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RESEARCH ARTICLE

SILVER DIAMINE FLUORIDE AND ITS CLINICAL APPLICATION: A NEW APPROACH TO CARIES PROPHYLAXIS

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ABSTRACT

Dental Caries is a common chronic disease and a serious public health problem which affects children growth and well being. Economical issues for restorative treatment and poor access to oral health care affects more of children from low socioeconomic area and are affected by untreated caries so Arresting Caries Treatment (ACT) is proposed to treat untreated dental caries in children of this strata of the community. Many biocompatible chemical agents have been used in experiments or in ex-vivo studies to prevent caries. Antimicrobial agents containing Silver (Ag), regarded as bioactive agent is used for arresting dentinal caries. Some topical fluoride agents like sodium fluoride and Silver diamine fluoride(SDF) have a pragmatic strategy for arresting caries, particularly in young and apprehensive children. A thorough literature review states that SDF is a safe, nontoxic and effective caries-preventive agent. Although, there are reports suggesting the efficacy of 38% SDF agent in arresting caries in the deciduous dentition. Some laboratory investigations have concluded that SDF has potent antibacterial action on biofilm, and obstructs caries progression process. Furthermore, SDF application is simple and an affordable in developing countries. Medline, PubMed, Ebsco and Google scholar databases, are the primary sources of review research.

INTRODUCTION

Background

Dental caries is a multifactorial, bacterial driven, chronic, site-specific and vital process resulting from the physiologic imbalance in the equilibrium between the tooth mineral and the plaque fluid.[1] Dental caries and periodontal disease have historically been considered the most important global oral health burdens.[2]Dental caries is also one of the most common chronic childhood diseases and in underprivileged parts of the world, many decayed teeth are left untreated.[3]

Dental caries is usually associated with the imabalanced microbial load between acidogenic/aciduric pathogens and basic environment generating microbes within the dental biofilm[4]and Streptococcus mutans is considered as the main etiologic microorganism for causing dental caries.

According to the World Health Organization (WHO), the global average of decayed-missing-filled teeth (DMFT) is 2.4.[5]It is still a paramount in most of the developed countries as it affects 60–90% of school going children. In several industrialized countries, there have been positive trends in the prevention of dental caries in children.[6]

In India, where more than 70% of population lives in rural areas with limited health services and expensive restorative treatment, peoplefail to attend the dental needs of their children, resulting in untreated dental caries. Some recent studies also reported the alarming increase in caries prevalence in primary and permanent dentition in families with low income, lower education level of parents, poor parental dental attitude. While cause for this increase in caries prevalence is unclear. The probable cause may be unubiquitous supply of sources of prevention.[7]

There are many conventional noninvasive caries management techniques involving application of topical fluoride agent for the prevention of carious lesions.[8] As per the literature it is estimated that only approximately 2 % of the global population understands the preventive role of fluoride in dental health.[9]

Presence of fluoride in plaque and saliva inhibits demineralization process and remineralization with fluoride results in a more stable and compact crystalline structure which is considered to be more resistant to acid challenge.[10] Thus, since ages treatment of early carious lesion with fluoride agent has been proven to be the cornerstone of caries preventive strategies.[7]

SDFa colorless solution containing fluoride ions, which is used to promote remineralization of enamel crystals which is constantly being attacked by bacterial acids produced in the oral cavity.[7] The use of SDF can be attributed to the early 1960's where it was shown to be successful cariesarresting agent with no major side-effects on oral health.[11,12]

Traditional restorative therapy of early childhood caries is no longer acceptable to tackle this prevalent disease, and arresting caries using SDF has become a pragmatic strategy, particularly for young children.[13]ACT of primary teeth with SDF is useful for managing caries in uncooperative young children and differently abled persons. Although SDF has been used in Japan to arrest dental caries since 1970s, it was not much in use by the dentists in other parts of the world. This article reviews the efficacy of SDF in arresting caries which is a global dental public health problem.

METHOD OF LITERATURE SEARCH

Search strategy was developed for articles indexed in Pubmed and Ebsco Host data bases. All studies in which SDF was used as caries arresting are included. The search was limited to reports written in English only and published from 1980 to June 2015. Reports present in the grey literature were not included. The studies selected for this review were reviewed by two reviewers independently.

A total number of 55titleswere reviewed for inclusion. Based on inclusion and exclusion criteria, 7 titles were dropped down and a total of 48 articles were then reviewed.

