



Effectiveness of Clinpro Tooth Crème in comparison with MI Varnish with RECALDENT™ for treatment of white spot lesions: a randomized controlled trial

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Abstract

Background Unightly opaque white impaired enamel may ruin a great aesthetic orthodontic outcome. This study aims to evaluate effectiveness of Clinpro Tooth Crème (0.21% w/w NaF anti-caries dentifrice with 950 ppm fluoride and f-TCP) and MI Varnish with RECALDENT™ (CPP-ACP) for treatment of white spot lesions (WSLs).

Materials and methods This was a randomized (1:1:1), single-blind, 3-armed, active-controlled, parallel-group trial. The study comprised three groups of 35 patients randomly assigned in blocks of 3 or 6 to one of the three following arms of the study-

Group I: Clinpro™ Tooth Crème 0.21% Sodium Fluoride Anti-Cavity Paste with functional–Tri Calcium Phosphate(f-TCP) group.

Group II: Fluoride varnish group (MI Varnish with RECALDENT™).

Group III: Home-care group (control).

For the subjective assessment, a blinded panel of 4 dental experts rated the improvement in WSLs over the eight weeks using a visual analog scale (VAS).

Results In total, 240 WSLs were identified, with maxillary lateral incisors and canines showing the highest incidence. Group I achieved the highest success rate of 67.61 (%) followed by group II (60.59%). There were no significant differences between the success rates of treatment in groups I and II. A minimum decline in WSLs was found in the control group, with a success rate of only 32.43%, significantly less than the first two groups ($P < .001$).

Conclusion Both the test agents in consideration were comparable in their remineralization potential. Clinpro Tooth Crème provides additional protection against decalcification of enamel compared to MI Varnish with RECALDENT™ (CPP-ACP).

Trial/project registration no. and date 4857/2017 on 21 June 2017.

Keywords Enamel remineralization · White spot lesions · Fluorides · Randomized controlled trial · Enamel decalcification

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Introduction

White spot lesions (WSLs), clinically illustrated as opaque white areas on the tooth surface caused by the loss of minerals below the outermost protective enamel layer, can be an unfortunate sequel of any orthodontic treatment [1]. Although prevention of these unsolicited lesions is the objective of every orthodontist, the prevalence of WSLs after orthodontic therapy has been reported to be between 5 to 97% [2, 3]. Once established, WSLs compromise esthetics and can be challenging or even impossible to reverse.

Saliva can remineralize these lesions to some extent, but this process is dawdling and rarely results in their complete resolution [4]. Fluoride too has been shown to

upsurge the initial pace of remineralization [5]. The course of enamel remineralization has been researched over many decades, leading to the development of technologies (e.g. ozone, bioactive glass, xylitol, calcium sodium phosphosilicate) that can boost remineralization and diminish enamel demineralization, thus providing potential oral health benefits [1, 4, 6].

Several approaches have been formulated to “counteract” demineralization of tooth structure. One method involves patient compliance and consists of in-depth oral hygiene instructions, in-office fluoride applications, and at-home fluoride rinses, gels, and varnishes. An alternative approach, which possesses potential benefits regardless of patient compliance, includes fluoride-releasing agents such as composites, glass ionomers, sealants, and elastomeric ties [7, 8].

A relatively new and promising approach is the introduction of functionalized tricalcium phosphate (f-TCP) combined with fluoride that not only causes greater remineralization in terms of microhardness and fluoride uptake, but also decreases the dose of fluoride required to achieve the same degree of remineralization [9]. Clinpro tooth crème (3 M ESPE) is a relatively new professional grade 0.21% w/w sodium fluoride (NaF) anti caries dentifrice that contains 950 ppm fluoride and f-TCP ingredient.

Another promising product launched by GC America is the MI Varnish with RECALDENT™ (CPP-ACP), which is advocated to transport bio-available calcium, phosphate, and fluoride to the tooth surface; working in concert with the sodium fluoride (NaF). Very few studies have addressed efficacy of these two relatively recent products for arresting areas of decalcification and preventing WSLs from progressing to carious lesions post-orthodontic treatment. The increasing awareness about oral health has made it clear that effective agents need to work synergistically with fluorides in achieving the desired goals of caries prevention.

