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The Use of Silver Diamine Flouride in Caries Arrest: A Review Article

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Abstract **Review Article**

Interest in the use of silver diamine fluoride (SDF) has been growing. SDF has been used as an alternative treatment for caries prevention and arrest. In 2014, SDF was approved by the US Food and Drug Administration as a treatment for dentinal sensitivity. A CDT code adopted by FDA in 2016 is D1354—interim caries arresting medicament application: "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".

Keyword: silver diamine fluoride, Food and Drug, dentinal sensitivity.

BACKGROUND

Dental caries is the most common infectious disease in the world in both children and adults, even though it is largely preventable [1, 2]. Dental caries is a biofilm (plaque)-induced acid demineralization of enamel or dentin, mediated by saliva [3]. The American Academy of Pediatric Dentistry (AAPD) identified the disease of early childhood caries (ECC) as the presence of one or more decayed (noncavitated or cavitated lesions), missing (due to caries), or filled tooth surfaces in any primary tooth in a child 71 months of age or younger [4].

In recent years, although reduction in overall caries indicators has been reported, an increase in ECC has been documented [5, 6]. ECC if remained untreated, can affect oral health–related quality of life, body weight, growth, school attendance, and school performance [7]. Arresting or preventing the caries process from resulting in cavitated lesions requires careful and systematic methods for documenting and monitoring disease at early stages and intervening prior to the development of advanced lesions [8].

Treating dental caries with a dental restoration has been a common job for a dentist. A survey in the United States found that a general dentist spends more than half (56%) of their clinical time providing dental restorations to their patients [9]. This prevailing restorative treatment for dental caries is often neither available nor affordable in many areas of the world. Nonrestorative caries treatment can be an alternative strategy for controlling dental decay, particularly for those who cannot tolerate more involved dental treatments. Many academics and clinicians advocate that the contemporary philosophy of caries management has shifted from a surgical approach to a medical approach [10].

As Dental caries is a condition that can be prevented, arrested, or slowed down, different agents have been used for this purpose [11]. Professional fluoride therapy is effective for the prevention of dental caries. Common fluoride agents include sodium fluoride (NaF), which can be acidulated and buffered with a phosphate to form acidulated phosphate fluoride (APF); sodium monofluophosphate; and stannous fluoride and silver diamine fluoride (SDF). They contain high concentrations of fluoride ranging from 12,300 ppm (APF) to 44,800 ppm (SDF) [12].

Interest in the use of silver diamine fluoride (SDF) has been growing. SDF has been used as an alternative treatment for caries prevention and arrest [13]. In 2014, SDF was approved by the US Food and Drug Administration as a treatment for dentinal sensitivity. A CDT code adopted by FDA in 2016 is D1354—interim caries arresting medicament application: "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." This new code allows for coding the off-label use of silver diamine fluoride for caries arrest [8, 14].

Ingredients and concentrations of SDF solution

SDF is a colorless alkaline solution with a pH value between 9 and 10. It can be tinted blue to facilitate SDF application. SDF products basically contain silver, fluoride and ammonia. Silver fluoride is unstable. Ammonia is added to form diammine silver fluoride which is more stable than silver fluoride [15].

Like most silver compounds, SDF is unstable under light irradiation and decomposes to silver. Hence, SDF must be stored in a light-proof bottle. It should be used as soon as possible once it is dispensed from the bottle in clinical practice. Although manufacturers produce SDF according to their own formulation, researchers mostly assume that a 38% SDF solution contains 253,870 ppm silver and 44,800 ppm fluoride ions. In other words, a 38% SDF solution is composed of 25% silver ions and 5% fluoride ions dissolved in an 8% ammonia solution. However, studies have found significant variations in silver and fluoride ion concentration in different SDF products [16, 17].

Safety of SDF

Apart from staining of the carious lesion, literature reported no other significant complications associated with SDF therapy. Many studies have shown that SDF use is safe. Castillo *et al.,* assessed the effectiveness and safety of topical diammine silver fluoride clinically on 126 adults. 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. They concluded that diammine silver fluoride is a clinically effective and safe tooth desensitizer [18]. Llodo *et al.,* mentioned in their controlled trial on Four hundred and twenty-five six-year-old children that SDF can cause transient gingival irritation requiring no treatment [19]. A systematic review by Zaeneldin *et al.,* concluded that SDF causes mild, reversible pulpal inflammation and is generally biocompatible [20]. Several clinical studies found that the fluoride concentrations in serum after SDF application is safe and posed little toxicity risk [21, 22]. A study showed that the risk of fluoride toxicity in a young child is low even SDF is applied to all the 20 primary teeth [23].

Figure: SDF causing staining of carious lesions

Mechanism of Action of SDF

Silver is antimicrobial and inhibits the growth of cariogenic biofilm. Fluoride promotes remineralisation and inhibits the demineralisation of teeth under an acid challenge. SDF also prevents the degradation of dentine collagen through the inhibition of proteolytic peptidases in dentine and saliva [23].