Rationale for Arresting Caries

Till date various fluoride releasing biomaterials have been promoted for the treatment of dental caries, including fluoride and silver nitrate mix which shows extensive caries inhibiting action. SDF among all fluoride releasing agents is gaining attention as it has the potential to arrest the caries process and simultaneously prevents demineralization.[14]

The sole purpose of ACT is to slow down the process of caries progression in an attempt to reduce children's discomfort and potential pulpal damage.[13]However, the factcan not be denied that dental caries is a dynamic process so it can only be theoretically arrested at any stage, even in the presence of frank cavitation.[13, 15]

History

Bactericidal activity of silver ion has been known since ancient times.[16] SDF has been accepted as a therapeutic agent for arresting dental caries by the Central Pharmaceutical Council of the Ministry of Health and Welfare in 1960. Dentists have termed silver nitrate solution as "Howe's solution" after Percy Howe, who reported its use for caries prevention.[1]

Mechanism of action of silver

Many studies have shown that silver interacts with sulfhydryl groups of proteins and with DNA, altering hydrogen bonding and inhibiting respiratory processes, DNA unwinding, cell-wall synthesis, and cell division At the macro level, these interactions affect bacterial killing and inhibit biofilm formation.[1,17,18,19]

Mechanism of action of SDF

Mei *et al* in his study mentioned that the use of 38% SDF solution arrested demineralization and preserved collagen from degradation in demineralized dentin.[20]

Proposed possible mechanisms of action of SDF on caries.[21]

The **first mechanism** can be: when SDF is applied on the tooth surface it reacts with mineral component of the teeth forming the product which is more resistant to the bacterial challenge. Selvig showed that SDF application increased the resistance of the peri and inter-tubular dentin to acid decalcification and thus retarding the penetration of acid into deeper layers of the dentin.[22]One study showed that SDF applied to dentin under clinical conditions penetrated to a depth of 50–100 μ.[23] It has been reported that SDF reacts with hydroxyapatite (HA) to release CaF_2 and silver phosphate. These CaF_2 ions thus released provides a reservoir of fluoride for the formation of Fluorapatite (FA) which is more resistant to bacterial challenge than HA resulting in decreased permeability of the tooth surface for acids due to blocking effect of the insoluble silver salts which stimulate sclerotic or calcified dentin and maintains the normal crystallinity of the tooth structure.

The overall reaction [1,15,24,25]

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

The **second mechanism** can be the blocking of dentinal tubules. According to Shimizu, dentin treated with SDF decreased in dye permeability and increased in electric resistance.[25]. Because of the blocked dentinal tubules, acid and microorganismcan not invade through this thus arresting the caries process. Because of this obturation of the dentinal tubules, the surface area of dentin, to be attacked by caries will decrease, and peri-tubular will be covered with obturating material (silver particles). Even if microorganisms invade through dentinal tubules, their growth will be inhibited by oligo-dynamic action of silver.[1,15]

Third mechanism can be binding of Ag ions with peptidoglycans in bacterial cell walls and disrupting membrane transport function, leading to cellular distortions and loss of viability. Binding to peptidoglycans, can inhibit bacterial enzyme activities, disrupt the metabolic processes, and ultimately causing death of the microbe[26] by inhibiting of biofilm formation on enamel and dextran-induced agglutination of *S. Mutans*.[1,15,27,28]

Procedure of SDF application

Followed by proper isolation thorough oral prophylaxis is performed. Carious tissue need not to be removed. Then gently apply the SDF with a micro brush. Wipe off the excess with a wet gauze or water. Make sure that the soft tissues are protected with Vaseline and cotton rolls during its application. Ideally one drop of SDF (380 mg per 1 ml) should be placed in a dappen dish, and using a cotton applicator or microbrush apply the SDF to carious surfaces of the teeth for 2 minutes. As such there is no recommendation in the available literature about the frequency of application of SDF solution. However some authors applied the solution annually and others biannually.

Advantages of SDF pointed out by Bedi and Infirri (1999)

Untreated dental caries which can lead to pain and infection later can be managed at early stages by the noninvasive application of SDF solution. Low cost of SDF treatment makes it available and affordable for many communities. The procedureis simple and allows non-dental professionals including primary health care workers to apply SDF to children. The treatment does not require expensive equipment or support infrastructure such as piped water and electricity. Therefore, the technique is easy to master and set up is inexpensive. And because of the simplicity of the armamentarium needed it allows the trained workers/non professionals to deliver the treatment to people living in

remote areas who can not usually access preventive services.[1,7,29]

Adverse effects of SDF

Despite of leading trend in the application of SDF, yet there are many disadvantages of using SDF solution**. SDF causes black discoloration of the carious dentin**, and it must be handled with care by using protective gloves.[30] This staining may be prevented by the use of potassium iodide (KI) following SDF application however this is not a proven phenomenon. It has got unpleasant metallic taste. In many cases mild gingival irritation has also been seen around gingival margins, but it undergoes spontaneous healing with in 2 days. Many instances of dental fluorosis and accidental toxic overdose from the regular use of 40% silver fluoride, haning same mode of action as SDF although these issues have been rejected.[31-34]

