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Management of White Spot Lesions

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Abstract

It has been reported that white spot lesions (WSLs) can be seen as a result of prolonged plaque accumulation on the affected surface of the teeth. They are more often associated with fixed orthodontic treatment and defined as “the presence of clinically detectable, localized areas of enamel demineralization.” These lesions are managed in the first step by establishing a good oral hygiene to enhance remineralization, and prophylaxis with products mostly containing fluoride, calcium, or phosphate. The aim of this chapter is to outline the risk factors and preventive measures of WSLs, and the currently used methods to manage it based on the latest evidence.

Keywords: white spot lesions, etiology, diagnosis, remineralization, fluoride

1. Introduction

White spot lesions (WSLs), defined as “white opacity,” occur as a result of subsurface enamel demineralization that is located on smooth surfaces of teeth [1].

The reason of the white appearance is the changes in light-scattering optical properties of the decalcified enamel [2]. Various risk factors such as acid-producing bacteria, fermentable carbohydrates, and many host factors, such as poor oral hygiene, low salivary volume, and a sugary diet, further the development of these incipient lesions [3].

A review of the literature has shown that WSLs develop as a result of prolonged “undisturbed” plaque accumulation on the affected teeth surface, commonly due to inadequate oral hygiene [4–9]. Under these conditions, acids diffuse into the enamel and the demineralization continues in the subsurface enamel, then the intact enamel surface collapses and becomes cavitated [10]. It has been shown that these lesions can appear within 4 weeks [11].
The concept of caries process was explained with a model; it was initiated by fluctuations in pH caused by the bacteria that are always metabolically active in the biofilm or dental plaque. These fluctuations may cause erratic loss and gain of mineral (“demineralization” and “remineralization”) [12]. As a total result of these continuous demineralization and remineralization processes of enamel that occur episodically based on the presence of cariogenic bacteria in dental plaque and the availability of refined carbohydrates for fermentation to organic acids [13], dissolution of the dental hard tissues develops and a caries lesion forms [14].

In the first stage of the enamel defect there is a lower mineral distribution and also a lower interprismatic mineral content in the surface layer [15]. It has been proposed that further dissolution of the outer 10–30 microns of enamel is prevented relatively by several metabolic formations. The protective roles of salivary proline-rich proteins and other salivary inhibitors like statherin have also been emphasized [16]. But they cannot penetrate the deeper parts of the enamel due to their macromolecule structures; so their stabilizing role is limited for the surface enamel [17]. The white-spot lesion’s shape is determined by the distribution pattern of the biofilm and the direction of the enamel prisms [18].

The presence of fixed orthodontic appliances causes an increasing number of plaque retention sites as a result of the presence of brackets, bands, wires, and other applications, which makes the cleaning of teeth more difficult [4, 5, 7, 9, 10, 19–22].

When the orthodontic bands are removed and the feasibility of tooth cleaning is provided, it results a reduced porosity of the deeper parts of lesions (Figure 1). The return of fluids to supersaturation condition causes a shift in equilibrium and reprecipitation of minerals at the sites of demineralization. As a result of this, the surface of the lesion may become hard and shiny, and then the white spot becomes less obvious, but some interior opacity remains [23].

It is important to understand how these lesions develop and what the risk factors are. Because it is a great challenge to make an early detection of WSL that would allow clinicians to apply preventive measures to control the demineralization process before lesions progress.

The aim of this chapter is to outline the risk factors and preventive measures of WSLs, and the currently used methods to manage them based on the latest evidence.

Figure 1. White spot lesions after completion of fixed appliance orthodontic treatment.
2. Prevalence

The prevalence of WSLs varies widely in the literature. It ranges from 23 to 95% when different evaluation methods and criteria are used [5, 20, 24–28].

Mizrahi [29] examined 527 patients before and 269 patients after fixed appliance orthodontic treatment to search the prevalence and severity of enamel opacities in a cross-sectional study. The results showed that both the prevalence (72.3–84%) and the severity (opacity index, 0.125–0.200) increased with the treatment. The study also concluded that there was a significant difference between male and female patients. Male patients experienced greater increases in the severity of enamel opacities than females did. However, there was no significant sex differential in the prevalence of enamel opacities either before or after the orthodontic treatment. Similar results about gender were obtained in another recent study [24]. This study also concluded that 23% of the patients developed WSLs during fixed appliance orthodontic treatment, and WSLs developed more frequently in the maxillary arch than they did in the mandibular. The researchers identified other risk factors during the treatment such as treatment time exceeded 36 months, patients with poor oral hygiene, and patients whose oral hygiene declined during treatment and pre-existing WSLs. They observed that the lesions are often symmetrical and occurred more frequently on the maxillary laterals, maxillary canines, and mandibular canines. In other studies, different results were obtained. According to these studies, the most inclined teeth to demineralization are the first permanent molars, the maxillary incisors, the mandibular lateral incisors, and canines [2, 26, 30].

Boersma et al. [31] examined caries lesions on the buccal surfaces of teeth in orthodontic patients by using quantitative light fluoroscopy versus visual examination immediately after removal of fixed appliances and concluded that 97% of the subjects had one or more lesions, and on average, 30% of the buccal surfaces in a person were affected and also highlighted that mutans streptococci counts, age, duration of treatment, socioeconomic status, and dietary habits showed no correlation with caries prevalence.

Results of a recent meta-analysis have demonstrated that in the 14 studies evaluated for WSLs, the occurrence of WSLs is common during fixed orthodontic treatment with an incidence and prevalence rate of 45.8 and 68.4%. It has been proposed that the risk of developing WSLs during orthodontic treatment should not be underestimated by orthodontists, necessitating the search for further methods to counter the risk of development of these lesions [32].

The reported prevalence of WSLs is quite variable, depending on the sample size, method of detection, the use of a fluoride regimen during treatment, inclusion of pre-existing developmental enamel defects, and selected patients groups [30].

3. Etiology

Dental caries is a community disease that develops due to biological factors that are present within the saliva and dental plaque and is closely related to the type and frequency of carbohydrate
ingestion, as well as the oral hygiene practiced by the individual. The protective factors also presented as salivary flow rate, buffering capacity, antimicrobial activity, microorganism aggregation, and clearance from the oral cavity, immune surveillance, and calcium phosphate binding proteins all interact to inhibit or reverse demineralization of exposed tooth surfaces [13].

