

Comparative Evaluation of Salivary Fluoride Concentration after Topical Application of Silver Diamine Fluoride and Sodium Fluoride: A Randomized Controlled Trial

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ABSTRACT

Background: The topical fluoride acts on the tooth in many ways and their most important action is inhibition of demineralization and enhancement of enamel remineralization.

Aim: The purpose of this clinical trial was to assess the fluoride concentration in saliva before and after 38% silver diamine fluoride (SDF) and 5% sodium fluoride (NaF) application on enamel and duration of its availability at different time intervals.

Methodology: A randomized clinical trial was conducted among 40 healthy children aged between 6 and 12 years. The participants were then randomly allocated into two different groups in which the first group (group I) was given 30% SDF and the second group (group II) were topically applied with 5% NaF solution. The fluoride concentration was measured in the salivary samples, which were collected at three time intervals, that is, at baseline (S1), 2 hours (S2), and 24 hours (S3) after application. Analysis of variance (ANOVA) test was used for evaluation and independent paired *t*-test was conducted for comparison between groups.

Results: When using an ANOVA with repeated measures with a Greenhouse–Geisser correction, the mean scores of fluoride concentration were statistically significantly different at different time intervals for both NaF ($F = 20.854, p < 0.0005$) and SDF ($F = 22.746, p < 0.0005$).

Conclusion: The present trial concluded that topical fluoride application increases fluoride bioavailability in saliva thereby increasing tooth remineralization. A steep rise in fluoride concentration was observed shortly post-SDF application at 2 hours and 24 hours time interval emerging a need for further research into the field of fluoridation with SDF.

Keywords: Enamel demineralization, Primary teeth, Saliva, Silver diamine fluoride.

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INTRODUCTION

The role of the fluoride agents for topical professional applications is well established. The topical fluoride acts on the tooth in many ways and their most important action is inhibition of demineralization and enhancement of enamel remineralization.^{1,2} At the neutral pH ecological balance is well maintained by the virtue of salivary fluoride which is present in saliva in approx. amounts of 0.01–0.08 ppm.^{3,4}

However, pH changes may disrupt this balance making the enamel vulnerable to demineralization. This situation poses an excess demand of fluoride to promote the remineralization. Hence, there is a need for retention of constant concentration of fluoride in oral environment for the prevention and reversal of early dental caries. Frequent use of fluoride agents for topical application (gels, solutions, and varnishes) may increase the bioavailability of fluoride ions in saliva but unfortunately it is short lived and does not provide complete protection, especially in high risk patients.

Fluoride has multiple ways of application and agents in preventive dentistry which can be delivered as topical (as in, gels, foams, silver fluoride, and fluoride varnish) or systemic (as in community water fluoridation) and self-administered (such as toothpastes and mouth rinses) and we can ignore the fact that fluoride transmission through topical or systematically and aim to deliver it to the oral cavity, so that it can play a role in caries control.⁵ Topical fluorides such as NaF varnish are used as preventive reagents due to their antimicrobial and remineralization

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abilities.⁶ Food and drug administration (FDA) approved SDF in 2014 for treating tooth sensitivity with an off-label use in caries treatment and prevention and also approved the marketing of SDF along with potassium iodide (Riva Star, SDI Limited) in the year 2018.⁷

SDF is a novel fluoride agent which is an alkaline, colorless solution, 38% weight/volume. Its main components are fluoride (44,800 ppm) and silver, along with ammonia which forms a highly stable silver halide complex.⁸ On interaction with hydroxyapatite crystals, fluoride ions react with free calcium leading to the formation of calcium fluoride (CaF₂) and silver phosphate. Calcium fluoride forms a reservoir of fluoride ions for the formation of fluorapatite.