Safety of SDF

Silver has been proven as both asset and a concern in arresting caries in primary dentition. However, there are many reported cases which have shown that use of 40% AgF could induce dental fluorosis. Studies in Japan evaluating the oral tissue response to SDF applications found self healingmild gingival irritation after its use, but no severe pulpal damage was reported. Another study on 55 primary carious teeth of children aged 6 to 13 years in Australia, found that over 90% of the teeth treated with AgF show histologically the presence of a wide odontoblast layer, thus favouring the pulpal[1,35,36]

Indications of SDF

SDF is a palliative treatment. When ART is not possible for infants and toddlers SDF plays an effective role in arresting caries because primary action of SDF is its germicidal nature.[1]It has got potential use in public health settings because it provides noninvasive treatment and prevention at the same time, easy to apply and handle. These qualities make it an excellent choice for arresting caries, especially among disadvantaged populations.[37]

Various indications for using SDF solution:

For inhibiting Caries process in primary dentition

A wide range of studies have reported the efficient use of SDF solution to arrest caries lesions in deciduousand permanent teeth. Sato *et al*, owing to its antibacterial property stated that SDF can be effective for the prevention of pits and fissures caries of posterior teeth as well. Nishino and Masslerin their study have mentioned that when teeths were treated with $Ag(NH_3)_2F$ they had significantly less caries scores compared to the fissures when they were treated with SnF_2 8%.[1]

Arresting root caries

Generally, it is observed that oral health is more compromised in geriatric people.[38] Therefore, WHO prioritized the prevention and treatment of root caries[9] Due to the mineral composition on rooth surface, these surfaces are naturally more susceptible to demineralizations.[4,9] This suggests to a double caries progression rate in dentin than in enamel.One of the study on institutionalized elderly patients concluded that the annual application of SDF demonstrated a greater benefit than oral hygiene instructions alone.[39]

For pulp protection

SDF can halt biofilm formation process as well as matrix metalloproteins(MMP) activities.[40] It also increases the microhardness of carious dentin, reduces loss of calcium and phosphate ions from tooth structure.[6,9,10] Sinha *et al*. suggested that SDF can be used as an alternative therapy to $Ca(OH)_2$ for indirect pulp capping.[15] Most laboratory studies have focused on changes in mineral content such as the calcium and phosphate level, fluoride content and microhardness of dental hard tissue.[15] A vitro study showed that carious primary teeth treated with SDF had favourable pulpal response histologically, which was evidenced by the presence of abundant reparative dentine and a wide odontoblast layer.[13]

As an effective intracanal medicament

The SDF is as effective as 2% CHX in removing E. faecalis from infected root canals. Silver interacts with the sulphydryl and thiol groups present in the bacterial amino acids and nucleic acids. This inhibits cell division, cellular respiration, metabolism, and biofilm formation. Several investigations conducted by Coward[24] and Bragg *et al* [25] have studied the cellular mechanisms that are affected by silver, thus proving its effectiveness as an anti‑bacterial agent.[13]

In treating dentinal hypersensitivity

Because of the thermal and physical changes, the fluid from oral environment enters into dentinal tubule causing dentinal hypersensitivity. The movement of fluid can be toward the the pulp or the outside the dentin. SDF acts by blocking these tubules and thus reducing the dentinal hypersentivity.[41]

It is also used to prevent pit and fissure caries, secondary, to treat infected root canals and to prevent the fracture of endodontically treated teeth.[12,25,28]

In Atraumatic Restorative Treatment

Chu and Lo in their review proposed the use of SDF as caries arresting agent in atraumatic restorative technique.[42]Gotjamanos *et al*. in his study on 55 carious primary teeth applied 40% AgF to residual caries followed by the placement of glass ionomer cement[22]and found benevolent pulpal response.[33] Proposed hypothesis regarding drill less atraumatic filling which will involve the application of SDF (38%) to arrest dental caries.[43]

DISCUSSION

Despite the wide variety of availability of fluoride releasing agents to prevent dental caries,it is still the most prevalent problem in dentistry. Infected tooth may go straight for the drill and when one does that, highly infected mist transports bacteria to new sites in the mouth and drive microbes deep into dentinal tubules and close to pulp and contaminates entire environment.

