

Root Sensitivity and the Possible Treatments with Nanomaterials

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Abstract

Root sensitivity is a common complication that occurs after periodontal therapy. The etiology is multifactorial, which causes the exposure of dentin. The hydrodynamic theory is the underlying mechanism that describes dentin sensitivity. However, the exact mechanism of how root sensitivity occur is still unknown. This review comprises the prevalence, etiology and managements of root sensitivity. The effect of mechanical debridement on the structure of root is also included. Due to the increasing attention in nanotechnology and nanomaterials, the use of nanomaterials in the management of dentin hypersensitivity are reviewed as a part of the management improvement. Finally, the understanding of root sensitivity and the possible applications of nanomaterials in the treatment together with some research questions that may lead to more understanding and more satisfying managements for root sensitivity are discussed.

Keywords: Root sensitivity/ Dentin sensitivity/ Dentin hypersensitivity/ Tooth structure/ Nanomaterials/ Nanotechnology

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Introduction

The aim of periodontal therapy is to create an environment that supports the patient in controlling plaque. Meticulous scaling and root planing are effective treatment modalities.¹ However, a complication of this treatment is gingival recession,² which exposes the dentin on the root surface due to the removal of infected cementum.³ The denuded dentin exposes dentinal tubules, which are the communication route between the oral cavity and pulp tissue, resulting in dentin sensitivity.⁴

Root sensitivity

1. Prevalence

The prevalence of root sensitivity reviewed by von Troil et al. demonstrates that 9-23% of root sensitivity occurs before periodontal treatment, and the prevalence increases to 54-55% after the treatment was performed.⁵ The severity of the root sensitivity increases during 1-3 weeks after periodontal treatment then slowly decreases.

2. Etiology

The etiology of cervical dentine sensitivity is multifactorial arising from exposed dentin. The cause may come from one or combination of following factors such as anatomical gap between cervical enamel and root cementum,

tooth brush abrasion, chemical erosion (extrinsic from acidic food and intrinsic from gastric regurgitation) and gingival recession.⁶ As cementum is thin and softer than enamel, the exposure of the root dentin from gingival recession can enable more rapid and extensive exposure of dentin. The factors involved in gingival recession are advancing age, chronic periodontitis, periodontal surgery, improper tooth brushing, orthodontic trauma, inadequate cervical restoration, dental malalignment, and high frenum attachment.⁶

The mechanism of dentin sensitivity is described by hydrodynamic theory.⁴ The movement of dentinal fluid within dentinal tubules can stimulate nerve fiber, leading to dentin sensitivity. The movement of dentinal fluid occurs when there is exposed dentin along with stimuli, including thermal changes, air blow, exploration, osmotic pressure and chemicals. To apply this mechanism to root sensitivity, it is possible that there is a gap between the enamel and cementum at the CEJ which appears in only 10% of all teeth.⁷

Considering the root structure together with this hydrodynamic theory, the cementum at the cervical 1/3 of the root length, which is commonly affected by periodontal

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treatment, presents acellular extrinsic fiber cementum with a thickness of 50-200 μm .⁸ When scaling and root planing are performed with hand curettes and a piezoelectric ultrasonic scaler, the thickness of cementum 1 mm below the cemento-enamel junction decreases by $22.28 \pm 15.22 \mu\text{m}$ and $13.08 \pm 7.59 \mu\text{m}$.⁹ When calculating the thickness of cementum loss with the thickness of total cementum, it appears that there should be a thin layer of cementum left after scaling and root planing. If root sensitivity occurs according to the hydrodynamic theory, the minimal thickness of cementum that can protect the movement of dentinal fluid is another point of concern. On the contrary, there might be other unknown mechanisms in addition to the hydrodynamic theory under the root sensitivity after scaling and root planing. However, the study of root sensitivity mostly emphasizes on the prevalence. Therefore, the mechanism of root sensitivity and its association with periodontal parameters or root structure is needed to be elucidated.

