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White Spot Lesions in Orthodontics: A Contemporary Review on Detection and Remineralization Strategies

Dr. Bharti Vyas*; Dr. Ramkishore Ratre; Dr. Sandhya Jain; Dr. Vijay Bhan Singh; Dr. U R Neelima; Dr. Yojna Atram

Department of Orthodontics and Dentofacial Orthopedics
Government College of Dentistry, Indore, Madhya Pradesh,
India.

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Abstract: White spot lesions (WSLs) represent subsurface demineralization of enamel which possess a significant challenge in orthodontics due to their prevalence and potential to progress. The recent studies from past decade were searched in electronic databases including Pubmed, Scopus and google scholar involving white spot lesions and effect of orthodontic treatment. The review evaluates the current state of knowledge regarding the etiology, diagnosis, and management of WSLs, with a specific focus on remineralizing agents. Diagnostic modalities are discussed in the context of their utility for early detection and monitoring of WSLs. Remineralization therapies utilizing fluoride, calcium phosphate-based compounds like anticay, casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) complexes, and bioactive glasses, are reviewed for their efficacy in promoting remineralization and inhibiting demineralization. Furthermore, clinical studies evaluating the effectiveness of remineralization therapies are critically analyzed, with an emphasis on their outcomes in terms of lesion remineralization, surface hardness, and long-term stability of remineralized tissues. Additionally, novel approaches, including nanotechnology-based delivery systems and biomimetic strategies, are highlighted as avenues for future research and development.

Keywords: *White Spot Lesions, Orthodontic Treatment, Enamel Dimineralization.*

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I. INTRODUCTION

Orthodontic procedures have been increasingly popular. However, the esthetic result of therapy is negatively impacted by side effects like white spot lesions (WSLs). Clinically, white, chalky patches are the first signs which may progress into dental caries and the development of a niche for bacterial plaque. Although a significant amount of mineral ion in hydroxyapatite crystals can be lost without impairing their structural integrity, the individuals develop sensitivity to temperature, pressure and chemicals. Nonetheless, the literature has inconsistent results about the relationship between orthodontics and the development of WSLs. Consequently, the review's objective is to evaluate recent research and literature to draw conclusions about a relationship between white spot lesions and the various strategies used to prevent or mitigate their progression

II. INCIDENCE

The prevalence in various studies has been reported to be variable with a wide range of 33.8% as reported by Geiger et al. to 97% as reported by Boersma et al. contingent on the method/criteria of analysis selected and whether the reference unit (surface, tooth, or patient) includes pre-existing enamel lesions or not [1,2]. According to Chapman et al. the order of incidence was lateral incisor (34%), canine (31%), premolar (28%), and central incisor (17%)[3]. When it comes to orthodontic treatments, these enamel lesions develop gradually and become irreversible

III. ETIOLOGY

New retentive regions created by orthodontic appliances, particularly brackets, ligatures, arches and adhesive remnants have the unintended consequence of causing plaque accumulation harboring cariogenic bacteria [4]. The cariogenic bacteria including Streptococcus mutans and Lactobacillus species are known to be part of the microbiome

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associated with WSLs. Actinomyces and Corynebacterium have also been linked to be involved in the early stages of caries

