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Review Article

Prospects of silver diamine fluoride (SDF) in reducing dentin hypersensitivity: An updated review

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ABSTRACT

Dental Hypersensitivity (DH) is a common clinical condition yet an annoying disease. Most of the time, clinicians fail to diagnose, leading to improper management and unsatisfied patients, negatively impacting their quality of life. The management involves various self-applied and in-office management modalities. This review briefly discusses several treatment options available for dentinal hypersensitivity and recommends Silver Diamine Fluoride (SDF) as a newer and more effective treatment option for dentinal hypersensitivity based on the available literature.

1. Introduction

Dentin hypersensitivity has been defined as a *"short, sharp pain arising from exposed dentin in reaction to stimuli that can be thermal, evaporative, tactile, osmotic or chemical and which cannot be attributed to something related to any other dental defect or pathology"*.[1–4] This pain ranges from slight to severe, can lead to physical, psychological, and social disability and may significantly impact patients' quality of life.[5,6] Patients may report changes in eating habits, oral hygiene neglect or modification, sensitivity while consuming cold food or drinks, or require local anaesthetic for routine dental appointments.[7] Depending on the types of diagnostic techniques used and the population explored, the prevalence of dentine hypersensitivity currently varies from 3% to 98%.[8,9] In older patients with periodontitis, the incidence of tooth hypersensitivity can reach as high as 60% to 98%.[7] Compared to men, women experience it more frequently, with the peak age of occurrence between 30–49 years of age and canines followed by premolars being the most commonly affected teeth.[4,10] Based on these demographic and health trends, there is a probability that the number of patients reporting pain due to DH will increase. Accordingly, to reduce life-long discomfort linked to DH, dental professionals should be trained to accurately diagnose and manage the condition if it is not preventable.[7]

There is still no agreement about the underlying mechanism that causes tooth hypersensitivity. Based on the direct innervations theory, the nerve's endings from the pulpal complex enter the dentin and extend to the dentinoenamel junction,[11,12] and mechanical stimuli directly transmit the pain. However, there is little evidence to support the existence of nerve in the superficial dentin. Presently, the most widely accepted hypothesis is Brannstrom's hydrodynamic theory,[9] which states that any thermal, tactile, or chemical stimuli close to the dentinal tubules can change the direction or increase the flow of fluid within dentinal tubules, and, this alteration would lead to stimulation of the A-δ fibres surrounding the odontoblasts. This presumptive theory necessitates the tubules be open inside the pulp and on the exposed dentin surface so that

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the fluid movement triggers baroreceptors and causes neural discharge, resulting in painful sensations.[12]

The first step toward treating dentine hypersensitivity is making sure the clinician makes the right diagnosis through a clinical examination and thorough history taking, and the aetiology is addressed by providing proper oral hygiene instruction and dietary advice.[13] Also, before establishing a final diagnosis of DH, the other causes of dental pain, similar to tooth hypersensitivity, should be ruled out.[1] The diagnosis of DH involves the usage of a jet of compressed air or water, which act like the stimulation factors and an exploratory probe in a mesiodistal direction on the exposed dentinal surface of affected teeth the patient points and allowing the dentist to determine the extent of the problem. Palpation of the teeth can help to rule out pain due to pulpitis or periodontitis. Transillumination and biting tests can confirm the presence of a cracked tooth, if any.[11,14]The severity or degree of pain can be recorded according to a categorical scale (slight, moderate or severe pain) or utilising a visual analogue scale.[15]

Treatment option for Dentin hypersensitivity ranges from non-invasive, self-performed therapy to professional treatments involving in-office procedures and applications of medicaments.[16] Before proceeding with any treatment, the predisposing factors (such as acidic drinks or excessive tooth brushing) should be removed or modified for long-term success and relief.[1] The present therapies lay emphasis on reducing fluid movement in the dentin tubules, blocking the dentin tubules, and preventing the reactionary nerve response in the pulp.[17] This can be achieved by techniques involving desensitisation, formation of a physical barrier on the exposed dentin, obliteration of dentinal tubule by crystalline structures, and iontophoresis.[18] Several treatment methods and medicaments have been utilised to control pain caused by dentin hypersensitivity. Though studies have found that oxalates, calcium phosphate, fluoride solutions, sodium fluoride varnish, and gels may decrease sensitivity,[19] there isn't a single, clear-cut approach that is better throughout the corpus of scientific data. Oxalic acid has a pH of 2.3, which is sufficiently acidic to etch dentine, resulting in the formation of calcium oxalate crystals. These crystals can block open dentinal tubules but may not last long as they may get dislodged or dissolve in the salivary fluids.[20]