A study by Chu et al. described the ability of 38% SDF to inhibit demineralization and promote preservation of collagen of demineralized dentine by forming a protective layer on and within the dentinal tubules *in vitro*.⁹ It is also suggested that SDF might be an effective preventive protocol and potentially a replacement of the commonly used NaF. This, however, requires a further assessment of clinical efficacy of each reagent in management of dentine caries especially in childhood as dental caries is more common among the young aged children. Thus, keeping this in mind the present clinical trial was conducted to assess the fluoride concentration available in saliva following professional application of 38% SDF and 5% NaF and the duration of its availability in saliva at different time intervals.

METHODOLOGY

A double blinded randomized clinical trial was conducted among 40 healthy children aged between 6 and 12 years in the Department of Pedodontics and Preventive Dentistry in accordance to the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. CONSORT guidelines for planning and reporting clinical trials were followed during the different stages of the study (Fig. 1).

Ethical Approval and Trial Registration

Ethical approval was obtained from the institutional review board (STP/SDMDS2015PED42D) and the trial was registered prospectively with the Clinical Trial Registry of India at <http://ctri.nic.in> on 15th December 2020 (REF/2020/12/038,731) prior to conduct of the study.

Informed Consent

Verbal as well as written informed consent was obtained from parents or caretakers of the children who participated in the study prior to the clinical procedure. Also, they were duly informed about the nature of study and written instructions along with study schedule were handed over to them.

Inclusion and Exclusion Criteria

The study participants with any medical history were excluded and only participants with sound teeth, good oral hygiene, and normal salivary rate (0.25–1.0 mL/min) were included in the study.

The sample size was determined considering the result of pilot study conducted on nine subjects with a power level of 80% in detecting the true statistical significance among the two groups. A total of 105 children were examined out of which 40 children fulfilled the inclusion criteria. The participants were clinically examined by a single examiner with the help of a mouth mirror and an explorer. Participants were instructed to avoid fluoride-rich diet and use of fluoride dentifrice was restricted during the study period.

Randomization

A computer-generated randomization method was used to allocate the selected tooth into two groups. The allocation concealment of the participants was based on SNOSE concealment using opaque sealed envelopes (sealed sequentially numbered envelopes

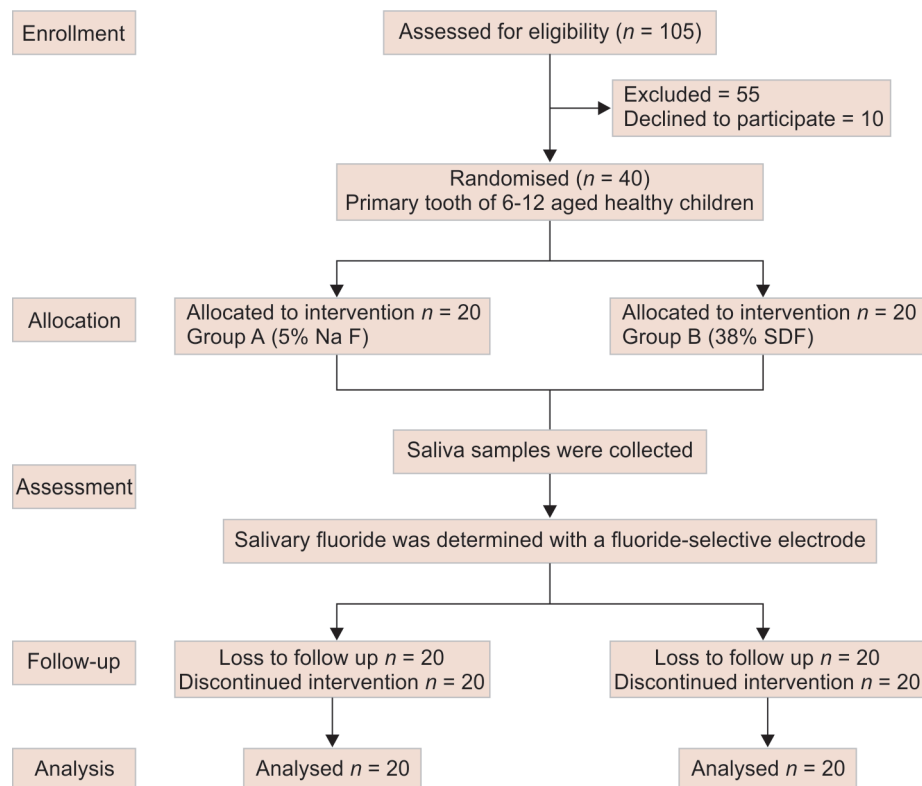


Fig. 1: CONSORT flowchart followed during different stages of the randomized controlled trial

