Review Article

Reverse The Adverse: A Review

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ABSTRACT

Dental caries is a major public health problem and is highly prevalent diet related disease. Early detection and intervention of dental caries (before cavitation), can stop and even reverse the caries process. Saliva's natural remineralization process cannot keep pace with altered biological and behavioral factors. As it is said that the fluorides help to prevent dental caries, but due to the increasing prevalence of caries and its severity, treatment with fluoride alone may not be sufficient. To overcome the same problem several technologies have been developed to supplement calcium and phosphate, maintain homeostasis, and to restore the salivary pH. A goal of modern dentistry is to prevent disease progression and improve esthetics, strength and function, non-invasively through remineralization. This article details the various agents that enhance and/or promote remineralization and their clinical implications.

Keywords: Dental caries, Dental enamel, Demineralisation, Fluorides, Remineralisation

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INTRODUCTION

Tooth enamel is the hardest tissue in the human body. It is a crystalline latticework composed of various minerals, the principal component of which is a complex calcium phosphate mineral called hydroxyapatite, which has a general formula of ($Ca_{10}[PO_4]_6[OH]_2$).[1] It is the most common apatite found in mammalian bones and teeth enamel. The rest of the enamel is made up of water and organic matter including proteins and lipids. As enamel is the outer layer of the teeth, it has to withstand a range of physical and chemical changes that include compressive forces (up to about 700 N), abrasion, attrition and importantly acid challenges from plaque and diet.[2,3]

The oral cavity is a combat zone for activities such as demineralization and remineralization. The ratio between remineralization and demineralization is of utmost importance, as it determines the hardness and strength of the tooth structure. The complex chemistry exists between bacteria, diet and salivary components, which result in demineralization of the enamel. Bacterial action on dietary fermentable carbohydrates leads to the production of acids, which diffuses into the tooth and dissolves the carbonated hydroxyapatite mineral a process called demineralization. A decline in the pH in the oral cavity results in demineralization and the oral environment becomes under saturated with mineral ions, relative to tooth's mineral content. If the demineralization phase continues for a longer period, excessive loss of minerals, leads to loss of the enamel structure and at the end cavitation. When the pH rises, the reverse takes place, resulting in the deposition of mineral back to the tooth structure.[4] Thus, remineralization is defined as the process whereby calcium and phosphate ions are supplied from a source external to the tooth to promote ion deposition into crystal voids in demineralized enamel to produce net mineral gain.

The process of remineralization have been studied over many decades of research and has led to the development of technologies that can promote enamel remineralization and reduce enamel demineralization thus giving potential oral health benefits.[5] This article provides an outline of various available agents and their roles in the remineralisation of tooth structure as well as their modes of action and clinical implications.

REMINERALIZING AGENTS

Fluoride

Fluoride has long been known to be effective in protecting the dental enamel from caries by reducing enamel dissolution and enhancing enamel remineralization processes, and is introduced into the oral environment via self (e.g., dentifrices, rinses) or professional applications (e.g., varnishes, foams, and gels fluoride-releasing restorative materials).

During the process of demineralization of enamel, apatite is reduced to simpler compounds or ions and apatite can be reformed during the process of remineralization. Apatite is the most stable and least soluble form of calcium phosphate compounds and its formation during mineralization, is therefore, desirable. One of the most important actions of fluoride is its ability to increase the formation of apatite during remineralisation. Brown *et al.*[6] suggested that due to its ability to enhance remineralization of carious enamel, the outer layer of the apatite crystal may take up fluoride that gets incorporated into the new crystal structure in increased amounts to form fluorapatite. This remineralized enamel will thus be more resistant to future demineralization than the surrounding unaffected enamel.

