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White spot lesions risk management prior and during the orthodontic treatment

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SUMMARY

Objective. To evaluate the efficiency of various interventions performed before and during orthodontic treatment which aim to reduce the incidence of WSL.

Materials and methods. Using PRISMA guidelines in search of clinical trials published between 2017 and 2022, a literature analysis was performed. This search was conducted using following Medical Subject Heading (MeSH) terms in 2 databases: "prevention and control" AND "Orthodontics" AND "Tooth Demineralization". Supplementary, a manual search was conducted in Google Scholar.

Results. The literature search resulted in a total of 3626 study articles, of which 8 publications were used in the present review, according to a selection based on the pre-established eligibility criteria. The review showed that F varnish, 10% Xylitol varnish had positive outcomes in comparison with placebo. 0.44% APF formulated daily oral rinse and nanosilver mouthwash were better than 0.2% NaF weekly rinse and CHX, F mouthwashes respectively. NovaMin toothpaste (TP), MIPP and MIV, examined in different studies, proved no significant difference over regular F TP. MIV compared to ProSeal provided no statistically significant between-group differences as well. Clinpro 5000 provided superior protection against enamel decalcification when compared to Clinpro Tooth Creme and MI Paste.

Conclusion. The white spot lesions have improved, regressed, or eliminated using topical agents including fluoride, xylitol, or casein phosphopeptide-amorphous calcium phosphate during the fixed orthodontic treatment. More research is needed in order to determine the most effective therapeutic approach for the treatment of surface and subsurface demineralization of the enamel.

Keywords: CPP-ACP, fluorides, prevention, treatment, white spot lesions.

INTRODUCTION

Fixed orthodontic appliances are the most commonly used type of appliance in orthodontics. Although they are reliable for an effective treatment, there are some adverse effects related to their usage.

White spot lesions (WSL) that are caused by demineralization of enamel, occur indeed frequently after orthodontic treatment, with some reports of numerous teeth affected, and approximately a third of orthodontic patients have at least one white spot lesion which is aesthetically unpleasant and may become permanently damaging (1). The principal cause for development of the lesion is plaque stagnation around the appliance, mostly between the gingival margin and the bracket as well as underneath the arch wires (2).

Acids from acidogenic bacteria in plaque, most notably *Streptococcus mutans (S. mutans)* start to diffuse into the tooth and demineralize subsurface enamel as long as conditions for bacterial growth are maintained. Eventually, the intact enamel surface will crumble and cavitate if the demineralization process is not stopped (3). It may also become a reason for the dissatisfaction of the patient due to esthetic appearance (4).

There have been numerous studies performed to find a solution of preventing caries around fixed orthodontic appliances. Some of the studies have focused on the bonding of brackets to the tooth surface (5, 6), some described the differences between the buccal and lingual brackets, their impact to caries development (7). However, the prevention of

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orthodontically induced tooth demineralization using topical agents in the form of rinses, varnishes or gels remains the easiest and most accessible way for the patients to avoid white spot lesions (8). Therefore, clinicians should have a huge interest in making the possibility of WSL occurrence reduced to a minimum and have comprehensive knowledge about the existing prevention methods. The aim of this study was to evaluate the efficiency of various interventions performed before and during orthodontic treatment which aim to reduce the incidence of WSL.

MATERIAL AND METHODS

This systematic review was registered in the International Prospective Register of Systematic Reviews (PROSPERO CRD42022356724) and was conducted and reported following international guidelines (9).

Focus question

The focus question was developed according to the population, intervention, comparison, and outcome (PICO) design (Table I).

Data source and search strategies

An electronic search was performed in online databases PubMed and the Science Direct for articles published between September 2017 and September 2022. This search was conducted using Medical Subject Heading (MeSH) terms. The search was undertaken with the following terms: "prevention and control" AND "Orthodontics" AND "Tooth Demineralization". Supplementary, a manual search was conducted in Google Scholar.

Selection of studies

Following the elimination of duplicates, the abstracts in the resulting publication were evaluated for eligibility in accordance with the inclusion and exclusion criteria in the first step of data selection. The study selection process was done by three independent reviewers.

The reviewers compared their results and resolved differences through discussion, consulting the fourth person when consensus could not be reached. The person was an experienced senior reviewer. Full-text articles were screened and finally, reports were obtained for all the studies that were deemed eligible for inclusion in this paper.