irreversibly) containing codes. The first group ($n = 20$) was given a topical application of 38% SDF (Fagamin TM) whereas the second group ($n = 20$) was given 5% NaF (TM) solution.

Clinical Evaluation

The salivary samples were collected from the study participants during morning hours in the department. They were instructed to have an early morning breakfast that day, to maintain a specified gap of 90 minutes prior to collection of samples. This time gap was ensured to avoid any influence of food consumption on the salivary composition. Saliva sampling was planned between 9 and 10 a.m. in the morning to minimize the effect of diurnal variation. Oral prophylaxis was done for all participants before the application of topical fluoride agents. Participants were made to sit in an erect position and each was handed over a sterile container for saliva collection. Saliva samples were collected from each participant at three intervals. The first sample was collected at baseline for which participants were instructed to spit for 2 minutes in sterile containers.

After collection of baseline samples preparation for topical application was initiated. Oral cavity was isolated by cotton rolls and saliva ejector. Both SDF and NaF were applied on all teeth for a period of 4 minutes by the applicator tip as per the group division. After application the dental surfaces were cleaned with gauze in order to prevent the swallowing of any residual topical agent. The participants were instructed not to consume food and beverages for 2 hours after the fluoridation. After 2 hours they were asked to spit for 2 minutes in sample collection containers for the second saliva sample collection. The participants were then further called after 24 hours for the third saliva sample collection.

Fluoride Estimation

The concentration of fluoride in saliva was determined with a fluoride-selective electrode. The fluoride concentration was measured in the salivary samples which were collected at three time intervals, that is, at baseline (S1), 2 hours (S2), and 24 hours (S3) after application.

Table 1: Comparative evaluation of salivary fluoride concentration of both groups at three time intervals at baseline (S1), 2 hours (S2), and 24 hours (S3) after application

Time	Group	Fluoride concentration Mean \pm SD	Independent sample t-test	
			p-value	Significance
Baseline	NaF	533.80 \pm 27.72	0.604	NS
	SDF	529.20 \pm 27.84		
2 hours	NaF	552.30 \pm 33.99	0.697	NS
	SDF	548.35 \pm 29.50		
24 hours	NaF	513.65 \pm 28.74	0.651	NS
	SDF	509.20 \pm 32.78		

NS, not significant; SD, standard deviation

Table 2: Intragroup comparison of salivary fluoride concentration at three time intervals at baseline (S1), 2 hours (S2), and 24 hours (S3) after application of both the groups

Group	Mean fluoride concentration Baseline	Mean fluoride concentration 2 hours	Mean fluoride concentration 24 hours	Repeated measures ANOVA with Greenhouse–Geisser correction	
	Mean \pm SD	Mean \pm SD	Mean \pm SD	p-value	Significance
NaF	533.80 \pm 27.72	552.30 \pm 33.99	513.65 \pm 28.74	0.000	Significant
SDF	529.20 \pm 27.84	548.35 \pm 29.50	509.20 \pm 32.78	0.000	Significant

STATISTICAL ANALYSIS

The values of fluoride levels were obtained from lab and were tabulated accordingly. These numerical data were later subjected for statistical analysis using SPSS software. The mean values and ANOVA test were used for evaluation of the data. Comparative testing between the groups were done using the independent paired t-test.

