitivity. Clinical trials document arrest and prevention of dental caries by silver diamine fluoride. This off-label use is now permissible and appropriate under U.S. law. A CDT code was approved for caries arresting medicaments for 2016 to facilitate documentation and billing. We present a systematic review, clinical indications, clinical protocol and consent procedure to guide application for caries arrest treatment.

AUTHORS

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Conflict of Interest

Disclosure: Dr. Horst is co-founder and CSO at OraViz.

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Conflict of Interest

Disclosure: None reported.

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Conflict of Interest

Disclosure: Dr. Milgrom is a principal in ADP Silver Dental Arrest LLC, which licenses permission to market Advantage Arrest to Elevate Oral Care LLC.

Until now, no option for the treatment of dental caries in the U.S. besides restorative dentistry has shown substantial efficacy.¹ Silver diamine fluoride is an inexpensive topical medicament used extensively in other countries to treat dental caries across the age spectrum. No other intervention approaches the ease of application and efficacy. Multiple randomized clinical trials — with hundreds of patients each — support its use for caries treatment, thus substantiating an intervention that addresses an unmet need in American dentistry. In August 2014, the Food and Drug Administration (FDA) cleared the first silver diamine fluoride product for market, and as of April 2015, that product is available.

Since its approval in Japan more than 80 years ago,² more than 2 million containers have been sold. The silver acts as an antimicrobial, the fluoride promotes remineralization and the ammonia stabilizes high concentrations in solution.³

Because silver diamine fluoride is new to American dentistry and dental education, there is a need for a standardized guideline, protocol and consent. The University of California, San Francisco, School of Dentistry paradigm shift committee assembled a subcommittee with the following goals:

- Use available evidence to develop a list of clinical indications.
- Define a protocol that maximized safety and efficacy and minimized inadvertent staining of clinical facilities.

- Build an informed consent document at the eighth-grade reading level.

We conducted a systematic review, inquired of authors of published clinical and in vitro studies about details and considerations in their protocols and consulted experts in cariology and materials chemistry where evidence was lacking. The work of this committee resulted in the adoption of silver diamine fluoride use in the UCSF student clinics.

Methods

A literature review was designed by a medical librarian to search PubMed and the International Association of Dental Research abstract archive with the following search terms: “33040-28-7” OR “1Z00ZK3E66” OR “silver diamine fluoride” OR “silver fluoride” OR “silver diamine fluoride” OR “diammine silver fluoride” OR “ammonical silver fluoride” OR “ammoniacal silver fluoride”. Differences in nomenclature have led to confusion around this material. Another review was completed with the terms “dental” OR “caries” AND “silver nitrate” AND “clinical.”

Material

Silver diamine fluoride (38% w/v $\text{Ag}(\text{NH}_3)_2\text{F}$, 30% w/w) is a colorless topical agent comprised of 24.4-28.8% (w/v) silver and 5.0-5.9% fluoride at pH 10,⁴ and marketed as Advantage Arrest by Elevate Oral Care LLC (West Palm Beach, Fla.). Other companies may market silver diamine fluoride in the future following determination of substantial equivalence and FDA clearance.

Mechanisms

Silver diamine fluoride is used for caries arrest and treatment of dentin hypersensitivity. In the treatment of exposed sensitive dentin surfaces,

topical application results in the development of a squamous layer on the exposed dentin, partially plugging the dentinal tubules.⁵ High concentration aqueous silver has been long known to form this protective layer.⁶ Decreased sensitivity in treated patients^{7,8} is consistent with the hydrodynamic theory of dentin hypersensitivity.⁹

Dental caries is a complex progression involving dietary sugars, bacterial metabolism, demineralization and organic degradation. The collagenous organic matrix is

Silver diamine fluoride outperforms other anticaries medicaments in killing cariogenic bacteria in dentinal tubules.

exposed once a dentin surface is demineralized and destroyed by native and bacterial proteases to enable a lesion to enlarge.¹⁰ Upon application of silver diamine fluoride to a decayed surface, the squamous layer of silver protein conjugates forms, increasing resistance to acid dissolution and enzymatic digestion.¹¹ Hydroxyapatite and fluorapatite form on the exposed organic matrix, along with the presence of silver chloride and metallic silver.⁵ The treated lesion increases in mineral density and hardness while the lesion depth decreases.⁵ Meanwhile, silver diamine fluoride specifically inhibits the proteins that break down the exposed dentin organic matrix: matrix metalloproteinases,¹¹ cathepsins¹² and bacterial collagenases.⁵ Silver

ions act directly against bacteria in lesions by breaking membranes, denaturing proteins and inhibiting DNA replication.^{13,14} Ionic silver deactivates nearly any macromolecule. Silver diamine fluoride outperforms other anticaries medicaments in killing cariogenic bacteria in dentinal tubules.¹⁵

Silver and fluoride ions penetrate ~25 microns into enamel¹⁶ and 50-200 microns into dentin.¹⁷ Fluoride promotes remineralization, and silver is available for antimicrobial action upon release by re-acidification.¹⁸ Silver diamine fluoride arrested lesions are 150 microns thick.¹⁹

Artificial lesions treated with silver diamine fluoride are resistant to biofilm formation and further cavity formation, presumably due to remnant ionic silver.^{20,21} More silver and fluoride is deposited in demineralized than nondemineralized dentin. Correspondingly, treated demineralized dentin is more resistant to caries bacteria than treated sound dentin.²² When bacteria killed by silver ions are added to living bacteria, the silver is re-activated so that effectively the dead bacteria kill the living bacteria in a “zombie effect.”²³ This reservoir effect helps explain why silver deposited on bacteria and dentin proteins within a cavity has sustained antimicrobial effects.