Most of the dentists in a survey preferred sensitivity toothpaste or desensitising pastes as the first line of therapy, and only 6.6% of the dental professionals suggested invasive procedures like gingival grafts or operative procedures for the same.[21] The use of desensitising products can relieve pain. These agents might function in two different ways during therapy. The first is by obstructing the tubular structure of dentin; the second is by altering or suppressing the pulpal nerve response. Desensitising pastes can be self-applied every day or professionally applied regularly. Potassium nitrate-containing desensitising toothpaste is an easy-to-use self-applied therapy. This option effectively treats dentine hypersensitivity; however, it frequently takes 4 to 8 weeks for pain alleviation. Some desensitising agents require regular application in dental settings on exposed dentine, like sodium fluoride varnish (NaF) and Silver Diamine Fluoride (SDF) solution. Till now, there has been no gold standard for professional therapy for treating hypersensitivity.[22,23]

1.1. SDF as a treatment option for DH: Experiences from clinical trials

We have surplus information on the anti-caries efficacy of SDF; however, the data on its effectiveness as a desensitiser is still uncertain and inconclusive. Silver Diamine Fluoride (38% w/v Ag $(NH_3)_2$ F, 30% w/w) is an alkaline solution consisting of two main ingredients -Silver in 24.4-28.8% (w/v) and Fluoride in 5.0-5.9% concentration (about 44,800 ppm) along with 7.5%–11.0% of ammonia. It is a colourless and odourless solution with a pH of 10.SDF is not a simple compound of silver, fluoride and ammonium ions, but rather a complex heavy-metal halide. The silver functions as an antimicrobial, while fluoride is present in sufficient concentration to promote remineralisation and the ammonia (NH3) in the solution keeps it stable and in constant concentration for a certain duration.[24–26]While silver-based materials have long been utilised, their advantageous antibacterial qualities and low toxicity were discovered in the 1970s, prompting considerable interest in the compound. Studies published in the dental field in recent years provided evidence supporting the application of chemicals containing silver nitrate in cavity disinfection, dentin desensitisation and the reduction of dental decay. SDF became available for therapeutic use in Japan in the 1960s,and also been used to treat caries in Australia, Brazil, Argentina and China since long.[27] Many researchers have used 38% Silver Diamine Fluoride solution at a pH of 8-9 for controlling dental caries.[28] However, its use for managing dental hypersensitivity is less common among dentists. As a non-invasive treatment for dentin hypersensitivity, 38% SDF was first introduced into the United States of America (USA) market in 2015, and the US Food and Drug Association cleared SDF as a dentine desensitising agent.[19,25,29]

Clinical trials supporting the efficacy of Silver Diamine Fluoride in treating tooth sensitivity are limited. On PubMed search, only four clinical studies related to SDF were available exploring its efficacy and safety in managing dentin hypersensitivity in adults. There was no uniformity in the clinical trials as the sample size and methodology varied. Some clinicians evaluated SDF efficacy immediately after application, after 24 hours and even on 7^{th} day.[19,30] A study investigated the anti-hypersensitivity effects even after14 days and compared the effectiveness of SDF used alone and in combination with a CO_2laser.[31] In another

recent study, authors evaluated DH at baseline and 4- and 8-week follow-up visits post applications and simultaneously compared SDF with 5% potassium nitrate solution on the exposed areas of root of the selected hypersensitive tooth.[32] The common objective in all the studies was to evaluate the efficacy of topically applied SDF in reducing the pain caused by dental hypersensitivity. Authors in all four studies utilised the visual analogue scale (VAS) to assess the pain or sensitivity score of their patients. Three of the trials[30–33] utilised 1-10 mm scale and one of the studies used the 100mm scale.[19] The above mentioned clinical trials have been summarised in Table 1.

