A Randomized Trial on the Inhibitory Effect of Chewing Gum Containing Tea Polyphenol on Caries

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Objective: *The purpose of the study was to determine the cariostatic potential of a chewing gum containing tea polyphenol.* ***Study design****: A total of 157 schoolchildren aged 8-9 years were randomly allocated into three groups. Two groups received chewing gum with or without tea polyphenol. A third group did not receive any chewing gum. A single examiner assessed the caries status for all participates at baseline, 12 months and 24 months. A one-way analysis of variance (ANOVA) was performed to evaluate differences among the groups at each interval. The Chi-square test was used to compare the caries-free rate among the three groups.* ***Results****: The mean DMFT increment was 0.17 for the polyphenol gum group, 0.60 for the control gum group, and 1.15 for the no gum group. Children who chewed gum containing tea polyphenol had a significantly lower mean DMFS increment over the 24-month period than did the other two groups (p < 0.05). The caries-free rate in the polyphenol gum group was significantly higher than that in the other two groups (p < 0.05) after two years.* ***Conclusion****: These findings indicated that the oral application of chewing gum with tea polyphenol has an inhibitory effect on dental caries.*

Keywords: *Chewing gum, tea polyphenol, dental caries, prevention*

INTRODUCTION

Dental caries is a common dental disease in many populations and arises from the interplay of four groups of factors: host, microorganism, diet and duration of exposure to a cariogenic environment.[1] Caries treatment can be an uncomfortable and costly experience and thus, caries prevention has attracted increasing attention worldwide. Many caries-control strategies just focus on the individual host and on dietary factors.[2]

Recently, there has been an increased interest in the effects of chewing gum on oral health. Salivary flow rate and pH are significantly increased during periods of gum chewing.[3-5] It has been suggested that sugar-free chewing gum may help prevent and arrest active caries. Gum chewing can stimulate salivation, which neutralizes plaque pH by increasing the alkalinity and buffering power of saliva. Salivation also accelerates the clearance of food debris and microorganisms from the oral cavity. Moreover, chewing gum not only acts as a salivary stimulant, but may also be a useful vehicle for some agents such as chlorhexidine, fluoride, and calcium phosphate.

Tea is a widely accepted drink, and has a long history. Green tea polyphenol, extracted from natural green tea, has been shown to inhibit the growth and metabolism of oral microorganisms as well as salivary amylase activity.[6] Evidence also supports the hypothesis that tea consumption is effective in reducing the cariogenic potential of starch-containing foods.[7,8]

Human tooth enamel acid resistance *in vitro* assay has been used to demonstrate the efficacy of tea polyphenol in increasing acid resistance [9]. These results demonstrate that the organic components of tea are capable of increasing the acid resistance of tooth enamel.

Despite the abundance of evidence demonstrating the many beneficial effects of chewing gum and tea polyphenol, there have been few clinical studies that investigate the cariostatic effects of chewing gum containing tea polyphenol. The objective of this study was to describe the caries-preventive effect of sugar-free gum containing 0.5% tea polyphenol.

MATERIALS AND METHOD

The protocol and informed consent form were reviewed and approved by the Independent Ethics Committee of Shanghai Ninth People's Hospital affiliated to Shanghai Jiao Tong University School of Medicine. Signed informed consent forms were obtained from the parents or guardians of all the participants.

The study was carried out in a district of Shanghai, China, a city with a population of almost 18 million. The water supply in Shanghai is non-fluoridated, and the naturally occurring fluoride concentration of the drinking water is around 0.5 ppm. Most of

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Table 1. Main ingredients (% wt) of the chewing gum, with and without tea polyphenol, used in the study

	Gum with tea polyphenol	Gum without tea polyphenol
Gum base	80	80
Sorbitol	11	11
Xylitol	6	6.5
Mannitol	2.5	2.5
Tea polyphenol	0.5	0

the study participants used fluoride dentifrices, which are readily commercially available. Most participants had lunch and dessert (cake or bread in the afternoon) at their school.