IV. METHODS OF DETECTION OF WHITE SPOT LESIONS

- Visual Inspection: Visual inspection is the first method to identify lesions with white spots. To check for surface defects, the teeth must be air dried for at least five seconds after cleaning with pumice and later be visually inspected. Various assessment scales have been devised till date, recent is the International Caries detection and Assessment System II ICDAS-II 2005 [5].
- Photographic examination: Intraoral photographs recorded pretreatment and post treatment changes can be a useful aid in comparison of the incidence of the WSLs occurring post-treatment. Teeth are assessed in proper axial position i.e. occlusal plane must be parallel to the horizontal plane [6]. Followed by assessment of frontal and lateral photographs using Gorelick Index scoring criteria. However, this method can't be beneficial in terms of quantifying the depth of lesions [7].
- Radiography: White spot lesions can be assessed with radiography for the extent and intensity, particularly if they are situated below the margin of the gingiva or in interproximal region.
- Electrical Impedance Spectroscopy (EIS): EIS is a non-invasive technique that measures the tooth's impedance by applying a little electric current.
- Fluorescence: As demineralization activity rises, tooth tissue's autofluorescence falls. Protoporphyrin, a photosensitive pigment produced by bacterial metabolic processes and found in demineralized tooth tissues, may be the cause of this [8].
- Certain instance include: multiphoton imaging, laser fluorescence (LF), quantitative light-induced fluorescence (QLF), near-infrared digital imaging transillumination (NIDIT), and fiber-optic transillumination (FOTI).

V. REMINERALIZING AGENTS

Numerous materials have been studied for their potential of remineralization of enamel. Below enlisted are those showing to have an effect on reducing the demineralization or to enhance remineralization potential of the dental enamel, hence, proven to be efficacious for white spot lesions (Table *1*).

Table 1: Remineralizing Agents

A. Studies Employing Fluoride in form of Paste, Varnishes and Oral Rinses.

Since, the carrier form of delivery of remineralizing agent plays an important aspect, further studies were evaluated to understand the effect of fluoride in various forms and how substantivity can add in reduction of demineralization at enamel level (Table *2*).

Studies have shown that higher concentration of fluoride in paste and varnishes have resulted in reduction of white spot lesions. Sonesson et al. evaluated the efficacy of fluoride toothpaste to find reduced white spot lesions with prevented fraction of 32% [18]. However, comparison of paste, varnish and rinse indicated more efficacy of varnish over the use of paste or rinse, reason aimed to substantivity.

Table 1: Remineralizing Agents

Fluoride
Non- Fluoride remineralization agents:
Amorphous calcium phosphate (ACP)
Casein Phosphopeptide- Amorphous Calcium phosphate (CPP- ACP)[9]
Alpha tricalcium phosphate(α-TCP) & Beta- tricalcium phosphate (β-TCP)
Sodium calcium phosphosilicate (Bioactive glass; BAG)
Dicalcium phosphate dihydrate (DCPD)
Calcium sucrose phosphate (Anti-Cay) [10,11]
Nanoparticles for remineralization:
Calcium fluoride nanoparticles
Calcium phosphate-based nanomaterials
Nano-HAP particles
ACP nanoparticles
Nanobioactive glass materials
Biomimetic Agents
Polydopamine
Polyamidoamine[12]
Oligopeptides
Theobromine[13]
Arginine [14]
Self-assembling peptides (P11-4)[15]
Methods:
Low level laser therapy
Microabrasion[16,17]
Resin infiltration method[17]

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Table 2: Studies Employing Fluoride in form of Paste, Varnishes and Oral Rinses.

RCT: Randomized controlled trial; ppm: parts per million; MIPP: Minimally invasive paste plus; MIV: Minimally invasive varnish; ICDAS: International caries detection and assessment system; WSL: white spot lesions; NaF: Sodium fluoride; CHX: Chlorhexidine; QLF: Quantitative light induced fluorescence; RMGIC: Resin modified glass ionomer cement; CPP-ACP: Casein Phosphopeptide-Amorphous Calcium Phosphate.

B. Studies Associated with Etching Time of the Enamel Surface

Orthodontic bonding of the bracket involves etching of enamel surface for mechanical interlocking of the adhesive with the created surface roughness. However, the etching time can be questionable between 15 seconds to 30 seconds. To reach to a consensus regarding the effect of etching, several studies were referred to reach to a conclusion that partial etching is favorable in terms of nonseparation of brackets and doesn't increase the susceptibility for demineralization in short term with no significant difference in long term [25].

