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Desensitizing Agents

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Abstract: Dentin hypersensitivity (DH) is the short, sharp pain derived from exposed dentin in response to chemical, thermal, tactile, or osmotic stimuli which cannot be explained as arising from any other dental defect or disease[1-3]. The development of DH involves two phases: lesion localization and lesion initiation. Lesion localization is the enamel and/or root surface denudation by attrition, abrasion, erosion, and abfraction resulting in the exposure of the underlying dentin, while lesion initiation follows dentine exposure and the dentinal tubules become patent from the pulp to the oral environment[4, 5]. Treatment of DH has two approaches which are removal of the etiological factor and prevention of DH, and application of desensitizing agents. Desensitizing Agents could be applied at home or in office. Desensitizing Agents treats DH by two mechanisms which are disturbance of the neural response to stimulus, and occlusion of dentinal tubules to block the flow of tubular fluid.

Keywords: *Dentin hypersensitivity;* ***Desensitizing agents; Immediate Dentin Sealing; Fluoride; Oxalates; Iontophoresis.***

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I. Etiology of Dentin Hypersensitivity:

Dentin hypersensitivity is mainly due to the exposure of dentinal tubules by removal of enamel and cementum.

II.1. Removal of Enamel:

The enamel layer can be removed by attrition due to occlusal wear, parafunctional habits (bruxism), improper tooth brushing (toothbrush abrasion), erosion from acids (Gastroesophageal reflux disorder - GERD), fracture of crown, abfraction, defective restoration (improper marginal seal) and bleaching.

II.2. Removal of Cementum:

Poor periodontal health due to incorrect tooth brushing and faulty restorations can lead to gingival recession and periodontal disease. This leads to the exposure of the root surface. Once exposed, the thin cementum layer (20 - 25 μm) can be easily removed by periodontal root scaling, abrasive pastes, acidic foods and toothbrushing, exposing the dentinal tubules.

N.B. In about 10% of the individuals, the enamel and cementum do not meet exposing the dentinal tubules leading to hypersensitivity[1].

III. Mechanisms of dentin hypersensitivity:

III.1. Direct Innervation (DI) Theory:

According to this theory the nerve endings enter dentin through pulp and extend up to the dentin-enamel junction (DEJ) and the mechanical stimuli directly transmit the pain. However, there is not enough evidence that can support the existence of nerves in the superficial dentin where dentin is more sensitive[1, 5].

III.2. Odontoblast Receptor Theory:

According to this theory, odontoblasts act as receptors of pain and transmit signals to the pulpal nerves. But this theory has also been rejected because the cellular matrix of odontoblasts is not capable of exciting and producing neural impulses and there is no synapse between odontoblasts and pulpal nerves[1, 5].

III.3. Fluid Movement / Hydrodynamic Theory:

This theory is the most widely accepted theory for dentin hypersensitivity. The theory based on the movement of the fluid inside the dentinal tubules and claims that tubules are open between the dentin surface which is exposed to the oral environment and pulp. Dentin hypersensitivity is made as the result of fluid movement inside the dentinal tubules, which is due to the thermal, physical changes, and osmotic stimuli. This fluid movement stimulates a baroreceptor and leads to neural stimuli. The number of tubules in sensitive dentin more than the number of tubules in non-sensitive dentin. Also, the tubules of sensitive dentin are wider than those in non-sensitive dentin[1, 6].

IV. Treatment of Dentin Hypersensitivity:

IV.1. Removing the Etiological Factor and Preventing Dentin Hypersensitivity[1, 5]:

Etiological Factor	Solution
Improper Tooth Brushing	The patient should be taught the correct method of tooth brushing and avoid the use of abrasive toothpastes.
Premature Occlusal Contacts	Dentin hypersensitivity can be resolved through correction of occlusion or the use of an occlusal splint
Gingival Recession and Periodontal Diseases	Periodontal treatment and root coverage procedures such as graft or positioning

	flap might be adopted to treat dentin hypersensitivity
Exogenous Acids such as carbonated drinks, citrus fruits, yogurt, and dairy products.	The patient's diet concerning the quality and the frequency of consumption of acidic foods should be monitored.
Endogenous Acids that enter the mouth through reflux or gastro-esophageal regurgitation	The patients are recommended to medical referral.

