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PROPHYLACTIC PROPERTIES OF FLUORIDE-RELEASING DENTAL MATERIALS

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ABSTRACT

The process of dental caries is determined by a delicate balance between pathological factors (bacteria and carbohydrates) that lead do demineralization and protective factors (saliva, calcium, phosphate and fluoride) that lead to remineralization. Contemporary approach to the treatment of dental caries includes preventive and prophylactic measures based on the notion of "demineralization and remineralization" in a micro phase in order to retain healthy teeth. Development of dental materials which release fluoride, calcium and phosphate throughout a considerable period of time certainly contributed to that. The purpose of this article was to review prophylactic and therapeutic properties of fluoride-releasing dental materials, and discuss the current status concerning the prevention or inhibition of caries development and progression.

Key words: demineralization, remineralization, prophylaxis, fluoride-releasing materials

APSTRAKT

Etiopatogeneza karijesa određena je ravnotežom između patoloških faktora (bakterije i ugljeni hidrati) koji vode demineralizaciji i protektivnih faktora (pljuvačka, fluoride, joni kalcijuma i fosfata) koji dovode do remineralizacije zubnih tkiva. Savremeni pristup u terapiji karijesa podrazumeva preventivne i profilaktičke mere koje su bazirane na dobrom poznavanju demineralizacionih i remineralizacionih procesa u gleđno-plakovnoj interfazi, sa ciljem očuvanja zdravih zubnih tkiva. Tome svakako doprinosi i razvoj savremenih stomatoloških materijala koji oslobađaju fluoride, kalcijum i fosfate u dužem vremenskom periodu. Cilj rada je bio da se predstave profilaktički i terapijski efekti stomatoloških materijala koji oslobađaju fluoride, kao i trenutne mogućnosti u prevenciji i zaustavljanju progresije karijesa.

Ključne reči: demineralizacija, remineralizacija, fluoroprofilaksa stomatoloških materijala

INTRODUCTION

Caries progression, as opposed to reversal, consists of a delicate balance between pathological factors- namely, a bacterially generated acid challenge and a combination of demineralization inhibition and reversal by remineralization [1]. The balance between pathological factors (such as bacteria and carbohydrates) and protective factors (such as saliva, calcium, phosphate and fluoride) is a delicate one that swings either way several times a day in most people [2]. If the pathological factors predominate, then caries progresses. If the protective factors predominate, caries is halted or reversed. The development of a carious lesion occurs in three distinct stages. The earliest stage is the incipient lesion; the second stage includes the progress of the demineralization front toward the dentinoenamel junction and/or into the dentin, while the final phase is the development of frank lesion which is characterized by a cavitation [3].

Modern concept of minimally invasive dentistry comprises maximum preservation of healthy tissues. Many dentists no longer take a narrow surgical view seeking to apply invasive treatment as a one-off event at a certain trigger point of disease severity and the evidence that caries is an initially reversible, chronic disease with a known multi-factorial aetiology. It is now clear that, by itself, restorative treatment of the disease does not "cure" caries. The caries process needs to be managed, in cooperation with patients, over the changing challenges of a lifetime [4]. Contemporary approach to the treatment of dental caries includes preventive measures based on the notion of "demineralization and remineralization" in a micro phase in order to retain healthy teeth. In addition, this idea is allowed by the development of dental supplies. The purpose of this article was to review prophylactic and therapeutic properties of fluoride-releasing dental materials, and discuss the current status concerning the prevention or inhibition of caries development and progression.

INFLUENCE ON DEMINERALIZATION AND REMINERALIZATION OF ENAMEL

Topical fluoride therapy refers to the use of systems containing relatively large concentrations of fluoride that are applied locally to erupted tooth surfaces to prevent formation of dental caries. It encompasses the use of fluoride rinses, dentifrices, pastes, gels, lacquers, and solutions that are applied in various manners. The continued deposition of fluoride into enamel during the later stages of enamel formation results in elevated concentrations of fluoride in surface enamel. Fluoroapatite and fluorohydroxyapatite are more resistant to acid dissolution [5,6], so the tooth surfaces are more resistant to the development of dental caries. Prolonged exposure of the enamel to low concentrations of fluoride will result in formation of calcium fluoride deposits on the enamel surface. Calcium fluoride may serve as a fluoride reservoir for enamel remineralization [7,8]. The release of fluoride increases the mineral saturation of oral fluid, and can promote the repair of lesions and reduce demineralization during periods of cariogenic attack [9,10].

