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Antibacterial Effect of Surface Pre-Reacted Glass Ionomer Filler and Eluate – Mini Review

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Abstract

A composite resin containing surface pre-reacted glass ionomer(S-PRG) has become widely used as filler or other dental materials in dental treatment. In this mini-review, we briefly summarizethe antibacterial activities of S-PRG on different oral bacteria. The inhibitory effect of S-PRG on plaque formation in the oral cavity has been observed. *Streptococcus mutans* adherence has been shown to be inhibited by S-PRG. S-PRG is also considered to be effective in caries prevention because S-PRG eluate could inhibit biofilm formation and disrupt salivary mature polymicrobial biofilm. S-PRG eluate has suppressed the protease and gelatinase activities of *Porphyromonas gingivalis*, which is one of the most important periodontopathic bacteria. Coaggregation by *P. gingivali* sand *Fusobacterium nucleatum* was also inhibited by S-PRG eluate. Other work has shown that an endodontic sealer containing S-PRGhad an antibacterial effect on some endodontic bacteria. Oral rinsing with S-PRG eluate was also effective in reducing oral malodor production. In this way, S-PRG has antibacterial effect, and it will be further applied for various dental materials and contribute to preventing oral diseases.

Keywords: Surface pre-reacted glass ionomer; Antibacterial effect; Adhesion; Ion release

Introduction

Dental caries and periodontitis are two major causes of tooth loss in adults. To reduce dental caries, it is necessary to prevent demineralization of the intact tooth surface and to promote remineralization of early stage tooth decay. Once irreversible caries are formed, restorative materials are applied as a treatment. However, secondary caries, which is caries lesion developed adjacent to restorations, is the next problem and is the main cause for the replacement of restorative materials.

To overcome these problems, much research on dental materials has been performed. Glass ionomer cement (GIC) is known to have an ion exchange and fluoride release activity, which results in interfering with cariogenic bacteria and remineralization [1-5]. However, because of the lack of hardness, GICs are not applied in cases where high occlusal loading is expected [6]. A composite resin containing pre-reacted glass ionomer(S-PRG) filler has become widely used in dental treatment [7]. The S-PRG filler particles are formed by an acid-base reaction between fluoroaluminosilicate glass and polyacrylic acid [8]. S-PRG fillers are capable of fluoride release and recharge [9-11]. S-PRG is also known to release several types of ions, including Al, B, Na, Si, Srand F [12]. The functions of these ions are summarized in Table 1. Anti-demineralization effects of S-PRG have been observed in denture base resin [13], fissure sealant [14, 15], and coating materials [16-18]. S-PRG has like-re-mineralizing ability [19-21], which is considered to come from its ion-releasing ability. The effects of S-PRG filler and its released ions on hard tissue were extensively investigated, including the anti-demineralization and re-mineralization activity. The bioactivity was also detected when using an S-PRG eluate [12]. It is also important to control cariogenic bacteria to prevent caries formation, and work has been done to describe the antibacterial effects of S-PRG. Oral microorganisms cause other diseases such as periodontitis, periapical lesions, oral malodor and so on. In this mini-review, the information on S-PRG was collected through Pub-Med and Japanese journal index system, and the effects of S-PRG on cariogenic and periodontopathic bacteria are briefly summarized.

Ions	Functions
F	fluoroapatite production, antibacterial effect, remineralization of demineralized lesions
Sr	improvement of bone formation and mineralization
Al	suppression of hypersensitivity
Si	remineralization of tooth
B	antibacterial effect, promotion of bone formation

Table 1: Ions released from S-PRG and their functions.

Inhibitory effect of S-PRG on plaque formation in the oral cavity

Controlling the levels of bacteria is an effective strategy to maintain dental health. It is important to reduce the amount of plaque on the surface of dental materials in the oral cavity. Early-stage research was performed on *in vivo* antiplaque activity. Small resin blocks were attached to the tooth surface and the amount of bacteria on the resin surface was observed after removing the blocks from the oral cavity. Scanning electron microscopy revealed many bacteria on the control resin blocks. In contrast, a much smaller amount of bacteria was attached to the S-PRG resin surface [22-26]. Bacterial adherence is the first step in caries initiation, and S-PRG-containing materials are considered to be less susceptible to cariogenic bacteria.

Film-like layers on saliva-soaked S-PRG

When S-PRG resin blocks were soaked in human saliva, thin film-like layers were observed [23] and more albumin was absorbed onto

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the S-PRG surface when compared with control blocks [27]. Using X-ray energy-dispersive spectroscopy, several ions such as Al, Si and Sr were predominantly detected [24]. The amount of these ions was much higher in the layers on S-PRG resin blocks than on other resin surfaces. The ions are considered to be released from S-PRG and these ions may be responsible for the prevention of bacterial adherence.

