

A Randomized Controlled Trial Evaluating the Effectiveness of Nanosilver Fluoride in Arresting Dental Caries in School Children

Chigurupati Devi¹, Rayala Chandrasekhar², C Vinay³, KS Uloopi⁴, Kakarla Sri RojaRamya⁵, Manumanthu V Ramesh⁶

ABSTRACT

Aim: The study evaluated the effectiveness of nanosilver fluoride (NSF) in arresting dental caries in 4–8-year-old school children.

Materials and methods: The two-arm, parallel-group randomized controlled trial included a total of 148 children aged 4–8 years with active carious lesions. Children were randomly divided into two groups: group I—NSF ($n = 74$); and group II—water (placebo and $n = 74$). Baseline data were recorded using the International Caries Detection and Assessment System (ICDAS) II criteria, and the teeth were treated with either of the solutions. Later, the teeth were evaluated by two blinded examiners for the lesion activity using ICDAS II criteria at 1, 3, and 6-month intervals. The obtained data were analyzed using the Chi-squared test for intergroup comparison and Cochran's Q test for intragroup comparison. Cohen's κ test was used to check the interexaminer and intraexaminer variability.

Results: Carious teeth treated with NSF have shown 56.3, 59.2, and 62% arrested carious lesions, whereas the placebo group has shown 0, 2.9, and 4.4% arrested lesions at 1, 3, and 6-month intervals, respectively. NSF showed a high statistically significant difference ($p < 0.001$) in arresting dental caries compared to the control group at all the time intervals.

Conclusion: Nanosilver fluoride (NSF) is found to be effective in arresting dental caries without staining carious lesions. Therefore, it can be used to reduce the bacterial load for caries stabilization in the initial phase of the comprehensive treatment protocol for the management of children with active caries lesions.

Clinical significance: Most of the decayed teeth in the primary dentition remain untreated either because of inaccessible dental services or the uncooperativeness of children. Hence, there is an absolute need for a cariostatic agent which arrests the progression of caries in a simple and noninvasive manner. The results of this study evidence that NSF effectively arrests dental caries in primary teeth. Hence, this can be a very economical way of arresting caries in the population who don't have access to regular dental treatment.

Keywords: Caries arrest, Cariostatic agent, Nanosilver fluoride, Randomized controlled trial.

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INTRODUCTION

Dental caries in children is one of the major public health problems since it impairs the masticatory function and reduces the quality of life. As oral healthcare services are not readily available everywhere, many decayed teeth in children go untreated. Traditionally, a surgical restorative approach has been used to treat dental caries, which is relatively expensive and calls for sophisticated dental equipment and trained professionals. Therefore, there is a need for a less invasive simple clinical technique to treat decayed teeth in children of underprivileged areas as well as uncooperative children.

Remineralization of caries lesions has become more popular recently in the field of minimally invasive dentistry, and the caries arrest approach is being popularized as a part of fundamental oral care. Several cariostatic agents, which apparently ensure the reduction of remaining microorganisms, have been developed. Earlier reviews have advocated the use of silver diamine fluoride (SDF) for the control of caries. However, an adverse effect, black staining of the tissues that it comes into contact has been reported after its application.^{1–3} SDF-treated caries lesions remain black indefinitely, posing a considerable aesthetic concern, particularly in the anterior teeth. As a result, despite its therapeutic effects, dentists tend to limit its use.³ Therefore, there is an evident need for a cariostatic agent with

^{1–5}Department of Pediatric Dentistry, Vishnu Dental College (VDC), Bhimavaram, Andhra Pradesh, India

⁶Department of Public Health Dentistry, Vishnu Dental College (VDC), Bhimavaram, Andhra Pradesh, India

Corresponding Author: Kakarla Sri RojaRamya, Department of Pediatric Dentistry, Vishnu Dental College, Bhimavaram, Andhra Pradesh, India, Phone: +91 8985774540, e-mail: roja.ramya86@gmail.com

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the least adverse effects and ease of use in children with active caries lesions.

Nanosilver fluoride (NSF), a novel formulation with both caries prevention and antimicrobial properties, has been developed.⁴ It contains nanosilver particles, chitosan, and fluoride. NSF has been shown to be safe and effective, having excellent antibacterial characteristics against the principal microorganisms responsible for the onset and progression of dental caries.^{5,6} To date, very few studies have been carried out

to authenticate its clinical efficacy in arresting dental caries. Therefore, the current investigation was performed to assess the effectiveness of NSF in arresting dental caries in school children's primary teeth.

