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SILVER DIAMINE FLUORIDE: A MAGIC BULLET FOR CARIES MANAGEMENT

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ABSTRACT: In the past few years, silver diamine fluoride (SDF), a medicament for topical use, has increasingly gained recognition amongst clinicians and patients as an effective tool for arresting caries, treating dentinal hypersensitivity, and enhancing tooth bond strength. Because of its cost-effectiveness and ease of application, SDF is now a treatment of choice in many clinical scenarios. SDF is a colorless topical compound constituting 24.4–28.8% (w/v) silver and 5.0–5.9% fluoride at pH 10. Upon application, SDF leads to the development of a hypermineralized layer, resulting in a decrease of dentinal sensitivity. The hypermineralized layer also helps to arrest caries by providing resistance against acid dissolution and enzymatic digestion on decayed surfaces. This article presents a quick overview of SDF, the current clinical evidence on its use, clinical indications, limitations, application protocol, and patient considerations.

Keywords: Dental caries; Dentinal hypersensitivity; Remineralization; Silver diamine fluoride.

INTRODUCTION

Nowadays, many patients are self-aware about the choices in dental materials that are available in the market for a given treatment. Silver diamine fluoride (SDF) is becoming a known dental material among the patients.

Mizuho Nishino first investigated silver diamine fluoride (SDF) in 1969 as part of her PhD thesis.[1] The idea of the compound revolved around combining a high dose of fluoride with the potent antimicrobial properties of silver and to analyze the results of its use. The entire experiment resulted in the formation of a precipitate that occluded dentinal tubules and led to a reduction in hypersensitivity.[2] Immediately after this, the Central Pharmaceutical Council of the Ministry of Health and Welfare of Japan granted approval to "silver diamine" fluoride as a cariostatic agent.

SDF is a colorless topical compound constituting 24.4–28.8% (w/v) silver and 5.0–5.9% fluoride at pH 10. Silver and fluoride are the two main components of this topical compound.[3] These two key components are made soluble in water with the help of ammonia. Chemically, metallic silver is inert, while silver ions are of major importance as they act as anti-microbial silver bullets on bacterial cell walls. These silver ions are biocompatible and are found to be of low toxicity in humans.[4] The topical application of this material is safe, simple, cost effective, and is able to arrest the development of dental caries. In August 2014 the US Food and Drug Administration (FDA) granted clearance to SDF as a Class II medical device.[5] SDF has the highest concentration of fluoride available in the market with the 5% SDF

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solution containing 44,800 parts per million (ppm) of fluoride, almost twice that of 5% sodium fluoride varnish containing 22,600 ppm.[5]

When SDF is applied to a carious lesion, two significant products form a physical barrier on the lesion. The first product, silver phosphate (Ag_3PO_4), serves as a reservoir of phosphate ions and the second one, calcium fluoride ($CaF_{2)}$, plays a crucial role in the supply of fluoride.[6,7] Free silver ions on the lesion or on other surfaces are reduced by environmental oxygen and stain the lesion black, which is the major side effect of this medicament. The aesthetic zone remain a challenge that is still to be dealt with.[8]

Upon application, SDF leads to the development of a layer on the exposed dentin resulting in a decrease in the dentinal sensitivity. This layer also helps to arrest caries by providing resistance against acid dissolution and enzymatic digestion on the decayed surface. The double effect of the high doses of fluoride that are delivered and the precipitated barrier formed with the silver makes SDF a unique caries arresting medicament. The disruption of the bacterial cell wall, DNA synthesis, replication, and metabolic activity leads to bacterial cell death.[9] The dead bacterial cells can also result in a "zombi effect" by acting as a carrier for silver ions in a process that kills bacteria living nearby.[10]

The aim of this review article is to provide a brief overview of silver diamine fluoride (SDF) including the evidence in the literature, the indications for its use in dentistry, contraindications to its use, and application protocols.

INDICATIONS FOR THE USE OF SDF IN DENTISTRY

Currently SDF is used selectively in dentistry and the possible indications are shown in Figure 1.

