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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 results to pain, unesthetic look and difficulty in mastication and function. 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 paediatric patients. The knowledge, the exact mechanism and its method of use is a primary requirement of the dental professional. The present article emphasizes a detailed review on silver diamine fluoride.

Keywords: silver, fluoride, silver, silver diamine fluoride.

INTRODUCTION

International data on caries epidemiology confirm that dental caries remains a significant disease of childhood that is found in a subset of at-risk children in both developing and developed countries.[1] According to WHO, the global average of DMFT is 2.4.[2]

Fluoride is primarily anti-caries effects are topical and its presence in plaque and saliva inhibits demineralization. Remineralization with fluoride leads to a crystalline structure more resistant to bacterial acid and thus caries inhibition and progression.[3]Silver diamine fluoride (SDF) $Ag(NH_3)_2F$, is used to arrest caries since 1969.[4] SDF has a unique anticariogenic ability to be a "silver-fluoride bullet."

SDF has been used to deal with high caries prevalence by arresting or slowing down the rate of caries progression, used in management of dental caries in young children, to arrest root caries, to prevent pit and fissure caries, to prevent secondary caries, to desensitize sensitive teeth, to treat infected root canals and to prevent the fracture of endodontically treated teeth.[3-8]

MECHANISM OF ACTION:

1. Action of Silver Diamine Fluoride on Bacteria

Multiple modes 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

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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 are due to the interaction of silver with thiol groups by the following mechanism.[11]

$$A/N\text{-}SH + AgX \rightarrow A/N\text{-}S\text{-}AgX + HX$$

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). This interaction indicates how silver diamine fluoride, when applied to caries lesions, might interact with bacteria and results in caries arrest through bacterial killing and inhibit caries progress through the inhibition of biofilm formation.[3]

It is noted that the nature of silver in silver compounds is not clearly stated in the literature. Silver ions (Ag+) are expected to have antibacterial effects, but metallic silver (Ag or Ag0) is relatively inert. However, metallic silver can interact with moisture in the oral environment and releases silver ions which is a crucial point for the antibacterial effects on pathogenic organisms.[12]

There are three main antibacterial effects of silver ions:

1. Destruction of cell wall structure;
2. Denaturation of cytoplasmic enzyme and
3. Inhibition of microbic DNA replication.

Firstly, silver ions can bind with disulphide in membrane proteins; thereby allowing easy penetration through membranes. It is also reported that silver ions can electrostatically bind negatively-charged peptidoglycans in the bacterial cell wall which is negatively-charged and disturb the membrane transport functions leading to cellular distortion and loss of viability.[13]

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

Thirdly, it was reported that silver ions can also attach to guanine, a major component of DNA, thereby disabling the replication ability of bacteria. Microorganisms in biofilms are more resistant to antibacterials than planktonic pathogens and it is reported that biofilms may require more than 100 times the concentration required for planktonic bacteria.[14]

2. Action of Silver Diamine Fluoride onTeeth

Investigators found that the 2 compounds have complex mechanisms.[7] The most commonly recognized interaction is sodium fluoride with calcium phosphate to form fluorapatite and sodium hydroxide (and a basic environment).

$$Ca_{10}(PO_4)_6(OH)_2 + NaF \rightarrow Ca_{10}(PO_4)_6F_2 + NaOH$$

The less commonly seen interaction is the combination of tooth calcium to form calcium fluoride and a basic environment.

$$Ca_{10}(PO_4)_6(OH)_2 + NaF \rightarrow CaF_2 + Na_3O_4 + NaOH$$

When hydroxyapatite of the enamel reacts with silver nitrate it results in the formation of calcium nitrate, silver phosphate, and silver oxide.

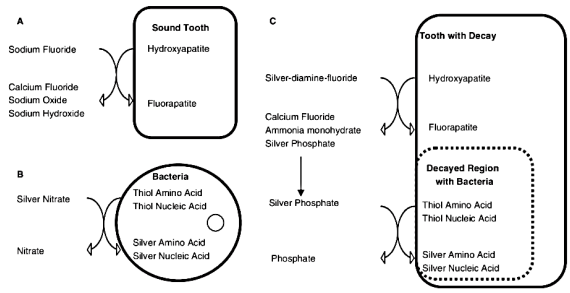
$$Ca_{10}(PO_4)_6(OH)_2 + Ag(NO_3) \rightarrow Ca(NO_3)_2 + Ag_3PO_4 + Ag_2 + H_2O$$

When fluoride and silver interact, it leads to the formation of fluorapatite. At first there is formation of calcium fluoride and silver phosphate in a basic environment.

$$Ca_{10}(PO_4)_6(OH)_2 + Ag(NH_3)_2F \rightarrow\rightarrow\rightarrow CaF_2 + Ag_3PO_4 + NH_4OH$$

Later, there is subsequent dissociation of calcium and fluoride.

$$CaF_2 \rightarrow Ca + 2F^-$$



Courtesy: Rosenblatt A et al

Effect of Silver Diamine Fluoride on teeth and bacteria

The last step is the formation of fluorapatite. The net result of these interactions is as follows.

$$Ca_{10}(PO_4)_6(OH)_2 + 2F^{-} \rightarrow\rightarrow Ca_{10}(PO_4)_6F_2 + 2OH$$

(A) In a sound tooth, when fluoride reacts with hydroxyapatite to form fluorapatite. Fluorapatite is less acid-soluble than hydroxyapatite resulting in inhibition of the caries process.