MATERIALS AND METHODS

With the approval of the Institutional Review Board (IRB/VDC/ MDS14 PEDO 3), a two-arm, parallel-group randomized controlled trial was conducted. The experimental protocol complies with the ethical guidelines for conducting human experimentation set forth in the Helsinki Declaration.

With the consent of the school administration, a total of 375 children between the ages of 4 and 8 years were screened from three schools in the West Godavari district of Andhra Pradesh. Among them, 148 children who met the inclusion criteria were chosen. The parents and school administration were informed of the study's objectives and procedures before giving their written consent.

Children who have an active carious lesion at the dentine level (ICDAS II code 5) in primary teeth were considered for the study. Children having systemic illnesses, special healthcare needs, and those who have proximal caries were excluded from the study. The study outcome is the assessment of the effectiveness of NSF in arresting caries lesions where the baseline data is compared with the postintervention data at 1, 3, and 6-month intervals.

Sample Size and Allocation

Based on the findings of the earlier study, the sample size was determined.⁴ The study required 67 samples per group, which was determined using G*Power 3.1 software with a level of significance set at 5% and power at 80%. With a 10% loss to follow-up considered, each group was comprised of 74 children.

The total number of children involved in the study was 148, with random allocation evenly dividing them into two groups: group I—NSF; and group II—water (placebo), using computer-generated randomization of block size four. The allocation details were recorded on cards, sealed in numbered envelopes, and kept hidden from the outcome assessor and data analyst to maintain blinding.

Preparation of NSF Solution

Nanosilver fluoride (NSF) solution of concentration 33989.8 µg/mL was prepared by Nanolabs, Jamshedpur, Jharkhand, India, according to the formulation given by Santos et al.⁴ For the preparation of colloidal silver, 200 mL of 2% acetic acid (V/V) was taken, and 1.0 g of chitosan was dissolved in that, which was then filtered under a vacuum after stirring overnight. Next, the 60 mL of chitosan solution was stirred while being cooled in an ice bath. Then 4.0 mL of 0.012 mol/L silver nitrate (AgNO₃) solution was introduced 30 minutes prior to mixing sodium borohydride (NaBH₄). NaBH₄ solution was added dropwise so that the 1:6 mass ratio of AgNO₃ and NaBH₄ was maintained. The solution's stability was enhanced by the addition of sodium fluoride (NaF) toward the end. The silver nanoparticles had an average size ranging from 3 to 5 nm. The concentrations of chitosan, silver, and NaF in the prepared solution were 28585, 376.5, and 5028.3 µg/mL, respectively.

Procedure

The children were examined using diagnostic instruments under daylight. Prior to the intervention, the children were asked to rinse their mouths with water. Then the carious primary teeth were

isolated with cotton rolls. No attempt was made to remove the caries in both groups.

In the experimental group, a micro brush was employed to apply two drops of NSF solution (33989.8 µg/mL) onto each tooth surface for 2 minutes before gently removing any excess with a cotton pellet. In the placebo group, the same procedure was followed with water. After the treatment procedure, the children were instructed to refrain from consuming any food or beverages for a period of 1 hour. Treatments in both groups were performed by a single operator. Oral hygiene and dietary instructions were given to all the children after the completion of the procedure.

Follow-up examinations were performed by two blinded examiners at the time intervals of 1, 3, and 6 months. Two examiners have been trained to evaluate active and arrested carious lesions using visual and tactile inspection according to the ICDAS II criteria. When a blunt probe penetrates the dentin easily with light force, they were recorded as active carious lesions. If the dentine could not be penetrated, they were recorded as arrested carious lesions.

To standardize the examiners, 10% of the sample size was allocated. Cohen's κ test was used to determine the reproducibility of caries diagnosis between the examiners and within the same examiner. The results showed a κ value of 0.90 for active caries and 0.83 for arrested caries in terms of the interexaminer agreement, whereas intraexaminer reliability was 0.88, and 0.86 for active and arrested lesions, respectively, and this indicates an almost perfect consistent agreement.