3. Management

Management of root sensitivity should start with a correct diagnosis. The clinical management comprises of identification and treatment of the etiologic factors. Elimination of these factors by providing the patient with education, such as instruction on tooth brushing techniques and avoidance of dietary acids can lead to the prevention and slow progression of root sensitivity. Once the factors are controlled with the persistent symptoms, desensitizing agents are recommended to manage sensitivity. In general, the actions of the agents are categorized by two mechanisms, which are stabilizing/desensitizing nerve and occluding the exposed dentinal tubules.¹⁰ Commercial desensitizing agents are available as over-the-counter products and in-office treatment. The formers have advantages in the ease of use, convenience of self-application and easier access. However, they might require a long action time, such as several weeks. An in-office treatment is stronger and more powerful. It provides instant relief, but the effects may not last¹⁰.

Numerous desensitizing agents have been incorporated into toothpaste for daily use. Fluoride is known as an essential component adding to toothpaste or mouthwash to remineralize dentin in order to prevent caries. In addition,

fluoride can form calcium phosphorous precipitates, calcium fluoride (CaF_2) and fluorapatite (FAP) within the dentinal tubules, which then decrease the dentin permeability.¹¹ The crystals that occur are partially insoluble in saliva. However, there are various types of fluoride for dentin sensitivity management. As reviewed by Petersson in 2013, toothpaste containing sodium fluoride (NaF), sodium monofluorophosphate (MFP), or amine fluoride (AMF) with a concentration between 1,000 and 1,500 ppm can be simply used for prevention and control of dentin hypersensitivity.¹¹ Bioglass-containing toothpaste (Novamin[®]) showed the ability to occlude tubules of dentin discs and relatively reduce the permeability by 81.5%.¹² It also represented effective occlusion after brushing treatment and immersing in artificial saliva. A randomized clinical study showed that twice-daily brushing with an anhydrous 0.454 w/w stannous fluoride (SnF_2) dentifrice for 8 weeks significantly reduces dentin hypersensitivity.¹³

Various desensitizing agents are used for in-office treatment. Resin impregnation is considered to reduce dentinal fluid flow and can control dentin sensitivity. A study using unfilled bonding agents showed immediate and lasting blockage of sensitivity in both cats and humans.¹⁴ A randomized, double-blind, controlled clinical study in 2017 also confirmed the efficacy of resin-based materials in reducing dentin hypersensitivity for up to 6 months after treatment.¹⁵ In addition, there is a clinical study that evaluated the effectiveness of light-cured, resin-based dentin sealer to treat root sensitivity.¹⁶ The results showed a quick and effective reduction in root sensitivity after periodontal surgery and its desensitizing effect lasted beyond 30 days. Gluma Desensitizer[®] is another desensitizing product used nowadays. A double-blind, controlled, split-mouth designed clinical trial assessed the efficacy of Gluma Desensitizer[®] on dentin hypersensitivity in periodontally treated patients.¹⁷ The result indicated no significant difference between baseline and 4 weeks after treatment and also no significant differences between Gluma-treated group and water-treated control. Another short-term (4-week) randomized, double-blind, placebo-controlled, split-mouth study compared the efficacy of fluoride varnish (Clinpro XT varnish) with Gluma

Desensitizer[®].¹⁸ Both desensitizing agents showed decreased tooth sensitivity from baseline, in which Clinpro XT varnish significantly lowered the sensitivity score compared to Gluma and control. In addition to the desensitizing agents, many studies evaluated the effectiveness of laser or light amplification by stimulated emission of radiations in the management of dentin hypersensitivity. There are various proposed mechanisms of action of certain laser types in the relief hypersensitivity. Nd-YAG laser occludes dentinal tubules, while diode laser acts by coagulating proteins inside the dentinal tubules and blocking dentinal fluid movement.¹⁹

