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RESEARCH ARTICLE

WISDOM TOWARDS REMINERALIZATION, A LITERATURE REVIEW

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Abstract

Aim/ Objective: The article aims to explore the remineralizing agents used in dentistry, in concern to decrease the occurrence of dental caries.

Background: Human enamel and dentin destruction are subjected to various factors within the oral cavity. Once formed human enamel is biologically irreparable but it is remineralized by saliva. Saliva serves as a provider of Fluoride, Calcium, and Phosphate ions which is responsible for remineralisation. This review aims to traverse the role of enamel and dentine in demineralization, role of Fluoride, Non-fluoride and Herbal remineralizing agents- their mechanism of action, advantages and disadvantages.

Clinical Significance: This review will replenish the interest of the readers in the prompt use of preventive technique thus facilitates in the reduction of dental caries.

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Introduction:-

On a global scale, dental caries is the **foremost predominant** and **persistent** non-communicable disease. It has influenced significantly, both on the healthcare sector and on each person's quality of life. ^[1] The pathophysiology of dental caries could be an energetic process which alternates between stages of demineralization and remineralization, instead of simply a dynamic misfortune of tooth minerals. The equilibrium between pathogenic elements that promote demineralization such as cariogenic bacteria, fermentable carbohydrates, salivary dysfunction and those that promote remineralization such as antibacterial agents, enough saliva, remineralizing ions, determines whether a lesion advances or reverses. ^[2]

Literature has extensively documented the use of fluoride as the principal preventative measure against dental diseases ^[1].

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Methods:-

An extensive search was done on PUBMED, ELSEVIER, GOOGLE SCHOLAR, with the keywords remineralising agents in pediatric dentistry, Non fluoride remineralizing agents, enamel and dentine demineralization, herbal remineralizing agents.

An overview of enamel structure and a detailed explanation of the mineralization process that occurs in salivary fluids and the commercially available remineralizing agents are the goals of this paper.

Enamel and Its Role on Demineralization

Human dental enamel which is an intense, acellular, and avascular tissue. It contains hydroxyapatite (HAP) crystals as an inorganic component (96%), as a result it is acellular, and it cannot be supplanted or repaired consequently if destroyed. Crystal cross section of enamel contains calcium, phosphate and hydroxyl ions. [3] The rise in causticity causes the crumbling of hydroxyapatite crystals within the tooth enamel and the diffusion of ions such as calcium and phosphate. [1] In the oral cavity the carbonate ions can supplant hydroxyl or phosphate ions, magnesium can supplant calcium, and fluoride can supplant hydroxyl ions. Ionic substitution of enamel is a widespread process in demineralization and remineralization cycle. It plays a key role by having a substantial impact on apatite behavior, particularly on its solubility. [3]

Dentin and Its Role on Demineralization

Human dentin is a calcified collagen framework made up of inorganic, organic matrix and water. The organic substance present in dentin is type I collagen, with a tiny amount of non-collagenous proteins (NCPs). Collagen fibrils binds themselves to generate collagen matrix scaffolds which latter helps in mineral production. Non-collagenous proteins (NCPs) are thought to be important regulators of mineralization. Caries and corrosive disintegration initiate dentin demineralization, which uncovered the collagen framework and leads to advance degeneration. [4]

Remineralization

It is the process of replenishing the tooth with minerals in order to prevent decay. Saliva has the capacity to remineralize the demineralized tooth. At some stage in remineralization, fluoride in saliva comes into touch with tooth and replaces the hydroxyl (OH⁻) ion inside the apatite crystal shape, changing hydroxyapatite to Fluorapatite, that's more immune to acidic attacks. The development of newer technologies that encourage enamel remineralization through saliva, but do not rely on fluoride treatments has been discussed here. [3]

