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Intervention of White Spot Lesions. A Contemporary Review of 20 years

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ABSTRACT

White spot lesion is incipient caries and it manifests as white opacity lesion on the demineralised enamel surface. White spot lesions are a common adverse effect among post orthodontic patients. The prevalence of white spot lesions in post orthodontic patients varies from 2% to 97%. Therefore, it is imperative for dental practitioners to be able to manage white spot lesions. Thus, this article is a contemporary review on the management of white spot lesions. After reviewing this article, it comes to a consensus that non- invasive treatments should be the first line management of white spot lesions. Non-invasive treatments such as patient education, motivation, oral hygiene reinforcement, and attempts to remineralise with various forms of fluoride preparation should be prioritised in the treatment plan. If the white spot lesions fail to respond more invasive treatment options might be considered.

INTRODUCTION

Dental caries is defined as a dental disease causing the destruction of enamel, dentine, and/or cementum eventually affecting the pulp. It has a multifactorial aetiology and one of the main causative factor is ascribed to acid-producing bacteria [1]. Dental caries may present in various forms from subsurface and subclinical changes to the full blown pattern with cavitation involving enamel, dentine, or even pulp [2, 3]. White spot lesions (WSLs) otherwise known as early, initial, or incipient dental caries is the predecessor of caries formation [4,5]. WSLs are characterized as subsurface enamel porosity from carious demineralisation that presents as a milky white opacity on a smooth surface. At this onset of caries staging, WSLs can be reversed and regressed by remineralisation of the lesion [5].

WSLs are encountered mostly during orthodontic treatment and are prevalent in orthodontic patients, ranging from 2% to 97%, depending on oral hygiene and preventive measures [5-7]. Dental caries results by the imbalanced relationship between oral hygiene, fluoride intervention, diet and saliva will affect the equilibrium between the microbial activities with the tooth. If the balance between the above mentioned factors are tilted, it would cause demineralisation on the involved tooth surface and therefore lead to formation of dental caries [8]. Many studies were carried out on WSLs. It is assumed that WSLs can be reversed and regressed naturally. The natural regression of WSLs perhaps can be described by remineralisation through buffering capacity of saliva along with the presence of fluoride, surface abrasion of porous layer, or removal of etiological factor [9-11]. However, most WSLs persist up to 12 years follow-up. Therefore, the natural recovery of WSLs may not be optimal. Some of the persisting WSLs could be aesthetically unacceptable for patients [7, 9, 11, 12]. A considerable amount of studies available in treating or alleviating of WSLs. Therefore, the aim of this paper is to review the management of WSLs based on the latest evidence for the past 20 years. There are two methods to manage WSLs, either by remineralising or masking the lesions. According to the current concept of minimally invasive dentistry, non- invasive treatment through remineralisation should be the first option before a more invasive treatment option is chosen [13].

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1. NON-INVASIVE TREATMENT

1.1 Oral hygiene instruction

In 1987, Holmen et al. [14] conducted research where he left biofilm on tooth samples undisturbed for two weeks and examined for any changes on the surface. Initially, the WSLs were only seen following air-drying. Subsequently, another layer of biofilm was left untouched for the next two weeks period, after which, they discovered that WSLs formed were more distinct and present even without air-drying. Hence, the hypothesis proved that biofilm is the main cause in WSLs formation. In order to prevent WSLs, the logical method would be removing the biofilm from the tooth surfaces [15]. According to American Dental Association, mechanical tooth brushing is effective in removing biofilm from teeth. The technique used and the duration of tooth brushing plays a significant role in reducing biofilm. The recommended regime for general population is to brush twice daily for two minutes with circling and sweeping motion using a fluoridated toothpaste. This recommendation however is not well known by the public and is often neglected by many patients. It is not surprising that brushing teeth with an incorrect method may cause the appearance of WSLs. Therefore, it is prudent to educate and instil good oral hygiene practices in all patients [16,17]. From the authors' perspective, it is crucial to encourage patients to be actively involved and advocate for self-responsibility in maintaining good oral hygiene, thereby eliminating the possibility of developing WSLs.