Clinical Evidence

Silver Nitrate Plus Fluoride Varnish

Before the FDA cleared silver diamine fluoride, some U.S. dentists sequentially applied silver nitrate then fluoride varnish to dentinal decay as the only available noninvasive option for caries treatment. Duffin rediscovered silver nitrate from the early literature,²⁴ which had been lost

to modern cariology. Surprisingly, there is no mention of silver nitrate in either of the American Dental Association Council on Scientific Affairs reports on *Nonfluoride Caries-Preventive Agents*²⁵ or *Managing Xerostomia and Salivary Gland Hypofunction*,²⁶ and it is not part of standard dental school curricula. Case series of carious lesions arrested by silver nitrate date to the 1800s. For example, in 1891, 87 of 142 treated lesions were arrested.²⁷ Percy Howe, DDS, then director of the Forsyth Institute in Boston, added ammonia to silver nitrate, making it more stable and effective as an antimicrobial for application to any infected tooth structure from early cavitated lesions to infected root canals.²⁸ Duffin added the application of fluoride varnish following silver nitrate, simulating silver diamine fluoride. While his clinic doubled in patients, cases needing general anesthesia disappeared. His review of randomly selected charts showed only seven of 578 treated lesions progressed within two and a half years to the point that extractions were needed.²⁴ Thus, with the exception of Duffin's and one other report, attention to silver nitrate largely disappeared by the 1950s. The lore is that use and teaching of this intervention were lost with the introduction of effective local anesthetic to enable painless restorations and fluoride for caries prevention. Because no high-quality clinical trials have been performed, we did not include the silver nitrate plus fluoride varnish regimen in our recommendation.

Silver Diamine Fluoride

We found nine published randomized clinical trials evaluating silver diamine fluoride for caries arrest and/or prevention of at least one year in duration. These

studies each involved hundreds of children aged 3 to 9 or adults aged 60 to 89 (**FIGURES 1** and **2**). Most participants had low (< 0.3 ppm) fluoride in the environmental water and reported using fluoride toothpaste (e.g., 73 percent).²⁹ Silver diamine fluoride was applied with cotton isolation. Lesions were detected with mirror and explorer only. All studies were registered and met the Consolidated Standards of Reporting Trials requirements. Clinical cases and studies not meeting these criteria can be found elsewhere.³⁰

When stannous fluoride was used to activate color change, a break in the black color within a lesion at six months was highly sensitive and specific for active caries.

Caries arrest increased dramatically after reapplication from one year posttreatment³¹⁻³³ to one and a half years,^{31,34} and increasingly to two to three years (**FIGURE 1**).^{29,31,35} Single application without repeat lost effect over time in the elderly.³² Twice per year application resulted in more arrest than once per year.^{31,35} Twelve percent silver diamine fluoride was markedly less effective.³²

Darkening of the entire lesion indicated success at follow-up and is suggested to facilitate diagnosis of caries arrest status by nondentists. A longitudinal study reported that color activation of silver diamine fluoride with 10% stannous fluoride resulted in less first molar caries.³⁶ Tea extract was used in one group to activate color change for improved follow-up diagnosis; no differences

in arrest were seen.³² Indeed, when stannous fluoride was used to activate color change, a break in the black color within a lesion at six months was highly sensitive and specific for active caries.³⁷

Silver diamine fluoride greatly outperformed fluoride varnish for caries arrest²⁹ and was equivalent or better than glass ionomer cement (GIC) (**FIGURE 1**).^{31,33} The addition of semiannual intensive oral health education with the application of silver diamine fluoride in the elderly increased the arrest of root caries (**FIGURE 1**).³⁸

Caries Prevention

When silver diamine fluoride was applied only to carious lesions, impressive prevention was seen for other tooth surfaces.^{29,35} Fluoride-releasing GIC can have this effect but it is limited to surfaces adjacent to the treated surface and of short duration. Direct application to healthy surfaces in children also helps prevent caries (**FIGURE 2**).^{29,35,39} Two studies show great difference in the level of prevention in the elderly;^{38,40} the difference is hard to reconcile. As seen for arrest, prevention is less after one year without repeat application.⁴¹

Annual application of silver diamine fluoride prevented many more carious lesions than four-times-per-year fluoride varnish in both children²⁹ and the elderly.⁴⁰ Prevention was roughly equivalent to twice-per-year varnish in one study (**FIGURE 2**).³⁹ The addition of semiannual intensive oral health education in a study of the elderly increased prevention.³⁸ Although many fell out, GIC or resin sealants outperformed silver diamine fluoride in preventing caries in the first molars of children,^{39,41} though the cost was ~20 times more.

Ongoing Trials

Unpublished reports of clinical studies unanimously confirm better caries arrest and/or prevention by silver diamine fluoride over control or other materials. A one-year report of a study of the elderly demonstrated that the addition of a saturated solution of potassium iodide (SSKI) to decrease discoloration did not significantly alter caries arrest or prevention.⁴² This was confirmed in the two-year examinations (personal communication, Edward Lo). A one-year report of a study in children showed that the application once per week for three consecutive weeks, once per year, was more effective than that of single annual application.⁴³ Other studies have recently begun to evaluate the ability of silver diamine fluoride to arrest interproximal carious lesions, to compare the relative efficacy of silver diamine fluoride to the combination of silver nitrate plus fluoride varnish and to compare the effects on populations with or without access to fluoridated water. Final reports from these studies will follow in the coming years.

Recommendations From the Literature on Clinical Efficacy

These studies show that 38% silver diamine fluoride is effective and efficient in arresting and preventing carious lesions. Application only to lesions appears to be similarly effective in preventing cavities in other teeth and surfaces as applying directly. Single application appears insufficient for sustained effects, while annual re-application results in remarkable success, and even greater effects with semi-annual application. From these data, we recommend twice-per-year application, only to carious lesions without excavation, for at least the first two years.

