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

Masahiro Yoneda*, Nao Suzuki and Takao Hirofuji
Section of General Dentistry, Department of General Dentistry, Fukuoka Dental College, Japan

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 summarize the 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-PRG had 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 that 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 rechter [9-11]. S-PRG is also known to release several types of ions, including Al, B, Na, Si, Sand 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.

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 the surface.
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 Streptococcus mutans, the most cariogenic bacterium, to the surface of S-PRG was lower than that 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]. The adhesion 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        | SEM¹                                                | 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 adeherence* | 27         |
|                          | albumin                    | ¹H-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 diffusion 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* | ³H-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  |            |
| Sakura et al.            | *S. mutans*                | SEM, ³H-labeled bacterial count                     | adherence           | less adherence  | 29         |
|                          | *S. mutans*                | colony count                                       | antibacterial test  | no difference  |            |
| Tamura et al.            | *S. sanguine 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, gelatin film assay                          | enzyme activities   | less enzyme activities |            |

1°scanning electron microscopy
2Na-benzoyl-L-arginine 4-nitroanilide hydrochloride
3polymicrobial biofilm
4volatile 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 Streptococcis 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 compared with 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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