

Preventing and Arresting the Appearance of White Spot Lesions around the Bracket by applying Fluoride Varnish: A Systematic Review

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Abstract

Introduction: White spot lesions are the first clinical sign of dental caries, and they occur frequently in patients with orthodontic appliances. Currently, there are no systematic reviews that have evaluated fluoride varnish compared with other methods to prevent or arrest the development of dental caries. The aim of this systematic review (SR) was to evaluate the effectiveness of the use of fluoride varnish compared with other methods to prevent or arrest initial lesions of caries in patients with corrective orthodontics.

Methods: A search was conducted for articles in the MEDLINE, EMBASE and Google Scholar databases. This SR included randomized clinical trials and prospective interventional studies that used fluoride varnish for the prevention and/or arrest of white spot lesions in orthodontic treatment or during the 3-month period after removal of orthodontic fixed appliances. To assess the risk of bias in the studies, we used the Cochrane collaboration tool.

Results: The search strategy showed 115 possible eligible articles, and we included 10 articles in this SR. The reviewed studies showed high and moderate methodological quality. Four studies out of 10 agreed that fluoride varnish is as effective as the advised and guided oral hygiene technique. Overall, most of the included studies did not show significant advantages to fluoride varnish application in terms of preventing the development of white spots around orthodontic brackets when the patients were submitted to regular professional oral hygiene control.

Conclusions: Fluoride varnish is an effective material to prevent and arrest white spot lesions in patients with orthodontic treatment.

Keywords: White spot; Orthodontics treatment; Fluoride varnishes; Tooth demineralization; Dental caries; Orthodontics brackets

Introduction

White spot lesions are the first clinical sign of dental caries that can be clinically detected [1,2]. These lesions appear as a result of the cyclic demineralization and remineralization of the enamel due to an alteration in pH levels when protective factors as saliva and fluorides are not able to maintain a balance in favor of remineralization, resulting in an initial lesion of caries on a specific surface of the tooth [3]. Initial lesions can be arrested and turned into inactive lesions, and the diagnostic can be performed at initial stages using visual inspection after drying the surface [4] with photographs (permanent method to register size of the lesion) and with laser fluorescence (QLF) [5,6] which is a validated method to monitor the early stages of caries and remineralization [7]. Likewise, initial lesions can be detected with diagnodent 8, which evaluates dental caries through a laser fluorescence detector and is an accurate method to identify caries in pits and fissures, as well as approximal caries. Another method is the International Caries Detection and Assessment System (ICDAS), which is a visual index for detection and classification of caries from white spot lesions to extensive cavities that gives a numerical value ranging from 0 to 6 [8].

Similarly, demineralization has been shown to be a collateral effect associated with poor oral hygiene in patients with a fixed orthodontics appliance [9] due to a greater accumulation of plaque produced by difficulties in performing adequate oral hygiene [1]. Initial lesions can be detected in 2 to 4 weeks as white spots along the periphery of the bracket; in patients with a continuous imbalance between dental plaque and the surface of the tooth, there is a loss of integrity in the surface that results in a cavity [10,11].

Data on the prevalence of initial lesions of caries in patients

undergoing orthodontics treatment are variable, i.e., from 2-96% and 74% [11]. Studies have indicated that white spot lesions (WSLs) can be controlled and prevented using non-operative treatments, such as fluoride toothpastes, oral rinses, reinforcement of oral hygiene instructions, and topical application of fluorides. Fluoride varnishes can revert, arrest or prevent demineralization processed in a WSL when combined with other preventive measures, such as dental plaque control and diet [12] because of the reduction of demineralization in the surface-reducing enamel solubility [13,14].

Among the products containing fluorides, varnishes are one of the most evaluated agents for remineralization of white spot lesions. The use of varnish increases the time of contact between the enamel, prolongs reactivity of NaF with the surface of the tooth [15] and is easy to use and secure. Therefore, varnishes have been the first choice for dentists [16,17]. The stability of varnishes has been shown for a period of 3 months, and the benefits can be the result of the CaF₂ precipitation that favors remineralization [18].

Currently, there are no systematic reviews that evaluated the effectiveness of fluoride varnishes in preventing and arresting white

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Received July 10, 2018; Accepted July 16, 2018; Published July 22, 2018

Citation: Sandra CD, Maria D, Ingrid MD, Vanessa HD, Katia VR, et al. (2018) Preventing and Arresting the Appearance of White Spot Lesions around the Bracket by applying Fluoride Varnish: A Systematic Review. Dentistry 8: 500. doi:10.4172/2161-1122.1000500

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spot lesions around the brackets compared with other preventive methods.

Objective

The aim of this systematic review was to assess the effectiveness of fluoride varnish applications compared with other techniques for the prevention or arrest of initial lesions of caries in patients with corrective orthodontics.

Consequently, the following research PICO question was suggested: Is the fluoride varnish application effective compared with other techniques to prevent or arrest white spot lesions in patients with corrective orthodontics?