In patients with gingival recession, surgical periodontal procedures, such as root coverage, might be considered. However, the dentist should confirm that patients can follow oral hygiene care to control the condition and the underlying etiologic factors. In this group of patients, the management consists of initial phase of non-surgical periodontal therapy and dentin hypersensitivity treatment followed by re-evaluation of periodontal status and dentin hypersensitivity, then surgical periodontal surgery, including root coverage for corrective phase. Patients should subsequently enter the maintenance phase for supportive periodontal therapy, including follow-up dentin hypersensitivity and motivation for oral hygiene care.²⁰

According to the hydrodynamic theory, blocking the exposed dentinal tubules is an effective way to lessen sensitivity. The size of dentinal tubules is considerable to deal with the properties of materials used. There are three types of dentinal tubule branches; major branches, fine branches and microbranches.²¹ Major branches, 0.5-1.0 μm in diameter, locate at peripheral part of the dentin. Fine branches, 300-700 nm in diameter, are abundant in the root dentin. Microbranches, 25-200 nm in diameter, extend from the dentinal tubules in all parts of the dentin. The character of root dentin surface where there is sensitivity from grinding with bur shows higher numbers of dentinal tubules than those without sensitivity.²² The effect of dentinal tubule occlusion in currently used desensitizing agents is mostly short-term. They may be easily degraded by an acidic condition in the oral cavity or washed out by salivary flow. To find the

effective way for management dentin hypersensitivity, the ideal properties of material should be able to penetrate deep into the dentinal tubule, remineralize the exposed dentin and resist to acid challenge. Nanoparticles have been widely studied as they are candidates for management of dentin hypersensitivity.

Nanoparticles and nanotechnology used in dentistry

Nanotechnology is defined by International Organization for Standardization (ISO) as “application of scientific knowledge to manipulate and control matter predominantly in the nanoscale to make use of size-and structure-dependent properties and phenomena distinct from those associated with individual atoms or molecules, or extrapolation from larger sizes of the same material”.²³

According to the definition provided by ISO, nanoparticles are nano-objects with all external dimensions in the nanoscale where the lengths of the longest and the shortest axes of the nano-object do not differ significantly.²³ If the dimensions differ significantly (typically by more than 3 times), terms such as nanofiber or nanoplate may be preferred to the term nanoparticle. The term nanoscale is defined as the length range approximately from 1 nm to 100 nm.

Nanoparticles can be divided into various types depending on their morphology, size and chemical properties. Based on their physical and chemical properties, nanoparticles may be classified by Khan et al. as carbon-based nanoparticles, metal nanoparticles, ceramics nanoparticles, semiconductor nanoparticles, polymeric nanoparticles and lipid-based nanoparticles.²⁴

To date, nanotechnology has been incorporated in various fields, including dentistry. The research and innovation in nanodentistry will help the treatment in dentistry become increasingly effective. The application in dentistry has been reported in diagnosis, drug delivery, local anesthesia, orthodontic treatment. Moreover, nanomaterials have been incorporated in many types of dental materials such as materials for restoration, impression, dental implant, tissue engineering and dentin hypersensitivity treatment. In addition, various types of nanoparticles have been studied for

the management dentin hypersensitivity in order to improve the mechanical and chemical properties of the materials.

Hydroxyapatite is a major inorganic component of enamel, dentin and cementum. Nano-hydroxyapatite (nano-HA) has been widely studied due to dentin occlusion and remineralization properties. Dentifrices containing two different sizes of nano-HA were used to brush the dentin discs and evaluated for their effect on plugging the dentinal tubules.²⁵ The result showed that both dentifrices containing nano-HA provided better capacity on tubule occlusion and surface remineralization than calcium carbonate dentifrice. However, the plugging rate and atomic percentage of Ca and P of 80 nm nano-HA dentifrice group showed higher than those of 300 nm nano-HA dentifrice. Recently, a systematic review and meta-analysis showed that nano-HA containing desensitizing agent relieved dentin hypersensitivity from evaporation and tactile stimuli better than nano-HA-free treatment or placebo.²⁶ Besides the pure nano-HA, there is an attempt to increase the effectiveness of nano-HA with fluoride. The nano-fluoridated hydroxyapatite successfully penetrated into the dentinal tubules with a higher plugging rate and deeper penetrating depth than nano-HA, which exhibited the potential of this modified nano-HA to be used for treatment of dentin hypersensitivity.²⁷