IV.2. Desensitizing Agents:

IV.2.1. Requirements of the ideal dentin desensitizing agent:

- Should be rapidly acting.
- Should has long-term effect.
- Should be harmless to pulp and painless.
- Should be easy to apply.
- Should not stain the teeth[1].

IV.2.2. Classifications of Desensitizing Agents:

IV.2.2.1. Classification based on the mode of administration:

a) At home: this mode is simple and reasonable.

a.1. Desensitizing Tooth Dentifrice and Toothpastes:

Desensitizing toothpastes containing strontium salts, fluorides, calcium phosphates, 8% arginine/calcium carbonate, carbonated hydroxyapatite, and potassium salts.

a.2. Mouthwashes: Mouthwashes used for dentin hypersensitivity are broadly classified into non fluoride desensitizing mouthwash and fluoride containing desensitizing mouthwash.

a.3. Chewing Gums containing potassium chloride and CPP-ACP[1].

About 2-4 weeks after at- home therapies, the degree of dentin hypersensitivity should be reinvestigated. If the pain still existed, the patient should start the next phase of the therapy; in-office therapy[1].

b) In office: This is a complicated and expensive mode but more effective than at home therapy such as varnishes, laser, bonding agents, gels, etc.[5].

IV.2.2.2. Classification based on the mechanism of action:

IV.2.2.2.1. Disturbance of the neural response to stimulus.

Agents that reduce the excitability of the intra-dental nerves, making them less likely to respond to dentinal fluid shifts such as low output power lasers and potassium salts (potassium nitrate and potassium chloride).

IV.2.2.2.2. Occlusion of dentinal tubules and block the flow of tubular fluid.

Treatments that reduce dentine permeability to the extent that stimuli such as air blasts and probing do not cause dentinal fluid shifts that activate the intra-dental nerves. This can be accomplished by treatments that deliver materials such as particulates that occlude the tubules or agents that interact with the oral environment to encourage the formation of mineral in the dentinal tubules can reduce dentine permeability such as fluoride, oxalates, and bonding agents[1, 7].

IV.2.2.2.1. Disturbance of the neural response to stimulus.

a) Low output power (low-level) lasers [(He-Ne) helium-neon and (GaAlAs) gallium-aluminum arsenide (diode) lasers]:

Laser treatment of exposed dentinal tubules provides a non-invasive, pain free and safe treatment[8]. In low output power lasers, a small fraction of the laser's energy is transmitted through enamel or dentin to reach the pulp tissue. It minimizes pain, reduces inflammatory processes, and discharges the internal tubular nerves[9]. Diode laser leads to increase in mitochondrial ATP through bio-stimulation, therefore formation of secondary dentin by odontoblast is enhanced. Moreover, it increases pain threshold of free nerve ending, provides analgesic effect by increase in endorphins[8].

b) Potassium salts:

Potassium salts such as potassium nitrate and potassium chloride are known as nerve-numbing agents. Potassium salts depolarize nerves resulting in transient excitation. Following this transient activation, the excitability of the nerves becomes depressed, making the nerves unresponsive to stimulus[3,7]. *Potassium nitrate* which is available as *aqueous solution, adhesive gel, toothpastes, and mouth rinses* is considered one of the most used agents for managing DH [1,10].

Mode of action:

Diffusion of potassium salts along the dentinal tubules, resulting in an increased extracellular potassium ion concentration that is significantly higher than physiological levels. A sustained depolarized state is achieved, during which few or no action potentials can be evoked, decreasing the excitability of the intra-dental nerve fibers. This is referred to as '*axonal accommodation'*. However, once the potassium ions are within the tubules, they must build up and remain at an elevated concentration for axonal accommodation to occur. If treatment with potassium-containing agents is discontinued, the concentration of potassium ions around the nerve fibers will diminish and sensitivity relief will be lost[1, 4, 10, 11].