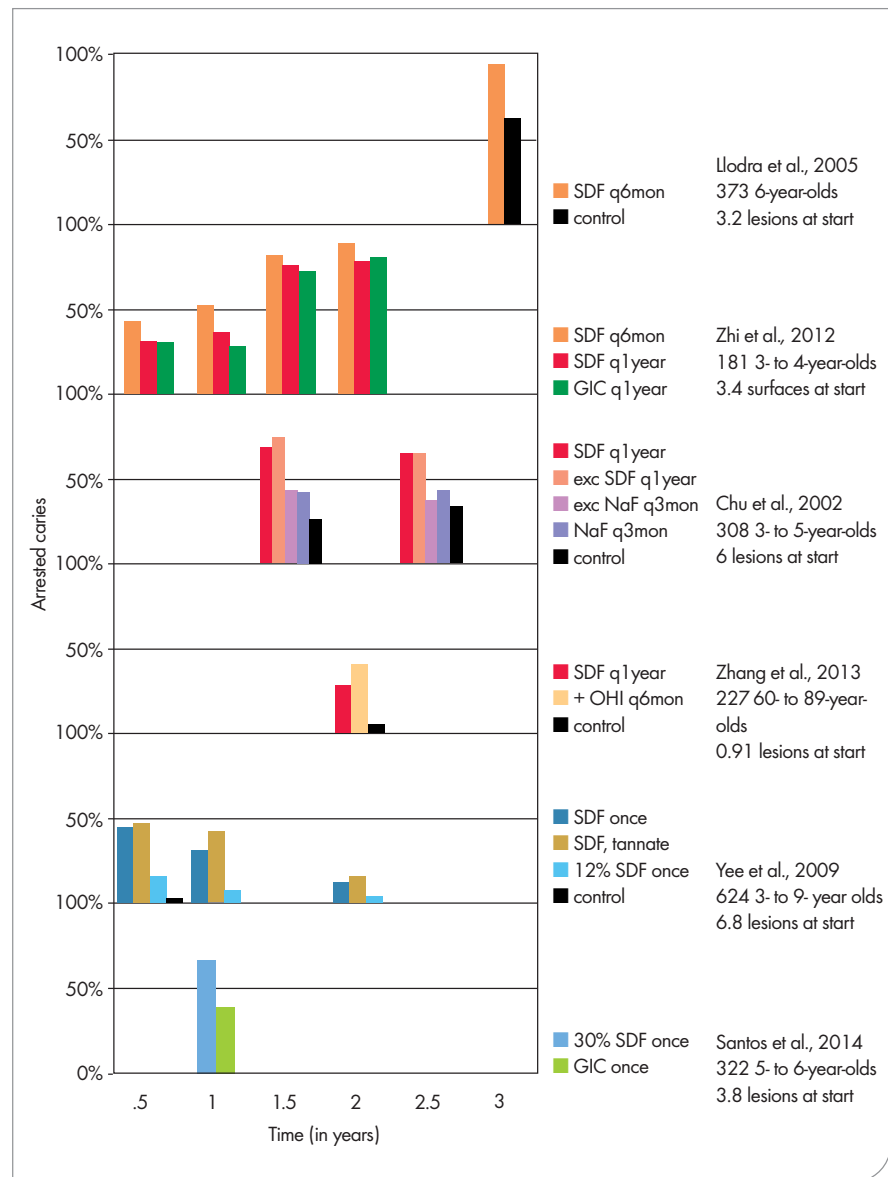


FIGURE 1. Graphic summary of randomized controlled trials demonstrating caries arrest after topical treatment with 38% silver diamine fluoride (SDF). Studies are arranged vertically by frequency of silver diamine fluoride application. Caries arrest is defined as the fraction of initially active carious lesions that became inactive and firm to a dental explorer. SDF (38% unless noted otherwise); q6mon, every six months; q1year, every year; q3mon, every three months; GIC, glass ionomer cement; NaF, 5% sodium fluoride varnish; + OHI q6mon, SDF every year and oral hygiene instructions every six months.

For any patient with active caries, we recommend considering replacement of fluoride varnish as the primary means to prevent new lesions, with application of silver diamine fluoride to the active lesions only. For patients without access

to both sealants and monitoring, silver diamine fluoride is the agent of choice for prevention of caries in permanent molars — particularly as there is no margin to leak and thereby facilitate deep caries and it does not stain sound enamel.