1.2 Fluoride

Fluoride plays a pivot role in the prevention and management of WSLs. This is primarily due to its ability to inhibit the activity of acidogenic bacteria thereby able to halt the demineralisation of the crystalline structure on enamel surface [18]. During the remineralisation of WSLs, fluoride can be incorporated into the crystalline lattice of demineralised enamel. This newly integrated crystalline lattice is known as fluroapatite crystal which is more resistant against future episodes of demineralisation attack [19]. Based on a previous study, use of high fluoride concentrated products in treating WSLs is not recommended as this might hyper-mineralise the outer surface of the lesions [20]. The hyper-mineralised lesion will remain opaque and might be at risk for extrinsic staining [21]. However, there are limited studies which supports this hypothesis [20,21]. More studies are required to support the above finding and if the hypothesis is verified, it is important to further study on the maximum level of fluoride concentration which will cause the hyper-mineralisation of the WSLs.

Fluoride can be dispensed in different modes such as toothpaste, mouthwash, varnish, gel, and tablets form which will be further discussed in the following subheadings.

1.2.1 Fluoridated toothpaste

Fluoridated toothpaste is the most common and easiest route for fluoride exposure. The proposed fluoride concentration for fluoridated toothpaste is 1000 to 1500 parts per million (ppm F) [22]. As for the brushing regimen, it is recommended to brush twice daily with fluoridated toothpaste [17]. Rinsing after tooth brushing is not recommended. In fact, spitting the excessive remaining toothpaste after brushing is preferred as this can maximize the caries protection effect of fluoridated toothpaste [23]. Studies have been carried out in utilizing fluoridated toothpaste in treating WSLs. It is proven that the use of fluoridated toothpaste of 1000 ppm/ 1100ppm is effective in the remineralisation of WSLs [24-26]. Agarwal et al. [27] proved that fluoridated toothpaste of 1450 ppm is capable to remineralise the WSLs significantly as compared to non-fluoridated toothpaste. Based on the eight weeks clinical trial, the authors concluded that fluoridated toothpaste has superior remineralising effect against the non-fluoridated toothpaste. Incorporating hydroxyapatite into the toothpaste has been a spotlight lately. Based on the review by Chen et al 2021, they demonstrated the effect of hydroxyapatite in remineralisation was comparable to fluoride. Despite with the comparable outcome in remineralising the white spot lesions, its biomimetic property might provide an advantages over the conventional products [28]. In our opinion, we are in agreement with Chen et al. 2021 that more clinical studies are needed to highlight the potential of hydroxyapatite in remineralisation as compared to the fluoride and to justify the use of hydroxyapatite fluoridated toothpaste.

1.2.2 Mouth rinses

Daily uses of fluoridated mouth rinses containing 0.05% sodium fluoride (NaF) or weekly rinsing with 0.2% NaF were proven to lower the risk of enamel demineralisation [29]. A randomised clinical study showed the antimicrobial activity potential of fluoridated mouth rinse. It demonstrated the ability of the sodium fluoride mouth rinse in reducing the bacteria count of *Streptococcus mutans* significantly in the subjects [30]. This finding was promising as the reduction of *Streptococcus mutans* loads in the oral cavity, the enamel demineralisation process might be halted and reversed. Weyant et al. [31] conducted systematic review to study the potential of topical fluoride in caries prevention which the application of topical fluoride is beneficial for individuals who were above 6 years old and at risk of dental caries, to rinse with 0.09% of fluoridated mouthwash in a daily, weekly, or fortnightly basis. Following the development of nanotechnology, the addition of hydroxyapatite nanocrystals in mouth rinses have proven to be effective in reducing the number of *Streptococcus mutans* in plaque and capable to form a protective layer on top of enamel surface that can shield the underlying enamel from demineralisation attacks [32-34]. When hydroxyapatite nanocrystal encounters WSLs, it is able to incorporate minerals into WSLs in depth which can improve the mineral contents in WSLs and further strengthen the existing layer by chemically altering the structure and forming fluorapatite [32,35,36]. Hegazy and Salama [37] conducted a randomized clinical trial to evaluate the effect of hydroxyapatite nanocrystal mouthrinse in remineralising early enamel caries by comparing against the mouthrinse containing fluoride and chlorhexidine. They reported that both the hydroxyapatite nanocrystal and fluoridated mouthrinse showed significant result in remineralising early enamel caries and the effect of remineralisation by hydroxyapatite nanocrystal was noticed one week earlier than fluoridated mouthrinse (0.02%). They concluded that the hydroxyapatite nanocrystal mouthrinse is effective in remineralising early enamel caries lesions. Hydroxyapatite nanocrystal mouth rinse could be a good alternative in managing of early enamel caries. Clinicians need to weight among the efficacy and cost effectiveness of hydroxyapatite nanocrystal mouthrinse in managing WSLs. Therefore, in the author's standpoint, strong research evidences are needed to determine the efficacy and justify the use of hydroxyapatite nanocrystal mouthrinse.