C. Studies Involving Effect of Modification in Resin Adhesive/ Varnish on WSLs

Fixed orthodontic brackets offer the most retentive niche for bacterial plaque, due to the rough surface structure of the adhesive materials. Multiple remineralizing agents have been incorporated with the resin adhesives as a means to reduce the demineralization, further reducing the incidence of White spot lesions (Table *3*). The study by Kim et al. took bioactive glass as an additive to the resin adhesive and concluded BAG-containing dentin adhesive decreased the permeability of demineralized dentin via its remineralization potential while maintaining bond strength to dentin [26]. Study by Xie et al. concluded the effect of tricalcium phosphate-based drugs and fluoride is not very conclusive. Overall, self-assembling peptide (P11-4) based drugs and resin infiltration will be effective therapies [27].

Table 2: Studies Employing Fluoride in form of Paste, Varnishes and Oral Rinses.

Author	Study design	Intervention	Control group	Assessment method	Results/ Outcomes
Rechmann et al. 2018 [19]	Prospective Randomized control trial (RCT)	1100 ppm fluoride toothpaste twice daily, MIPP daily and MI Varnish quarterly.	1100 ppm fluoride toothpaste twice daily and fluoride rinse	Evaluation of Enamel decalcification index and ICDAS assessment.	Fluoride reduces WSLs incidence in the experimental group. Daily MIPP and MIV doesn't appear to reduce significantly WSLs.
Restrepo et al. 2016[20]	RCT	Group 1- 5% NaF Varnish Group 2- 2% CHX gel	Home Care	DIAGNOdent pen	Fluoride induced faster remineralization than CHX
Van der Kaaij et al. 2015[21]	RCT	NaF and amine fluoride combination rinse	Placebo rinse	QLF	In the fluoride group, 31% of participants developed at least one demineralization, compared with 47% in the placebo group.
Jena et al. 2015[22]	RCT- Split mouth study	RMGIC varnish	No varnish application	DIAGNOdent and visual inspection	RMGIC varnish seem favourable in prevention of WSLs
Yetkiner A et al. 2014[23]		CPP-ACP	Fluoride toothpaste	Laser fluorescence+ visual	Statistically significant
Du et al. 2012[24]		Fluoride varnish	Saline	Laser fluorescence	Statistically significant in intervention group.

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Table 3: Studies Involving Effect of Modification in Resin Adhesive/Varnishs on WSLs

TiF4: Titanium tetrafluoride; Ti: Titanium; ICDAS: International caries detection and assessment system; HAC:

Nanohydroxyapatite with chitosan; SP-HA: Hydroxyapatite with self-assembling peptide; Ca: Calcium; P: phosphorus; SEM-EDAX: Scanning electron microscopy and energy dispersion X-ray spectroscopy; NACP: nanoparticles of amorphous calcium phosphate; SN15: salivary statherin protein; PAMAM: Polyamidoamine dendrimer.

D. Studies Employing Additional Methods

Microabrasion, resin infiltration, low level laser therapy and photodynamic therapy have been studied for their effect on White spot lesion reduction (Table *4*). Studies utilizing the therapies like resin infiltration and microabrasion have reached a similar conclusion that both the procedures are effective in reducing the WSLs with former being more effective than latter [31]. Gomez et al. did research involving the introduction of photodynamic therapy in comparison to ultrasonic cleaning to find delay in undesired side effects and less caries risk associated with photodynamic effect [32]..

Table 3: Studies Involving Effect of Modification in Resin Adhesive/Varnishs on WSLs

