Journal of Dentistry and Oral Care Medicine
Volume 5 | Issue 2
ISSN: 2454-3276

Review Article Open Access

Remineralization Activities of Bioactive Materials and Nanotechnological Products Used in Pediatric Dentistry

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Citation: Oznurhan F, Keskus B (2019) Remineralization Activities of Bioactive Materials and Nanotechnological Products Used in Pediatric Dentistry. J Dent Oral Care Med 5(2): 201

Received Date: October 07, 2019 **Accepted Date:** December 17, 2019 **Published Date:** December 19, 2019

Abstract

Tooth decay is a progressive disease caused by acid fermentation of carbohydrates by pathogenic microorganisms in the mouth, leading to demineralization of teeth. Many factors such as diet, socioeconomic and sociocultural level, individual risk factors, and hygiene habits of the patient play a role in caries formation. There is a dynamic balance between pathological factors (demineralization) and protective factors (remineralization) in formation of dental caries. It is important to maintain this balance in prevention of dental caries and in the recycling of the caries process at a certain level. In order to prevent tooth decay, especially in children, it may be necessary to manage nutrition and oral hygiene education as well as applying protective agents by the physician. Fluoride is known as the most widely used caries prevention agent in dentistry. Fluoride has led to the search for alternatives as a result of disadvantages as well as NaF varnish deficiencies. The purpose of this research is to evaluate the remineralization activities of bioactive materials and nanotechnological products offered as an alternative to fluoride.

Keywords: Remineralization- Demineralization; Non- Fluoridated Agents; Casein Derivatives

Introduction

Demineralization is a reversible chemical process defined as mineral loss in enamel caused by acid attacks caused by food or bacteria. When appropriate media is present in the mouth, minerals such as calcium and phosphate precipitate again on the enamel surface and this process is called 'remineralization'. When the equilibrium is deteriorated during the demineralization cycle, the loss of minerals on the tooth surface increases and the first stage of caries formation occur [1]. Remineralization agents are used to protect tooth tissue and to stop the progression of caries. Fluoride is known as the most widely used caries prevention agent in dentistry. Fluoride has led to the search for alternatives as a result of disadvantages [2,3] as well as NaF varnish deficiencies [4]. The purpose of this research is to evaluate the remineralization activities of bioactive materials and nanotechnological products provided as an alternative to fluoride.

Methodology

Source of Data

The bulk of this evidence based review will deal with contemporary nonfluoride technologies. A search of articles from "PubMed" and "Medline" and databases like Google and Google scholar with the keywords remineralization, demineralization, and nonfluoridated demineralizing agents was conducted in the month of September 2019. We retrieved a total of which 105 articles that discussed current technologies of nonfluoridated demineralizing agents were read and 44 most relevant articles were included in this paper.

Literature Review

Tooth enamel is a translucent, hard tissue that protects the dentin-pulp complex from external factors. Enamel plays an important role in providing function and aesthetics. Compared to other tissues, enamel is the hardest and most mineralized tissue in the human body [5,6].

Initial enamel caries is the first stage of the caries lesion, where it is possible to stop and treat the lesion. These lesions are usually seen in the region of the cole (Figure 1), although the superficial structure of the lesion is more porous than healthy enamel, a

solid, uninterrupted surface is felt in the examination by catheter [7]. In enamel, demineralization-remineralization is a dynamic physicochemical process that occurs when the oral bacteria form a biofilm on the enamel surface and breaks down the fermentable carbohydrates and the cycle of the response to it [8].

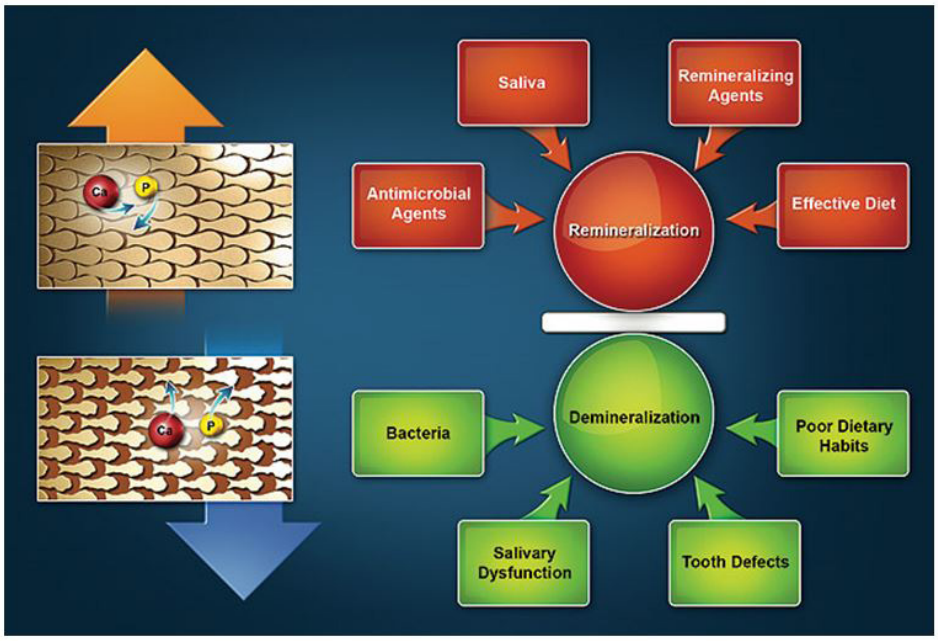

Figure 1: Illustration showing factors affecting the remineralization/demineralization process in the oral environment [9]