Inclusion criteria

- Studies written in English;
- Studies regarding the information on orthodontically induced WSL interventions prior and during the orthodontic treatment
- Patients of any age undergoing orthodontic treatment;
- Studies in which participants had at least 1 clinically visible lesion;
- Articles published in the preceding 5 years (2017-2022);
- Human studies.

Exclusion criteria

- Patients not on orthodontic treatment;
- In vitro and animal studies;
- Patients undergoing any non-remineralizing therapy for WSLs treatment
- Case reports;
- Systematic reviews.

Data extraction

Descriptive and quantitative information including study design, sample size, patient age, intervention method, follow-up periods, outcomes and conclusions were independently extracted by three authors.

Assessment of methodological quality

The quality of included study protocols was assessed after study selection by investigating full-text articles. The Cochrane Collaboration's two-part tool was used to assess the risk of bias across the studies, evaluating random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias (10).

Data synthesis

A narrative synthesis of the results was made. The data of interest were collected and put into a table in order which was described earlier. Meta analysis was not performed due to high heterogeneity of studies.

RESULTS

Study selection

A total of 3626 articles which were up to 5 years old were identified in the online search engine. Following the removal of duplicates and the review of article titles and abstracts, 17 articles were chosen. The present review uses 8 articles that meet all the selection criteria. The study selection process was illustrated in a flowchart in Figure 1.