Materials and Methods

This review was structured according to the guidelines of PRISMA [19], the Cochrane Handbook for Systematic Reviews of Intervention [20] and the checklist for reviews [21]. Likewise, the protocol for this SR was registered at the National Institute for Health Research PROSPERO, International Prospective Registry of Systematic Reviews (<http://www.crd.york.ac.uk/PROSPERO>, registration number CRD42016038888).

Type of study and participants (inclusion criteria)

This review included all articles that met the following criteria: studies on human, controlled clinical trials and prospective intervention studies that compared the effectiveness of fluoride varnish applications versus other techniques to prevent or arrest white spot lesions in patients with permanent dentition undergoing corrective orthodontics treatment or after removal of orthodontic fixed appliances in a time less than or equal to 3 months.

Exclusion criteria

Authors discarded studies that evaluated the effectiveness of fluoride varnish on teeth with orthodontics bands or loops, cavitation caries, dental whitening, enamel defects, dental restorations in the buccal surface and lesions microscopically assessed. Likewise, we excluded studies that evaluated the effectiveness of simultaneous application of a fluoride varnish with another product.

Measurement of results

This review evaluated the following variables of the results:

- 1) Prevention of white spot lesions, measured by visual clinical examination and other visual diagnostic tests.
- 2) Arrest of white spot lesions, measured by visual clinical examination and other visual diagnostic tests.

Search strategies

Detailed search strategies were developed for MEDLINE (for Medical Literature Analysis and Retrieval System Online), EMBASE (Excerpta Medica Database), Google Scholar, as well as other sources of information such as the gray literature and manual search.

There was no restriction of language. Databases were reviewed until February 2017 using MeSH terms (Medical Subject Headings), keywords and other free terms with Boolean operators (OR, AND).

Search strategies were based on the algorithm used for MEDLINE:

#1 orthodontics or orthodontics treatment or orthodontics brackets or multibrackets appliance therapy

#2 white spot or dental caries or tooth demineralization

#3 #1 and #2

#4 topical fluoride or fluoride varnishes or varnishes, fluoride or varnishes or fluoride or fluor protector or remineralizing agents

#5 prevention or prevention and control

#6 #4 or #5

#7 #3 and #6

Validity assessment and data extraction

Two independent reviewers evaluated titles, abstracts and full texts of the articles and disagreement between reviewers was resolved through discussion. When no agreement could be reached, a third reviewer was consulted. If important data were missing or unclear, we attempted to contact the authors to resolve the ambiguity of the information. Information from the articles was extracted and recorded taking into account the following data: year of publication, location of the trial, study design, characteristics of the participants, measure of outcomes, methodological quality of the trials and conclusions.

Assessment of risk of bias and quality assessment in included studies

The methodological quality of the randomized clinical trials and prospective intervention studies was evaluated using the Cochrane Collaboration tool for assessing risk of bias, as described in the Cochrane Handbook for Systematic Reviews [20,21] (Table 1).

The risk of bias was classified according to the following characteristics:

- (1) low risk of bias: all criteria were achieved (adequate methods of randomization and concealment of allocation, adequate follow-up, blinding of examiners);
- (2) uncertain risk of bias: one or more criteria partially achieved (i.e., unclear criteria were established); or
- (3) high risk of bias: one or more criteria were not achieved [21].

Data synthesis

Data were grouped into tables of evidence, and a descriptive summary was created to determine the quantification of data and variations of the studies.

Results

Search results

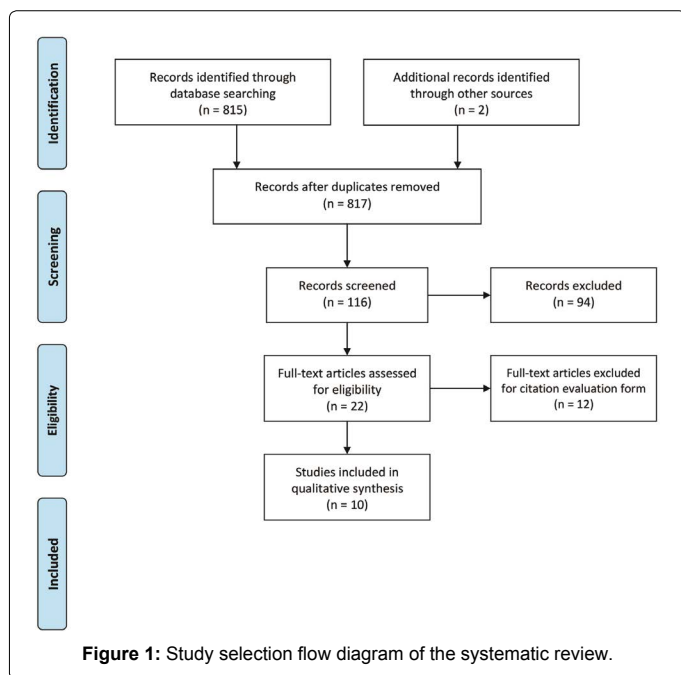
The search strategy identified 817 potentially eligible articles in the database (Embase, PubMed y Google Scholar). Then, 701 articles were excluded based on the title of each article, and 116 abstracts from the remaining articles were analyzed and 94 were excluded; 22 full texts were then analyzed and 12 were excluded due to the selection criteria not being met (Figure 1).

