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Silver Diamine Fluoride, an alternative in the management of caries

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Abstract

Silver diamine fluoride (SDF) is a magic alternative in caries management. SDF is an alkaline solution constituting a complex of silver, fluoride and ammonia. Dental caries can be reduced and crystallized with SDF in a simple non-invasive treatment approach avoiding the use of painful local anesthetic injections and loss of tissue. This treatment modality is well accepted by children and the application technique is quick and easy without the need for extensive excavation. During this unprecedented time of the COVID-19 pandemic, SDF eliminates the need for aerosol generating equipment. Silver Diamine Fluoride is truly a silver bullet as the high fluoride content allows for more effective diffusion into enamel and dentin, the silver kills bacteria upon contact, and stays in the demineralized tooth structure, hardening them and reactivating upon exposure to bacteria and the ammonia stabilizes the solution and serves as an antiseptic.

Keywords: Early Childhood caries, Primary teeth, Silver diamine fluoride.

Introduction

One of the most common diseases in children all over the world remains to be dental caries [(1)]. Early childhood caries is the form of decay in primary teeth seen in

children under the age of 6 years, found to be associated with frequent sugar consumption in the presence of acid-producing bacteria. The occurrence of new carious lesions, acute and chronic pain, sepsis, emergency room visits, hospitalization for procedures under general anesthesia, delay in growth and development, and diminished quality of life are some of the different consequences of ECC.[2]. Until their natural exfoliation, the primary teeth are essential to maintain the space for the permanent teeth. More than 600 million children worldwide are currently affected by ECC despite the fact that it is a preventable disease. This disease affects the quality of life of children and their families and becomes an unnecessary hindrance to society [3].

The prevalence of ECC is found to be more among children coming from lower socio-economic groups. Various studies have shown that in preschool children, the cavitated carious primary teeth are largely left untreated [4]. The treatment of ECC is faced with a number of obstacles [5]. Due to their young age and uncooperative behavior, restorative treatment for children is challenging [6]. The prerequisites for the management of caries in the primary dentition can vary from those in the permanent dentition, given that they are replaced within 6–8 years [7].

The significant decline in the incidence of caries witnessed universally over the past decades is attributed to the use of fluoride in dentistry.[8] However, a high number of untreated caries lesions is still seen in preschool children.[9]Traditionally, the treatment of the carious lesions follows surgical removal of the carious tissue and the replacement with a suitable restorative material.[10]The new paradigm in oral health care, minimal invasive dentistry (MID), aims at the preservation of sound tooth structure using noninvasive techniques.[11]

Silver Diamine Fluoride (SDF) is a cost-effective, easy-to-use alternative to reduce sensitization and arrest caries. The surgical management of caries, “the drill and fill technique”, can be shifted to a medical management with SDF.[12]Even though silver diamine fluoride (SDF) had been in use in different countries for years, there has been an intensified attention of late by dentists globally due to its efficacy in arresting the development of carious lesions. [13][14]The U.S. Food and Drug Administration (FDA) gave SDF clearance in August 2014 for dental use in the United States and designated SDF with “Breakthrough Therapy Status” in 2016. [15]The ease of application makes SDF suitable for almost all patient populations, including those with developmental, behavioral, or medical considerations that complicate traditional restorative techniques. [16][17]

The coronavirus disease 2019 (COVID-19) pandemic is an unprecedented and difficult time for dentistry since oral healthcare workers are deemed to be at the highest risk of getting infected with SARS-CoV-2.However, this disarray should enforce creative and collaborative solutions. Silver Diamine fluoride is an excellent alternative in such a situation as it does not require aerosol generating equipment, is inexpensive and effective. [18]

History

There has been a long history of use of silver in medicine. Earliest medical use of silver was for water disinfection and storage. Silver vessels were used by Alexander the Great (335 BC), the Greeks and the Romans in order to keep water fresh.[19]

Use of silver in dentistry was reported as early as the 1840s, where silver nitrate was reported for its use in arresting caries. [20] Howe in 1917 reported the use of an ammoniacal silver nitrate solution which could be applied directly to carious lesions.[21] Howe’s solution was believed to have antibacterial properties, and was used up until the 1950s. [22]