The earliest stage in the development of a carious lesion is the incipient lesion. The early lesion is macroscopically evidenced on the tooth surface by the appearance of an area of opacity- the white spot lesion. At this stage, the subsurface demineralization at the microscopic level is well established with four recognizable zones. Starting from the tooth surface, the four zones are (1) the surface zone, (2) body of the lesion, (3) dark zone, and (4) the translucent zone [11]. When conditions are optimal, the interface between surface and subsurface of the lesion can be remineralized (repaired) either by calcium, phosphates and other ions from saliva, or by preventive and prophylactic strategies (fluoride therapy and adequate nutrition). It is well-known that incipient enamel lesion can be arrested and/or remineralized by use of topical fluorides, and that extent and efficacy of the remineralization process are related to the concentration of fluorides [12,13] (Fig 1).

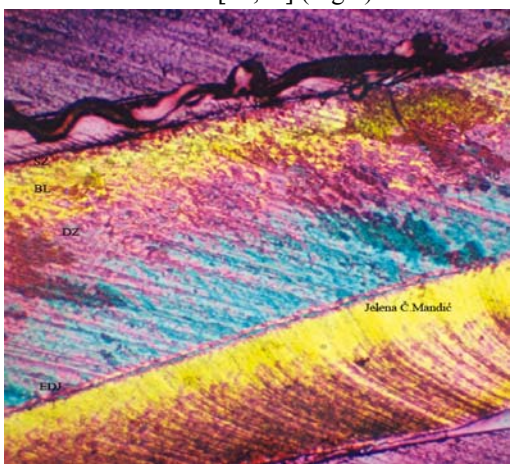

Figure 1. Picture of the remineralized incipient carious lesion showing: ***SZ*** *(surface zone);* ***BL*** *(body of the carious lesion);* ***RZ*** *(dark remineralization zone);* ***EDJ*** *(dentinoenamel junction)*

Both atraumatic restorative treatment (ART) and minimally invasive (MI) dentistry approaches use glass-ionomer cements as restorative materials and fissure sealants and combine preventive and restorative procedures. The objective of sealing the fissures is to prevent and/or arrest fissure caries. According to the technique, glass-ionomer sealants are recommended: (1) where there is fissure caries restricted to the enamel; (2) for caries-free teeth with a deep pit and fissures morphology; (3) in patients who are assessed to be of high caries-risk.

Fissure sealing with glass-ionomer cement was first introduced by Mc Lean and Wilson in 1974 [14]. Glass-ionomers bond to enamel by physicochemical mechanisms following polyacrylic acid conditioning. Existence of a hybrid layer is not exclusive characteristic of resin based materials, this layer is formed during demineralisation and ion exchange at the interface zone between glass-ionomer and tooth structure. In the *in vitro* studies, the wave-like interfacial zone, approximately 5-10 μm wide, without gap

formation, was visualised. Rarely, discreet tags of glass-ionomer material penetrating shallow microporosities were observed [15]. The surface contact between glass-ionomer and the enamel indicate predominant chemical bonding (Fig 2).

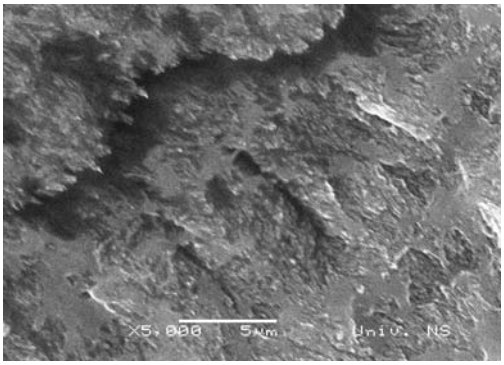

Figure 2. SE microphotograph of enamel after conditioning with polyacrylic acid. The integrity of enamel prisms is maintained which indicates predominant chemical bonding (5000×).

An important advantage of glass-ionomer cement as a sealant is fluoride release which results in increased resistance of the fissures to demineralization. High levels of fluoride assist remineralization of the surrounding area as well. Glass-ionomer sealant has anti-caries effect by fluoride uptake of enamel. Fluoride present in the glass-ionomer fissure sealant is readily exchangeable for hydroxyl and chloride ions from the adjacent enamel. Fluoride uptake and the microhardness increase after application of glass-ionomer have been shown [16]. In an *in vitro* study, Retief et al. [17] showed fluoride uptake of enamel and cementum from glass-ionomer cement. Incorporation of released fluoride into adjacent enamel may enhance caries resistance, remineralize enamel caries and alter the bacterial byproducts of plaque [18]. There is an evidence of increased concentration of fluoride in saliva for as long as 1 year after placement of glass-ionomer sealants [19].

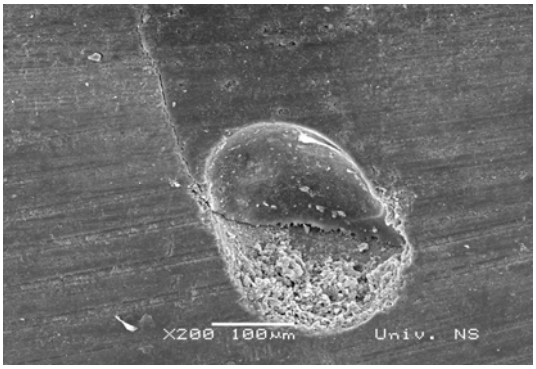

Figure 3. Air-bubble beneath glass-ionomer fissure sealant (200×).

