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Review Article

Precautionary Measures and Clinical Solutions to Overcome the Negative Aspects of Silver Diamine Fluoride: A Comprehensive Review of Literature

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Abstract

Dental caries has a multifactorial etiology and has been a public dental health concern worldwide. Dental caries influences various aspects of the health of pediatric patients. Multiple advantages of using silver diamine fluoride (SDF) have been described in the available published literature. The existing literature reveals that, in recent years, SDF has emerged as a promising option to address the global burden of dental caries in certain clinical scenarios. However, the literature also mentions the negative aspects and demerits of SDF in clinical dentistry. Dental clinicians using SDF should have updated, evidence-based knowledge for its safer and more effective use in managing dental problems, especially dental caries in pediatric patients. Hence, the aim of the current review article was to thoroughly explore and present the literature regarding the negative facets (shortcomings) of silver diamine fluoride and also the precautionary/preventive measures and clinical solutions for its safer and more effective use in clinical practice.

Keywords: Adverse effects, clinical procedure, complications, detrimental effects, evidence-based dentistry, pediatric dentistry, safer use, SDF, side-effects, Silver diamine fluoride, systemic effects

Introduction

Dental caries has a multifactorial etiology and has been a public dental health concern worldwide.[1] The global prevalence of early childhood caries (ECC) in children has been reported to be 48%.[1] Dental caries influence various aspects of health in growing children. ECC has negative effects on the oral health-related quality of life (OHRQoL) of affected children and their families.[2] Pediatric patients suffering from severe forms of ECC experience a greater negative impact. Physical and psychological components of OHRQoL have been reported to be the most influenced components.[2] The current scientific concept or philosophy for managing dental caries has shifted from the traditional surgical approach to a newer medical model/approach, which majorly incorporates the utilization of fluoridated and antimicrobial agents.[3] The traditional "surgical approach" for addressing dental caries has been invasive in nature for dental hard tissue and, in addition, has a higher probability of pulp exposure or loss of pulp vitality in teeth with deep/extensive carious lesions.[3,4] In contrast, the medical model/approach for managing dental caries is considered a non-invasive or minimally invasive modality.[3,4]

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Fluoride in certain forms has been reported to show favorable attributes in caries control and prevention. Dental literature exhibits that, in recent years, silver diamine fluoride (SDF) has emerged as a promising option to address the global burden of dental caries in certain clinical scenarios.[5,6] Many previous studies have revealed that SDF is efficacious in arresting or halting the progress of carious lesions, which is attributed to several mechanisms, such as antibacterial effects, enhanced remineralization of dentine tissue, and preservation of collagen in demineralized dentine of carious teeth.[6,7] Relevant systematic reviews concluded that SDF use can be a therapeutic modality for caries management in cavitated carious teeth among preschool children, especially those with poor access to dental health care facilities/services.[8] Furthermore, uncooperative pediatric patients and children with special health care needs pose a great challenge to dental clinicians in delivering or providing effective and optimal dental treatment for dental caries. In such situations or scenarios, SDF has also been reported as a viable therapeutic or preventive option with clinical success.[9]

Multiple advantages of using SDF have been described in pertinent published literature.[3,5–9] However, the available literature also reflects the demerits or undesirable negative aspects of SDF use in dentistry.[9] Dental clinicians/practitioners using SDF should have evidence-based knowledge and updated information for its safer and more effective use in managing dental problems, particularly dental caries in pediatric patients. Hence, the objective of the current narrative review was to explore and summarize or highlight the relevant literature about the negative aspects of silver diamine fluoride and also the precautionary/preventive steps or measures for its safer and more effective use in clinical practice.

Methods

The relevant literature for the current narrative review was searched in various online databases (PubMed, SCOPUS, Web of Science) and also through manual/hand searches in the Google Scholar search engine, from the list of references of relevant articles, and some relevant dental journals. Pertinent keywords/MeSH terms and combinations were used, such as "Silver diamine fluoride," SDF, "adverse effects," "side effects," complications, adverse systemic effects, acute adverse effects, "negative aspects," drawbacks, limitations, shortcomings, demerits, "SDF in pediatric dentistry," preventive measures, precautionary measures, and clinical solutions to overcome/tackle drawbacks/shortcomings. The full text of relevant published articles was read carefully, and the retrieved literature or information related to the negative aspects of SDF and precautionary clinical solutions/steps/measures to prevent or tackle them has been presented in narrative form in this review article.