Effect on streptococci

Streptococci are known as early-colonizers in dental plaque formation. An effective method of caries and secondary caries prevention is to reduce the attachment of these bacteria onto the surface of dental materials. The adherence of Streptococci has been examined in various ways. The adherence of *Streptococcus mutans,* the most cariogenic bacterium, to the surface of S-PRG was lower than that to other control resins [28-32]. There was a weaker or no effect on the attachment by other Streptococci such as *S. oralis*, *S. salivarius*, and *S. sanguinis* [22,25,26]. Theadhesion inhibition activity of S-PRG seemed to be limited to only some bacteria. The reason for this is not clear and the mechanism of bacterial adherence and inhibition by S-PRG need to be clarified. S-PRG also affected the pH decrease and demineralization caused by *S. mutans* [33]. S-PRG did not have a bactericidal effects on Streptococci [26,29], but it had some growth inhibition in liquid medium [34].

Effect on *in vitro* polymicrobial biofilm

In the oral cavity, the plaque is not composed of one bacterium, but composed of many different microorganisms. Therefore, it is important to examine the effect of S-PRG on the polymicrobial biofilm. Kuramochi et al. showed that S-PRG had a suppressive effect on the polymicrobial biofilm with salivary bacteria [35]. Suzuki et al. reported

Authors	Target	Assay methods	Function	Result	References
Nishio et al.	human dental plaque	SEM[1]	plaque formation	less plaque formation	22
	S. oralis	SEM, labeled bacterial count	adherence	no difference	
Honda et al.	human dental plaque	SEM	plaque formation	less plaque formation	23
	huma saliva	EDS	film-like interface substance	anti-bacterial layer formation	
Hirose et al.	Streptococci	SEM	adherence	less *S. sanguinis*adherence	27
	albumin	^{125}I-labeled albumin	albumin adsorption	more albumin adsorption	
Tamoto et al.	human dental plaque	SEM	plaque formation	less plaque formation	24
		EDS	film-like interface substance	Al, Si, and Sr were detected from the thin layer	
Han et al.	*P. acnes, A. israelii, E. faecalis*	agar difusion method	antibacterial test	anti-bacterial effect on *P. acnes, A. israelii*	37
Daneshmehr et al.	*S. mutans*	SEM	biofilm formation	less biofilm formation	28
Yoshida et al.	human dental plaque	SEM	plaque formation	less plaque formation	25
	S. sanguinis, S. salivarius, S. oralis	^{3}H-labeled bacterial count	adherence	no difference	
Idono et al.	human dental plaque	SEM	plaque formation	less plaque formation	26
	S. oralis	SEM	adherence	less adherence	
	S. oralis	colony count	antibacterial test	no difference	
Saku et al.	*S. mutans*	SEM, ^{3}H-labeled bacterial count	adherence	less adherence	29
	S. mutans	colony count	antibacterial test	no difference	
Tamura et al.	*S. sanguie and S. oralis*	growth curve examination	growth inhibition	growth inhibition	34
Kimyai et al.	*S. mutans*	SEM, bacterial count	adherence	less adherence	30
Ma et al.	*S. mutans*	pH electrode	pH change	less pH decrease	33
	S. mutans	micro-CT scanning, SEM	demineralization	less demineralization	
Yoneda et al.	*S. mutans*	safranin-based micoplate assay	adherence	less adherence	38
	P. gingivalis	BAPNA[2], gelatin film assay	enzyme activities	less enzyme activities	
	*P. gingivalis*and *F. nucleatum*	coaggregation assay	coaggregation	less coaggregation	
Hotta et al.	*S. mutans*	SEM, labeled bacterial count	adherence	less adherence	31
	S. sanguinis	SEM, ^{3}H-labeled bacterial count	adherence	no difference	
Kuramochi et al.	huma saliva	bacterial count of PM biofilm[3]	biofilm formation	less biofilm formation	35
Hahnel et al.	*S. mutans*	MTT-based microplate assay	biofilm formation	less biofilm formation	32
Suzuki et al.	huma saliva	colony count	antibacterial test	less viable bacteria	36
	huma saliva	safranin-based micoplate assay	biofilm formation and disruption	less biofilm formation and biofilm disuruptive effect	
	oral molodor	halimeter assay	VSCs[4]produciton	less VSCs production	

[1]scanning electron microscopy
[2]Na-benzoyl-L-arginine 4-nitroanilide hydrochloride
[3]polymicrobial biofilm
[4]volatile sulfur compounds

Table 2: Antibacterial effect of S-PRG.

that S-PRG could disrupt salivary mature polymicrobial biofilm as well as inhibit the formation of the biofilm [36].