1.2.3 Fluoride varnish

Fluoride varnish tends to stay on teeth surface for a longer period credited to its unique viscous consistency. Hence, fluoride varnish can release fluoride ions for a substantial period on the tooth surface which can promote surface, subsurface remineralisation and formation of a protective barrier around the enamel surface [26,38,39]. In addition, its application is one of the few methods that does not require high patient compliance. Several studies proved that fluoride varnish (Duraphat® Colgate ®, New York, USA) is favourable in treating WSLs. Application of fluoride varnishes over 2-4 applications annually have been reported being effective in caries prevention [25,26,38,40, 41]. Perrini et al. [42] noticed with periodic application of fluoride varnish every 6 months, it reduced the incidence of WSLs on orthodontic patients with moderate or fair oral hygiene. Besides Duraphat®, an ammonium fluoride varnish, (Fluor Protector S, Ivoclar Vivadent, Zurich, Switzerland) which contains of 1.5% ammonium fluoride, equivalent to 7700 ppm is launched in the market. Despite initially having a lower fluoride concentration (compared to Duraphat® contains 2.26%, equivalent to 22600ppm), after setting, the fluoride concentration of Fluor Protector S increases by 4 folds. A study by Sonesson et al. [43] showed positive outcomes with the management of WSLs with ammonium fluoride varnish. They reported the routine application of ammonium fluoride varnish every 6 weeks can reduce the incidents of WSLs by 14%, and lower the prevalence of progressed WSLs during orthodontic treatment. In the author's point of view, it is encouraged to have recent and strong evidence based studies in comparing and evaluating the effect of the different type of fluoride varnishes in the market. This piece of evidence would be beneficial for the clinician in managing WSLs.

1.2.4 Fluoride gel and foam

Fluoride gel application can be carried out by dental practitioners over 2-4 times annually either in 1.23% sodium fluoride or acidulated phosphate fluoride (APF) gel type. Both fluoride gels are applied through the aids of mouth tray. Sodium fluoride gel application has been proven to be effective in managing white spot lesions. It was reported sodium fluoride gel is able to remineralise the white spot lesions. Based on the study by Jamil and El Sharkawy [44] , the use of 1.23% sodium fluoride gel in remineralising white spot lesions can be enhanced with the natural materials such as ginger and honey. Although there was an improvement in the action of sodium fluoride gel in combination with natural material, more studies are required to identify the efficacy of the natural materials in managing white spot lesions. APF gel contains phosphoric acid of pH 3.0 which helps to etch the outer surface of enamel. With the increment in the numbers of pores on the mildly etched enamel, it is expected for the fluoride in the gel to penetrate the body of lesion. Therefore, demineralisation is stopped and remineralisation is promoted [29,45]. Similarly, the APF foam is having same fluoride concentration as the APF gel and its application is done with mouth tray [46]. Molaasadollah et al. [47] reported that 1.23% of APF gel alone or combination use of 1.23 % APF gel and Erbium, Chromium doped yttrium, Scandium, Gallium, and Garnet (ErCr: YsGG) laser can promote remineralisation of WSLs and reduce the surface area of WSLs. However, there is no significant difference in terms of remineralisation of WSLs in the presence of laser radiation compared to using fluoride foam alone. The application of laser irradiation in management of WSLs would be further discussed in this review.

