

Review Article

Silver Diamine Fluoride and its Applications in Pediatric Dentistry: A Review Article

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Abstract

Dental caries continues to be the most prevalent chronic disease across the world despite advances in prevention and treatment options. Caries management has shifted from the traditional approach to minimum intervention dentistry, that frequently use fluoridated and antimicrobial agents. Among these agents, silver diamine fluoride (SDF) has gained significant recognition due to its antibacterial properties and ability to remineralize carious lesions. It has been used as anti-caries agent and dentin desensitizer for hundreds of years around the world. SDF is an effective, inexpensive, and non-invasive option for children with high caries risk, special health care needs and those with behavioral or medical management problems. Its application is simple and requires no expensive equipment. No adverse systemic effects due to SDF application have been reported. However black staining of tooth structure following its application is a matter of concern. The current review gives insight of the action and clinical application of SDF based on published literature.

Keywords: Dental caries, Minimum intervention dentistry, Silver diamine fluoride, Caries prevention, Caries arrest.

Introduction

Dental caries continues to be the most prevalent chronic disease across the world despite advances in prevention and treatment options.(Tarfa and Al Jubouri, 2023) Thus it represents a major public health issue. Traditionally, carious lesion had been treated by removal of bacterially contaminated infected dentin as well as demineralized affected dentin and replacing it with a restoration.(Schwendicke *et al.*, 2021)

Owing to the increased understanding of the caries process and the development of adhesive

and biomimetic restorative materials, minimum intervention dentistry (MID) became the contemporary caries management approach. It adopts a philosophy that incorporates prevention, early interception and treatment of carious lesions with minimum intervention.(Jingarwar, Bajwa and Pathak, 2014) It implies removal of the outer highly infected, denatured caries-infected dentin (CID) while preserving the inner demineralized, bacteria-free remineralizable caries-affected dentin (CAD) as the clinical bonding substrate.(Thompson *et al.*, 2008; Kidd, 2010; Schwendicke, Dörfer and Paris, 2013;

Schwendicke *et al.*, 2021) The use of adhesive restorative materials promotes a more conservative cavity design, which relies on the effectiveness of adhesion with enamel and dentin.(Migliau, 2017) This enables the dentist to attain maximum intervention, with minimum invasive treatment.(Walsh and Brostek, 2013)

Minimal invasive dentistry approaches include atraumatic restorative technique (ART), air abrasion, Sono abrasion, laser, chemo-mechanical caries removal (CMCR), and application of topical fluorides.(Showkat *et al.*, 2020)

Review of Current Literature

Topical fluoride has been used as an anti-caries agent since the 1960's. It has been delivered via dentifrices, gels, foams, and varnishes. These products have shown to be effective in the prevention and control of caries.(Mohan, Chidsey and Rosivack, 2020) Also silver compounds such as silver nitrate, silver fluoride and silver diamine fluoride (SDF), have been used as anti-caries agents and dentin desensitizers for hundreds of years around the world.(Peng, Botelho and Matinlinna, 2012)

The World Health Organization (WHO) recognised SDF as an important medicine that is safe and effective to meet the most important health needs for adults and children.(Chai *et al.*, 2022) It also meets the U.S. Institute of Medicines 6 quality aims of being: safe (i.e. without adverse events); effective (i.e. reduces caries initiation and progression by almost 80% on treated teeth); efficient (i.e. can be applied by health professional in different health and community settings with minimal preparation); timely (i.e. takes less than 30 seconds for application); patient centred (i.e. meets immediate needs of the patient in one minimally invasive and painless treatment session);and equitable (i.e. equally effective and affordable for all socioeconomic groups, races, ethnicities, and cultures).(Crystal and Niederman, 2016)

In 2014, the US Food and Drug Administration (FDA) cleared SDF as a dentin desensitizer.(US Food and Drug Administration, 2014) Silver diamine fluoride had been used off-label for caries arrest; however, the American Dental Association

(ADA) has approved SDF as an interim caries-arresting medicament in 2018.(American Dental Association, 2018) Topical application of SDF became one of the effective minimally invasive treatment modalities for managing dental caries.(Crystal and Niederman, 2019) It has the potential to arrest dentin caries in primary and permanent teeth.(Zaffarano *et al.*, 2022; Mungur *et al.*, 2023)

Composition and concentrations

Silver diamine fluoride is an alkaline colourless solution that contains silver, ammonia and fluoride.(Hendre *et al.*, 2017) The ammonia ions combine with the silver ions to produce a stable complex ion called the diamine-silver ion. SDF is claimed to be more stable than silver fluoride and can be kept in a constant concentration for a longer time.(Chu and Lo, 2008)