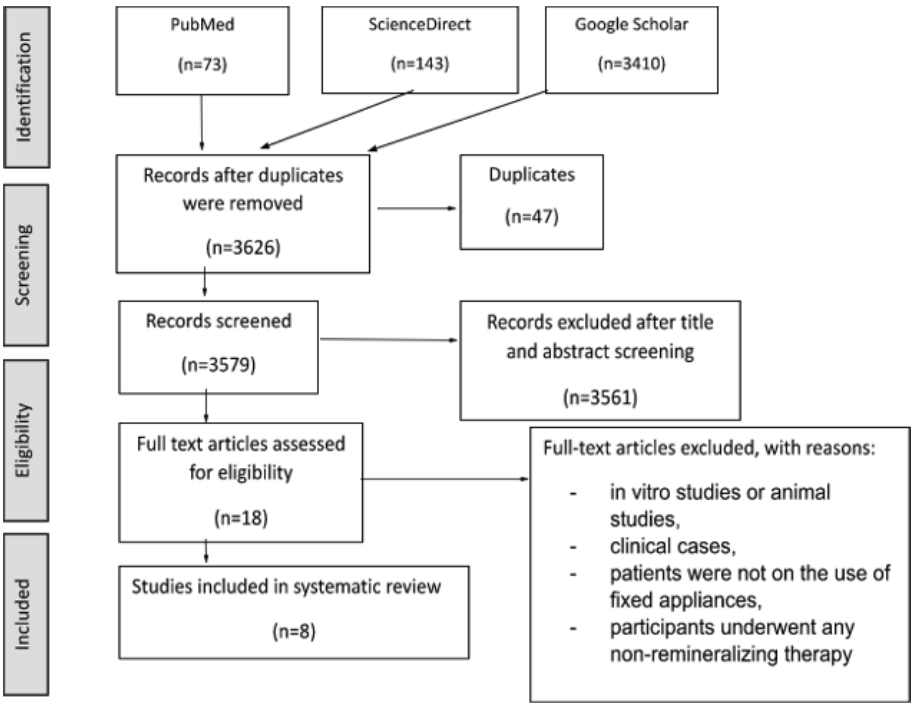

Fig 1. PRISMA selection criteria flow chart

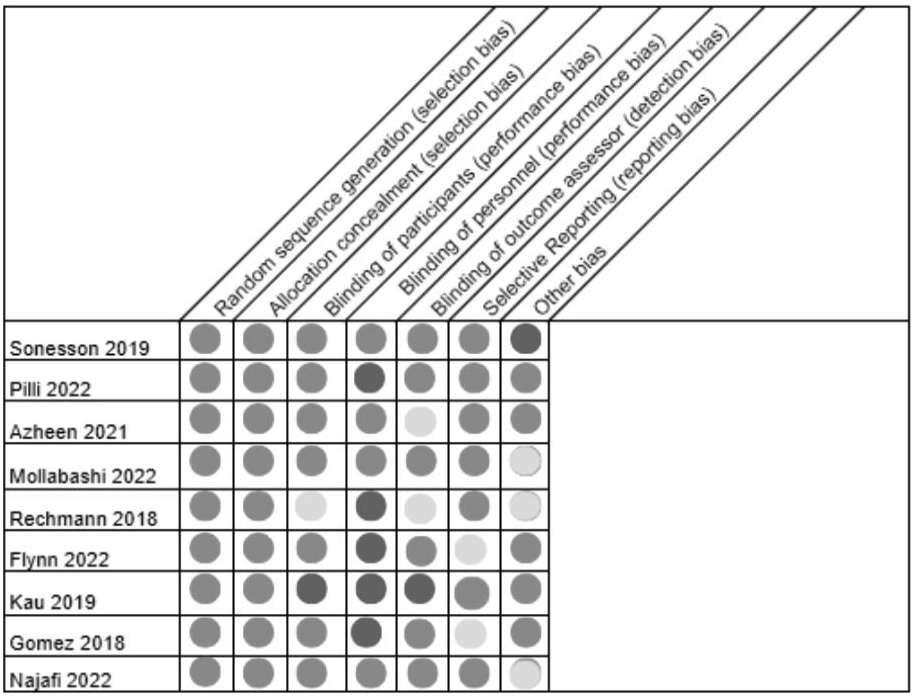

Fig 2. Risk of bias

Table 1. The focus question development according to the PICOS study design

Component	Description
Population (P)	Patients undergoing orthodontic treatment.
Intervention (I)	Interventions for orthodontically induced white spot lesions.
Comparison (C)	Comparison between different intervention methods.
Outcome (O)	Intervention effectiveness – regression or disappearance of lesions
Study design (S)	Randomized and non-randomized controlled trials.
Focus question	What are the most effective remineralization therapies for the patients undergoing orthodontic treatment?

Study characteristics

All selected studies were randomized controlled trials, including two double-blinded (14-15).

Fundamental data extracted from individual studies are presented in Table 1. A total of 615 patients with ages ranging from 12 to 35 were included in the studies. The average number of patients per study was approximately 77 patients (with a minimum of 37 and a maximum of 148 patients). Patient follow-up periods ranged from 2 weeks after the intervention to 2 years.

All of the studies (11-18) received ethical approval from their ethical committee/review board.

Demineralization was evaluated and measured with different techniques including visual assessment (International Caries Detection and Assessment System (ICDAS), enamel decalcification index (EDI), prevalence of WSL), and DIAGNOdent pen value.The findings of each study's evaluation and the main conclusions were also extracted and summarized in Table 1.

Methodological quality assessment of included studies

The Cochrane collaboration's two-part methodology (10) was used to assess the risk of bias (Figure 2). The studies that were reviewed all had a medium to high level of bias when assessing "blinding of personnel." The primary investigators could not be blinded due to operational constraints, and the interventions applied in separate groups were too diverse to be concealed, therefore even though all studies did not meet the "personnel blinding" criteria, they are not deemed to be of low quality. Also, studies

