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Use of silver diamine fluoride in dentistry: a review

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Abstract

Silver Diamine Fluoride (SDF) is a solution containing ionic silver, fluoride, and ammonia that arrests the progress of carious lesions. The fluoride penetrates deeper into the tooth with SDF as compared with other fluoride solutions, creating a fluoride reservoir in the tooth structure. The fluoride component of SDF contributes to remineralization and fluorapatite formation, producing harder, more caries-resistant tooth structures. The silver provides the antimicrobial activity for the material and inhibits biofilm formation. The solution was recently approved by the Food and Drug Administration for desensitizing cold sensitive teeth and has been used off-label to treat carious lesions. SDF will produce a caries lesion darker (brown to black) than the original, which is the major criticism of the material. The application of SDF is easily adapted for public health programs. The lesion is isolated, and the solution is painted onto the clean caries lesion and dried. This simple application process requires little equipment, and its low cost per application makes the material ideal for large populations.

Keywords: Dental caries, Silver Diamine Fluoride, Remineralization

Introduction

Dental caries is among the most common multifactorial chronic dental disease. Many risk factors contribute to their initiation and progression. The risk factors can be categorized as biological, environmental or socio-behavioral [1&2]. In preschoolers, high consumption of sucrose, sweet drinks, high sugar intake between meals, and frequent snacking have all been associated with dental caries [3]. Both the American Academy of Pediatric Dentistry (AAPD) and The American Academy of Pediatrics (AAP) view Early Childhood Caries (ECC) as a major public health issue, recommending that caregivers and oral health care providers need to be more assertive in implementing added preventive practices that can reduce caries risk in children [4].

ECC is a serious public health problem in both developing and industrialized countries. It continues to affect babies and preschool children worldwide [5]. The burden of untreated caries is increasing due to limited financial resources, poor access to basic oral care and the high cost of restorative treatment [6]. Consequences of untreated caries may remember the expanded danger of future caries for essential and lasting dentition, pain and infection, changed eating and sleeping habits, delayed growth and development, high treatment costs, loss of school days and low confidence. Managing and treating dental caries in children and in individuals with special health care needs is challenging and the treatment often requires advanced pharmacologic behavior guidance such as sedation and general anesthesia, which can be expensive [7]. To reduce the burden of caries in young children and to avoid possible serious consequences of untreated decay, it is important to identify an effective, low-cost method of treating caries in children [6].

A variety of evidence-based approaches for caries prevention have been reported however, these strategies demand significant financial investment and depend upon the availability of oral health workforces and facilities. In recent years thanks to a better understanding of caries etiology and pathology along with the evidence from various clinical trials a new perspective has been evolved which is focused towards preventing and arresting the disease process itself [1]. The effective ECC preventive measures include the use of fluoridated and non-fluoridated remineralizing agents. In the management of cavitated ECC, Atraumatic Restorative Treatment (ART) has also been recommended. It is painless, low cost and can be applied outside the clinical setting or when conventional treatment is not available. Though, a major disadvantage of this treatment is its high rate of failure [3]. To overcome these disadvantages Silver Diamine Fluoride (SDF) has been incorporated into the practice. It is being used as an alternative treatment option for caries prevention and arrest. Its least invasive property which preserves the maximum dental hard tissue, low cost and ease of the application makes it a favourable treatment of choice in dental offices and community dental health projects. Thus, the interest in the use of SDF has been growing widely [3]. SDF is believed to have antimicrobial properties while also promoting re-mineralization and has the potential to address the epidemic of untreated decay in young children [5]. Carious lesions treated with SDF increase in mineral density and hardness, and decrease in size. It is also very effective in reducing hypersensitivity in the tooth [4].

SDF solution was approved for use as a therapeutic agent in Japan in the 1960s [8]. In 2014, the US Food and Drug Administration (FDA) cleared the first SDF product for use in the USA [9]. Since 1969, SDF has been used to arrest caries of the primary teeth in children [10]. The literature has considered it as the “silver-bullet” with relatively minimal adverse events, such as tooth discoloration and some gingival irritation [11]. It is effective at arresting existing caries in the primary teeth of children, especially toddlers and children with behavioral issues by being an effective, efficient, equitable and safe caries-preventive agent. It can be widely used in the demographics that suffer from the highest rates of tooth decay in children, bed-bound patients, people with mental disabilities, post-radiation and chemotherapy patients with xerostomia, and members of the community in very low socioeconomic situations [11]. Thus, this review article explores in depth about SDF solution, including its usage as caries preventing and arresting agent in primary as well as permanent tooth.

