ORIGINAL ARTICLE

Comparative Evaluation of the Remineralizing Efficacy of Fluoride Varnish and its Combination Varnishes on White Spot Lesions in Children with ECC: A Randomized Clinical Trial

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Abstract

Aim: The aim of the study was to assess the remineralizing efficacy of fluoride and its combination varnishes on white spot lesion (WSL) in children with early childhood caries (ECC).

Materials and methods: Sixty children with active WSL on primary maxillary anterior teeth were randomly selected. At baseline, the WSL activity was evaluated using ICDAS II [lesion activity assessment (LAA)] and its dimensions through photographic method. They were allocated to group I (GI) (5% NaF), group II (GII) [5% NaF with amorphous calcium phosphate (ACP)], and group III (GIII) [5% NaF with casein phosphopeptides – amorphous calcium phosphate (CPP –ACP)]. First, oral hygiene instructions and diet counseling were given followed by application of fluoride varnishes in their respective groups. The same parameters were recorded at follow-up of 2, 4, 12, and 24 weeks intervals. Data were collected and subjected to statistical analysis using Friedman Chi-square and Mann–Whitney tests.

Results: Overall, the active WSL changed to inactive over a period of 24 weeks in GI was 90%, GII was 95%, and 100% in GIII. There was a significant reduction in dimension of WSL in GI from 4.119 to 2.525 ($p = 0.0001$). Likewise, there was a significant reduction in dimension of WSL in GII and GIII from 4.586 to 3.258 and 4.696 to 1.2155, respectively ($p = 0.0001$, $p = 0.0001$). Comparatively, group III (MI varnish) showed statistically significant reduction in the dimension of WSL from baseline to 24 weeks ($p = 0.002$). But the results were statistically insignificant with change of active lesions to its inactivity ($p = 0.349$).

Conclusion: Fluoride varnish with CPP–ACP was found to be an effective preventive strategy in reversing WSL in children with ECC.

Clinical relevance: These combination varnishes could prove to be a promising preventive measure for pediatric dentists in reversing white spot lesions of ECC.

Clinical trial registry: NCT03360266.

Keywords: Casein phosphopeptides and amorphous calcium phosphate, Child, Diet, Oral hygiene, Sodium fluoride, Tooth.

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Introduction

Early childhood caries (ECC) is a virulent form of caries occurring in children under 71 months of age, develops on smooth surfaces, and progresses rapidly.[1] In the initial phase, it is observed on the cervical margins of the maxillary primary incisors as dull, white spot lesions (WSL) which quickly advance to obvious decay if left untreated.[2] White spot lesion is caused by demineralization of enamel with subsurface porosity; at this stage, the lesion is usually reversible.[3]

The caries diagnostic system, Nyvad criteria, was the first classification to define clearly the activity assessment of both cavitated and noncavitated lesions. Later, International Caries Detection and Assessment System (ICDAS) was developed in a workshop.[4] Subsequently, ICDAS I was modified to ICDAS II, which represents a foundation upon which new caries assessment tools could be embedded to aid in making more accurate decisions for clinical practice as well as for clinical and epidemiological research.[5]

Fluoride varnishes such as sodium fluoride, stannous fluoride, casein phosphopeptides, and amorphous calcium phosphate prolong the contact time between fluoride and the tooth surface.[6] Furthermore, biannual applications have been proven to be efficient in decreasing the WSL of early childhood caries.[7] Although numerous fluoride varnishes are available, till date only sodium fluoride varnish was widely investigated to be effective in children. Based on the recent concept, calcium and phosphate ions are considered to be the primary constituents

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of tooth mineral, and adequate quantities of these ions must be present in the remineralizing medium for remineralization to occur. Recaldent™ (GC America), a complex of casein phosphopeptides and amorphous calcium phosphate (CPP–ACP), has been added to NaF, which was proved to be effective in preventing and even reversing white spot lesions.[8] Another study tried only ACP fluoride varnish in *in vitro* and found it to deliver more fluoride to both intact and demineralized enamel than the fluoride varnish containing tricalcium phosphate.[9] Hence, there is a need to investigate these newer combination varnishes on WSL in ECC children.