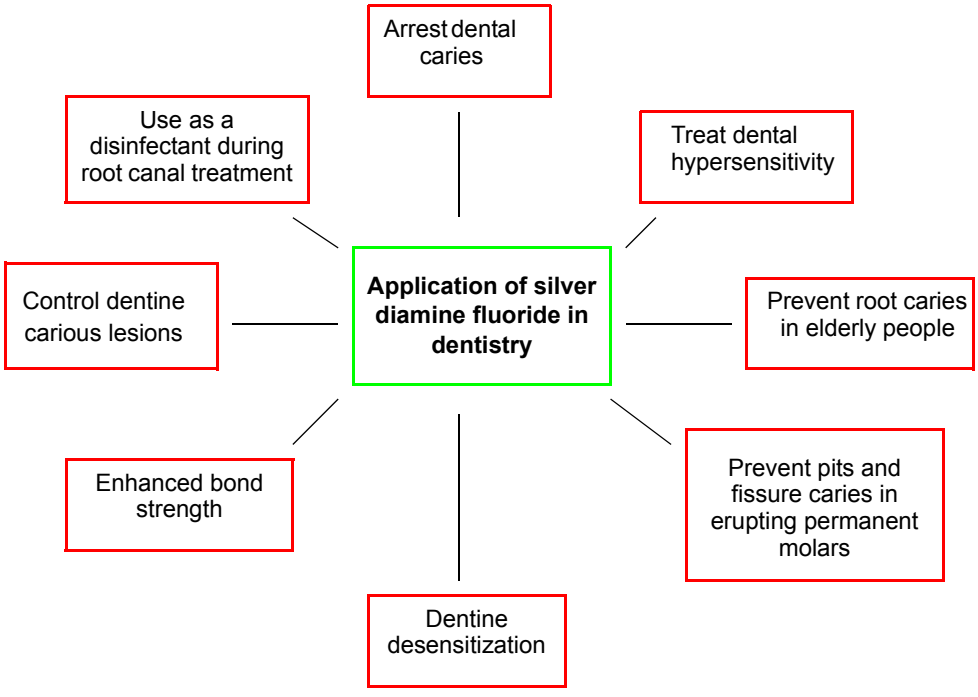

Figure 1. Possible indications for the application of silver diamine fluoride (SDF) in dentistry.[11-14]

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Studies have shown SDF to be useful in high caries risk patients who have active cavitated caries lesions in the anterior or posterior teeth with multiple cavitated caries lesions that may not all be treated in one visit or for patients with difficulty accessing dental care.[15,16] Its ease of application allows it to be applied in an office without the need for sedation or other invasive measures, or even out of office in kindergartens, schools, old people's homes, and nursing homes.[17]

CONTRAINDICATIONS IN DENTISTRY

On the other hand, the contraindications to the use of SDF includes individuals with a silver allergy. SDF application may irritate already sensitive open mouth sores and therefore it should be used with caution until the symptoms subside. Also, the application of petroleum jelly for protection during the application may prevent irritation of the oral mucosa. SDF does not restore the function or form and therefore adjunctive treatments should be planned for cases with large carious lesions reaching the pulp in order to be effective.[18]

Research has also proposed innovative ways to complement the use of SDF. The silver modified atraumatic restorative technique (SMART), which is the placement of a glass ionomer cement (GIC) over a SDF-treated lesion, is a prime example.[19]

EVIDENCE IN DENTISTRY

Most of the studies related to SDF have come from teams of researchers in various countries including Argentina, Brazil, China, Cuba, Japan, and Nepal.[20] The popularity of the use of SDF in less developed countries may be increased due to the limited access to better oral health care. Llodra et al. reported on the efficacy of SDF for caries reduction in the primary teeth and first permanent molars in Cuban school children whose drinking water had a low fluoride content. The 36-month clinical trial revealed a preventive fraction of 79.7% for the deciduous teeth and 65% for the first permanent molars compared to a control group not receiving SDF. This preventive effect was achieved by a six-monthly application of SDF during the study period [21].

