Dentine Hypersensitivity

David G. Gillam
Editor

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Foreword

Dentine hypersensitivity has gained increasing interest in recent years due to several reasons. For example, the success of caries prevention programs and improved periodontal treatment modalities are factors considered to be responsible for an increased number of patients of all ages having more natural teeth than in the past. Consequently, these patients apparently suffer more frequently from what they call "sensitive teeth" (dentine hypersensitivity), mainly after exposure to cold and sweet drinks/food or to tactile stimuli. The quality of life of these patients is markedly compromised, and they may ask the clinician for pain relief. This is a challenge for both the dental clinician and the dental scientific community. It is reflected, for example, in a constantly increasing number of publications in the scientific literature, scientific workshops, and continuing education courses over the past two decades on the topic. It is known that patients with dentine hypersensitivity also exhibit gingival recession, sometimes as a sequel of periodontal treatment. They also experience the loss of enamel, e.g., due to increased consumption of erosive drinks and other acidic food products, extensive tooth brushing with abrasives in the toothpaste, or other factors. This may lead to exposed dentine surfaces, which are a prerequisite for dentine hypersensitivity. However, it should be noted that not all exposed dentine surfaces lead to dentine hypersensitivity. Further light on the topic was provided by the introduction of the hydrodynamic theory, as first proposed by Gysi around 1900 and then further elaborated by Martin Brännström in the middle of the last century. The open dentine tubules on the exposed dentine surface have been considered essential for the fluid shifts in the dentine tubules following thermal, osmotic, or other stimulation, subsequently activating mechanoreceptors at the nerve endings associated with the odontoblast processes close to the pulp. However, not all phenomena can be satisfactorily explained by this theory. For instance, the role of pulp inflammation, tertiary dentine formation, nerve transduction, occlusal stress responsible for cervical abfractions, and periodontal involvement is still being discussed in this context. Thus, further research on dentine hypersensitivity needs a multidisciplinary approach, involving the classical discipline of operative dentistry but also periodontology, endodontics, including pulp biology, immunology, occlusal stress, and the essential aspects of prevention of the condition.

Manufacturers of cosmetics (e.g., toothpaste and mouth rinse products) and dental materials (e.g., dentine adhesives and desensitizing products) have rapidly responded to the needs of both patients and dental professionals by

introducing a wide range of products into the consumer market for the treatment of dentine hypersensitivity. Different approaches to reduce dentine hypersensitivity have been developed; most of these products are based on the concept of covering or obturating the tubule openings on the exposed dentine surface. Both the potential effectiveness and clinical efficacy have often been demonstrated by in vitro studies and mainly short-term clinical trials, respectively. Again, several problems have arisen, for example, the clinical relevance of the in vitro tests used in this context, the mainly limited efficacy of these treatments, with the need for constant application, the lack of pain relief in certain cases, or the question of possible pulp damage induced by certain therapies. Dentine hypersensitivity is a challenge, and this book addresses the challenge posed by this condition. Here, all aspects of dentine hypersensitivity are comprehensively covered and updated. The array of topics ranges from basic research on etiology to treatment modalities and finally to preventive aspects, including patient communication, motivation, and compliance. A group of well-known authors from both clinical and laboratory research, under the wise guidance of David Gillam, have not only provided a compilation of the relevant evidence from the published literature but also critically pinpointed the weaknesses of the presently available information and the missing gaps in our understanding of dentine hypersensitivity. Finally, interesting ideas for the formulation of new products and an innovative design for future studies are presented. Reading this book is certainly a gain not only for researchers but also for the clinician.

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Disclosure Statement

The authors have one or more patents on the bioactive glass formulations and other oral care products and are currently directors of BioMin Technology Ltd, UK.

Contents

1 Introduction and Overview: Statement of the Problem

Martin Addy and David G. Gillam

1.1 Aim and Objective

It is more than four decades since dentine hypersensitivity (DH) was described as "an enigma being frequently encountered but ill-understood" (Johnson et al. 1982). Since this time, the "three R's" of research, writing and review have, considerably but not completely, improved the understanding of DH. This said surveys, in several countries, suggest that DH remains ill-understood by a considerable proportion of dental healthcare professionals (Canadian Advisory Board on Dentine Hypersensitivity 2003; Rao et al. 2010). With respect, it would not seem unreasonable or derogatory to suggest that the topic of DH has received limited attention in dental undergraduate and postgraduate curricula. Also, it would appear the plethora of literature on the subject which has grown enormously over relatively recent years has been read by a minority of dental professionals. The overall aim of this book must be therefore to address this imbalance in the understanding of the problem. Specifically using question-based, section headings, the aim of this first chapter is to provide a brief overview of DH, including current concepts of the condition and possible future innovations in diagnosis, management and treatment. The hoped-for objective is to provide a basis for subsequent chapters and authors to detail specific aspects of the diagnosis, management and treatment of DH.

