REVIEW ARTICLE

The Rising Horizon of Silver Diamine Fluoride as an Anti-Caries Agent in Pediatric Dentistry: A Narrative Literature Review

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ABSTRACT

The field of pediatric dentistry has been greatly evolving, bringing forth a vast repertoire of innovations, techniques, and advances in its different streams. Among the various domains of pediatric dentistry, it is the arena of preventive pediatric dentistry or more aptly called "minimally invasive dentistry" that has emerged as an important concept in the modern oral health care system. Out of the several preventive regimens available in pediatric dentistry, silver diamine fluoride (SDF) has been the material of choice as an anti-caries agent for arresting further progression in incipient carious lesions. SDF is known for its excellent antibacterial, anti-cariogenic, remineralizing, and desensitizing properties that enhance patients' acceptability toward a non-invasive preventive approach than for an invasive oral procedure. Not only its superior properties but also its better handling characteristics of an easy, quick, and hassle-free application have made SDF highly convenient to use in day-to-day clinical practice. SDF has proved to be a boon in the case of children who lacks access to the conventional oral health-care set-up or in children with special healthcare needs to maintain a caries-free oral environment. However, there is a major disadvantage associated with SDF application and it is the appearance of blackish stains on the teeth surfaces applied with SDF. This unaesthetic appearance, however, can be easily overcome by the use of a saturated potassium iodide solution or the use of glass ionomer cement or composite to mask the stained teeth surfaces. Several evidence-based studies and clinical trials have been conducted to gain insight into the mechanism of action of SDF, which is yet to be unraveled. Hence, this narrative literature review presents a succinct account of SDF emphasizing strongly on its evolutionary trend, debated mechanism of action, and specific procedural steps to use it in a clinical set-up.

Key words: Anticariogenic, minimally invasive dentistry, potassium iodide solution, preventive dentistry, remineralization, silver diamine fluoride

INTRODUCTION

"Prevention is better than cure" - this well-known adage given by the famous Dutch philosopher "Desiderius Erasmus" in 1500 still holds high significance and has become a fundamental principle of modern healthcare, especially in the rising horizons of oral health care. The management of dental caries was based on an earlier notion that it was a progressive infectious bacterial disease, which eventually results in loss of tooth structure until and unless any restorative or surgical intervention is undertaken to rehabilitate the tooth structure. However, in the present era of modern dentistry, there has been a paradigm shift in the management of dental caries moving from a restorative or surgical approach to a preventive or conservative mode of treatment, which strongly highlights the importance of the preventive aspect in the domain of cardiology.[1] Preventive dentistry helps in the early diagnosis and management of incipient carious lesions which enables clinicians

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to halt the caries progression with the help of suitable preventive approaches.[1] Dental caries is undoubtedly preventable in nature and early identification of its risk factors along with the implementation of preventive oral treatment at a young age can reduce the onset of new carious lesions and its further progression since preventing the initiation of caries through the use of different advanced approaches is more cost-effective than treating its advanced form.[2,3]

The American Academy of Pediatric Dentistry (AAPD, 2008) has defined "Early childhood caries" (ECC) as the presence of one or more decayed (non-cavitated or cavitated lesions), missing (due to caries) or filled tooth surfaces in any primary tooth, in a child of 71 months of age or younger.[4,5] ECC is the most prevalent chronic infectious oral disease in children globally that causes serious life-threatening consequences if left untreated. Uribe *et al.*, (2021) stated the overall prevalence of ECC to be 48% worldwide and 49.6% in India.[6] ECC clinically manifests as white-spot lesions in the upper primary incisors along the margin of the gingiva. ECC, if remains untreated can progress rapidly affecting the entire primary dentition leading to complete loss of teeth and eventually affecting the overall quality of life in a child.[7] Early diagnosis and treatment of ECC is highly important for preventing severe pain, infection, impairment of masticatory function, phonetics, aesthetics, and further deterioration in the quality of life. However, further progression of the incipient carious lesions can be prevented by the application of different anti-caries agents and a conservative mode of treatment. Early detection, use of evidence-based preventive approaches, and prompt management of incipient lesions can greatly improve a child's oral and general health, leading to a healthy life and well-being.[8]

Different kinds of anti-caries preventive agents are available in pediatric dentistry such as different forms of fluoride agents (fluoride gels and varnishes), pit and fissure sealants, nano silver fluoride, atraumatic restorative treatment, silver-modified atraumatic restorative treatment (SMART) materials (amorphous calcium phosphate releasing pit and fissure sealants, casein phosphopeptide-amorphous calcium phosphate), preventive resin restoration, resin-based flowable composite, composite adhesive resin restoration, and silver diamine fluoride (SDF).[9-18] Out of all the preventive agents available in pediatric dentistry, SDF is one of the widely used anti-caries agents known for its superior remineralizing and excellent caries-arresting properties.[19]