SDF Inhibits Bacterial Growth and Biofilm Formation

SDF inhibits the growth of cariogenic bacteria [24]. It has been shown that SDF is more effective compared to silver ammonium nitrate and sodium fluoride in inhibiting bacterial growth. SDF possesses strong antimicrobial action against S. mutans, A. naeslundii and L. acidophilus [25]. S. mutans is an important pathogen associated with the initiation and progression of carious lesions. SDF can inhibit the adherence and growth of S. mutans on the surface of carious lesions [26]. L. acidophilus is often found abundantly in dentine carious lesions. Aeslundii can invade rapidly through dentinal tubules and is attributed to the development of root caries. Studies have shown that SDF inhibited the growth of multispecies cariogenic biofilms on the tooth surface [27]. An in vitro study by Chu *et al.,* found silver particles, together with dead bacteria on the dentine surface after SDF application [26].

SDF Promotes Remineralisation and Counteracts Demineralization

Arrested carious lesions treated with SDF generally have a black and hard surface. This clinical observation is corroborated by an ex vivo study that reported an increase in microhardness of the dentine surface layer after SDF application [28]. Laboratory studies found the surface layer of dentine carious lesions was rich in calcium and phosphorus after SDF treatment [28, 29]. Saliva is supersaturated with calcium and phosphate. In the presence of saliva, SDF fosters remineralisation of teeth in the oral cavity when the pH value is higher than 5.5 [30]. SDF also inhibits calcium dissolution from hydroxyapatite and prevents the

demineralisation of enamel and dentine [31]. Rosas *et al.*, found that enamel carious lesions, after SDF application, had significantly less mineral loss compared to those without SDF treatment [32]. The plaque on the tooth surfaces absorbs fluoride after SDF application. When bacteria produce acids, the fluoride in the plaque fluid, along with the acids produced, penetrates subsurface of enamel. The fluoride is adsorbed to the crystal surface and protects the crystal from dissolution [33]. In addition, calcium fluoride, silver phosphate and silver protein can be formed and precipitate on the dentine surface after SDF application [34]. These precipitates developed dense granular structures of spherical grains on the intertubular area of dentine and occluded orifices of dentinal tubules [35].

SDF Inactivates Proteolytic Activity and Prevents Collagen Degradation

In an acidic environment, such as an active carious lesion, or when cariogenic bacteria produce lactic acid, collagenases are activated which destroy dentine collagen. SDF has an inhibitory effect on collagenases, such as matrix metalloproteinases (MMPs) and cysteine cathepsins. Activation of MMPs and cysteine cathepsins contributes to collagen breakdown in dentine carious lesions. Inactivation of collagenases and prevention of collagen degradation contributes to the arrest of carious lesions using SDF [36].

SDF Occludes Dentinal Tubules and Promotes Tertiary Dentine Formation

The fluorohydroxyapatite produced after SDF application promotes remineralisation, which can block or decrease tubule diameter, resulting in relief of dentine hypersensitivity. Silver also precipitates as silver salts on the dentine surface and within the dentinal tubules after SDF application [37, 38].

Effectiveness of Silver Diamine Fluoride in Caries Prevention and Arrest

A solution of 38% SDF has been reported as an effective treatment for caries arrest [39, 40]. SDF is a promising strategy to manage dental caries in very young children, high caries risk children, those who have special needs or those living in poor conditions or developing countries [39, 41]. SDF is an alternative treatment for controlling dental caries when other approaches are not available. It is a minimally invasive, low-cost, and simple method that can reduce fear and anxiety in young children. In addition, it could be applied in community settings [40].

Based on several in vitro studies findings, it is hypothesized that fluoride and silver components of SDF protected the dentin surface against surface loss through formation of fuoroapatite, CaF_2 and insoluble silver products like silver phosphate, silver chloride or metallic silver [42, 43]. On the other hand, formation of the insoluble silver compounds on dentin surface may increase the surface roughness of dentin [44].

A systematic review by Gao *et al.*, found that there are certain inconsistencies regarding the study design for the clinical trials on SDF because the studies were conducted using SDF at different concentrations, application frequencies, and follow-up periods. In the mentioned review, clinical trials using the most common concentration of SDF (i.e., 38%) were chosen for meta-analysis. All studies using SDF with concentration (38%) reported a statistically significant caries-arresting effect on children. Although the fluoride concentration was high (44,800 ppm in 38% SDF), no significant complication was reported in these studies. Studies of SDF used not only different concentrations but also different application frequencies. The application frequency could be one-off or repeated applications every 3, 6, or 12 mo [39]. A study reported that increasing the application frequency increased the caries arrest rate of SDF application [45]. However, more clinical trials are necessary to formulate the optimal treatment strategy to arrest caries among children.

Studies also reported that using SDF was better than glass ionomer cement or fluoride varnish in arresting caries in primary teeth [45, 46]. Caries removal was not necessary before SDF application [47]. SDF is low cost and does not require sophisticated instruments or techniques for application. It is a cost-effective agent to manage dental caries. The risk of cross infection is low. The application is painless and simple and can be used for young children or patients with special needs [39].