The concentration of commercial SDF solutions varies from 3.8 to 38 wt.%. The 38 wt.% SDF solution achieves the greatest effect. Researchers assume that 38% SDF is composed of 25% silver ions and 5% fluoride ions dissolved in 8% ammonia solution. Thirty eight percent SDF contains 44,800 ppm fluoride which is the highest fluoride concentration among the fluoride agents available in dental market.(Zheng *et al.*, 2022)

However, studies on different SDF products have found significant variation in silver and fluoride ion concentration. For example, Advantage Arrest™ has a pH of 10 and contains 24.4–28.8% silver and 5.0–5.9% fluoride. SDI Riva Star™ has a pH of 13 and contains 35–40% silver fluoride and 15–20% ammonia. The manufacturer also provides a solution of potassium iodide (KI) to be applied immediately onto the surface to scavenge precipitated silver.(Almuqrin *et al.*, 2023)

Mechanism of action

Silver and fluoride ions infiltrate enamel (up to 50 μm) and dentin (up to 200 μm). (McConnachie, Friedman and Abrams, 2018) It has been proven that SDF [$\text{Ag}(\text{NH}_3)_2\text{F}$] reacts with tooth hydroxyapatite (HA) [$\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$] forming insoluble precipitate of calcium fluoride (CaF_2) and silver phosphate (Ag_3PO_4) over the tooth surface. This decreases calcium and phosphorous loss from carious lesion. (Yu, Kimura and Fujita, 2001) Silver phosphate and calcium fluoride have synergistic effect on prevention of new carious lesion development, harden and arrest existing ones. (Rosenblatt, Stamford and Niederman, 2009; Mei et al., 2017) The chemical reaction between SDF and HA can be summarized as follow: (Peng, Botelho and Matinlinna, 2012)

$$\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2 + \text{Ag}(\text{NH}_3)_2\text{F} \rightarrow \text{CaF}_2 + \text{Ag}_3\text{PO}_4 + \text{NH}_4\text{OH} \text{ (Alkaline environment)}$$

Reaction products:

a. Calcium fluoride (CaF_2):

(1) SDF provides an alkaline environment that renders CaF_2 less soluble and, therefore, serves as a fluoride ion reservoir for the next acidic challenge. (Mei et al., 2013)

(2) CaF_2 Acts as a pH-regulated slow-release fluoride ion reservoir during cariogenic challenges. The released fluoride ions (F^-) replace hydroxyl groups in HA to form fluoroapatite [$\text{Ca}_{10}(\text{PO}_4)_6\text{F}_2$] which is more resistant to acid attack and demineralization than HA. (Rošin-Grget and Linčir, 2001) The chemical reaction can be summarized as follow: (Peng, Botelho and Matinlinna, 2012)

$$\text{CaF}_2 \rightarrow \text{Ca}^{++} + 2\text{F}^-$$

$$\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2 + 2\text{F}^- \rightarrow \text{Ca}_{10}(\text{PO}_4)_6\text{F}_2 + 2\text{OH}^-$$

In addition, fluoride ions restore lattice imperfection and improve the crystallinity of HA. (Shah et al., 2014) They also enhance the remineralization process by accelerating the precipitation of HA calcium & phosphate minerals, which is evident by high calcium and phosphorus level in the outermost layer of the arrested dentin carious lesion. (Chu and Lo, 2008; Mei et al., 2014) Kinney et al., 2003 observed a dense granular

spherical grains under scanning electron microscope on the surface of demineralized dentin treated with SDF, which indicates extrafibrillar mineral formation. Chu et al., 2012 found that the micro-hardness of remineralized dentin increased after SDF treatment. It is plausible that the remineralization of the demineralized dentin occurred in both extrafibrillar and intrafibrillar manner. (Mei et al., 2013)

b. Silver phosphate (Ag_3PO_4):

(1) Deposited Ag_3PO_4 is responsible for the increased hardness and black staining of the SDF arrested lesion. (Hiraishi et al., 2022)

(2) Ag_3PO_4 acts as a reservoir of phosphate ions that facilitates the transformation of CaF_2 to fluoroapatite. (Peng, Botelho and Matinlinna, 2012)