History of SDF

In ancient times around 1000 B.C. bactericidal activity of silver ion has been known. It was used in the form of silver nitrate in medicines for ages. Its dental use can be traced back to Japan around 1000 AD, where it was used for cosmetic blackening of teeth [12]. **In 1846** the first dental use of silver nitrate was incorporated as a remedy for hypersensitivity of dentin, erosion and pyorrhoea, as a sterilizing agent and caries inhibitor in deciduous as well as in permanent teeth [13]. **In 1970** came the use of ammonical silver fluoride for the arrest of dental caries which was pioneered by Dr. Nishino and Dr. Yamaga et al in Japan [14], who developed it to combine the actions of fluoride (F) and silver ions (Ag+) and led to the approval of the first SDF product, Saforide [15]. In the same year it was accepted by The Central Council of the Ministry of Health and Welfare in Japan for dental treatment [12]. **In 1980** it was widely used in Australia and Brazil, Argentina and China for many years to treat dental caries. After that it lost it charm and was not used in other countries due to its unesthetic property [12]. **21st century**, it started to be used again in China as well as in many countries such as Japan, Australia, Nepal, Philippine, Cuba and several African countries. In USA, before the Food and Drug Administration (FDA) cleared SDF, some American dentists sequentially applied silver nitrate followed by fluoride varnish to carious lesion as the only available "atraumatic" procedure to treat dental caries [12]. **In 2014**, the U.S. FDA cleared the use of SDF in the United States as a topical agent to decrease sensitivity. Its use in arresting caries is an off-label use, defined by the FDA as an "unapproved use of an approved drug" [12]. **In 2015**, the first commercial product became available in the United States: Advantage Arrest [9]. **In October 2016,** the FDA awarded SDF the designation of "breakthrough therapy" based on its arrest of dental decay in children and adults, a first for an oral health therapy [12].

Composition, Properties And Availability of SDF

It is a color less, alkaline liquid with composition of silver 24-27%, ammonia 7.5-11%, fluoride 5-6% and water. Specific gravity of 1.25 and a pH of 10. It is available in aqueous form in 8 mL and 5 mL dropper-vials which approximately contains 250 drops (1mL=20 drops), 1 drop can treat 4-5 teeth surfaces [16]. SDF is available in various concentrations depending upon the ppm of fluoride, silver and amine present in it and its pH value. Available concentrations of SDF 38% (44,800ppm and pH 10), 30% (35,400ppm and pH 9), 12% (14,100ppm and pH 8.5) and 10% (11,800ppm and pH 8.5-9) [17].

Table 1: The various commercially available brands that supplies SDF [18].

SDF (%)	Product Brand	Manufacturer	Country	Ingrdients	Package
12 and 30	Cariestop	Biodinamica	Brazil	flouric acid, silver nitrate, ammonia	5-ml or 10ml dropper bottle
38	Saforide	Toyo seiyaku kasei	Japan	SDF	5-ml dropper bottle
38	Advantage arrest	Elevate oral care	United States	SDF	8-ml dropper bottle
38	e-SDF	Kids e-dental	India	SDF	5-ml dropper bottle
38	FAgamin	Tedequim srl	Argentina	SDF	5-ml dropper bottle
30-35	Riva star	Sdi dental ltd.	Australia	SDF	unit 1- 0.05 ml unit 2- 0.10ml

Mechanism of action

SDF is used for caries arrest and treatment of dentin hypersensitivity. In treatment of exposed sensitive dentin surfaces, topical application results in development of a squamous layer on the exposed dentin, partially plugging the dentinal tubules [19]. Dental caries is a complex progression involving dietary sugars, bacterial metabolism, demineralization, and organic degradation. The collagenous organic matrix is exposed once a dentin surface is demineralized and destroyed by native and bacterial proteases to enable a lesion to enlarge [20]. Upon application of SDF to a decayed surface, the squamous layer of silver-protein conjugates forms, increasing resistance to acid dissolution and enzymatic digestion [21].

$Ag(NH_3)_2F(aq) \rightarrow Ag(s) + 2NH_3(g) + F^-(aq)$

The fluoride and silver ions so formed as contained in the SDF appear to have the ability to inhibit the formation of cariogenic biofilms. Hydroxyapatite and fluoroapatite form on the exposed organic matrix, along with the presence of silver chloride and metallic silver. The treated lesion increases in mineral density and hardness while the lesion depth decreases. Meanwhile, SDF specifically inhibits the proteins that break down the exposed dentin organic matrix: matrix metalloproteinases [21], cathepsins [22] and bacterial collagenases [19]. Silver ions act directly against bacteria in lesions by breaking membranes, denaturing proteins, and inhibiting DNA replication [23&24]. 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” [25]. This reservoir effect helps explain why silver deposited on bacteria and dentin proteins within a cavity has sustained antimicrobial effects.