Table 2. RAS treatment with lasers

	No.	Author, year	Design	Patients	Age (year range)	Intervention	Other F sources	Follow-up	Outcome	Start (G1/ G2 (/G3/G4))	End (G1/ G2(/G3/G4))	Conclusions
Fluorides	1.	Sonesson 2019 (11)	RCT	148	12-18	G1: Ammonium F Varnish G2: Placebo	TP 1450 ppm F-	every 6th week	prevalence of WSLs (%)	8%/ 10%	41.8%/ 43.8% Index of Goerlick: 1: 76.9%/ 78.0% 2:19.6%/ 15.8% 3: 3.5%/ 6.2%*	Ammonium F could prevent the development of advanced WSLs in adolescents
	2.	Najafi *et al.* 2022 (12)	RCT	120	12-20	G1: 10% Xylitol varnish G2: 20% Xylitol varnish G3: 5% F varnish G4: Placebo	TP 1450 ppm F-	T1: before treatment T2: after 3 mos T3: after 6mos	DIAGNOdent pen value	1.2±0.74/ 1.1±0.88/ 1.09±0.89/ 1.1±1.05	1.3±0.63/ 1.73±0.76/ 1.23±0.45/ 1.78±0.90	The short-term effects of 10% xylitol varnish on caries management were significantly better than those of 20% xylitol varnish and placebo, but were comparable to those of fluoride varnish.
	3.	Pilli 2022 (13)	RCT	90	12-18	G1: 0.2% NaF (weekly) group G2: APF group (daily)	TP:1100 ppm F-	T0: start of treatment; T1: 4 weeks; T2: 12 weeks; T3: 24 weeks	ICDASi	0.025/ 0.014	0.113/ 0.015	APF formulated daily oral rinse—0.044% w/v of NaF—is more effective than the weekly once regimen of 0.2% NaF oral rinse to prevent white spot lesions.
	4.	Ali 2021 (14)	RCT	42	18-37	G1: nano-silver mouthwash; G2:CHX mouthwash; G3: fluoride mouthwash	TP 1450 ppm F-	T0: before bonding; T1: after 1 mo; T2: after 3 mos; T3: after 6 mos;	incidence of WSL per teeth	2.38%/ 6.54%/ 8.92%	9.52%/ 24.4%/ 24.4%	The mean of WSLs in nanosilver group is lower than CHX and fluoride group in T2 and T3 of follow-up ($P < 0.05$)
	5.	Mollabashi 2022 (15)	RCT	38	15-30	G1: F toothpaste G2: F+ NovaMin	-	T0: before bonding; T1: after 1 mo; T2: after 3 mos;	DIAGNOdent pen value	18.33±3.65/ 18.72±4.4	11.4±3.73/ 9.56±2.85	NovaMin/F toothpaste did not provide significant effect compared to F toothpaste
Fluorides with CPP-ACP	6.	Rechmann 2018 (16)	RCT	37	13-26	G1: MI Varnish + MI PastePlus G2: F toothpaste	TP:1100 ppm F-	T0: before bonding; T1: after 3 mos; T2: after 6 mos; T3: after 12 mos;	EDI, ICDAS	EDI scores: 0: 51%/ 56% 1: 35%/ 33% 2: 5%/ 3% 3: 9%/ 8% EDI sum: 37.7/42.9 ICDAS score: 21.1/ 21.9;	EDI scores: 0: 45%/ 46% 1: 47%/ 45% 2: 1%/ 3% 3: 8%/ 6% EDI sum: 41.3/ 40.2 ICDAS score: 22.6/ 22.3;	Applying daily MIPP and quarterly MIV resulted in no statistically significant differences in EDI sum and ICDAS scores, only higher salivary fluoride levels were achieved
	7.	Flynn 2022 (17)	RCT	40	12–17	G1: ProSeal sealant G2 :MI Varnish	-	G1 every 3 months G2 every 4–6 weeks 12 mos	EDI	-	EDI scores: 0: 91.8% / 95.8% 1: 7.1% / 3.99% 2: 0.62% / 0.11% 3: 0.62% / -	MI Varnish and ProSeal sealant provide similar levels of protection during orthodontic treatment
	8.	H. Kau 2019 (18)	RCT	100	12-	G1: Clinpro 5000 G2: Clinpro Tooth Creme G3: MI Paste Plus	-	T0: before bonding; T1: after 1 mo; T2: after 2 mos; T3: after 3 mos;	EDI	EDI scores: 0: 100%/ 97.7%/ 99.8% 1: 0%/2%/0% 2:0%/0.3%/0.2%	EDI scores: 0: 86.8%/ 74.7%/79.6% 1: 7.2%/ 18.4%/ 13.9% 2: 3.7%/ 4.5%/ 3.4% 3: 1.7%/ 1.2%. 2.2% 4: 0.3%/ 1.2%/ 0.6% 5: 0%/0%/0.2% 6: 0.3%/ 0%/ 0%	Clinpro 5000 has a better effect than the two other pastes.

– - not defined.

did not show a conflict of interest between the authors.

Among the 8 included studies, 5 randomized controlled trials (11-15) evaluated the effects of fluorides, of which two evaluated the effect either of Ammonium F (11) or single F containing varnish (12) compared with placebo and Xylitol varnish, two included studies compared the effect between fluoride, nanosilver or CHX mouthwash (13, 14), and one assessed the effect of different F containing pastes (15).

In a study that evaluated the efficacy of Ammonium F varnish with intraoral photography, studies observed a significant reduction ($P < 0.05$) in the number of WSLs in the test group concerning WSL Score 3 (excessive white spot formation (thicker bands)) (11). Both the fluoride and 10% xylitol groups in the other study had significantly lower DIAGNOdent mean readings at T2 and T3 than the placebo group. However, at any moment, there was no discernible difference between 20% xylitol and placebo (12).