This two-year, double-blind, randomized, controlled, clinical trial was carried out in a typical primary school in Shanghai among children aged 8-9 years old who were generally healthy. Children with any severe medical condition, undergoing orthodontic treatment, or participating in an oral health program involving the use of topical fluorides were excluded.

Use of chewing gum

To avoid the exchange of gum among the participants, classrooms in the study school were used as the unit of randomization, and were randomly allocated to one of the three groups. An independent research assistant carried out the random assignment by drawing numbers from a box. Assignment was concealed until the time of gum distribution by the research assistant. Each parallel group consisted of two classes of children and six classes were involved in total. After the baseline evaluation, one group received chewing gum with tea polyphenol (experimental group) and one group received chewing gum without tea polyphenol (positive control group) each day at school. The third group did not receive any chewing gum (negative control group). The research assistant distributed the chewing gum twice daily (one midway between breakfast and lunch and the other just after eating dessert in the afternoon), supervised an 8-minute chewing period, and then collected all of the chewed gum.

The experimental and positive control gums contained the same ingredients, namely, gum base, sorbitol, xylitol, and mannitol (Table 1), with the exception of the inclusion of green tea polyphenol in the experimental gum. Both types of gum sticks were virtually identical in terms of size, hardness, shape (slab gum), color, and packaging. All gum was supplied by the Shanghai Gaojing food company.

The double-blind study was designed so that only the research assistant responsible for the distribution of the chewing gum could distinguish between the types of gums. Both the examiners and the participants were blinded to the group allocation. All subjects were instructed to continue their regular daily tooth brushing and other oral health procedures over the course of the two years.

Clinical examination

Clinical examinations were performed in the schools by a single examiner using a portable chair and a fiber-optic examination light (Rolux, Guangzhou, China). The criteria for the diagnosis of dental caries followed those recommended by the World Health Organization (1997). A positive diagnosis of a carious cavity was made only when both visual and tactile criteria were met simultaneously. All children were given a clinical caries examination at baseline and after 12 and 24 months of follow-up. Only permanent teeth were examined for the purpose of this study.[10] Examinations were performed with a standard explorer and plain mouth mirror.

Calibration of the examiner was conducted prior to the baseline examination.[11] 10% of children were re-examination to evaluate the intra-examiner reliability at the baseline and follow-up examinations. The primary study outcome was the development of new carious cavities in the sound tooth surfaces of the participants during study period.

In the sample size calculation, the ratio of mean to standard deviation of caries increment was anticipated to be around 2:3 and a difference of 1 or greater in caries increment between the highest and lowest values among the groups was regarded as clinically significant. The results of sample size calculation, based on a 5% statistical significance level and an 80% power, showed that 50 children in each group would be required. A 15% drop-out rate over the study period was expected. Thus, around 54 children in each group or a total of 162 children were required.

Statistical analysis

Statistical analyses were performed using the SPSS 16.0 (SPSS Inc, Chicago, IL, USA). One-way analysis of variance (ANOVA) was performed to investigate differences among the three groups in the children's age, DMFT and DMFS scores at baseline, 12-month and 24-month follow-ups. Chi-square test was used to investigate the gender distribution of children among the three groups. The caries increment was computed by counting the number of teeth or tooth surfaces that had changed from sound to caries or filled in the 24-month study period. ANOVA was also used to assess the differences among the three groups in the mean caries increment. The Student-Newman-Keuls post-hoc analysis was used for multiple comparisons in the case of statistically significant differences. The proportion of children with a zero DMFT score among the three groups was compared across different time points by the Chi-square test. The statistical significance level was set to be 0.05 in all statistical tests.