SDF is a topical fluoride solution that has been used in a concentration of 38% (44,800 ppm fluoride) globally since the early 1970s.[20] SDF is known to possess excellent anti-cariogenic, remineralizing, and desensitizing properties.[19] It is cost-effective, safe, and easy to use for arresting incipient carious lesions. The U.S. Food and Drug Administration (FDA) gave its clearance in August 2014 for the first preparation of SDF to be used orally in the United States and has been made available for use since April 2015.[20] Horst *et al.* (2016) have reported that SDF can be suitably used for community oral health programs due to its cost-effectiveness and has been extensively used as an anti-caries agent with a recommended annual or biannual application.[21]

SDF has been extensively used to prevent the caries progression in the primary teeth of children and in the occurrence of pit and fissure caries in the erupting permanent molars.[22] Use of SDF has been highly suggested in children with high caries risk indicators, medically compromised, and in children with special healthcare needs.[23] Apart from the management of carious lesions, SDF is also used to treat teeth hypersensitivity and in sterilizing the infected root canals of the teeth. SDF has also been shown to be effective in reducing the enamel carious lesions affecting both primary and permanent teeth.[24] The effectiveness of SDF in arresting dentinal caries of primary teeth has been stated to range from 65% to 91%.[25]

The American Dental Association has stated that arresting early carious lesions have become an important aspect of caries management to prevent its serious consequences.[26] Following the caries arrest with the use of SDF, an atraumatic restoration of the tooth is done to make the surface more cleansable so that a combinational therapy of caries arrest and subsequent restoration can yield higher treatment outcomes, popularly known as the SMART.[27] SMART procedures combine both the advantages of the anti-bacterial and remineralizing characteristics of SDF to arrest caries along with the additional properties of being an atraumatic, minimally invasive, and highly effective caries preventive technique. However, the most significant disadvantage associated with SDF application is the occurrence of blackish staining of

the teeth caused due to the formation of the silver oxide precipitate, which can be overcome by two suggested alternatives. One of the alternatives is to use a saturated potassium iodide solution, which can react with the residual silver ions to eliminate this staining effect. The other alternative technique is to apply glass ionomer cement or composite over the SDF-applied surfaces to mask the stained carious lesions.[28]

SDF has therefore proven its mark as an excellent anti-caries agent in the domain of pediatric dentistry and it continues to be used globally as an effective preventive approach due to its advanced clinical and better handling properties. Hence, this scientific narrative review of the literature highlights the various important aspects of the SDF and its use in pediatric dentistry to aim toward a more conservative mode of treatment in children, thereby instilling a positive attitude toward dental treatment.

EVOLUTION OF SDF

The use of silver in dentistry was reported as early as the 1840s, which dates back to the use of silver nitrate for arresting dental caries. Silver nitrate was used mostly due to its disinfectant nature for the management of caries based on the infectious nature of dental caries.[29] Howe (1917) reported the use of an ammonical silver nitrate solution referred to as "Howe's solution," which was directly applied onto the surface of the carious lesions.[30] Howe's solution was believed to penetrate caries-affected dentin to demonstrate its antibacterial effect. It was used until the 1950s and eventually, its oral use got diminished with the introduction of fluorides as an anti-caries agent.[29] The combined effect of silver and fluorides have been hypothesized to not only halt the ongoing caries progression but also to further prevent the development of new carious lesions.[31] A combined application of silver nitrate solution having strong antibacterial action and sodium fluoride varnish with good remineralizing properties was also introduced for managing carious lesions.[32]

The use of ammonical silver fluoride to arrest dental caries was first pioneered by Dr. Nishino and Yamaga in Japan, who developed it to combine the actions of fluoride (F^-) and silver (Ag^+) ions that led to the approval of the first SDF product: "Saforide" (Bee Brand Medico Dental Co, Ltd, Osaka, Japan) in the 1970s.[33] In the 1970s, SDF was accepted as a therapeutic agent for arresting dental caries by the Central Pharmaceutical Council of the Ministry of Health and Welfare in Japan. It has also been widely used in countries such as Argentina, Australia, Brazil, and China for many years to treat dental caries.[34] In 2014, the FDA gave the clearance for the use of the first SDF product in the USA.[20]