Statistical Analysis

The data collected was exposed to descriptive statistical analysis, utilizing the Chi-squared test for comparison between groups and Cochran's Q test for comparison within groups. Statistical significance was computed with a *p*-value of ≤ 0.05 considered significant, and a *p*-value of ≤ 0.001 considered highly significant.

RESULTS

The CONSORT flow diagram (Flowchart 1) illustrates the involvement of the participants throughout the duration of the study. The study's sample comprised 71 males and 77 females, with a mean age of 6.19 ± 0.56 years among the participants. There were three dropouts in the NSF group; in which two children discontinued school, and one child migrated to another city. In the control group, six children were lost to follow-up since they migrated to other cities.

On intragroup comparison, NSF has shown 56.3, 59.2, and 62% of arrested carious lesions at 1, 3, and 6-month intervals, respectively. The statistical analysis indicated a significant difference between the time intervals (*p* = 0.05). The water group showed 0, 2.9, and 4.4% arrested lesions at 1, 3, and 6-month intervals, respectively (Table 1).

On intergroup comparison, a high statistically significant difference (*p* = 0.000) was noticed between the groups at all the time intervals. NSF showed a higher percentage of arrested carious lesions compared to the water group at all the time intervals (Table 2).

DISCUSSION

With a greater understanding of caries pathology and evidence from clinical studies, it is now believed that the caries arresting approach can effectively prevent caries progression. NSF has shown promising properties as a cariostatic agent.⁴ However, efforts are

Flowchart 1: CONSORT flow diagram

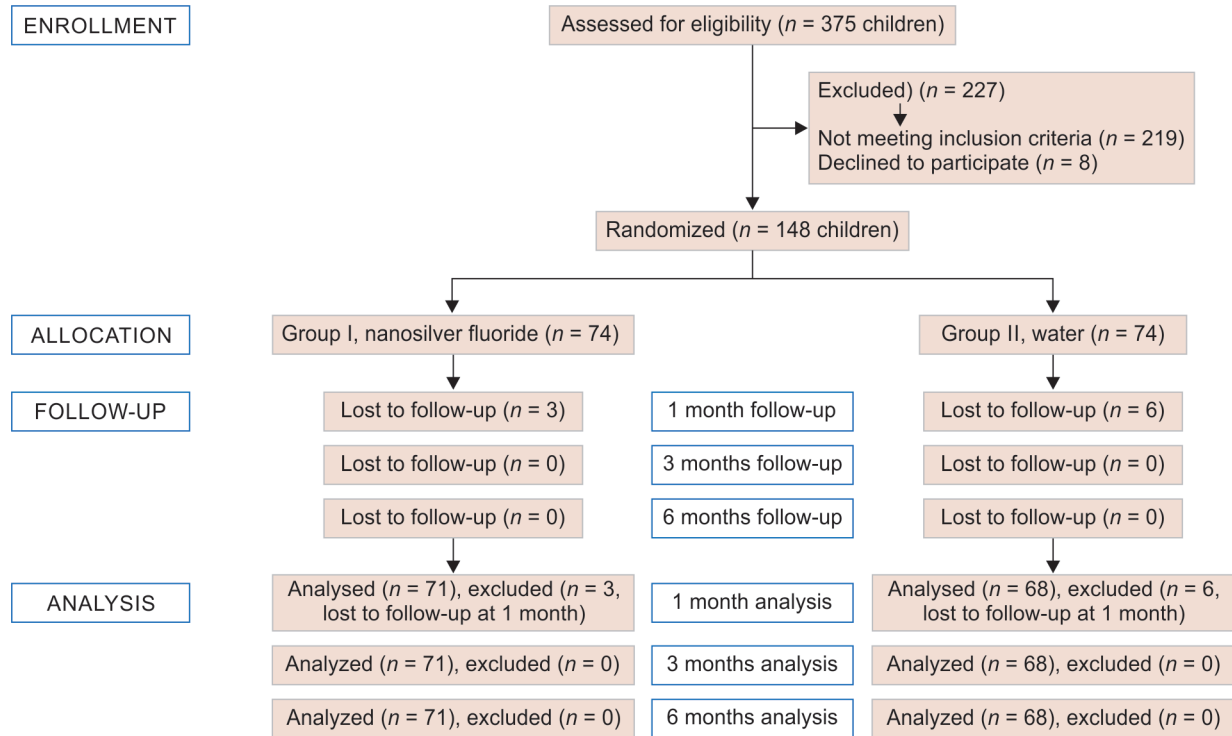


Table 1: Intragroup comparison of the cariostatic effect of NSF at different time intervals