Materials and methods

This was a randomized (1:1:1), single-blind, 3-armed, active-controlled, parallel-group trial. The sample size calculation Sample size calculation was based on the results of a previous study by Robertson et al. with similar groups of subjects [10]. Based on the 1:1:1 ratio between the groups, a sample size of 30 participants per group would give more than 80% power to detect significant differences with a 0.40 effect size and at the a 0.05 significance level. The study comprised of three groups of 35 patients, each with random assignment to each treatment group (total recruitment of 105 subjects). The patients were randomly assigned in blocks of 3 or 6 to one of the three following arms of the study:

Group I: Clinpro™ Tooth Crème 0.21% Sodium Fluoride Anti-Cavity Paste with functional-Tri Calcium Phosphate(f-TCP) (3 M ESPE, Saint Paul, MN, USA) group

These patients received an 8-week supply of Clinpro Tooth Crème at the start of the study and instructions to apply a pea-sized amount to each arch twice daily. They were given the usual home-care oral hygiene instructions of brushing after every meal (thrice daily) with a fluoride toothpaste (1100 ppm of fluoride), a manual toothbrush, and dental floss. Questions checked compliance at the follow-up visit about the frequency of application of the Clinpro Tooth Crème (Fig. 1).

Group II: Fluoride varnish group

These patients received 0.55 ml unit dose 5% sodium fluoride varnish (MI Varnish with RECALDENT™) as a single application at the start of the study. They were also rendered the same home-care oral hygiene instructions (Fig. 2).

Group III: Home-care group {control}

This group of patients was enlightened with the usual home-care oral hygiene instructions of brushing with a fluoride toothpaste (1100 ppm of fluoride), a manual toothbrush, and dental floss (all three of the same brand and type as used by other two groups).

Patients in all the groups were bonded with a 0.018-inch slot Roth pre-adjusted appliance (Centrino series Libral Traders). These metal brackets were bonded using a light-cured composite resin and adhesive (Transbond XT; 3 M Unitek) in accordance with the manufacturer’s instructions. One week after bracket placement, all patients received thorough oral prophylaxis and each patient was given the same oral hygiene instructions.

Patients were carefully selected for the study and included and excluded on the following criteria:

Inclusion criteria:

- Patients completed fixed appliance orthodontic therapy within the past 2 months in the participating orthodontist’s unit.
- Had at least 1 WSL on the facial surface of a maxillary central, lateral incisor or canine that was not present before orthodontic treatment (assessed with pretreatment photographs that were available as part of the routine initial records before orthodontic treatment).
- 12 years and older (permanent dentition).