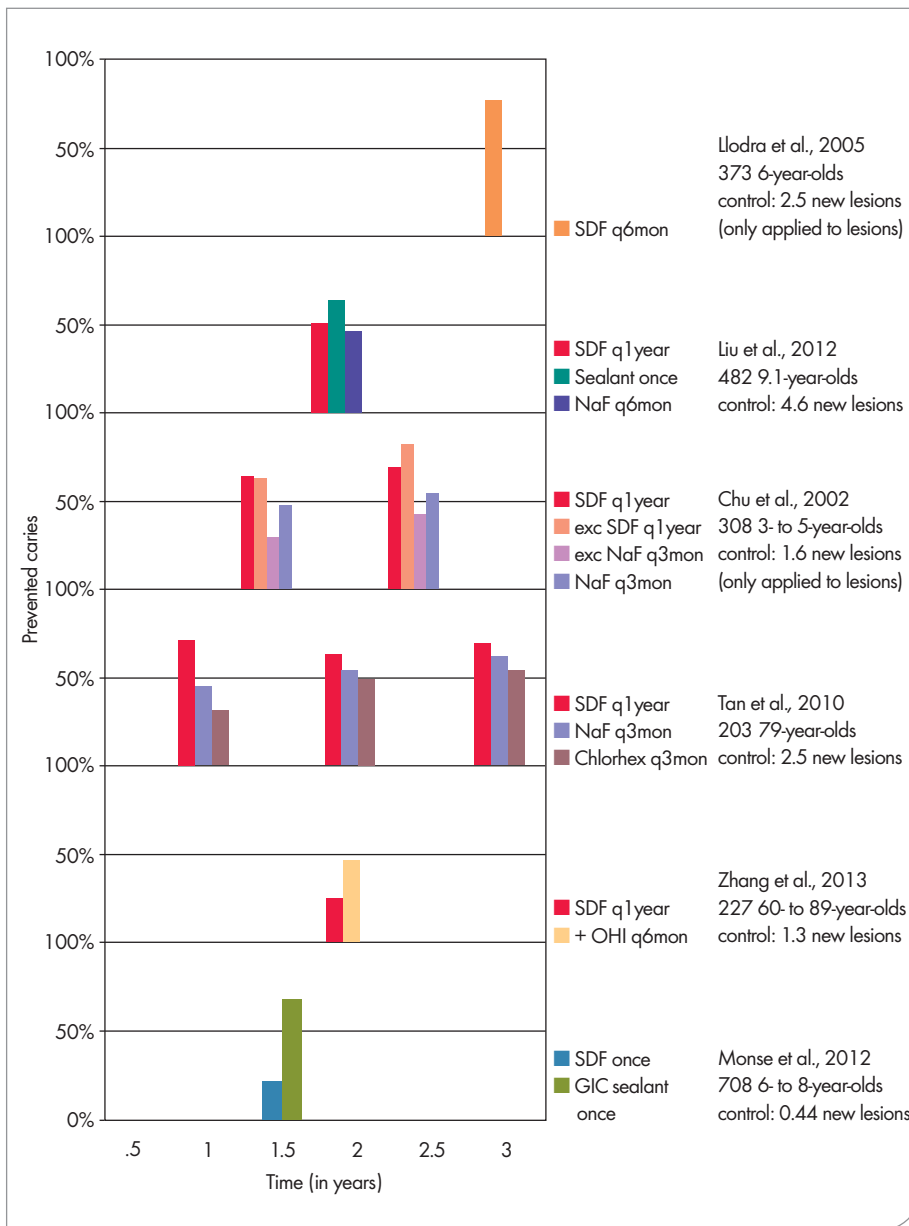


FIGURE 2. Graphic summary of randomized controlled trials demonstrating caries prevention after topical treatment of carious lesions with 38% silver diamine fluoride. Prevented caries is defined as the fraction of new carious lesions in treatment groups as compared to those in the placebo or no treatment control group. Chlorhex, 1% chlorhexidine varnish.

Longer studies are needed to determine whether caries arrest and prevention can be maintained with decreased application after two to three years, and whether more frequent use would enhance efficacy. Traditional or

nontraditional restorative approaches, such as the atraumatic restorative technique (ART)⁴⁴ and Hall crowns,⁴⁵ should be performed as dictated by the response of the patient, disease progression and the nature of individual lesions.

Safety

Maximum Dose and Safety Margin

The margin of safety for dosing is of paramount concern. In gaining clearance from the FDA, female and male rat and mouse studies were conducted to determine the lethal dose (LD50) of silver diamine fluoride by oral and subcutaneous administration. Average LD50 by oral administration was 520 mg/kg and by subcutaneous administration was 380 mg/kg. The subcutaneous route is taken here as a worst-case scenario. One drop (25 μ L) is ample material to treat five teeth and contains 9.5 mg silver diamine fluoride. Assuming the smallest child with caries would be in the range of 10 kg, the dose would be 0.95 mg/kg child. Thus, the relative safety margin of using an entire drop on a 10 kg child is 380 mg/kg LD50/0.95 mg/kg dose = four-hundredfold safety margin. The actual dose is likely to be much smaller, for example 2.37 mg total for three teeth was the largest dose measured in six patients.⁴⁶ The most frequent application monitored in a clinical trial was weekly for three weeks, annually.⁴³ Thus, we set our recommended limit as one drop (25 μ L) per 10 kg per treatment visit, with weekly intervals at most. This dose is commensurate with the Environmental Protection Agency's (EPA) allowable short-term exposure of 1.142 mg silver per liter of drinking water for one to 10 days (Agency for Toxic Substances and Disease Registry, ATSDR, 1990).

Cumulative exposure from lower-level acute or chronic silver intake has no real physiologic disease importance, but the bluing of skin in argyria should obviously be avoided. The EPA set the lifetime exposure conservatively at 1 gm to safely avoid argyria. The highest applied dose for three teeth measured in the pharmacokinetic study, 2.37 mg, would enable > 400 applications.⁴⁶ Silver

nitrate (typically a 25% solution) has been used for more than 100 years in the U.S. without incident, including acceptance by the ADA, and in other countries for arresting dental caries.³

Adverse Effects

Not a single adverse event has been reported to the Japanese authorities since they approved silver diamine fluoride (Saforide, Toyo Seiyaku Kasei Co. Ltd., Osaka, Japan) more than 80 years ago.⁴⁷ The manufacturer estimates that more than 2 million multi-use containers have been sold, including > 41,000 units in each of the last three reporting years.

In the nine randomized clinical trials in which silver diamine fluoride was applied to multiple teeth to arrest or prevent dental caries, the only side effect noted was for three of 1,493 children or elderly patients monitored for one to three years who experienced “a small, mildly painful white lesion in the mucosa, which disappeared at 48 [hours] without treatment.”^{29,31-33,35,38,40,41,48} The occurrence of reversible localized changes to the oral mucosa was predicted in the first reports of longitudinal studies.⁴⁹ No adverse pulpal response was observed.