It has been observed from the literature review that *in vitro*[9,10] and clinical studies using fluoride varnish and CPP ACP varnish[11] have been conducted in orthodontic patients.[12] To our knowledge, there exist few *in vitro*[13,14] and clinical studies[15,16] which assessed the efficacy of CPP–ACP fluoride varnish in permanent teeth but no clinical study has been done using combination varnishes (NaF with ACP) pertaining to remineralization of white spot lesions in ECC patients. Thus, the purpose of this study was to compare the effect of fluoride varnish and combination of fluoride and CPP–ACP, fluoride with ACP varnishes in reducing the activity and dimension of white spot lesions occurring on smooth surfaces of primary anterior teeth of children with ECC.

Materials and Methods

This single-blinded, randomized clinical trial (Clinical trial registry: NCT03360266) was conducted among children aged 3–6 years after obtaining approval from the Internal Review Board (IRB Reference No: IGIDSIIRB2015 NDP20PGRSPPD) and Institutional Ethical Committee (IEC Reference No: IGIDSIEC2016 NDP20PGRSPPD), Puducherry for a period 6 months from February 2016 to November 2016 in outpatients (OPD) of Department of Pedodontics and Preventive dentistry.

Sample Size Calculation

$$n = \frac{2\sigma^2\left(Z_{1-\beta} + Z_{1-\alpha/2}\right)^2}{\left(\mu_1 - \mu_2\right)^2}$$

The mean dimension at initial period and after four weeks was 4.05 ± 1.27 and 2.86 ± 1.33, respectively, with a reduction of 0.31 mm (29.38%) as observed from the previous literature.[3] The significance level $\alpha = 0.05$ with power = 80%, and the sample size was calculated to 18 per arm. By adding a dropout of 10%, the actual sample size was 20 per group.

Selection of Subjects

Children with white spot lesions were identified based on history, clinical examination, inclusion, and exclusion criteria.

Inclusion Criteria

- Preschool children aged 3–6 years with ECC.
- Children with active white spot lesions on labial surface of 1 or more primary maxillary anterior teeth.
- Children whose parents signed the informed consent form/willing to participate in the study.

Exclusion Criteria

- Preschool children with cavitated lesions on primary maxillary anterior teeth.
- Developmental enamel alterations (hypoplasia, fluorosis).
- Children with systemic diseases.
- Children with allergy to milk products.
- Apart from fluoride varnish and fluoridated tooth paste, subjects exposed to no other forms of fluoride were excluded.

Procedure

Patient Preparation

Initially, after screening case history was recorded using the case sheet which consisted of name, age, sex, class, ICDAS II, decayed filled tooth/decayed filled surface index, diet history, and provisional diagnosis. A written informed consent from the parents was obtained after explaining them the study protocol. Permission was obtained from the Department of Oral Medicine for using orthopantomogram machine.

Allocation Concealment

Since availability of the three fluoride varnishes used in this study were in different packages, allocation could not be concealed.

Randomization

Primary maxillary anterior teeth with active WSL in ECC children were selected by the first investigator after prolonged air drying the tooth for 5 seconds. Random sequencing was generated by an independent observer using computerized randomization method. According to random numbers, second investigator applied the respective fluoride varnishes over the WSL. The baseline and follow-up evaluation of both the activity and dimension of WSL were determined by the first investigator.

Children were then randomly allocated to:

Group I—5% sodium fluoride (Profluorid, VOCO),

Group II—5% sodium fluoride with amorphous calcium phosphate (Enamel Pro, Premier Dental Products Company), and

Group III—5% sodium fluoride with casein phosphopeptide and amorphous calcium phosphate (MI Varnish, CPP–ACP, GC Australasia Dental Pty Ltd).

Blinding

First investigator was blinded to randomization and the procedure of applying different fluoride varnishes for children in their respective groups; wherein the investigator only evaluated the activity and dimension of WSL throughout the study period.

Detection of White Spot Lesions

The white spot lesions were visualized on the labial surface of teeth close to the cervical margin after prolonged air drying of 5 sec and evaluated using two visual criteria activity (A) and dimension (D).