Fig. 1 Clinpro™ Tooth Crème and the instructions list

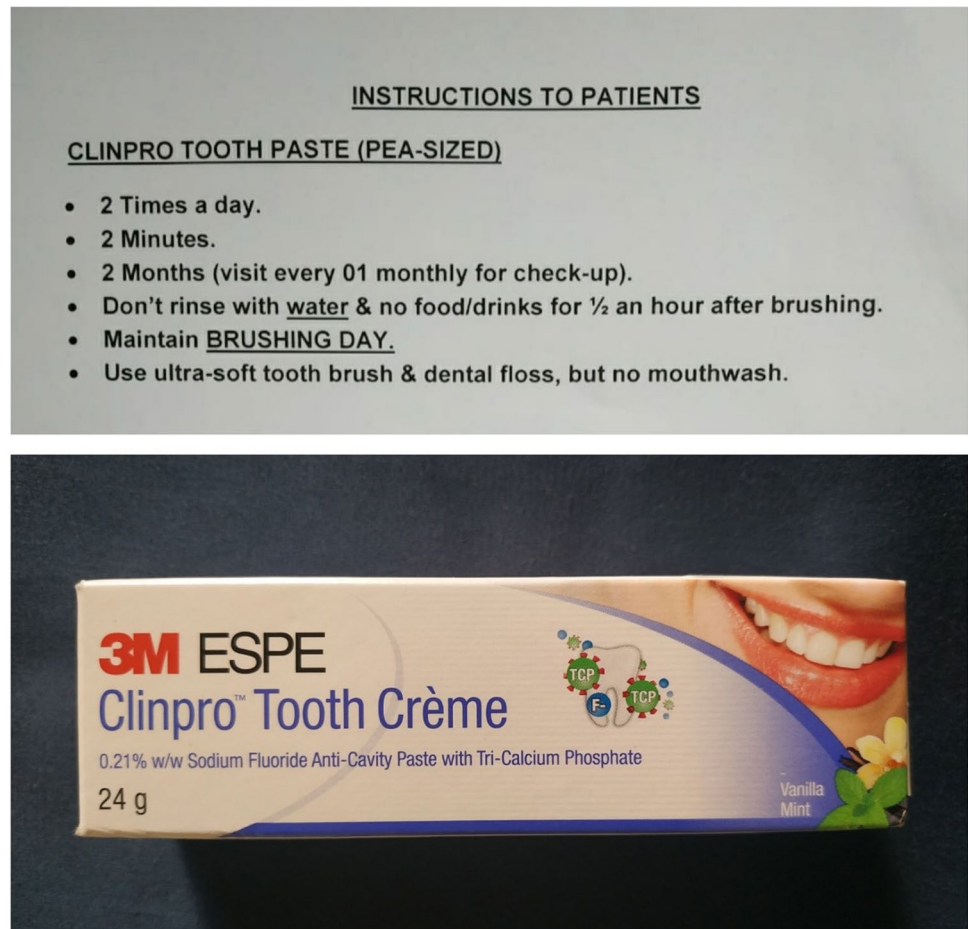


Fig. 2 MI Varnish with RECALDENT™



- Patients that in the investigator's opinion would be compliant with the use of the paste.
- Patients who had not used extensive fluoride regimes.
- Subjects must use non-fluoridated toothpaste for 1 week prior to starting this trial.
- Exclusion criteria:
 - Any medical or dental condition that, in the opinion of the investigator, could impact study results.
 - Patient planning to relocate or move within three months of enrolment.
 - Patients who had or were undergoing fluoride treatment for white spot lesions.
 - Any WSLs present on qualifying teeth with frank cavitation.
 - Patients with f-TCP/casein allergy or known allergies to fluoride or other components of the test materials.
 - Pregnant women.

Instructions for paste delivery

Prior to start, patients were instructed to brush for 1 week with a non-fluoride toothpaste. Then, it was advised that the selected product be brushed on for 2 min twice daily for 8 weeks. After brushing with the product, patients did not rinse their mouth with water. Instead, they were guided just to expectorate (spit) so they did not clear out the actives from the product. Patients also did not have to eat or drink for 30 min following this therapy.

Administration of the study (recall visits)

Subjects were examined every 4 weeks when they came for their appointment. At the end of each appointment, the next one was scheduled. Reminders were sent to the participants to confirm their visits. At each visit, 3 intraoral photos were taken with the digital camera available in the unit (frontal and buccal views). The brushing diary was reviewed.

Visual analog scale

For the subjective assessment, a blinded panel consisting of 4 dental experts rated the improvement in WSLs over the 8-week period using a visual analog scale (VAS). The scoring was performed under direct illumination using a dental chair light after gentle pumicing and drying with compressed air for 5 s, along with tactile consideration by dental probing.

The Dental experts had to point out their finger on the line ranging from 0 to 10 to indicate what they thought was the severity of the WSLs with '0' score indicating the teeth with least WSL and '10' depicting the most severely affected teeth with WSLs (Fig. 3).

Statistical analysis

Statistical analysis was accomplished using SPSS for Windows (version 26.0, SPSS Inc., Chicago, Illinois, USA). The aggregate average VAS score was calculated for each group.

One-way analysis of variance with post hoc analysis using Tukey's test was used to find the difference between the three groups at the end of 8 weeks.

Method error assessment

To determine the intra-observer reliability of the measurements, 4 patients at a time were evaluated by each of the 4 dental experts in the same dental operatory. The reproducibility of the measurements was tested by intraclass correlation coefficient and the kappa coefficient (k) for the interrater reliability. The intraclass correlation coefficients were 0.97 of WSLs for 1st dental expert, 0.93 for 2nd dental expert, 0.91 for 3rd dental expert, and 0.95 for 4th dental expert. The kappa coefficients were interpreted using the guidelines outlined by Landis and Koch and it was 0.78 in our study.

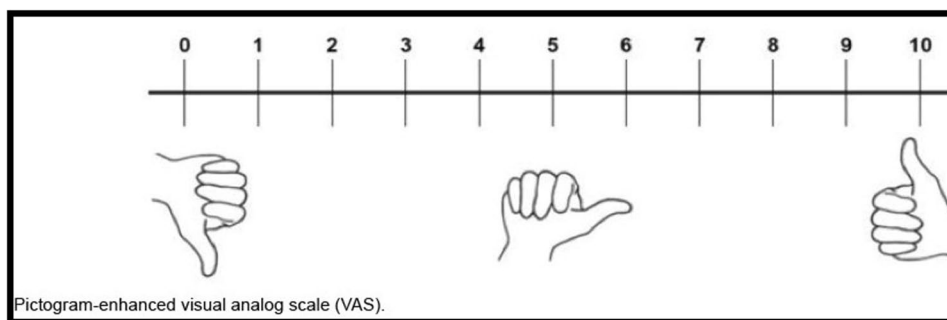
Results

The WSL analysis on visual analog scale by 4 dental experts was done immediately post debonding and oral prophylaxis (T0), and after 08 weeks of debonding and application of the respective products under consideration (T8). The values of differences were used for the calculation of paired t -test.