Included studies

A total of 10 clinical trials were selected for this systematic review that were conducted in the United States [22,23] Brazil [24-26] Sweden [27], Iran [28], Germany [29], China [30] and Italy [31]. Three of the studies used fluoride varnish as a preventive therapy in the appearance of white spot lesions around the bracket [24,25,31] with a split mouth design, and 7 studies used varnish to treat white spot lesions around the bracket with a parallel design [22,23,26-30].

Domain	Support for judgement	Review authors' judgement
Selection bias		
Random sequence generation.	Describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.	Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence.
Allocation concealment.	Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment.	Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment.
Performance bias		
Blinding of participants and personnel Assessments should be made for each main outcome (or class of outcomes).	Describe all measures used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.	Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Detection bias		
Blinding of outcome assessment Assessments should be made for each main outcome (or class of outcomes).	Describe all measures used, if any, to blind outcome assessors from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.	Detection bias due to knowledge of the allocated interventions by outcome assessors.
Attrition bias		
Incomplete outcome data Assessments should be made for each main outcome (or class of outcomes).	Describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. State whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomized participants), reasons for attrition/exclusions where reported, and any re-inclusions in analyses performed by the review authors.	Attrition bias due to amount, nature or handling of incomplete outcome data.
Reporting bias		
Selective reporting.	State how the possibility of selective outcome reporting was examined by the review authors, and what was found.	Reporting bias due to selective outcome reporting.
Other bias		
Other sources of bias.	State any important concerns about bias not addressed in the other domains in the tool. If particular questions/entries were pre-specified in the review's protocol, responses should be provided for each question/entry.	Bias due to problems not covered elsewhere in the table.

Table 1: Cochrane Collaboration tool for assessing risk of bias.



Articles were published between 2006 and 2016; 6 articles were randomized controlled trials [22,23,26-30] and 4 were non-randomized clinical trials [24,25,28,31] (Tables 2 and 3).

Altogether, 866 subjects were examined in the evaluated articles. It

is noteworthy that the following visual diagnostic methods were used to measure the effectiveness of fluoride varnish: Diagnodent [24,26,31] clinical photographs, QLF, QLF and ICDAS, ICDAS, and Nyvad index [23-28].

Methodological quality of the included studies, assessment of the effectiveness of fluoride varnish to prevent and arrest white spot lesions:

Evaluation of studies: Six studies showed high methodological quality [22,23,26-30], and four showed moderate methodological quality [24,25,28,31]. Additionally, eight clinical trials showed adequate methods of randomization, and six studies [22,23,26-30] described clear and adequate allocation concealment as well as results regarding the completeness of the follow-up. Only four clinical trials reported blinding of examiners and participants [23,26,29,30]. Regarding “selective outcome reporting” and “sources of bias”, information was not clear for the trials [25,28] (Figure 2). The follow-up period ranged from approximately 0 months to a year, considering that some articles had time intervals of 3-months [24,25,30,31].

Assessment of the effectiveness of fluoride varnish to prevent white spot lesions: According to Demito et al. [24] teeth not treated with fluoride varnish showed a greater tendency to demineralize, 0.89 +/- 1.94 in the control group vs 0.53 +/- 1.33 (p<0.05) in the varnish group. Rodrigues et al. [25], reported similar results with an increase of 0.34 +/- 0.64 in the experimental group and 0.61 +/- 1.15 in the control group; for both studies, these differences were statistically significant. The study carried out by Huang et al. [23] found no differences between MI Paste Plus and PreviDent fluoride varnish compared to a