Literature Reporting Concerns Regarding Negative Aspects of SDF

To date, although no single adverse effect/acute systemic illness associated with the use of SDF in dentistry has been reported in the available literature,[6] published dental literature reports various undesirable/negative facets of SDF application in dentistry, such as black discoloration (black staining), gingival irritation (gingival pain and swelling), gum bleaching, pulpal inflammation, pulp necrosis, argyria, temporary tattoo on skin or submucosa, silver allergy, metallic/bitter taste, white reversible lesions of the oral mucosa, influence on bond strength with adhesive agents/restorative materials, and risk/concern of toxicity (nausea, vomiting, and generalized discomfort).[4,6,9–16]

Before discussing the unfavorable or gloomy facets of SDF in clinical dentistry, we should first look into the indications and contraindications described by substantial previous published studies for SDF use in dentistry.

Indications for SDF Use

Certain indications for the use of SDF in various clinical dental conditions/scenarios have been described in the available published literature, such as caries arrest and caries prevention in pediatric dental patients; dental management of high caries-risk patients with active cavitated lesions; dentinal hypersensitivity; root-surface caries; secondary/recurrent caries; remineralization of hypomineralized coronal surfaces of molars; patients with uncooperative behavior; patients with special health care needs (SHCN) or with medical management challenges/medically compromised patients having high caries risk; active cavitated carious lesions without any clinical signs of pulpal involvement; and in clinical scenarios where cavitated dental caries lesions are difficult to treat, such as patients having inaccessible dental care facilities, patients with carious teeth which may not all be managed in a single visit/appointment, and in indirect pulp therapy (IPT).[9,13,17–23]

Contraindications for SDF Use

The contraindications of silver diamine fluoride in clinical dentistry include silver allergy, soft tissue ulcerations

(ulcerative gingivitis or stomatitis), active cavitated carious lesions with clinical signs/symptoms of pulpal involvement, symptomatic carious teeth, teeth with periapical pathology, pediatric patients' parents/guardians not giving consent for SDF use, and concerns regarding the blackish discoloration/black staining and unaesthetic appearance of SDF-treated carious teeth.[15,16,23–25]

Various Types of Adverse Effects of SDF and Their Precautionary Measures

Black staining/discoloration

Blackish discoloration/staining is the most common undesirable side effect reported, and it has been directly proportional to the concentration and frequency of application of the SDF agent/solution on the affected tooth.[9,12] Black staining is formed due to the formation of reactionary products of SDF on carious tooth structure (silver phosphate and silver sulfide). Clinically visible discoloration occurs 2 minutes following SDF application, with major visual changes observed after 5 minutes of application. Staining has been mentioned to occur more in regions of carious coronal structure with surface irregularities.[9,24]

Preventive Measures and Clinical Solutions to Overcome the Black Discoloration Problem

SDF should be applied only on the affected carious tooth surface.[15] Prior to SDF application, excavation/removal of carious dentinal tissue of the tooth is not essential.[15,23] However, it may be carried out to achieve comparatively better aesthetic outcomes. Excavation of carious tissue before SDF application may reduce the amount of affected coronal dentinal surface that transforms into a dark black color after SDF application.[15,23]

Optionally, fluoride varnish may be applied over the SDF-treated surface to keep the SDF agent in contact with the carious lesion as far as possible, preclude saliva from diluting the applied SDF from the tooth, and lessen the risk of unacceptable blackish stain on other tooth surfaces.[25]

Discoloration/staining may be removed/polished off through more invasive measures/modalities.[15] Sometimes, even with polishing methods, discoloration remains, especially at the restoration margins of the affected tooth. Owing to the metallic nature of the blackish stain/discoloration, bleaching modalities do not remove this black discoloration.[15] It is crucial that pediatric patients' parents/guardians are informed pre-operatively about the potential for black discoloration/staining of the carious tooth structure and restoration margins due to SDF use.[15]