1.3 Casein phosphopeptide- amorphous calcium phosphate (CPP-ACP)

Depending on the preparation, casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) can provide calcium and phosphate, with (CPP-ACFP) or without fluoride, (CPP-ACP) to enamel surfaces. CPP-ACP can promote the solubility of calcium phosphate regardless of pH of the environment. Abundance of calcium and phosphate is detected on the tooth surface when CPP-ACP is in its amorphous state. This inhibits demineralisation and induces remineralisation on the outer and sub enamel surface [48-50]. CPP-ACP can strengthen the crystalline structure of remineralised enamel and reduce the microstrain which can further enhance the protection of enamel to subsequent acid challenge [51]. Additionally, it can reduce rate of demineralisation by increasing the buffering capacity of saliva and elevate the pH rapidly on the affected enamel surface. Several groups of researchers tested the outcome of CPP-ACP in treating WSLs. They found that routine application of CPP-ACP has the potential to remineralise the surface and subsurface of WSLs with or without the additional preparation of fluoride. They also found that CPP-ACP enhances the appearance of WSLs [24,25,52,53]. Karabekiroglu et al. [54] conducted a randomized clinical trial to evaluate the effect of CPP-ACP paste in treating post orthodontic WSLs over a 3 year follow up period. Daily application of CPP-ACP paste, showed reduction in severity of WSLs, *Streptococcus mutans* and *Lactobacillus* bacterial load, and better salivary buffering capacity compared to fluoridated toothpaste, although the finding was not significant. This could be attributed to low patient compliance which was not evaluated in this study. According to manufacturer's instructions, CPP- ACP should be applied once or twice daily and left on the surface of tooth for 2-5 minutes before rinsing and therefore requires high patient compliance. This may have been a confounding factor that could have affected the outcome of this study. Closer monitoring of compliance and higher number of samples are recommended for future randomized clinical trial in evaluating the efficacy of CPP-ACP in treating WSLs. A recent systematic review reported that CPP-ACP and CPP-ACPF were both effective against WSLs during/after orthodontic treatments and was seen to promote remineralisation of WSLs [55].

1.4 Polyols

Xylitol is a type of polyol, an alcohol derivative of sugar, shown to have anti-cariogenic effect. It has been proven to have the potential to reduce the number of *Streptococcus mutans* by disrupting the energy production processes leading to cell death. Xylitol has also been seen to limit plaque formation and bacterial adherence by increasing salivary flow rate and therefore able to inhibit demineralisation and promote remineralisation [56,57]. Turku sugar study conducted in 1976 was the first xylitol human study to demonstrate the relationship of xylitol in caries prevention [58]. Following that several other studies have also demonstrated the effect of xylitol in caries prevention [57,59]. Cocco et al. [59] performed a randomized clinical trial on low, medium and high caries risk subjects. They evaluated the subjects by exposing to low dose (2.5g) xylitol chewing gum daily over a one-year period. Results found significant reduction in patient's caries risk and concentration of salivary *Streptococcus mutans* especially in the incipient caries group. Similarly, in a recent review, Janakiram et al. [60] reported the effectiveness of xylitol in caries prevention, leading to reduction in the decayed, missing, filled (DMF) values and *Streptococcus mutans* counts. The current finding on the use of Xylitol is still immature and further randomized controlled clinical trials are required to identify the frequency of xylitol usage, suitable delivery vehicles, and the exact caries preventive effects of xylitol.

1.5 Probiotic

Probiotic bacteria is defined as live microorganisms, when administered in adequate amounts confer a health benefit on the host [61]. Probiotics work by combining the local and systematic events including adhesion, co-aggregation, growth inhibition, bacteriocin production and immunomodulation. It was also reported that probiotics might be able to reduce *Streptococcus mutans* count, thereby contributing positively to caries protection [62,63]. A study by Gizani et al. [64] showed daily intake of probiotic lozenges did not have significant effect in preventing the development of WSLs during orthodontic treatment. However, using intraoral photography to detect WSLs in this study may potentially introduce error and bias. A recent randomized clinical study in Egypt studied the effect of probiotic chewable table on the plaque, gingival indices, salivary pH, and the WSLs. They found statistically significant difference in improvement of plaque and gingival indices, and the salivary pH reading between the intervention group and control group. The authors inferred that, probiotics play a significant role in oral health improvement and may aid in caries prevention in the presence of fluoride. The potential positive caries prevention effect of probiotics has been discussed and published in recent critical appraisal and systematic reviews [65-68]. There are conflicting opinions in the role of probiotics in prevention of white spot lesions. In the latest systematic review by Pietri et al. 2020 and Hadj-Hamou et al. 2020 suggested that more randomized clinical trials are required to determine the effect of probiotics, the appropriate effective dose and the duration of treatment required in caries prevention.