Study	Participants /Type of material/ study design	Groups	Postoperative Follow Up	Postoperative sensitivity evaluation	Outcome	Conclusions
Demito et al., [21]						
	15 patients (274 teeth).	Test group: 137 teeth	Measures at 3 months and 6 months after application.	0-10 = sound dental surface.	Control group showed 32% more progression of demineralization than varnish group at 6 months, no significance.	The fluoride varnish is less expensive and easier to apply than fluoride gel and unlike home rinses, this do not require patient collaboration. The disadvantages include the need to wait 1 hour before eating or drinking and 12 hours before brushing, re-apply the varnish at least every 12 weeks to maintain its effectiveness. At the end, when comparing fluoride varnish with other alternatives to reduce enamel decalcification, varnishes can be the first option.
	Fluoride varnish Duraphat/ Without fluoride varnish.	Fluoride varnish application Duraphat.		11-20 = caries in enamel (external half).		
	Randomized Clinical Trial.			21-30 = caries in enamel (internal half)	Most of the demineralization was in the gingival third.	
	Split-Mouth.	Control group: 137 teeth, no Fluoride application.		>30 = caries.	Teeth without intervention.	
				Diagnodent.	Gingival third: 0.89 +/- 1.94.	
Perrini et al., [25]						
	24 patients.	Test group: Quadrant 1 and 3 using Duraphat.	Evaluation at the intervention, 3, 6, 9, y 12 months after placing brackets.	0 a 13: sound enamel.	The sample showed a greater tendency to demineralization in the untreated vs treated teeth, although both linear analyzes and coefficient showed not significant difference at any of the measured times. Conclusions indicate that the gingival third was slightly more susceptible to demineralization. Particularly, at 9 months, incisors treated with fluoride varnish showed significantly less demineralization compared to non-treated teeth.	Regular application of fluoride varnish may protect against white spots, but will not be statistically significant if patients have excellent oral hygiene.
	Duraphat/ without fluoride varnish.			14 a 20: initial demineralization.		
	Randomized Clinical Trial.			21 a 29: moderate demineralization.		
	Split-Mouth.	Control group: Quadrants 2 and 4, without fluoride varnish.		>30: dental caries.		
Rodrigues et al., [26]						
	10 patients (200 teeth).	Test group: 100 teeth with Duraflo application.	Varnish was applied every 3 months during a year.	0: without decalcification	The average number of varnish application was 10 (range 4-20) in both groups. Incidence of WSL during treatment with orthodontic fixed appliances was 7.4% in the fluoride varnish group compared to the placebo group 25.3% (P 0.001). The absolute risk reduction was 18%.	The results of this prospective evaluation of quarterly application of fluoride varnish have shown to be an effective auxiliary method to reduce white spot lesions during treatment with orthodontic fixed appliances. During a 12-month observation, there was a 44.3% reduction in enamel demineralization index of teeth treated with fluoride varnish compared to control group.
	Duraflo/ without fluoride varnish.			1: decalcification less than 50% of the Surface.		
	Randomized clinical trial.			2: decalcification greater than 50% of the surface.		
	Split-Mouth.	Control group: 100 teeth without fluoride varnish application.		3: decalcification 100% of the surface, or severe decalcification with cavity.	Progression was significantly lower in fluoride varnish group than the placebo group, 0,8 +/- 2,0 vs. 2,6 +/- 2,8 (P 0.001).	Although fluoride varnish does not completely prevent the development of enamel lesions, the reduce in the incidence and severity of the lesions deserves a clinical consideration. The regular application of fluoride varnish in patients undergoing orthodontic treatment can be accepted as a contemporary standard of care to limit enamel lesions.
				Banks and Richmond index through photographs.		

Table 2: Characteristics of included studies in preventing white spot lesions with fluoride varnish application.

Study	Participants /Type of material/ study design	Groups	Postoperative Follow Up	Postoperative sensitivity evaluation	Outcome	Conclusions
Huang et al., [30]						
	115 patients	Test group 1: 34 patients, application of MI Paste Plus	Measures in the 8 th week of intervention	0: without improvement or deterioration	The measures evaluated by the expert panel were 21% MI Paste Plus, 29% PreviDent and 27% in the control group. The results of the expert panel were 29%, 31%, and 25%, respectively. Scores for objective improvements were 16%, 25% and 17%, and scores for autoperceived improvement were 37% in the 3 groups.	In this randomized clinical trial, there was no difference between the effectiveness of MI Paste Plus, fluoride varnish PreviDent compared with conventional and toothpaste regimen for remineralization of white spots during a period of 8 weeks.
	MI Paste Plus/ Fluoride varnish PreviDent/ without fluoride varnish	Test group 2: 40 patients, application of 0.4 mL of 5% sodium fluoride varnish PreviDent		100: completely improved in mm		
	Randomized clinical trial	Control group: 41 teeth, without fluoride varnish		Photographs	No significant differences	
Stecksén et al., [20]						