RESULTS

A total of 184 children from 6 classes were invited to participate in this study in March 2008. A total of 168 children (mean age: 8.4±0.5 years) with 91 boys and 77 girls fulfilled the inclusion criteria. Among them, 56 children were randomly assigned to the polyphenol gum group, 54 to the control gum group, and 58 to the no gum group. The mean age and the gender ratio of the children in the three groups were similar ($p > 0.05$). By the end of the study, 11 children had withdrawn from the trial and 157 subjects were followed for two years. The main reason for the children who dropped out was school transfer. The drop-out rates among the three study groups were similar ($p > 0.05$). No subjects reported side effects related to the chewing gum during the use of either of the two gums. There was no statistically significant difference between the children who were followed for 2 years and those who dropped out in terms of their age, gender, baseline DMFT and DMFS scores ($p > 0.05$). Intra-examiner reliability was good, as Kappa statistics on tooth status was 0.80.

Table 2 shows the mean DMFT and DMFS scores at baseline, 12-month and 24-month follow-ups of the 157 participants who completed the two-year study. At baseline, no significant difference

Table 2. Mean DMFT and DMFS of the study participants at baseline, 12-month and 24-month follow-ups

		Baseline		12-month		24-month	
		DMFT	DMFS	DMFT	DMFS	DMFT	DMFS
Group	N	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Polyphenol Gum	52	0.44 (0.85)	0.56 (1.13)	0.52 (0.90)	0.63 (1.22)	0.62 (1.05)	0.75 (1.38)
Control Gum	52	0.31 (0.61)	0.33 (0.68)	0.48 (0.75)	0.52 (0.85)	0.90 (1.14)	1.12 (1.60)
No Gum	53	0.28 (0.60)	0.36 (0.79)	0.62 (0.88)	0.81 (1.23)	1.43 (1.46)	2.06 (2.30)
All Groups	157	0.34 (0.70)	0.41 (0.88)	0.54 (0.84)	0.66 (1.11)	0.99 (1.27)	1.31 (1.88)
p-value		0.455	0.355	0.674	0.402	0.003	0.001

was found among the three groups in terms of mean age, gender proportion, and mean DMFT or DMFS scores ($p > 0.05$).

After one year, the differences in DMFT and DMFS scores among the three groups were not statistically significant but were statistically significant after two years (Table 2).

Statistically significant differences in mean DMFT and DMFS increments ($p < 0.05$) were found among the three groups at both the 12- and the 24-month follow-ups (Table 3). In addition, multiple comparison shows that the DMFT increment at the 24-month follow-up was significantly different between the polyphenol gum group and the positive control group ($p < 0.05$).

The proportion of children with a zero DMFT score among the three groups is shown in Table 4. There were no significant differences among the three groups either at baseline or at 12 months ($p > 0.05$). However, after two years, the proportion of children with a zero DMFT score in the polyphenol gum group was significantly higher than that of the other two groups ($p < 0.05$).

DISCUSSION

Tea, following water, is the most popularly consumed beverage worldwide, and the extract of this natural food, tea polyphenol, which includes epigallocatechin gallate, epicatechin gallate (ECG), gallocatechin gallate (EGCG), and catechin gallate, has attracted extensive attention.[12] Several findings have suggested that tea catechins may have the potential to improve periodontal status.[12-15] Other studies have shown that tea polyphenol is effective in inhibiting the growth of halitosis-correlated bacteria and in preventing the odor induced by cysteine.[16,17]

Tea polyphenol has an anti-cariogenic property, and has been shown to provide a direct bactericidal effect against *Streptococcus mutans* and *S. sobrinus*.[1] Moreover, tea polyphenol has been shown to exert substantial inhibition of *S. mutans* adherence to saliva-coated hydroxyapatite, and to inhibit the synthesis of insoluble glucan by glucosyltransferase (GTF) in *S. mutans*.

The present study found that children in the polyphenol gum group had significantly lower DMFT increment when compared with those in the positive and negative control groups at the 24-month follow-up. This finding confirmed the inhibitory effect of tea polyphenol on dental caries.[1] However, there are few clinical studies which have investigated the inhibitory effect of tea polyphenol in chewing gum on dental caries. No further comparison could be made with other studies.