A range of both *in vivo*[23,24,25] and *in vitro* studies[26,27,28] documented the effectiveness of silver fluoride compounds at arresting caries lesions towards the end of the twentieth century and the beginning of the twenty-first century, leading to the commercial use of silver fluoride compounds in Mexico, Australia and Japan. Ammonium has since been included with the compound, resulting in the formation of SDF.[29]

Silver diamine fluoride was first studied by Nishino, at Osaka University in Japan in 1969, incorporating the potent antimicrobial properties of silver with the benefits of a high dose of fluoride. [30]This formulation produced a precipitate that occluded dentinal tubules and reduced hypersensitivity. Japan's Central Pharmaceutical Council of the Ministry of Health and Welfare approved "diammine silver fluoride" as a cariostatic agent and was available in the market. [31]

Composition

Silver diamine fluoride (SDF) is a complex of silver, fluoride and ammonia. Silver shows an antimicrobial effect, remineralization is promoted by fluoride, and the solution is stabilized by ammonia.[29]The most commonly used concentration of SDF is 38% w/v Ag(NH3)2F (30% w/w) and it is comprised of 24.4-28.8% (w/v) silver and 5.0-5.9% fluoride, at pH 10.The concentration of fluoride present in SDF is about 48,0000 ppm. [32]

SDF mechanism of action

The effectiveness of SDF is due to the combination of silver nitrate and fluoride. The caries arresting properties of SDF is produced by the action on cariogenic bacteria as well as the organic and inorganic structures of teeth.[33]

Actions of SDF on cariogenic bacteria

Cariogenic bacteria is inhibited by both fluoride and silver ions present in SDF. Knight *et a.* in 2005 showed that dentine surfaces on to which SDF had been applied exhibited significantly reduced levels of *Streptococcus mutans*, the most important pathogen associated with the initiation and progression of the caries lesion. [34] The antimicrobial action of the SDF has also been demonstrated on multi-species cariogenic biofilms[35] and *Lactobacillus*[36] species.

High-concentration of fluorides inhibit biofilm formation by binding to bacterial cellular components and influencing enzymes related to both carbohydrate metabolism and sugar uptake.[35] Silver ions' antibacterial action is threefold: penetrating and destroying bacteria cell wall structures, inhibiting enzymatic activity thus influencing metabolic processes, and inhibiting the replication of bacterial DNA.[37]

Effects of SDF on inorganic content of enamel and dentine

Remineralization of dentinal caries is shown to be brought about by SDF.[38]It has been hypothesized that the chemical reaction between SDF and hydroxyapatite of teeth results in the formation of silver phosphate and calcium fluoride, generating an elevation of pH and formation of fluoride reservoirs.[39]Fluorapatite which is insoluble is formed by the dissolution of fluoride and calcium. The reaction between SDF and hydroxyapatite also leads to the formation of nanoparticles of metallic silver that get attached to hydroxyapatite crystals.[38] The incorporation of silver particles into the hydroxyapatite is significant due to the antibacterial and anti-cariogenic nature of the silver, hence inhibiting the development of future caries on the arrested lesion.[29]

Effects of SDF on the organic content of dentine

Larger amounts of intact collagen were shown to be remaining on the dentine surface after treatment with SDF than after treatment with water in a study using immunolabeling. [36]The liberation of hydroxyproline which is seen as a result of collagen degradation was significantly lesson dentine treated with SDF than on

dentine treated with water3. SDF had an inhibitory effect on matrix metalloproteinases (MMPs), which play an important role in the enzymatic degradationof collagen, by inhibiting the proteolytic activities ofMMP-2, MMP-8 and MMP-942. The activities of cathepsins, which are proteolytic enzymes that contribute to dentine collagen degradation, were also inhibited by SDF. [38]

Caries Management: Caries arrest and caries prevention

SDF is most commonly used as a caries-arresting and preventive agent. Several randomized control trials have examined the effectiveness of SDF as a caries-arresting agent. [29]

In 2002, Chu *et al.*[12] undertook a 3–5-year prospective controlled clinical trial comparing the use of annual application of 38% SDF (48,000 ppm F) to the use of 5% sodium fluoride (NaF) varnish (22,600 pp F). Both products were applied every three months to Chinese schoolchildren with carious primary anterior teeth. The study found that SDF's prevented fractions for caries arrest and prevention in primary teeth were >96% and >70%, respectively. In contrast, for fluoride varnish, the highest prevented fractions were 21.3% and 55.7% for caries arrest and prevention, respectively.[33] The study also found no significant benefit of caries excavation before application of SDF implying that minimal equipment was needed for caries arrest with SDF. [29]