To avoid inadvertent black staining/discoloration of the permanent anterior teeth in patients with non-cavitated carious lesions (e.g., white spot lesions/incipient caries), care should be taken to prevent contact between the SDF solution and these teeth during its application on carious posterior teeth or anterior primary teet.[15,23] A separate/new applicator tip/brush should be used to apply fluoride varnish over the SDF-treated surface of the tooth (if varnish is used optionally after SDF application).[25]

The aforementioned blackish discoloration, a side effect of SDF, can be mitigated by using potassium iodide, as described in the relevant published literature.[26,27] The chemical reaction behind such an advantage of potassium iodide is that SDF reacts with potassium iodide, forming silver iodide and tri-potassium phosphate. Tri-potassium phosphate is "white" in color, which hides/conceals the black discoloration of arrested carious dentin.[27]

Procedure for Masking Black-Stained Arrested Carious Dentin Using Potassium Iodide

Petroleum jelly can be applied to the adjacent gingiva, and the tooth can be isolated using a rubber dam. Then, the affected carious tooth surface should be dried, and SDF should be applied over the caries using a microbrush. After waiting for one minute, excess SDF can be removed from the carious surface with cotton. Potassium iodide can then be applied over the SDF-treated tooth using a disposable micro applicator. Finally, the tooth can be restored with appropriate adhesive restorative materials (GIC or RMGIC).[27]

Zhao et al[26] reported that potassium iodide in combination with SDF does not impact the bonding strength of GIC to the SDF-treated dentin. However, a systematic review (2020) concluded that there is weak evidence for potassium iodide in diminishing the black discoloration caused by SDF application.[28] No serious adverse events were reported with either material (SDF alone or SDF with potassium iodide), as per recent studies.[28]

Although guardians/parents of pediatric patients perceived black discoloration, they were satisfied with the beneficial effects of SDF on dental caries and were open to compromising aesthetics (black staining) in favor of using the minimally invasive approach of SDF.[29,30] Thus, SDF use for caries management has been accepted by the majority of parents and children.[29,30]

Other solutions/methods to tackle the black discoloration drawback of SDF agents have been mentioned in recent literature.[31] There is a need to explore addi-

tional antimicrobial agents to augment or substitute silver, decreasing the need for high concentrations of ionic silver. Such substitutions with other antimicrobial metals have been reported to decrease the tendency of SDF to cause blackish staining of carious lesions.[31]

Silver nanoparticles (AgNPs) and nanoparticles of silver fluoride (nano-silver fluoride) have been suggested in the relevant literature to overcome the above-mentioned undesirable demerits of SDF use for caries arrest.[31,32] Since oxidation appears to be a primary cause of black staining/discoloration of SDF with carious tissue, incorporating selenium nanoparticles (SeNPs), which possess antioxidant properties, may have an anti-staining beneficial role.[31] SeNPs can also be employed for their antimicrobial nature.[31] Recent literature has suggested future research in the context of SeNPs.[31]

Oral Mucosal Lesions

Literature describes that, owing to the higher alkalinity (high pH) of the SDF agent, mucosal or skin burns may occur during contact with mucosal/skin surfaces in patients after SDF use on carious teeth. It has been reported that these burn-like lesions tend to be small (localized), slightly painful, white lesions on the oral mucosa. However, these lesions disappear/resolve after about 48 hours (2 days) without any active treatment.[10,13,16]

Precautionary Clinical Measures and Management

The aforementioned smaller, white-colored mucosal lesions in the oral cavity can be managed clinically by following some preventive or precautionary steps/measures such as complete isolation using a rubber dam during SDF therapy.[16] However, since this is not always feasible, other alternative ways of isolation should be considered, e.g., light-cure liquid dam material or at least petroleum jelly and a cotton roll can be used for isolation purposes to protect the soft-tissue surfaces adjacent to the treated carious tooth.[16] Pertinent literature reveals that SDF-treated carious lesion surfaces should be dried gently with a cotton pellet or a moderate stream of compressed air, keeping the rubber dam in place for approximately 3 minutes.[15,23] However, drying the SDF-treated tooth surface with a cotton pellet instead of employing compressed air avoids the generation of aerosols containing microbes during SDF application.[25]

