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Microhardness Analysis After Remineralization Agents in Orthodontics: A Systematic Review

Alba Belanche Monterde[1*], Patricia Lasierra [2]and Javier Flores-Fraile[1]

[1]Department of Surgery, Faculty of Medicine and Dentistry, University of Salamanca, 37008 Salamanca, Spain
[2]Department of Medicine and Medical Specialties, Faculty of Health Sciences, University of Alcalá de Henares, 28801 Madrid, Spain

[*]**Corresponding author:** Alba Belanche Monterde, Department of Surgery, Faculty of Medicine and Dentistry, University of Salamanca, 37008 Salamanca, Spain

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Abstract

Background: Enamel microhardness can be reduced after orthodontic treatment caused by enamel demineralization. White spot lesions (WSLs) are prevalent after bracket debonding and its treatment is crucial for enhancing health and aesthetics. The aim of the systematic review is to compare microhardness changes in WSLs with different remineralizing compounds after bracket debonding.

Methods: An electronic database was performed in PubMed, Cochrane, WOS and Scopus. Initially a total of 223 in vivo and in vitro trials were obtained. After duplicates removal and title and abstract reading 65 were obtained for the screening. Finally, only 11 trials were included in the review.

Conclusion: CPP-ACP alone and combined with fluoride molecules are effectives in increasing microhardness of WSLs after brackets treatment.

Keywords: CPP-ACP, microhardness, white spot lesion, WSLs, orthodontics **Conclusion:** This report advocates for further exploration of conservative surgical options in treating OKCs, balancing efficacy with patient-centered outcomes.

Introduction

White spot lesions (WSLs) are common after orthodontic treatments and are the first step of caries development. If they are not treated it can lead with cavitation. In the current population WSLs are only 2% prevalent but in the orthodontic it is 49% prevalent. That is caused by the biofilm changes and the oral hygiene difficulty that orthodontics leads to. The oral biofilm produces acids that start to demineralize the enamel. The high amounts of Streptococcus Mutans (SM) showed a higher risk of caries development in the orthodontic patient. This does not seem to be dependent of the type of orthodontics and happen even on the aligner attachments. In order to avoid or reverse the demineralization some remineralizing agents are disposable. For example, the nano-hydroxyapatite agent is a synthetic material with crystals that avoid the demineralization process and resemblance the affected enamel [1, 2, 3]. Other agents used are amorphous calcium phosphate (CPP-ACP) and fluoride content varnish or adhesives. In addition, CPP-ACP combined with fluorides are used and have shown significantly better results than both agents alone [4]. Lingual multibracket appliances have been also recommended because they seem to have fewer incidences of WSLs [5]. However, the patient compliance on hygiene is an important factor to take into account in the prevention. In addition, the orthodontic adhesives are essen [6]. So remineralizing agents into the adhesive are also studied and used to prevent the caries lesion. Bioactive glass particles are included into the adhesive including silver, zinc and fluoride molecules. Other biomaterials included in the adhesive are mesoporous bioactive nanoparticles, ammonium bromide and calcium fluoride with di-methylamino hexadecyl methacrylate [6, 7, 8]. A recent meta-analysis has showed that theobromine is also an effective compound to avoid WSLs demineralization equivalent to fluorides [9, 10].

The aim of the present systematic review is too comprehensive analyze the current evidence in remineralizing agents to avoid white spot lesions after bracket debonding. As a secondary aim the microhardness values will be collected to compare the effect of the compound on the enamel after its application.

Methodology

Search strategy

The electronic search was conducted in four databases PubMed Medline (125 papers), Cochrane (85 papers), Scopus (11 papers) and Web of Sciences (2 papers) with the PICO question “Do the remineralizing agents affects to enamel microhardness after brackets debonding?” For searching the papers it was used the following strategy search “((brackets) OR (orthodontics) OR (braces)) AND (microhardness) AND ((remineralizing agents) OR (white spot lesions) OR (WSL))?” In the beginning, a total of 223 papers were found, only trials were selected. After eliminating duplicates 215 articles were screened and for the after reading the title a total of 65 were selected for abstract reading. In the end,

applying the inclusion and exclusion criteria a total of 18 were fully read and a total of 11 papers were included in the systematic review (Figure 1).