In 2005, Llodra*et al.*[40] undertook a three-year prospective controlled clinical trial examining the efficacy of applying 38% SDF solution twice a year for caries reduction in carious primary and permanent teeth. The study found that, for primary teeth, the prevented fractions for SDF were 55.6% and 78.6% for caries arrest and prevention, respectively. In permanent teeth, the prevented fractions for SDF were 100% and 63.6% for caries arrest and prevention, respectively.[33]

Braga *et al.*[41] compared the effectiveness of SDF to other non-invasive approaches (cross-tooth brushing technique [CTT] and glass-ionomer cement [GIC] fissure sealants) in arresting occlusal caries in erupting permanent first molars. The study found that, after three and six months, 10% SDF showed a significantly higher capacity than CTT and GIC for arresting caries. A general reduction in active lesions was noted in all groups.

Dos Santos Jr *et al.* [42] compared caries-arresting properties of 30% SDF with those of GIC as an intermediate restorative technique (IRT). The study demonstrated that, after 12 months, SDF was 1.73 (95% CI, 1.38–2.18) times more effective in arresting caries (RR, 66.9%) than IRT (RR, 38.6%).

Duangthip *et al.*[43] examined the effect of 30% SDF applied three times with a weekly interval and compared this to three applications of 5% NaF varnish and a single 30% SDF application. The study found that SDF was significantly more effective at arresting caries than NaF. The study also found no significance between the three-time application of SDF and the single application of SDF.

Summary of published studies on caries arrest in children by SDF

Study (year)	Objective	Results
Chu et al. (2002)[12]	effectiveness of topical fluoride applications in arresting dentin caries	Silver diamine fluoride was found to be effective in arresting dentin caries in primary anterior teeth in pre-school children.
Llodra et al	Assess the effectiveness of 6-month	SDF was more effective for caries reduction in

(2005)[40]	application of 38% SDF in preventing and arresting caries in primary and permanent teeth and compare with results in a control group	primary teeth(80%) and first molars (65%) than a control group.
Braga et al (2009)[41]	Compare the effectiveness of SDF in arresting occlusal caries in erupting permanent first molars with the effectiveness of other noninvasive approaches (CTT and GIC)	After 3 and 6 months, 10% SDF showed a significantly higher capacity than CTT and GIC for arresting caries. A general reduction in active lesions was noted in all groups
Yee et al (2009)[44]	Compare the effectiveness of a single application of 38% or 12% SDF, with or without the use of a reducing agent (tea), in arresting caries	The number of arrested carious surfaces was significantly higher in 38% SDF and 38% SDF plus tea groups at 6 and 12months ($P < 0.001$) and 24 months ($P < 0.01$) than it was in12% SDF and control groups.
Dos Santos et al (2012)[42]	Compare the caries-arresting properties of 30% SDF with those of IRT using GIC	After 12 months, SDF was 1.73 (95% CI, 1.38-2.18) times more effective in arresting caries (RR, 66.9%) than IRT (RR,38.6%) ($P < 0.05$).
Monse et al (2012)[45]	Compare the effectiveness of 1 application of 38% SDF with that of ART sealants and no treatment in the prevention of dentinal caries (D3 lesions)	The caries increment was lower in toothbrushing children than in non-toothbrushing children. HR was statistically significant for the non-treated children (HR, 0.43; CI, 0.21-0.87; $P < 0.02$) and the sealant-treated children (HR, 0.15; CI, 0.03-0.072; $P < 0.02$).
Zhi et al (2012)[46]	Compare the effectiveness of annual and semiannual topical application of SDF solution with that of annual application of GIC in arresting active dentin caries in primary teeth	The group receiving 6-month applications of SDF showed higher caries arrest rates (OR, 2.98; CI, 1.35-6.69; $P = 0.007$)than groups receiving annual applications of SDF or GIC.
Duangthip et al (2016)[43]	Compare the effectiveness of 3 topical fluoride application protocols (weekly SDF [3×], annual SDF, and NaF [3×]) in arresting	At 6 and 12 months, groups receiving intensive application of SDF had higher caries arrest rates than other treatment groups (annual SDF and weekly NaF varnish applications).At 18