As previously explained, the WSLs can occur on any tooth surface in the oral cavity, where prolonged “undisturbed” plaque accumulation exist; in other words, the surfaces that microbial biofilm forms on exist. The other important factors that impact this process are the patient’s modifying factors, including medical history, dental history, medication history, diet, levels of calcium, phosphate, and bicarbonate in saliva, fluoride levels, and genetic susceptibility [33].

No change was seen clinically on the enamel after 1 week in the presence of undisturbed biofilm even after samples had been carefully air-dried. The outer surfaces of the enamel showed dissolution from the crystal’s peripheries, and inter-crystalline spaces enlarge. Two weeks later, the changes in WSLs become visible after air-dried. After 4 weeks, the lesions could be seen without air-drying and as opaque on a matte surface [34].

Orthodontic treatment has been reported as the most frequent factor for this situation, and equal susceptibility has been reported whether teeth are banded or bonded [2, 4, 5, 7, 9, 10, 19–22, 35, 36].

Tufekci et al. [5] demonstrated a sharp increase in the number of WSLs during the first 6 months of treatment and it continued to increase at a slower rate up to 12 months in a clinical study. They suggested evaluating the oral hygiene status of patients during the initial months of treatment and, if necessary, implementing extra measures to prevent demineralization.

Fixed orthodontic appliances cause inaccessible areas for plaque and make tooth cleaning difficult. The oral musculature and saliva cannot clean tooth surfaces caused by the limitation of irregular surfaces of brackets, bands, and wires [33], furthermore, excess bonding, long etching time (>15 s), decayed/treated molars, and the duration of treatment are considered other risk factors [26, 37]. The colonization of aciduric bacteria encourages biofilm formation resulting in a rise in the levels of mutans streptococci and lactobacilli [38, 39]; in time, this causes active WSLs, and, if not treated, a cavitated caries lesion can develop.

Demineralization areas without cavitation are colonized by mutans streptococci (11–18% of total streptococcal count) in about 12–18 months prior to becoming clinically visible. In the remineralization process, mutans streptococci are reduced substantially (2–5% of total streptococcal count) [40, 41].

The critical pH for dissolution of dental hydroxyapatite is 5.5, but mutans streptococci and lactobacilli have pH of 3.9–4.1, which is well below it. Dental plaque buffering capacity and degree of calcium and phosphate supersaturation will determine the demineralization process [42–48].

The goal of modern dentistry is to determine all the risk factors and preventive measures by understanding all mechanisms responsible for demineralization leading to WSLs in order to intervene non-invasively and improve the strength, esthetics, and functions of teeth.
4. Diagnosis of white spot lesions

WSLs are opaque, white, and soft lesions characterized by demineralization on the tooth surface [36, 49]. The early diagnosis and treatment of these lesions, which are difficult to diagnose because of their characterization by submerged enamel demineralization, can prevent tooth decay and clinical caries formation.

Many tools can be used to diagnose WSLs including traditional visual inspection, mirror-sound applications and radiographies, trans-illumination methods, fluorescence methods, electrical conductivity, ultrasonic methods, and other newly developed technologies.

4.1. Visual inspection and radiography

The simplest method of detecting WSLs is the mirror-sound application and visual inspection. The demineralization of the enamel and microporosity affects the transmission of light within the enamel. Thus, the enamel layer loses its bright color and appears opaque-white due to optical refraction. Using a standard examination light and mirrors, opaque white lesions can be detected through the clinician’s visual examination. These lesions are often seen as opaque, matt, or chalky white areas around the labial cervical third and under orthodontic brackets, where bacterial plaques accumulate, they vary in size and are not clearly distinguishable. The surface of the enamel is protected, but roughness and micro-ridges (perikymata) are visible on the surface. In addition, it is possible to detect small defects using small rounded probes. The use of spiked probes is not recommended because it can cause defects in the softened enamel [50]. Yassin [51] showed that with micro radiological methods in an in vitro study, the use of spiked probes in a robust demineralized enamel model can cause cavitation in WSLs.

The addition of conventional radiographs to visual examination increases the diagnostic probability. However, ionized radiation exposure is the most obvious disadvantage. Other possible disadvantages are cases, where the outermost layer of enamel is intact and cases, where occlusal lesions without macroscopic deterioration are hard to diagnose. There is a lack of radiographic examination in more than 40% of approximal caries of enamel [52]. Previous studies showed no difference in diagnostic efficacy between conventional and digital bite-wing radiographs [53].

With computer aided diagnosis, a computer program, we can interpret the radiographs to distinguish between robust, demineralized, and caries teeth. The Logicon System (Carestream Dental LLC, Atlanta, GA) is an example of this technology. The program matches the radiographs with clinical images, compares them, and provides a dental density chart in graphical format [54].

4.2. Trans-illumination methods

The rapid development of imaging technology is beginning to help in the early detection of caries development. Fiber optic trans-illumination (FOTI) and digital imaging fiber optic
trans-illumination (DIFOTI), where light transmission is used, are among the methods. The use of fiber optic light makes it possible to see smaller superficial white lesions; it undergoes optical refraction by passing an intense light beam through the tooth. In the DIFOTI method, focused images can be taken with the help of a CCD camera installed in the system. The images can be analyzed by a computer and the diagnosis of approximal, occlusal, and soft surface caries can be done simultaneously. It allows documentation of the lesion and follow-up of the progression [55]. The DIFOTI method can detect demineralization as early as 2 weeks, but DIFOTI fails to measure the depth of the lesion [56].

4.3. Fluorescence methods

There are also systems that use the natural fluorescence that occurs in tooth enamel. The light emission coefficient of a caries lesion is higher than healthy enamel resulting in lower fluorescence in caries lesions [57]. Quantitative light measuring fluorescence (QLF) is associated with light changes in the natural fluorescence of hard tissue. The 50-W-xenon light, produced by the QLF hand tool, passes through the blue filter and reaches the tooth. The fluorescence light emitted from the tooth is collected by a camera mirror, passes through a yellow filter that eliminates light below 520 nm, and is sent to a computer program for examination. With QLF, the tooth is exposed to blue light, which stimulates green fluorescence from the hard tissues. In demineralized foci, a decrease is detected in this natural fluorescence and is seen as darker areas. Red fluorescence is seen due to porphyrins metabolized by bacteria in tartar, plaque, or infected caries lesions. Computer-aided QLF methods can also be used to evaluate the progression of the lesion and treatment response [58, 59]. The QLF system has high interobserver consistency and is effective at preventing false negatives [59].