Gingival responses have been minimal. In a pharmacokinetic study of silver diamine fluoride application to three teeth in each of six 48- to 82-year-olds, no erythema, bleeding, white changes, ulceration or pigmentation was found after 24 hours. Serum fluoride hardly went up from baseline, while serum silver increased about tenfold and stayed high past the four hours of measurement.⁴⁶ In a two-site hypersensitivity trial of 126 patients in Peru, at baseline 9 percent of patients presented redness scores of 2 (1 being normal, 2 being mild to moderate redness and 3 being severe); and after one day, 13 percent in silver diamine fluoride treated patients versus 4 percent

in controls. All redness was gone at seven days. Meanwhile, gingival index improved slightly in silver diamine fluoride treated patients.⁷ Nonetheless, gingival contact should be minimized. In our experience, it has been adequate to coat the nearby gingiva with petroleum jelly, use the smallest available microsponge and dab the side of the dappen dish to remove excess liquid before application.

Concerns for fluoride safety are most relevant to chronic exposure,⁵⁰ whereas this is an acute exposure. Chronically high systemic fluoride results in dental

At least for children, many parents have seen the color changes as a positive indication that the treatment was effective.

fluorosis. The ubiquitous use of fluoride-based gas in general anesthetics has shown that the first acute response is transient renal holding, and is rare.⁵¹ Concerns have been raised about poorly controlled silver diamine fluoride concentrations⁵² and fluorosis appearing in treated rats.⁵³ However, silver and fluoride levels are closely monitored for the U.S. product, and the Health Department of Western Australia conducted a study that found no evidence of fluorosis resulting from long-term proper use of silver diamine fluoride.⁵⁴ Therefore, we have concluded that the development of fluorosis after application of the U.S.-approved product is not a clinically significant risk.

Silver allergy is a contraindication. Relative contraindications include any significant desquamative gingivitis or

mucositis that disrupts the protective barrier formed by stratified squamous epithelium. Increased absorption and pain would be expected with contact. Heightened caution and use of a protective gingival coating may suffice.

A saturated solution of potassium iodide (SSKI) is contraindicated in pregnant women and during the first six months of breastfeeding because of the concern of overloading the developing thyroid with iodide; thyroid specialists suggested a pregnancy test prior to use in women of childbearing age uncertain of their status.

Nonmedical Side Effects

Silver diamine fluoride darkens carious lesions. At least for children, many parents have seen the color changes as a positive indication that the treatment was effective.²⁹ Application of an SSKI immediately following silver diamine fluoride treatment is thought to decrease staining (patent US6461161). This is an off-label use; potassium iodide is approved as an over-the-counter drug to facilitate mucus release to breathe more easily with chronic lung problems and to protect the thyroid from radioactive iodine in radiation emergencies. In our clinical experience, SSKI helps but does not dramatically effect stain; arrested lesions normally darken. Most stain remains at the dentin-enamel or cementum-enamel junction. However, SSKI maintains resistance to biofilm formation or activity in laboratory studies.²⁰ Also, SSKI maintained caries arrest efficacy in the early results of an ongoing clinical trial.⁴² Meanwhile, silver diamine fluoride-treated lesions can also be covered with GIC or composite (see below for discussion on bonding).

Patients note a transient metallic or bitter taste. In our experience, with judicious use, the taste and texture

response is more favorable than the response to fluoride varnish.

Even a small amount of silver diamine fluoride can cause a “temporary tattoo” to the skin (on the patient or provider), like a silver nitrate stain or henna tattoo, and does no harm. Stain on the skin resolves with the natural exfoliation of skin in two to 14 days. Universal precautions prevent most exposures. Long-term mucosal stain, local argyria akin to an amalgam tattoo, has been observed when applying silver nitrate to intraoral wounds; we anticipate similar stains with submucosal exposure to silver diamine fluoride.

Silver diamine fluoride stains clinic surfaces and clothes. The stain does not come out once it sets. Spills should be cleaned up immediately with copious water, ethanol or bleach. High pH solvents such as ammonia may be more successful. Secondary containers and plastic liners for surfaces are adequate preventives.

Effects on Bonding

Using a contemporary bonding system, silver diamine fluoride had no effect on composite bonding to noncarious dentin using either self-etch or full-etch systems.⁵⁵ In one study, simply rinsing after silver diamine fluoride application avoided a 50 percent decrease in bond strength for GIC.⁵⁶ In another study, increased dentin bond strength to GIC was observed.⁵⁷ Silver diamine fluoride decreased dentin bonding strength of resin-based crown cement by approximately one-third.⁵⁸ Thus, rinsing will suffice for direct restorations, while excavation of the silver diamine fluoride-treated superficial dentin is appropriate for cementing crowns.

Indications

Countless patients would benefit from conservative treatment of nonsymptomatic active carious lesions. We discuss the following indications.

First, extreme caries risk is defined as patients with salivary dysfunction, usually secondary to cancer treatment, Sjogren’s syndrome, polypharmacy, aging or methamphetamine abuse. For these patients, frequent prevention visits and traditional restorations fail to stop disease progression. Similar disease recurrence occurs in severe early childhood caries.

Second, some patients cannot tolerate standard treatment for medical or psychological reasons. These include the preoperative child, the frail elderly, those with severe cognitive or physical

Countless patients would benefit from conservative treatment of nonsymptomatic active carious lesions.

disabilities and those with dental phobias. Various forms of immunocompromise mean that these same patients have a much higher risk of systemic infection arising from untreated dental caries. Many only receive restorative care with general anesthesia or sedation and others are not good candidates for general anesthesia due to frailty or another medical complexity. The Centers for Disease Control and Prevention (CDC) estimates 1.4 million people in the U.S. live in nursing homes and 1.2 million live in hospice.⁵⁹ These individuals tend to have medical, behavioral, physical and financial limitations that beg a reasonable option.

