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Nano Silver Fluoride for Arresting Dental Caries

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INTRODUCTION:

Dental caries is one of the most prevalent diseases affecting mankind right from childhood to elderly. It is a multifactorial disease affecting both primary and permanent dentition [1]. According to Global Oral Health Data Bank, the prevalence of dental caries usually varies from 49% to 83% across countries throughout the globe. Dental caries has a negative impact on health related quality of life, irrespective of age. Though the prevalence of dental caries worldwide has decreased, the rates are different in high and middle or low income countries. There is a greater decline in prevalence of dental caries among the high income countries, while in some low and middle income countries, there is less or inverse decline which may be due to various risk factors [2]. Risk factors associated with dental caries include frequent exposure to dietary sugar and refined carbohydrates, inappropriate bottle feeding, low salivary flow rates, developmental defects of tooth enamel, low socioeconomic status, caries susceptibility, maternal caries, high maternal levels of cariogenic bacteria, and poor maternal oral hygiene [3] [4].

Many advances have been seen in treating dental caries. There is a drastic shift in the method of treatment of dental caries from invasive procedures to minimal invasive procedures [5]. Minimally invasive techniques have gained importance mainly for preventing caries and arresting the progress of carious lesion. These treatments can be given at the community level and the application procedure is less time consuming.

Topical fluorides has gained its popularity as an effective measure in caries prevention as it exerts anti-caries property since decades [6]. Various topical fluoride agents have evolved over years such as Sodium fluoride (NaF) (1941), Stannous Fluoride (SnF2) (1947), Acidulated Phosphate Fluoride (APF) (1963), Varnish containing Fluoride (1964) and Amine Fluoride (1967) [7]. Since 1969, SDF has been used to arrest caries of the primary teeth in children, prevent pit and fissure caries of the erupting permanent molars and prevent root caries in elderly people and was approved by US Food and Drug Administration (FDA) in 2014 [8].

Silver (Ag) ions or salts are known to have been widely used in dentistry since 19th century as main component in restorative material because of its antimicrobial effect due to sustained ion release and low bacterial resistance [9]. With the advancement of nanotechnology in recent days, silver nanoparticles (AgNPs) have been synthesized which has potent antimicrobial properties and has unique interactions with bacteria and fungi species [10].

A newer innovative material called Nano Silver Fluoride was introduced by Targino et al which has combined efficiency of Nano silver particles and fluoride [11]. It combines preventive and antimicrobial properties, has overcome the drawbacks of other materials and has been emerging as an effective anti-caries agent.

MECHANISM OF ACTION:

Antimicrobial properties of nanostructured silver-based formulations have been demonstrated against microorganisms such as bacteria, viruses, and fungi [12]. Various theories have been discussed in the literature on the mechanism of action. Silver ions are capable of acting on different structures of the bacterial cell. Silver ions (Ag+) bind to molecules containing sulphur or nitrogen, results in defects in bacterial cell membrane, leads to loss of their cell contents and death of bacteria. Another mode is free radical formation by the silver nano particles when in contact with bacteria, and these radicals have the ability to damage the cell membrane and make it porous which can ultimately lead to cell death. Studies also stated that silver interact with sulfhydryl groups of proteins and with DNA, altering hydrogen bonding, respiratory processes, DNA unwinding, cell wall synthesis, and cell division [13]. Silver Nano particles also stimulate oxidative stress response causing bacterial cell destruction. Cell membrane disruption and DNA modification via reactive oxygen species (ROS) as the principal agent were also described in the literature [9].

The size of Nano Silver particles has effect on the antimicrobial activity. Antimicrobial efficacy of Nano silver particles is inversely proportional to the size of silver nano particles. Lesser the size of particles, higher the antimicrobial efficacy [14]. Nano silver fluoride also prevents the mineral loss on the enamel and have shown significant ability to prevent bacterial biofilm formation by disrupting its adhesion (anti-adherence) and also has anti-cariogenicity. Also fluorides is effective in controlling cariogenic biofilms and causes significant reductions in bacterial extracellular polysaccharide formation. They are also effective for acidogenicity reduction on cariogenic biofilm and has remineralizing capacity [15].