(B) In bacteria, when silver reacts with thiol groups of amino and nucleic acids, the bacteria is unable to carry out metolic and reproductive functions, resulting in bacterial lysis.

(C) In teeth with decay, silver diamine fluoride reacts with hydroxyapatite to form fluorapatite, and the by-product is silver phosphate. Silver phosphate later reacts with bacterial amino and nucleic acid thiol groups to form silver amino and nucleic acids.

REACTIONS OF CARIOUS AND NON-CARIOUS DENTIN TO SILVER NITRATE:

The following four layers could be distinguished in dentin treated with silver nitrate:[16]

1. A thin, superficial layer of black precipitate seen on the surface of the dentin. This layer consisted of free silver precipitated by the eugenol. The precipitate was on the dentin which indicated that the eugenol acted on the surface of the dentin only or penetrated the dentin only superficially.
2. A layer of carious dentin is stained brown. This was the result of the reduction of the silver nitrate to brown free colloidal silver or a combination of the silver nitrate with the altered available protein by the carious matrix. The deepest border of this brown staining mass was irregular, that outlines the advancing carious lesion into the underlying dentinal tubules and matrix. Carious dentin which was not treated by silver nitrate stained a deep purple with hematoxylin and eosin. Carious dentin treated with silver nitrate stained a deep brown and did not take the purple stain of the hematoxylin and eosin. Hence it was concluded that the brown staining was a specific result of the silver nitrate.
3. An intermediate zone was seen relatively free of silver staining. This zone may represent a zone of reduced dentinal vitality (metamorphosed or sclerotic

UNIVERSITY OF CALIFONIA, SAN FRANCISCO (UCSF) PROTOCOL FOR ARRESTING DENTAL CARIES LESION

Indications	*Contraindications*
Extreme caries risk (Xerostomia or S-ECC)	Absolute: silver allergy
Difficult to treat dental carious lesion	Relative: ulcerative gingivitis, stomatitis
Patients without access to dental care	SSKI contraindication: pregnancy, breast-feeding
Patients with carious lesion that may not all be treated in one visit.	
Treatment challenged by behavioural or medical management.	

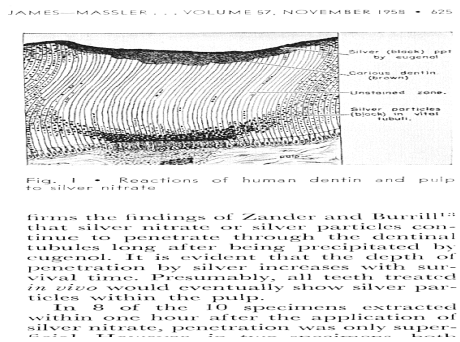


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Fig. 1. • Reactions of human dentin and pulp to silver nitrate.

firms the findings of Zander and Burrill[13] that silver nitrate or silver particles continue to penetrate through the dentinal tubules long after being precipitated by eugenol. It is evident that the depth of penetration by silver increases with survival time. Presumably, all teeth treated *in vivo* would eventually show silver particles within the pulp.

In 8 of the 10 specimens extracted within one hour after the application of silver nitrate, penetration was only super-

Courtesy: Englander HR

Reactions of human dentin and pulp to silver nitrate.

dentin). This zone coincides with the region which has tubular contents that are degenerated in advance of the carious lesion.

4. A deeper zone containing large black globules of reduced silver particles. These were observed deep within the vital dentinal tubules and within the pulp cells.[16]

Conventional-thickness sections (6-7 Fm) showed silver granules extending for variable distances through primary dentine and in some areas of reparative dentine. The amount of reparative dentine formed was substantial and was mainly of the irregular tubular variety. The predentine layer was wider than normal (in some cases up to 5 times the normal width). Regardless of its increased width, the predentine showed a comparatively small degree of mineralization.