One study was conducted to compare nanosilver, 0.05% CHX and 0.05% F mouthwashes. At T2 and T3, there was a significant difference between the groups in the gingival, incisal and mesial surfaces with lower number of WSLs in nanosilver group compared to F and CHX groups, but no significant difference in the distal surface (14). Pilli *et al.* (13) conducted a study to compare the efficacy of a weekly once regime of NaF mouth rinse with APF daily mouth rinse. Intergroup comparison of mean severity white spot lesions (ICDAS scores) showed the significant difference at the T1, T2 and T3 time points, indicating the 0.44% APF formulated daily oral rinse is more effective than the weekly once regimen of 0.2% NaF oral rinse. The properties of calcium sodium phosphosilicate bioactive glass commercially called NovaMin in a toothpaste were evaluated in the study by Mollabashi *et al.* (15) comparing simple F toothpaste with both NovaMin and F containing toothpaste. The DIAGNOdent pen scores decreased significantly in both groups, but NovaMin toothpaste did not show significantly better results; therefore, there is no interaction between NovaMin and F for remineralisation of WSLs at different observation intervals in orthodontic patients.

3 articles (16-18) compared the effects of fluorides with phosphopeptides compounds: 1 compared Clinpro5000 and Clinpro Tooth Creme with MI PastePlus (18) and another 2 (16, 17) compared MI Varnish either with ProSeal sealant or with simple F toothpaste.

In comparison with Clinpro 5000, Clinpro Creme showed higher levels of EDI (significant at the 95% level) whereas MI Paste exhibited marginal significance (at the 90% level) in having a higher decalcification index than Clinpro 5000 (18). Other 2 articles studied the effectiveness of MI Varnish. Rechmann *et al.* (16) investigated whether daily MIPP and quarterly MIV application versus twice-daily 1100ppm F toothpaste is more effective. The mean percentage of sites per patient with an EDI score > 0 in the MIPP+MIV group (T0: 44.4%, T1: 46.1%, T2: 47.9%, T3: 55.2%) was slightly lower than in F toothpaste group at every time point, except for 12th month (T0: 49.1%, T1: 48.4%, T2: 53.3%, T3: 54.1%), but mean EDI sum score differences at each time point were not statistically significant. Coequal results for ICDAS scores were found, only salivary F levels were significantly higher at 12 months for the MIPP+MIV than for the control group (0.20±0.26 versus 0.04±0.04 ppm). The other study investigated the efficacy of the same MI Varnish compared to ProSeal (PS) sealant in prevention of WSL. The incidence of patients (50% for PS vs 35% for MIV) and teeth (17.5% vs 12.5%) developing WSLs were higher in the PS than in the MIV group, but the differences were not reported as statistically significant, suggesting both materials provided similar protection against WSLs during fixed orthodontic treatment.

DISCUSSION

Despite current achievements in caries prevention, one of the biggest issues faced by clinicians is the prevention and control of demineralization during orthodontic treatment. Current dentistry is focused on a preventative strategy rather than invasive restorations of carious lesions, therefore, early detection of WSL is important when considering the short period of time during which WSLs can form and become irreversible. The leading techniques for evaluating WSLs are following: the optical caries monitor, DIAGNOdent™ pen (19), quantitative laser and light-induced fluorescence (QLF), digital imaging with fiber-optic transillumination and computer analysis of digital images (20, 21). However, budget constraints limit these methods from being used in the majority of studies. Six out of eight studies included in this review used visual evaluation and digital intraoral photographs for WSL assessment (11, 13, 14, 16-18). These methods tend to underestimate the actual prevalence of enamel demineralization due to remains of bonding materials, moisture contamination, and blurry/

overexposed pictures (11). This evaluation should, wherever possible, be conducted using quantitative techniques, such as Diagnodent (22, 23) and QLF (24) - the widely used and approved technique for evaluating WSL. In study, it's critical to assess lesions in order to standardize the diagnosis using the same scales, such as ICDAS (International Caries Detection and Assessment System) or EDI (Enamel Decalcification Index) (25).

A requirement for inclusion in this review was the presence of a control group study design, such as another agent as a control, a placebo, or no intervention. Under ideal circumstances a positive (another agent or placebo) and a negative (no treatment) control group should always be included (26). This standardization study design might strengthen the evidence by improving the probability of quantitative comparison studies and reducing research bias. In certain studies, the number of participants is limited. However, due to the restriction of this limitation to some patient groups, this issue can be addressed with the standardization of methodologies.

It should be noted that some studies included in this review did not consider other fluoride sources (15, 17, 18). Other authors included data of other fluoride sources in their studies (11-14, 16), however, in this review it is not standardized. This factor might influence the results, since combination of additional fluoride (e.g. toothpaste) and remineralization agent can provide synergistic effect on WSL treatment (27).

Over the last five years, a lot of experimental studies have been conducted to assess the efficacy of various remineralization technologies used after debonding of orthodontic appliances. However, the lack of studies appraising the efficacy of remineralization methods during orthodontic treatment is a huge limitation of this review.