Mesoporous silica nanoparticles have gained attention in biomedical applications due to their advantage properties, such as high internal surface area, tunable pore sizes and colloidal stability.²⁸ In 2014, an *in vitro* study of mesoporous silica nanoparticles showed that they could almost completely occlude dentinal tubules and seal about 105 μm deep into the tubules.²⁹ Mesoporous silica nanoparticles were also fabricated with nano-HA which effectively occluded dentinal tubules, resisted to acid and did not disturb the immediate bond strength between dentin and self-etch adhesive system.³⁰ Moreover, mesoporous silica was used as a carrier for nano-sized calcium carbonate particles mixed with phosphoric acid in order to develop biomaterials mimicking the dentin components, which precipitate deeper into the dentinal tubules.³¹ This biomaterial enabled Ca^{2+} and $\text{PO}_4^{3-}/\text{HPO}_4^{2-}$ ions to permeate the dentinal tubules and form

biomimetic crystals at the depth of approximately 40 μm with biocompatibility. The animal model in this study also confirmed the efficacy of the biomaterial in growing biomimetic crystals within dentinal tubules without irritating pulp after 70 days of application.³¹

Nano-scaled bioactive glass is another interesting nanomaterial. It demonstrated satisfactory results in total tubule occlusion with continuous homogeneous minerals to a depth of 20.6–24.7 μm .³² Since both bioactive glass and mesoporous silica nanoparticles show effective properties in tubule occlusion, Jung et al. coated mesoporous silica nanoparticles with bioactive glass nanoparticles and studied their effect on dentinal tubule occlusion and mineralization.³³ The coated nanoparticles effectively occluded tubules and formed a membrane-like layer. When the tooth discs were treated with these nanoparticles followed by acid challenge, the material with smaller size and larger surface area was more effective in acid resistance and remineralization. In addition, bioactive glass-coated mesoporous silica nanoparticles demonstrated higher rate of tubule occlusion and faster remineralization than uncoated ones.³³

Polymeric-based nanoparticles were loaded with various chemicals including zinc, calcium and doxycycline to improve the effectiveness for reducing dentin permeability and viscoelastic properties of cervical dentin.³⁴ The polymeric nanoparticles in the study were composed of 2-hydroxyethyl methacrylate backbone, ethylene glycol dimethacrylate cross-linker and methacrylic acid functional monomer. The polymeric nanoparticles themselves have approximately 90% of tubule occlusion after 7 days of application, while zinc-loaded and calcium-loaded nanoparticles increased the percentage of tubule occlusion to be 100%, which reflects the highest reduction of dentinal fluid flow. Moreover, the dentin treated with zinc-loaded nanoparticles showed higher complex modulus values at intertubular and peritubular dentin than those treated with calcium-loaded nanoparticles. Therefore, the results possibly assume that zinc-loaded nanoparticles were effective in dentin remineralization and tubule occlusion. However, doxycycline-loaded nanoparticles failed to show this effect.³⁴