To treat initial caries without drilling some remineralization agents were used for this purpose

Remineralization Agents Used in Pediatric Dentistry

-Fluorine, Fluorine Compounds and Ions
a. Fluoride
b. Titanium Tetrafluoride (Tif4)
c. Silver Diamine Fluoride
d. Ammonium Hexafluorosilicateto
e. Silver Ion
- Plant Based Agents
a. Green tea
b. Coffee
c. Propolis
d. Cocoa
e. GallaChinensis
- Chitosan
- Ozone
- Probiotics

Bioactive Materials and Nanotechnological Products

a. Calcium Phosphate
1) Tricalcium Phosphate
Nano - B - Tricalcium Phosphate
2) Amorphous Calcium Phosphate (ACP)
I. Casein Phosphopeptide - Amorphous Calcium Phosphate (CPP - ACP)
II. Nanoparticulate Amorphous Calcium Phosphate Composites
3) Dicalcium Phosphate Dehydrate
4) Trimetaphosphate Ion
b. Hydroxyapatite
c. Bioactive Glasses (Calcium Sodium Phosphosilicate)
d. Calcium Carbonate Carrier – Sensistat

Disadvantages of Fluoride

Fluorine and its derivatives are highly effective on flat surface decay; however, its effect is limited on pit and fissure caries. High levels of fluoride are not recommended because of toxic potential [10].

Ideal Requirements for Remineralizing Agents

- Can diffuse under the outer surface or transmit calcium and phosphate under the outer surface
- Excessive amount of calcium should not release
- Does not support the formation of calculus
- Can be applied at acidic pH
- Can be used in xerostomiato increase the remineralizing properties of saliva
- The new material should benefit more from the fluoride effect [11].

Bioactive Materials and Nano technological Products

Calcium Phosphate

Since calcium phosphate particles are one of the main inorganic components of dentin, they are among the promising materials for remineralization [12]. Commercially available pure calcium phosphates are not suitable for use in remineralization studies due to their low activity and penetration in the lesion depending on their particle size. However, in the use of nano-sized calcium phosphates, demineralized dentin has been reported to increase the existing surface area for the regulation of the organic matrix [13].

Tricalcium Phosphate (TCP)

It is available in different forms, such as tricalcium phosphate (TCP), alpha tricalcium phosphate (α-TCP) and beta tri-calcium phosphate (β-TCP). The main problem with the use of TCP-containing remineralization products is the formation of calcium-phosphate compounds or calcium-fluoride compounds in the presence of fluorine in the medium. This partially reduces remineralization by reducing the concentration of free calcium and fluorine in the medium. In order to prevent this undesirable situation, TCP may be used in remineralization agents at less than 1% or by combining with ceramics such as titanium dioxide or other metal oxides. Another technique is to coat the particles that make up TCP with surfactants such as sodium lauryl sulfate, carboxylic acid, polymers or copolymers [14].

Nano - β - Tricalcium Phosphate

Shibata *et al.* [15] exposed carious human molar teeth with colloidal hydroxyapatite and β-tricalcium phosphate solutions for 10 days and evaluated their mineral density and micromechanical properties in their *in vitro* study. It has been shown that dentin elastic modulus and mineral density increase after remineralization in samples immersed in β-tricalcium phosphate more than those immersed in hydroxyapatite. However; they reported that mineral density alone was not an indicator of mechanical properties because the increase in mineral density was not commensurate with micro-mechanical recovery.

Amorphous Calcium Phosphate (ACP)

ACP is the initial solid phase which precipitates from the supersaturated calcium phosphate solution. They are used in many sides of dentistry because of their excellent bioactivity, high cell adhesion, non-cytotoxic and osteoconductive properties [16,17]. Octacalcium phosphate or apatitic products such as stable crystal phases can be easily converted to the formation of apatite in bio mineralization is thought to play a role as a transient [18,19].

Ning *et al.* [20], applied calcium phosphate loaded agarose gel for 10 days to non-carious human permanent third molar teeth after the demineralization process and showed that dentin surface was completely covered with hydroxyapatite crystals

Casein Phosphopeptide - Amorphous Calcium Phosphate (CPP - ACP)

Casein phosphopeptide in CPP-ACP complex provides phosphate and calcium ions by stabilizing the amorphous calcium phosphate for remineralization of dental hard tissues with its phosphoserine [21,22].