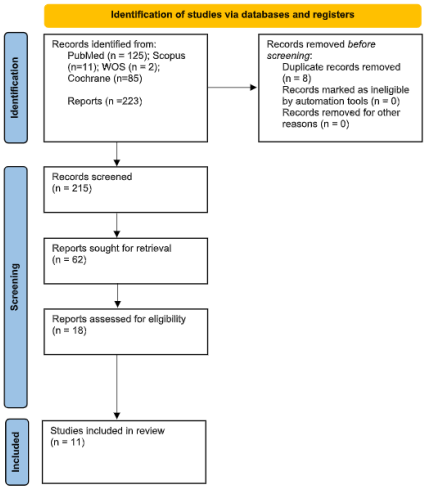

Figure 1: Identification of studies via databases and registers.

Inclusion and exclusion criteria

The systematic review was performed taking into account previously selected by the three authors' inclusion and exclusion criteria. The exclusion criteria were articles performed in animals, systematic reviews and metanalisis, experimental biochemical issues, paper in which the remineralizing agent was used in a common caries lesion for restorative, papers which do not evaluate bracket demineralization and pediatric patient evaluations. The inclusion criteria were clinical and in vitro trials, which brackets were bonded and debonded, which white spot lesions happened or simulated and which compared different remineralizing agents for WSLs.

Analysis of results

The 11 trials included in the systematic review were selected for two authors (J.F-F and A.B.M) separately and after that it were selected in common. The data of these articles was summarized in Table 1 [11-21]. In Table 1.

Author/year	Study type	n treatment	Remineralization compound	Follow-up	Outcomes	Measurement methodology	Variables analysed
Agha N., 2024 (12)	In vitro study	11	CPP-ACP	1 month	Sesamum indicum oil 5% ($p<0.05$) higest values	SEM	Microhardness
		11	Sesamum indicium oil 5%				
		11	Sesamum indicum oil 10%				
Pavethynath V., 2024 (13)	RCT	25	CPP-ACP	3 months	All groups showed improvements ($p<0.05$).	Microhardness tester	Microhardness
		25	Calcium phosphate				
		25	Fluoride varnish				
Ding L., 2024 (14)	RCT	54	CPP-ACP	6 months	Resin infiltration significantly decreased enamel porosity ($p<0.05$)	SEM	Color and fluorescence parameters and microhardness
		54	Fluoride varnish				
		54	Infiltrating resin				
Senthilkumar I., 2024 (15)	In vitro study	10	Fluoride adhesive	28 days	Fluoride+CPP-ACP significantly ($p>0.001$) got higer hardness values.	Microhardness test	Shear bond strength (SBS), microhardness, adhesive remnant index (ARI)
		10	CPP-ACP				
		10	Fluoride adhesive and CPP-ACP				
Chevitarese AB., 2023 (16)	Controlled clinical trial	20	Aqueous 4% TiF4 solution	1 month	Microhardness was higer ($p<0.05$) in the treatment group.	Microhardness test, SEM	Microhardness, fluoride uptake, enamel layer analysis
Ghaly YS., 2023 (17)	In vitro study	20	SAP (P_{114})	2 months	SAP (P_{114}) got the best	Microhardness test	Surface microhardness, Ca/P
		20	CPP-ACP				

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		20	Fluoride varnish		remineralizing effect.		ratio
Rangarajan S., 2022 (18)	n-RCT	15	CPP-ACP	28 days	CPP-ACP showed better results in the cervical area.	Private laboratory analysis	Surface microhardness
		15	5% NaF varnish				
Pourhajibagher M., 2021 (19)	In vitro study	nAv	Zeo/ZnONPs	3 months	Greatest remineralization and anti-biofilm efficacy.	TEM image, laboratory analysis	Citotoxycity, biofilm evaluation, hemolysis effect, anti-metabolic activity
Nalawade VA, 2021 (20)	In vitro study	20	Sensitive toothpaste	15 days	The three treatment improve the microhardness.	SEM	Microhardness
		20	Amflor				
		20	Enafix				
Uy E., 2019 (21)	In vitro study	17	Funcionalized tricalcium poshosphate	nAv	CPP-ACP obtained a significant remineralization	Thermocycling	Shear bond strength
		17	CPP-ACP				
Nam HJ., 2019 (22)	In vitro study	nAv	Graphite Fluoride BAG (FGtBAG)	nAv	Resins containing have antibacterial and remineralization efficacy.	Fluorine dissolution test, remineralization test, antibacterial test, Instron machine.	Antibacteria capability, shear bond strength

nAv: not available, nRCT: not randomized clinical trial, RCT: randomized clinical trial, CPP-ACP: casein phosphopeptide-amorphous calcium phosphate, SEM: electron microscopy scanning, SAP: self-assembling peptide, NaF: sodium fluoride, Zeo/ZnONPs: zinc oxide nanoparticles, TEM: trassmision electron microscopy.