IV.2.2.2.2. Occlusion of dentinal tubules and block the flow of tubular fluid.

a) Fluorides:

Fluoride is commonly used in *varnishes, mouth rinses, gels, and dentifrices*. Moreover, it can be incorporated into bioactive glasses to form fluoride-containing bioactive glasses (FBaG). FBaG can form fluorapatite (FAp) instead of carbonated hydroxyapatite[12].

Mode of action:

Fluorides form an insoluble compound calcium fluoride (CaF_2) with the tooth substance. This forms a physical barrier and narrows the diameter of dentinal tubules, reducing its permeability. Moreover, fluoride penetrates the pulp and interferes with its function, lowering its vitality. Thus, it is no longer receptive to pain and a reaction between fluoride and the free ions of some electrolytes, such as calcium, makes these ions unavailable for the normal mechanism of pain conduction [8,13].

Fluoride agents:

Sodium fluoride forms a precipitate that can be removed by the saliva or mechanical scrubbing. Therefore, acid has been added to the formula so that the resultant acidulated sodium fluoride can form precipitates deep in the tubules[1].

Stannous fluoride has the same effect as sodium fluoride. If the precipitate of apatite fluoride forms, it can resist salivary action, tooth brushing and dietary substances' action[1]. Moreover, it causes tubule occlusion by the chemical precipitation of a tin-rich surface deposit that provides nearly complete coverage of the dentine surface[4].

b) Oxalates:

The application of oxalate such as potassium oxalate has dual mechanism in treating dentine sensitivity by blocking excitation of the pulp sensory nerve and occluding patent dentinal tubules. However, potassium oxalate can lead to some digestive disorders so it should not be used for a long term[1].

Mode of action:

The decrease in hypersensitivity after application of potassium oxalate is due to nerve depolarization by K^+ ions and tubular occlusion due to the deposition of calcium oxalate crystals within the tubules[14]. Oxalates have the advantage of insolubility in acid, making them resistant to dissolution after treatment[2].

c) Bonding agents:

Bonding agents exhibit a long-term or permanent effect and can effectively seal dentinal tubules through forming a hybrid layer. The old adhesives formed the hybrid layer through removing the smear layer and etching the dentinal surface so that deep resin tags could be formed. The new adhesives modify the smear layer and incorporate it into the hybrid layer[1].

Gluma desensitizing agent contains hydroxyethyl methacrylate (HEMA), benzalkonium chloride, glutaraldehyde, and fluoride. Glutaraldehyde leads to protein coagulation within dentinal tubules. HEMA causes resin tags to be formed and dentinal tubules to be occluded[1].

Immediate Dentin Sealing:

The immediate application of a dentin-bonding agent after tooth preparation and before impression-taking decreases bacterial microleakage, dentin hypersensitivity, gap formation, and bond strength[15].

d) Bioactive glass:

Bioactive glasses (BGs) are highly biocompatible materials; their active ingredient is calcium sodium phospho-silicate. The use of bioactive glass is a promising treatment for DH due to the formation of a bioactive barrier on dentin surface that has the ability to occlude the dentinal tubules and form a mechanically strong layer of hydroxyapatite on the dentin surface, which can resist degradation by acids[16].

Mode of action:

Dissolution of BG in physiological liquid environments induces the formation of calcium phosphate precipitates which are effective in hard tissue regeneration and remineralization. This effect of Bio active glass may be referred as it forms a hydroxycarbonate apatite (HCA) layer on the surfaces of the particles, and to its ability to occlude dentinal tubules mechanically. The presence of HCA layers over BG particles surfaces allows them to bind to each other and to the walls of dentinal tubule (collagen type I), which enhance their effect on the occlusion of dentinal tubules[1, 6, 12, 17].

e.g., NovaMin® toothpaste.

e) Casein-Phosphopeptide-Amorphous Calcium Phosphate (CPP)-(ACP):

Casein-Phosphopeptide is a remineralizing agent containing amorphous calcium phosphate (ACP) and casein phosphopeptide (CPP) proteins that contains phosphoseryl sequences which is helpful in attaching and stabilizing ACP. CPP-ACP remineralizes the early lesions of enamel subsurface,

therefore, it is effective in prevention and treatment of dentin hypersensitivity. CPP-ACP is incorporated into various oral health care products such as *mouth rinses, toothpastes, tooth mousse and sugar-free chewing gums* [1].