1.2 How Common Is Dentine Hypersensitivity?

There have been several surveys on the prevalence and distribution of DH in a variety of subject groups (for reviews, see Addy 2000, 2002; West 2006) (Chap. 2), but whether any used selection protocols for classical population based epidemiological studies is open to question. Indeed, some were only from patients attending dental practices or hospitals, or question and answer only based studies and several predated the now agreed definition of the condition and may have included subjects that would be excluded by the said definition: one frequently quoted study was published only as an abstract (Graf and Galasse 1977). This all said, averaging across studies spanning nearly 35 years, that used a dental inspection, suggests that 15% of adults suffer from DH from one or more teeth at any one time, although much lower, 3%, and much higher, >50%, prevalence figures have been published (for review, see West 2006). A recent review on

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the burden of DH by Cuhn-Cruz and Wataha (2014) from the published studies would appear to suggest that the best estimate of the prevalence of DH is 10% with an average of 33% across the studies. Even though DH can be diagnosed in persons at the extremes of age, teenagers to octogenarians, most commonly it appears to afflict young people between 20 and 40 years. Females have been reported to be more commonly affected than males and at a younger mean age but not all data reached statistical significance. Available distribution data mostly indicate four features of DH: canines and first premolars, then incisors and second premolars and finally molars is the order of teeth most affected; left-sided teeth are more frequently afflicted than their right-sided, contra-lateral counterparts; the site of predilection by far is buccal cervical; lesions show little or no plaque (Addy et al. 1987; Fischer et al. 1992).

What is largely missing from the prevalence and distribution data is numbers of teeth affected and range of pain scores experienced per individual. This lack of information makes difficult an accurate judgement of how DH impacts on the quality of life of sufferers (see Chap. 3). Thus, although DH is stated to be a common painful condition of the teeth, do 15% of all populations in developed countries visit the dentist at anyone time to report suffering from the condition? Unlikely! Indeed, do 15% of adults who regularly attend the dentist report voluntarily, as suffering from DH? Also, most unlikely! Furthermore, over many years authors have reported DH to be cyclical, which suggests lesions "self-heal" through tubule occlusion and then restart by tubule exposure: is this really the case? Possibly, but other explanations are available, including seasonal variation in aetiological factors and stimuli, stimuli avoidance tactics by sufferers and periodic self-medication with home use desensitising products: all of these would preclude the need for professional intervention. At this early stage of this chapter, it is apparent that there are important gaps in our knowledge of DH. In summary, prevalence and distribution data associates DH more commonly with younger adults, specific teeth, tooth sides and sites, good oral hygiene, and possibly females. Such information must beg the question: are these associations indicative even supportive of present-day thoughts on the aetiology of DH? Probably!

1.3 Awareness of Dentine Hypersensitivity by Dental Professionals

As previously indicated, DH remains ill-understood by a considerable proportion of dental healthcare professionals (Canadian Advisory Board on Dentine Hypersensitivity 2003; Rao et al. 2010), which can have an impact in the awareness and treatment of the condition in practice. Recent surveys have indicated that DH is poorly understood by clinicians, possibly due to lack of education on the topic at both dental undergraduate and postgraduate schools, although it is evident that this may be changing in some areas of the world. Nevertheless, most surveys still indicate that there is confusion with the underlying mechanism of DH, its prevalence, diagnosis and management (see Chap. 2). Despite the plethora of literature on the subject which has continued to grow enormously over relatively recent years, it is apparent that only a minority of dental professionals show an interest in the topic as most clinicians consider DH to have a limited impact on the QoL of their patients (Chap. 2). Is there still a need for further education on? Definitely?

1.4 Definition and Terminology: Hypersensitivity or Sensitivity?

At an international meeting, DH was defined as: short sharp pain arising from exposed dentine in response to stimuli, typically thermal, evaporative, tactile, osmotic or chemical, and which cannot be ascribed to any other form of dental defect or pathology (Holland et al. 1997). Essentially, the definition is a clinical descriptor of DH as a specific dental condition which needs to be distinguished from other causes of dentinal pain and

- Medicaments (for example, non-encapsulated HCL replacement, chewing ascorbic acid tablets (vitamin C) and acetylsalicylic acid tablets (aspirin), iron tablets, salivary stimulants)
- Occupation (for example, jobs involving wine tasting or working near acidic industrial vapours)
- Sports (for example, improperly chlorinated swimming pools)

There is an increasing body of literature indicating that acid erosion caused by relatively small acidic challenges will lead to loss of enamel and dentine and expose the dentine tubules and initiate DH. This literature included laboratory research (Addy et al. 1987b; Absi et al. 1992; West et al. 1999; Vanuspong et al. 2002; Gregg et al. 2004; Ganss et al. 2009), review papers (Addy and Hunter 2003; Addy 2005; Zero and Lussi 2005; Lussi 2006), clinical research (Absi et al. 1992; Hughes et al. 1999; Hunter et al. 2000; Olley et al. 2012, 2014a, 2015; O'Toole and Bartlett 2017), and prevalence studies (Lussi and Schaffner 2000; Smith et al. 2008; West et al. 2013b).

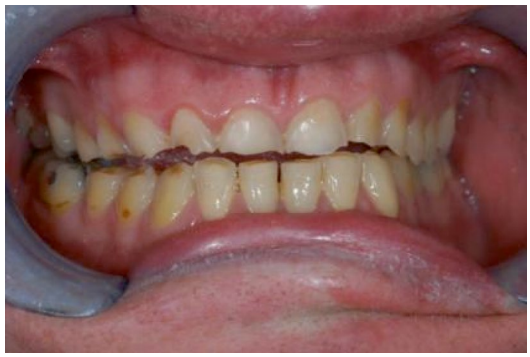

Fig. 4.1 An example of a patient with severe erosion, which has initiated a loss of crown height and an anterior open bite due to gastric erosion