The coronal pulp was normal except for the presence of diffusely distributed lymphocytes in some instances. Lymphocytes and plasma cells were observed in greater numbers in areas of the root canal pulp where resorption was seen. Under conventional light microscopy, silver particles were detected within the odontoblastic and subodontoblastic layers, and in the central region of the coronal pulp, but not in the root canal pulp. Examination using confocal laser scanning microscopy revealed a much greater density of silver in the coronal pulp. Particles were observed lying within odontoblasts, fibroblasts and endothelial cells lining capillaries.[16]

CLINICAL APPLICATIONS OF SILVER DIAMINE FLUORIDE:

- To arrest Initial dental caries: *In-vitro* studies by Yamaga et al 1972, Gotjamanos and Orton 1998, klein et al 1999, and *in-vivo* studies by McDonald and Sheiham 1994, clinical trials in primary and permanent dentition by Nishino et al 1969, Almeida 1994, Chu et al 2002, Llodra et al 2005, Wong et al 2005, has been effective in controlling and preventive dental caries.[3]
- To prevent pit and fissure caries: Nishino and Massler 1997 in their study mentioned that caries score of SDF treated teeth was significantly lower than the fissures treated with 8% SnF_2 or $Ag(NO)_3$.[19]
- To prevent secondary caries: Shimizu and Kawagoe in 1976 found no recurrent caries was seen on amalgam restoration on primary teeth which was pre-treated with SDF after 24 months.[19]
- To arrest root caries: Root caries usually increases as age increases. A study done on Hong Kong's elderly community where 38%SDF was used resulted in arresting dentin caries on exposed root surface. In this clinical study the group who received SDF and oral hygiene education had 18% more arrested active root surfaces when compared to those who received SDF alone.[20]
- To desensitize sensitive teeth: SDF has the ability to occlude dentinal tubules. Hatsuyama et al 1967, Murase et al 1969, and Kimura et al 1971 have shown that SDF was effective against abrasion, erosion, hypersensitive dentine and also it was suggested 4 times application was most appropriate.[19]
- To treat infected root canals: Mathewson et al showed that SDF is as effective as 2% chlorhexidine in removing E. faecalis from infected root canals.[21]

- As an indirect pulp capping agent: The main objective of SDF treatment is to maintain pulp vitality by arresting dental caries, promoting dentin sclerosis which results in decreased permeability and stimulating tertiary dentine formation.[22] Yamaga et al 1972 described that SDF will arrest the progression of caries when applied in presence of softened caries or when removal of softened caries can cause pulpal exposure.[7] Chu and Lo proposed SDF can be applied in IPC and ART procedures. An in-vitro study by Gupta et al 2011 concluded that highest zone of bacterial inhibition was seen when SDF was used. In-vivo part of the same study by Sinha et al found SDF was a re-hardening, remineralizing and antibacterial and therefore can be used as an IPC material.[19]

PROTOCOL FOR APPLICATION BY UCSF[17]

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

Considerations

- Decayed dentin will darken as the caries lesions arrest. Most will be dark brown or black
- SDF can stain the skin, which will clear in 2-3 weeks without treatment.
- SDF can permanently stain operatory surfaces and clothes.
- A control restoration may be considered after SDF treatment.
- Saturated Solution of Potassium Iodide (SSKI, Lugol's Solution, various sources) can be used after SDF to decrease color changes.
- Re-application is usually recommended, biannually until the cavity is restored or arrested or the tooth exfoliates.

PROCEDURE

1. Standard Personal Protective Equipment (PPE) for provider and patient.
2. 1 drop of SDF into the deep end of a plastic dappen dish. Obtain 1 drop of SSKI in a separate dappen dish if selected)
3. Remove bulk saliva with saliva ejector.
4. Isolate tongue and cheek from affected teeth with "2x2" gauze or cotton rolls.
5. If near the gingiva, consider applying petroleum jelly with a cotton applicator for safety.
6. Dry affected tooth surfaces with triple syringe, or if not feasible dry with cotton.
7. Remove excess on side of dappen dish.
8. Apply directly onto the affected tooth surface/s with microsponge.
9. Allow SDF to absorb for up to 1 minute if reasonable, 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.)
10. Rinse with water.
11. Place gloves, cotton, and microbrushes into plastic waste bags.

ADVERSE EFFECTS

- Argyria: Irreversible pigmentation of the skin due to prolonged exposure to silver
- 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 increase in erythema in the gingiva of the teeth which disappears 48 hours without any treatment.[23]
- Metallic taste
- Accidental ingestion of large amount of SDF, vomiting can be induced to avoid its absorption in the body. 10% calcium gluconate (10ml) solution can be administered. Calcium ions reacts with fluoride ions to form insoluble calcium fluoride which cannot be absorbed in the GIT. [18]

- Staining of teeth: Staining of SDF could be due to formation of silver phosphate. Several studies with SDF/KI or SiF were tried to reduce the staining, but none were effective and further studies are necessary to provide promising results.[23]

CONCLUSION

SDF is safe, effective treatment for dental caries. Application twice a year outperforms all minimally invasive treatment including ART and sealants. Traditional approaches often provide only temporary benefit results to the highest rates of recurrent caries are in patients with the worst disease burden. The advent of treatment for non-symptomatic caries not requiring general anaesthesia or sedation addresses long-standing 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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