1.6 Laser

Laser irradiation shows its potential in caries prevention with its capability to decrease enamel permeability by melting the enamel surface and recrystallisation of enamel surface. With laser irradiation, demineralisation of enamel surface can be inhibited [69,70]. The use of carbon dioxide (CO_2) laser irradiation can alter the structure of enamel and form a new structural composition which has better resistance against subsequent acidic attacks [71]. Combination of laser and fluoride have been reported to have synergistic effect in preventing or treating WSLs with a reduction in demineralisation on enamel surface and increase in enamel hardness. This might be explained by crystal growth in the enamel surface when subjected to temperature changes, leading to bigger crystals, and less crystallographic imperfection [72,73]. Yassaei and Motallaei [72] tested the combined use of Er: YAG laser and CPP-ACPF in treating WSLs in an in-vitro study. They microhardness of WSLs were significantly higher in the Er: YAG with CPP-ACPF group against the sole application of Er: YAG laser or CPP-ACPF group. In a randomized clinical trial, Mahmoudzadeh et al. [73] reported that CO_2 laser was effective in preventing WSLs during orthodontic treatment over an observation period of 6-months. In addition, CO_2 laser has the potential to change the subsurface crystalline structure of the enamel, thereby preventing demineralisation. Molaasadollah et al. [47] reported no significant difference with the application of Er, Cr: YSGG laser and 1.23% APF gel in increasing remineralisation of WSLs. This study however had a small sample size and the study was in-vitro study, the results should be evaluated cautiously. With the different outcomes of using laser in managing WSLs, it would be prudent to have robust in vitro studies followed by randomized clinical trials to determine the outcome of laser therapy in caries prevention.

1.7 Ozone

Ozone is a naturally occurring compound, present in the form of gas in the stratosphere. It possesses the ability to destruct cell walls and cytoplasmic membranes of bacteria and fungi leading to cell death [74,75]. Holmes and Lynch [76] reported ozone's potential to convert pyruvic acid, a byproduct of acidogenic bacteria, into acetic acid. The presence of acetic acid can promote remineralisation of incipient carious lesion [77]. A systematic review by Azarpazhooh and Limeback [78] concluded that ozone application is beneficial in the management of incipient caries . Still the evidence is indecisive, and ozone application is not cost effective. A recent clinical study revealed the promising result of ozone application in antibacterial properties. Based on the outcome of the study, ozone application was able to inhibit the growth of the different kinds of *Streptococcus*, *Staphlylococci*, and *Lactobacillus* on the WSLs significantly. Therefore, Makeeva et al. [79] strongly recommended the use of ozone in the management of WSLs. However, there are still uncertainties regarding the efficacy, cost-effectiveness, duration of application, frequency, concentration, and any potential side effects of ozone application. More research required in this field for its effectiveness against WSLs.

1.8 Tooth bleaching

External bleaching has been proposed as one of the treatment modalities for WSLs. It can improve the appearance of WSL.s However, there were reports of reduction in microhardness of the treated WSLs [80,81]. Depletion of calcium and phosphate on treated enamel surface might be the causative factor that leads to the reduction of microhardness on enamel surface. Despite the possibility of mineral depletion post-external bleaching, the depth of the demineralised lesion did not increase significantly [82], and therefore, some researchers suggested the additional use of fluoride with external bleaching [83,84]. Kim et al. [83] compared the efficacy of external bleaching with the use of CPP-ACPF in the treatment of WSLs. They reported external bleaching with CPP-ACPF application can improve the aesthetic outcome of WSLs without lowering the chemical and mechanical properties of WSLs. This might be because the presence of fluoride in CPP-ACPF may increase mineral deposition in the subsurface lesion of WSLs. Similarly, Choi et al. [84] also reported the additional fluoride application with home or in-office external bleaching protocols is beneficial as it can promote remineralisation of WSLs.