There may be voids and/or gaps unintentionally left between the sealant and the tooth [20] (Fig 3). If there is a strong initial fluoride release from the filling, the content of the void or gap will be concentrated with fluoride. Thus the viability of the bacteria is decreased and the defect may not result in negative bacterial effects and/or secondary caries.

Fissure sealing with glass-ionomer cement may arrest caries on an affected surface [21, 22]. Paradoxically, although the caries prevention was acceptable, retention of glass-ionomer sealants was poor. Even the retention of sealant is incomplete, the caries inhibition is sufficient to endorse their use as a public health measure. Mejàre and Mjör [23] used a replica scoring technique and recorded clinically extensive loss of 61% of glass-ionomer sealants after 6-12 months, but all occlusal surfaces sealed with this material remained caries-free. This finding may be explained by the fact that even after the glass-ionomer sealant had been clinically registered as lost, the replicas revealed areas of retained sealant remnants in 93% after 30-36 months. The probable reason for this observation is that sealants even being clinically lost still remain on the bottom of the fissure protecting the tooth from occlusal caries development [24-28]. This may be due to the better penetration and retention of glass-ionomer sealant in the depth of the fissure, relative to resin-based materials, which was not apparent macroscopically. Glass-ionomer cements can probably be recommended as a fluoride depot rather than as a conventional mechanical barrier occluding a susceptible fissure.

Apart from fluoride, there must be sufficient calcium and phosphate ions present before the enamel is possible to remineralize. Milk and milk products (cheese) have been shown to have anticariogenic properties in animal and human *in situ* models [29-32]. The mechanism of action is due to a direct chemical effect from phosphoprotein casein of the cheese [31,33]. Casein phosphopeptides (CPP) have the ability to stabilize calcium phosphate in solution through binding amorphous calcium phosphate (ACP). Phosphoseryl residues of the CPP and calcium phosphate will form CPP-ACP nanocomplexes. In dental plaque CPP-ACP binds onto the surfaces of bacterial cells, as well as to components of the intercellular plaque matrix [34]. Incorporation of casein peptides into the plaque will increase plaque's content of calcium and phosphate by forming a stabile solution that is supersaturated with respect to the calcium phosphates. Studies in human caries *in situ* models [34,35] showed that CPP-ACP increased the levels of calcium and phosphate in plaque up to five fold. Although the majority of the calcium phosphate in the CPP-stabilized solutions is in the form of ACP, the solutions still contain free calcium and phosphate ions. Since CPP-ACP acts as a calcium-phosphate reservoir and helps plaque fluid to maintain a state of supersaturation with respect to enamel, it will depress enamel demineralization and enhance remineralization.

Anticariogenic potential of the CPP-ACP nanocomplex is well documented in laboratory, animal and human *in situ* caries models. Microradiographic and microdensitometric analyses [34,36-38] showed that short-term use (14 days) of CPP-ACP products provided reduction of the lesion depth from 5.7% to 18.36%, and increasement of the mineral content in the surface zone (65.7%). CPP-ACP has also been shown to remineralize enamel with mineral that is more resistant to acid challenge

than normal tooth enamel mineral [39]. If fluorides are added to the CPP-ACP solution, the CPP-ACFP solutions will produce greater remineralisation than the CPP-ACP solutions [40].

REMINERALIZATION OF DENTINE ADJACENT TO FLUORIDE-RELEASING RESTORATIVES

Studies of carious dentine revealed that it consists of two layers that have remarkably different structure, biochemical and physiological properties [41-44]. The superficial outer layer is characterized by extensive decalcification and irreversibly denatured collagen fibers. No odontoblastic processes are present. The tissue is softened, nonsensitive, invaded by a large number of cariogenic microorganisms, and has to be removed. The inner layer shows intermediate decalcification, regularly arranged collagen fibbers, and living odontoblastic processes. This layer can be physiologically remineralized due to the presence of odontoblastic processes and collagen network which is a good basis for precipitation of calcium and other ions. The aim of a modern concept of treatment of dentine caries is to remove only the outer, permanently damaged 'infected' layer of carious dentine, but to preserve the demineralised 'affected' dentine which can be healed [43].

It has been suggested that dentine is a reactive tissue, both for demineralization and remineralization, due to the high content of water and the low level of mineral (comparing to enamel). Fluoride treatments have potentials to assist in remineralizing previously demineralized dentine and a dose response between fluoride levels and the remineralization of dentine has been shown. Hypermineralization of dentine is a real phenomenon when dentine is in close contact with a fluoride releasing restorative material [45,46]. To date, both ultrastructural and analytical evidence is available on the existence of an intermediate layer along the GIC-dentin/enamel interfaces that is caused by ion exchange between the material and tooth substrate [47-53].

