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Silver Diamine Fluoride: A Literature Review

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Abstract

Dental caries is one of the most common oral diseases. It is always better to prevent the disease before it advances which may result in pain, an unaesthetic look, and difficulty in mastication and function. The application of silver diamine fluoride is one of the preventive measures performed by the dentist to prevent and arrest initial dental caries. It is very effective in all age groups especially in pediatric patients. Knowledge about the exact mechanism of action of silver diamine fluoride and its method of use is a primary requirement for the dental professional. The present article emphasizes a detailed review on silver diamine fluoride.

Keywords: Silver diamine fluoride, preventive dentistry, pediatric patient

INTRODUCTION

Dental caries remains a significant disease of childhood and is at-risk in children in both developing and developed countries. This is confirmed by international data on caries epidemiology.[1] World Health Organization reported in 2003 that the global average of decayed, missing, filled tooth (DMFT) is 2.4.[2]

Basically, fluoride has anti-caries effect, and its presence in oral environment under plaque and saliva inhibits the demineralization process. Remineralization of tooth with fluoride results in a crystalline structure, which is more resistant to bacterial acid and helps to inhibit caries progression.[3] Since 1969, silver diamine fluoride (SDF), $Ag(NH_3)_2F$, is used to arrest caries.[4] Silver diamine fluoride has a unique anti-cariogenic ability to be a "silver-fluoride bullet."

Silver diamine fluoride has been used to treat high caries prevalence by arresting or delaying the rate of caries progression, used in treating dental caries in young children, to prevent secondary caries, to arrest root caries, to desensitize sensitive teeth, to prevent pit and fissure caries, to prevent the fracture of endodontically treated teeth, and to treat infected root canals.[3-8]

MECHANISM OF ACTION

Action of Silver Diamine Fluoride on Bacteria

Several mechanism of action have been proposed for silver and can be explained by the multiple biological organisms like bacterial, protozoan, fungal, and viral in origin, subcellular targets like cell membranes, cell organelles, nuclei and mechanisms such as metabolism, replication of the cell have been examined. Studies have indicated that when silver interacts with sulfhydryl groups of proteins and DNA, it alters the hydrogen bond and results in inhibiting the respiratory processes, DNA unwinding, cell wall synthesis, and cell division.[9] At the macro level, these interactions lead to bacterial killing and inhibit biofilm formation.[10] The central mechanism for these effects is the interaction of silver with thiol groups by the following mechanism.[11]

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A/N-SH+ AgX → A/N- S- AgX+HX
where A/N is amino (A) or nucleic (N) acids (respectively), SH is a thiol group, Ag represents silver, and X represents an anion (diamine fluoride). The above reaction indicates that when SDF is applied to caries lesions, there is interaction with the bacteria resulting in inhibition of biofilm formation, arrest of caries by bacterial killing, and inhibition of further progression of caries.[3]

The nature of silver in silver compounds is not clearly stated in the literature. Metallic silver is inert, whereas silver ions (Ag+) are expected to have antibacterial effects. When metallic silver interacts with moisture in the oral environment, it releases silver ions.[12] The 3 main antibacterial effects of silver ions are denaturation of cytoplasmic enzyme, destruction of cell wall structure, and inhibition of microbic DNA replication.

First, silver ions can bind with disulfide in membrane proteins thereby allowing easy penetration through membranes and silver ions can electrostatically bind negatively charged peptidoglycans in the bacterial cell wall and disturb the membrane transport functions leading to distortion of cell and loss of viability.[13]

Secondly, silver ions can bind to sulphydryl groups (–SH, the thiol group of cystine) which is essential for enzyme activities. Such interactions with cystine can inhibit enzyme activities and disrupt various metabolic activities leading to the death of the microbe.[11]

Thirdly, guanine is a major component of DNA in pathogens, and silver ions have the ability to attach to guanine disabling the replication ability of bacteria.[14]

Action of Silver Diamine Fluoride on Tooth
The most commonly recognized interaction of SDF on tooth is when sodium fluoride reacts with calcium phosphate, it forms fluorapatite ($Ca_{10}(PO_4)_6F_2$) and sodium hydroxide (NaOH) in a basic environment. The less commonly seen interaction in a basic environment is the combination of tooth calcium to form calcium fluoride (CaF_2). When hydroxyapatite of the enamel reacts with silver nitrate, it results in the formation of calcium nitrate ($Ca(NO_3)_2$), silver phosphate (Ag_3PO_4), and silver oxide.

When fluoride and silver react, it results in the formation of fluorapatite. At first, there is formation of calcium fluoride (CaF_2) and silver phosphate (Ag_3PO_4) in a basic environment. Later, there is dissociation of calcium and fluoride leading to the formation of fluorapatite ($Ca_{10}(PO_4)_6F_2$) (Figure 1).