Erosive acid challenges are important in removing the smear layer and pellicle (on the tooth surfaces exposed to saliva) and initiating DH. In two clinical studies, cavities were prepared in dentine, and hydrostatic pressures were applied to the exposed dentine. Patients reported sensations of short sharp pain in those lesions in which an acid challenge was used to remove the smear layer from the surface of the prepared cavity, but not in lesions in which the smear layer was present (Brannstrom 1965; Ahlquist et al. 1994). This can be easily demonstrated in the laboratory. Figure 4.2 shows a high-powered scanning electron microscopy image of the surface of root dentine taken from the buccal cervical region of a premolar tooth. Following treatment of the surface of the dentine with a 6% solution of citric acid under agitation, the smear layer was removed, and the dentine tubules become visible. This work is supported elsewhere (Pashley et al. 1981) (Addy et al. 1987a). Most of the dentine tubules are greater than 1 μm diameter post-acid challenge. This is greater than 0.83 μm, the minimum diameter reported as being required to elicit DH at the cervical area of

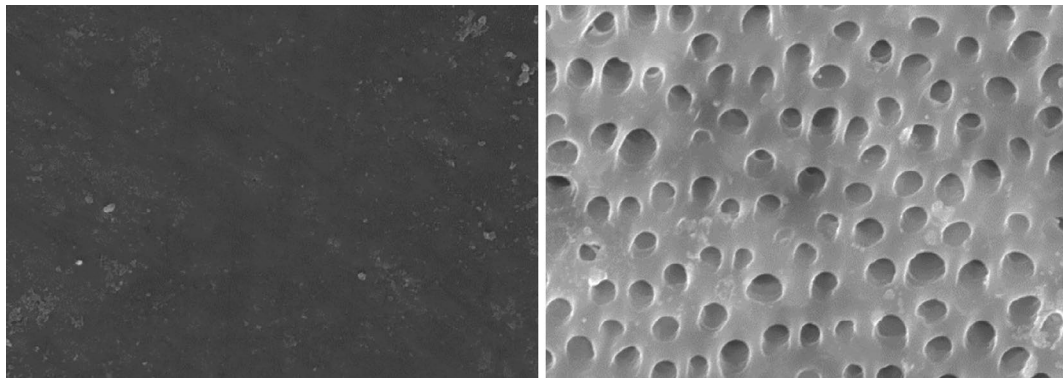

Fig. 4.2 Scanning electron micrograph (SEM) images (×2000) of untreated root surface (left) and root surface following a 1 minute 6% citric acid challenge with gentle agitation (right). Scale bar 2 μm

The importance of a mature salivary pellicle in providing a protective role during erosion must not therefore be underestimated; in particular, the phosphate, calcium, and fluoride content of an erosive challenge may prevent dental wear (Zero and Lussi 2005) and sleeping medications (which may reduce salivary flow) are associated with more reported DH (West et al. 2013a). Currently there is ongoing research in this area and clinical experiments have demonstrated that the salivary pellicle forms a protective layer against erosion (Moazzez et al. 2014).

Regarding the timing of erosion, clinical studies show that DH is more likely if acidic beverages are consumed more recently, within an hour (Olley et al. 2015). It has also been shown that contact time between the tooth and the acid leads to more DH, for example, patients who spent more than 10 min eating fruit per sitting or habits include sipping an erosive beverage or holding it in the mouth (O'Toole and Bartlett 2017).

4.6 Abrasion, NCCLs, and DH

Abrasion is a physical process, which occurs because of the mechanical wear of dental tissues by foreign bodies. Toothbrushing and dentifrices are common forms of dental abrasion (Addy and Hunter 2003; Addy and West 2013). Toothbrush abrasions are influenced by brushing habits, force applied, and the time spent brushing (Hooper et al. 2003). There are additional habits linked to abrasion, for example, onychophagia, clips, and other tools, which may contact the teeth. There is less data than erosion to support the role of abrasion in causing DH, but toothbrushing with a toothpaste has been implicated in the aetiology of DH (Addy and Hunter 2003; Abrahamsen 2005; Bartlett and Shah 2006; Ganss et al. 2009; Addy and West 2013), and more recent studies are identifying a greater role of toothbrushing force and filament type as being important in DH (Sehmi and Olley 2015; O'Toole and Bartlett 2017). A recent systematic review by Teixeira et al. (2020) demonstrates a high proportion of adults in the population with NCCLs and therefore exposed cervical dentine. This study reported that the average prevalence in the adult population for NCCLs is 46.7% and that older individuals were more likely to present with NCCLs (Teixeira et al. 2020). Enamel cervically on the tooth is thinner and hence in patients with extreme abrasion habits (perhaps in combination with erosion), the NCCL lesion will occur sooner, persist longer, and, with ongoing aetiology, continue to increase in size throughout life. Figure 4.3 shows a NCCL caused predominantly by excessive abrasion.