Author	**Study design**	**Intervention**	**Control group**	**Assessment method**	**Results/ Outcomes**
Chevitarese A B et al. 2023[28]	Controlled clinical trial	Aqueous 4% TiF_4 solution application	No treatment	Microhardness testing. Ion chromatography for fluoride uptake	Enamel microhardness and fluoride uptake were higher in intervention group, while the Ti layer could be seen over teeth that received TiF4 application.
Gohar et al. 2022[15]	Randomized control trial	Self-assembling peptide	Varnish containing 22.600 fluoride ppm and tricalcium phosphate	DIAGNOdent, Laser fluorescence and ICDAS scoring	Self-assembling peptides reveal higher performance in subsurface remineralization than the fluoride-based varnish material
Rangappa et al. 2022[29]	In- Vitro Study	Group 1-HAC, Group 2- SP-HA	Control group	Mineral content (Ca, P) and surface morphology using SEM-EDAX	All restored the mineral content to the baseline levels with more favorable surface morphologic results in the HAC group.
Gao et al. 2020[12]	In- Vitro Study	Group 1-Enamel with NACP, Group 2- Enamel with [SN15-PAMAM], Group 3- Enamel with SN15-PAMAM + [NACP]	Enamel control- no intervention	Surface examination and hardness testing	SN15-PAMAM + NACP adhesive method could achieve 90% higher enamel remineralization of the artificial caries than the control under acid challenge
Alabdullah et al. 2017 [30]	RCT 12 months	Fluoride containing adhesive resin	Non-Fluoride containing adhesive resin	Visual examination, DIAGNOdent pen	The fluoride containing resin do not have a desirable preventive effect to prevent demineralization.

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Table 4: Studies Employing Additional Methods

RI: Resin infiltration method; MA: Microabrasion; CPP-ACP: Casein Phosphopeptide-Amorphous Calcium Phosphate; ICDAS-II: Internal caries detection and assessment system II; ΔE: color change.

E. Studies of Various Orthodontic Treatment: Fixed vs. Removable Appliance System.

Due primarily to their esthetic qualities, the introduction of clear aligners system is regarded as innovative in the field of orthodontics. In order to examine the connection of demineralization followed by fixed orthodontic therapy and an aligner (CA-clear aligner), Studies have been conducted to observe demineralization in both groups treated with a removable or fixed appliance with higher incidence in the fixed appliance [34]. The key distinction was the development of multiple new WSLs with a greater depth but a smaller surface size in the fixed appliance group attributed by high levels of plaque index, compared to bigger but less developed lesions in the CA group [35].

Knösel M et al. in the study revealed that individuals treated with the lingual fixed appliance experienced fewer WSLs overall than those treated with conventional labial fixed appliances [36].

F. Studies of Various Orthodontic Treatment Modalities and WSLs

Orthodontic treatment utilizing Rapid Maxillary Expansion (RME) have shown to promote demineralization. Considering the luting cements, demineralizing potential has been studied to conclude that compomer cements have lower enamel decalcifying effect followed by glass ionomer cement and polycarboxylate to the lower end on the preference [37]. Bonding technique has also been studied as a factor to find indirect bonding technique contributes to lesser degree of WSL formation, which can be attributed to lesser adhesive remnants around the brackets [38].

Table 4: Studies Employing Additional Methods

Author	Study design	Intervention	Control group	Assessment method	Results/ Outcomes
Puleio et al. 2022[31]	Systematic review	RI therapy	Remineralisation and MA therapy	-	RI therapy to be most effective and predictable.
Simon et al. 2022[33]	RCT	RI	CPP-ACP	Spectrophoto-metry, ICDAS-II scoring	There was significant reduction in lesion area, and improvement in color of white spot lesions with both of the treatment modalities.
ShanD et al. 2021[16]	RCT	Group 1: RI therapy Group 2: MA	No treatment	Integrated optical density	The highest ΔE improvement was obtained by RI, but there was no significant difference between MA and control group
Gu Xi et al. 2019 [17]	Split mouth, RCT	Group 1: RI therapy Group 2: MA	-	Lesion area ratio (R value) on standardized clinical photographs. ΔE of each tooth measured with a Crystal eye spectrophotometer	RI and MA (RI>>MA) improved the esthetic appearance of WSLs and showed sufficient durability for 12 months.
Gomez et al. 2018[32]	RCT	Prophylactic method: Photodynamic therapy	Prophylactic method: Ultrasonic scaling	ICDAS and Periodontal assessment	Both the procedures delayed undesired side effects and exhibit low caries risk.