Reactions of Carious and Noncarious Dentin to Silver Nitrate
The following 4 layers could be seen in dentin treated with silver nitrate and is depicted in Figure 2:[16]

1. The presence of thin black precipitate is appreciated in the superficial layer mainly consisting of free silver.
2. Carious dentin usually stains brown as a result of reduction of silver nitrate leading to alteration of protein in the carious matrix. Deepest border of this brown staining indicates the advancement of carious process into dentin. H & E section of carious dentin-stained deep purple whereas deep brown stains were seen when carious dentine was treated with silver nitrate, and it did not take up the purple stains, suggesting that deep brown stains are due to silver nitrate itself.

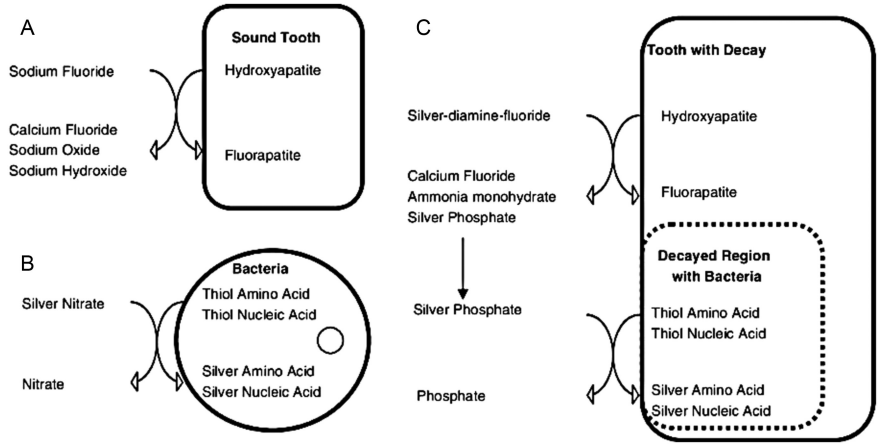

Figure 1. A-C. Effect of silver diamine fluoride (SDF) on tooth and bacteria. (A) In a sound tooth, fluoride reacts with hydroxyapatite to form fluorapatite. (B) In the presence of bacteria, silver reacts with thiol groups of bacteria leading to inability to carry out metabolic and reproductive functions, resulting in bacterial lysis. (C) In tooth with dental caries, SDF reacts with hydroxyapatite to form fluorapatite and silver phosphate as a by-product. Silver phosphate reacts with bacterial thiol groups of amino and nucleic acid to form silver amino and nucleic acids (courtesy: Rosenblatt et al[3]).

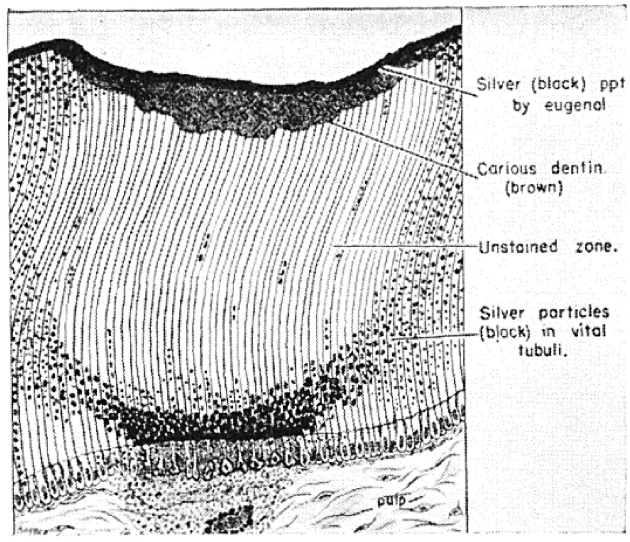

Figure 2. Reactions of human dentin and pulp to silver nitrate (courtesy: Englander et al[16]).

3. An intermediate zone did not show any staining due to reduced dentinal vitality, that is the presence of sclerotic dentin.
4. The deeper layer mainly contains vital dentinal tubules consisting of large black globules of reduced silver particles.[16]

Clinical Applications of Silver Diamine Fluoride

- To arrest initial dental caries.
- To prevent pit and fissure caries.
- To prevent secondary caries.
- To arrest root caries.
- To desensitize sensitive teeth.
- To treat infected root canals.
- As an indirect pulp capping agent.

***Protocol for Application by* University of California, San Francisco[17]**

Maximum dose: 25 µL (1 drop)/10 kg per treatment visit

Considerations:

- Decayed dentin will stain dark brown or black
- SDF can stain the skin; however, it will clear in 2-3 weeks without treatment.
- SDF can permanently stain operatory surfaces and clothes.
- A control restoration if required can be considered after SDF treatment.
- Saturated solution of potassium iodide can be used after SDF to decrease color changes.
- Re-application is usually recommended biannually.