According to Addy (2005), the effects of normal toothbrushing on wear of enamel are negligible and unlikely to lead to exposure of the underlying dentine alone unless erosion is also occurring. Normal toothbrushing, even for extended periods of time (measured in years) will also cause limited wear of dentine and the wear may be limited to the smear layer, which would presumably have a subsequent effect on DH (Absi et al. 1992). Increasing the force of toothbrushing can, in addition, cause increased tooth surface loss in dentine. Manual, as opposed to electric toothbrushing has been demonstrated to cause more dentine wear because of the force applied with a manual toothbrush (Knezevic et al. 2010; Van der Weijden et al. 2011). However, studies have also demonstrated that electric toothbrushing causes more wear than manual brushing (Bartlett et al. 2013). Nonetheless, the type of toothbrush alone is not the only factor in dentine wear. Studies have shown that brushing

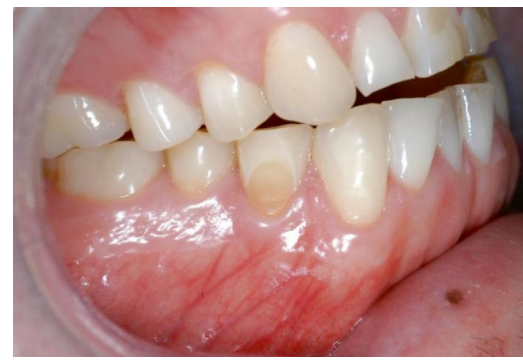

Fig. 4.3 An example of abrasion on the buccal cervical region commonly referred to as a non-carious cervical lesion (NCCL). Clinical features may include aesthetic concerns and perhaps DH

may also remove the smear layer and have been seen in practice to contribute DH symptoms.

Concerning dentifrices, although these are unlikely to cause DH lesion localisation, dentifrices of higher abrasiveness or overzealous use of brushing with dentifrice may initiate more dentine wear and DH lesion initiation by removal of the smear layer and establishment of patent dentine tubules (Addy and Hunter 2003; Sehmi and Olley 2015). Some dentifrices, especially those containing silica, may have a therapeutic effect in preventing DH by partially occluding the dentine tubules over time (Addy and Mostafa 1989; West et al. 2002) and may also contain active ingredients capable of increasing this effect over shorter periods (Olley et al. 2012, 2014a). Due to a reduction in DH symptoms, it has been shown that dentifrices with active ingredients to occlude the dentine tubules may reduce DH irrespective of brushing force applied (Mullan et al. 2017). In these situations, overzealous brushing aetiology may continue, unidentified, to increase the size of the NCCL lesion over time.

4.7 Attrition and DH

Attrition is the physical wear of dental hard tissues due to tooth-to-tooth contact on occlusal or incisal tooth surfaces. In normal function, the teeth only contact for a short period of time for eating or swallowing. However, when this contact occurs at other times, it is termed parafunction or bruxism. This often occurs nocturnally as a form of stress relief (Bartlett and Smith 2000). Although DH is more common on buccal tooth surfaces in association with gingival recession, prevalence studies which have also investigated occlusal surfaces show that the occlusal surfaces also demonstrate DH (Bamise et al. 2008; Olley et al. 2013) (Fig. 4.4). The severity of DH on occlusal surfaces is associated with the severity of tooth wear clinically (Olley et al. 2015).

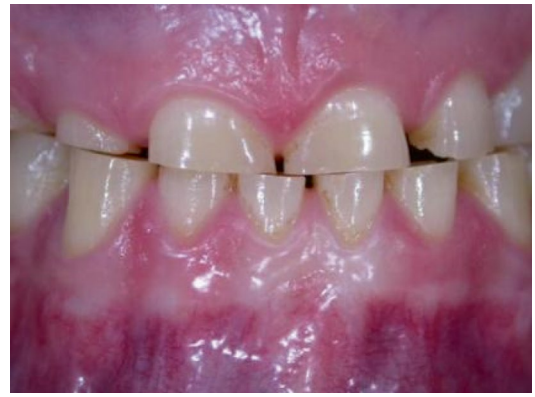

Fig. 4.4 An example of severe attrition associated with bruxism. Note the incisal surfaces are flattened

4.8 Abfraction and DH

Abfraction (later named in 1991) was first suggested by Lee and Eakle (1984) and Grippo (1991). Abfraction was attributed to those tooth wear lesions that could not be explained due to erosion and/or abrasion and which occurred due to occlusal stress, often occurring near to the cervical margin of teeth (Nascimento et al. 2016). As a cause of NCCLs, they have been associated with DH (Addy 2002). Limited inconclusive data, however, supports the correlation between occlusal stress, abfraction, and NCCLs (Nascimento et al. 2016), which will be further explained in relation to the multifactorial aetiology of NCCLs, below. Sarode and Sarode (2013) also challenged the theory behind abfraction lesions in a review indicating that the theory is not proven and that there is evidence against the theory. Some papers globally continue to utilise the term abfraction, perhaps as a multifunctional tooth wear umbrella term for NCCLs. It is therefore important to be aware of the term. Anecdotally, occlusal stress may become more important for lesions that are extremely deep (Nascimento et al. 2016). Here, there is so little tooth remaining cervically due to tooth wear/NCCL (perhaps initially caused by erosion and abrasion) that any excessive occlusal stress, may

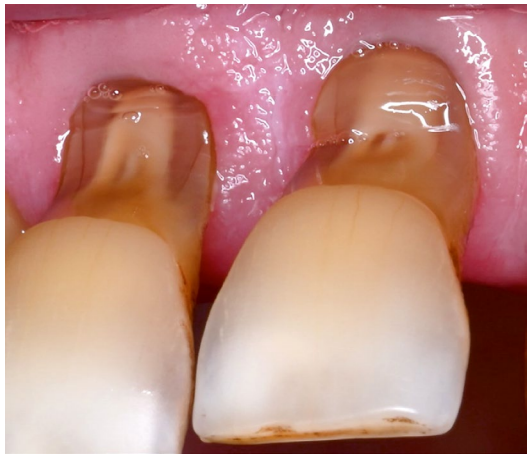

Fig. 4.5 Example of the 'abfraction' lesion misnomer, likely caused initially by Erosion - Abrasion (and referred to commonly as an NCCL). Due to little tooth structure now, occlusal forces may pose a risk for future de-coronation

now not simply be a difficult to prove aetiology of cervical wear, but more likely a risk factor for future de-coronation (see Fig. 4.5).