Mode of action:

ACP-CCP complex creates a firm binding with the biofilm on teeth and form calcium and phosphate reservoir as it delivers bio-available calcium and phosphate for remineralization, resulting in occlusion of dentin tubules[18].

RecaldentTM is a special milk-derived protein containing

amorphous calcium phosphate (ACP) and casein

phosphopeptide (CPP). ACP-CCP complex creates a ◎rm

binding with the bio◎lm on teeth and form calcium and

phosphate reservoir, which is combined into both enamel

and dentin surfaces. Due to its ability to block opened

tubules it is recommended in dentin hypersensitivity

e.g., Recaldent™ and GC Tooth Mousse.

f) Middle output power (Carbon Dioxide Laser (CO_2), Nd:YAG, and Er:YAG):

The high-power lasers increase the surface temperature which can result in the complete closure of dentinal tubules after recrystallization of the dentinal surface. Occlusion occurs through coagulation of the proteins of the fluid inside the dentinal tubules. Moreover, absorption of the laser energy by carbonate and phosphate minerals in dentine can lead to the melting of the tubular structure without cracking and results in reducing the permeability and hydraulic conductance[1, 8, 9].

g) Nano hydroxyapatite:

The major advantage of nanohydroxyapatite is its resemblance to the mineral structure of teeth, bioactivity, and biocompatibility. Nanohydroxyapatite has been integrated into products for oral care such as dentifrices, mouthwash, and pastes (such as Desensibilize Nano P) to reduce dental sensitivity by obstructing open dentinal tubules on the surface of the dentin, or for the purpose of promoting the remineralization of enamel by replacing calcium and phosphate ions in the areas from which minerals dissolved, restoring its integrity[19].

Mode of action:

Nano hydroxyapatite promotes tubule occlusion by the deposition and/or penetration of nano-sized particles into the dentin tubules. The particulate nano calcium phosphate exhibits mechanical

obliteration properties twice as good as the traditional calcium phosphate compositions. However, the deposits formed by a hydroxyapatite paste is not resistant to acidic and mechanical challenges[13, 17, 20].

h) Resin modified glass ionomer:

Resin modified glass ionomer provides a physical barrier at the dentin surface which can release fluoride, calcium, and phosphate to the aqueous medium. The two latter are a result of the presence of calcium glycerophosphate in the composition of resin modified glass ionomer based desensitizing gent. The released calcium, phosphate, and fluoride during the erosive challenge, increasing their saturation regarding tooth minerals, thereby reducing the demineralization rate[13].

e.g., Clinpro XT Varnish.

i) Arginine/calcium carbonate (Pro-Argin) system:

The proargin system is composed of a positively charged amino acid at physiological pH (arginine), a source of calcium (calcium carbonate) and bicarbonate as pH buffer[4]. Arginine has the capacity to interact directly and rapidly with the dentine surface. Arginine contains several nitrogen atoms that can carry positive charges making this amino acid cationic over the range of physiological pH values. Cationic molecules have a high affinity for dentine since dentine has a negative surface charge. Cationic agents can also facilitate the attachment of other materials to the dentine surface by charge interactions and hydrogen bonding[7].

Mode of action:

Interaction between calcium carbonate and arginine leads to the formation of positively charged agglomerate by the adsorption of the arginine onto the calcium carbonate forming a surface layer rich in calcium (dentin like material) which binds to the negatively charged dentin surface leading to occlusion of dentinal tubules. Moreover, the arginine–calcium carbonate agglomerate has an alkaline pH which enables the precipitation of calcium and phosphate from dentin fluid and saliva[6,17].

j) Strontium salts:

Strontium is an alkaline metal and shares similar biological and chemical properties with calcium. It has a similar charge-to-size ratio and readily substitutes the calcium in hydroxyapatite within dentine. Strontium salts such as strontium chloride and strontium acetate have been widely used in toothpastes to relief DH pain[4].