$Ca_{10}(PO_4)_6(OH)_2 + Ag(NH_3)_2F = CaF_2 + Ag_3PO_4 + NH_4OH$

Silver and fluoride ions penetrate ~25 microns into enamel [26] and 50-200 microns into dentin [27]. Fluoride promotes remineralization, and silver is available for antimicrobial action upon release by re-acidification [28]. SDF arrested lesions are 150 microns thick [29]. Recently, Mei et al. (2013)[19] mentioned that the use of 38% SDF inhibited demineralization and preserved collagen from degradation in demineralized dentin [Figure 1].

Clinical implications and mechanism of action of SDF are summarized in Figure 2.

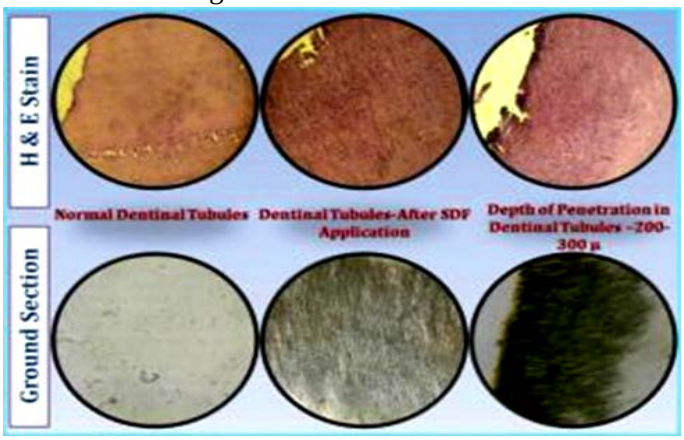

Figure 1: Depth of penetration of silver phosphate crystals.

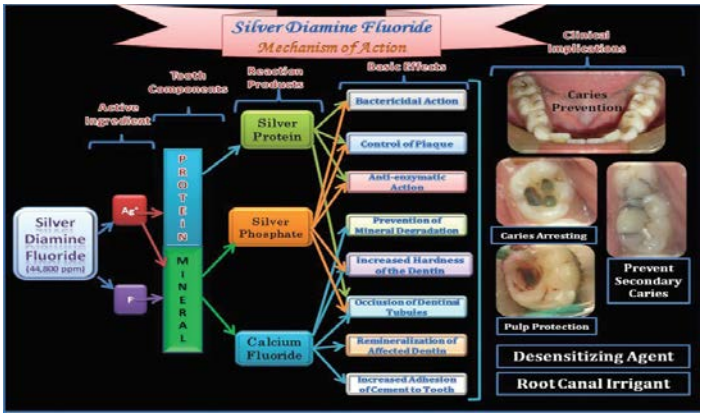

Figure 2: Summary of mechanism of action and clinical application of silver diamine fluoride

Indications [9, 30-32]

1. The pre-cooperative child including the ones suffering from Severe Early Childhood Caries.
2. High caries-risk patients with anterior or posterior active cavitated lesions with no clinical signs of pulp involvement.
3. Treatment challenged by behavioral or medical management. This includes the frail elder, those with severe cognitive or physical disabilities, and dental phobias.
4. Preventing secondary caries below to the conventional restorations.
5. SDF solution seem to be appropriate to reduce pain caused by dentin hypersensitivity.
6. To treat infected root canals.
7. Extreme caries risk patients like those suffering from salivary dysfunction like xerostomia, sjogren syndrome, polypharmacy, aging, or methamphetamine abuse which is usually secondary to cancer treatment.
8. Can be helpful in preventing pit and fissure caries.

Contraindications [9, 30]

1. Patient with silver allergy.
2. Suffering from desquamative gingivitis or mucositis.
3. Teeth showing clinical signs of pulpal inflammation or reports of unsolicited/spontaneous pain.

Advantages [32-34]

1. It effective in arresting dentin caries in primary and permanent teeth, less caries increment is seen in children receiving SDF compared with those without the SDF therapy.
2. Remineralisation of demineralised inorganic tooth mineral thereby nhibiting the progression of caries.
3. Control of pain and infection.
4. Ease and simplicity of use, the clinician just need to use a microbrush to apply it on the surface of the tooth.
5. Cost effective.
6. Minimal requirement for personnel time and training.
7. It is non-invasive as there is no need for surgical intervention because the caries can be inhibited without excavation.