4.9 Multifactorial Aetiologies of Tooth Wear and DH

In tooth wear, it is unusual that attrition, abrasion, or erosion occur individually and it may be more accurate to describe them, as in a previous review, through dental tribology terminology as two body, three body, and chemico-physical wear, respectively (Addy 2000, 2005). For patients, these wear processes may include oral hygiene practices, dietary habits, stress, and their effects on the occlusion (Bartlett and Shah 2006; Bartold 2006; Shah et al. 2009).

A common multifactorial lesion that may present with aesthetic concerns and/or DH is the NCCL. These often occur on labial or buccal tooth surfaces perhaps due to anatomy and/or effects and degree of brushing force. It has been broadly suggested that NCCLs may be due to chemical degradation of enamel and/or dentine as well as flexural biomechanical loading forces originating from some location distant from the actual point of loading (Glossary of Prosthodontic Terms. 2018). The impact of occlusal forces as a predominant concern in NCCL aetiology might be true, for example, in a deep buccal cervical NCCL with limited cervical tooth tissue remaining and excessive occlusal loading (see also Fig. 4.5). Such a lesion may warrant restoration due to the force from occlusal loading. However, in the case of most NCCLs, such as the one shown in Fig. 4.3, the principal early aetiologies are toothbrushing and toothpaste abrasion often combined with erosion. Indeed, the evidence for predominant aetiologies involved in NCCLs and DH in the published literature have evolved over the last few decades. In 1984, a case study and review reported that the predominant aetiologies were more likely to be due to abfraction, erosion, and abrasion (Lee and Eakle 1984). Subsequently, in 1996, a prevalence study on 1007 dental hospital patients attributed the main aetiologies as erosion and abrasion (Smith and Robb 1996) and erosion has been described as the predominant aetiology (Addy and Hunter 2003). A further recent review of the literature continues to support the notion that NCCLs are multifactorial in nature with erosion and abrasion, as well as perhaps some occlusal forces in particular eccentric loading having an effect in some situations (Bhundia et al. 2019). However, the role of occlusal loading is not fundamental, and the important aetiologies are therefore now more likely to be erosion and abrasion (Bartlett and Shah 2006; Smith et al. 2008). The term abfraction is, as explained previously, misleading, considering the multidisciplinary nature of NCCLs.

Overall, the research would suggest that erosion is most important for DH in both the exposure of dentine and initiation of a DH lesion. If these aetiologies are to be avoided, then the protection afforded to the dentine by the acquired pellicle and the smear layer must play an important role in the transient nature of DH in both NCCL and post-surgical recession. For example, dental erosion often works in synergy with abrasion, in the aetiology of NCCLs and DH (Lussi 2006) and toothbrushing will at the very least remove the acquired pellicle, which has been shown to offer protection against erosion in vitro (Wetton et al. 2006). Combinations of tooth-

showed by João-Souza et al. (2019). As recently demonstrated (Pini et al. 2020) in vitro with a toothpaste formulation containing AmF, $SnCl_2$, and chitosan, brushing itself seems to play an important role in the formation of stannous compounds formed on the surface of the tooth. Also, the viscosity (i.e., the molecular weight) of chitosan also seems to be important for the control of ETW. Chitosan that is too fluid might not reduce tissue loss, whilst chitosan that is too thick could create excessive friction, which is undesirable (Pini et al. 2020). Thus, future studies on the use of chitosan for the prevention of ETW should also be conducted, especially in more complex study designs such as in situ models.

To this day, there is currently no published randomized clinical trial testing the effect of F^-, Sn^{2+}, and chitosan toothpaste in the control of DH. Therefore, twice daily application of self-applied fluoride toothpaste containing either tin, potassium with or without tin, or arginine with calcium carbonate can be recommended for the reduction of DH pain. Nonetheless, there is a need for standardized methodology guideline development to improve the conduct, analysis, and reporting of DH in clinical studies (Pollard et al. 2023).

7.7 Potassium Salts in In-Office Products

One of the most investigated agents to treat DH are those containing potassium salts, such as potassium oxalate (Wang et al. 2016; Osmari et al. 2018; Sgreccia et al. 2020, 2022). The mechanism of action of this product is based on the presence of potassium and the formation of calcium oxalate. Potassium ions can prolong the duration of the repolarization stage of the nerve fibre, which is essential for a stimulus to occur (Nanjundasetty and Ashrafulla 2016). A study by Peacock and Orchardson (1995) demonstrated that 8–16 mM concentrations of potassium ions around axons are necessary to sustain the nerve depolarization. However, there has been a degree of controversy because of its proposed mode of action (nerve desensitization) based on an animal model (Markowitz et al. 1991; Schmidlin and Sahrmann 2013; Boneta et al. 2013). Several investigators have, however, challenged this mode of action as indicated above and have suggested that these formulations may instead be through tubule occlusion and attributed to other constituents (e.g., abrasives or even the presence of fluoride salts) than the potassium ion per se (Addy and Mostafa 1989; Gillam et al. 1996; West et al. 1997; Orchardson and Gillam 2000). Conversely, the oxalate is known to react with calcium and precipitate calcium oxalate, which can occlude the patent dentinal tubules and has been shown to resist a subsequent erosive challenge (Calabria et al. 2014; Francisconi-Dos-Rios et al. 2021) (see also Chap. 6).