Newly erupted permanent first molars are more prone to decay because they are difficult to clean by mechanical actions such as tooth brushing or chewing, in addition to the presence of the gingiva partially covering the occlusal tooth surface. In a comparative study by Braga et al., SDF and GIC were applied on non-cavitated carious lesions in erupting permanent first molars. The study found that all the conventional techniques are equally effective in the prevention of the initial occlusal caries on the permanent first molar but SDF is faster in its action of inactivating caries.[22] Systematic reviews have revealed an effective role for SDF in the prevention of dental caries in the primary dentition.[23,24]

In addition, Li et al. have demonstrated a greater effectiveness of SDF, compared to placebo, in the treatment of root caries in older adults.[25] They studied the application of SDF solution for arresting dental caries in centers for the elderly in Hong Kong. In randomized clinical trials (RCT) they found that the annual application of 38% SDF and SDF/KI significantly prevented root caries in the community-dwelling elders.[25] In another RCT, the same group of researchers reported on the long-term efficacy of SDF with or without potassium iodide (KI) in arresting root caries.[12] The treatment significantly arrested the root caries but the long-term application of KI did not significantly reduce the blackening effect of the SDF on the arrested caries.[15]

In terms of dental hypersensitivity, a short-term study by Castillo et al. reported on the effects of SDF application on tooth sensitivity in Peru. In this study, a micro brush was dipped into SDF solution and applied to the surface for one second and this application found a reduction in tooth sensitivity after 7 days and concluded that SDF was able to reduce dental hypersensitivity.[13]

Another study conducted in Australia by Craig et al. on nineteen patients compared the application of a 38% solution of SDF/KI (SDI Ltd, Melbourne, Australia) with an oxalic acid-based product (Superseal, Phoenix Dental Inc, USA).[26] They found while the oxalic acid-based product failed to produce a reduction in dentine hypersensitivity, this was reduced by the application of the SDF/KI.[26] In an *in vitro* evaluation, Patel et al. found that potassium iodide (KI) was able to minimize the staining effect of SDF.[27]

Gao et al. found that a concentration of 38% SDF was more effective for arresting caries compared to lower levels of SDF such 10% or 12%.[5] Peng et al. recently reported on the amount of silver found in dentine discs with different concentrations of SDF.[10] They found that 38% SDF was more effective in a basal medium mucin (BMM) saliva substitute than in human saliva.[10] The information collected from the various studies indicates that SDF performs better at arresting dental caries than fluoride varnish, fluoride releasing GIC used in interim therapeutic restorations, chlorohexidine, and using only oral hygiene instructions.[28] However, this was not true in all of the cases, such as for non-cavitated molar grooves where it under performed or, at times, had an effect equal to the effect of GIC or resin sealants.[22] The time interval and optimal frequency of usage still remains unclear as the data available are inconsistent but an application every six to twelve months is being promoted.[12] Regarding its efficacy, Chu et al. reported on the microhardness of active carious lesions after the application of 38% SDF every 12 months, and found that there was an increase the hardness of the arrested caries area compared to an area of active caries.[8] The chemical reaction between silver and potassium iodide (KI) is as follows:[29]

$$Ag\,(NH_3)_2F + KI \rightarrow AgI + KF + 2NH_3$$

Glutathione (GSH) is a reducing agent in mammalian cells and acts as an intracellular non-protein thiol (NPSH).[30,31] Sayed et al. studied the effect of GSH on the tooth discoloration by SDF of bovine enamel and dentine specimens and found that, with its reducing agent activity, GSH decreased the color changes after the SDF application, with the results being better for enamel than for dentine.[29]

CLINICAL APPLICATION

A recent publication by the American Academy of Pediatric Dentistry (AAPD) issued an evidence-based clinical guideline that recommends the stepwise chair-side use of SDF for the non-restorative treatment of carious lesions in primary and permanent teeth.[32] This indicates a massive shift from restorative approaches towards preventive approaches with SDF playing a key role in the change.