Several mechanisms have been proposed to achieve the anti-caries effects of fluoride, including the formation of fluorapatite, the enhancement of remineralization, interference with ionic bonding during pellicle and plaque formation and the inhibition of microbial growth and metabolism.[5] Fluoride can be used along with other components such as sodium, zinc, tin, titanium. The newly introduced titanium fluoride (TiF) exhibits enhanced uptake of calcium and TiF pretreated enamel also shows decreased loss of calcium during demineralization.[7]

Bioactive Glass

Even though, the fluorides are still the keystone of non-invasive dental caries management, many of the alternative methods to the fluoride have been developed and extensive research is still going on for the same.[8] In recent times, bioactive glass materials have been known to many fields of dentistry. This material has several distinctive features; the most significant among them is its ability to act as a biomimetic mineralizer, matching the body's own mineralizing traits. Bioactive glass was considered as a step forward in remineralization technology.[9] Bioactive glass consists of minerals that occur naturally in body fluids and it reacts when it comes in contact with water, saliva or body fluid to release calcium, phosphorous, sodium and silicone ions in such a way that it results in the formation of hydroxyapatite crystals (HAP).[10] An important finding in the remineralization concept was the effect of the concentration of calcium ions on the remineralization process.

CALCIUM SODIUM PHOSPHOSILICATE

NovMin™, a bioactive glass, containing calcium sodium phosphosilicate, which comprises of 45% SiO_2, 24.5% Na_2O, 24.5% CaO and 6% P_2O_5 that result in the formation of new hydroxyl carbonate apatite crystals.[11] There is some evidence of desensitizing actions of NovaMin™, as seen in a 6 weeks clinical trial[12] and some evidence regarding reductions in plaque and gingival index.[13] An unpublished data[14] describes a laboratory study employing enamel slabs and pH cycling that compared two dentifrices, both containing fluoride at a level of 1100 ppm, but with the NovaMin test product, containing 5% by weight bioactive glass particles in place of an equivalent amount of silica abrasive as a control. There was progressed execution of the NovaMin product in mineral gain compared with the control. NovaMin has been incorporated into a number of products, such as dentifrices and gels. One of these dentifrices is Oravive Tooth Revitalizing paste™, which is explicitly free of fluoride. Recent data suggest only a low bioavailability of calcium and phosphate from NovaMin.

CASEIN PHOSPHOPEPTIDES (CPP)

CPP are milk products containing the cluster sequence-ser (P)-ser (P)-ser (P)-glu-glu-bind fluoride as well as calcium and phosphate, and thus can also stabilize calcium fluoride phosphate as soluble complexes. They are used alone or as amorphous calcium phosphate (ACP). Clinical studies of mouth rinses and dentifrices have provided synergistic effect between CPP-ACP and fluoride. For example, addition of CPP-ACP to fluoride mouth rinse increases the incorporation of fluoride into dental plaque. A dentifrice containing CPP-ACP with fluoride provides remineralization, which is superior to both CPP-ACP alone and to conventional and high fluoride dentifrices.[15] This synergy between CPP-ACP and fluoride had been identified in laboratory studies using GC MI Paste/Tooth Mousse, which showed that Tooth Mousse without fluoride remineralized initial enamel lesions better when applied as a topical coating after the use of a fluoride dentifrice.[16] Addition of CPP-ACP complex into restorative dental materials can be a potential area for further research. Some researchers have already added CPP-ACP into glass ionomer cements (GIC) and have concluded after their *in-vitro* study that GIC containing CPP-ACP provided increased protection to dentine during acid attack.[17] CPP-ACP has also been added to dentifrices, mouth rinses, chewing gums, lozenges, and bovine milk. A study by Walker *et al.*[18] found that although milk contains casein phosphate, addition of CPP-ACP results in enhanced remineralization. A dose of 5 g of CPP-ACP produced 148% more mineralization compared with 2 g of CPP-ACP per liter of milk.