RESULTS

The present clinical was undertaken to know the salivary fluoride concentration of the participants who reported to the Department of Pedodontics and Preventive Dentistry. Forty study participants were recruited in the study and were randomly assigned into two different groups each comprising of 20 participants. After normality testing was conducted, comparative tests were performed between the groups using the independent sample t-test. The mean values of salivary fluoride concentration of both the groups at three different time intervals, that is, at the baseline (S1) prior to the application of fluorides and postapplication at 2 hours (S2) and 24 hours (S3) time interval are depicted. The fluoride concentration is comparatively slightly higher for the group receiving NaF (533.80 \pm 27.72) than SDF (529.20 \pm 27.84) at baseline, 2 hours later (NaF = 552.30 \pm 33.99) (SDF = 548.35 \pm 29.50), and 24 hours time interval (NaF = 513.65 \pm 28.74) (SDF = 509.20 \pm 32.78) but is not statistically significant (Table 1).

The intragroup comparison between the two groups of mean fluoride concentration at different time intervals, that is, baseline, 2 hours, and 24 hours interval is described in Table 2. When using an ANOVA with repeated measures with a Greenhouse–Geisser correction, the mean scores of fluoride concentration were statistically significant at different time intervals for both NaF ($F = 20.854, p < 0.0005$) and SDF ($F = 22.746, p < 0.0005$) (Table 2).

DISCUSSION

The present study investigated the retention of fluoride in saliva by measuring its fluoride concentration at different time periods after SDF application on sound tooth enamel. Since the discovery

of its anticariogenic potential, fluorides have been considered the forefront of preventive dentistry. SDF has been widely used as antihypersensitivity agent and for caries arrest for over two decades. It has been further proposed for complex-to-treat carious lesions and to treat high probability of caries risk patients. It can add as a boon to those with medical or behavioral complications, those needing numerous treatment visits, and the ones without access to dental care.¹⁰

The high fluoride content of SDF renders it with a great potential for remineralization. Application of SDF increases the microhardness by facilitating the penetration of fluoride ions to a depth of 50–100 μ .¹¹ However, literature lacks in evidence showing its role as remineralizing agent and studies researching its caries preventive action is scarce. This action was attributed to its prolong retention in saliva due to the formation of silver halide complex which is more stable. Although topical application of conventional fluorides like NaF supports remineralization process but their sustenance in saliva is for shorter duration unlike SDF 38%. It was stated that the bioavailability of fluoride in saliva depends on several factors like dietary fluoride intake, rate of salivary secretion, and use of fluoridated products.^{12,13} Thus, patients were instructed against the intake of fluoride rich food/beverages and use of fluoride dentifrice was forbidden. This was done to ensure that saliva does not get fluoride from any additional source and the fluoride concentration is purely attributed to topically applied fluoride. In the present study, the concentration of fluoride in saliva after SDF application was calculated at different time intervals and was compared with baseline measurements. SDF contains 24.4–28.8% silver and 5.0–5.9% fluoride, containing 55,800 ppm fluoride ions; 249,000 ppm silver ions; and pH of 10.2.^{8,14} In this study, unstimulated saliva was used instead of stimulated saliva since that would increase the rate of F clearance from the oral cavity, also artificially lowering the F levels in subsequent samples which is similar to a study done by Vincent and Thomas.¹⁴ SDF application will lead to CaF_2 layer formation on the enamel surface, and this CaF_2 layer will later release bioavailable fluoride ions.¹⁵ The present study results showed that the average salivary fluoride concentration at baseline was 533.80 ± 27.72 for NaF and 529.20 ± 27.84 for SDF. An overall comparison showed a significant difference in fluoride levels at all time intervals among the groups. A steep rise in fluoride concentration was observed shortly post-SDF application at 2 hours and 24 hours time interval.

The constant presence of fluoride in saliva aids in replenishing the net mineral lost from tooth surface due to pH changes in oral cavity.^{16,17} This presence can be ensured by using SDF, which is a novel fluoride agent. The time effect plays an important role in oral bioavailability of fluoride.¹⁸ It was suggested that the presence of ammonia in SDF stabilizes the fluoride in solution for extended periods, thereby increasing its bioavailability. The present study results were in accordance with this fact. A previous study, showed that fluoride concentration returned to initial level 1 hour after SDF application, while in our study the levels remained elevated up to 2 hours.