Assessment of WSL Activity (at Baseline)

The activity of the WSL was evaluated using ICDAS II, that is, whitish/yellowish enamel which was opaque with loss of luster, rough on probing across surface, and usually identified at plaque stagnation areas was considered as an active lesion. But, if the enamel is whitish/brownish/(or)black and shiny, which felt hard and smooth on probing, located usually away from plaque stagnation areas was considered as an inactive lesion[5] with the aid of a ball-ended periodontal probe (CPITN probe). Active WSL were selected for the present study based on the above criteria (Fig. 1).

White spot lesion dimensions were measured by photographic method.

Fig. 1: Assessment of white spot lesion activity—preoperative photograph

Assessment of WSL Dimensions (At Baseline)

Standardization of photographs: Intraoral photographs were taken with Nikon D3200 camera, which were standardized by placing the patient and the camera along with tripod at a distance of 40 cm, aperature maintained at maximum focal equal to 3.6 in a light controlled room. Patients' head was stabilized using cephalostat of OPG machine, while they were made to bite on specially made occlusal plate with vertical and horizontal scale incorporated to standardize photographs.

Measurement of WSL dimension: The standardized photos were then transferred to the laptop, and maximum lesion dimension was measured using computer software (Adobe photoshop 7.0). After opening Adobe photoshop 7.0 software in a laptop, the photos to be analyzed were displayed, polygonal Lasso tool was clicked from the tool bar and with its help the area of white spot lesions were selected and pixels were measured (Figs 2A and B) using the following formula:

$$\text{WSL\%} = \frac{\text{Number of pixels occupied by the lesion} \times 100}{\text{Number of pixels in the labial surface}}$$

Application of Fluoride Varnish

At baseline, both activity and dimensions were recorded as mentioned above. Irrespective of groups, all received oral hygiene instructions and diet counseling before start of the study. Fluoride (NaF—Profluorid) and combination varnishes (NaF + ACP—Enamel Pro) (NaF + CPP–ACP—MI varnish) were applied on white spot lesions as per manufacturer's instructions. After isolation, the labial surface of the tooth was dried and the respective varnishes were applied over the WSL using an applicator brush. Post varnish instructions were given, wherein the patient was instructed to avoid hard, hot, or sticky foods for 4 hours. At follow-up period of 2 weeks, 4 weeks, 12 weeks, and 24 weeks intervals, lesion activity and dimensions were again recorded similar to baseline by the first investigator (Fig. 3).

The recorded values were tabulated and subjected to statistical analysis using Epi-info software version 7.

Percentage, mean, standard deviation, Chi-square, Friedman Chi-square/Mann–Whitney test were used.

Results

In each group, a sample of 20 active WSL was included at the baseline and over a period of 24 weeks; the active status was measured at 2th week, 4th week, 12th week, and 24th week. Till 2nd week, there was no change in lesion activity of all the 3 groups. At 4th week, 50% of the active lesion changed into inactive in GIII while it was only 5% in GII and nil in GI. At 12th week, it was 85% in GIII, 25% in GII, and 20% in GI. At 24th week, a 100% change occurred in GIII and it was 95% and 90% in GII and GI, respectively. It shows that the change of active WSL to inactivity was earlier in GIII (Table 1).

The mean dimension of WSL in GI, GII, and GIII at baseline was 4.11 ± 1.8, 4.58 ± 2.46, and 4.69 ± 2.63, respectively. There was a decreasing trend in dimension of all the groups and at 24th week, it was 2.52 ± 1.42, 3.25 ± 2.22, and 1.21 ± 0.78, respectively. The reduction in dimension of WSL was high in GIII compared to GI and GII (Table 2).

The remineralization efficacy of WSL among the three groups, that is, 5% sodium fluoride, 5% sodium fluoride with amorphous calcium phosphate, and 5% sodium fluoride with casein phosphopeptide and amorphous calcium phosphate, was tested using Chi-square in children with ECC. The results revealed that at 2 weeks, changes in activity of WSL were same among the three groups ($x^2 = 2.034$, $p = 0.362$). At 4th week, group III had a higher level of reduction in the activity of WSL compared to other two groups and it was significant ($x^2 = 20.26$, $p = 0.001$). At 12th week, group III also showed higher level of reduction in the activity of WSL compared to other two groups and it was significant. At 24th week, although group III showed maximum reduction, it was statistically insignificant (Table 3).