SDF in this regard is one of the most trending and approachable technique for arresting caries in both primary and permanent dentition.Presently various biomaterials are available which leads to minimal loss of healthy dental tissue, especially by using minimally invasive operative techniques and by applying caries arresting substances like 38% SDF, which has been used to minimize premature loss of primary teeth affected by carious lesions close to their age of normal exfoliation.[44]There are few studies which support the use of

SDF in primary dentition, while few studies reject it due to its reported adverse effects.[25,35]

The success rate of SDF in arresting caries was found to be 70% after 30 months of its use. SDF is available in various concentrations such as 38%, 30% and 12% and among these 38% is the most commonly used concentration. It has been reported that 38% SDF could reduce mineral loss and collagen exposure from acid challenge by pH cycling.[20] In a clinical trial in Cuba, SDF solution was applied onto primary canines and molars, permanent first molars every 6 months for 3 years showed positive results of arrestment of 77% of the treated carious lesions. Another clinical trial in Nepal elucidated 35% arrestment of the active carious lesions in primary teeth after 2years.[32]

Various clinical trials have demonstrated that SDFcan arrest caries. However, the mechanism of action is not yet fully known. Previous studies on mechanism of SDF have mostly focused on antimicrobial effects and mineral changes in tooth structure.[45]Although SDF has been used in many European countries but, the use of SDF is not yet cleared by the US Food and Drug administration. Based on the different studies there were many factors responsible for benificial effects of SDF in arresting caries: frequency, concentration of the solution, and the method of caries assesment. According to the study conducted by Qing Hui Zhi *et al*, biannual 38% SDF application is appropriate in arresting the active carious lesion and the frequency of SDF application was found to bedirectly proportional to the proportion of active dental cariest that had became arrested.[46]

Chu and Lo also proposed the use of SDF as caries arresting material in atraumatic restorative technique and as an indirect pulpcapping agent.[31] Gotjamanos *et al* in his study used 40% AgF to residual caries followed by atraumatic glass ionomer cement placementand found commendable pulpal response.[33,34] Santos *et al*. examined underprivileged school children and concluded that 30% SDF was far more better than intermediate restorative technique (IRT)for arresting caries. indicating that its use for disadvantaged communities can declare a paradigm shift in pediatric practice.[47]
Overall success rate of SDF in arresting active caries was found to be 70% with a suggestion of replacing with SDF for indirect pulp capping.[48]

Various clinical trials have demonstrated that the beneficial effects of SDF. Targino *et al* also evaluated the cytotoxic effects of Nano Silver Fluoride (NSF) against S. mutans in comparison to chlorhexidine and silver diamine fluoride and concluded that the NSF is a better bacteriostatic/ bactericidal compound. Zhang *et al* also suggested the use of silver nanoparticles in adhesives, composites, cements and sealants to inhibit biofilms and caries.[39]

In a study conducted by Lodra *et al* in 2005, around 77% of the active caries that were treated became inactive during the study, and the efficacy of preventing new caries was 80% in the primary teeth and 65% for the first permanent molar. [32,39]Murase *et al* and Kimura *et al* have shown that $(Ag(NH_3)_2F)$ was the most effective against erosion and abrasion and dentinal hypersensitivity.[1]

Proposed riskattributed to SDF is itsability to cause pulpal damage.Because of the growing interest in the use of SDF for arresting active carious lesion, a study on the pharmacokinetics of silver fluoride has been reported by Vasquez *et al*.who suggested that serum concentrations of fluoride and silver after application of SDF produces minimal toxicity risk when used in permanent dentition.[50] But stillas per the literature available, the issue of acute toxicity or the chances of fluorosis with the use SDF is debatable.[34,49]

Some authors have reported transient lesions in oral mucosa through direct contact with SDF solution.[25]After application of SDF solution, black discoloration of the carious dentin occurs which is probably the most undesirable side-effect thus produced. This staining may be prevented by applying potassium iodide (KI) after the SDF application however.[30]

Some issues like dental fluorosis and accidental toxic overdose from the routine use of 40% silver fluoride are also linked with its use, which has mechanism of action as SDF [34] Although these concerns have been rejected, with the application of low concentrations of.[49]

The advantages and disadvantages of this ACT approach have been elucidated in studies.[31] It is interesting to note that professionals are using SDF solution internationally. Currently SDF does not have FDA approval i.e. experiments are still needed to refute the concerns regarding SDF safety.[7] The need for agents such as SDF should be evaluated in terms of WHO Millennium The advantages and disadvantages of this ACT approach have been elucidated in studies.31 It is interesting to note that professionals are using SDF solution internationally. Currently SDF does not have FDA approval i.e. experiments are still needed to refute the concerns regarding SDF safety.7 The need for agents such as SDF should be evaluated in terms of WHO Millennium Development Goals for Health, particularly the oral health goals, because it is highly effective, arrests caries and has no major adverse effects.[49]

CONCLUSION

To address the unmet treatment needs of million of people it is necessary to find a solution to the dental caries problem. New and renewed efforts must be amalgamated together to focus on combating serious emerging increase in dental caries. Dentistry has the capability and resources to deal with this challenge and the time is now. The potential benefit of SDF is worthy of attention: its ability to arrest dental caries; minimal armammentatrium for its use, and reduced cost of treatment makes its use more recommendable in dental practice. By implication, SDF could provide a new quantitative preventive benefit for individuals and populations.

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