302 patients	Test group: 132 patients. Application of Fluor protector 0.1% F with silane fluoride varnish based on polyurethane.	Until complete orthodontic treatment	1: No development of white spot	The incidence of WSL during treatment with an orthodontic fixed appliance in the fluoride varnish group was approximately one-third of the placebo group, 7,4 vs. 25.7% (P< 0.05).	The results of this study strongly suggest that regular applications of fluoride varnish may reduce the development of white spot lesions around the bracket during treatment with orthodontic fixed appliances. Therefore, fluoride varnishes should be advocated as a professional preventive measure in orthodontic practice.
Fluoride varnish Duraphat/ without fluoride varnish	2: mild development of white spot (thin border)				
Randomized clinical trial	Control group: 125 patients. Application of a colorless varnish placebo similar to the one used in the treated group but without fluoride.		3: severe development of white spot (thick band)	The mean score of progression was 0.8 ± 2.0 in the intervention group compare with 0.8 ± 2.0 in the control group; this difference was statistically significant (P <0.001).	
Parallel			4: development of white spot and cavity. Photograph		
Kirschneck et al., [27]					
90 patients	Test group 1: 30 patients with 1 application of fluoride varnish Elmex® at the beginning of the orthodontic treatment	Measures were done on week 4, 12 and 20	0: Sound 1: White spot seen after air drying	None of the 3 studied groups showed significant differences in ICDAS scores on any of the 4 measured times (T0 to T3). However, the median of the ICDAS index increased in the three groups during the period of study (T0 to T3)	The one-time application of Elmex Fluid® or Fluor Protector S varnishes at the beginning of the orthodontic treatment with fixed multibracket appliance did not provide any additional benefit in prevention compared to the home use of fluoride toothpaste in patients with low to moderate risk of caries.
Randomized clinical trial			4: Underlying dark shadow from dentin 5: Distinct cavity with visible dentin less than 50%		
Parallel	Control group: 30 patients with 1-time application of a placebo free of fluoride at the beginning of the orthodontic treatment		ICDAS		
He et al., [28]					
240 patients (597 teeth)	Test group 1: upper anterior teeth of 80 patients, application of Duraphat 1 time per month	Measures were done at 0, 3 y 6 month	ΔF (%): is the percentage of fluorescence loss, comparing sound enamel with a lesion. The fluorescence loss less than 5% was considered harmful. Area (mm ²) is calculated as pixels considered by the software to represent demineralized enamel (i.e., those with fluorescence loss of 5% or more). ΔQ (mm ² x%): is the product of ΔF and the area and indicates the volume of the lesion.	Significant decrease in ΔQ in all groups after 6 months. In the statistical analysis, the interaction between the group and time indicated that the ΔQ values of the 3 groups followed different trends over time (varnish vs. control: estimate, -11.83; 95% CI: -15.39 a -8.26, P <0.0001, the film against Control: estimate, -7.72, 95% CI, -11.34 to -4.10, P <0.0001, Table IV).	White spot lesions around the brackets may self-healing in some cases, after removal of the brackets. However, not all patients experienced remineralization by themselves. Daily use of fluoride toothpaste and education in oral hygiene can support enamel remineralization and treatment with fluoride varnish or a fluoride film can induce greater amount of remineralization after orthodontic treatment. Fluoride varnish may be slightly more effective than fluoride film.
Duraphat/ fluoride film Sheer/ placebo without fluoride	Test group 2: upper anterior teeth of 80 patients, application of fluoride film (Sheer) 1 time a month				
Randomized clinical trial	Control group: upper anterior teeth of 80 patients, application of placebo 1 time a month		QLF (images)		
Parallel					
Miresmaeili et al., [29]					

	65 teeth in 20 patients	Test group: 10 patients (33 teeth) Fluoride varnish	Measures were done at 0 and 4 months	The pre- and post-intervention images were superimposed using the same tooth size to match the two images. Edges of the lesion were marked before and after treatment with black and red lines, respectively. The lesion / tooth area ratio was calculated based on the number of pixels using the following formula: WSA% = Number of pixels occupied by the lesion / Number of pixels on the surface of the labial tooth 100	Oral hygiene was good in both groups. The mean size of the lesion in the test group was 8.3% ± 3.07 before treatment, decreasing to 5.9% ± 2.9 after treatment (P = 0.009). The mean size of the lesion in the control group was 7.7% ± 4.2 before treatment, decreasing to 5.9% ± 3.6 after treatment (P = 0.001). No statistically significant differences were detected between the two groups (P = 0.307).	Based on the results, the application of fluoride varnish has no superiority over the process of natural remineralization of saliva in reducing the size of white spot lesion on the enamel in patients with good oral hygiene.
	Fluoride varnish (VOCO)/ prophylaxis					
	Randomized clinical trial	Control group: 10 patients (32 teeth). No application of any product, just dental prophylaxis				
	Parallel			Photos superimpose in photoshop		
Wulc et al., [31]						
	20 patients	Test group: 10 patients with fluoride varnish application in white spot lesion	Measures were done at 0 and 2 months	ICDAS 0: Sound 1: White spot seen after air drying for 5 seconds 2: White spot seen when wet.	ICDAS median, Code count 1 and 2 was 2.71 with a range from 0 to 12 and a standard deviation of 3.58 in the control group. In the experimental group the mean ICDAS count of codes 1 and 2 was 6.72 with a range from 0 to 17 and a standard deviation of 6.69	Data collection should be completed and sample size increased to make conclusions about the role of fluoride varnish application in white spot lesions. Applying fluoride varnish to white spot lesions appears to be ineffective in reducing the lesions compared to good oral hygiene.
	Fluoride varnish Enamel Pro®/ without fluoride varnish application	Control group: 10 patients with oral hygiene instructions		QLF Three images were taken for each patient. 2 images of buccal segments and 1 front image. Loss of fluorescence (Df) and changes in caries volume (ΔQ) were calculated with QLF – D software by tracing all lesion.		There can be no correlation between IMC and the susceptibility to white spots. Changes in patient recruitment and appointments could enhance the data collection process, allowing a successful long-term experiment
	Randomized clinical trial					
	Restrepo et al., [32]					