Another method that uses the fluorescence characteristic of teeth is laser fluorescence (DIAGNOdent—KaVo, Germany). The fluorescence of the laser beam is less in demineralized enamel than normal enamel. With the method developed by Lussi in 2004, a red diode laser beam of 650 nm is applied to the occlusal surface of the tooth. It is collected using an optical fiber located at the same end, filtered by high frequency light wavelengths, and counted by a photodiode. Only low-frequency fluorescence that passes through the caries lesion is measured and quantified. Thus, the name “quantifiable laser fluorescence” is used as a value of the measurement scale, and when it increases, the likelihood of decay increases. A value of 5–25 indicates early lesions, 26–35 indicates early dentin caries, and over 35 indicates deep dentin caries. The most important disadvantage of this system is that it can give false positive results in the presence of painted fissures, plaque and calculus, pit and fissures sealant, and in the presence of restorative material [57, 60]. Therefore, it is important to clean the tooth surface when using DIAGNOdent. A study by Pretty [59] showed that laser fluorescence technology has higher specificity compared to electrical resistance, FOTI, and QLF. Although it has the advantages of allowing very early caries detection, reproducibility, and measurement on approximal, buccal, and lingual surfaces with different tips without any destruction, it has the disadvantages of being expensive and having the sensitivity to give false positive results. Çınar et al. [61] compared the DIAGNOdent and DIAGNOdent pen with visual examination and bitewing radiographs for detection of occlusal caries. They found that for outer enamel lesions DIAGNOdent pen has higher sensitivity than radiographs.
4.4. Electrical conductivity

Difference arises in the electrical transmission of solid and demineralized enamel surfaces due to porosity. Saliva penetrates the enamel and increases the electrical permeability of the tooth [62]. This electrical conduction is measured by a connector placed on a region with high conductivity such as the gingiva or skin and a probe placed into the fissure.

Today, the most important device used for this purpose is the electronic caries monitor (ECM) (LODE Diagnostic, Groningen, The Netherlands). The ECM has a limited capacity on the occlusal surface in general. It is more successful on smooth and approximal surfaces. Compared with clinical visual methods, the sensitivity of this system is higher but the specificity is lower [63].

Another method based on electrical conductivity measurement is alternating current impedance spectroscopy (CarieScan). In this method, multiple electrical frequencies are used to detect occlusal and soft surface caries. A surface of the tooth is isolated by drying with compressed air and the suspicious area is examined. If the entire surface is to be examined, an electrolyte solution is used and the probe tip is placed in a larger area. This method, which is unaffected by dyes and discoloration, is more accurate and reliable than the ECM [64].

4.5. Ultrasonic methods

The high frequency sound waves applied by the probe are converted back to electrical impulses as they return from the textures and the echo (reflection) they form is detected. Ng et al. [65] reported that high-frequency pulse-echo ultrasound waves (18 MHz) produce different echoes in robust and demineralized enamel.

Studies have shown that ultrasound is a successful method in deep dentin lesions, but it is even more useful in evaluating remineralization. A study comparing ultrasound against radiography and histology in mandible molar teeth for detection of WSLs reported the sensitivity and specificity of the method as 88 and 86%, respectively. It was concluded that ultrasound was a useful tool for detection of these lesions [66].

4.6. Optical coherence tomography and polarization sensitive optical coherence tomography

Optical coherence tomography (OCT) uses infrared light to obtain high-resolution images of approximately 10–20 microns with confocal microscopy and low coherence interferometry. The accuracy of OCT is quite high and it can show early mineral changes in the in vivo environment with exposure to acid for only 24 h using near infrared reflectivity. Polarization sensitive OCT (PSOCT) has also been used to study the spatially resolved scattering and polarization phenomena of teeth, which are known to have a strong polarization effect [67, 68].

4.7. Frequency-domain laser-induced infrared photothermal radiometry and modulated luminescence

Frequency-domain laser-induced infrared photothermal radiometry and modulated luminescence technology (PTR/LUM) is based on the principle that infrared laser light absorption
of the tooth is measured depending on the resulting temperature change (exchange interval of less than 1°). In this method used by Canary System (Quantum Dental Technologies), the thermal energy conversion of the optical energy provides better evaluation of tissue density and lesion depth than visual techniques [62]. In another laboratory study, it was stated that radiography is more sensitive than visual or laser fluorescence technology [69].

5. Differential diagnosis of white spot lesions

WSLs occur due to hypomineralization of the enamel. Conditions causing hypomineralization such as fluorosis, traumatic hypomineralization, molar-incisor hypomineralization, genetic defects causing enamel hypoplasia, as well as environmental factors should be considered during the diagnosis. WSLs appear translucent when the surface is moist, and opaque-white when the surface is dried with air spray. Other hypomineralized lesions are often opaque-white when the surface is moist. The surface of WSLs is softer and rougher, and dental plaque accumulation is often observed in these areas.

Fluorosis is a hypomineralization that occurs as a result of excessive incorporation of fluorides during the formation of enamel. Excessive fluoride uptake and the use of fluoride-containing substances occur after symmetrical interaction of the homologous teeth and influence different tooth groups. In the early phase, convergent horizontal white lines cause a parchment-like appearance accompanied by irregular chalky areas. Histopathologically, hypermineralization occurs in the superficial layer of teeth with dental fluorosis and hypomineralization occurs in the subsurface of the external third of enamel. Then, a brown color change occurs due to the infiltration of exogenous chromophoric proteins [70].

Traumatic hypomineralization occurs as a consequence of periodontal trauma affecting deciduous teeth. The severity of the trauma is not related to the level of hypomineralization. Even a simple, unobtrusive shock can cause the formation of these defects [70]. Periapical inflammation after trauma affects germ mineralization. Traumatic hypomineralization can occur in many different shapes, borders, localizations, and colors. They often occur as punctiform lesions in the dental crowns of the incisal third. They usually affect one tooth asymmetrically with respect to the corresponding contralateral teeth. Although the trauma story gives an idea for the diagnosis of these lesions, it is sometimes difficult to remember simple shocks, so the diagnosis of these lesions is often made by excluding other causes [71].