PREPARATION:

Targino AG et al prepared Nano Silver Fluoride by following method. To prepare Nano silver fluoride, 1 g of chitosan was dissolved in 200 mL of 2% (V/V) acetic acid solution. The solution was stirred overnight and then vacuum filtered. Later, it was added to 60mL of chitosan solution and placed in an ice bath while stirring. Then, 4mL of 0.012 mol/L silver nitrate solution (AgNO3) was added and incubated for 30 minutes before adding sodium borohydride (NaBH4). A mass ratio of 1:6 between AgNO3 and NaBH4 was maintained by adding the solution drop wise. After 45 minutes in the ice bath, the colloid was removed from the bath and allowed to reach room temperature before being stored at 4°C [11] [15]. The flask was then removed from the ice bath and the

sodium fluoride (10,147 ppm of fluorine) was incorporated. The stirring was maintained overnight [11].

Preparation of 5% Nano Silver Fluoride:

Haghoo et al (2014) described the preparation of 5% Nano Silver Fluoride using weight dilution method. Silver nano-particle powder (0.5 grams) (99.5% pure; Particle size of less than 100 nanometre containing polyvinyl pyridoline as a dispersant) was added to 10 ml of 22,600 ppm of slow release Sodium fluoride varnish in a light proof brown bottle and vigorous stirring is performed to achieve uniform dispersion of Nano-silver particles [5].

APPLICATION PROCEDURE OF NANO SILVER FLUORIDE VARNISH:

Nano Silver Fluoride varnish is applied using the following simple steps [11]:

Thorough oral prophylaxis is done.

No effort would be made to remove the caries or unsupported enamel.

Cotton roll isolation is done

Initial cleaning of cavity to be performed by using small cotton pellet

Apply a single drop (0.1 mL) of 5% Nano silver fluoride with a disposable micro applicator tip for 10 seconds. Only single application is done and no repetition.

Cavity will be closed with a cotton pellet for ten minutes.

One micro applicator tip would be used and discarded after single use.

DIFFERENT STUDIES:

In-vitro Studies

Before the introduction of Nano Silver Fluoride by Targino AG et al in 2014, in-vitro studies using Silver nano particles were done by Sondi I et al (2004), Kim JS et al (2007), Shahverdi AR et al (2007), Espino-Cristobal LF et al (2009). These studies exhibited antimicrobial effect of Silver Nano particles against Escherichia coli, Staphylococcus aureus, Yeast and Streptococcus mutans [16] [17] [18] [19].

Targino AG et al (2014) conducted a study to evaluate the antimicrobial activity of Nano Silver Fluoride on Streptococcus mutans and its cytotoxic effect in comparison with Chlorhexidine and Silver Diamine Fluoride. The study showed that Nano Silver Fluoride had antimicrobial activity comparable to that of Silver Diamine Fluoride and it also exhibited lower cytotoxicity than Silver Diamine Fluoride [11].

Haghgoo R et al (2014) conducted an in vitro study which demonstrated the antimicrobial effect of Nano Silver Varnish on Streptococcus mutans and Streptococcus salivarius [20].

Nozari A et al (2017) conducted an in vitro study to determine the remineralisation ability of Sodium Fluoride Varnish, Nano-Hydroxyapatite Serum and Nano Silver Fluoride on Enamel of primary anterior teeth. The study results showed that the greatest remineralisation was observed in the Nano Silver Fluoride Group [21].

Teixeira JA et al (2018) tested Nano Silver Fluoride and Sodium Fluoride dentifrice in-vitro against Streptococcus mutans and their performance in enamel remineralisation. It was found that Nano Silver Fluoride dentifrice had better antibacterial effect than Sodium Fluoride dentifrice and it prevented mineral loss on enamel surface during pH cycling similar to Sodium Fluoride dentifrice [15].

Randomized Controlled Trials

Santos VE Jr et al (2014) investigated the effectiveness of Nano Silver Fluoride Solution in arresting dental caries in primary teeth in children. Water was used as the control group. The Dental caries was assessed using International Caries Detection and Assessment System II (ICDAS II) criteria. It was observed that at the end of 12 months 66.7% of the dental caries treated by Nano Silver Fluoride was arrested, while the control group showed that 34.7% of the dental caries were arrested and the difference was statistically significant. Nano Silver Fluoride was found to be effective in arresting dental caries and there was no staining of teeth observed [22].

Tirupathi S et al (2019) conducted a study to compare the effectiveness of 5% Nano Silver Fluoride Varnish with 38% Silver Diamine Fluoride varnish in arresting dental caries in primary molars of school children . Dental caries was assessed using International Caries Detection and Assessment System II (ICDAS II) criteria. At the end of 12 months, it was observed that there was no significant difference between the two groups in arresting dental caries. Nano Silver Fluoride Varnish did not result in staining of teeth as observed in case of Silver Diamine Fluoride [5].