Protocol of SDF Therapy for Arresting Caries

Although SDF use is simple and straightforward, published SDF application protocols are not the same. Some protocols suggested the use of protective barriers, such as petroleum jelly, to prevent soft tissue irritation and/or staining. However, Young *et al.*, opined that the protection of intraoral soft tissues is not necessary. On the contrary, the protective barrier could inadvertently get on the lesion or surface and inhibit SDF uptake [48]. Fung *et al.*, found that gingival irritation was uncommon, and no staining of oral mucosa was reported after SDF application [49].

The ADA mentioned that SDF therapy is a noninvasive way in which to arrest caries without drill and fill. A clinical trial showed that caries removal did not affect the caries-arresting effect of SDF [47]. Caries removal is not necessary prior to SDF application. This simplifies and shortens the treatment time for SDF therapy. Moreover, it allows for SDF use in the outreach setting with inexpensive, simple, and disposable dental tools [50].

The ADA and the AAPD recommended an application time of 60 seconds for SDF application [51, 52]. The AAPD suggested drying an SDF-treated lesion with a gentle blow of compressed air using a 3-in-1 syringe. However, an author team suggested no blowing

with compressed air or rinsing while the SDF is being absorbed [48]. Another author team did not recommend removing excess SDF with air or water spray because it can splash the SDF and stain the lips and face. In addition, compressed air may cause momentary and transient pain in the applied tooth [53].

Table: Recommendations by national dental organizations for silver diamine fluoride (SDF) use to arrest caries

No.	Organisation, year; topic [web link]	SDF application protocol
P1	American Dental Association, 2018; Silver Diamine Fluoride Application: Evidence-Based Recommendations [https://www.youtube.com/watch?v=a0HH7GifdM4]	Isolate the carious tooth with cotton roll or gauze Clean the carious lesion with cotton pellet or micro brush Dry the carious lesion with gauze or cotton Apply SDF to the carious lesion using micro brush Leave the SDF-treated lesion for 60 seconds Remove excess SDF with gauze if necessary (SDF therapy is a noninvasive way in which to treat carious lesion without drill)
P2	American Academy of Pediatric Dentistry, 2018; Chairside Guide: Silver Diamine Fluoride in the Management of Dental Caries Lesions [https://www.aapd.org/globalassets/media/policies_guidelines/r_chairsideguide.pdf]	Protect gingiva and mucosa with a protective coating Protect skin with a temporary henna-appearing tattoo Clean the carious lesion Isolate the tooth with cotton roll or other methods (Removing carious dentine prior to SDF application is not necessary) Apply SDF to the carious lesion using micro brush Leave the SDF-treated lesion for 60 seconds Dry the SDF-treated lesion with 3-in-1 syringe Leave the SDF-treated lesion up to 180 seconds Remove excess SDF with gauze, cotton roll, or cotton pellet Cover the entire dentition with fluoride varnish
P3	British Society of Paediatric Dentistry, 2020; How to Apply Silver Diamine Fluoride, [https://www.youtube.com/watch?v=tELmH9jRvv8&t=17s]	Protect any exposed gingival tissues and lips with petroleum jelly Isolate the carious tooth with cotton roll Clean the carious lesion with cotton roll Dry the carious lesion with cotton roll or 3-in-1 syringe Apply SDF to the carious lesion using micro brush Leave the SDF-treated lesion for 60 seconds (best for 180 seconds) Remove excess SDF with gauze or micro brush if necessary Cover the SDF-treated lesion with toothpaste or fluoride varnish

Some papers suggested applying potassium iodide solution to remove the dark staining that occurs following SDF application [54, 55]. A clinical trial found that the application of potassium iodide was associated with better aesthetic outcomes but poorer caries control compared with SDF application only [54]. A review concluded that insufficient evidence exists to support a demonstrable benefit of potassium iodide application to reduce tooth staining [56]. Furthermore, the application of potassium iodine takes a further 60 seconds or until the precipitation of insoluble white silver iodide. It prolongs the treatment time of SDF therapy and may reduce patient cooperation [57].

Some researchers speculated that applying fluoride varnish after SDF application prevents saliva from diluting the applied SDF. However, a laboratory study found that the adjunctive application of SDF solution and sodium fluoride varnish had a similar remineralising effect to that of SDF solution alone on enamel caries [58]. Another laboratory study found that a sodium fluoride varnish could reduce the antibacterial effects of SDF and might affect the arrest of dentine caries [59]. Direct application of SDF on a vital pulp is not recommended because it causes pulp necrosis [60]. Rinsing or washing to be necessary when SDF contacts gingivae or oral mucosa. SDF may cause gingival irritation, but the irritation is transient and will resolve without treatment [50]. More clinical studies are needed to establish best practices.

CONCLUSION

SDF at concentrations of 38%, is more effective than other preventive management strategies for arresting dentinal caries in the primary dentition and show potential as a caries preventive treatment in primary teeth and permanent first molars. Although SDF therapy is simple and straightforward, the recommended application protocols were principally based on experts' opinions and could be different. Standardized SDF protocols must be developed to allow meaningful study comparisons and establish treatment guidelines.

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