At a single appointment/visit, only a very calculated amount of SDF solution (one drop) should be used wherever possible for caries management. It has been reported in the literature that one drop of SDF solution is usually adequate to treat 5–6 carious teeth.[15,23] To further reduce the amount of SDF solution before application, the brush should be dipped into the SDF solution and tapped against the side/wall of the plastic dappen dish.[15] Therefore, using an appropriate amount/volume of SDF solution and employing effective isolation methods during SDF therapy can minimize or eliminate the possibility of SDF contact with oral mucosal surfaces and white lesion occurrence.[15,16]

For carious proximal surfaces, woven unwaxed floss should be used carefully by placing the dry "fuzzy" portion of the floss into the dry, isolated contact. The SDF should then be applied to the floss with a micro-brush applicator on the buccal, lingual, and occlusal aspects of the carious tooth.[25] The floss should not be moved, and after 1 minute, it may be removed carefully. It is also imperative to protect the adjacent soft tissues in the oral cavity (e.g., with the help of a gloved finger) from any SDF solution migrating along the floss.[25] Literature also suggests that placing a gauze pack inside the oral cavity is necessary to protect the tongue and cheek during SDF use.[13,16]

Gingival Lesions After SDF Application and Precautionary Measures

Relevant literature reveals that transient gingival irritation, gingival erythema, gingival swelling, gingival bleaching, and gingival pain may seldom occur after SDF application for dental caries treatment, although its incidence is reported to be very low.[12,15,16,33,34] The precautionary clinical measures mentioned in the previous paragraph/section should similarly be undertaken to prevent this side effect.[15,16,23,34]

Dermatologic Problems

Temporary henna-appearing tattoos (skin pigmentation) have been mentioned in the available literature as occurring when SDF remains in contact with the skin (e.g., lips).[14] This effect is temporary in nature because silver does not penetrate into the dermis. Desquamation of the skin (natural exfoliation) along with pigmentation occurs. Keratinocytes shed off over a period of 2–4 weeks, and thus, the problem resolves spontaneously.[14]

Argyria, a dermatologic side effect characterized by greyish or bluish discoloration of the skin or mucosal surfaces, occurs due to prolonged or frequent exposure/ingestion of silver metal.[14]

Precautionary Clinical Measures and Clinical Solutions

The above-mentioned adverse effects of SDF can be avoided by following precautionary clinical measures/steps such as applying a protective coating of petroleum jelly over the lips/vermilion border to prevent transitional henna-appearing pigmentation (tattoo). The decayed teeth to be treated should be isolated using rubber dams, cotton rolls, or other appropriate alternative methods. Careful application and handling of SDF using a microbrush applicator tip can prevent intra-oral and extra-oral soft tissue exposure to SDF. Minimal (appropriate) volumes of SDF solution should be used.[15] Additionally, dental clinicians should wear masks, gowns, gloves, etc., to avoid skin staining from the SDF agent.[25]

Metallic/Bitter Taste and Precautionary Clinical Measures

Published literature reports that patients may experience a metallic or bitter taste during or after SDF application.[13,16] This drawback can be overcome by removing/wiping any excessive amount of SDF liquid from the carious tooth surface with a cotton pellet or gauze piece.[13,16] Optionally, applying fluoride varnish over the SDF-treated tooth surface may help mask the undesirable bitter or metallic taste.[25]

Pulpal Necrosis and Precautionary Clinical Measures

Substantial literature reveals that SDF demonstrates promising or favorable attributes as an indirect pulp-capping (IPC) material and for use in deep dentinal caries.[4,12,16] Its capacity to arrest dentinal caries can also minimize the risk of iatrogenic pulpal exposures by decreasing the amount of carious tooth structure requiring excavation.[16]

Relevant literature describes that SDF does not cause severe pulp damage. Mild inflammatory responses in the underlying pulp and reactionary/reparative dentin formation have been reported after using SDF as an IPC material, suggesting that SDF is usually biocompatible for IPT procedures.[4,35] However, direct application of SDF to pulp tissue has been reported to cause necrosis in limited cases.[4]

Systemic Adverse Effects

None of the published studies related to SDF use in pediatric dentistry have reported symptoms of acute toxicity or systemic illness, including nausea, vomiting, or generalized discomfort after treatment.[12,13,15,17,21,36] However, due to the higher concentrations of fluoride and silver in SDF, there is concern about adverse consequences, particularly for young pediatric dental patients.