Table 1: Charasteristics of the studies included in the systematic review including the remineralizing agents, results, methodology and variables analyzed.

It was collected the n treatment of each group of study in which a remineralizing agent was used for WSL treatment and the type of agent used for that. In addition, it was collected the methodology of measuring and the variables analyzed in each paper. The type of trial was also showed to better understanding the final approach of the results.

Analysis of biases

The risk of biases was evaluated by the JADAD scale (Table 2).

	JADAD CRITERIA					
Author/Year	Is the Study Described as Randomized?	Is the Study Described as Double-Blinded?	Was There a Description of Withdrawals and Dropouts?	Was the Method of Randomizatio n Adequate?	Was the Method of Blinding Appropriate?	Score
Agha N. et al, 2024 (11)	NA	NA	NA	NA	NA	0
Pavetgtnath V. et al, 2024 (12)	1	0	1	1	0	3
Ding L. et al, 2024 (13)	1	0	1	1	0	3
Senthilkumar I. et al, 2024 (14)	NA	NA	NA	NA	NA	0
Chevitarese AB. et al, 2023 (15)	0	1	1	0	0	2
Ghaly YS. et al, 2023 (16)	NA	NA	NA	NA	NA	0
Rangarajan S. et al., 2022 (17)	0	1	1	0	0	2
Pourhajibagher M. et al., 2021 (18)	NA	NA	NA	NA	NA	0
Nalawade VA et al., 2021 (19)	NA	NA	NA	NA	NA	0
Uy E. et al. , 2019 (20)	NA	NA	NA	NA	NA	0
Nam HJ. et al., 2019 (21)	NA	NA	NA	NA	NA	0

NA: Not applicable.

Table 2. Assessment of methodological quality according to the Jadad scale.

The evidence is low and moderate quality. The majority of the trials are performed in vitro [11,14,16,18, 19-21]. but some of them were in vivo trials [12, 13, 15, 17]. Only two of the clinical trials were randomized [12, 13. and it were correctly randomized showing moderate quality assessment. The non randomized clinical trials even being blinded obtained low quality assessment with a 2 score in the JADAD scale. The articles of Ding L. et al. and Pavetgynath et al. obtained the highest score with 3 points in the JADAD [12,13].

Results

Sample size

The sample size variable between the trial. The randomized clinical trials had higher sample sized [12, 13]. The sample of each study groups was ranged from10 to 54. Some articles used 20 for study group as sample size [15, 16, 19]. Other in vitro trial selected 17 [20]. other clinical trial 15 [17]. and two in vitro trials 11 [11] and 10 [14] as sample size. The randomized clinical trials selected 25 [12] and 54 [13] for each study group. The study of Ding L. also is the study in which more sample is included.

Remineralizing agents used to WSLs after bracket debonding

The remineralizing effectiveness of the compounds was evaluated by the microhardness evaluation. This variable was measured before and after the agent use on the white spot lesion [12, 14, 15, 16]. In addition, the antibacterial capability and the shear bond strength was measured and compared between the study groups [18, 20, 21]. Citotoxycity was also an important factor because of the high importance of biocompability dental compounds needs to have [18]. Another variable but less important in remineralizing WSL is the adhesive remnant index (ARI). This visual index is commonly used when studying polishing after bracket debonding [11]. The majority of the articles used CPP-ACP as a treatment group [11, 12, 13, 14, 16, 17, 20]. CPP-ACP showed statistically better results when compared with fluoride varnishes (17 and 20). But this result remains controversial. Other articles showed that Fluoride+CPP-ACP is better in microhardness values than CPP-ACP alone ($p>0.001$) [14]. The fluoride varnish might not be highly recommended to obtain high microhardness in WSL because in the greatest number of trials another compound got better outcomes [11, 13, 17]. Whereas, one trial did not find statistical differences between groups and also fluoride varnish increased microhardness [12]. In addition, resin infiltration showed higher microhardness and was recommended to WSL treatment [21].