Mode of action:

Dentin has a high affinity for strontium ions as the application of strontium onto a dentine surface results in the formation of a very compact continuous layer, composed of a high-density calcium–strontium hydroxyapatite (CaSr HA), which can penetrate and fill the dentinal tubules. The formation of CaSr HA results from an ion exchange between strontium and calcium in the dental

tissues. CaSr HA has enhanced acid resistance. Moreover, strontium ions can alter neural transmission, calm the dentin nerve, slowing the conduction of the odontoblastic process, and relieve pain. Finally, strontium stimulates the formation of tertiary dentin[4,21].

V. Iontophoresis:

Iontophoresis is based on the principle like charges repel and opposite charges attract. By applying charged direct electrical current, concentrated ionized drugs can be driven rapidly into the tissue and effectively reaches to the therapeutic levels by iontophoresis[8].

Mode of action:

Desensitization by iontophoresis has been explained by several mechanisms. The first mechanism proposed is that electrical current produces paresthesia by altering the sensory mechanism of pain conduction. The second mechanism describes that it causes microprecipitation of the precipitates produced by desensitizing agents such as calcium fluoride around the tubules, thus blocking the hydrodynamically mediated stimuli that induce pain[22]. Another mechanism states that iontophoresis acts by influencing ionic motion by electric currents, thus enhancing ion uptake by the dentinal tubules and achieving desensitization[8].

VI. Natural desensitizing agents:

VI.1. Propolis:

Propolis is a natural, nontoxic, resinous substance, which is yellow brown. This is collected by honeybees from accessible parts of the plants. Chemically is made up of phenolic acids in addition to microelements such as aluminum and calcium. Propolis exhibits properties such as anti-inflammatory, antioxidant, antimicrobial, antiviral, antiparasitic, anesthetic, and that of a free-radical scavenger. The flavonoids present as a component of propolis are the main active and reactive agents capable of stimulating reparative dentin formation. This is one of the main factors that enable propolis to reduce dentin permeability efficiently[18,23,24]. Propolis has sustained effect due to stable nature of the propolis deposits[25].

VI.2. Moringa oleifera:

Moringa oleifera could have a promising effect in treatment of DH. This effect could be attributed to the presence of various nutrients in it such as calcium, phosphorus and others that are associated with dentinal tubule occlusion[6].

References

1. Pranati, T., et al., Etiology and Management of Hypersensitivity of Teeth -A Review. Journal of Pharmaceutical Research International, 2022. 34: p. 317-329.

2. Cunha-Cruz, J., et al., Dentin hypersensitivity and oxalates: a systematic review. J Dent Res, 2011. 90(3): p. 304-10.

3. Kanehira, M., H. Ishihata, and M. Saito. Dentin Hypersensitivity: Etiology, Prevalence and Treatment Modalities. in Interface Oral Health Science 2014. 2015. Tokyo: Springer Japan.

4. Wainer, C., How do desensitising agents in dental products work? BDJ Student, 2020. 27(3): p. 43-45.

5. Davari, A., E. Ataei, and H. Assarzadeh, Dentin hypersensitivity: etiology, diagnosis and treatment; a literature review. Journal of dentistry (Shiraz, Iran), 2013. 14(3): p. 136-145.

6. Ali, M.-A.S., M.A. Niazy, and M.A. El-Yassaky, Effect of Application of Natural versus Synthetic Desensitizing Agents on Dentin Permeability. Al-Azhar Dental Journal for Girls, 2021. 8(3-A): p. 355-359.

7. Markowitz, K., A new treatment alternative for sensitive teeth: a desensitizing oral rinse. J Dent, 2013. 41 Suppl 1: p. S1-11.