Even with all the limitations, it is noticeable in almost all studies included in this review that remineralizing techniques reduce the white spot lesions (size or visual appearance). In some clinical studies, it was proved that high-concentration fluoride varnish is effective remineralization method, however, the main finding of the present studies was that the fluoride varnish could alleviate but not totally prevent the development of WSLs during treatment with fixed orthodontic appliances (11, 12). The similar to F varnish effect of 10% Xylitol varnish was found in the investigation by Najafi *et al.* (12) The prolonged release of xylitol from this concentration, in line with a study by Pereira *et al.* (28), may be responsible for the minimal changes in mineral loss from the start of the treatment up to the sixth month in the 10% xylitol group, and the high concentration of 20% xylitol appeared to be similar to placebo varnish due to curtailed time in the saliva (Pereira). Some scientists reported that fluoride and CHX combination is more effective than fluoride alone for dental caries prevention and keeping a healthy microbiome during orthodontic treatment (29). However, reversible adverse effects, such as impaired taste sensation (30), tooth staining (31), and occasional mucus membrane irritation (30), could be associated with prolonged use of CHX application. In the other study the effectiveness of acidulated fluoride used daily was greater compared to neutral fluoride used once a week (32). The explanation for this outcome might be that solutions with a low pH increase calcium fluoride (CaF2) formation as well as the regular application boosts the effectiveness of intervention (32, 33). Therefore, compared to neutral NaF, acidulated fluoride formulations provide more calcium fluoride to the enamel within a short period of time.

Recent scientific studies assessed the impact of CPP-ACP on WSL remineralization. It has been proved that the combination of casein phosphopeptide and amorphous calcium phosphate (CPP-ACP) can reduce WSLs (34, 35). Comparing casein phosphopeptide-amorphous calcium phosphate fluoride (CPP-ACP) and tricalcium phosphate fluoride (TCP-F), TCP-F provided better results in remineralization than CPP-ACP (Kau; 14). Rechman *et al.* () concluded that there is no difference between daily application of CPP-ACP together with quarterly application of CPP-ACFP and fluoride toothpaste twice a day. However, some studies discovered that applying CPP-ACP and other fluoride remineralization products (regular 1100 ppm fluoride toothpaste, 5% NaF varnish) provided significant reduction in the number, size, and activity of WSLs in comparison to fluoride (36-39). Finally, comparing MI Varnish and ProSeal there was no significant difference, however Flynn *et al.* (17) suggested that deviations likely would have been statistically significant with larger sample numbers.

CONCLUSIONS

The white spot lesions have improved, regressed, or eliminated using topical agents including fluoride, xylitol, or casein phosphopeptide-amorphous calcium phosphate during the fixed orthodontic treatment. More research is needed in order to determine the most effective therapeutic approach for the treatment of surface and subsurface demineralization of the enamel.