Furthermore, our results show that the control chewing gum group also received caries prevention benefits from gum chewing. It should be noted that the control gum was a sugar-free gum containing xylitol. Results from published information have indicated that xylitol chewing gum can prevent dental caries. The predominant sugar substitutes used in chewing gum are xylitol and sorbitol. Evidence from other studies has indicated that sorbitol-sweetened gum offers fewer benefits with respect to reduction of the risk of caries than does xylitol-sweetened gum because sorbitol is a low-cariogenic sweetener.[18-21]

Xylitol has generally been considered to be a non-cariogenic sugar substitute because it is not fermentable by most plaque microorganisms.[19] It can decrease the levels of *S. mutans* in both plaque and unstimulated saliva,[22,23] and reduces the accumulation of plaque on the tooth surface.[24] It has been shown that there is a reduction in the incidence of dental caries after the use of xylitol chewing gum.[25,26]

In a two-year investigation,[26] in which children were given one, two, or three pieces of chewing gum per day, it was shown that daily consumption of two and three pieces of gum led to 33% and 58% reductions in the DMF(S) increment, respectively. However, children who received one piece of gum per day exhibited no significant caries reduction, suggesting a potential dose-response relationship. In this study, subjects chewed the gum twice daily, and this frequency of gum-chewing was lower than that in other studies. Moreover, this clinical trial lasted for only two years. This period is shorter than that of other studies, with some studies even running for as long as

Table 3. Mean DMFT and DMFS increment of the study participants at the 12-month and 24-month follow-ups

	12-month		24-month	
	DMFT increment	DMFS increment	DMFT increment	DMFS increment
Group	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Polyphenol gum	0.08 ± 0.27	0.08 ± 0.27	0.17 ± 0.43	0.19 ± 0.44
Control gum	0.17 ± 0.51	0.19 ± 0.60	0.60 ± 1.05	0.79 ± 1.49
No gum	0.34 ± 0.68	0.45 ± 0.82	1.15 ± 1.43	1.70 ± 2.25
Comparison	Gp1<Gp3	Gp1,Gp2<Gp3	Gp1<Gp2<Gp3	Gp1,Gp2<Gp3
p-value	0.033	0.006	<0.001	<0.001

Table 4. The proportion of children with a zero DMFT score among the three groups

Group	N	Baseline n (%)	12-month n (%)	24-month n (%)
Polyphenol gum	52	38 (73.1%)	36 (69.2%)	35 (67.3%)
Control gum	52	40 (76.9%)	35 (67.3%)	27 (51.9%)
No gum	53	42 (79.2%)	32 (60.4%)	22 (41.5%)
All groups	157	120 (76.4)	103 (65.6)	84 (53.5)
p-value		0.754	0.630	0.029

40 months.[27] It is therefore speculated that the tea polyphenol gum may demonstrate a more marked reduction in the incidence of caries if chewed more frequently and for longer periods.

In this study, all participants presented with a mixed dentition. Since it was expected that many primary teeth in the study subjects would exfoliate during the study period the primary teeth were not included in the clinical assessments. As expected, the vast majority of the carious cavities in this study were found in the first permanent molars of the study children. The results of this study provide evidence to support that the regular use of tea polyphenol chewing gum is a promising way to prevent dental caries, especially in places where professionally applied topical fluorides and fissure sealants are not widely used.

Chewing gum has been suggested to be one of the most appropriate delivery vehicles for dental-protective agents,[28] as it can be readily fitted into a regimen that includes frequent fluoride exposure, good oral hygiene and regular dental appointments. Incorporation of tea polyphenol into chewing gum may be an effective supplement to daily tooth brushing for the prevention of dental caries.

CONCLUSION

Results of this clinical trial show that regular use of chewing gum containing xylitol and tea polyphenol is safe and effective for caries prevention in school children. The results further suggest that, in a school-based caries prevention program, using chewing gum with a combination of tea polyphenol and xylitol may be superior to gum containing xylitol alone.

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