Formulations are launched in different vehicles to the dental profession (Fig. 7.1) (Sgreccia et al. 2020, 2022) or for OTC use (Orchardson and Gillam 2000; Lynch et al. 2018; Burnett et al. 2018; Anderson et al. 2020; Chapman et al. 2020), including solutions (Lynch et al. 2018; Burnett et al. 2018) and strips (Amini et al. 2016; Lynch et al. 2018; Chapman et al. 2020). Regardless of the vehicle, potassium oxalate shows reliable and long-lasting effect compared with other occluding products. Along the clinical effect, the self-reported quality of life (QoL) has also been investigated, in which the individuals demonstrate satisfaction once treated with potassium oxalate (Sgreccia et al. 2022). Agheli et al.

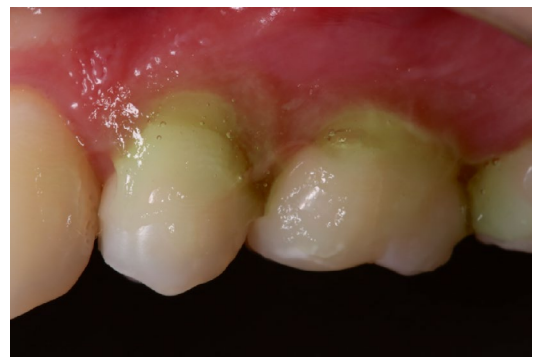

Fig. 7.1 Application of an in-office potassium oxalate gel on sensitive dentine. As recommended by the manufacturer, the product was kept on the exposed dentine for 3 min and removed without rinsing. (Images provided by Dr. Victor Mosquim and Dr. Mariele Vertuan)

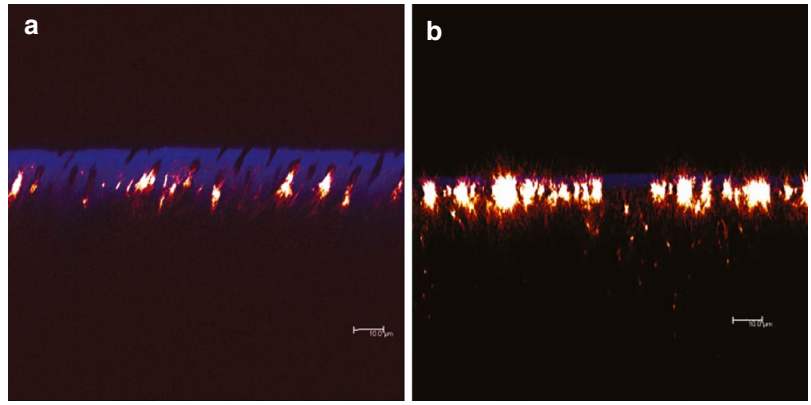

Fig. 7.3 Confocal laser scanning microscopy (CLSM, XZ axis) of dentine treated with 3% potassium oxalate before (**a**) and after (**b**) a citric acid challenge. (Images provided by Dr. Linda Wang, Dr. Marcela Pagani Calabria and Dr. Luciana Fávaro Francisconi-dos-Rios)

However, according to Jackson (2000) and Panagakos et al. (2009), potassium-containing toothpastes are no more effective than regular fluoride toothpastes. Conversely, a systematic review with meta-analysis (Bae et al. 2015) reported that potassium-containing toothpastes were more effective than placebo, and a network meta-analysis also reported that potassium worked better against the symptoms of DH when in combination with stannous fluoride or hydroxyapatite, especially for tactile and air stimuli, with a moderate certainty of the evidence (Martins et al. 2020).

As described above, the focus in most of the earlier desensitizing studies was on toothpaste formulations and relatively few studies have been conducted examining the effectiveness of potassium-containing mouthrinse formulations. Several investigators have reported that these mouthrinse formulations containing potassium nitrate and sodium fluoride (Gillam et al. 1996; Pereira and Chavas 2001), potassium citrate or sodium fluoride (Yates et al. 1998), or a mixture of fluorides (Yates et al. 2004) may reduce DH. Gillam et al. (1996) demonstrated that the 3% potassium nitrate and sodium fluoride mouthrinses significantly reduced DH compared to the sodium fluoride mouthrinse after 2 and 6 weeks of use. Pereira and Chavas (2001) also demonstrated that, after 2 weeks, there were no statistically significant differences between the two groups using tactile and thermal stimuli. At 6 weeks, however, the 3% potassium nitrate and 0.2% sodium fluoride mouthwash demonstrated a significant difference in DH when stimulated by cold air, as compared to the control 0.2% sodium fluoride mouthwash.