REFERENCES

1. Willmot, Derrick. (2008). White Spot Lesions After Orthodontic Treatment. Seminars in Orthodontics. 14: 209-219. doi: 10.1053/j.sodo.2008.03.006.
2. Øgaard B. (2008). White spot lesions during orthodontic treatment: mechanisms and fluoride preventive aspects. Semin Orthod. 14:183–193. doi: 10.1053/j.sodo.2008.03.003
3. Chambers C, Stewart S, Su B, Sandy J, Ireland A. (2013). Prevention and treatment of demineralisation during fixed appliance therapy: a review of current methods and future applications. Br Dent J.215(10):505–11. doi:10.1038/sj.bdj.2013.1094
4. Bishara, Samir & Ostby, Adam. (2008). White Spot Lesions: Formation, Prevention, and Treatment. Seminars in Orthodontics. 14. 174-182. doi: 10.1053/j.sodo.2008.03.002.
5. Paschos E, Kleinschrodt T, Clementino-Luedemann T, Huth KC, Hickel R, Kunzelmann K-H, et al. (2009) Effect of different bonding agents on prevention of enamel demineralization around orthodontic brackets. Am J Orthod Dentofacial Orthop.135(5):603–12. doi:10.1016/j.ajodo.2007.11.028
6. Schmidlin PR, Schätzle M, Fischer J, Attin T. (2008). Bonding of brackets using a caries-protective adhesive patch. J Dent. 36(2):125–9. doi:10.1016/j.jdent.2007.11.005
7. an der Veen MH, Attin R, Schwestka-Polly R, Wiechmann D. (2010) Caries outcomes after orthodontic treatment with fixed appliances: do lingual brackets make a difference?: Lingual brackets and caries prevention. Eur J Oral Sci.118(3):298–303. doi:10.1111/j.1600-0722.2010.00733.x
8. Weyland, M.I., Jost-Brinkmann, PG. & Bartzela, T. (2022). Management of white spot lesions induced during orthodontic treatment with multibracket appliance: a national-based survey. Clin Oral Invest 26, 4871–4883. doi: 10.1007/s00784-022-04454-5
9. Sarkis-Onofre R, Catalá-López F, Aromataris E, Lockwood C. (2021) How to properly use the PRISMA Statement. Syst Rev.;10(1):117. doi: 0.1186/s13643-021-01671-z
10. Higgins, J., Altman, D., Gotzsche, P., Juni, P., Moher, D., Oxman, A., Savovic, J., Schulz, K., Weeks, L. and Sterne, J. (2011). The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ, 343(oct18 2), pp. d5928-d5928.doi: 10.1136/bmj.d5928
11. Sonesson M, Brechter A, Abdulraheem S, Lindman R, Twetman S. Fluoride varnish for the prevention of white spot lesions during orthodontic treatment with fixed appliances: a randomized controlled trial. Eur J Orthod [Internet]. 2020;42(3):326–30. Available from: http://dx.doi.org/10.1093/ejo/cjz045
12. Zarif Najafi H, Shavakhi M, Pakshir HR. (2022). Evaluation of the preventive effect of two concentrations of xylitol varnish versus fluoride varnish on enamel demineralization around orthodontic brackets: a randomized controlled trial. Eur J Orthod. May 24;44(3):243-251. doi: 10.1093/ejo/cjab049
13. Pilli LN, Singaraju GS, Nettam V, Keerthipati T, Mandava P, Marya A. (2022). An extensive comparison of the clinical efficiency of acidulated phosphate fluoride (APF) and neutral sodium fluoride (NaF) oral rinses in the prevention of White Spot lesions during fixed orthodontic treatment: A randomized controlled trial. Biomed Res Int 2022:6828657. doi:10.1155/2022/6828657
14. Ali A, Ismail H, Amin K. (2022). Effect of nanosilver mouthwash on prevention of white spot lesions in patients undergoing fixed orthodontic treatment - a randomized double-blind clinical trial. J Dent Sci. 17(1):249–55. doi: 10.1016/j.jds.2021.03.016
15. Mollabashi V, Heydarpour M, Farhadifard H, Alafchi B. (2022). DIAGNOdent pen quantification of the synergy of NovaMin® in fluoride toothpaste to remineralize white spot lesions in patients with fixed orthodontic appliances: A double-blind, randomized, controlled clinical trial. Int Orthod.20(2):100632. doi:10.1016/j.ortho.2022.100632
16. Rechmann P, Bekmezian S, Rechmann BMT, Chaffee BW, Featherstone JDB. (2018). MI Varnish and MI Paste Plus in a caries prevention and remineralization study: a randomized controlled trial. Clin Oral Investig. 22(6):2229–39. doi:10.1007/s00784-017-2314-9
17. Flynn LN, Julien K, Noureldin A, Buschang PH. (2022) The efficacy of fluoride varnish vs a filled resin sealant for preventing white spot lesions during orthodontic treatment. Angle Orthod. 92(2):204–12. doi:10.2319/052521-418.1
18. Kau CH, Wang J, Palombini A, Abou-Kheir N, Christou T. (2019). Effect of fluoride dentifrices on white spot lesions during orthodontic treatment: A randomized trial: A randomized trial. Angle Orthod. 89(3):365–71. doi:10.2319/051818-371.1
19. Hamdan WA, Badri S, El Sayed A. (2018).The effect of fluoride varnish in preventing enamel demineralization around and under orthodontic bracket. Int Orthod. 16(1):1–11. doi:10.1016/j.ortho.2018.01.005
20. Lucchese A, Gherlone E. (2013). Prevalence of white-spot lesions before and during orthodontic treatment with fixed appliances. Eur J Orthod. 35(5):664–8.doi:10.1093/ejo/cjs070
21. Akin M, Basciftci FA. (2012). Can white spot lesions be treated effectively? Angle Orthod. 82(5):770–5. doi:10.2319/090711.578.1
22. Du M, Cheng N, Tai B, et al. Randomized controlled trial on fluoride varnish application for treatment of white spot lesion after fixed orthodontic treatment. Clinical oral investigations 2012;16(2):463-68.
23. Andersson A, Sköld-Larsson K, Hallgren A, Petersson LG, Twetman S. Effect of a dental cream containing amorphous cream phosphate complexes on white spot lesion regression assessed by laser fluorescence. Oral health & preventive dentistry 2006;5(3):229-33.
24. Beerens M, Van Der Veen M, Van Beek H, Ten Cate J. Effects of casein phosphopeptide amorphous calcium fluoride phosphate paste on white spot lesions and dental plaque after orthodontic treatment: a 3-month follow-up. European journal of oral sciences 2010;118(6):610- 17.
25. Robertson MA, Kau CH, English JD, et al. MI Paste Plus to prevent demineralization in orthodontic patients: a prospective randomized controlled trial. American Journal of orthodontics and dentofacial orthopedics 2011;140(5):660-68.
26. Memarpour M, Fakhraei E, Dadaein S, Vossoughi M. Efficacy of fluoride varnish and casein phosphopeptide-amorphous calcium phosphate for remineralization of primary teeth: a randomized clinical trial. Medical Principles and Practice 2015;24(3):231-37.
27. Iman I. El-Sayad, Amal K. Sakr, Yahia Abdel Hamid Badr, "Combining casein phosphopeptide-amorphous calcium phosphate with fluoride: synergistic remineralization potential of artificially demineralized enamel or not?," J. Biomed. Opt. 14(4) 044039 (1 July 2009) https://doi.org/10.1117/1.3210780
28. Pereira A de FF, Silva TC da, Silva TL da, Caldana M de L, Bastos JRM, Buzalaf MAR. (2012). Xylitol concen-