At the restoration/tooth interface on the floor of a prepared cavity both the restorative material and any pulpal fluid that can reach the interface will provide mineral ions required for the remineralization. Pulpal fluid will provide both calcium and phosphate ions and, if glass-ionomer cement is a restorative material, there will be a further increase of phosphate as well as either calcium or strontium. Immediately after placement of cement, pH at the restoration/tooth interface will be around 2.0 and this will stimulate the release of ions from both sides. The rapid interdiffusion of elements occurs when the cement is not completely set and will enable the glass-ionomer to adhere to the dentine. Long-term interactions occur over a long period of time. They correspond to the slow diffusion of some elements of the glass-ionomer cement through the dentin. Ions will penetrate into demineralised dentine on the floor of the cavity and re-precipitate onto the remaining apatite crystallites. This will assist in the healing of the lesion. From the clinical point of view, the caries process is arrested after removal of infected dentine and placement of an appropriate restoration. Some bacteria can persist under the restorations for the considerable time period, but the conditions are unfavourable for bacterial growth and metabolism when they are separated from the oral environment [54,55].

Several laboratory studies investigated the ability of fluoridated materials to prevent or inhibit demineralization of adjacent dentine. It was demonstrated that fluoride release from restorative glass-ionomers increased the resistance of dentine to demineralization and bacterial challenge [56]. Tarn et al. [57] reported that the size of artificially created dentine caries lesions adjacent to conventional or resin-modified glass-ionomers was inhibited by 30–40% compared to lesion size adjacent to a non-fluoridated material. Microradiographic analysis of human decalcified dentine [58] showed that fluoride-releasing adhesive systems enhanced mineralization of decalcified dentine. Gilmour et al. [59] investigated the effectiveness of a conventional glass-ionomer compared with a fluoride-releasing composite when exposed to a microbial artificial caries system and reported that glass-ionomer cement was more successful in reducing caries-like lesion production in the adjacent dentine.

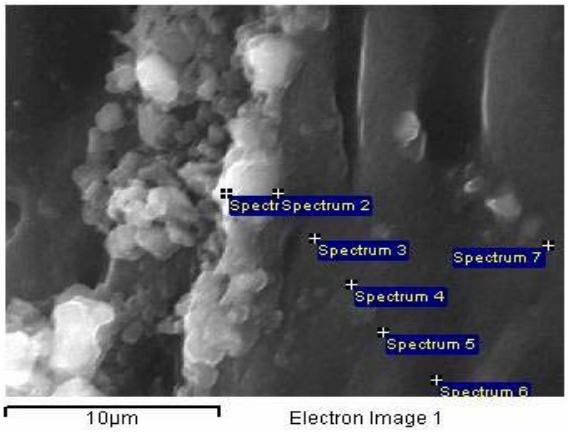

Figure 4. SE microphotograph of glass-ionomer/dentine interface showing penetration of strontium ions up to 10 µm

There have been numerous attempts to demonstrate the phenomenon of ion exchange between glass ionomer cements and dentine. Ultrastructural evaluations of a material based on a strontium glass (Fuji IX GP, GC Int) demonstrated that both fluorine and strontium ions had penetrated deep into the underlying demineralized dentine. The strontium ions were found to have penetrated the entire depth of the remaining carious uninfected dentine while fluoride ions traversed 94% [60]. The pattern of uptake of strontium and fluorine by the demineralized dentin suggests that this is due to the remineralizing process, the extent of which is dependent on the nature of the diseased dentin left behind [60]. Fig. 4 shows morphology of the glass-ionomer/dentine interface and penetration of ions from the material into dentine. Following placement of new prophylactic glass-ionomer cement (Fuji-VII, GC Int), electron-probe microanalysis of the demineralized dentine showed significant increase in calcium and phosphate content; fluoride and strontium also were present to a depth corresponding with the advancing front of each lesion [60].

When compared to unaltered materials, the incorporation of CPP-ACP [61] or bioactive glass [62] into a glass-ionomer cement was associated with an increase of fluoride release and an enhanced protection of the adjacent dentin during acid challenge.

CONCLUSION

There is a continuum of fluoride-releasing dental materials. *In vitro* studies showed that fluoride-releasing materials may act as a reservoir for fluorides from topical fluoridation and may lead to an elevation of the fluoride level in plaque or saliva in the immediate vicinity of the restorative. In addition, several laboratory studies showed the ability of fluoridated materials to prevent or inhibit demineralization of adjacent dentine. However, clinical studies exhibited conflicting data. Therefore, further clinical studies are needed to evaluate the impact of fluoride-releasing restoratives on caries development and progression.

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