30 patients (51 lesions)					
5% NaF Varnish (Duraphat®)	Test group 1: F group: 5% NaF varnish: 10 patients, 17 lesions	At the moment of application, 1 week, 1, 2, 3 months after application.	Diagnodent: Previously calibrated measuring sound surface of each tooth. Measures were performed after air drying for 5 seconds. The peak reading shown on the DDpen panel was recorded twice for each tooth surface.	Fluorescence values decreased during the course of the study. The average reading of the lesions in DDpen on the baseline F group: 17.2 ± 2.3, CHX group: 16.8 ± 1.8, CO group: 17.0 ± 1.7, which decreased to 7, 2, 9.2 and 10.5, respectively, at the end of the study (3 months).	After 3 months, F, CHX or CO groups were able to control white spot lesions around to the bracket. However, the treatment with fluoride varnish was able to control the progression of the lesion in a shorter period of time.
2% Chlorhexidine gel (Clorexal gel 2%)	Test group 2: CHX group: 2% Chlorhexidine gel: 10 patients, 17 lesions			At the end of the study, 70.58% of the lesions were classified as inactive with intact surface (NY, score 4) and 29.42% as active with intact surface (NY, score 1).	
Saline solution					
Randomized clinical trial	Control group: CO group: Saline solution: 10 patients, 17 lesions		Nyvad Index: 0: Sound 1: Active caries (intact surface) 2: Active caries (superficial discontinuity) 3: Active caries (cavity) 4: Inactive caries (intact surface)	One week after the first application, fluorescence values in F group were significantly lower than those at baseline (P <0.01) and CHX (P <0.01). Significant differences in baseline were found only for the control group one week after the second application (P <0.01). Fluorescence values for F remained constant from the 1st to 3rd month and were significantly different from baseline (P <0.05). At the third month, fluorescence values for F were similar to CHX (P > 0.05) but were significantly different from CO (P <0.05). However, CHX values were similar to CO values (P > 0.05).	

Table 3: Characteristics of the included studies in arresting white spot lesions with fluoride varnish applications.

conventional oral hygiene and toothpaste regimen for remineralization of white spot lesions over a period of 8 weeks. In contrast, Stecksén-Blicks et al. [27], affirmed that regular applications of topical fluoride varnish can reduce the development of white spot lesions along the periphery of the bracket during treatment with orthodontics fixed appliances.

Therefore, fluoride varnish should be considered as a professional preventive measure in orthodontics practice.

Demito et al. [24], showed 32% more progression of demineralization in the control group than in the varnish group at six months; however, the differences were not statistically significant. Likewise, they affirmed that the greatest demineralization occurred in the gingival third [24,31].

One of the evaluated studies found that the incidence of WSL with fluoride varnish application during the treatment with orthodontics fixed appliances was 7.4%, while it was 25.3% ($p < 0.001$) in the placebo group, and the absolute risk reduction was 18%. The progression was significantly lower in the fluoride varnish group than in the placebo group, 0.8 +/- 2.0%. 2.6 +/- 2.8 ($p < 0.001$) [25]. Likewise, Perrini et al. [31], reported similar results, concluding that there was a greater tendency towards demineralization in the untreated vs. the treated teeth, although statistical analysis showed that the difference was not significant at any of the measurement times. Therefore, at 9 months of follow-up, the treated incisors showed significantly less demineralization than the previous non-varnished (untreated) teeth.

Assessment of the effectiveness of fluoride varnish to arrest white spot lesions: Four of the 10 studies [23,28-30], agreed that good oral hygiene associated with the use of fluoride toothpaste was able to remineralize white spot lesions and did not find statistically significant differences in the progress or detention of the lesions with fluoride varnish application compared to other techniques, suggesting that the use of fluoride varnish does not have superiority in the remineralization of white spot lesions in relation to oral hygiene reinforcement.