The non-invasive procedure for SDF application is simple to execute in terms of clinical dexterity. However, the choice of this treatment modality for a specific patient/caregiver, and tooth should be taken carefully after considering the

contraindications and indications for the use of SDF. In order to achieve a successful SDF application the following steps are recommended:

• Application of a protective coating, such as petroleum jelly, on the lips and skin to avoid temporary staining of the soft tissues if they come in contact with SDF.

• Isolation of the teeth to be treated with cotton rolls or other isolation methods in order to protect the gingival tissues.

• To avoid staining, care should be taken when applying SDF on primary teeth neighboring a permanent anterior tooth that may have a white spot lesion.

• The application of the SDF should be done using a micro brush with careful attention in order to prevent intraoral and extraoral soft tissue contact with the SDF. No more than a single drop of SDF should be used for the entire appointment.

• Before applying the SDF, the lesion should be dried gently with a flow of compressed air.

• Care should be taken while transferring the microsponge brush after dipping it in SDF and application of SDF should take place only to the affected tooth surface.

• Excess SDF should be removed with a cotton roll or a gauze to reduce systemic absorption.

• The time of application should be at least one minute if possible. It will differ according to the patient type and it is most likely that it will be shorter for uncooperative and young patients. In these situations the arrest status of the lesions should be reevaluated in recall visits and the possibility of reapplication considered.

• After the SDF has been applied, the medicament should be dried by a gentle flow of compressed air. The isolation can be kept in place for 3 minutes.

• An additional treatment with five percent sodium fluoride varnish can be used to treat the entire dentition to help prevent caries on the teeth at the sites not treated with SDF.

Figures 2A and 2B illustrate a clinical case, a 3 yr-old-boy with early childhood caries, before and after the application of SDF. The hypersensitivity present before treatment was absent after 10 days of treatment with SDF/KI.

SDF has the highest concentration of fluoride available in the market. the 5% SDF solution contains 44,800 ppm of fluoride, almost twice that of 5% sodium fluoride varnish containing 22,600 ppm of fluoride. However, the smaller amount of fluoride in 5% SDF remains enough for it to play its role within safety levels. There are several other products available in the market with different concentrations of SDF (Table).

In 2014, SDF was approved by the US Food and Drug Administration for caries inactivation and the treatment of tooth hypersensitivity.[33] However, in Germany and other European countries SDF has so far mainly been used through an SDF containing product as a desensitizer for hypersensitive teeth (Riva-Star®). The need for using such a product can be represented by the observed caries levels in children.[34-36]

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Figures 2A and 2B. Clinical case before and after the application of SDF. 2A: A three-year-old boy with early childhood caries and a dmft=7. All the cavitated carious lesions were considered as active (score=5; Bjørndal criteria). Hypersensitivity was present; 2B: Arrested carious lesions after 10 days of treatment with SDF/KI. Hypersensitivity was now absent.

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Table. Commercially available silver diamine fluoride (SDF) products

Product	Manufacturer/Country	SDF concentration (%)	Main components
Advantage Arrest	Elevate Oral Care/USA	38%	Silver diamine fluoride
Cariestop	Biodinamica/Brazil	12%	Fluoridic acid, silver nitrate, ammonia hydroxide, deionised water
Fagamin	Tedequim SRL/Argentina	38%	Silver diamine fluoride
Saforide	Toyo Seiyaku Kasei Co. Ltd./Japan	38%	Silver diamine fluoride
Riva Star	SDI Dental Limited/Australia	30–35%	Unit 1: Silver, fluoride, ammonia Unit 2: Potassium, iodine

CONCLUSIONS AND FUTURE CONSIDERATIONS

In conclusion, silver diamine fluoride (SDF) is an inexpensive means of arresting cavitated carious lesions. It is cost effective due to the over-all low cost of the material and the relatively short chair time required for the application. The acceptability can be improved by enhancing the aesthetic side of the treatment. It has a great potential, especially for the treatment of early childhood caries, geriatric patients, as an interim solution for fearful adults, special needs children and patients whose treatment challenged by behavioral or medical issues. The impact of the use of SDF at the epidemiological level can be further evaluated in the future.

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