A total of 96 patients (32 using Clinpro Tooth Crème, 34 receiving MI varnish and 30 of the control group) were available at T8. Of these, 67 cases (70%) were females and 29 (30%) were male. A total of 74 patients (77%) developed white spots in only one arch and the remaining 22 patients (23%) got them in both the arches. Out of 74, 53 patients (71.6%) got WSLs in the maxillary arch, and 21 (28.4%) incurred lesions in the mandibular arch.

In total, 240 lesions were identified on the teeth in consideration in our study (maxillary centrals, laterals, and canines) with 83 white spots in Group I, 79 in Group II, and 78 in control group. The maxillary lateral incisors and canines showed the highest incidence of WSLs. The mandibular laterals and canines showed the lowest incidence of WSLs.

Fig. 3 Visual Analogue Scale (VAS)



Success rate calculation

Figure 4 illustrates the considerable reduction in WSLs in Group I. The average VAS score by four dental experts post-debonding of 318 reduced to 103 after the 08-week application of Clinpro™ Tooth Crème as per instructions given to the patient at the start of the study. In Group II, the average VAS score abridged from 302 to 119 as depicted in Fig. 5. In groups I and II, there was a significant decrease in the value on VAS between T0 and T8 ($P < 0.001$). Control group showed the least remineralization of WSLs with their cumulative average score reducing from 296 to just 200 on brushing with 1100 ppm fluoride toothpaste with a manual toothbrush (Fig. 6). The

aggregate VAS value of all the dental experts had no significant changes over time from T0 to T8 ($P = 0.0914$).

Figure 7 describes the success rates in percentage achieved by the three participant groups. Group I achieved the highest success rate of 67.61% ($318 - 103 / 318 \times 100$) followed by group II (60.59%) $\{302 - 119 / 302 \times 100\}$. There were no significant differences between the success rates of treatment in groups I and II. Minimum decline in WSLs was found in the control group, with success rate of only 32.43% ($296 - 200 / 296 \times 100$), which was significantly lesser than the first two groups ($P < 0.001$).

Figures 8, 9, and 10 are the representative intraoral clinical photographs of groups I, II, and III respectively, further justifying the success rates as mentioned in Fig. 7. Altogether, the results strongly supported that Clinpro Tooth

Fig. 4 Average VAS score before and after Clinpro™ Tooth Crème application (Group I)

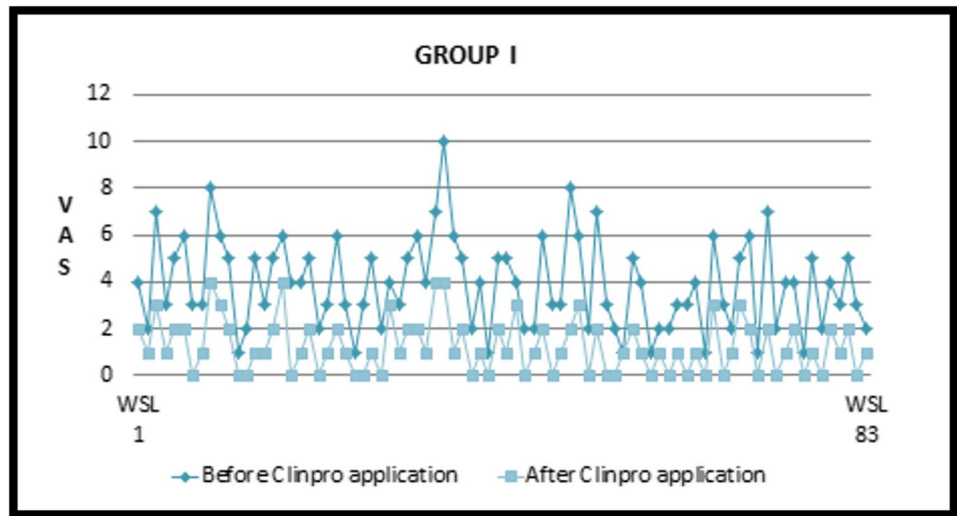


Fig. 5 Average VAS score before and after MI Varnish application (Group II)