2. MICRO-INVASIVE TREATMENT

2.1 Resin Infiltration

Resin infiltration is an intermediary treatment for WSLs. It was launched as ICON®, (DMG, Berlin, Germany) infiltration in 2009 [85]. Before proceeding to resin infiltration, conditioning the lesions with 15% of hydrochloric acid is required. This conditioning procedure will remove 34-58 µm outer enamel surface in depth to allow resin to penetrate WSLs [86,87]. ICON® works through the infiltration of low viscosity resin which consists of triethylene glycol dimethacrylate (TEGDMA). TEGDMA has high penetration coefficient properties which allows penetration into the microporosities of WSLs [88]. Demineralisation can be impeded by occluding the microporosities in WSLs [88]. Besides, resin infiltration is proven to be capable forming an enamel hybrid layer with the treated white spot lesions which has higher resistance against the acid attack than sound enamel [89]. Having a refractive index (RI) of 1.46 which is close to RI of sound enamel (1.62), ICON® is able to enhance the appearance of WSLs immediately after resin infiltration [90]. Several studies have demonstrated the use of resin infiltration in masking WSLs [91-93]. It is shown that aesthetic outcome following resin infiltration therapy has a promising result and good stability in colour for a minimum of 24 months. Therefore, resin infiltration is considerably safe and suitable as a long term management of WSLs [94]. Bourouni et al. [95] appraised the efficacy of resin infiltration in masking post orthodontic WSLs in a systematic review. The authors felt that resin infiltration provided a significantly better outcome in masking WSLs than natural remineralisation and regular application of fluoride varnish. However, more robust clinical data from long-term follow-up studies are required to evaluate the clinical success of resin infiltration as this material is susceptible to staining and secondary caries at margins of WSLs.

2.2 Microabrasion

Enamel microabrasion is one of treatment options to improve the appearance of WSLs, [29,96]. The material needed for microabrasion is hydrochloric acid ranging from 6.6% -18% along with silica carbide particles ranging from 20-160 µm in size [97]. It was proven that microabrasion can modify the optical appearance of WSLs by eliminating the topmost superficial demineralised enamel layer. Demineralised layer on outer enamel would be compacted, producing a dense prism-free region after microabrasion therapy [98,99]. In an in-vitro study, Segura et al. [100] claimed that post microabrasion, WSLs are more resistant against acid challenge and colonization of *Streptococcus mutans*. In a randomized control clinical trial to evaluate the potential of microabrasion in managing WSLs, it was reported that both resin infiltration and microabrasion is capable of improving the appearance of WSLs. The improved WSLs showed good colour stability for a minimum of 12 months [101]. Shan et al. 2021 conducted a randomised clinical trial comparing the efficacy of resin infiltration and microabrasion in managing of white spot lesions, it was shown that both the microinvasive treatment were effective, although resin infiltration had better aesthetic outcome [102]. Despite the positive enhancement in the appearance of WSLs, enamel microabrasion has its limitation. Enamel microabrasion is only effective in improving the appearance of WSLs if and only the lesion depth is not more than 0.2-0.3 µm [13,21,103].

CONCLUSIONS

WSLs are a common problem encountered in dental practice. It is crucial for dental practitioners to be able to manage WSLs. Currently, there is no gold standard in managing WSLs. However, in line with a more conservative approach, dental practitioners should start with non-invasive treatment, followed by minimally invasive options, and, if the WSLs do not respond to first two options, could then proceed with the more invasive treatment options.

Therefore, the present authors recommend starting with the aim to remineralise the WSLs. via patient education, motivation and improving oral hygiene practices and application of topical fluoride using the various preparation and concentrations. However, aesthetic concerns of white spot lesions predominantly dictate the clinical management of WSLs, with patients seeking immediate and significant improvement. As reviewed in this article, clinicians now have various treatment options which are able to bring about immediate aesthetic improvement using microinvasive approaches such as, resin infiltration, microabrasion and external bleaching.

Treatment of professionally applied fluoride varnish or self-administered fluoride mouthwash, CPP-ACP with or without fluoride can be implemented depending on the extension of WSLs. However, the aesthetically concerned WSLs need to take into consideration, because many patients with WSLs would prefer immediate improvement in the appearance of WSLs. Among all the treatment modalities, microinvasive treatment can improve the appearance of WSLs on a single visit. In such cases, microinvasive treatment such as resin infiltration, microabrasion, or external teeth bleaching would be advocated. Nevertheless, instilling a good oral hygiene habits is the most crucial in the prevention of WSLs.

DECLARATION OF INTEREST

The review paper is part of the literature review of the author's MclinDent dissertation report. There is no known conflict of interest.

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