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White spot lesion remineralization by sugar-free chewing gum containing bio-available calcium and fluoride: A double-blind randomized controlled trial

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ABSTRACT

Objectives: To assess the effect of chewing gum containing phosphoryl oligosaccharides of calcium (POs-Ca) and fluoride on white spot lesion (WSL) remineralization in comparison with POs-Ca or placebo (control) chewing gums, in double- blind, randomized, controlled trial.
Methods: Thirty-seven healthy subjects, who had at least one WSL, with an ICDAS score of 2 or 1, were recruited for this study. The subjects were randomly divided into three groups (control, POs-Ca, POs-Ca + F) and chewed two slabs of each gum three times every day for 3 months. WSLs were assessed using ICDAS criteria and optical boundary depth (BD) by optical coherence tomography (OCT) system at a monthly recall. Data were analyzed by Wilcoxon rank-sum test and Wilcoxon signed rank test with Bonferroni corrections at 0.05 significance level.
Results: Visual score changes from ICDAS score 2 to score 1 over the course of the study were observed; control (30%), POs-Ca (48%) and POs-Ca + F (45%). Unlike the control gum, chewing POs-Ca and POs-Ca + F gums resulted in significant changes in the mean value of BD over the 3 months course of the study ($p < 0.05$). There was a significant difference in mean value of BD after first month between POs-Ca + F and control groups ($p < 0.05$).
Conclusions: This study highlighted the importance of calcium and fluoride ion bioavailability in the reinforcement of demineralized enamel lesions by chewing gums. Furthermore, adding fluoride to POs-Ca might speed up the remineralization progress on natural WSL.

1. Introduction

White spot lesion (WSL) is an initial non-cavitated enamel carious lesion that has reached the stage, where the subsurface mineral loss has produced changes in the optical properties of enamel such that these are visibly detectable as a loss of translucency, resulted in a white appearance of the enamel surface [1,2]. According to the minimal intervention (MI) concept, non-cavitated lesions such as enamel WSL should be managed initially by remineralization techniques.

It has been reported that substances containing bioavailable calcium such as casein phosphopeptide-amorphous calcium phosphate (CPP-ACP), which increases the concentration of calcium and phosphate ions, have potential for enhancement of the remineralization of subsurface lesions of enamel [3,4]. Also phosphoryl oligosaccharides of calcium (POs-Ca), a highly soluble calcium material prepared from phosphoryl oligosaccharides (POs), were found to remineralize enamel lesions effectively in a previous *in situ* study [5–10]. On the other hand, remineralization would also be accelerated or enhanced by the effect of fluoride [11]. There is substantial evidence on the effectiveness of topical

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fluoride in the form of mouthwash, gel or varnish, as an agent for preventing caries and promoting remineralization of early lesions [12].

Sugar-free chewing gums may be an effective vehicle for bioavailable compounds such as calcium promoting enamel remineralization, while exerting an anticariogenic effect through the stimulation of saliva [7,13,14]. Recently, manufacturers have been adding calcium and fluoride in various forms to enhance the potential anti-cariogenic and remineralization potential of gums [7,8,14,15].

It is well known that early diagnosis of the enamel caries lesions may allow the health care provider to implement non-invasive strategies to reverse the lesion. Visual inspection is one of the most common diagnostic methods in lesion assessment. The International Caries Detection and Assessment System (ICDAS), based on visual examination, has been introduced as a novel system to diagnose dental caries [16]. Also, various optical methods have been explored to detect caries such as DIAGNODent and quantitative light induced fluorescence (QLF) since optical properties of enamel change during demineralization [17,18]. Introduction of optical coherence tomography (OCT), which is a noninvasive and nondestructive, real-time high-resolution cross-sectional imaging system that can visualize the internal structures [19], has brought recent advancements in the field of diagnostic sciences [20]. In dental literature, several *in vitro* and *in vivo* studies have utilized OCT to assess enamel demineralization and remineralization [21–30]. Nevertheless, no single clinical evaluation provides adequate reliability for detection of demineralization and remineralization of enamel in WSL; therefore, it may be beneficial to combine at least two detection methods together for a clinical trial.