MECHANISM OF ACTION OF SDF

SDF is known to possess excellent antimicrobial, remineralizing, and desensitizing properties.[19] The exact mechanism of action of SDF is not yet known. However, it is hypothesized that F^- ions act mainly on the tooth structure, while Ag^+ ions like any other heavy metals are antimicrobial in nature. Owing to this antimicrobial nature, the Ag^+ ions can easily destroy the cell wall structure of bacteria and inhibits not only the enzymatic activities of collagenase but also cell processes such as deoxyribonucleic acid (DNA) replication, formation of the cell membrane, functioning of the cell wall, and biofilm formation. To conclude, the Ag^+ ions can highly influence the metabolic process of a bacterial cell.[35]

SDF is also known to inhibit the demineralization process of hydroxyapatite crystals in teeth which eventually helps in preserving the collagen fibers from further degradation in the demineralized dentinal tissue. SDF reacts with the hydroxyapatite crystals of a tooth in an alkaline medium to form calcium fluoride (CaF_2) and silver phosphate (Ag_3PO_4) as the major reaction products. CaF_2 provides sufficient fluoride release for the formation of fluorapatite crystals [$Ca_{10}(PO_4)6F_2$] which is less soluble than hydroxyapatite crystals in an acidic environment, while (Ag_3PO_4) and (CaF_2) together aid in reducing the patency of dentinal tubules.[36] Collagen is usually degraded by matrix metalloproteinases (MMPs) and cathepsins, which get activated due to the low pH in carious dentine. Thus, SDF inhibits the enzymatic activity of MMPs and cathepsins to further prevent any breakdown of collagen fibers.[37]

SDF also has a pivotal role to play in the disruption of the biofilm and promoting anti-caries effect through a phenomenon known as the "zombies effect." The concept explains that the biocidal-killed bacteria are capable of killing the living bacteria since the dead bacteria acts as a reservoir of silver, which due to the Le-Chatelier's principle gets retargeted towards the living bacteria.[38,39] The Ag^+ ions affect the bacteria by interacting with their proteins and DNA to inhibit bacterial cell wall synthesis, DNA synthesis, and induce mitochondrial

failure. Therefore, these bactericidal properties as well as bacteria killed by silver plays an important role in the dental plaque biofilm's disruption and provides full mouth caries protection through the "zombie effect," whereby living bacteria are killed on contact with silver-affected bacteria.[39-41]

Despite the well-known notion that the mechanism of action of SDF is still highly contested and only partially understood in the scientific domain, however, the most important underlying concept explains that the demineralized dentinal surfaces treated with SDF demonstrate significantly less growth of cariogenic species compared with those not treated with SDF.[40,41]

IMPORTANCE OF SDF

The present era of modern dentistry greatly emphasizes the concept of minimally invasive dentistry that aims toward a multitude of preventive approaches and one such promising tool in the field of preventive dentistry is the emergence of SDF. SDF has undoubtedly proven its mark as an efficient anti-caries tool in the management of carious lesions developing at an incipient stage.[18] The combined effects of the remineralizing and antibacterial properties of SDF make it as one of the most effective cariostatic agents along with the added advantages of better handling properties such as easy, fast, and hassle-free application in children at different clinical set-ups.[31] SDF serves an indirect advantage of facilitating space maintenance in case of primary/mixed dentition by avoiding the extraction of a tooth through the process of caries arrest at an incipient stage. SDF is also known to help improve the level of cooperation in case of anxious or pre-cooperative children mostly due to its minimally invasive approach.[20,37] Horst *et al.* (2016) stated that SDF can be suitably implemented for use in community oral health programs due to its cost-effectiveness, easy mode of application, and superior anticaries properties, thereby recommending its application annually or biannually as an anti-caries preventive agent.[21] However, SDF has certain disadvantages as well, such as an unpleasant metallic taste, staining clinical surfaces and clothes, and gingival and mucosal irritation, while the most important disadvantage associated with SDF after its application has been the characteristic irreversible blackish staining of teeth.[42]