SDF proved to be safe and clinically efficient in treating tooth hypersensitivity after 24 hours and seven days post application in a study conducted in Peru.[19] Craig et al.[30], in their pilot study, compared the effectiveness of 38% Diamine Silver Fluoride followed by potassium iodide with an oxalic acid-based reagent and concluded that SDF/KI combination was better at reducing the dental pain associated with tooth hypersensitivity. The authors observed a high difference in the mean VAS scores between the baseline and seventh day for patients receiving 38% Silver Diamine Fluoride/ Potassium Iodide application than those receiving an oxalic acid-based preparation (p = 0.0134). Also, a higher number of patients (p=0.0129) reported relief with the Diamine Silver Fluoride/Potassium Iodide therapy than from the other treatment.[30] In a comparative study conducted in Indonesia, researchers reported a significant reduction in VAS and DIAGNOdent values on the 7^{th} and 14^{th} day with the Silver Diamine Fluoride and CO_2 laser application on the affected teeth surface. However, there was no statistical difference between SDF alone and SDF combined with a CO_2 laser.[31] In a recently published clinical trial, Chan AKY et al.[32] reported that the topical application of 38% SDF on the exposed root surface of older adults was more effective than 5% potassium nitrate solution in reducing pain due to dentin hypersensitivity.[32] Some prosthodontists have also reported effective desensitisation with SDF application following vital tooth preparations for definite prosthesis.[33] Since potassium iodide might further lower dentin permeability after topical fluoride therapy, Knight et al.[34] recommend using potassium iodide right after applying SDF. Research indicates that one week following treatment, both SDF and SDF in combination with potassium iodide are harmless and efficient at desensitising teeth. Potassium iodide (KI) and silver Diamine Fluoride (SDF) include a number of components, resulting in a notable decrease in tooth hypersensitivity, as experienced in these studies. Additionally, the interaction reaction between SDF and KI may produce sufficient silver iodide (AgI) further reduce dentine tubule patency.[19,30]

SDF application is simple, economical and possible in any setting, as it does not need extensive infrastructure support and types of equipments.SDF is a suitable therapeutic option for geriatric dental patients who are medically compromised, have difficulty adapting to routine oral care and cannot bear invasive operative procedures.[26,28] Few researchers recommend SDF in managing pain and dentin sensitivity associated with root caries.[19] The protocol of SDF application for Dentin Hypersensitivity is the same as for treating caries. SDF is applied with a disposable micro brush on the affected areas of the hypersensitive teeth under isolation. There is no established protocol for SDF application in literature. The application can be single or can be repeated. There are no post- application restrictions for the patients receiving SDF application. The application time may vary from ten seconds to three minutes, and based on clinical findings, there occurs no association between application time and clinical results.[26]

1.2. Mechanism of action of SDF as a desensitiser

Silver-based products have an extensive record as dentine desensitisers because silver ions are capable of precipitating proteins in the dentinal tubules.[35] SDF contains both silver and fluoride ions, which may contribute to lowering dentine hypersensitivity. There is an assumption that the chemical interactions between fluoride ions and free calcium ions result in calcium fluoride that can block the dentinal tubules and decrease the dentinal permeability,[15] and is partially insoluble in saliva,[13,36] and silver ions cause protein denaturation and aggregation in the dentinal tubules.[37] SEM studies have demonstrated granular precipitates in the peritubular dentin after topical application of fluorides. The traditional understanding is that, a layer of silver and dentin organic matrix protein conjugates forms when SDF is applied on sensitive dentin surfaces, which partially closes the exposed dentinal tubules.[24,25] The analyses of SDF-treated dentin using scanning electron microscopy and energy-dispersive X-ray spectroscopy have shown that after treatment, the diameter of the dentinal tubules is markedly decreased by the deposition of silver particles within and on the surface of tubules, eventually reducing the tubular fluid movement.[38,39]

Also, an in-vitro experiment reported that when compared to a placebo, standard(solution) and experimental viscous forms of 38% SDF were able to occlude dentinal tubules, thus potentially providing relief from dentin hypersensitivity. For both types of SDF forms, silver precipitates were seen on the dentin surface and inside dentinal tubules, with a slight tendency for the experimental gel SDF type to be more abundant than the widely marketed solution of 38% SDF, though the difference was not statistically significant.[40] This observation was also confirmed in a Nano-CT- enabled three-dimensional visualisation of the dentinal tubules.