(3) Deposited Ag_3PO_4 on the tooth surface is insoluble in acidic attacks and causes partial or complete obliteration of dentinal tubules with silver particles. This obliteration of the dentinal tubules is good for reducing dentinal hypersensitivity and hinders invading microorganisms to go further through them which helps to increase resistance to secondary caries. (Shah et al., 2014) In addition, silver has antibacterial properties. Its antibacterial properties arise from inhibition of bacterial enzyme activities which disrupts bacterial metabolic processes causing death of the cariogenic bacteria. (Shounia, Atwan and Alabduljabbar, 2017) It also reduces the colonization of cariogenic bacteria by inhibiting biofilm formation on the enamel surface and dextrin induced agglutination of cariogenic streptococcus mutans. (Shah et al., 2014; Cm et al., 2016; Shounia, Atwan and Alabduljabbar, 2017)

(4) Ag_3PO_4 reacts with alkali chloride solutions to form silver chloride (AgCl). The solubility product of AgCl (6.5×10^{-4} g/100 ml) is lower than that of Ag_3PO_4 (8.9×10^{-5} g/100 ml). (Mei, Ito, et al., 2013) AgCl is also known for its antibacterial properties and is used in dentistry as an antimicrobial agent. (Peng, Botelho and Matinlinna, 2012; Mei, Ito, et al., 2013)

(5) A study by **Mei et al., 2012** showed that silver ions have a potent inhibitory effect on the activity of Matrix metalloproteinases (MMPs) as well as bacterial collagenase, which preserves the collagen of dentin from degradation. The inhibitory effect of 38% SDF on MMP-2, MMP-8 and MMP-9 was significantly higher than that of the equivalent F in sodium fluoride solution.

Clinical applications

The use of SDF has been drawing increasing attention over years in the following cases:

1. Management of patients with high caries risk like those suffering from xerostomia.(Jain, 2020)

2. Management of patients with behavioral or medical management problems. For young patients or those with special health care needs, SDF application can be a good alternative to restorative treatment under sedation or general anesthesia.(Shounia, Atwan and Alabduljabbar, 2017)

3. Management of patients with multiple carious lesions that cannot be treated in one visit. Silver diamine fluoride arrests caries during the control phase until definitive treatment is performed.(Jain, 2020)

4. Root caries arrest.(Jain, 2020)

5. Caries arrest in community-based caries control programs especially in developing and low-income countries.(Jain, 2020)

6. Secondary caries prevention. **Mei et al., 2016** evaluated SDF's effectiveness to prevent secondary caries under glass ionomer cement (GIC) and composite resin restorations and observed reduction in secondary caries under the restorations following pretreatment with SDF.

7. Management of dentinal hypersensitivity.(Castillo *et al.*, 2011)

8. Root canals disinfection. Silver diamine fluoride can be effectively used as an endodontic irrigant.(Shabbir *et al.*, 2022)

Contraindications:

Silver diamine fluoride is contraindicated to be used in the following cases:

1. Patients with allergy to silver.(Horst, Ellenikiotis and Milgrom, 2016; Contractor, M.S. and M.D., 2021)

2. Pregnant females.(Horst, Ellenikiotis and Milgrom, 2016)

3. Breastfeeding females.(Horst, Ellenikiotis and Milgrom, 2016)

4. Patients with ulcerations in the oral cavity.(Horst, Ellenikiotis and Milgrom, 2016; Contractor, M.S. and M.D., 2021)

5. Patients with desquamative gingivitis or mucositis.(Greenwall-Cohen, Greenwall and Barry, 2020)

6. Teeth showing signs or symptoms of pulpal or periapical pathosis.(Contractor, M.S. and M.D., 2021)

7. Concerns regarding discolouration and failure to get consent to use SDF.(Contractor, M.S. and M.D., 2021)

Advantages (Shah *et al.*, 2014; Cm *et al.*, 2016; Shounia, Atwan and Alabduljabbar, 2017)

1. Silver diamine fluoride is effective in arresting and preventing dental caries.

2. It is inexpensive and therefore affordable in most communities.

3. Its application is simple and requires no expensive equipment or support infrastructure. So even trained dental auxiliaries or non-dental professionals can easily apply SDF to children in remote areas who cannot usually access preventive services.

4. It is non-invasive, and thus it is painless and does not require local anaesthesia prior to its application. In addition, its application limits the risk of spreading infection.