Procedure

1. One drop of SDF was added into the deep end of a plastic dappen dish. Obtain 1 drop of saturated solution of potassium iodide (SSKI) in a separate dappen dish if required.
2. Remove bulk saliva with saliva ejector. Isolate tongue and cheek from affected teeth with "2×2" gauze or cotton rolls.
3. Near the gingiva, the application of petroleum jelly with a cotton applicator can ensure safety.
4. Dry affected tooth surfaces with a triple syringe or with cotton.
5. Remove excess of SDF using microsponge on side of dappen dish.
6. Apply directly onto the affected tooth surface/s with microsponge.
7. Allow SDF to absorb for up to 1 minute, then remove excess with gauze or cotton roll. (If using SSKI, apply with a different microsponge. Repeat 1-3 times until no further white precipitates are observed. Wait 5-10 seconds between applications. Remove excess with cotton.)
8. Rinse with water.

ADVERSE EFFECTS

- Argyria
- Temporary tattoo on skin or submucosa which will resolve in 2 to 14 days by natural exfoliation of skin.[18]
- Silver allergy results in transient erythema in the gingiva of the teeth which usually disappears in 48 hours without any treatment.[22]
- Metallic taste
- In case of accidental ingestion of a large amount of SDF, vomiting can be induced to avoid its absorption in the body. 10% calcium gluconate (10 mL) solution can be administered. Calcium ions react with fluoride ions to form insoluble calcium fluoride which cannot be absorbed in the gastrointestinal tract.[18]
- Staining of SDF could be due to formation of silver phosphate. Several studies with silver diamine fluoride/potassium iodide (SDF/KI) were tried to reduce the staining, but none were effective and further studies are necessary to provide promising results.[22]

***Studies on* Silver Diamine Fluoride**

To arrest the initial dental caries, many studies have been conducted. *In vitro* studies by Yamaga et al.[7] Gotjamanos and Orton 1998,[23] klein et al 1999,[24] *in vivo* studies by McDonald and Sheiham 1994,[25] and clinical trials in primary and permanent dentition by Nishino et al 1969,[26] Almeida 1994,[27] Chu et al 2002,[28] Llodra et al 2005,[29] and Wong et al 2005[30] have been effective in controlling and preventive dental caries.

Nishino and Massler in 1997,[31] concluded that the caries score of SDF-treated teeth was significantly lower than the fissures treated with 8% SnF_2 or $Ag(NO)_3$. Shimizu in 1974[32] concluded that there was no recurrent caries seen on amalgam restoration on primary teeth which was pre-treated with SDF after 24 months.

Root caries usually increases as age progresses. A study done on Hong Kong's on elderly community where 38% SDF was

Table 1. University of California, San Francisco Protocol for Arresting Dental Caries Lesion

Indications	Contraindications
Extreme caries risk (xerostomia or severe-early childhood caries)	Absolute: silver allergy
Difficult to treat dental carious lesion	Relative: ulcerative gingivitis, stomatitis
Patients without access to dental care	Saturated solution of potassium iodide contraindication: pregnancy, breastfeeding
Patients with carious lesion that may not all be treated in one visit	
Treatment challenged by behavioral or medical management	

used resulted in arresting dentin caries on exposed root surface.[20] To treat infected root canals, Mathew et al[21] reported that SDF is as effective as 2% chlorhexidine in removing *E. faecalis* from infected root canals.

Silver diamine fluoride has the ability to occlude dentinal tubules and desensitize the dentinal tubules. Hatsuyama et al in 1967,[33] Murase et al in 1969,[34] and Kimura et al in 1971[35] concluded that SDF was effective against erosion, abrasion, and hypersensitive dentine.

The prime objective of SDF treatment is to maintain pulp vitality by arresting dental caries resulting in decreased permeability and stimulating tertiary dentine formation.[22] Yamaga et al[7] in 1972 described that SDF has the capacity to arrest the progression of caries when applied in the presence of softened caries or when removal of softened caries can result in pulpal exposure. Chu et al[15] proposed that SDF can be applied in indirect pulp capping (IPC) and atraumatic restorative treatment (ART) procedures. An *in vitro* study by Gupta et al 2011[36] concluded that the highest zone of bacterial inhibition was seen when SDF was used. *In vivo* part of the same study by Sinha et al in 2011[37] found SDF as a re-hardening, remineralizing, and antibacterial agent and therefore can be used as an IPC material.

Silver diamine fluoride is a safe and effective treatment for dental caries. Application of SDF twice a year outperforms all minimally invasive treatments including ART and sealants as depicted in Table 1. Traditional approaches often increase the rates of recurrent caries in patients with severe caries. This method does not require general anesthesia or sedation addressing concerns about expense, danger, and practical complexity of these services. This is a powerful new tool against dental caries particularly suited for those with high risk.

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