Microhardness differences between agents

The microhardness after the remineralizing agent use was measured in all the studies recorded but three [18, 20, 21]. The methodology of measuring was variable but the most used machine was the microhardness tester [12, 14, 15, 16]. The microhardness tester was found with different names in the trials but all of them have the same measuring protocol so the values obtained are comparable between each other. In addition, scanning electron microscopy was also used to evaluate the enamel microhardness before and after the agent usage [11, 13, 15, 19]. The digital approach that SEM allows seems a good methodology for the issue as it also allows to evaluate the anatomical changes produced on the enamel by image. Another image test that was used in an in vitro trial was the trassmision electron microscopy [18].

Novel approaches

Other and less used compounds are currently being studied to remineralizing WSLs. For example, Graphite Fluoride BAG (FGtBAG) has been used into the infiltration resins showing good outcomes [21]. In addition, for reducing biofilm accumulation Zeo/ZnONPs and to obtain a better calcium phosphate rates SAP (P11-4) were used (16 and 18). SAP (P11-4) obtained the highest values of microhardness compared to CPP-ACP and fluoride varnish measured by the microhardness tester [16]. The most novel compound which was used as remineralizing agent is sesamum indicium oil. Sesamum indicium oil 5%

was compared with CPP-ACP measuring microhardness and showed the highest microhardness values ($p<0.05$) in SEM analysis [11]. More trials are needed to obtain more quality results about these novel compounds that can enhance microhardness. The application in vivo of these agents might be incredible important in the demineralization of white spot lesions.

Discussion

The systematic review showed that CPP-ACP is recommended to remineralizate white spot lesions created after the bracket debonding. As the interfase adhesive-composite-mesh is the weakest part for biofilm retention, novel compound which can be included in the adhesive were studied showing good outcomes. Also, CPP-ACP combined with fluorides was recommended obtained significantly higher microhardness than CPP-ACP and fluoride varnishes alone. Enamel microhardness was evaluated by the microhardness tester and the scanning microscopy electron. Both methodologies were correct to evaluate this variable before and after the compound usage.

White spot lesions are an orthodontic side effect consequent to an imbalance between minerals loss and gain which causes demineralization of the enamel. The 4th week of treatment WSLs might be visible and should be correctly treated because they can affect the oral health and aesthetics. Probiotics during this period were used to avoid gastro-intestinal imbalances and reduce the Streptococcus amounts [22, 23]. Probiotic also showed to reduce halitosis and traumatic lesions during the initial phase of orthodontics. A recent meta-analysis suggests its ability in WSLs reduce [22]. WSLs are more frequent in central incisors ranging from 27 to 97%. They are also more frequent in in growing patients because of their lower compliance (11 to 15 years old) but it is also high in 20 years old patients because of they might need longer treatments.

It was shown that the applications of fluoride varnish each 2 or 3 months significantly decreases the WSL development and the fluoride toothpaste is recommended to avoid it [23]. But the concern about fluorides excess exists. High values of fluorides typically lead to fluorosis and other authors did not recommend the very frequent usage [24]. Moreover, it has been controversial which orthodontic appliance allows to reduce the WSL incidence. Clear aligners were recommended because less plaque retention was observed in the aligner patients. However, these results are controversial because clear aligner patients are normally more aged than bracket patients so risk of biases could exist in this kind of papers [25].

Novel compounds were used to avoid WSLs cavitation trying to reestablish the enamel structure to the previous situation. Silver diamine fluoride (SDF) 38% was evaluated in caviated lesions in primary molars showing to be effective for its detention [26, 27, 28]. SDF was effective for primary caries treatment in a 12 months follow-up and allowed to reduce the number of clinical appointments. SDM showed better results when compared with a common restorative material [28]. This compound might be interesting to future researches of WSL. A high number of orthodontic patients are kids and primary teeth are sometimes included in the treatment [29]. However, in the present systematic review this compound was not used in orthodontic WSL. But another novel compound was contrasted as self-assembling peptides or graphite fluoride BAG on resin infiltration showing an interesting future for the WSLs treatment [16, 20].

Conclusion

The CPP-ACP compound showed effectiveness in WSLs reduction and in microhardness increase. CPP-ACP combined with fluorides obtained good outcomes. Also, novel remineralizing compound included in the orthodontic adhesive are interesting for future researches.

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