Disadvantages

1. Patients may experience a transient metallic or bitter taste following SDF application.(Jain, 2020)

2. Silver diamine fluoride causes significant black staining to carious lesions, oral mucosa, and skin. Superficial black staining of the oral mucosa and skin tends to resolve within days as epithelial cells slough off. On the contrary, SDF arrested carious enamel or dentin remains permanently black due to the formation of silver phosphate.(Greenwall-Cohen, Greenwall and

Barry, 2020) Initially, carious lesion remains with the same colour, but after 2-3 weeks it becomes dark brown to black.(Vennela *et al.*, 2021) This stain is caused by oxidation of ionic silver to metallic silver and silver oxide, with subsequent precipitation of silver–protein and silver phosphate complexes on tooth structure.(Almuqrin *et al.*, 2023) SDF can also stain non-carious dentin if an adhesive was applied over the SDF and light cured. Studies have also pointed out marginal staining of restorations with previous SDF application.(Nguyen *et al.*, 2017)

It is mandatory to inform the parents/patients pre-operatively about the potential for discolouration and to have their written consent. Brown-black discolouration can be polished off or removed through more invasive procedures. Occasionally, polishing cannot remove the discolouration, particularly at restoration margins. Dental bleaching cannot remove the discolouration because of its metallic nature.(Greenwall-Cohen, Greenwall and Barry, 2020) Application of potassium iodide (KI) after SDF may have the potential to reduce SDF staining.(Roberts *et al.*, 2020) Potassium iodide reacts with SDF forming a white creamy precipitate of silver iodide (AgI), which removes the excess free silver ions. The KI is agitated until the solution turns clear and is rinsed and dried.(Greenwall-Cohen, Greenwall and Barry, 2020; Vennela *et al.*, 2021) The chemical reaction between SDF and KI can be summarized as follow:(Nguyen *et al.*, 2017)

$$\text{Ag}(\text{NH}_3)_2\text{F}(\text{aq.}) + \text{KI}(\text{aq.}) \rightarrow \text{AgI}(\text{s}) + 2\text{NH}_3(\text{g}) + \text{F}^-(\text{aq.})$$

Safety

Silver diamine fluoride has been successfully used since the 1960s for caries arrest. Apart from staining of the tooth structure, no other significant complications were reported with SDF therapy.

However, SDF can cause mild transient gingival irritation that requires no treatment.(Castillo *et al.*, 2011) A systematic review also concluded that SDF can cause mild, reversible pulpal inflammation and is generally biocompatible.(Zaeneldin, Yu and Chu, 2022) Clinical studies found that fluoride concentration

in serum following SDF application posed little toxicity risk.(Vasquez *et al.*, 2012; Ellenikiotis *et al.*, 2022) Risk of fluoride toxicity in a young child is low even if SDF is applied to all the 20 primary teeth.(Yan *et al.*, 2022)

Clinical practice guidelines for silver diamine fluoride application:

Informed consent highlighting expected staining of treated lesions and need for reapplication for disease control, is required.(Crystal *et al.*, 2017)

Gross debris should be removed from carious lesion to allow better contact between SDF and denatured dentin.(American Academy of Pediatric Dentistry, 2017; Crystal *et al.*, 2017) However, excavation of carious dentin before SDF application is not necessary.(Chu, Lo and Lin, 2002) Excavation of carious dentin can be considered for aesthetic purposes because it reduces the proportion of arrested carious lesion that becomes black.(American Academy of Pediatric Dentistry, 2017)

Protective coating to the lips and skin should be applied to prevent black staining of SDF to soft tissues.(American Academy of Pediatric Dentistry, 2017) Teeth to be treated should be isolated with cotton rolls or any other isolation methods along with saliva ejector to remove excess saliva from the site of application. Cocoa butter, petroleum jelly or other products, used to protect surrounding gingival tissues, should be carefully applied away from the surfaces of the carious lesions.(American Academy of Pediatric Dentistry, 2017; Crystal *et al.*, 2017)

The University of California, San Francisco (UCSF) protocol recommends a limit of 1 drop (25 µL) per 10 kg for the entire appointment, with weekly intervals at most. One drop is enough to treat five teeth. It contains 9.5 mg SDF.(Horst, Ellenikiotis and Milgrom, 2016)

Carious lesion should be dried with gentle flow of compressed air.(Horst, Ellenikiotis and Milgrom, 2016; American Academy of Pediatric Dentistry, 2017; Crystal *et al.*, 2017) Careful application of SDF with a microbrush should be

adequate to prevent intraoral and extraoral soft tissue exposure. SDF should be applied cautiously on primary teeth adjacent to permanent anterior teeth that may have white spot lesions to avoid inadvertent staining. (American Academy of Pediatric Dentistry, 2017)

Clinical studies report application time ranging from 10 seconds to 3 minutes, but AAPD recommends application time of at least 1 minute if possible. When using shorter application time in very young and difficult to manage patients, consider reapplication along with careful monitoring at post-operative and recall visits to evaluate caries arrest. (Crystal et al., 2017)