Chibinski *et al.* (2017) and Trieu *et al.* (2019) have stated that SDF is highly effective in arresting further caries progression and development of new lesions,[43,44] thereby suggesting it to be indicated in children with high caries risk, active carious lesions on any surface of the anterior or posterior primary teeth, newly erupted permanent first molars, children with multiple lesions requiring frequent, and also in children with special health care needs.[26] Use of SDF is highly recommended in children who lack access or have difficulty with conventional oral care such as in special care children, where the availability of extensive treatment approaches are very limited, or in children not very amicable towards dental treatment. SDF is also indicated in teeth affected with molar incisor hypomineralization to reduce dentinal hypersensitivity and to slow down the rate of caries progression.[21] Despite its several clinical indications, SDF has also been found to be highly contraindicated in teeth showing clinical signs or symptoms of irreversible pulpitis, dental abscess, fistula, radiographic signs of pulpal involvement, and peri-radicular pathology. Furthermore, SDF cannot be applied in children having active non-arrestable carious lesions.[45,46] However, SDF is relatively contraindicated in children having oral ulceration, mucositis, stomatitis, and a history of allergy or intolerance toward silver, fluoride, or ammonia.[46]

PROCEDURAL STEPS TO USE SDF

SDF has a wide range of applications in pediatric dentistry because of its easy, simple, quick, and non-invasive nature of the application. Better handling properties of SDF allow clinicians to use it in a short duration of time and with minimal clinical expertise.[23] The clinical use of SDF has important steps, which start with removing gross debris from the incipient lesions to facilitate better contact of SDF with denatured dentin. However, AAPD guidelines have stated that excavation of carious dentin before SDF application is not always mandatory.[23] After the removal of debris from the carious lesions, a protective coat of petroleum jelly is applied to the lips and skin to prevent the temporary staining associated with SDF. This is followed by the isolation of teeth using cotton rolls or under a rubber dam. A microbrush is used to apply SDF onto the tooth surface and its careful use will prevent exposure of intraoral and extraoral soft tissue to SDF.[23,47] The microbrush is dipped into the plastic dappen dish containing SDF followed by dabbing the microbrush onto the side of the dappen

dish to remove excess fluid before application. The dampened microbrush with SDF is then applied onto the affected tooth surface for a duration of at least one minute. Thorough isolation of the teeth for 3 min along with a gentle flow of compressed air after the application of SDF will facilitate drying. Post-application of the SDF, the entire dentition needs to be treated with 5% sodium fluoride varnish to prevent any occurrence of caries in untreated teeth with SDF.[47]

A follow-up after 2–4 weeks of post-treatment is highly recommended to inspect whether the treated lesions are arrested or not, whereas reapplication of SDF is recommended if the treated lesions do not appear arrested (dark and hard in consistency).[44] Additional coats of SDF can be applied on recall appointments based on the color and hardness of the lesion or in case of any evidence of lesion progression. Post-application of SDF, the arrested lesions can be restored using suitable restorative material.

ADVANCED ANTI-CARIES AGENTS

Antibacterial and Antimicrobial Agents

Antimicrobial peptides

They are produced by the salivary glands and the oral epithelium having defensive action. Short antimicrobial peptide molecules include histatins, human lactoferrin 1-11 (hLF1-11), cathelicidins (LL37), $(CKPV)_2$, histatin 5 derivative (P-113), and LKW peptides.[48]

Probiotics

They are living microorganisms that are safe for human consumption and provide multiple health benefits on adequate intake. It improves the adaptive immune response and serves as an efficient anti-caries agent.[49]

Ozone

Recently, ozone is used as a caries preventive agent since it eliminates the bacteria associated with caries. It should be applied for a period of 10–50 s to make a carious lesion reversible in nature. Remineralizing solution and fluoride rinses can be effectively used following ozone application which deactivates almost 99% of the bacteria.[50]

Use of fissure sealants in combination with ozone treatment

A combination of sealant and ozone treatment can be used as a preventive approach since ozone pretreatment favorably affects the marginal sealing ability of the fissure sealant.[51]

Nanoparticles of amorphous calcium phosphate (NACP)

NACP is a novel mineralizing material in preventive dentistry. The "smart" NACP nanoparticles exhibit excellent physical and mechanical properties, which significantly increase the Ca^{2+} and PO_4^{3} ions to be released at a low pH while possessing mechanical properties nearly 2 times that of $Ca_3(PO_4)_2$ composites.[52]

CONCLUSION

The existing scientific evidence has strongly proved SDF to be a golden bullet having superior clinical properties meant for caries prevention and has brought about a transformative change in the present era of modern preventive dentistry. However, not only the clinicians should be adept in using this miraculous caries-preventive agent but also there has to be adequate awareness amongst the parents/caregivers regarding the use and benefits of SDF. Its superior properties and better handling characteristics further ignite extensive clinical research and broaden its horizon toward the innovation of newer materials with added advantages such as the ongoing trials over the efficacy of nanoparticles-infused SDF material. Undoubtedly, SDF is a promising caries-preventive agent that halts further caries progression and prevents several of its serious consequences.

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