Diagnostic Criteria

A preliminary determination can be made using a visual-tactile examination, which may at that point be endorsed and authenticated by the foremost suitable hardware utilizing ICDAS II criteria. Depending on the sort of data advertised, demonstrative tests can be separated into subjective and quantitative categories. Following a clinical examination, radiographs are habitually utilized as the primary help in conclusion, since they give a subjective guess for the specialist. Caries detection dyes are basically applied to assist in caries evacuation. In spite of the availability of variety of applications, Fiber Optic Transillumination (FOTI) is habitually utilized. [5] Light-induced fluorescence gives quantitative data on the area, measure, and bacterial action of the lesion. [6]

Remineralizing Agents

Fluoride

Fluoride, an **anticaries agent** is now discovered in each and every dental product, as it have anticaries activation. [7] Various fluorides which are professionally in-use applied are: Fluoride Varnish, Fluoride gels, Fluoride Foams, and Fluoride dentrifices. Systematic surveys by Benson et al., 2013; Marinho et al., 2003, 2015, 2016; Shahid, 2017 have affirmed that fluoride products helps in avoiding dental caries [2] [8] [9] [10] Studies by Agustsdottir et al., 2010; Dye et al., 2017 showed that despite the regular use of fluoride dentrifices the apparent slowdown in the decrease of dental caries has been ascribed to the reality that diets all over world are changing to incorporate progressively handled and sugary nourishments, diminishing fluoride's repair capacity. [11] [12] Whereas, fluoride and homeostatic components present in saliva are regularly used to remineralize early lesions in ordinary physiological settings, but they are deficient in profoundly cariogenic verbal environments. [2]

Electric field-induced remineralization

One of the various biomimetic mineralization strategies to regenerate hydroxyapatite is the electrophoresis-aided mineralization system. This technique transfers ions more efficiently through gels or liquids. Agarose hydrogels can be utilized to stimulate hydroxyapatite production. This technology specifically permits calcium as well as phosphate ions to travel forward in a single direction in the agarose hydrogels.^[13] Wu et al. 2014 used an electrophoresis-aided biomimetic mineralization system to successfully remineralize, a totally demineralized dentin collagen framework.^[14] Zhang et al. 2018 in his study on electrophoresis and CPP-ACP found that the demineralized enamel floor was absolutely remineralized after 5 hours of treatment.^[15] Khosalim et al 2022 used Graphene oxide (GO) to boost the production of hydroxyapatite with electrophoresis, the blockage of dentinal tubules with tooth enamel like substance on dentin surfaces treated with electrophoresis and Graphene oxide was observed. This demonstrated a promising method for mineralizing dentin biomimetically. ^[13]

Non-Fluoride Remineralizer

CPP-ACP (Casein Phosphopeptide-Amorphous Calcium Phosphate): Created by Eric Reynolds. ^[16] CPP-ACP complexes can diffuse into the damaged enamel body. In addition, CPP has been shown to retain fluoride ions, thereby helping in remineralizing the enamel. CPP-ACP is available under the brand name Recaldent and is used in chewing gum, mouthwash, and candy. There are also commercially available as sugar-free syrups containing RECALDENT™ (CPP-ACP).

Amorphous Calcium Phosphate (ACP) Technology:

Pioneered by Dr. Ming S. Tung. It was first employed in toothpaste called Enamelon in 1999. Yet, one impediment of this is that, the calcium and phosphate particles are not stabilized and they combine to form insoluble accelerates, indeed, before they come in association with enamel or saliva. ^[17]

Self-Assembling Peptide:

Peptide treatment has been illustrated to boost net mineral profit by expanding mineral gain and repressing mineral misfortune within the tooth. P114, a circle of beta-sheet-forming peptides that themselves bring together the three-dimensional frameworks under natural situations, has been found to nucleate hydroxyapatite. The presentation of a biomimetic peptide, inclusive of P114, has the advantage of causing spontaneous, genuine mending, by renewing the mineral itself. ^[16]

Nanohydroxy Apatite:

Due to its Nano sized structure similar to apatite crystals, the Nano hydroxyapatite crystals dissolve faster, allowing for a speedier reaction, resulting in a more compact surface and avoiding further demineralization ^[18]