TRI-CALCIUM PHOSPHATE (TCP): A NEW APPROACH

Functionalized TCP helps in controlling the delivery of phosphate and calcium ions to the teeth, it works synergistically with fluorides without any unwanted interactions with fluorides during storage of the product. TCP is a moderately soluble antecedent to HAP, and is specially prepared to co-exist with fluoride in both aqueous and non-aqueous product forms. It is designed for a particular fluoride vehicle (e.g., dentifrice or varnish), and to create a functionalized TCP ingredient it is milled with pure organic materials. This process ensures that preceding utilization, the active calcium sites are shielded from premature interactions with fluoride, which could otherwise render both calcium and fluoride inactive. Since the structure of TCP is similar to hydroxyapatite, once the functionalized calcium ions are released, they readily interact with the tooth surface and subsurface. Functionalized TCP can offer optimal benefits when delivered in a neutral pH environment while other calcium phosphate added substances may require an acidic pH, which could restrict the benefits to the tooth.[19] As functionalized TCP is less soluble relative to other forms of calcium phosphate,[20] when applied as a dentifrice in formulation with fluoride, this TCP ingredient can enhance mineralization and help build a high-quality, acid-resistant mineral without the need of high levels of calcium. It has been stated that the organic coating prevents undesirable interactions with fluoride that might dissolves away when particles come in contact with saliva. Particles of TCP or TCP alloys can be covered with sodium lauryl sulfate or other surfactants, or with carboxylic acids (such as fumaric acid), polymers and copolymers. This is the premise for the 3M Espe ClinPro™ fluoride dentifrices. According to the manufacturer, this naturally altered TCP technology ought to work best as a remineralizing agent at neutral or slightly alkaline pH. There is some research evidence utilizing bovine enamel models, which show increased surface micro hardness and fluoride incorporation into the outer layers of the enamel.[21]

XYLITOL

Xylitol is a commonly used sugar substitute. The most common way for xylitol delivery has been chewing gum,[22] as chewing gum is considered as a most common habit in many countries. It has been also reported that chewing sugar-free gum have beneficial effects, particularly in reducing caries. A study conducted in Turku, Finland, evaluated the effectiveness of xylitol on dental plaque reduction. Xylitol has been widely researched and universally acknowledged as a characteristic sweetener approved by the US Food and Drug Administration and the American Academy of Pediatric Dentistry.[23] The mechanisms of action include enhanced remineralization of the enamel by acting as a carrier for calcium ions into white spot lesions.[24] Funoran, a high molecular weight sulfated polysaccharide extracted from the red seaweed Gloiopeltis furcata has been demonstrated to inhibit cariogenic and periodontopathic bacteria, and thus contributing to the prevention of periodontal disease and dental caries.[25-27] Chewing gum containing funoran and calcium hydrogen phosphate has a remarkable ability to enhance remineralization throughout all layers in initial caries-like enamel lesions *in-vitro*.[28]

During the period of xylitol use the caries preventive effect was observed to be long term in relation to the teeth erupting.[29] Despite of the abundant literatures available, there is a need for extensive research to understand the exact mechanisms of action, the effect of xylitol on the plaque-saliva distribution of mutans streptococci and the clinical significance of xylitol resistance. Furthermore, suitable delivery vehicles for xylitol and the degree to which xylitol can be "diluted" with different polyols without losing the caries-preventive effects must be determined efficiently.

OZONE

Ozone is the layer of earth's stratosphere which shields us from the harmful sunlight that causes skin cancers. It is a chemical compound, which is an effective oxidizing agent. It acts by attacking thiol groups of cysteine amino acid and annihilates the cellular membrane of carious bacteria.[30] Ozone can shift microbial flora from acidogenic and aciduric microorganisms to normal commensals permitting remineralization to occur.[31] Presently HealOzone (KaVo GmbH, Germany) remineralizing solution consisting of xylitol, fluoride, calcium, phosphate and zinc is approved for the treatment of caries. It can be used as 2100 ppm of ozone ± 5% at a flow rate of 615cc/min for 40 s.[32] It has been proposed that tooth remineralization might be promoted with the assistance of salivary minerals and usable fluorides or remineralizing chemicals, bringing about a tooth surface that is more impervious to future acid attacks. The mechanism of Heal Ozone's action is related to ozone's strong antimicrobial properties and its capability to oxidize proteins associated with the dental caries process.

CONCLUSION

The awareness about oral health is increasing in present days. Most of the patients are now shifting from the curative to preventive health care. The increasing demand about the same made it clear that there are needs of another agents, which can work together with fluorides in achieving the desired goal of caries prevention. Achievements in the concept of bone repair and regeneration by bioactive materials were the inspiring base for gaining the same results to maintain the health of tooth enamel. These agents played significant role in the prevention of dental caries in modern dentistry and aimed at controlling the demineralization/remineralization cycle, depending on the microenvironment around the tooth. The oral care providers should change their treatment plan from curative to preventive aspects with the help of these simple remineralization tools, techniques and products. This will help in maintaining the hard tissue health throughout the patient's life.

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