Although a higher concentration of SDF is more efficacious compared to a lower concentration in halting active dental caries [6,11,12], the long-term effects of repeated or prolonged exposure to silver compounds have not been fully described in the published literature.[36,37]

Precautionary Clinical Measures and Clinical Management

The probability of occurrence of the aforementioned systemic effects from SDF use can be minimized through appropriate and judicious application at the dental clinic.[13,15] Excessive SDF solution should be removed using cotton to reduce the risk of systemic absorption into circulation.[13,15] SDF should be applied for a duration of 1 minute and gently dried using compressed air.[15] The SDF-treated tooth/teeth should remain isolated for at least 3 minutes after application.[13,15]

In cases of accidental ingestion of a larger amount of SDF during treatment, vomiting can be induced to prevent systemic absorption. Relevant literature suggests that administering 10% calcium gluconate solution (10 mL) may help mitigate systemic absorption. Calcium ions (Ca^{2+}) react with fluoride ions (F^-) to form insoluble calcium fluoride (CaF_2), which cannot be absorbed systemically in the gastrointestinal tract.[14,38]

Impact on Bond Strength of Restorative or Adhesive Materials

Literature shows inconclusive findings about the influence of SDF application on the bond strength or bonding with restorative materials.[16,39,40] A study by Markham et al[41] reported that SDF application on the tooth surface reduces the bond stability of composite or GIC to both enamel and dentinal surfaces when universal adhesives are used. Most of the failures or drawbacks have been described as due to adhesive failure and surface contamination by the SDF agent [41]. Hence, it was suggested that SDF solution should not be applied to the entire surface of the tooth that is to be bonded.[41] However, Siqueira et al[42] reported that the application of silver diamine products enhances the micro-tensile bond strength. Similarly, Firouzmandi et al[43] mentioned that SDF use increases the bond strength of decay-affected dentin of the tooth; however,

it does not have any impact on normal dentin. It has also been mentioned in pertinent literature that using a contemporary bonding system, SDF application had no negative influence on composite bonding to the non-carious portion of dentin by either full-etch or self-etch systems.[43] Therefore, further research is still required to explore deeply the effect of SDF on bond strength or bonding with other dental restorative materials.

Precautionary Clinical Measures and Management

Preventive measures to overcome the above-mentioned unwanted effects of SDF on bonding are as follows: SDF should be applied carefully or precisely onto the carious dentinal surface wherever feasible to decrease the SDF contamination of the sound enamel surface.[16] Simply rinsing after SDF application can avoid a 50% decline in GIC bond strength.[13] Rinsing of the SDF-treated surface will be sufficient for direct restorations, whereas excavation of the SDF-treated superficial dentin of the tooth is appropriate for cementing artificial crowns.

If SDF and potassium iodide (KI) are to be used together, then it is necessary that the generated precipitate be washed (rinsed) and then air-dried properly prior to the application of the adhesive agent or restorative material.[16] Furthermore, literature exhibits that the use of a conditioning agent or acid etching process after (SDF + KI) application can further ameliorate bond strength.[16] Literature has also mentioned that the adhesive bond strength may be improved by the process of surface abrasion.[16] However, there is a lack of clinical research to demonstrate this.[16] If adhesive resin cement is to be used for cementation or luting of the prosthetic crown, then more invasive measures may be needed, such as partial (superficial) excavation of SDF-treated dentin.[13,16] A risk of iatrogenic exposure of the underlying pulp must be assessed on a clinical case-based basis prior to the partial removal of superficial carious dentin.[16]

Non-Restoring/Non-Rehabilitating Nature and Clinical Solutions

Pertinent literature mentions another shortcoming of SDF: it does not actually treat or eradicate dental caries; instead, it halts or arrests the carious process of the tooth surfaces.[15] It may aid in the remineralization of the carious lesion if the intra-oral environment is favorable or conducive. However, SDF is unable to restore the lost tooth structure.[15,44] Furthermore, when there is a substantial breakdown or loss of coronal tooth structure, the occlusal relationship and long-term clinical outcomes may worsen or deteriorate if rehabilitation of form and function of the SDF-treated tooth is not performed.[15,44]