The available desensitizing agents action through either stabilizing nerves or occluding the exposed dentinal tubules. On the other hand, when considering root sensitivity in periodontitis patients, there is the loss of cementum thickness from mechanical instrumentation. Thus, repair and regeneration of cementum may be another possible management of root sensitivity. Nuñez et al. mentioned the role of cementum-related and enamel-related proteins produced by Hertwig's epithelial root sheath cells in the differentiation of cementoblasts specifically in producing acellular extrinsic fiber cementum (AEFC).³⁵ The studies on cementum regeneration have been focused on these proteins, which could induce undifferentiated mesenchymal stem cells into the cementoblast phenotype.³⁵ The type and function of the newly-formed cementum are also important. The regenerated cementum should resemble AEFC, which was responsible for the attachment function and was usually affected by periodontitis.³⁶ Current researches on the cementum regeneration were reviewed as a part of periodontal tissue engineering.³⁷ Various methods were developed including the differentiation of cementoblast progenitors themselves, co-culture several cell types and cell sheet application.³⁶ There is a study showing the possible use of nanomaterial as a scaffold for cementogenic differentiation.³⁸ The author demonstrated that HA bioceramics with the hybrid of nanorods and microrods could promote cell adhesion, proliferation, alkaline phosphatase activity and osteogenic/ cementogenic-related marker expression *in vitro*.³⁸ The study about the efficacy of the nanomaterials to regenerate cementum on the denuded root is challenging due to the availability of blood supply, cell viability and containment of defect. Furthermore, the characteristics and properties of newly-formed cementum *in vivo* are required to be elucidated.

Various desensitizing agents in nanoscale have been shown the effective relief of dentin hypersensitivity. However, long-term follow-up clinical trials and meta-analysis are needed to be confirmed before definitive recommendations will be provided. In addition, the use of nanomaterials on cementum regeneration is another possible approach to treat root sensitivity, which requires tremendous exploration.

Conclusion

Root sensitivity is the common complication occurs after periodontal treatment. The mechanism is explained by the hydrodynamic theory. However, when considering root structure and the effect of mechanical debridement, there are some questions still needed to be answered. The management of root sensitivity is mainly focused on the materials that can either stabilize the nerve or occlude the dentinal tubules. Various studies have been investigated to get the ideal properties of materials, which can occlude the exposed dentinal tubules to a certain depth, resist to acidic condition in oral cavity and remineralize the affected tooth surface. Nanomaterials have become more interesting materials for the management since their nano-size can penetrate into the dentinal tubules with improved properties in acid resistance and remineralization. However, the clinical trials with long-term follow-up are important for the future application in clinical practice.

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อาการเสียวรากฟันและการรักษาด้วยวัสดุนาโน

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บทคัดย่อ

อาการเสียวรากฟันเป็นภาวะแทรกซ้อนที่เกิดขึ้นได้หลังการบำบัดรักษาโรคปริทันต์ อาการเสียวรากฟันเกิดจากปัจจัยหลายอย่างประกอบกัน ซึ่งปัจจัยเหล่านี้ทำให้มีการเผยตัวของท่อเนื้อฟัน กลไกการเกิดอาการเสียวฟันได้มีการอธิบายด้วยทฤษฎีไฮโดรไดนามิก อย่างไรก็ตามกลไกของการเกิดอาการเสียวรากฟันยังคงไม่ทราบแน่ชัด บทความนี้จึงมีการทบทวนวรรณกรรมเกี่ยวกับความชุก สาเหตุ และการจัดการกับอาการเสียวรากฟัน รวมถึงผลของการการอุดหินน้ำลายและเกลารากฟันที่ส่งผลต่อโครงสร้างของผิวรากฟัน ปัจจุบันนาโนเทคโนโลยีได้รับความสนใจเพิ่มขึ้นเนื่องจากวัสดุนาโนมีคุณสมบัติที่ต่างไปจากวัสดุเดิม จึงได้รวบรวมการศึกษาที่พัฒนาการใช้วัสดุนาโนเพื่อจัดการกับอาการเสียวฟัน บทความปริทัศน์นี้ได้อภิปรายถึงกลไกการเกิดอาการเสียวรากฟัน ความเป็นไปในการนำวัสดุนาโนมาใช้เพื่อรักษาอาการเสียวรากฟันและคำถามงานวิจัยที่เกิดขึ้น ซึ่งอาจนำไปสู่ความเข้าใจเกี่ยวกับกลไกการเกิดอาการเสียวรากฟันและการรักษาที่มีประสิทธิภาพมากขึ้น

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