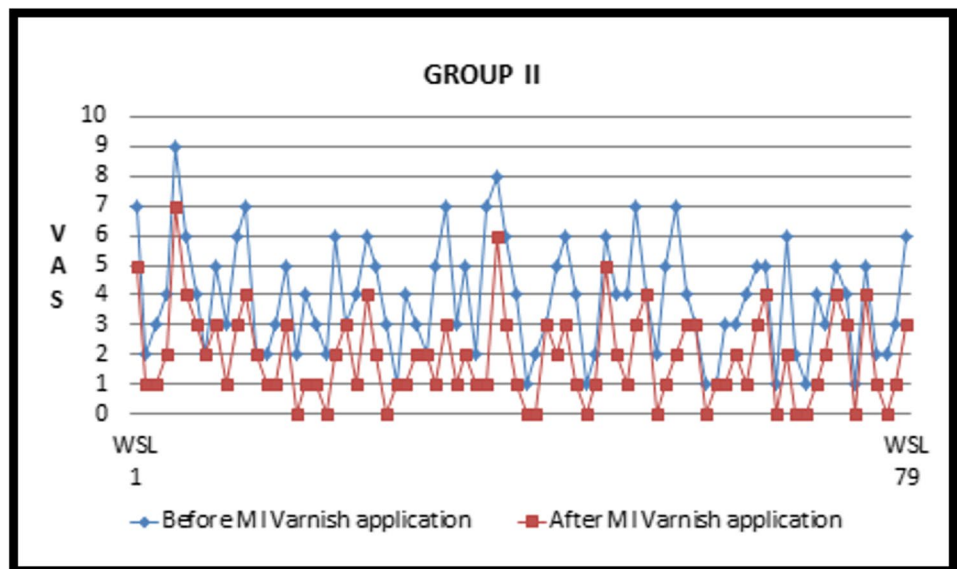


Fig. 6 Average VAS score in Control Group (Group III)

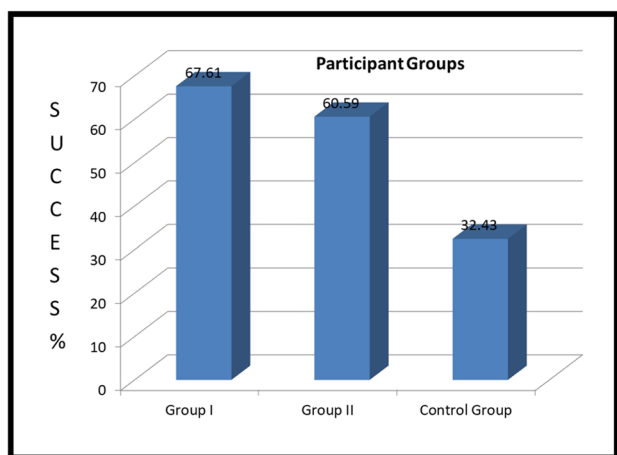
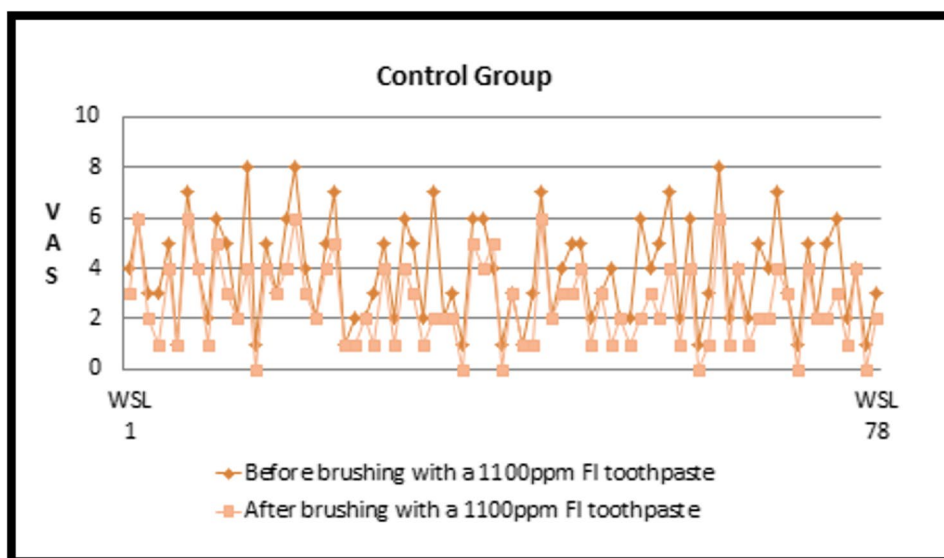


Fig. 7 Success rates in percentage achieved by the three participant groups

Crème provided enhanced remineralization potential of decalcified enamel when compared to MI varnish and regular 1100 ppm fluoride toothpaste.