Nagireddy VR et al (2019) evaluated the effectiveness of Nano Silver Fluoride Solution in arresting dental caries in deciduous molars of children. Saline was used as the control. Dental caries was assessed using International Caries Detection and Assessment System II (ICDAS II) criteria. At the end of 12 months, arrest of dental caries was seen in 65.21% of teeth in Nano Silver Fluoride group while it was observed only in 28.88% of teeth in the control group and the difference was statistically significant. In the Nano Silver Fluoride group there was no staining of teeth, no complaint of metallic taste in the mouth nor were any lesions found in the oral mucosa [23].

ADVANTAGES [5]

1. **Control of pain and infection**: NSF is effective in arresting caries progression that if left untreated will cause pain and infection
2. **Affordable cost**: The cost of NSF treatment is low and should be affordable in most communities
3. **Simplicity of treatment**: The procedures are simple and enable non dental professionals including primary health care workers to be trained in the application of NSF hence making it more available and affordable.
4. **Minimal armamentarium and support required**: The treatment being simple does not require any expensive equipment or support infrastructure such as piped water and electricity like other conventional dental treatments.
5. **Non-invasive procedure**: Prevents the risk of spreading any sort of infection in very low. Also improving patient compliance and attitude towards dental treatment.

COMPARISON OF NANO SILVER FLUORIDE AND SILVER DIAMINE FLUORIDE

Silver diamine fluoride is a material used for arresting dental caries which has been gaining popularity in the recent times. Some of the differences between nano silver fluoride and silver diamine fluoride (Table 1).

Table 1: Comparison between nano silver fluoride and silver diamine fluoride

NANO SILVER FLUORIDE	SILVER DIAMINE FLUORIDE (SDF)
Nano silver particles has enamel remineralizing potential mainly in case of deciduous teeth.	SDF is known to effectively prevent and control dental caries. It is used in different concentrations in deciduous teeth with a high risk of disease or caries activity.
Nano silver particles has powerful antimicrobial activity even at a lower concentration due to its reduced size and increased contact area. It has bactericidal activity against Streptococcus mutans, Enterococcus faecalis and Escherichia coli. It also has anti-biofilm properties.	SDF has been proven to be effective in inhibiting growth of cariogenic bacteria associated with dentinal caries formation such as Streptococcus mutans and Lactobacillus acidophilus. It has also been effectively used as root canal medicament because of its effect against Enterococcus faecalis.
Nano-silver compounds do not form oxides when contacting oxygen in the medium and so there is no darkening of the demineralized enamel. So no staining of teeth is seen and doesnot cause esthetic modification.	Use of SDF causes staining of caries tissues as dark brown due to formation of oxides, which may be unacceptable in anterior teeth with esthetic concern.
Clinical trails with Nano silver fluoride has shown promising results for the prevention and treatment of dental caries in deciduous teeth of children.	Clinical trials demonstrated that SDF is effective in preventing and arresting dental caries in primary teeth and permanent teeth
Laboratory study has shown the use of silver nano particles with sodium fluoride has inhibited collagen degradation and remineralized artificial dentine caries.	Laboratory studies showed that SDF increases the resistance of dentine to demineralization and collagen degradation.
Nano silver fluoride has low cytotoxicity to living cells	SDF causes slight irritation of gingival and mucosal tissues when contacted.
Nano silver fluoride formulation is mostly prepared in 5% concentration.	SDF is available in various concentration such as 38%, 30% and 12%.

TOXICITY:

At the concentrations used in dental materials, there are no reports on toxicity and adverse effects far till now. Cytotoxic studies have reported that Nano silver has lower cytotoxicity when compared to other dental materials.

SCOPE FOR FURTHER RESEARCH:

Studies should be done to know the effectiveness of the material on root caries, dentinal sensitivity and in prevention of dental caries. Randomised Controlled trials to know the effectiveness of Nano silver fluoride in arresting dental caries on permanent teeth hold scope for further research. Effectiveness of Nano silver fluoride in comparison with silver diamine fluoride and sodium fluoride varnish should be further assessed. Also further extensive cytotoxic studies are required to gather thorough knowledge regarding toxicity of the material. Studies can also be done to assess the cost effectiveness of the material.

CONCLUSION:

Nano silver fluoride has great potential in the treatment to arrest and prevent dental caries as it is simple, non-invasive and less technique sensitive. Owing to its advantages there is great scope in the use of this material in public health programs.

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