8. Patil, A.R., et al., Comparative Evaluation of Efficacy of Iontophoresis with 0.33% Sodium Fluoride Gel and Diode Laser Alone on Occlusion of Dentinal Tubules. Journal of clinical and diagnostic research : JCDR, 2017. 11(8): p. ZC123-ZC126.

9. Biagi, R., et al., Laser-assisted treatment of dentinal hypersensitivity: a literature review. Annali di stomatologia, 2016. 6(3-4): p. 75-80.

10. Vlasova, N., et al., Clinical efficacy of hydroxyapatite toothpaste containing Polyol Germanium Complex (PGC) with threonine in the treatment of dentine hypersensitivity. The Saudi Dental Journal, 2022.

11. Zhu, M., et al., The Effect of Calcium Sodium Phosphosilicate on Dentin Hypersensitivity: A Systematic Review and Meta-Analysis. PLoS One, 2015. 10(11): p. e0140176.

12. Dessai, A., N. Shetty, and N. Srikant, Evaluation of the effectiveness of fluoridated and non-fluoridated desensitizing agents in dentinal tubule occlusion using scanning electron microscopy. An in-vitro study. Dent Res J (Isfahan), 2020. 17(3): p. 193-199.

13. Garofalo, S.A., et al., In Vitro Effect of Innovative Desensitizing Agents on Dentin Tubule Occlusion and Erosive Wear. Oper Dent, 2019. 44(2): p. 168-177.

14. Farook, M.S., et al., Comparing the Effectiveness of Different Dentinal Desensitizing Agents: In Vitro Study. BioMed Research International, 2021. 2021: p. 6652250.

15. Samartzi, T.-K., et al., Immediate Dentin Sealing: A Literature Review. Clinical, cosmetic and investigational dentistry, 2021. 13: p. 233-256.

16. Freitas, S.A.A.d., et al., Bioactive toothpastes in dentin hypersensitivity treatment: A systematic review. The Saudi Dental Journal, 2021. 33(7): p. 395-403.

17. Kulal, R., et al., An In-vitro Comparison of Nano Hydroxyapatite, Novamin and Proargin Desensitizing Toothpastes - A SEM Study. J Clin Diagn Res, 2016. 10(10): p. Zc51-zc54.

18. Hongal, S., N. Torwane, and B.R. Chandra shekar, The effect of 30% ethanolic extract of Indian propolis on replica of human dentin compared against commercially available desensitizing agent: A methodological SEM study in vitro. Pharmacognosy research, 2014. 6: p. 113-9.

19. Carrouel, F., et al., Nanoparticles as Anti-Microbial, Anti-Inflammatory, and Remineralizing Agents in Oral Care Cosmetics: A Review of the Current Situation. Nanomaterials (Basel), 2020. 10(1).

20. Kulal, R., et al., An In-vitro Comparison of Nano Hydroxyapatite, Novamin and Proargin Desensitizing Toothpastes - A SEM Study. Journal of clinical and diagnostic research : JCDR, 2016. 10(10): p. ZC51-ZC54.

21. Yang, Z.-Y., et al., Arginine-containing desensitizing toothpaste for the treatment of dentin hypersensitivity: a meta-analysis. Clinical, cosmetic and investigational dentistry, 2016. 8: p. 1-14.

22. Kumar, S., et al., Iontophoresis and topical application of 8% arginine-calcium carbonate to treat dentinal hypersensitivity. Nigerian Journal of Clinical Practice, 2018. 21(8): p. 1029-1033.

23. Kripal, K., et al., Treatment of dentinal hypersensitivity using propolis varnish: A scanning electron microscope study. Indian J Dent Res, 2019. 30(2): p. 249-253.

24. Puranik, M., Y. Harish, and M. Anushri, Herbs: A Good Alternatives to Current Treatments for Oral Health Problems. International Journal of Advanced Health Sciences, 2015. 1: p. 26-32.

25. Purra, A., et al., A comparative evaluation of propolis and 5.0% potassium nitrate as a dentine desensitizer: A clinical study. Journal of Indian Society of Periodontology, 2014. 18: p. 466-71.