Third, some patients have more lesions than can be treated in one visit, such that new lesions arise or existing lesions become symptomatic while

awaiting completion of treatment. This is particularly relevant to the dental school setting where treatment is slow. American dentistry has been desperately lacking an efficient instrument to be used at the diagnostic visit to provide a step toward controlling the disease.

Fourth, some lesions are just difficult to treat. Recurrent caries at a crown margin, root caries in a furcation or the occlusal of a partially erupted wisdom tooth pose a challenge to access, isolation and cleansability necessary for restorative success.

Following the above considerations, we developed four indications for treatment of dental caries with silver diamine fluoride:

1. Extreme caries risk (xerostomia or severe early childhood caries).
2. Treatment challenged by behavioral or medical management.
3. Patients with carious lesions that may not all be treated in one visit.
4. Difficult to treat dental carious lesions.

Finally, these indications are for our school clinics. They do not address access to care. The U.S. Department of Health and Human Services estimates 108 million Americans are without dental insurance, and there are 4,230 shortage areas with 49 million people without access to a dental health professional.⁶⁰ Unlike fillings, failure of silver diamine fluoride treatment does not appear to create an environment that promotes caries, and thus needs to be monitored. Thus, a final important indication is:

5. Patients without access to dental care.

Clinical Application

We considered practical strategies to maximize safety and effectiveness in the design of a clinical protocol for the UCSF dental clinics (**FIGURE 3**).

The key factor is repeat application

Silver Diamine Fluoride (SDF) UCSF Protocol for Arresting Dental Carious Lesions or Treating Tooth Sensitivity

Material: Advantage Silver Arrest (38% SDF, purified water) from Elevate Oral Care.
Shelf life: three years unopened. Do not refrigerate. Avoid freezing or extreme heat.

Indications:

1. Extreme caries risk (xerostomia or severe early childhood caries).
2. Treatment challenged by behavioral or medical management.
3. Patients with carious lesions that may not all be treated in one visit.
4. Difficult to treat dental carious lesions.
5. Patients without access to dental care.

Maximum dose: 25 µL (1 drop) / 10kg per treatment visit.

SDF Contraindication: Silver allergy.

SDF Relative Contraindications: Ulcerative gingivitis, stomatitis.

SSKI Contraindications: Pregnancy, breastfeeding.

Considerations:

- Decayed dentin will darken as the caries lesions arrest. Most will be dark brown or black.
- SDF can stain the skin, which will clear in two to three weeks without treatment.
- SDF can permanently stain operatory surfaces and clothes.
- A control restoration (e.g., GI via ART or other material) may be considered after SDF treatment.
- Saturated solution of potassium iodide (SSKI, Lugol's Solution, various sources) can be used after SDF to decrease color changes.
- Re-application is usually recommended, biannually until the cavity is restored or arrested or the tooth exfoliates.

Procedure:

1. Plastic-lined cover for counter, plastic-lined bib for patient.
2. Standard personal protective equipment (PPE) for provider and patient.
3. One drop of SDF into the deep end of a plastic dappen dish (also obtain one drop of SSKI in a separate dappen dish if selected).
4. Remove bulk saliva with saliva ejector.
5. Isolate tongue and cheek from affected teeth with 2-inch by 2-inch gauze or cotton rolls.
6. If near the gingiva, consider applying petroleum jelly with a cotton applicator for safety.
7. Dry affected tooth surfaces with triple syringe or if not feasible dry with cotton.
8. Bend microsponge, immerse into SDF, remove excess on side of dappen dish.
9. Apply directly onto the affected tooth surface(s) with microsponge.
10. Allow SDF to absorb for up to one minute if reasonable, then remove excess with gauze or cotton roll. (If using SSKI, apply with a different microsponge. Repeat one to three times until no further white precipitates are observed. Wait five to 10 seconds between applications. Remove excess with cotton.)
11. Rinse with water.
12. Place gloves, cotton and microbrushes into plastic waste bags.

FIGURE 3. Clinical protocol for the UCSF dental clinics.

over multiple years. We believe that dryness of the lesion during application is also important. Isolation with gauze and/or cotton rolls is sufficient, while air drying prior to application is thought to improve effectiveness. Allowing one to three minutes for the silver diamine fluoride to soak into and react with a lesion is thought to effect success.

Allowing only a few seconds to soak in due to the cooperation limits of very young patients commonly results in arrest. Application time in clinical studies does not correlate to outcome. However, our committee decided to be cautious in our recommendations for initial use. Longer absorption time also decreases concerns about removing silver

diamine fluoride with a posttreatment rinse. Removing any excess material with the same cotton used to isolate is routine to minimize systemic absorption.

Many clinicians place silver diamine fluoride at the diagnostic visit, then at one and/or three-month follow ups, then at semiannual recall visits (six, 12, 18, 24 months). Whether application needs

to continue after two or three years to maintain caries arrest is not known. Another approach is simply to substitute silver diamine fluoride for any application of fluoride varnish to a patient with untreated carious lesions. Increased frequency with higher disease burden follows the caries management by risk assessment (CAMBRA) principles.⁶¹ It is relevant to take photographs to track lesions over time.