Until now, no randomized, controlled trial study has reported on the effect of chewing gum containing both bioavailable calcium and fluoride on enamel remineralization *in vivo*. The aim of this double-blind, randomized, controlled trial study was to assess the effect of chewing gum containing POs-Ca and fluoride on natural WSL remineralization in comparison with POs-Ca or placebo (control) chewing gums. The null hypothesis was that there were no differences in the degree of enamel remineralization of subsurface lesions between the three chewing gums.

2. Materials and methods

2.1. Study design and subject recruitment

Thirty-seven healthy subjects (median age: 26 year) were recruited following obtaining ethical approval for the study from the Ethics Committee of the Tokyo Medical and Dental University and signing the informed consent forms. Each of the volunteers completed the medical history forms and underwent intraoral examination for caries experience. For inclusion in the study, the subjects were required to have at least one WSL, with an ICDAS score of 2 or 1 as described below [16]. Exclusion criteria included smoking, evidence of poor oral health including periodontal disease, recent professional fluoride therapy (<2 weeks), uptake of fluoridated water or any medication that could affect oral flora, and pregnancy. Each subject had between one and eleven WSL(s) with a total of 124 WSLs examined throughout the course of this study, as described in Fig. 1.

This clinical trial was based on a double-blind, randomized, controlled design with three sugar-free gums. One of the gums was a placebo sugar-free chewing gum without POs-Ca (Ezaki Glico, Osaka, Japan) and the other two contained 2.5 wt% POs-Ca or 2.5% POs-Ca and 1.2% fluoride-containing green tea extract, namely POs-Ca and POs-Ca + F (Ezaki Glico) (Table 1). The placebo and intervention chewing gums were identical in appearance, taste and smell without any observable differences. The chewing gum slabs were received in code-labelled packages stored at room temperature. The codes were randomly assigned by a controller and remained unknown to the volunteers and operators until all remineralization data had been obtained. The subjects were randomly divided into three groups and chewed two slabs of each

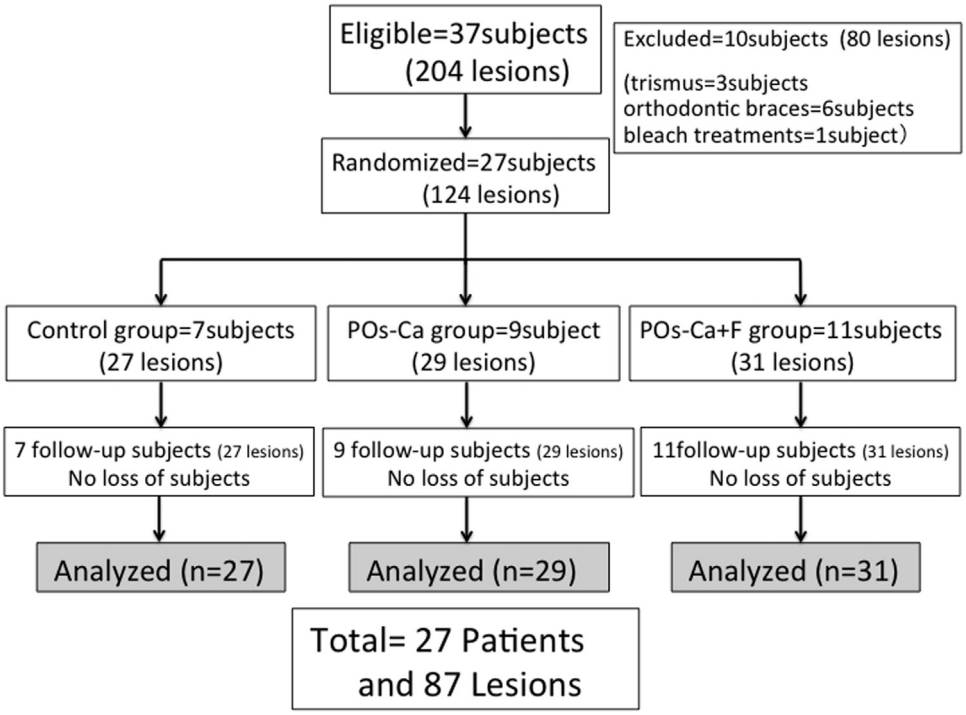

Fig. 1. Participant disposition for the randomized control trial. Thirty-seven healthy subjects were recruited. After the intraoral examination, 10 subjects were excluded because of trismus or under orthodontic treatment or bleach treatment.