Molar incisor hypomineralization is the least known lesion in differential diagnosis. In the clinic, at least one of the four most permanent molar teeth must have a qualitative enamel defect. Permanent incisors can also be affected. Sometimes the cusps and second molars can also be affected. It is important that the molars and permanent incisors have well-defined white, yellow, or brown opacities on the occlusal surface of the crown. Enamel splints are present and they modify the occlusal anatomy of the first molar teeth. Excessive tooth sensitivity and anesthesia difficulties secondary to underlying pulpal inflammation occur. The shapes and edges of restorations are atypical and early failures of restorations can be seen. It should be considered in unexplainable extractions of the first molars in patients without
caries. Respiratory diseases causing hypoxia, episodes of recurrent febrile infections, and exposure to dioxin should be questioned [69, 72].

Genetic factors causing enamel hypoplasia and hypomineralization include Amelogenesis Imperfecta, Congenital Erythropoietic Porphyria, Ectodermal Dysplasia, Epidermolysis Bullosa, Tricho-dento-osseous Syndrome and syndromes causing Hypoparathyroidism (Velocardiofacial Syndrome, DiGeorge Syndrome, 22q11.2 deletion syndrome, Kenny-Caffey Syndrome). Smoking habits of the mother, low birth weight, Celiac disease, and Vitamin D deficiencies like Rickets can also cause hypomineralization. Infections such as Congenital Syphilis, Chicken Pox, Rubella, Measles, Mumps, and Cytomegalovirus can cause enamel defects. Apart from fluoride, tetracycline and cytotoxic drugs, lead intoxication, and Pica ingestion can lead to discoloration, and enamel defects in teeth [70].

6. Management of white spot lesions

6.1. Oral hygiene

The aim of modern dentistry is to manage initial caries lesions non-invasively through remineralization to prevent disease progression [73]. Oral hygiene is very important in protecting teeth against WSLs. This can be firstly achieved by both motivation and education of patients [74].

It is well known that tooth brushing, which is an effective way to remove plaque/biofilm from the tooth surfaces prevents oral diseases such as caries, gingivitis, and periodontitis to a significant extent. Therefore; today, it is a standard to use a toothbrush as a personal daily oral hygiene procedure in developed countries.

Mechanical cleaning is provided by brushing teeth with fluoride containing toothpaste and flossing [74]. The effective removal of plaque from the tooth surface by proper brushing is well known to prevent dental caries [75]. The technique and frequency vary according to the patient’s disease pattern and oral hygiene needs [76]. Kuhnisch et al. [77] recommended that twice-daily removal of the dental biofilm by brushing teeth with fluoride toothpaste prevent new caries lesions.

Although manual brushing of teeth is a very simple and effective method, a number of studies have stated that the time and effectiveness of tooth brushing are inadequate. Most children brush their teeth regularly, but for only 30–45 s. Depending on their age and manual skills, teeth may be insufficiently cleaned [78, 79]. While the timer of the power toothbrushes makes sure that children spend adequate time brushing their teeth, the inherent bristle movement may make up for their limited dexterity particularly in cleaning hard-to-reach areas like interproximal tooth surfaces [80].

6.2. Fluoride

The initial stage of WSLs can be treated successfully with good oral hygiene, topical fluoride application, and/or other caries-mineralizing agent [81]. Ideal remineralization material
should be bioavailable in order to diffuse or deliver calcium phosphate into the lesion or boost the remineralization properties of saliva and oral reservoirs, without calculus formation [73, 82].

Topical fluoride application is the first choice of many clinicians to treat WSLs. During topical fluoride application, a calcium fluoride-like material (CaF$_2$) develops in plaque, on the tooth surface or initial caries lesion. When the pH value decreases during a caries attack, CaF$_2$ is used as a reservoir of fluoride ions for release [2, 83]. Also when there is fluoride on the enamel surface, fluoroapatite, which has a more durable structure than hydroxyapatite, is formed [36]. This is believed to be a major mechanism of fluoride action in enamel remineralization [84–86]. In addition, topical fluoride application increases plaque pH and inhibits bacterial metabolic pathways indirectly, thus enamel demineralization reduces and remineralization enhances [87].

Low-dose topical fluoride is recommended over long periods of time with frequent exposures in order to avoid dental fluorosis [87, 88].

High concentration applications of fluoride to WSLs are usually preferred in clinical practices; however, highly concentrated fluoride leads to hypermineralization of surface layer of WSLs. Therefore, the penetration of calcium and phosphate ions into the body of lesion is blocked. This is referred to as lamination. It may have some undesirable esthetic consequences [36, 89].

A slow calcium, phosphate, and fluoride ion penetration from saliva or low concentrations of fluorides should be allowed to the WSLs firstly. In this way, more esthetically agreeable results will be achieved. This kind of treatment regimen may remineralize the mild WSLs from the deeper parts of the lesion to the outer surface layers of the enamel. Therefore, the chance to get a successful and more esthetic treatment result increases [36].

Remineralization with saliva is a small and slow process. There is a tendency for the mineral gain to be in the surface layer of the lesion because low ion concentration gradient occurs from saliva into the lesion [73]. Frequent exposure to low levels of fluoride is the most important part of the prevention and remineralization of caries. This can be achieved by using fluoride toothpaste, mouthrinses with fluoride, and fluoride varnish. Systemic fluorides seem to have a limited role; mostly its primary effect is topical [87]. Many fluoride-containing products, such as toothpaste, mouthrinses, gels, and varnish can be used alone or in combination [90].

6.2.1. Toothpastes

Fluoride toothpaste is the most commonly used form of fluoride to provide a constant and low amount of fluoride in oral environment [91, 92]. Various fluoride compounds have been added to toothpaste either alone or in combination in the formulations, including sodium fluoride, sodium monofluorophosphate, amine fluoride, and stannous fluoride [90, 93].

The concentration of fluoride in toothpastes recommended by WHO is between 1000 and 1500 parts per million (ppm F). In many countries, toothpastes containing low fluoride (usually 450–500 ppm fluoride) are marketed for children. High fluoride containing toothpaste more than 1500 ppm (up to 5000) is commonly prescribed for adults at increased risk of caries [91]. Higher fluoride containing toothpaste provides more protection against caries [90, 94].
American Academy of Pediatric Dentistry (AAPD) recommended that using a smear or rice-size amount of fluoridated toothpaste is appropriate for children under 3 years old, and a pea-size amount of fluoridated toothpaste is appropriate for children 3–6 years old [95]. However, Marinho et al. [90] recommended that children no more than 6 years of age should be supervised when brushing their teeth, and that no more than a pea-size amount, approximately 5 mm, should be used. Teeth should be brushed twice a day so that the toothpaste has a better effect. Moreover, rinsing with water must be held at bare minimum or it should not be done at all [95].