G. Studies of Ligating Techniques and WSLS Formation

In order to determine the correlation between the type of ligature material utilized and the quantity of plaque and pathogenic bacteria accumulation around the orthodontic appliances, studies have been conducted to conclude the self-ligating brackets and conventional elastomeric ligation has no difference in plaque retention and WSLs but contrary to it, study by Buck et al. concluded self-ligating appliances promote less retention of oral bacteria [39].

VI. DISCUSSION

The review's findings show that WSLs are still a major issue after receiving orthodontic treatment. Upon assessment of all the available articles and comparison, it was concluded that the clinicians face challenges in detecting enamel defects during orthodontic treatment. To identify the occurrence, extent and intensity of WSLs, it is needful to adjunct the simple visual examination with QLF or other newer florescence-based techniques.

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Despite the limitations of this review resulting from the use of different diagnostic and monitoring methods, non-standardization of assessment methods, and small patient numbers in some studies, a recent systematic review indicated no differences in the therapeutic approach for the treatment of WSLs, regardless of the type of diagnosis used [40].

Fluoride has historically been the gold standard but newer remineralizing techniques based on the integration of calcium and phosphates at the level of demineralized tooth surfaces have been developed recently. One of the systems to be identified is hydroxyapatite, which is employed in a novel biomimetic technique that seeks to fully integrate with the enamel structure. Conversely, fluoride lacquer or varnish pre-orthodontic treatment results in reduced bond strengths, which is probably going to cause a higher frequency of premature bracket separation.

Biomimetic remineralizing agents, including self-assembling peptides like P11-4, and amelogenins, chitosan, polyamidoamine (PAMAM) dendrimers, gel methyl-methacrylate, offer promising solutions for managing white spot lesions. Chitosan, a biopolymer derived from chitin, aids in remineralization by binding calcium ions and facilitating their incorporation into enamel. PAMAM dendrimers enhance the delivery and stabilization of calcium phosphate compounds, promoting effective mineral deposition [41]. Gel methyl-methacrylate serves as a matrix material for delivering remineralizing agents and supporting hydroxyapatite crystal formation. Self-assembling peptides, such as P11-4, mimic the natural enamel matrix proteins and self-organize into nanofibers that guide the remineralization process by providing a scaffold for mineral deposition. Amelogenins, natural enamel matrix proteins, holds an essential role in the formation and mineralization of enamel by promoting the organization of hydroxyapatite crystals.

Recent research, suggests resin infiltration and micro-abrasion procedures can both reduce the diameters of WSLs with comparable effectiveness, but resin infiltration has a better esthetic result. A systematic review by Karad et al. reviewing in-vitro studies showed Calcium sucrose phosphate (CaSP) to be a better remineralizing agent in comparison to casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) [11]. Concerning the enhancement of enamel's microhardness, casein phosphopeptide-amorphous calcium phosphate with fluoride (CPP-ACPF) and other remineralizing agents are effective. Furthermore, it was observed that the administration of CaSP was advantageous in restoring the color of the lesions with white spots to that of healthy enamel. Several sessions are typically required for WSL therapy, and recollection intervals should be modified to account for evaluation of preventive measures, observation of early lesions, and potential instruction in improving the patient's behavioral and oral hygiene.

The literature reports that the severity of WSLs corresponds with the length of treatment, and comparison studies have clinical significance only when they are carried out within the same orthodontic treatment time. Despite the relatively modest number of publications covered, the implications for the discipline are noteworthy because they bring a sophisticated systematization of the data found in the literature.

VII. CONCLUSION

Remineralization represents a promising approach for managing WSLs, offering a conservative and minimally invasive alternative to traditional restorative techniques. Biomimetic agents offer a multifaceted approach to restoring the mineral content and structural integrity of enamel, providing a non-invasive means to address and reverse white spot lesions. Continued research efforts aimed at refining remineralizing agents and elucidating their mechanisms of action, with in-vivo research are crucial for advancing the field and improving patient outcomes in preventive dentistry.

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