Table 1: Summary of in-vivo studies followed SDF application for DH

Author,Year and Country	Objective	Sample size and Participant's age group	Study design(s), Treatment agent(s) and Methodology	Main Findings	Side effects on soft tissue	Conclusion
Castillo JL,2011:[19] Lima and Cusco, [Peru]	To assess the clinical effectiveness and safety of topical application of Diamine Silver Fluoride as a desensitising agent	126, Adults	i)Multi-Center Randomized Clinical Trial Japan] ii)Experimental group-38% SDF and Control group-Sterile water iii)The participants with at least one sensitive tooth were randomly allocated to either the Experimental group or the Sterile water Group. iv)The pain was measured with a 100-mm visual analogue scale after 24 hours and on 7^{th} day. iv)Single Application of Diamine Silver Fluoride was done.	In Lima, post SDF application, mean variance in pain scores between the baseline and 7^{th} day in experimental group was-35.8 (SD = 27.7) mm vs. 0.4 (SD = 16.2) for the controls (P < 0.0001). In Cusco, the average variation in pain score between baseline and day 7 in the experimental group(SDF) was -23.4 (SD = 21.0) mm vs. -5.5 (SD = 18.1) mm (P = 0.0015) in the control group.	No abnormal gingival or soft tissue ulceration was reported. Some patients experienced a slight but temporary gingival inflammation in areas near the teeth post SDF application. No staining of the gingival tissues was observed. Gingival Index was unaltered..	SDF is safe and clinically efficient in treating tooth hypersensitivity following its application after 24 hours and 7 days.

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Table 1 continued

Craig et al,2012;[30] Australia	To compare the efficacy of an experimental Diamine Silver Fluoride/potassium iodide product with an oxalic acid-based preparation in reducing dentine hypersensitivity.	19, Adults, [Mean Age 38.7 years]	i)Double-Blind Randomized Clinical Trial With A Split-Mouth Design ii)Silver fluoride/potassium iodide product (SDI Limited, Melbourne, Australia) which contains 38% (w/v) Diamine Silver Fluoride and a saturated solution of potassium iodide and Oxalic Acid-Based Product (Super seal, Phoenix Dental Inc, Fenton, MI, USA) iii)Group1-38%Silver Fluoride/Potassium Iodide Group2-Oxalic Acid-Based Product (SuperSeal, Phoenix Dental Inc, Fenton, MI, USA) iv)In each quadrant ,the most sensitive tooth was chosen and given a cold stimulus. The patients recorded their responses on a visual analogue scale (VAS) with a scoring range of 1 to 10.	The mean difference in the VAS scores at baseline and after seven days in group 1 [SDF/KI]was −1.71 Whereas for teeth treated with the oxalic acid-based preparation[group 2] the value was −0.69	No abnormal signs of gingivitis or other alterations, and none of the teeth presented evidence of staining.	Silver Diamine fluoride/potassium iodide application resulted in a significantly larger reduction in dentine hypersensitivity (p = 0.0134) than the oxalic acid-based preparation.

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Table 1 continued

Permata N et al.[31] 2018; Indonesia	To analyse the efficacy of Silver Diamine Fluoride and CO2 laser in reducing dentin hypersensitivity	16, Adults, Mean Age 25.5years	i)Single-blind randomised Clinical Trial with a Split-Mouth Design ii)Group 1 [Silver Diamine Fluoride application only] Group 2 [Silver Diamine Fluoride followed by CO2 laser application] iii) Dentin hypersensitivity was measured: VAS (evaporative and thermal stimuli), DIAGNOdent (an objective measurement tool) Hypersensitivity scores were recorded four times: Before treatment, immediately after material application(baseline), 7^{th} day and14 days after material application without reapplication.	Silver Diamine Fluoride application alone and Silver Diamine Fluoride followed by CO2 laser exposure can significantly reduce dentin hypersensitivity (measured with VAS) to evaporative and thermal stimuli on the teeth surface compared with baseline data (p = 0.000) But that there was no statistical difference between SDF alone and SDF combined with a CO_2 laser scores.	No adverse reactions or side effects were reported	There was a notable reduction in VAS and DIAGNOdent scores following the Silver Diamine Fluoride application alone or in combination with CO2 laser application