More recently, a mouthrinse containing 1.4% potassium oxalate (Listerine Advanced Defence Sensitive, LADS) has been developed (Johnson and Johnson Consumer and Personal Products Worldwide, Skillman and Morris Plains, NJ, USA). There are limited data on its long-term effectiveness on DH with only three published studies (five different randomized clinical trials (RCTs)) (Sharma et al. 2013a, b; Burnett et al. 2018). In two of the studies, the investigators reported that the potassium oxalate mouthrinse significantly reduced DH compared to the negative control groups (Sharma et al. 2013a, b). However, in the study of Burnett et al. (2018), which included three different RCTs, only one of them found that a 1.5% potassium oxalate mouthrinse, and a 2% potassium oxalate + 45 ppm F mouthrinse were superior to the placebo mouthrinse after 4 and 8 weeks. In this publication, the authors discuss the importance of the placebo effect, which has been estimated to be responsible for 20–60% of symptom relief in DH studies. The authors then conclude that, due to the high sensitivity of DH investigations to a placebo effect, further research is necessary to evaluate the effectiveness of this mouthrinse when used as an adjunct to a fluoride-containing toothpaste (Burnett et al. 2018).

Table 10.1 reviews selected commercial and experimental products that claim to remineralize enamel in the early caries lesions (including white spot lesions)

Authors	Type of study	Authors comments
Self-assembling peptides Wierichs et al. (2021)	Systematic review and meta-analysis on the efficacy of a self-assembling peptide compared to any other (placebo) treatment or untreated/ standard control.	"Self-assembling peptides may be a viable option to remineralize enamel caries. However, results should be interpretated with caution due the low number of clinical trials, the short follow-up periods and the limiting grade of evidence."
Gohar et al. (2023)	Randomized controlled trial on post-orthodontic white spot lesions. Biomimetic self-assembling peptides compared to fluoride-based delivery systems:	"The visual assessment using ICDAS reveals that the biomimetic remineralization using self-assembling peptides and the fluoride-based varnish material showed a similar effect in masking post-orthodontic white spot lesions. However, the laser fluorescence using DIAGNOpen showed that the self-assembling peptides reveal higher performance in subsurface remineralization than the fluoride-based varnish material. Therefore, self-assembling peptides are considered a promising material for lesion regression in post-orthodontics white spot lesions".
Atteya et al. (2024)	Randomized controlled clinical trial on the effect of nanosilver fluoride, self-assembling peptide and sodium fluoride varnish on salivary cariogenic bacteria:	"In general, the antimicrobial effect of P11-4 and NSF on salivary S. mutans and Lactobacilli was not significantly different from NaF varnish. P11-4 induced greater reduction more quickly than the two other agents and NSF antibacterial effect was lost after one month. *Clinical relevance*: NSF varnish and P11-4 have antimicrobial activity that does not significantly differ from NaF by 3 months. P11-4 has the greatest antibacterial effect after one month with sustained effect till 3 months. The antibacterial effect of NSF lasts for one month. NaF remains effective till 3 months."
Keeper et al. (2023)	Systematic review and meta-analysis on the effect of self-assembling peptide P_{11}-4 on arrest, cavitation, and progression of initial caries lesions	"Six clinical trials met the inclusion criteria. Results of this review represent 2 primary and 2 secondary outcomes. When compared with parallel groups, use of CR likely results in a large increase in caries arrest (relative risk [RR], 1.82 [95% CI, 1.32 to 2.50]; 45% attributable risk [95% CI, 24% to 60%]; number needed to treat [NNT], 2.8) and likely decreases lesion size by a mean (SD) of 32% (28%). The evidence also suggests that use of CR results in a large reduction in cavitation (RR, 0.32 [95% CI, 0.10 to 1.06]; NNT, 6.9) and is uncertain about lowering merged International Caries Detection and Assessment System score (RR, 3.68 [95% CI, 0.42 to 32.3]; NNT, 19). No studies used Curodont Repair Fluoride Plus. No studies reported adverse esthetic changes. *Practical implications:* CR likely has clinically important effects on caries arrest and decreased lesion size. Two trials had nonmasked assessors, and all trials had elevated risks of bias. The authors recommend conducting longer trials. CR is a promising treatment for initial caries lesions"

(continued)

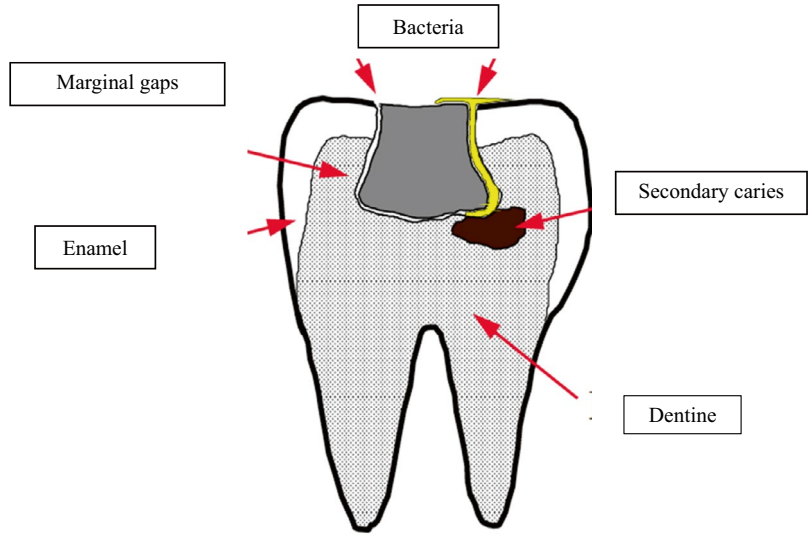

Fig. 10.1 Diagram illustrating the problems with dental composite materials

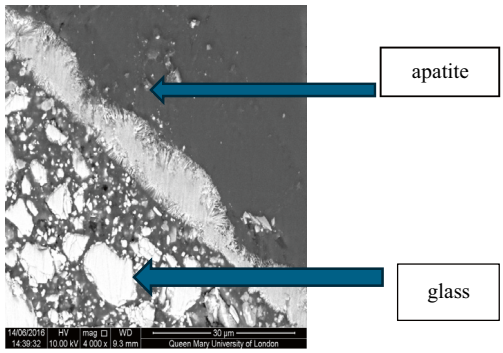

Fig. 10.2 Back Scattered SEM Cross-Section BG Composite ReMin AS pH = 7

tite layer may form in marginal gaps on surface of carious lesions within cracks and voids.