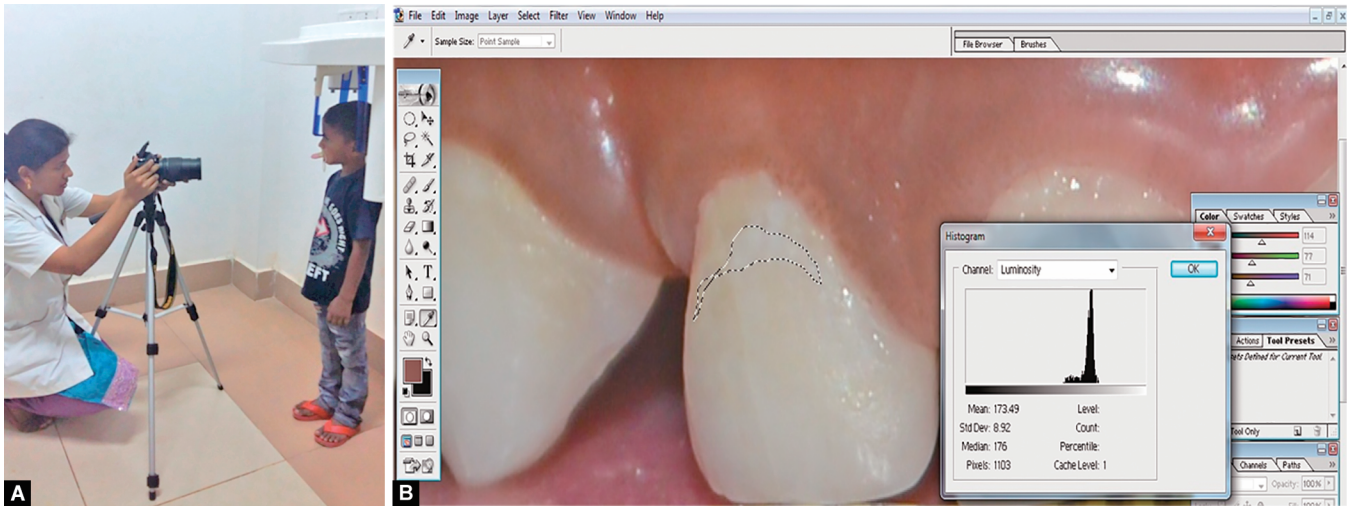
A repeated measures of ANOVA was employed to find the reduction in the activity of WSL in 5% sodium fluoride (group I) from baseline to 2nd week, 4th week, 12th week, and 24th week. The difference in the reduction in WSL over a period of 24 weeks was found to be significant ($p = 0.001$). A *post hoc* test showed that the reduction started as early as second week and continued till 24th week of measurement.

Likewise, a repeated measures of ANOVA was employed to find the changes in the activity of WSL from baseline to 2nd week, 4th week, 12th week, and 24th week for group II and group III.

The difference in changes over a period of 24 weeks in both the groups were statistically significant ($p = 0.001$). A *post hoc* test showed that the reduction started as early as second weeks and continued till 24th week of the measurement in both the groups (Table 4).

Comparison of changes in the dimension of WSL between baseline, 2 weeks, 4 weeks, 12 weeks, and 24 weeks follow-up of group I Profluorid varnish was performed. While comparing within the group, the mean rank at baseline, 2 weeks, 4 weeks, 12 weeks, and 24 weeks were 4.55, 3.58, 3.25, 2.33, and 1.30, respectively, with a p value of 0.0001, which was found to be statistically significant. Therefore, it could be inferred that Profluorid varnish showed gradual reduction in the size of the WSL from baseline through 24 weeks follow-up (Table 5).

Comparison of changes in the dimension of WSL between baseline, 2 weeks, 4 weeks, 12 weeks, and 24 weeks follow-up of (group II) Enamel Pro varnish was performed. Within group comparison displayed the mean rank of 1.6 at baseline, 1.3 at 2 weeks, 1.39 at 4 weeks, 1.09 at 12 weeks, and 0.05 at 24 weeks, respectively. The p value of 0.0001 was found to be statistically significant. Thus, similar to Profluorid varnish, Enamel Pro also



Figs 2A and B: (A) Standardization of photographs; (B) Measurement of WSL dimension on displayed images using Adobe Photoshop software