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Table 1 continued

Chan AKY,et l.[32] 2023; Hong Kong	To investigate the effectiveness of topically applied 38% SDF solution in reducing dentine hypersensitivity in teeth with an exposed root surface in older Chinese adults.	139, adults,65 years and older	i) Double-Blind Randomised Clinical Trial ii)Group1-38%SDF Group2-5%KNO_3 ii)The participants received 38% SDF solution [Group 1] or 5% Potassium Nitrate [Group 2] solution on the exposed root surface of the selected hypersensitive tooth after clinical examination at baseline visit and at 4- and 8-week follow-up visits.[after every 4 weeks] iii)The participants gave a sensitivity score (SS) in visual analogue scale from 0 (no pain) to 10 (agonizing) at the baseline visit.	There was a significant difference ($P < 0.001$) in the percentage reduction in Sensitivity score(SS) between the two groups with the test (SDF) group showing a greater percentage reduction in SS than the control group did at the 8-week follow-up. At the 8-week follow-up, the sensitivity ratings significantly decreased in both the SDF and potassium nitrate groups. Participants who received SDF, however, had a consistent and notable decline in their Sensitivity scores(SS) between baseline up to the 8-week follow-up, while those who got Potassium Nitrate showed a similar decline in SS up to the 4-week follow-up, but no remarkable reduction in SS was noted between the 4-week and 8-week follow-up visits	No adverse consequences documented	38% SDF solution reduced hypersensitivity on the exposed root surface of older adults. In addition, 38% SDF was superior to 5% Potassium Nitrate solution in lowering hypersensitivity in older patients presenting with exposed radicular dentin.

The samples treated with the novel and more viscous SDF preparations had more precipitates present deeper into the tubules. Most of the silver particles were clustered near the point of application on the tooth surface, and the amount varied between the two types of SDF formulations (36.7% for commercially available SDF and 40.7% for experimental gel-type SDF).[41] Sizes of the silver precipitates ranged from almost a tubule's diameter to much below 1 μm and were found to penetrate as deep as 500 μm.[38,40]

1.3. Safety parameters with SDF use

SDF has outstanding safety features. The younger generation also tolerates it well. There is no evidence in the literature of potential risks or adverse outcomes related to SDF application to carious lesions in healthy population groups. The primary obstacle to its use is the discolouration it leaves behind upon application. Therefore, it's critical to comprehend the patient's worries about SDF treatment.[42] Patients with a known allergy to Silver products are absolutely contra-indicated to SDF application, while relative contraindications are apparent desquamative gingivitis or mucositis that may compromise the protective barrier produced by stratified squamous epithelium. Patients may complain of increased absorption and pain with SDF applications. Dental professionals should follow strict isolation techniques and apply a protective gingival coat to prevent unnecessary contact with healthy soft tissues. Since the Japanese government authorised Silver Diamine Fluoride (Saforide^{TM}, Toyo Seiyaku Kasei Co. Ltd., Osaka, JP) more than 80 years ago, barely a serious adverse occurrence has been reported to them.[25] In the clinical trials related to SDF, post-SDF application, most authors documented no adverse effects like tissue ulceration or abnormal colour changes. The gingival tissues exhibited no discolouration. Teeth were only stained when the surfaces had untreated decay. Abnormal gingival inflammation was minimal,[30,31] though they did not follow any standard scale to record gingival inflammation or colour changes. Castillo J et al.[19] reported a few patients with SDF application experienced mild and temporary gingival inflammation next to the tooth. Gingival symptoms of irritation usually get better within 2 days of SDF application.[19,43] Many researchers have raised concerns due to the presence of high concentrations of silver (255,000ppm) and fluoride ions (44,800ppm) in SDF; however serum levels of silver and fluoride are less likely to cause any toxicity when used less frequently in adults.[44] In short term study, following topical SDF treatment in adults, the amounts of plasma silver and fluoride were below the concentrations associated with toxicity.[45] The evidence related to SDF use as a desensitising agent is limited, and more studies with prolonged evaluation periods are required to gain a better understanding of its efficacy and safety in the long term.

2. Future Prospects

Dentine hypersensitivity is a commonly experienced dental problem and a significant burden for dental patients and dentists. Though SDF is an efficient option, most studies using SDF for DH have been for short-term effects. For a better understanding, we need randomised, placebo-controlled and double-blinded long-term follow-up clinical studies using the SDF application for managing DH.

3. Conclusion

Despite its established advantages and supporting data, SDF is still not widely used in clinical dentistry. The primary cause is the long-lasting, black staining that SDF leaves behind after treatment. Also, dental patients usually demonstrate their pain differently. Prospective research studies could look into the anti-hypersensitivity effects of SDF using diverse assessment and evaluation strategies.

4. Source of Funding

None.

5. Conflict of Interest

None.

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