Results from another study showed that fluoride concentration returned to initial levels after 6 hours. The present study results are in accordance to previous studies and support the hypothesis that topical fluoride application increases fluoride bioavailability in saliva thereby increasing tooth remineralization.¹⁹ In the present study, SDF was applied to healthy enamel, which is free of caries and has no dentin exposed.

Although SDF has remarkable benefits when used as a preventive agent, however, it does have minor side effects like the staining of lesions. The color changes where silver tarnishes to black is an index of the effectiveness of the treatment, it indicates success and all lesions that are completely black are apparently arrested. Some lesions that are arrested do not turn entirely black, but this is fairly obvious from the shiny dentin; all demineralized (cariou) or hypomineralized dentin or enamel will stain black. Parents and caregivers generally do not object to the stains in primary teeth when the treatment is explained and the alternative is operative treatment.¹⁹ The carious dentin is hardened by the treatment to twice normal dentin hardness.^{20,21} Application is simple (dry and apply), such that any dental or medical provider can provide the treatment. Nurses and hygienists who can provide care at remote sites such as schools or nursing homes should be encouraged to adopt SDF to manage dental caries lesions. This can lead to an effective monitoring and low economic cost that can commensurate with fluoride varnish.

The present study has some limitations as well which might be the small number of subjects due to time constraints. Apart from that capacity of unstimulated saliva was examined in the present study. Although unstimulated saliva represents the state of saliva daily, its collection consumes more time and its viscosity makes it more difficult to examine. SDF application can increase fluoride concentration in saliva, which in turn can inhibit the tooth demineralization process. In the present study, SDF was applied to healthy enamel, which is caries free and has no dentin exposed. This may be a limitation of this study as SDF is best recommended for at-risk caries treatment, treatment in which subjects cannot medically or psychologically tolerate standard treatment, carious lesions that are difficult to treat, and subjects with dentin hypersensitivity. However, the application of SDF in healthy subjects is sufficient to demonstrate the purpose of this study, which was to measure increases in fluoride concentration in saliva. Thus, further studies are needed to be done in this prospect to throw more emphasis on SDF and its effective quality to inhibit demineralization and thereby dental caries.

AUTHOR CONTRIBUTIONS

Zohra Jabin: conception and design, sample preparation and analysis, drafting the article, and acquisition of relevant literature.

Iffat Nasim: critical revision.

Vishnu Priya V: critical revision.

Nidhi Agarwal: critical revision.

REFERENCES

1. Twetman S, Sköld-Larsson K, Modéer T. Fluoride concentration in whole saliva and separate gland secretions after topical treatment with three different fluoride varnishes. *Acta Odontol Scand* 1999;57(5):263–266. DOI: 10.1080/000163599428670
2. Li X, Wang J, Joiner A, et al. The remineralisation of enamel: a review of the literature. *J Dent* 2014;42(Suppl 1):S12–S20. DOI: 10.1016/S0300-5712(14)50003-6
3. Al Dehailan L, Lippert F, González-Cabezas C, et al. Fluoride concentration in saliva and biofilm fluid following the application of three fluoride varnishes. *J Dent* 2017;60:87–93. DOI: 10.1016/j.jdent.2017.03.005
4. Byeon SM, Lee MH, Bae TS. The effect of different fluoride application methods on the remineralization of initial carious lesions. *Restor Dent Endod* 2016;41(2):121–129. DOI: 10.5395/rde.2016.41.2.121