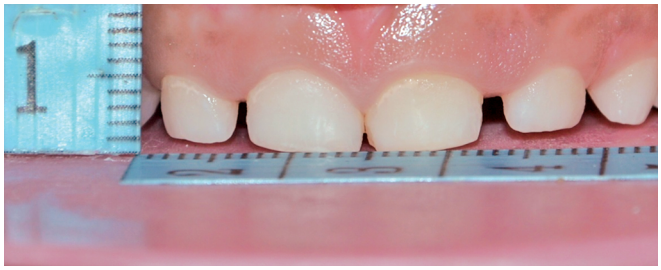


Fig. 3: Postoperative photograph showing resolution of WSL in maxillary primary anterior teeth

Table 1: Descriptive data of baseline characteristics for activity of WSL

Activity		*GI*	*GII*	*GIII*
Baseline	Active	20 (100%)	20 (100%)	20 (100%)
	Inactive	0	0	0
2 weeks	Active	20 (100%)	20 (100%)	19 (95%)
	Inactive	0	0	1 (5%)
4 weeks	Active	20 (100%)	19 (95%)	10 (50%)
	Inactive	0	1 (5%)	10 (50%)
12 weeks	Active	16 (80%)	15 (75%)	3 (15%)
	Inactive	4 (20.0%)	5 (25.0%)	17 (85%)
24 weeks	Active	2 (10.0%)	1 (5%)	0
	Inactive	18 (90.0%)	19 (95%)	20 (100%)

Table 2: Descriptive data of baseline characteristics for dimension of WSL

Dimension	*GI*	*GII*	*GIII*
Baseline	4.11 ± 1.8	4.58 ± 2.46	4.69 ± 2.63
2 weeks	3.74 ± 1.63	4.33 ± 2.45	4.39 ± 2.44
4 weeks	3.44 ± 1.5	4.09 ± 2.43	3.51 ± 2.19
12 weeks	2.99 ± 1.52	3.85 ± 2.29	2.2 ± 1.40
24 weeks	2.52 ± 1.42	3.25 ± 2.22	1.21 ± 0.78

showed gradual decrease in the size of the WSL from baseline through a 24 weeks follow-up (Table 6).

Comparison of changes in the dimension of WSL from baseline through 24 weeks follow up of (group III) MI varnish

Table 3: Comparison of changes in activity of WSL among 3 groups of fluoride varnishes from baseline to 24 weeks follow-up

		Inactive			
Groups	*Active (n)*	*2 weeks*	*4 weeks*	*12 weeks*	*24 weeks*
GI	20	0	0	4 (20.0%)	18 (90.0%)
GII	20	0	1 (5.0%)	5 (25.0%)	19 (95%)
GIII	20	1 (5.0%)	10 (50.0%)	17 (85.0%)	20 (100%)
x^2		2.034	20.26	21.312	2.105
df		2	2	2	2
p		0.362	0.0001	0.0001	0.349

was performed. On comparing within group follow-up intervals, the mean rank at baseline, 2 weeks, 4 weeks, 12 weeks, and 24 weeks was 4.83, 4.08, 3.10, 1.93, and 1.08, respectively. Statistical significance was observed with a *p* value of 0.0001. Hence, MI varnish showed greater changes in reducing the size of the WSL within a shorter period of time from baseline to 24 weeks follow-up (Table 7).

Freidman test was applied to find the changes in dimension of WSL among the three groups at 2 weeks, which was statistically insignificant ($Z = 0.992$, $p = 0.609$); hence, *post hoc* test was not carried out.

At 4th week, the result shows that the three different types of fluorides significantly differed in reducing the dimension of WSL in children with ECC ($X^2 = 7.33$, $p = 0.001$). A *post hoc* test, Mann–Whitney, showed that the sum of ranks for group III was 507 which was higher than the sum of rank 313 for group II. The reduction in dimension was high in group III compared to group II and significantly higher ($Z = 111.0$, $p = 0.016$). However, the comparison between group I and II and group I and III was not significant ($p = 0.148$ and $p = 0.164$).