A further study to assess the remineralization potential of a fluoride BAG composite restoration demonstrated the ability to remineralize dental tissue around the restoration. (Figs. 10.3, 10.4 and 10.5).

To summarize Figs. 10.2, 10.3, 10.4, 10.5, 10.6, 10.7 and 10.8, it can be suggested that calcium, phosphate, and fluoride release is possible from a bioactive composite restoration and can result in the remineralization of a carious lesions which could be beneficial in minimally invasive dental procedures such as atraumatic restorative treatment (ART). There is also evidence of the exchange of H^+ for Ca^{2+} resulting in a basic pH particularly in water filled marginal gaps that inhibit acidophilic bacteria as well the presence of apatite formation within the marginal gaps (between the restoration and dentine) resulting in the infill within the gap and potentially stopping bacterial penetration and secondary caries.

A final example of the work ongoing at QMUL is the development of a fluorine containing bioactive glass orthodontic adhesive, see Fig. 10.9.

The ability to prevent demineralisation of teeth during orthodontic treatment is a major advantagem.

10.2 Conclusions

It is evident from reviewing the effectiveness of the available remineralization products that while some of the products appear to be of promise, the consensus from the published reviews such as systematic reviews with/without meta-analysis appears somewhat inclusive. Part of the problem as expressed in several reviews is the lack of standardization of both in vitro and in vivo studies and perhaps this should be addressed in the future.

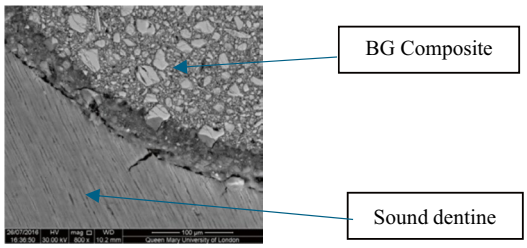

Fig. 10.7 SEM showing sound dentine and the BG composite interface

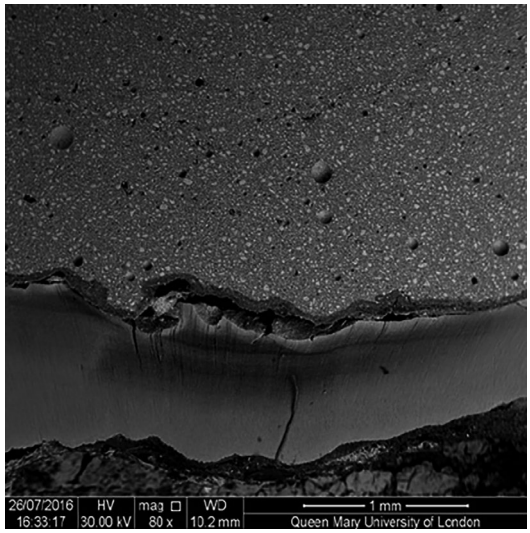

Fig. 10.8 SEM showing the carious dentine BG composite interface

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Future Research

Although the bioactive glasses being developed at QMUL show promise as remineralizing agents, there is a need for further clinical research in well controlled randomized clinical trials.

Disclosure Statement

The authors have one or more patents on the bioactive glass formulations and other oral care products and are currently directors of BioMin Technology Ltd., UK.

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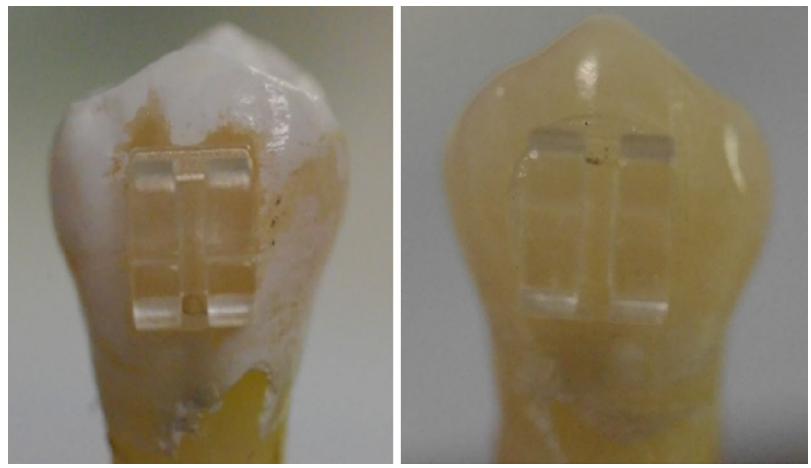

Fig. 10.9 In vitro comparison of a leading inert glass orthodontic adhesive (left) with a novel fluorine containing bioactive glass orthodontic adhesive (right). (Premolars with orthodontic brackets after immersion in artificial saliva pH 4)