The widespread use of fluoride-containing toothpastes has caused a decline in tooth caries incidence. There has been a recently introduced additive, which is called Arginine, for toothpaste and other dental care products containing fluoride. Arginine is an amino acid that occurs naturally in a range of food products and in the saliva [96]. When applied in oral cavity, arginine is deaminated by the arginine deaminize system in saliva, producing ammonia, which is highly alkaline and leads to an increase in the pH in the oral biofilm, so that plays an active role with an insoluble calcium compound, and sodium monofluorophosphate for remineralization of WSLs [82, 97].

According to the statement of Zero [98], rinsing with tap water following the tooth-brushing, which is a widely seen practice, decreased oral fluoride retention considerably. Through the suggestion of this finding, the practice of brushing with fluoride toothpaste and a fluoride containing mouthrinse afterwards—used in combination—may be advantageous.

6.2.2. Fluoride mouthrinses

Fluoride mouthrinses have been successfully used to prevent dental caries and management of WSLs in children. Marinho et al. [99] suggested that supervised regular use of fluoride mouthrinse by children and adolescents is associated with a large reduction in caries increment in permanent teeth. Both daily uses of mouthrinses containing 0.05% NaF (226 ppm) and weekly rinsing programs with 0.2% NaF (900 ppm) were found to decrease the incidence of enamel demineralization. Because of the risk of fluoride ingestion, mouthrinsing is not recommended for children under 6 years old.

6.2.3. Fluoride varnishes

Fluoride varnishes were developed to make the contact time longer, to bond to the enamel for greater periods and prevent the immediate loss of fluoride after application. Therefore, they take the role of reservoir for slow release and facilitate greater fluoride uptake [100, 101]. Safety and efficacy methods of professionally practiced topical treatment for arresting active enamel caries are proven by fluoride varnishes. The fluoride concentration of fluoride varnishes is at a very high level (5% sodium fluoride, 22,600 ppm F). Since the amount of fluoride exposure can be kept under control, fluoride varnish application is thought to be safe [2]. They gradually release fluoride [102], and can be applied fast and effortlessly as well as setting in contact with moisture [103]. Dental prophylaxis in not necessary before varnish applications, thus chair time becomes shorter [81, 103]. Patients should avoid eating for 2–4 h after the application and to avoid brushing their teeth the night of the application, thus fluoride varnish may have more effect [104].
Douglas et al. [105] state that most guidelines recommended 5% (22,600 ppm F) concentration of sodium fluoride varnish. Even though there were differences upon the suggested frequency of application, applying fluoride varnish twice per year was a consensus.

AAPD guideline recommended that fluoride varnishes should be applied at least twice in a year for primary teeth and two or four times in a year for permanent teeth [95]. Marinho et al. [106] found that the use of fluoride varnishes two to four times a year, in permanent and primary dentition, leads to a considerable decrease in caries increment.

6.2.4. Fluoride gel

Fluoride gel can be applied both by professionals and by self-application of patients. In professional application, there are various methods for fluoride application. One of these methods is the application of fluoride with a mouth tray. In this method, fluoride gel is placed into a mouth tray and applied to entire dental arch at same time. Tray application is easily accepted by children. Other application methods include cotton balls and toothbrushes [91, 107]. The commonly used gels are 1.23% sodium fluoride gel (12,300 ppm F) and acidulated phosphate fluoride (APF) gel. The acidulation of this form is made with phosphoric acid at pH 3.0. The use of a fluoride vehicle with a lower pH value may extend the entrance of mineral ions into the body of the lesion. With this method, the microspores present on the surface of the enamel will not close because lamination due to fluoride of the surface layer will not happen. Thus, remineralization of the lesion will occur. On sound enamel surfaces, it acidulate dentifrices by mild etching. This results to an increase both in the microspores of the enamel layer and in the penetration of fluoride ions into the tooth [81]. Adding phosphate to an acid fluoride solution was practiced in order to depress calcium fluoride formation and increase fluoroapatite formation [100]. In pursuance of avoiding the likelihood of a low pH gel leading to etching in restorations, use of %2 neutral gels is recommended [91, 101]. Fluoride gel is professionally applied up to four times a year for 4 min [91, 101]. Due to risk of swallowing the fluoride gel, use in children under 6 years old is not recommended [108].

6.2.5. Fluoride foam

APF foam has the same concentrations (1.23%) and pH (3–4) of APF gel and applied in a same manner of APF gel [109]. Because of foam having a much lighter specific weight compared to a gel, it will take far less foam by weight in order to wholly fill a tray. Therefore, the amount of excess fluoride ingestion is reduced. It is seen that APF foam might be a beneficial alternative [110]. APF foam is professionally applied for 4 min and two times a year. This is effective in preventing dental caries in primary teeth [109, 111].

AAPD recommended that children with increased caries risk must undergo a professional fluoride treatment at least every 6 month. Since the risk categories might change in time, the types and intervals of preventive interventions should be adjusted accordingly [95].

6.3. Calcium-phosphate-based delivery systems

Calcium-phosphate based delivery systems are developed due to the difficulties of the solubility of calcium and phosphate remineralization systems; especially the presence of fluoride
ions. They can be examined under three headings: crystalline, unstabilized amorphous, and stabilized amorphous formulations [73].

Crystalline calcium phosphate remineralizing systems have poor solubility of the calcium phosphate phases, so it is difficult to achieve enamel remineralization [112]. It is a problem that excessive amounts of calcium phosphate phases present in the mouth [113]. Calcium sodium phosphosilicates referred as bioactive glasses, are a kind of crystalline calcium phosphates derivatives [114] and show maximum remineralizing potential [115]. Narayana et al. [116] reported that calcium sodium phosphosilicate paste has shown to release ions and transform them into hydroxy carbonate apatite for up to 2 weeks.

Unstabilized amorphous calcium phosphate (ACP) formulation is developed by mixing calcium ions with phosphate ions to produce an ion active phase so that it could be precipitated as quickly as ACP or, in the presence of fluoride ions, amorphous calcium fluoride phosphate (ACFP). The desired effect is dissolution into the saliva and to promote tooth remineralization [117], but these unstabilized forms can cause dental calculus [73].