Friedman test was applied to find the changes in dimension of WSL among the three groups at 12th week and found significant ($x^2 = 13.9$, $p = 0.001$). Hence, a *post hoc* was carried out. Mann–Whitney U test showed that the reduction in the dimension was not significant between group I and II ($p = 0.096$). The reduction in the dimension of WSL was high in group III compared to group I and significantly higher ($x^2 = 111.0$, $p = 0.01$). Likewise, the

Table 4: Repeated measures of ANOVA used for comparison of changes in the activity of WSL from baseline to 2 weeks, 4 weeks, 12 weeks, and 24 weeks

Source	*Type III sum of squares*	*df*	*Mean square*	*F*	*Sig.*
Group I					
Intercept	1131.515	1	1131.515	101.776	0.001
Error	211.237	19	11.118		
Group II					
Intercept	1619.902	1	1619.902	59.818	0.001
Error	514.527	19	27.080		
Group III					
Intercept	1026.433	1	1026.433	66.061	0.001
Error	295.217	19	15.538		

Table 5: Comparison of changes in dimension of WSL from baseline to 24 weeks follow-up of Profluorid varnish (Friedman Chi-square)

	N	*Mean*	*Std. deviation*	*Mean rank*	*Friedman Chi-square*	*p*
D_Baseline	20	4.119	1.8363	4.55	49.253	0.0001
D_2 weeks	20	3.740	1.6325	3.58		
D_4 weeks	20	3.4445	1.50764	3.25		
D_12 weeks	20	2.9905	1.51721	2.33		
D_24 weeks	20	2.5250	1.41639	1.30		

Table 6: Comparison of changes in dimension of WSL from baseline to 24 weeks follow-up of Enamel Pro varnish using Friedman Chi-square test

	N	*Mean*	*Std. deviation*	*Mean rank*	*Friedman Chi-square*	*p*
D_Baseline	20	4.586	2.4614	1.6	54.185	0.0001
D_2 weeks	20	4.330	2.4525	1.3		
D_4 weeks	20	4.0940	2.42895	1.39		
D_12 weeks	20	3.8565	2.28889	1.09		
D_24 weeks	20	3.2580	2.21717	0.05		

Table 7: Comparison of changes in dimension of WSL from baseline to 24 weeks follow-up of MI varnish (Friedman Chi-square)

	N	*Mean*	*Std. deviation*	*Mean rank*	*Friedman Chi-square*	*p*
D_Baseline	20	4.696	2.6350	4.83	75.236	0.000
D_2 weeks	20	4.394	2.4422	4.08		
D_4 weeks	20	3.5100	2.19349	3.10		
D_12 weeks	20	2.2040	1.40591	1.93		
D_24 weeks	20	1.2155	0.78493	1.08		

reduction in dimension was high in group III compared to group I and significant.

Comparison of changes in dimension of WSL among the three groups of fluoride varnishes at 24 th week was compared and found to be significant ($x^2 = 12.77$, $p = 0.002$). Mann–Whitney U test showed that the difference in dimension of WSL in group I and group II was not significant ($p = 0.398$). The difference in dimension of WSL was high in group III with sum of rank 510 compared to group I which was 310 and significant ($x^2 = 77.5$, $p = 0.001$).

Overall, the reduction in dimension of WSL was significant at 4th week, 12th week, and 24th week in group III compared to rest of two groups.

Discussion

In a systematic review by Petersson et al.[17] based on the clinical trials, it was determined that the use of fluoride varnish reduced caries by 30% in deciduous teeth during 6 months to 3 years of time periods. Another study[18] using sodium fluoride declared slow release of fluoride over a period of 6 months, wherein the greatest release occurred in the first 3 weeks and more gradual release thereafter. Hence, this study was planned for a period of 6 months.

From the results of our study, we observed that MI varnish initiated reversing active white spot lesions to inactivity at 2 week follow up. This result was consistent with the study by Manton et al.,[19] who over a period of 10 days application of CPP–ACP (Tooth mousse, using same combination in cream) noted more

remineralization of enamel WSL than placebo cream. At 4 weeks, we noticed that MI varnish converted 50% of active lesions to inactivity. This result was similar to Yazicioglu et al.'s[20] cohort study wherein the paste containing CPP–ACP produced remineralization of WSL on both smooth and occlusal surfaces over a period of 28 days. Another study by Autio-Gold and Courts[21] found that fluoride varnish converted 81% of active lesions to inactivity in the primary teeth after 9 months but in the present study, using MI varnish (5% NaF and CPP–ACP) almost 85% of lesions became inactive within 12 weeks follow-up. Nevertheless, after 6 months MI varnish enhanced remineralization and converted all active WSL into inactive lesions. Kitasako et al.[22] also observed the same effects with paste containing CPP–ACP (Tooth mousse) over a 6 months period, while it also increased the surface pH of the lesions. In addition, moderate change in lesion activity (90–95%) was observed with Profluorid and Enamel Pro varnishes during the period of study.