Effect on endodontic bacteria

Periapical lesions are caused by bacterial infection, and it is important to control bacteria to prevent recurrence. S-PRG is not only used for restoration, but is also used for endodontic sealer. Han et al. performed experiments on endodontic bacteria. An endodontic sealer containing S-PRG had an antibacterial effect on *Propionibacterium acnes* and *Actinomyces israelii*, but had no effect on *Enterococcus faecalis* [37]. It is impossible to make the endodontic environment free from bacteria, so antibacterial sealer is effective for preventing recurrence of periapical lesions.

Effect on enzyme activities of *Porphyromonas gingivalis*

Some dental materials are applied to the area adjacent to the gingival margin, and the antibacterial materials will be effective in preventing periodontal diseases. S-PRG suppressed the protease and gelatinase activities of *P. gingivalis* [38], which is associated with the progression of periodontal disease. Some materials that inhibit the protease activity of *P. gingivalis* have been developed, but most of them are in liquid form, while S-PRG shows antibacterial activity as both a solid form material or its eluate. S-PRG is considered to have long-lasting activity to prevent periodontal diseases. Gelatinase is also related to the progression of secondary caries underneath tooth restorations [39,40]. Santos et al. reported that zinc oxide cement and amalgam suppressed gelatinase activity, which may contribute to the caries preventive effects of these materials [41]. It is already known that S-PRG limits caries progression because it releases fluoride [12,42], but we found that it may additionally prevent secondary caries by inhibiting gelatinase activity at restoration sites.

Effect on co-aggregation of periodontopathic bacteria

It is well known that mixed infection of different kinds of bacteria is important to the initiation and progression of periodontal diseases [43]. We have previously shown that mixed infection of *P. gingivalis* and other microorganism enhances their virulence [44]. Co-aggregation of periodontopathic bacteria is associated with bacterial attachment in the gingival crevice [45]. *Fusobacterium nucleatum* is known to have a co-aggregation activity, which is considered to be its virulence factor [46]. Yoneda et al. reported that S-PRG also disturbed the co-aggregation between *P. gingivalis* and *F. nucleatum* in a dose-dependent manner [38].

Effect on oral malodor

Oral malodor is associated with volatile sulfur compounds (VSCs) produced by periodontopathic bacteria [47,48]. Clinically, oral malodor is caused by tongue coating, periodontitis, and deep caries. Unclean denture is also one of the causes of halitosis [49], and antibacterial denture made with S-PRG will contribute to malodor prevention. Suzuki et al. reported that S-PRG rinsing eliminated more bacteria from the oral cavity when compared with water rinsing [36]. They also revealed that oral rinsing with an S-PRG eluate was effective in reducing VSCs production.

Overall review of antibacterial activities of S-PRG

S-PRG is known to release various ions, including F, Al, Sr, SiO, B and Na [12,50]. Boron is known to have an antibacterial activity in cutaneous diseases and periodontitis [51,52], and inhibits bacterial and fungal quorum sensing [53]. Quorum sensing is a key factor in biofilm formation, so inhibition of this function in Streptococci may be a good candidate for the mechanism underlying the actions of S-PRG. In *P. gingivalis*, the mechanism responsible for S-PRG actions may involve the control of metal salts and ions that regulate bacterial enzyme activity. Gingipains, which are the major cysteine protease of *P. gingivalis* are known to require metal ions to achieve maximum enzyme activity [54], whereas gelatinases are inhibited by metal salts [55]. Thus, S-PRG may affect enzyme activity by modulating the concentrations of these metal salts and ions.

Bio-active properties of dental restorative materials are obtaining attention. Dental restoration is expected to induce "super dentin", which is more resistant to acid and base when comparedwith original dentin [56]. Antibacterial effects are highlighted as one of the bio-active properties [57]. Imazato reported the antibacterial effect of monomer methacryloxydodecyl pyridinium bromide [58]. In this way, the antibacterial activity of S-PRG will be more thoroughly investigated and it will be further applied for various dental materials and contribute to preventing caries, periodontitis and other oral diseases.

Conclusion

S-PRG has inhibited the adherence of cariogenic bacteria *in vitro,* and it had antiplaque activity *in vivo*. S-PRG eluate disrupted mature biofilm as well as inhibited biofilm formation. Enzyme and co-aggregation activity of periodontopathic bacteria was suppressed by S-PRG eluate. S-PRG-containing sealer suppressed endodontic bacteria. Oral rinsing with S-PRG eluate eliminated bacteria and diminished oral malodor. The various antibacterial effects were summarized in Table 2.

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