The casein phosphopeptides remineralization system is developed for replicating properties of the milk caseins and salivary statherin. Therefore, the casein phosphopeptide-stabilized amorphous calcium phosphate (CPP-ACP) [118] and casein phosphopeptide stabilized amorphous calcium fluoride phosphate complexes (CPP-ACFP) are developed [86]. CPP-ACP is a bioactive agent with a base of milk products able to bind calcium and phosphate ions to stabilize calcium phosphate in solution and to increase the level of calcium phosphate in dental plaque. CPP-ACP also adheres to hydroxyapatite, soft tissues, and supplies free calcium and phosphate ions, thereby helping to maintain reducing demineralization and promote remineralization by reforming into calcium phosphate crystals [119–122]. It can interact with hydrogen ions from the surface of the tooth and so it can penetrate to enamel's subsurface layer in order to produce mineral gain [30, 123]. Antibacterial and buffering efficacy has also been emphasized as interfering the growth and adherence of Streptococcus mutans and Streptococcus sobrinus to dental plaque [124].

It was used for the first time in 2009 to treat WSLs [125]. There have been many studies evaluating the effectiveness of fluoride and CPP-ACP in recent years and the positive effects of this in secondary prevention of WSLs has increased noticeably.

Andersson et al. [126] observed that daily topical application of CPP-ACP for 3 months followed by a 3-month period of daily tooth brushing with fluoridated toothpaste helped in the complete elimination of the post-orthodontic WSLs. They stated that visual evaluation suggested an esthetically more favorable outcome of the ACP treatments. Bailey et al. [125] claimed that CPP-ACP is effective when used for 12 weeks after debonding according to QLF and digital photographs. Even Brochner et al. [127] found usefulness of MI Paste when used for 4 weeks after debonding.

Robertson [128] has shown that according to the evaluations with intraoral digital photographs of 50 patients, MI Paste (GC America) (CPP-ACP containing paste) significantly reduced the incidence of WSLs during orthodontic treatment when used for 3–5 min each day at night after brushing for 3 months. Akin et al. [7] found that CPP-ACP can be more
beneficial than fluoride rinse for postorthodontic remineralization with 58% reduction in the WSLs in 6 months.

Recent findings of a 12-week clinical study showed that topical applications of 10% CPP-ACP paste twice a day as an adjunct to a standard oral hygiene program significantly improved the appearance and remineralization of WSLs [89]. Contrary, there are studies reporting that CPP-ACP did not appear to be more effective than 1450 ppm fluoridated toothpaste in improving the appearance of WSLs after 36 months [129].

In the presence of fluorides, the formation of CPP-ACFP nano-complexes occurs and when the pH falls, the dissolution of the nano-complex leads the formation of calcium ions, phosphate ions, and neutral species CaHPO$_4$ and HF [130]. The synergistic effect of CPP-ACP and fluoride results in increased concentration of bioavailable calcium and phosphate ions in reducing the WSLs [131]. They produce a larger and more rapid remineralization of WSLs [132]. Llena [132] observed that 4-week use of CPP-ACFP is superior to fluoride varnish in remineralizing smooth surface WSLs. There is another study supporting these results as CPP-ACFP on daily basis had better remineralization potential than once professional application of fluoride varnish and twice daily use of fluoride toothpaste [86]. However, Beerens et al. [133] indicated that the use of CPP-ACFP crème for 12 weeks has no clinical advantage over normal hygiene in the remineralization of WSLs. They also reported that the percentages of aciduric bacteria and S. mutans decreased significantly both in CPP-ACFP and control groups, but they found no differences between groups. Similarly, Huang et al. [122] observed that CPP-ACFP does not appear to be more effective than normal home care in improving the appearance of WSLs over an 8-week period. The use of CPP-ACFP in subsurface enamel lesions due to orthodontic fixed appliance treatment does not provide additional improvement measured by QLF imaging, microbiological composition as well as by digital oral photographs [134].

Tooth Mousse/MI Paste (GC, Tokyo, Japan) is a topical remineralizing cream containing CPP-ACP (10% w/v). It is suggested to be applied on tooth surfaces twice a day after brushing. The patients should refrain from drinking or eating for 30 min subsequent to application. In addition high fluoride toothpaste should be used for 6 months in order to succeed in treating postorthodontic demineralized WSLs [121].

In a recent review, it was concluded that CPP-ACP products did not show any significant benefits over brushing with fluoride toothpaste in the prevention of demineralization because of the limited quality of evidence. Also, there is insufficient evidence for the use of fluoride-containing formulation. Further well-designed randomized controlled trials are required to determine efficiency of these systems for the prevention and treatment of early dental caries [135].

6.4. Polyols

Polyols are the alcohol derivatives of sugars, which are metabolized more slowly than sucrose by the oral bacteria. This reduces the risk of caries. They were first developed for use in diabetic products, but nowadays they are used in sugar free products like chewing gum, chocolate, boiled sweets, and biscuits. Polyols are “bulk sweeteners” which include xylitol, sorbitol, mannitol, maltitol, and lactitol [136].
Especially, xylitol provides an anti-caries efficacy on dental plaque and cariogenic microorganisms [137]. This reduces mutans streptococci (MS) levels by disturbing the energy production process and leads to cell death [138]. It also reduces the adhesion and acid production of these microorganisms present in dental plaque and saliva [139, 140]. Xylitol is more unique than the other sugar alcohols because it promotes mineralization by increasing salivary flow rate and is nonfermentable by oral bacteria [141]. It was shown that xylitol exhibits a dose- and frequency-dependent effect and it is safe [142, 143].

In an in vitro enamel lesion remineralization study, Makinen and Soderling [144] have proposed that very high concentrations of sorbitol and xylitol may influence calcium bioavailability, so it can support the remineralization process of subsurface lesions of enamel.

Miake et al. [145] investigated the effects of remineralizing solutions; with and without 20% xylitol, for 2 weeks on artificially demineralized enamel. They indicated that xylitol could influence remineralization in the deeper layers of demineralized enamel by facilitating Ca$^{2+}$ movement and accessibility into the lesion.

A long-term study evaluated daily intake effects of erythritol, xylitol, and sorbitol on the development of enamel and dentin caries. It was found that the erythritol group showed a lower number of caries lesions than the xylitol or control groups and the longest duration of caries formation time [146].

Several studies indicated that using chewing gums containing xylitol controls cariogenic bacteria and plaque acidogenicity, and provide controlling caries increment [147, 148]. Sengun [149] reported that xylitol lozenges significantly helped neutralizing the acidity of dental plaque in patients undergoing fixed orthodontic appliance.