On comparing the changes in dimension of WSL at different follow-up periods of Profluorid varnish in the present study, it showed gradual reduction in the lesion size. This result was inconsistent with the study by Miresmaeili et al.,[12] who stated that use of fluoride varnish had no superiority over natural remineralization of saliva in decreasing WSL in patients with good oral hygiene. But correlating Shen et al.'s[6] study, wherein the release of fluoride from Enamel Pro, Clinpro, MI varnish, Duraphat and Profluorid varnish was compared and concluded that Profluorid released 16% of their added fluoride at 24 hours and 48 hours whereas MI varnish exhibited the highest release of fluoride till 48 hours. Thus it was proved that profluorid varnish without added calcium, was also effective for some point of time.

In the present study, when evaluating Enamel Pro varnish at different follow-up periods it was found to be similar to Profluorid varnish, as gradual reduction in the size of the WSL was observed. Conversely, an *in vitro* study by Cochrane et al.,[23] comparing MI varnish, Clinpro white Enamel Pro, Bifluorid, and Duraphat, showed that only MI varnish and Enamel Pro released significant levels of inorganic phosphate. Besides Schemehorn et al.[9] examined the fluoride uptake into or onto sound and demineralized bovine enamel treated with ACP (Enamel Pro) and fTCP (Omni vanish) and found that ACP varnish promoted significantly more fluoride deposition than fTCP containing varnish, as it contained higher levels of available calcium and phosphate ions. Additionally, Downey et al.[24] also displayed a greater cumulative amount of fluoride release from Enamel Pro compared to other fluoride varnishes. These could be possible explanations for gradual reduction in WSL with Enamel Pro varnish.

MI varnish is very effective in reducing the size of the ECC white spot lesions within a shorter period of time in the present study. It showed moderate to maximum changes in the dimension of the white spot lesion at 4, 12, and 24 weeks follow-up. The possible explanation for this result could be greater release of fluorides and calcium from CPP–ACP containing fluoride varnish over shorter time duration. This was consistent with the study by Cochrane et al.;[23] while comparing other varnishes, MI varnish had greatest release of both calcium and inorganic phosphate ions at 4, 72, and 168 hours. Also, Pithon et al.'s[10] and Akin et al.'s[25] studies in postorthodontic patients observed that the topical application of CPP–ACP was very effective in reducing the lesion size and increase the remineralization potential of enamel surface around orthodontic brackets.

Thus, in the present study, on comparing the overall changes in the dimension of WSL, MI varnish was found to be effective compared to Enamel Pro and Profluorid. Although the three varnishes (Profluorid, Enamel Pro, MI) presented the same concentration of fluoride, a probable explanation for this difference could be their composition, as MI Varnish contained CPP–ACP that might have greatly increased the anticaries efficacy of the product and considerably diminished the size of white spot lesions. This result was consistent with the study by Pithon et al.[10] who also found that this combination varnish was capable of reducing early enamel carious demineralization in orthodontic patients.

But within the limitation of our study, there is a need for further research investigating the efficacy of combination varnishes on all active WSL (ECC) in primary teeth with larger sample size on long-term basis as we had included only primary maxillary anterior teeth with smaller sample size and efficacy of varnish was assessed over a shorter period of time, that is, 6 months.

Conclusion

- Fluoride and its combination varnishes were capable of enhancing remineralization of ECC white spot lesion in children, hence proving the hypothesis.
- CPP–ACP in combination with NaF varnish was found to be more effective in reversal of lesion activity and dimension followed by ACP fluoride varnish and fluoride varnish alone in ECC children.
- To further substantiate the efficacy of combination varnishes on ECC white spot lesion, we recommend randomized controlled trials on larger sample size on primary teeth.

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