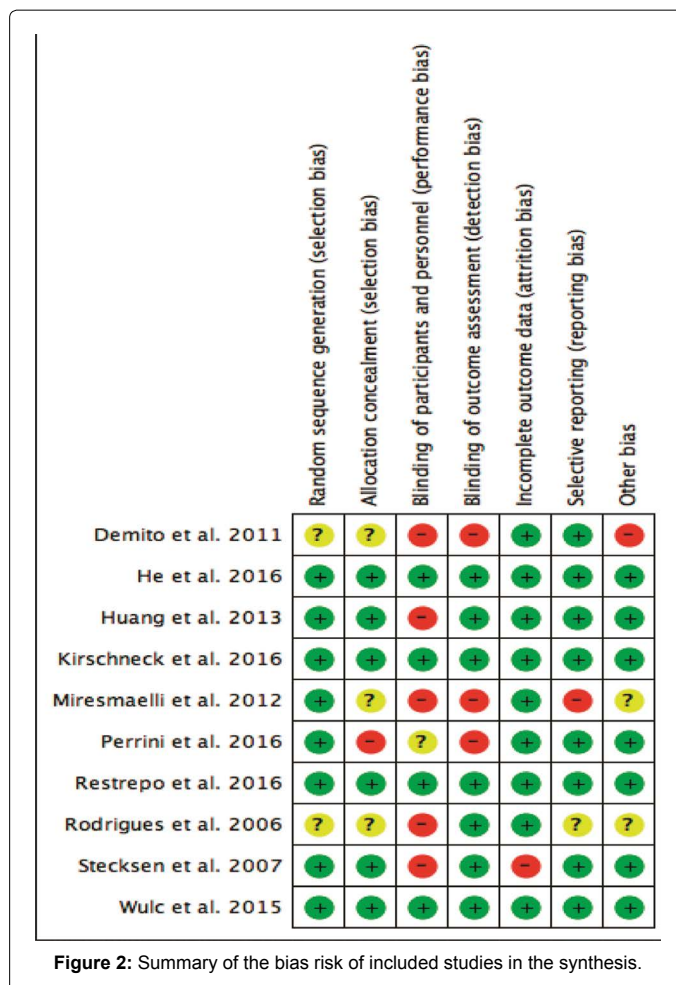


Figure 2: Summary of the bias risk of included studies in the synthesis.

Kirschneck reported that between the Elmex® fluid group, the Fluor Protector S group and the placebo group without fluoride, there was no significant difference in the measurements at any of the four evaluated times (T0 to T3). However, the mean ICDAS index significantly increased in the three groups during the course of the investigation (T0 to T3), and WSL and initial caries were significantly higher in the control group, which had only oral hygiene with fluoride toothpaste, and a placebo varnish [29].

Likewise, Miresmaeili et al. [28], showed good oral hygiene in both the fluoride varnished and the prophylaxis group, the mean lesion size in the test group was $8.3\% \pm 3.07$ before treatment, decreasing to $5.9\% \pm 2.9$ after treatment ($p=0.009$), and in the control group, the mean lesion size was $7.7\% \pm 4.2$ before treatment, decreasing to $5.9\% \pm 3.6$ after treatment ($p=0.001$); however, no statistically significant differences were detected between the groups ($p=0.307$).

In contrast, He et al. reported a significant decrease in white spot lesions in all groups after 6 months. The interaction between the group and time in the statistical analysis indicated that the values of the 3 groups followed different trends in time (varnish vs. control: estimate, -11.83; 95% CI: -15.39 to -8, 26, $p < 0.0001$, the fluoride vs. control film: estimation, -7.72, 95% CI, -11.34 to -4.10, $p < 0.0001$). It should also be noted that the authors emphasized the importance of explaining to patients and families about the risks of acquiring white spot lesions around the brackets during orthodontic treatment, taking into account oral hygiene care and the use of fluoride toothpastes.

Effectiveness of fluoride varnish application versus other therapies to prevent and arrest white spot lesions

Huang et al. did not find differences between the effectiveness of MI Paste Plus and PreviDent fluoride varnish compared to conventional oral hygiene and the use of toothpaste for the remineralization of white spots during a period of 8 weeks [22]. Steckslen-Blicks et al. stated that regular applications of topical fluoride varnish versus placebo may reduce the development of white spot lesions around the bracket during treatment with orthodontics fixed appliances, and then, the fluoride varnish can be used as a preventive measure as a professional routine in the practice of orthodontics [27].

Huang et al., noted that the improvements in white spot lesions evaluated by the expert panel were 29% MI Paste Plus, 31% Fluoride in PreviDent Varnish and 25% in the untreated group; however, there were no statistically significant differences. In contrast, Restrepo et al. reported that after 3 months, the 5% NaF varnish-F (Duraphat®) group, 2% chlorhexidine Gel and the saline-treated control group were able to control white spot lesions around the brackets. However, treatment with 5% NaF varnish was able to control the progression of the lesion in a shorter period of time [22,26].

Discussion

Summary of main findings

Overall, most of the included studies did not show significant advantages of fluoride varnish application in terms of preventing the development of white spots around orthodontic brackets when the patients were submitted to regular professional oral hygiene control.

Taking into account that the fluoride varnishes are made by different commercial manufacturers, the composition of the product can vary, mainly in the proportions of fluoride. However, the articles evaluated in this review presented the application protocols of fluoride varnish according to the criteria of each manufacturer.

Quality of evidence and potential biases and limitations in the review process

The studies included in this review showed differences in methodological quality, with greater control of bias in 6 of them [22,23,26-30] and 4 with moderate methodological quality [24,25,28,31]. Three studies used the same diagnostic method (Diagnodent). However, the evaluation scale to characterize the lesions had a different value. Likewise, other authors performed a photographic analysis of the lesions, but each one used different software and criteria to classify WSL. It is important to emphasize that none of the studies evaluated stated a conflict of interest [22,25,27,28].

Due to the heterogeneity of the measured parameters and the instruments used, an important methodological problem was generated for interpretation of the results, taking into account the variability of the measures used to determine white spot lesions. This allowed only the generation of qualitative analyses about the impact of fluoride varnishes on initial caries lesions.