Efforts to improve the penetration of silver diamine fluoride into affected dentin by chemical cavity preparation have not been studied but are being explored clinically. Pretreatment with ethylenediaminetetraacetic acid (EDTA) to remove superficial hydroxyapatite in affected dentin may open the dentinal tubules to further silver diamine fluoride penetration. Pretreatment with hypochlorite (bleach) may help breakdown bacteria and exposed dentin proteins, but this may be redundant to the action of the silver. Hypochlorite to decrease discoloration after silver diamine fluoride treatment is not recommended, as the color comes from silver that cannot be broken down like organic chromophores and might break down dentin proteins stabilized against the effects of bacteria and acid by interactions with silver.

Experience with the combination of silver nitrate plus fluoride varnish (see above) has many practitioners asking about a topical varnish after silver diamine fluoride placement to prevent silver diamine fluoride taste and keep the silver diamine fluoride in the lesion. We see no evidence that varnish would help achieve either goal. Varnish does not seal. Rather, allowing more time for residence and diffusion of silver diamine fluoride to react with and dry into the lesion is more likely to improve effectiveness. Also, in our experience, silver diamine fluoride results in less aversive taste and texture responses than to fluoride varnish.

Decreased darkening of lesions in the esthetic zone improves acceptance. SSKI is an option if the patient is not pregnant, though significant darkening should still be expected. SSKI and silver diamine fluoride are not to be combined prior to application — SSKI can be placed after drying the silver diamine fluoride-treated tooth. Silver diamine fluoride does not prevent restoration of a lesion, thus it does not prevent esthetic options. While silver diamine fluoride has been shown to be more effective than ART or interim restorative treatment

In our experience, silver diamine fluoride results in less aversive taste and texture responses than to fluoride varnish.

(IRT),³³ the two are compatible and can be combined across one or more visits.

The California Business and Professions Code permits dental hygienists and assistants to apply silver diamine fluoride for the control of caries because they are topical fluorides (Section 1910.(b)). Physicians, nurses and their assistants are permitted to apply fluorides in California and in many other states and federal programs. The recent decision of the Oregon Dental Board to allow dental hygienists and assistants to place silver diamine fluoride under existing rules for topical fluoride medicaments sets a precedent. Dental hygienists and assistants in Oregon were barred from providing silver nitrate in a previous decision. All providers need to be trained. Applications should be tracked if applied to the same patient by multiple clinics.

Documentation and Billing

A new code, D1354, for “interim caries arresting medication application” was approved by the Code on Dental Procedures and Nomenclature (CDT) Code Maintenance Commission for 2016. The code definition is “Conservative treatment of an active, nonsymptomatic carious lesion by topical application of a caries arresting or inhibiting medication and without mechanical removal of sound tooth structure.” The CDT Code is the U.S. HIPAA standard code set and is required for billing. The Commission includes representatives from the major insurers, Medicaid, ADA, AGD and specialty organizations. Insurers are in the process of evaluating coverage for this treatment.

Legal Considerations

Silver diamine fluoride is cleared by the FDA for marketing as a Class II medical device to treat tooth sensitivity. We are discussing off-label use as a drug to treat and prevent dental caries. This is a parallel situation to fluoride varnish, which has the same device clearance but is ubiquitously used off label by dentists and physicians as a drug to prevent caries. The same public health dentists who achieved the FDA device clearance are now applying for a dental caries indication. However, this is a more complicated process, normally only carried out by large pharmaceutical companies, and is likely to take longer.

Consent

Because silver diamine fluoride is new in the U.S., it is important to communicate effectively. In the UCSF clinics, we are using a special consent form (FIGURE 4) as a way to inform patients, parents and caregivers, and

UCSF Dental Center Informed Consent for Silver Diamine Fluoride

Facts for consideration:

- Silver diamine fluoride (SDF) is an antibiotic liquid. We use SDF on cavities to help stop tooth decay. We also use it to treat tooth sensitivity. SDF application every six to 12 months is necessary.
- The procedure: 1. Dry the affected area. 2. Place a small amount of SDF on the affected area. 3. Allow SDF to dry for one minute. 4. Rinse.
- **Treatment with SDF does not eliminate the need for dental fillings or crowns to repair function or esthetics. Additional procedures will incur a separate fee.**
- I should not be treated with SDF if: 1. I am allergic to silver. 2. There are painful sores or raw areas on my gums (i.e., ulcerative gingivitis) or anywhere in my mouth (i.e., stomatitis).

Benefits of receiving SDF:

- SDF can help stop tooth decay.
- SDF can help relieve sensitivity.



Risks related to SDF include, but are not limited to:

- **The affected area will stain black permanently.** Healthy tooth structure will not stain. Stained tooth structure can be replaced with a filling or a crown.
- Tooth-colored fillings and crowns may discolor if SDF is applied to them. Color changes on the surface can normally be polished off. The edge between a tooth and filling may keep the color.
- If accidentally applied to the skin or gums, a brown or white stain may appear that causes no harm, cannot be washed off and will disappear in one to three weeks.
- You may notice a metallic taste. This will go away rapidly.
- If tooth decay is not arrested, the decay will progress. In that case the tooth will require further treatment, such as repeat SDF, a filling or crown, root canal treatment or extraction.
- These side effects may not include all of the possible situations reported by the manufacturer. If you notice other effects, please contact your dental provider.
- Every reasonable effort will be made to ensure the success of SDF treatment. There is a risk that the procedure will not stop the decay and no guarantee of success is granted or implied.

Alternatives to SDF, not limited to the following:

- No treatment, which may lead to continued deterioration of tooth structures and cosmetic appearance. Symptoms may increase in severity.
- Depending on the location and extent of the tooth decay, other treatment may include placement of fluoride varnish, a filling or crown, extraction or referral for advanced treatment modalities.