In contrast to these studies, Shen et al. [150] purposed that polyols (xylitol, sorbitol, maltitol, and mannitol) do not promote remineralization of enamel subsurface at physiologically relevant concentrations by forming Ca$^{2+}$-polyol complexes and facilitating calcium uptake into the lesion. Also, it has been shown that daily consumption of chewing gum containing CPP-ACP reduces the level of salivary S. mutans more than xylitol chewing gum [151].

More randomized controlled clinical trials are required for understanding the mechanisms of action, resistance, suitable delivery vehicles, and caries-preventive effects of xylitol [152]. The American Academy of Pediatric Dentistry (AAPD) supports the use of xylitol and other sugar alcohols as non-cariogenic sugar substitutes. However, this underlines the lack of consistent evidence showing significant reductions in S. mutans and dental caries in children, and adds that the high dose and high frequency of xylitol used in clinical trials may be unrealistic in clinical practice [153].

### 6.5. Chlorhexidine

Chlorhexidine is a commonly used cationic bisbiguanide agent with a broad range of antiseptic effect [154]. The efficacy and antiplaque effect of the solution in the control and management of biofilms has been proved in gingivitis [155], but there is not enough evidence in preventing initial caries lesions or the reduction of mutans streptococci levels [156, 157]. The inconclusive results of some studies have shown that chlorhexidine varnishes are effective in decreasing
the prevalence of caries while others have not during orthodontic treatment [158–160]. It is likely that varnishes are more effective due to higher chlorhexidine concentration and longer contact time with the tooth surface [161, 162]. Chlorhexidine has bacteriostatic and bactericidal effects on Streptococcus mutans [163] and inhibits acid production in bacterial plaque; so during sucrose challenges, it reduces the fall in pH [164]. It was assumed that its remineralization effect on WSL’s might be due to electrostatic links with hydroxyapatite’s phosphate groups causing precipitation of phosphate salts on demineralized enamel surface [165]. When compared with weekly application of fluoride varnish period of 3 months, it was found that both were effective in controlling WSLs adjacent to orthodontic brackets but fluoride showed a faster remineralization [166]. The combined use of fluoride and chlorhexidine varnish was shown to be more effective in active WSLs than the use of one alone [167]. Studies using chlorhexidine vehicles alone or in combination with other agents are very limited, and a majority of the cases did not show a statistically significant reduction.

6.6. Laser

It has been shown that the use of laser irradiation is effective for caries prevention recently [168]. The mechanism is explained by decreased enamel permeability and alterations in the chemical composition and surface morphology for increased acid resistance of enamel exposed by laser irradiation [169, 170]. Melting and recrystallization of enamel surface cause reduction of permeability and the solubility of enamel, and thus prevent demineralization [171–174]. However, when laser is applied at high energy levels, it may cause undesired changes like cracks, glazed surfaces, columns separated by voids in the enamel surface during cooling [175, 176]. Irradiation of laser creates microspaces on the surface of the enamel so the released ions are trapped, and minerals are deposited into the enamel tissues [177]. It has been shown that using laser with topical fluoride leads a synergistic effect like increased uptake and less consumption of fluoride and decreased dissolution rate of the enamel [178, 179]. Also, the combination of laser and fluoride increase enamel acid resistance [180, 181] and transformation of hydroxyapatite to fluorapatite [169].

Erbium, chromium:yttrium-scandium-gallium-garnet (Er,Cr:YSGG) laser is strongly absorbed by the hydroxyapatite of tooth structure and it does not ablate the surface. It only changes chemical composition of the enamel [182]. Nd:YAG laser irradiation was demonstrated to be effective in preventing occlusal caries in pits and fissures of primary teeth by low energy level [183]. CO₂ laser was also effective in the control of demineralization, with the advantages like being quick, comfortable, and simple application, especially in children, considering the difficulty of using a fluoride [184]. More long-term studies are required for understanding the longevity of the laser therapies in preventing caries and remineralization effect on WSLs [179].

6.7. Probiotics

Probiotic bacteria are defined as “living microorganisms that ensure a health benefit for the host when administered in sufficient amounts” by the World Health Organization (WHO) [185]. These bacteria mechanisms of action, which are candidates for bacteriotherapy, are still an open question, but it is known that they can produce bacteriocins against pathogenic bacteria. They also have local and systemic effects involving immune-modulation, modulate the
inflammatory response, competitive inhibition, and binding instead of pathogens [186, 187]. Probiotics can be delivered in milk, yogurt, cheese, ice cream, tablets, lozenges, powder, and drops. No negative side-effects for the probiotic usage were reported [188]. It was stated that probiotics may have a positive effect on reducing the mutans streptococci counts and this may cause a positive effect on the development of caries [189].

The study by Näse et al. [190] in preschool children milk containing *Lactobacillus rhamnosus* GG showed decrease in dental caries development; especially in the age group with the 3–4-year-olds, with a fraction of 60%. They suggested 5-day a-week intake of probiotic for reducing risk for caries. Also, Stecksen-Blicks et al. [191] evaluated the effect of milk supplemented with *L. rhamnosus* and fluoride for 21 months on enamel and dentine caries, and concluded that daily consumption of milk containing probiotic bacteria and fluoride reduced caries in preschool children with a prevented fraction of 75%. The disadvantages associated with its usage are effect of the probiotic will disappear when the patient discontinues its use [186], and using a single group of bacteria is partly relevant for microbial shift to the biofilm structure with aciduric phenotypes [188].

There is a need for long-term and large-scale trials examining the positive effect of these products to adopt bacteriotherapy for preventing and controlling caries and also determining the most appropriate species, treatment time, the ideal concentration, and vehicle [189, 192].

6.8. Sealants

Sealant applications to the enamel surfaces adjacent to orthodontic brackets during orthodontic treatment to form a physical barrier for acidic conditions was investigated by researchers and conflicting results has been reported. Some studies showed a caries inhibition effect of sealant application [193, 194], while others did not and also found high cost [195–197]. Durability of sealants may vary due to mechanical abrasion from mastication and brushing. These factors cause sealant abrasion [195, 198], so sealant preservation should be evaluated with 3-, 5-month periods and renewed if necessary [199]. Repeated applications are recommended for preventing WSLs formation effectively [200]. Also, filled resin sealants may be preferred due to their wear resistance instead of unfilled resin sealants to provide a better protection as a physical barrier but at this time removal after treatment can cause problems [201, 202]. Glass ionomer cements were suggested as enamel surface sealants due to their property of better prevention of surface lesion formation [19]. It has been reported that excessive sealant material may cause retention sites for biofilm and new sites for caries around the brackets [203]. Further well-designed *in vitro* and *in vivo* studies should be performed to evaluate long-term effects and find more high-level evidence to guide the best clinical decision to use resin sealant [19, 204].