Discussion

The oral cavity is a battlefield of events of demineralization and remineralization; balance between the two is the crucial decisive factor of the caries process. Central to this vision is the aptitude to detect caries lesions at a primary stage and correctly compute the degree of mineral loss, ensuring that the precise intervention is instituted.

Many authors have described the effect of fluorides on preventing formation and inducing remineralisation of

WSLs. Donly et al. claimed in an in-vitro study that fluoride-releasing GIC for cementing bands helps diminish the incidence of WSLs [11]. Demito et al. reported that the mean depth of enamel demineralisation was found to be up to 38% lesser after fluoride varnish application in comparison with a control group [12].

Kalha et al. concluded that patients who rinsed daily with a 0.05% sodium fluoride mouth rinse had lesser severity of enamel decay adjacent to the brackets [13]. Another study done in 2021 compared the effect of CPP-ACP and fluoride with/without Erbium, chromium-doped yttrium, scandium, gallium, and garnet laser irradiation on enamel microhardness of permanent teeth concluded that fluoride varnish augmented the enamel microhardness, while GC Tooth Mousse had no such effect. Laser therapy before the application of remineralizing agents did not significantly boost enamel resistance to demineralization [14].

Our study was executed to assess the efficacy of Clinpro™ Tooth Crème (0.21% NaF with f-TCP) and MI Varnish with RECALDENT™ {CPP-ACP} in ameliorating white spot lesions. Their results were compared with those of a control group in which the patients were educated with the usual home-care oral hygiene instructions of brushing with a fluoride toothpaste (1100 ppm of fluoride), a manual toothbrush, and dental floss.

TCP is a relatively new hybrid material created with a milling technique that fuses beta tricalcium phosphate (β -TCP) and sodium lauryl sulphate (fumaric acid). This blending results in “functionalized” calcium and a “free” phosphate, intended to upsurge the efficacy of fluoride remineralization [15, 16].

In our study, 53 patients (71.6%) got WSLs on maxillary anteriors and 21 patients (28.4%) were identified with lesions on mandibular anterior teeth. The remineralizing

Fig. 8 Intraoral photographs of a Group I patient: (I) before orthodontic treatment, (II) mid-treatment, (III) immediate post-debonding exhibiting WSLs, (IV) after 08 weeks of Clinpro™ Tooth Crème application

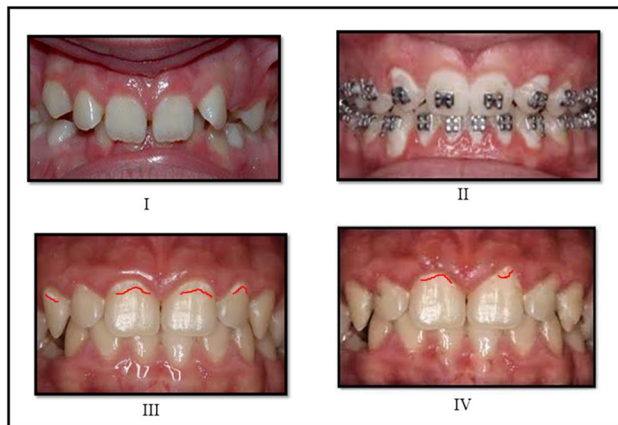
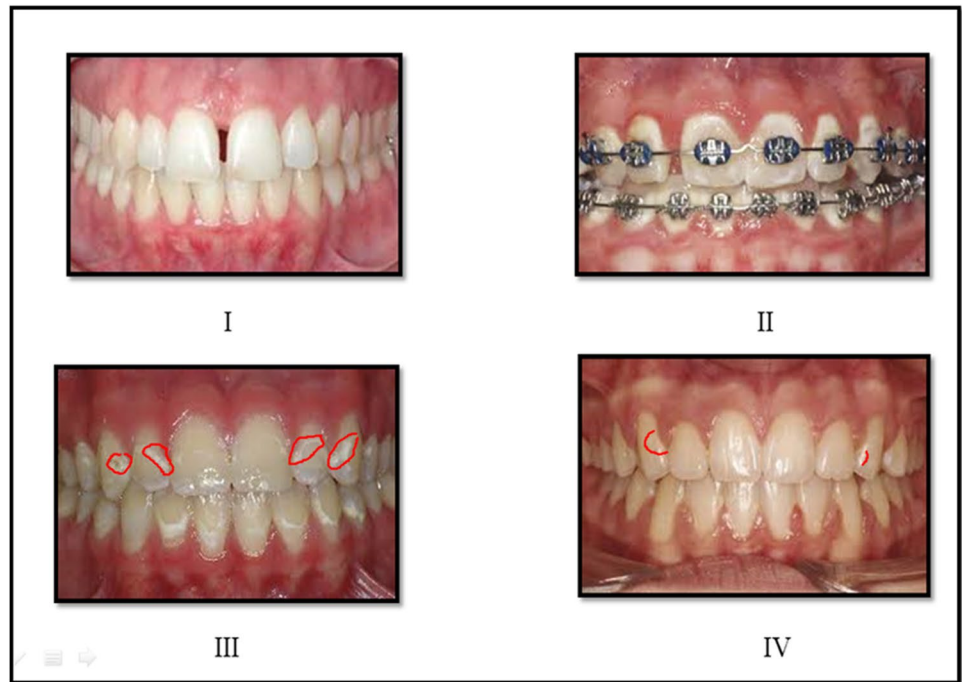