Time interval	Arrested n (%)	Not arrested n (%)	Cochran's Q	p-value
1 month	40 (56.3%)	31 (43.7%)	6.000 ^a	0.05, S
3 months	42 (59.2%)	29 (40.8%)		
6 months	44 (62.0%)	27 (38.0%)		

Cochran's Q test; S, significant

Table 2: Intergroup comparison of the cariostatic effect of NSF and water at different time intervals

Groups	1 month		3 months		6 months	
	Arrested n (%)	Not arrested n (%)	Arrested n (%)	Not arrested n (%)	Arrested n (%)	Not arrested n (%)
Group I (NSF)	40 (56.3%)	31 (43.7%)	42 (59.2%)	29 (40.8%)	44 (62.0%)	27 (38.0%)
Group II (water)	0 (0%)	68 (100%)	2 (2.9%)	66 (97.1%)	3 (4.4%)	65 (95.6%)

p-value = 0.000, HS

Chi-squared test; HS, highly significant

still needed to evaluate its clinical effectiveness in arresting caries. Hence, in the present study, NSF solution has been evaluated in halting primary teeth caries.

NSF has the advantages like the nonmetallic taste, low toxicity, better biocompatibility, and nonstaining of the carious tissue black compared to SDF.⁵ Targino et al. found that NSF is less toxic and more biocompatible than SDF.⁵ Santos et al. have demonstrated that the effectiveness of NSF (66.7%) was similar to that of SDF (66.9%).⁴ Similarly, Tirupathi et al. have shown that using a dental varnish containing 5% nanosilver-infused NaF on an annual basis is comparably efficient to using 38% SDF in halting the advancement of dental caries in primary molars.⁷

In the current study, the noncaries removal principle was followed, and no attempt was made to remove caries which made the application process easier and faster. As it is a noninvasive

therapy, it makes subject compliance possible, even for young children. According to Chu et al., the number of carious surfaces that were arrested showed no variation between teeth that underwent caries excavation before SDF application and those that did not.⁸ There is no confirmation that fluoride agents' ability to arrest dental caries is affected by the removal of carious tissues before their application.

In the present study, NSF has shown an overall success of 62% in arresting carious lesions at 6-month intervals. This impact might be due to the interaction between fluoride, chitosan, and silver nanoparticles. Silver nanoparticles and chitosan are primarily effective against cariogenic bacteria, whereas fluoride ions act primarily on the tooth structure. Nanosilver disrupts bacterial membranes, most likely as a result of the generation of reactive oxygen species, including free radicals.⁹⁻¹¹ The small-sized, spherical

NSF particles (3–5 nm) used in the present study further enhance the antibacterial efficacy by expanding the contact surface and might also lower the toxicity.^{12–14}

Similar to the present study, Santos et al. noticed a success rate of 72.7% at 5 months interval when NSF was applied once a year.⁴ Nozari et al. have reported higher posttreatment surface microhardness values with NSF compared to nanohydroxyapatite serum and NaF varnish, suggesting that NSF has a higher capacity for remineralization than the other two.¹⁵ e Silva et al. conducted the microhardness, fluorescence spectroscopy, and optical coherence tomography tests and demonstrated that in deciduous enamel remineralization, the action of NSF is comparable to NaF.¹⁶ They also reported that pH drops and *Streptococcus mutans* adhesion to the enamel surface were better prevented by NSF than by NaF.¹⁶

Nanosilver fluoride (NSF) showed superior effectiveness in arresting dental caries without staining carious lesions. Hence, this can be a very economical way of arresting caries in the population who don't have access to regular dental treatment. However, long-term clinical studies are necessary to validate the clinical efficacy of NSF in community programs.

CONCLUSION

Nanosilver fluoride (NSF) is found to be effective in arresting dental caries without staining carious lesions in primary teeth. Hence, it can be used to reduce the bacterial load for caries stabilization in the initial phase of the comprehensive treatment protocol for the management of children with active caries lesions.

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