	dentin caries in the primary dentition	months, the group receiving an annual SDF application presented a higher caries arrest rate (40%) than the groups receiving intensive SDF and NaF treatments ($P < 0.001$).
Duangthip et al.[47]	Compare the effectiveness of 3 applications of silver diammine fluoride (SDF) solution at yearly interval and three applications of SDF solution or sodium fluoride (NaF) varnish at weekly interval at baseline in arresting active caries in the primary teeth of preschool children.	Over a 30-month period, annual applications of SDF solution is more effective than three weekly applications of NaF varnish or SDF solution at baseline in arresting active cavitated dentine caries lesions in primary teeth.
Fung et al.[6]	This 30-mo randomized clinical trial compared the effectiveness of 2 concentrations (12% or 38%) of silver diamine fluoride (SDF) and 2 periodicity of application (once or twice a year) in arresting cavitated dentin caries in primary teeth.	SDF at a concentration of 38% is more effective than that of 12% in arresting active caries in primary teeth. For children with poor oral hygiene, caries arrest rate of SDF treatment can be increased by increasing the frequency of application from annually to semiannually

Abbreviations: ART, atraumatic restorative treatment; CTT, cross-toothbrushing technique; GIC, glassionomer cement; HR, hazard ratio; IRT, interim restorative technique; NaF, sodium fluoride; SDF, silver diamine fluoride.

Other Indications [29, 48]

- Treatment of dentinal hypersensitivity
- Treatment of molar incisor hypomineralization (MIH)
- Disinfection of the root canal system
- Indirect pulp treatment (IPT)
- As a substitute to sealants in children who cannot endure a scrupulous sealant procedure.
- SDF has significant inhibitory effect on MMPs and Cathepsin, which leads to the enzymatic degradation of the composite resin adhesive hybrid layer collagenous matrix and also reduces collagen degradation. These factors may help in increasing bond strength of resin to dentin.

Contraindications for SDF [29]

Contraindications for use of SDF include:

Silver allergy

Significant desquamative gingivitis or mucositis

Active cavitated caries lesions with pulp involvement as per the clinical judgment

Pregnancy

Breastfeeding

Restorations in the aesthetic zone

Caries in the aesthetic zone

Signs or symptoms of periapical pathology

Radiographic signs or symptoms of periapical pathology

If parents/guardians do not consent for using SDF due to concerns of the color change.

Silver allergy is a complete contraindication to SDF. Use of potassium iodide (KI) for discolouration, described later, is contraindicated in pregnant women and during the first six months of breastfeeding due to concern of overloading the developing thyroid with iodide. [16]

Side effects of SDF

SDF has been used in several countries for upwards of 80 years. Not a single adverse event has been reported to the Japanese authorities since they approved SDF over 80 years ago. [49]

There are, however, some localised potential side effects of SDF that have been discussed in the literature. [29]

Discolouration

One of the most frequently reported side effects of SDF is discolouration.[40]Discolouration tends to be black/dark brown and is thought to result from silver phosphate (Ag3PO4), which is formed when dental caries is treated with SDF. Silver phosphate readily turns black under sunlight or under the influence of reducing agent. [29]

The appearance of the staining causes aesthetic concern among patients and parents. Parental acceptance of SDF staining increased for teeth in less-visible locations and when the child exhibits uncooperative behavior. Many parents accepted SDF treatment only to avoid alternative treatment under sedation or general anesthesia. [50]

The staining potential of SDF may be modified by the application of Potassium Iodide (KI). KI reacts with free silver ions to produce silver iodide, a creamy white reaction product. [51] However, studies have reported significant color changes after long term storage. [52, 53]

Glutathione (GSH), a tri-peptide biomolecule, is considered the best candidate with silver as it contains a thiol group (-SH) which has a high affinity for adsorption onto metal surfaces and can produce long term effects. [54]

Bond Strength

It has been postulated that SDF reduces the bond strength to adhesive materials due to the introduction of a new interface at the tooth-restoration complex and the occlusion of dentinal tubules, thus reducing the penetration of the adhesive agents into the tubules. Interestingly, contradictory to this, some products even claim an improvement in bond strengths. Literature on SDF effects on bond strength, however, has inconclusive findings. [29]

An *in vitro* study by Quock*et al* [55] examined the effect of SDF (38% and 12%) on bond strength to dentine. The study found that SDF does not adversely affect the bond strength of resin composite to non-carious dentine. This finding was supported by Camacho *et al.* [56] who found that the *in vitro* application of SDF to etched non-carious enamel before orthodontic bracket bonding does not adversely affect bond strength.