Bioactive Glass or Bioglass (Sodium calcium phosphosilicate), pioneered by Dr. Len Litkowski and Dr. Gary Hack was commonly marketed as Novamin. It is a biomimetic mineralizer that releases sodium, calcium and phosphorus ions when it enters the saliva. The liberated ions immediately form hydroxycarbonate apatite (HCA) for upto 2 weeks, once formed they bind to the tooth surface aiding in remineralization ^[17]

Dicalcium Phosphate Dihydrate (DCPD) an apatite antecedent that effectively transforms into Fluorapatite within the nearness of fluoride. The DCPD in a dentifrice, boost the quantities of unfastened calcium debris within the plaque liquid, for up to 12 hours after brushing. ^[16]

Tri-Calcium Phosphate is made up of calcium settings and also shows structural similarities with the hydroxyapatite of tooth enamel. When TCP enters saliva, calcium, phosphate, and fluoride ions enter the enamel and induce remineralization. ^[17]

Polyamide, Theobromine and Arginine Bicarbonate:

Poly (amidoamine) dendrimers are manmade proteins with carboxylic acid groups that replicate self-synthesis of amelogenin to guide the creation of HAP crystals. ^[16] Theobromine, the xanthine observed in cocoa (240 mg/cup) and chocolate (1.89%), has been shown to accelerate the enamel crystal growth. Grace Syafira et al. 2012 discovered that theobromine treatment on the enamel surface increased enamel microhardness ^[20] Calcium Carbonate mineral has been found in an aminoacid, namely Arginine bicarbonate. ^[16] Cheng X et al. 2015 found that once blended with fluoride, arginine altogether, expanded fluoride uptake in comparison to fluoride on its own, and lesions dealt with arginine-containing toothpaste additionally contained more fluoride than lesions treated with fluoride toothpaste. ^[21]

Herbal Remineralizing Agents

Xylitol, a sugar alcohol that is not fermentable inhibits plaque's capacity to make acids and polysaccharides, resulting in anticariogenic actions. Xylitol is not fermented by cariogenic microorganisms and consequently does not reduce the pH of plaque, limiting teeth demineralization and bacterial growth

Proanthocyanidin (PA), a polyphenol, found in grape seed extract helps in the transformation of soluble collagen to insoluble collagen. It inhibits *Streptococcus mutans*-produced glucosyl-transferases ensuing in caries inhibition.^[17] Zhao et al [2014] observed that 1, 2 and 3mg/mL grape seed extract diminished the development of artificial enamel caries lesions.^[22]

Milk protein (yogurt) binds to the enamel surface and inhibits demineralization. Lactase also helps reduce the formation of cariogenic microorganism. At an acidic pH, yogurt releases calcium ions that help, to remineralize the tooth enamel. Varghese et al. [2013] showed that yogurt extract prevent demineralization of tooth enamel.^[23]

According to Brighenti et al 2012, **Psidium cattleianum leaf extract (strawberry guava)** contains flavonoids like kaempferol, quercetin and cyanidin, and additionally tannin (ellagic acid), own antibacterial activity. It works by suppressing the glucose metabolism and membrane-related proteins which includes glycosyltransferases in *S.mutans* biofilms, thus preventing demineralization.^[24]

Moringaoleifera (MO) also known as “miracle tree has high mineral and protein content. Moringaoleifera helps with the reconstitution of enamel surface lesions by chemical interplay with teeth minerals and peptide-led remineralization to deposit a new layer of healthy enamel.^[25]

Conclusion:-

Remineralization is the future frontier in dentistry. The main focus is to manage the demineralization remineralization cycle, in order to prevent the consequences of demineralization. The prevention and management becomes possible only by better understanding the demineralization stages and the remineralization drugs used.

Clinical Significance

Fluoride is a commonly used remineralizing agent in dentistry, but in certain situations when there is a chance of excess fluoride exposure, other nonfluoride remineralizing agents can be used. This review will replenish the interest of the readers in the prompt use of preventive technique that helps in the reduction of dental caries.

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