trations in artificial saliva after application of different xylitol dental varnishes. J Appl Oral Sci. 20(2):146–50. doi:10.1590/s1678-77572012000200004
29. Shimpo Y, Nomura Y, Sekiya T, Arai C, Okada A, Sogabe K, et al. (2022). Effects of the dental caries preventive procedure on the White Spot lesions during orthodontic treatment-an open label randomized controlled trial. J Clin Med. 2022;11(3):854. doi: 10.3390/jcm11030854
30. James, P.; Worthington, H.V.; Parnell, C.; Harding, M.; Lamont, T.; Cheung, A.; Whelton, H.; Riley, P. Chlorhexidine mouthrinse as an adjunctive treatment for gingival health. Cochrane Database Syst. Rev. 2017, 3, CD008676.
31. Emel, S.; Ilhan, B. Microbiological Evaluation of 0.2% Chlorhexidine Gluconate Mouth Rinse in Orthodontic Patients. Angle Orthod. 2007, 77, 881–884.
32. B. Øgaard, "White spot lesions during orthodontic treatment: mechanisms and fluoride preventive aspects," Seminars in Orthodontics, vol. 14, no. 3, pp. 183–193, 2008
33. D. Rios, H. M. Honório, L. F. Francisconi, A. C. Magalhães, M. A. . A. M. Machado, and M. A. R. Buzalaf, "In situ effect of an erosive challenge on different restorative materials and on enamel adjacent to these materials," Journal of Dentistry, vol. 36, no. 2, pp. 152–157, 2008.
34. Rollings S, Greene L, Borrie F, Lamont T. Small trial finds beneficial effect for MI Paste in preventing white spot lesions during orthodontic treatment. Evid Based Dent. 2012;13(4): 117–118. 9.
35. Robertson MA, Kau CH, English JD, Lee RP, Powers J, Nguyen JT. MI Paste Plus to prevent demineralization in orthodontic patients: a prospective randomized controlled trial. Am J Orthod Dentofacial Orthop. 2011;140(5):660–668.
36. Akin M, Basciftci FA (2012) Can white spot lesions be treated effectively? Angle Orthod 82(5):770–775
37. AnderssonA,Skold-LarssonK,HallgrenA,PeterssonLG, TwetmanS (2007)Effectofadentalcreamcontainingamorphouscreamphosphate complexes on white spot lesion regression assessed by laser fluorescence. Oral Health Prev Dent 5(3):229–233 21.
38. Bailey DL, Adams GG, Tsao CE, Hyslop A, Escobar K, Manton DJ, Reynolds EC, Morgan MV (2009) Regression of postorthodontic lesions by a remineralizing cream. J Dent Res 88(12): 1148–1153.
39. Wang JX, Yan Y, Wang XJ (2012) Clinical evaluation of remineralization potential of casein phosphopeptide amorphous calcium phosphate nanocomplexes for enamel decalcification in orthodontics. Chin Med J 125(22):4018–4021

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