Disadvantages [9, 18]

1. SDF does not restore tooth structure and function to normal.
2. The most prominent being the irreversible black staining of teeth which usually occurs after the application of SDF.
3. Metallic or bitter taste.
4. Staining of skin, lips gingival and cloths with which it comes into contact.

Adverse effects of SDF

Several studies have highlighted the black dental stains that appear after SDF application as one of its disadvantages. The black discoloration comes from a layer of silver phosphate (Ag3PO4), which is a hard and impermeable layer formed on the tooth upon application of SDF [35]. Ag3PO4 is yellow when it is first formed, but turns black under sunlight or reducing agents. The precipitation of silver sulphide also contributes to the dark color of caries lesions upon SDF application. SDF is sensitive to light and must be kept in dark containers [36].

Clinical application

Chair side guidelines by AAPD (2018-2019) [37]

- Remove gross debris from cavitation to allow better SDF contact with denatured dentin.
- Carious dentin excavation prior to SDF application is not necessary. As excavation may reduce proportion

of arrested caries lesions that become black, it may be considered for esthetic purposes.

- A protective coating may be applied to the lips and skin to prevent a temporary henna-appearing tattoo that can occur if soft tissues come into contact with SDF.
- Isolate areas to be treated with cotton rolls or other isolation methods. If applying cocoa butter or any other product to protect surrounding gingival tissues, use care to not inadvertently coat the surfaces of the caries lesions.
- Caution should be taken when applying SDF on primary teeth adjacent to permanent anterior teeth that may have non-cavitated (white spot) lesions to avoid inadvertent staining.
- Careful application with a microbrush should be adequate to prevent intraoral and extraoral soft tissue exposure.
- Not more than one drop of SDF should be used for the entire appointment.
- Dry lesion with gentle flow of compressed air.
- Bend micro sponge brush. Dip it into SDF and dab on the side of the plastic dappen dish to remove excess liquid before application.
- Use a plastic dappen dish as SDF corrodes glass and metal.
- Apply SDF directly to only the affected tooth surface. Remove excess SDF with gauze, cotton roll, or cotton pellet to minimize systemic absorption.
- Application time should be at least 60 seconds (60-120 seconds).
- Apply gentle flow of compressed air until medicament is dry. Try to keep isolated for as long as three minutes.
- The entire dentition may be treated after SDF treatment with 5% sodium fluoride varnish to help prevent caries on the teeth and sites not treated with SDF follow-up.

Follow up

Twice per year (biannual) application was shown to be more effective in caries control compared to once a year until the tooth is restored or exfoliates [38-40]. The effectiveness of one-time SDF application in arresting dental carious lesions ranges from 47% to 90%, depending on the lesion size and the location of the tooth [41]. Anterior teeth have higher rates of arrest than posterior teeth.

Therefore, follow-up for evaluation of caries arrest is advisable. Follow-up at 2-4 weeks after initial treatment to check the arrest of the lesions treated. Reapplication of SDF may be indicated if the treated lesions do not appear arrested (dark and hard). Additional SDF can be applied at recall appointments as needed, based on the color and hardness of the lesion or evidence of lesion progression. Caries lesions can be restored after treatment with SDF [42].

SDF + Fluoride Varnish

The combination of fluoride varnish after SDF placement to prevent SDF taste and keep the SDF in the lesion. No evidence that varnish would help achieve either goal. Rather, allowing more time for residence and diffusion of SDF to react with and dry into the lesion is more likely to improve effectiveness [9].

Maximum dose and safety margin

Due to the high concentrations of fluoride and silver, the toxicity of 38% SDF remains a concern when applying in very young children. In gaining clearance by the FDA, to determine the lethal dose (LD50) of SDF by oral and subcutaneous administration. Average LD50 by oral administration was 520 mg/kg, and by subcutaneous

administration was 380 mg/kg. One drop (25 µL) is ample material to treat 5 teeth, and contains 9.5 mg SDF. 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 = 400-fold safety margin. Actual dose is likely to be much smaller, for example 2.37 mg total for 3 teeth was the largest dose measured in 6 patients [43]. The most frequent application monitored in a clinical trial was weekly for 3 weeks, annually [44]. Thus we set our recommended limit as 1 drop (25 µL) per 10 kg per treatment visit, with weekly intervals at most [9].

Conclusion

SDF appears to be a useful immediate treatment for children who can't receive traditional restorative treatment for dental decay. It is effective for caries arrest and prevention of new lesions on the teeth where it is applied, and is a minimal intervention treatment that is safe and affordable.

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