Effect on dentino-pulp complex

It has been suggested that SDF should not be used in carious lesions with close proximity to the pulp, [57] due to the potential for silver ion penetration into the pulp complex. However, a study by Rossi *et al.* in 2017[58] examined the effect of SDF on the pulp complex by examining a histological study of human teeth treated with SDF and experimental studies on laboratory animals. In the *ex vivo* study of human teeth, microscopy demonstrated that SDF sealed dentinal tubules only at the site where it had been placed, with limited penetration beneath. The pulp tissue associated to treated caries showed chronic inflammatory infiltrate and formation of tertiary dentine, with no Ag precipitate. The study concluded that SDF induces minimal adverse effects to the pulp.

SDF effect on the gingiva

SDF has been reported to potentially result in gingival erythema, [59] gingival inflammation, gingival bleaching and gingival pain. [60] This was shown not to be significantly different to baselines, was noted as being transient as it was seen for less than a week and was not severe. Additionally, this erythema was not accompanied by any long-term staining of the gingiva. [59]

SDF effect on mucosa and skin

Due to the high pH of SDF, mucosal or skin burns may occur post-application. The burns tend to be small, mildly painful white lesions in the mucosa, which disappear after 48 hours without treatment. [40]

Moreover, SDF can stain clothes and skin of the body. Though it does not cause pain or damage, SDF skin staining cannot be easily washed away and takes around seven days to disappear. However, the staining of clothes with SDF is permanent. [29]

Clinical Technique [61]

Case selection for application of silver diamine fluoride

Patients who may benefit from SDF include those:

• With high caries risk who have active cavitated carious lesions in anterior or posterior teeth

• Presenting with behavioral or medical management challenges and cavitated carious lesions

• With multiple cavitated carious lesions that may not all be treated in one visit

• With dental carious lesions that are difficult to treat

Criteria for tooth selection include:

• No clinical signs of pulpal inflammation or reports of unsolicited/spontaneous pain.

• Cavitated carious lesions that are not encroaching on the pulp. If possible, radiographs should be taken to assess depth of caries lesions.

• Cavitated carious lesions on any surface as long as they are accessible with a brush for applying SDF.

SDF can be used prior to restoration placement and as part of caries control therapy. [62]

Informed consent, with emphasis on the expected staining of treated lesions, potential staining of skin and clothes, and the need for reapplication for disease control, is recommended.

Clinical application of silver diamine fluoride

• The gross debris should be removed from site of carious lesion so as to have a better contact of the SDF solution with denatured dentin.

• It is not necessary to excavate the caries. A protective coating may be applied to soft tissues.

• 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 carious 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.

• Soft tissue exposure should be prevented with careful application. The entire appointment can be completed with one drop of SDF.

• Dry lesion with gentle flow of compressed air.

• The micro sponge brush should be bent at an angle. It should be dipped into SDF and excess fluid removed before application. Apply SDF directly to the carious lesion. In order to minimize systemic absorption, the excess SDF should be removed with gauze, cotton roll, or cotton pellet.

• At least one minute application time must be followed if possible.

• Dry the solution with gentle force of compressed air. Isolation should be maintained for up to three minutes.

Follow-up

The success in arresting dental caries lesions with SDF ranges from 47 to 90 percent. Anterior teeth have higher rates of arrest than posterior teeth. There-fore, follow-up for evaluation of caries arrest is advisable.

• Recall visit should be made after 2-4 weeks in order to check whether the carious lesion has gotten arrested.

• 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.

• Restoration of the carious lesion can be done after treatment with SDF.

• Semi-annual application shows better caries arrest rate

Conclusion

SDF has enormous potential and is a magic alternative in caries management. This material which has been described as a silver bullet can do wonders in dentistry as it is non-invasive, inexpensive, easy and simple to use. The paint on technique has minimal requirement of personnel training and time and is well accepted by children. At this unprecedented time of the COVID-19 pandemic, this breakthrough therapy of Silver Diamine Fluoride, which eliminates the need for aerosol generating equipment is truly a magic drug for dentistry. As humans, we adapt to change and let us find a silver lining during the pandemic, the Silver Bullet, Silver Diamine Fluoride.

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