I CERTIFY THAT I HAVE READ AND FULLY UNDERSTAND THIS DOCUMENT AND ALL MY QUESTIONS WERE ANSWERED:

_____ (signature of patient) _____ (date)

_____ (signature of witness) _____ (date)

FIGURE 4. UCSF special consent form.

to standardize procedures because we have so many inexperienced student clinicians. All practices have established procedures for consent and an extra form may not be needed in the community. The normal elements of informed consent

apply. We sought to ensure awareness of the expected change in color of the dentin as the decay arrests, likelihood of reapplication and contraindications in the presence of silver allergy and stomatitis. Note the importance of distinguishing

between allergy to nickel and other trace metals rather than silver allergy, which is rare. We used readability measurements to guide intelligibility and included a progressively discoloring lesion to show stain of a lesion but not healthy enamel.

Conclusion

Silver diamine fluoride is a safe, effective treatment for dental caries across the age spectrum. At UCSF, it is indicated for patients with extreme caries risk, those who cannot tolerate conventional care, patients who must be stabilized so they can be restored over time, patients who are medically compromised or too frail to be treated conventionally and those in disparity populations with little access to care.

Application twice per year outperforms all minimally invasive options including the atraumatic restorative technique — with which it is compatible but 20 times less expensive. It approaches the success of dental fillings after two or more years, and again, prevents future caries — while fillings do not. Silver diamine fluoride is more effective as a primary preventive than any other available material, with the exception of dental sealants, which are > 10 times more expensive and need to be monitored.

Saliva may play a role in caries arrest by silver diamine fluoride. Lower rates of arrest are seen in geriatric patients.³⁸ The elderly tend to have less abundant and less functional saliva, which generally explains their higher caries rate. In pediatric patients, higher rates of arrest are noted for buccal or lingual smooth surfaces and anterior teeth.³¹ These surfaces bathe more directly in saliva than others. It is surprising that silver chloride is the main precipitant in treated dentin, as chloride is not a common component of dentin or silver diamine fluoride, so may come from the saliva.

Traditional approaches often provide only temporary benefit, given the highest rates of recurrent caries are in patients with the worst disease burden. The advent of a treatment for nonsymptomatic caries not requiring general anesthesia or sedation addresses long-standing

concerns about the expense, danger and practical complexity of these services.

Experience suggests that dryness prior to application enhances effectiveness. Good patient management is still profoundly relevant to the very young and otherwise challenged patients, though this one-minute intervention is more tolerable than other options. Silver diamine fluoride can readily replace fluoride varnish for the prevention of caries in patients who have active caries. This as a powerful new tool in the fight against dental caries, particularly suited for those who suffer most from this disease.

Clinical evidence supports continued application one to two times per year until the tooth is restored or exfoliates, and otherwise perhaps indefinitely. Some treated lesions keep growing, particularly those in the inner third of the dentin. It is unclear what will happen if treatment is stopped after two to three years and research is needed. ■

ACKNOWLEDGMENT

The UCSF paradigm shift committee subcommittee on silver caries arrest included Sean Mong, DDS, EdD; Spomenka Djordjevic, DDS, MS; Paul Atkinson, DDS, PhD; George Taylor, DMD, MPH, DrPh; Natalie Heavilin, DDS; Ling Zhan, DDS, PhD; John Featherstone, PhD; Hellen Ellenikiotis, DDS; and Jeremy Horst, DDS, PhD. Thanks to Linda Milgrom for designing the PubMed search. Thanks to Chad Zillich, DDS, for help with the literature review. Thanks to study authors, particularly Edward Lo, BDS, MDS, PhD; Chun Hung Chu, BDS, MDS, PhD; and Geoff Knight, BDS, MSc, MBA, for helpful discussions.

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CLINICAL USE OF SILVER DIAMINE FLUORIDE IN DENTAL TREATMENT

FEBRUARY 2016

Compendium of Continuing Education article provides an overview on the use of Silver Diamine Fluoride in dental treatment.

May L. Mei, BDS, MDS, PhD; Edward Chin-Man Lo, BDS, MDS, PhD; and Chun-Hung Chu, BDS, MDS, PhD.

ABSTRACT

The use of a topical fluoride solution, namely silver diamine fluoride (SDF), in dental treatment has been drawing increasing attention. SDF has been used in some countries in Asia, including Japan and China, as a caries-arresting and anti-hypersensitivity agent. It was recently cleared by the Food and Drug Administration in the United States as a fluoride to manage hypersensitive teeth. Topical application of SDF is a noninvasive procedure that is quick and simple to use. Promising results of laboratory studies and clinical trials have suggested that SDF is more effective than other fluoride agents to halt the caries process. A review concluded that SDF is a safe, effective, efficient, and equitable caries control agent that has a potentially broad application in dentistry and may meet the criteria of both the WHO Millennium Development Goals and the US Institute of Medicine's criteria for 21st century medical care. This article provides an overview of the clinical use of SDF in dental treatment.

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FRESH APPROACH TO CARIES ARREST IN ADULTS

SEPTEMBER/OCTOBER 2015

Decisions in Dentistry article on the use of Silver Diamine Fluoride in adult patients.

Dr. John Featherstone, Dean of the University of California San Francisco School of Dentistry and
Dr Jeremy Horst, DDS, PhD.

KEY TAKEAWAYS

- Cleared by the U.S. Food and Drug Administration for treating dentinal hypersensitivity, in off-label use silver diamine fluoride can be used to prevent and arrest caries.
- The agent acts as an antimicrobial that remains active well after application. It also promotes remineralization and resistance to demineralization in enamel and dentin.
- In order to effectively implement treatment, clinicians should know the indications and contraindications, and gain informed consent for use.
- Dentists and (if allowed by state practice acts) dental auxiliaries who apply this agent must understand precautions for handling silver diamine fluoride.
- Repeat application completely stops many, but not all lesions. Research is needed to determine why some caries are not arrested.

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