Fig. 9 Intraoral photographs of a Group II patient: (I) before orthodontic treatment, (II) mid-treatment, (III) immediate post-debonding exhibiting WSLs, (IV) after MI Varnish application

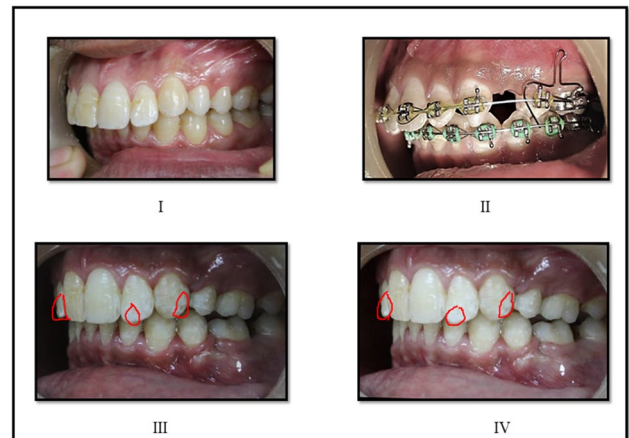


Fig. 10 Intraoral photographs of a Group III patient: (I) before orthodontic treatment, (II) mid-treatment, (III) immediate post-debonding exhibiting WSLs, (IV) after 08 weeks of brushing with 1100 ppm fluoride toothpaste

capacity of saliva could describe this difference, as it bathes exposed tooth surfaces diminishing plaque acidity and washing away sugary substrates [17]. The mandibular teeth may be more predisposed to this cleansing action because of their close proximity to salivary glands and saliva that is pooling around the dentition. Our study supports the analysis of Chapman et al., who reported that the order of incidence of WSLs was lateral incisors, canines, premolars, and central incisors [18].

Clinical detection of white spot lesions in our study was carried out using visual inspection after air drying and tactile consideration by dental probing. However, the subjectivity

and lack of reproducibility of these means have led to the introduction of various optical techniques during the past few years: the visual caries monitor, digital imaging with fibre-optic transillumination, computer analysis of digital photographs, and procedure of the use of quantitative laser and light-induced fluorescence to name a few [19].

We achieved success rates of 67.61% in supporting the regression of white spot lesions when Clinpro™ Tooth Crème 0.21% Sodium Fluoride Anti-Cavity Paste with functional-Tri Calcium Phosphate was applied by patients

over an eight-week observation period. After treatment, few trivial affected areas lingered due to cavitation. This is in analogy with a recent study which compared the effectiveness of three latest fluoride dentifrices in preventing WSLs in the orthodontic practice [20].

MI Varnish with RECALDENT™ (CPP-ACP) boosts enamel acid resistance and enhances salivary fluoride levels. It remains on the teeth longer than other fluoride varnishes and contains high levels of fluoride and calcium released into the oral cavity. Casein phosphopeptides (CPP) is a naturally occurring product in milk casein; and amorphous calcium phosphate (ACP) found in RECALDENT™ also acts as the source of calcium and phosphate [21].