5. Oliveira BH, Rajendra A, Veitz-Keenan A, et al. The effect of silver diamine fluoride in preventing caries in the primary dentition: a systematic review and meta-analysis. *Caries Res* 2018;53(1):24–32. DOI: 10.1159/000488686
6. Koo H. Strategies to enhance the biological effects of fluoride on dental biofilms. *Adv Dent Res* 2008;20(1):17–21. DOI: 10.1177/154407370802000105
7. Trieu A, Mohamed A, Lynch E. Silver diamine fluoride versus sodium fluoride for arresting dentine caries in children: a systematic review and meta-analysis. *Sci Rep* 2019;9(1):2115. DOI: 10.1038/s41598-019-38569-9
8. Horst JA, Ellenikiotis H, Milgrom PL. UCSF Protocol for caries arrest using silver diamine fluoride: rationale, indications and consent. *J Calif Dent Assoc* 2016;44(1):16–28. PMID: 26897901.
9. Chu CH, Mei L, Seneviratne CJ, et al. Effects of silver diamine fluoride on dentine carious lesions induced by *Streptococcus mutans* and *Actinomyces naeslundii* biofilms. *Int J Paediatr Dent* 2011;22(1):2–10. DOI: 10.1111/j.1365-263X.2011.01149.x
10. Cross KJ, Huq NL, Stanton DP, et al. NMR studies of a novel calcium, phosphate and fluoride delivery vehicle- α (S1)—casein(59-79) by stabilized amorphous calcium fluoride phosphate nanocomplexes. *Biomaterials* 2004;25(20):5061–5069. DOI: 10.1016/j.biomaterials.2004.01.045
11. Chu CH, Lo EC, Lin HC. Effectiveness of silver diamine fluoride and sodium fluoride varnish in arresting dentin caries in Chinese pre-school children. *J Dent Res* 2002;81(11):767–770. DOI: 10.1177/0810767
12. Dawes C, Weatherell JA. Kinetics of fluoride in the oral fluids. *J Dent Res* 1990;69:638–644. DOI: 10.1177/002203459006905125
13. Heijnsbroek M, Gerardu VA, Buijs MJ, et al. Increased salivary fluoride concentrations after post-brush fluoride rinsing not reflected in dental plaque. *Caries Res* 2006;40(5):444–448. DOI: 10.1159/000094292
14. Vincent S, Thomas AM. Fluoride levels in saliva and plaque following the use of high fluoride and conventional dentifrices—a triple blinded randomised parallel group trial. *ScientificWorldJournal* 2019;2019:1636209. DOI: 10.1155/2019/1636209
15. Rosenblatt A, Stamford TCM, Niederman R. Silver diamine fluoride: a caries “silver-fluoride bullet”. *J Dent Res* 2009;88(1):116–125. DOI: 10.1177/0022034508329406
16. Naumova EA, Kuehnl P, Hertenstein P, et al. Fluoride bioavailability in saliva and plaque. *BMC Oral Health* 2012;6(1):112–115. DOI: 10.1186/1472-6831-12-3
17. Vasquez E, Zegarra G, Chirinos E, et al. Short term serum pharmacokinetics of diammine silver fluoride after oral application. *BMC Oral Health* 2012;12:60. DOI: 10.1186/1472-6831-12-60
18. Vogel GL. Oral fluoride reservoirs and the prevention of dental caries. *Monogr Oral Sci* 2011;22:146–157. DOI: 10.1159/000325166
19. Weyant RJ, Tracy SL, Anselmo TT, et al. Topical fluoride for caries prevention: executive summary of the updated clinical recommendations and supporting systematic review. *J Am Dent Assoc* 2013;144(11):1279–1291. DOI: 10.14219/jada.archive.2013.0057
20. Crystal YO, Janal MN, Hamilton DS, et al. Parental perceptions and acceptance of silver diamine fluoride staining. *J Am Dent Assoc* 2017;148(7):510–518.e4. DOI: 10.1016/j.adaj.2017.03.013
21. Chu CH, Lo ECM. Microhardness of dentine in primary teeth after topical fluoride applications. *J Dent* 2008;36(6):387–391. DOI: 10.1016/j.jdent.2008.02.013