Gentle flow of compressed air should be applied until medicament is dry. (Crystal et al., 2017) Excess SDF should be removed with cotton pellet, cotton roll, or gauze to minimize systemic absorption. (Horst, Ellenikiotis and Milgrom, 2016) Isolation should be kept as much as possible for 3 minutes. No special post-operative instructions are needed. (Crystal et al., 2017)

Five percent sodium fluoride varnish can be used along with SDF to help prevent caries on the teeth and sites not treated with SDF. (American Academy of Pediatric Dentistry, 2017)

Follow-up at 2-4 weeks after initial treatment and at recall appointments for evaluation of caries arrest is advisable. Arrested caries appears dark and hard. Reapplication of SDF may be considered if the treated lesions do not appear arrested. (American Academy of Pediatric Dentistry, 2017; Crystal et al., 2017)

Cariou lesions can be restored following treatment with SDF. If they are not restored after SDF treatment, bi-annual reapplication of SDF should be considered to increase caries arrest rate. (American Academy of Pediatric Dentistry, 2017)

Silver Modified Atraumatic Restorative Technique (SMART):

Clinicians have begun to use a technique called Silver Modified Atraumatic Restorative Technique (SMART), in which GIC is placed after SDF application. (Modasia and Modasia, 2021) Partial

caries removal in Atraumatic Restorative Technique (ART) decreases the likelihood of pulp exposure, while SDF application arrests the activity of residual bacterial biofilm through its antimicrobial effect. Subsequent placement of a GIC restoration seals the cavity, cuts off fermentable carbohydrate substrate for residual bacterial biofilm, restores tooth form and masks the black stain caused by SDF. (Khor et al., 2022) This SMART technique can be performed with placement of GIC immediately following SDF application in a single appointment or after two applications of SDF, as recommended biannually to arrest the lesion. (Shah et al., 2022)

Mei et al., 2016 reported that application of 38% SDF increased the resistance of the GIC and composite resin restorations to secondary caries.

Restorations and Silver diamine fluoride:

It has been claimed that SDF decreases the bond strength to adhesive restorative materials due to the presence of silver phosphate at the tooth-restoration interface and the partial or complete occlusion of dentinal tubules with silver particles, which decrease the penetration of the adhesive materials into them. This is more problematic with composite resin restorations as the bonding mechanism of adhesives depends mainly on micromechanical retention and hybrid layer formation in dentin. (Burgess and Vaghela, 2018; Fröhlich, Rocha and Botton, 2020) Literature on SDF effect on bond strength, however, has inconclusive findings. (Greenwall-Cohen, Greenwall and Barry, 2020)

An in vitro study by **Puwanawiroj et al., 2018** investigated the effect of 38% SDF on bond strength of GIC to natural CAD. The study found that SDF did not adversely affect the bond strength of GIC to natural CAD. Similarly **Zhao et al., 2019** found that SDF with or without KI did not adversely affect the bond strength of GIC to artificial CAD.

A systematic review and meta-analysis by **Fröhlich et al., 2022** concluded that regardless of dentin condition, SDF application with or without the rinsing step did not influence the bonding of GIC to dentin.

A study by **Wu et al., 2016** found that pretreatment of dentin in primary teeth with 38% SDF had no significant effect on bond strength to composite resin. Similarly **Duker et al., 2019** found that SDF did not adversely affect the bond strength of composite resin to artificially demineralized dentin.

On the other hand, **Soliman et al., 2021** and **Sa'ada et al., 2021** found that pretreatment of non-cariious primary dentin with 38% SDF solution increased the bond strength to RMGIC. Similarly **Firouzmandi et al., 2020** found that SDF application increased the bond strength of composite resin to natural CAD. However, this effect disappeared after aging.

A systematic review and meta-analysis by **Fröhlich et al., 2022** concluded that SDF application significantly compromised the bonding of Adhesive systems to dentin. A rinsing step after SDF application eliminated this effect in sound dentin and improved the bond strength to CAD.

Further research is still required to determine the effect of SDF on bond strength and stability of different restorative materials.

Conclusion:

Silver diamine fluoride has been proven to be beneficial for caries prevention and arrest. It is considered a non-invasive procedure that is cheap, fast, and easy to use. It has great benefits, especially for management of early childhood caries, patients with special health care needs, and those with behavioural or medical issues. Moreover, SDF application does not require sophisticated training of the dental or health professionals. Black staining is a potential disadvantage of SDF; however, some parents chose it over other invasive techniques as it is painless and safe.

Conflict of Interest:

The authors declare no conflict of interest.

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