Permanent Black Staining of Working Surfaces at Dental Clinics

SDF has also been described as causing permanent black-colored stains on most surfaces of clinical armamentarium, instruments, counters or tables, and clothing when it comes into contact with the SDF solution.[17]

Precautionary Clinical Measures and Management

Spillage due to SDF should be cleaned up promptly with copious water, ethanol liquid, or a bleach agent.[13] A high pH (alkaline) solvent such as ammonia (NH_3) may be more effective in resolving the said problem.[13] Furthermore, secondary containers and plastic liners (sheets) for work surfaces or tabletops in dental clinics have been discussed in published literature as adequate preventive measures.[13] Plastic bibs or aprons for patients during dental procedures have been described as a precautionary step to tackle such staining drawbacks of SDF use.

Instructions to Patients After SDF Application

Relevant literature mentions that no post-operative instructions are available from SDF manufacturers.[15] However, several studies in the context of SDF suggested restricting the consumption of food and drinks after SDF application for 30 minutes to 1 hour.[15] Follow-up visits are advised at 2- to 4-week intervals after the initial SDF treatment to evaluate the arrest or halt of the SDF-treated carious teeth (i.e., hardened and darkened arrested carious lesions).[15] Re-application and additional SDF application at the recall visits may be needed based on the clinical evaluation in terms of hardness and the color appearance of the cavitated carious lesion or evidence of caries lesion progression.[13,15,17] The teeth with caries can be restored after SDF therapy using GIC (as SMART restoration procedure), resin-modified glass ionomer cement (RM-GIC), or composite resin materials. When carious lesions of teeth are not restored or rehabilitated after SDF application, biannual re-application (i.e., every six months) is advised to enhance caries arrest as a preventive approach.[15]

Significance of Informed Consent

One of the most important aspects before commencing the use of SDF on a patient in clinics is obtaining informed written consent from parents or guardians and

assent from pediatric patients after explaining the procedure with SDF, as well as the advantages and disadvantages of the SDF agent. Patients should be informed about the possibility of black discoloration of SDF-treated teeth, transient skin staining, clothing stains, and the need for re-application of SDF at follow-up visits.[15,17,45]

Global Perspective About SDF Use

Relevant published literature reflects that there are no unified guidelines or recommendations for using SDF for caries management from international associations or organizations related to dentistry.[6] A need for substantial research in the context of SDF has been advised to furnish more scientific evidence to support an identical protocol for SDF-based therapy in dentistry.[6] Almost all dental colleges or institutes usually incorporate SDF in their clinical training programs for dental students or clinicians, mainly in pediatric dentistry departments or sessions.[6] However, the training sessions for dental students are usually brief or shorter, and specific or definite clinical training for SDF therapy is rare to find.[6] It has been reported in a recent published article that dentists in several countries either did not know about SDF well or did not use it frequently in their dental clinics.[6]

Although SDF use has been accepted as a simple, non-invasive (conservative), and inexpensive (cost-effective) modality for managing dental caries in young children, older individuals, and people with special health care needs (SHCN), it has also been mentioned in literature that SDF use can be a cost-effective strategy adopted for community-based dental programs.[6]

In recent years, phosphorylated chitosan nanoparticles, NB-TCP modified by chitosan NPs, or chitosan nanoparticles have been evaluated by *in-vitro* studies and concluded that the aforementioned remineralizing agents showed promising results in terms of remineralization and microhardness of the enamel surface or caries in comparison to SDF or other traditional remineralizing agents.[46–48]

Conclusion

Various undesirable negative aspects of silver diamine fluoride (SDF) and their precautionary or preventive methods and clinical solutions have been reported in the available published literature to tackle or overcome the unfavorable outcomes of SDF. Dental clinicians, including pediatric dentists, should be aware of the aforementioned precautionary and preventive steps or measures and clinical solutions. Hence, proper case selection, clinical evaluation of the patient (past medical history, dental history, and clinical examination), regular follow-up, dentist's updated knowledge, and sound clinical skills (i.e., evidence-based dental practice) are significant facets to ensure safer and more effective SDF use in dentistry. In the future, more standard high-quality studies or research are needed to ameliorate treatment outcomes with SDF and to scientifically explore better alternatives to SDF with no such shortcomings.

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