According to the International Caries Classification and Management System (ICCMS), the time of fluoride varnish applications changes regarding the patient's level of risk for developing caries. Based on this, they recommend an average application of fluoride varnish twice a year in individuals with medium risk and 4 times a year in patients with high risk of development caries [32]. On the other hand, ICCMS mentions that for patients with a low risk of dental caries, it is not necessary to apply fluoride varnish, and only adequate oral hygiene is required, which agrees with the studies evaluated in this review. However, it is necessary to emphasize that this protocol is not standardized for patients with orthodontic appliances in which oral hygiene is more difficult to perform but is aimed at individuals in general.

The studies included in this systematic review used fluoride varnishes from different commercial manufacturers as follows: Bifluoride [33,34], PreviDent fluoride varnish, Elmex fluid, Duraphat, Fluor Protector S, 5% NaF Varnish-F [35-39]. However, the application methods were similar, since they were all applied on dry surfaces and were left to act on the dental surface as a biofilm without any kind of removal. Additionally, concentrations of fluoride levels varied from one to another as follows: Duraphat, PreviDent 5% and NaF Varnish-F have 22,600-ppm concentrations; while Fluor Protector S has a 7,700-ppm fluoride concentration, and ELMEX has a 1,200-ppm concentration, suggesting that these various concentrations of fluoride may directly influence the results obtained by the studies.

On the other hand, each varnish has a different coloring. In studies that used a placebo and a fluoride varnish with different pigments, such as Duraphat, the examiners could not be blinded, which could have generated biases in the measurements. Another difference between commercial manufacturers is the total amount of product contained in the bottle and the type of storage used; however, the authors did not report whether these characteristics influenced the results.

The included studies showed different diagnostic methods, making it difficult to associate and compare the results. Therefore, performing a meta-analysis was not possible. Additionally, finding articles with a high evidence level was complex.

Agreements and disagreements with other studies or reviews

It is important to emphasize that, so far, there are no specific systematic reviews of the studied subject. However, there have been

studies that evaluated the progression of white spot lesions with other prevention methods, even with fluoride varnish in combination with other materials such as chlorhexidine.

Øgaard B et al. evaluated the effectiveness of fluoride varnish in combination with an antimicrobial agent and compared it with only a fluoride varnish in the reduction of white spot lesions [16]. They found that a fluoride varnish combined with the antimicrobial agent reduced the levels of *Streptococcus* and other bacteria in the plaque during the first 48 hours, but for the reduction of white spot lesions, no statistically significant differences were observed between the two groups.

Benson PE et al., in their systematic review, evaluated the effects of fluoride on reducing the incidence of white spot lesions in teeth during orthodontic treatment, assessing several methods of prevention [39]. They found that the application of fluoride varnish every six weeks during orthodontic treatment was effective to prevent WSL. They concluded that more double-blind, randomized and controlled studies are necessary to determine the best way to prevent white spot lesions in patients undergoing orthodontic treatment, as well as the most accurate way of assessing compliance on treatment and possible adverse effects, which agreed with the results of this new systematic review.

The results found in this review were similar to those in the report by Baygin et al., in which they evaluated the effect of the chlorhexidine-thymol varnish, a fluoride varnish with chlorhexidine of toothpaste, the fluoride varnish in oral hygiene and the prevention of dental caries in patients with orthodontic applications [39]. The authors found that the use of Cervitec Plus or Cervitec gel, combined with the standard oral hygiene regimen, may be beneficial in orthodontic patients for maintenance of oral health by reducing bacterial colonization and gingivitis.

Based on the above, this review suggests that for future studies, the protocol for the application of fluoride varnish should be standardized, taking into account the periods of application for high risk individuals, such as patients with orthodontic appliances. Therefore, we recommend the parameters of ICCMS for the fluoride varnish application protocol in this type of patient (every three months for high risk patients).

In all but 4 studies included in this review, patients were aware that they were being evaluated, so a Hawthorne effect may be present, where patients were blinded. In addition, it can be inferred that patients were meticulously instructed to perform their oral hygiene routine, so the presence of plaque may have been lower. For unbiased results regarding the effectiveness of fluoride varnishes, the effects of fluoride should be studied with basic oral hygiene instructions that reflect the reality of the daily consultation [23,26,27,30].

Conclusions

Fluoride varnish seems to be an effective material to prevent and arrest white spot lesions in patients with orthodontic treatment who are at high risk of developing these lesions due to poor oral hygiene. However, neither statistical nor clinical advantages to fluoride varnish application in terms of preventing the development of white spots around orthodontic brackets could be identified when the patients followed a regular professional oral hygiene control routine.

Implications for practice and directions for future research

Professional guidance for oral hygiene is enough to prevent or arrest white spot lesions around brackets.

Future clinical trials should evaluate the effectiveness of a varnish

under true oral hygiene conditions so that it is possible to quantify the application of these materials and to develop a standardized protocol for the application of fluoride varnish for patients with orthodontic treatment.

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