CPP binds to various oral surfaces such as teeth, dentin, biofilm, and oral mucosa in the oral cavity. MI Varnish delivers bioavailable calcium and phosphate ions into the saliva, considered to be the building blocks for healthy teeth. CPP-ACP has been proven to slow the progression of caries and promote the regression of early lesions in randomized controlled clinical trials [22]. It might be incorporated in chewing gums, lozenges, or creams [23]. Systematic review with meta-analysis studies too have established that CPP-ACP has a short-term remineralization effect [24].

Few of the previous studies reported a similar favourable effect from either CPP-ACP or supplemental fluoride. Abufarwa and colleagues, in a recent study, concluded that CPP-ACP fluoride varnish prevents enamel demineralization for at least 4 weeks and limits demineralization up to 12 weeks [25]. Singal et al. in a study published this year reported that topical treatment using Calcium phosphate (CaP) derivatives along with fluoride group showed superior remineralization potential as well as the antibacterial effect as compared to no intervention and/or placebo or fluoride alone. Apart from CPP-ACP, other CaP derivatives like TCP and fTCP too had promising effects in remineralizing early lesions [26].

A recent study also reported that Clinpro Tooth Crème enhanced white-spot lesions remineralization on anterior deciduous teeth but did not adorn clinical appearance after its use within the suggested protocol [27]. Another study that evaluated the impact of two remineralizing agents reported that CPP-ACP containing varnish had higher remineralizing effect when compared to TCP containing varnish [28]. Few of the recent studies have suggested combinations too. Radha et al. concluded that fluoride and its combination varnishes were more capable in promoting WSL remineralization and fluoride uptake. CPP-ACP in combination with NaF varnish was reported to be additionally effective in reversal of lesion activity and dimensions followed by ACP fluoride varnish and fluoride varnish alone [29].

The use of MI Varnish with RECALDENT™ (CPP-ACP) would be ideal in patients with poor compliance who have not yet even developed enamel lesions, thus minimizing aesthetic damage and curtailing the need for future restorative

intervention. The success rate of WSL reduction with this product in our study was 60.59% which can be considered reasonably acceptable. A similar study undertaken to compare the efficacy of sodium fluoride (NaF), casein phosphopeptide amorphous calcium phosphate fluoride (CPP-ACP-F; MI Paste Plus) and a water-based cream (Remin Pro), which contains hydroxyapatite and fluoride for prevention of enamel demineralization advocated that 0.05% NaF was more efficient than Remin Pro and MI Paste Plus for prevention of white spot lesions (WSLs) [30].

The results of this study indicated that the size reduction of post-orthodontic WSLs when using 1100 ppm fluoride toothpaste with manual toothbrush was effective only on mild lesions (control group) as small lesions are relatively shallow, and fluoride ions can therefore, easily upkeep remineralization.

Our findings throw some light on two of the efficacious methods for treating white spot lesions. Considering the limitations of our *in vivo* study, it can be inferred that the appropriate use of Clinpro™ Tooth Crème would be more beneficial than other means for treating patients with WSLs.

Conclusion

Both the test agents in consideration were comparable in their remineralization potential. Clinprotooth crème (0.21% w/w NaF anti-caries dentifrice with 950 ppm fluoride and f-TCP) though provides additional protection against decalcification of enamel.

The use of MI Varnish with RECALDENT™ (CPP-ACP) would be beneficial in regression of WSLs in patients with poor compliance.

Fluoridated dentifrice alone as a remineralizing agent cannot be expected to serve as an effective therapeutic aid in averting WSLs.

Author contribution “This work was carried out in collaboration between all authors. The first author [Lt Col Ashish Handa] designed the study, wrote the protocol, and wrote the first draft of the manuscript; the second author [SurgCapt (D) DMM Chengappa] managed the formal analyses and data curation of the study; the third author [Lt Col Parvinder Sharma] performed the statistical analysis and was the patient care provider; and the fourth author [Dr Jasleen K. Handa] managed the literature searches and did the review and editing. All authors read and approved the final manuscript.”

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Declarations

Competing interests The authors declare no competing interests.

Ethics approval Armed Forces Medical Research Committee.

Consent to participate Verbal informed consent has been obtained from the patients (with prior approval from ethical committee) to undertake and publish this study.

Conflict of interest The authors declare no competing interests.

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