6.9. Tooth bleaching agents

Vital bleaching was recommended to camouflage WSLs that are seen after the fixed appliance of orthodontic treatment [205]. It is a minimal invasive conservative approach and provides a more uniform appearance [206], but the most important reason for not having a wide use is that microhardness of sound and demineralized enamel surfaces may decrease after bleaching treatment [207]. Therefore, the risk of developing caries increases [208].
6.10. Microabrasion

Enamel microabrasion treatment can improve enamel surface texture and remineralization and eliminate superficial staining or defects [209, 210]. This technique includes hydrochloric acid and pumice application to the enamel, which removes approximately 100 μ from the surface layer. The structure of this microabraded enamel surface appears polished because of no interprismatic space and it is more resistant to bacterial colonization and demineralization [211, 212]. Some researchers reported that the microabrasion technique can reduce the size of white spot lesions by 83% and they concluded that it could be a treatment option for post-orthodontic demineralized enamel lesions [213]. While, another group of researchers contended that the first option should be conservative methods such as topical fluoride application. But if the problem still persists, microabrasion can be the treatment choice [214]. Also, Pliska et al. [8] demonstrated that microabrasion treatment successfully reduces white spot lesions regardless the CPP-ACP paste. However, there is a limitation to its use. It was reported that the technique is effective if the lesion sizes do not exceed from 0.2 to 0.3 mm in depth [215].

6.11. Ozone

Ozone application due to its oxidizing power and a reliable microbiocidal effect in the gaseous or aqueous phases can be considered as an alternative treatment method [216]. It can reduce the total number of microorganisms [217] by breaking up the cell walls of bacteria, viruses, and fungi, and also kills the acid-producing bacteria causing decay [218]. It was reported that ozone application can reduce Streptococcus mutans and Streptococcus sobrinus counts on saliva-coated glass beads [217]. However, this treatment method can only remove the microorganisms and stop the demineralization activity only in the outer half of enamel lesions [219]. According to a systematic review published recently, ozone application’s clinical and cost effectiveness are still unknown; as well as the optimal concentration, application period, and how long effects might last, how deep it might penetrate, or whether having other side effects. More studies and evidence are needed to answer these questions as in the example of the application of ozone gas to decayed teeth is effective in preventing progression of dental caries, and ozone should not be considered as an alternative in general practice [220].

6.12. Resin infiltration

Resin infiltration is a technique used in improves the appearance of WSL. An opaque appearance of WSL is associated with the scattered of light as it passes through the lesion body. Scattering is caused at interfaces between two components with different refractive indices (RI), enamel (RI 1.62–1.65), water (1.33), or air (1.00). During the enamel-air interface, larger scattering is produced (Figure 2). Thus, early lesion stages need drying to be visually detected, as the RI of water is closer to that of enamel compared with air. Therefore, dehydrated enamel would show a decrease in translucency (Figure 3) [221, 222].

Resin infiltration technique obstructs the pores that provide diffusion pathways for acids and dissolved minerals in enamel. Thus, it prevents acid penetration into the lesions. Unlike fissure sealants, this technique creates the diffusion barrier inside the enamel lesions. Fissure sealants only form a barrier on the enamel lesions. Thus, resin infiltration could strengthen
the enamel structure and prevent cavitation or breakdown of enamel surface [223]. Moreover, lesion progression slowed down or even arrested [221].

Resin infiltration material (Icon, DMG; Hamburg, Germany), consist of triethylene-glycol-dimethacrylate-resin and has high penetration coefficient, high surface tension, and low contact angle with enamel that facilitates penetration of lesion body of carious enamel [224]. The hypermineralized superficial layer blocked penetration of resin infiltrant into the lesion body. To facilitate resin penetration into the lesion body, 15% hydrochloric acid gel applied to hypermineralized superficial layer (Figure 4) [225]. Paris et al. [226] concluded that etching for 2 min with 15% hydrochloric acid gel led to deeper resin penetration of lesion body than etching with 37% phosphoric acid gel.
After acid etching procedure, ethanol is applied for 30 s to remove the water from the lesion body (Figure 5); so that lesion desiccation is provided and resin penetration into the pores is facilitated by increased surface free energy [227, 228]. Paris et al. [228] showed that application of ethanol is an important step as pretreatment in preparation for resin infiltration.

Having completed the preparation of the lesion, a resin infiltrant is applied for 3 min on the lesion surface to occlude the porous of carious lesion, and to reduce diffusion of acids and minerals. Meyer-Lueckel et al. [229] reported that 3 min application of an infiltrant seems to be sufficient to achieve an almost complete penetration of natural caries lesions in vitro. Then excess resin was removed with cotton wad, before light curing [227]. Paris et al. [203] suggested that excessive material could be clinically a disadvantage, since sealants margins and excess resin could provide retention sites for biofilm and new caries lesion.

As a positive side effect of this application, this material was applied enamel lesions lose their whitish-opaque color appearance and look similar to sound enamel. Hence, this treatment could be used for arresting enamel lesions as well as improving the esthetic appearance of buccal WSLs [227]. The masking of enamel caries is caused by infiltrating the lesions by using resins with a similar refractive index (RI of infiltrant: 1.52) as apatite crystals (Figures 6 and 7). Thus, light scattering is reduced and visual color differences to enamel decreased [221].

Kim et al. [230] reported that resin infiltrant was wholly masked in 61% of the teeth, partially masked in 33% of the teeth and no change was observed in 6% of teeth in post orthodontic

Figure 5. View after rinsing of icon etch and ethanol application.

Figure 6. View after application of resin infiltrant and allowing penetration for 5 min.
defects. They also concluded that masking effect of resin infiltrant is depends on depth of the lesion and activity. When the lesion does not reach deeper and the superficial layer is thinner, successful results are obtained with this application.

7. Conclusion

The WSLs may become less noticeable spontaneously over a period of 5–12 years [231]; however, natural remineralization mechanism by saliva involving mineral gain in the surface layer of enamel has little improvement on the esthetic and structural properties of the deeper lesions [73]. Within the limitations of the available data, it may be concluded that there is a need for examining the most appropriate remineralizing agent, treatment, and vehicles in order to speed up this repair process of the deeper parts of the WSLs for better esthetic and structural reinforcement.

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