Cao *et al.* [23] kept dentin specimens of non-carious permanent third molar teeth in CPP-ACP solution for 10 days after demineralization process and showed the formation of hydroxyapatite crystals in the collagen fibrils of phosphorylated dentin in their study .In the light of the data obtained, it has been reported that CPP-ACP has the potential to induce biomimetic remineralization.

Rachiotis *et al.* [22] showed that when CPP-ACP applied to sound dentine it inhibits demineralization and when applied to artificial carious dentine it increases remineralization. Therefore, they recommend the application of CPP-ACP in the prevention of dental caries.

Nano-particulate Amorphous Calcium Phosphate Composites

Calcium phosphate filler embedded composites are materials that can remineralize dental caries by releasing calcium and phosphate ions [24,25]. Conventional calcium phosphate composites contain calcium phosphate particles of 1–55 μmm but have low mechanical properties. Recently, amorphous calcium phosphate nanoparticles having an average size of 116 nm have been synthesized. While nanoparticulated amorphous calcium phosphate composites release high levels of calcium and phosphate ions, mechanical properties have been reported to be twice as high as conventional calcium phosphate composites [26,27].

In an *in vitro* study, dentin samples obtained from human permanent molar teeth were coated with nanoparticulated amorphous calcium phosphate composite alone and in combination with the biomimetic analog after the demineralization process the samples were then subjected to a 21-day cycle that contains artificial saliva and lactic acid applications. As a result of different treatments, amorphous calcium phosphate composite with nanoparticles has been shown to increase the concentration of calcium and phosphate ions in demineralized dentin samples and neutralized the acid and promote dentin remineralization. In addition, the use of these composites with biomimetic analog has been reported to increase the remineralization and the hardness of demineralized dentin [28].

Dicalcium Phosphate Dehydrate (DCPD)

When DCPD added to the toothpaste, it increases the levels of free calcium ions in the plaque fluid and has a higher level of calcium ions when compared to toothpastes containing conventional silica for up to 12 hours after brushing. After brushing with DCPD toothpaste in combination with fluoride that promotes remineralization of teeth, calcium that released from DCPD diffuses into the enamel and calcium ion was seen in the plate 18 hours after the procedure [29].

Trimetaphosphate Ion (TMP)

The potential action of TMP is the absorption of the substance from the enamel surface. It forms as an effective barrier in preventing or delaying the reaction of enamel crystals with oral fluids and therefore reduces demineralization in case of acid exposure. Gonzales *et al.* [30], emphasized the role of sodium TMP as a template analogue of dentin matrix phosphoproteins to induce intrafibrillary remineralization of apatite Nano crystals in the incomplete resin infiltrated dentine collagen matrix.

Hydroxyapatite

Hydroxyapatite improves the mineral density and surface properties of the material enamel tissue, improving bacterial adhesion and resistance to tooth decay. Toxic or negative effects were not found [31]. It has been reported that toothpastes containing hydroxyapatite relieves dentin sensitivity and helps remineralization after whitening treatments [32]. Nano hydroxyapatites have been developed to increase solubility and release of Ca and P ions [33].

Nano hydroxyapatite is reported that they were more effective at low pH values than at high pH [34]. In studies, it has been shown that Nano hydroxyapatites prevent demineralization and provide remineralization [35,36]. Swarup and Rao [37] reported that Nano hydroxyapatite was more successful in remineralization of initial caries lesions when compared with fluoride.

Bioactive Glasses (Calcium Sodium Phosphosilicate)

Bioactive glasses provide the release of calcium and phosphate ions in the oral environment [38]. Gjorgievska *et al.* [39], stated that toothpastes with bioactive glass gives successful results in hard tissue repair. Bioactive glass and CPP-ACP showed similar remineralization ability as fluoride ions [40,41]. Matsuyoshi *et al.* [42], found that bioactive glass containing toothpastes were successful in terms of remineralization. In another study, bioactive glass was reported to be more effective than pastes containing CPP-ACP [38]. Milly *et al.* [43], was reported that t bioactive glass and polyacrylic acid containing form alone provides remineralization in white spot lesions, as well as by improving the mechanical properties of phosphate has been reported to increase.

Calcium Carbonate Carrier - Sensistat

SensiStat technology consists of an arginine, bicarbonate, an amino acid complex and calcium carbonate particles which are commonly used in toothpastes. The arginine complex is responsible for adhering the calcium carbonate particles to dentin or enamel surface and remineralize the tooth surface by releasing calcium. SensiStat Technology was developed in New York by Israel Kleinberg and was first used in Ortek'sProclude desensitizing prophy paste and then in Denclude [44].

Conclusion

Many methods have been used to prevent tooth decay and provide remineralization till now. However, although these methods have a certain degree of success and possible side effects, many have not been found to be sufficient to cope with caries formation alone. Therefore researches still go on to find an alternative agent which is more preservative and provides effective remineralization then these methods. Technological developments in the last decade have facilitated the development of remineralizing agents and the access and application of dentists to these products. More researches are needed in order to produce new materials, more effective and reliable methods to be used in preventing from caries.

Conflict of interest

The authors declare that they have no conflict of interest.

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