Xylitol Carryover Effects on Salivary Mutans Streptococci after 13 Months of Chewing Xylitol Gum

C. Shinga-Ishihara^a Y. Nakai^{a,b} P. Milgrom^c E. Söderling^d M. Tolvanen^d
K. Murakami^a

^aPediatric Dental Clinic, Okayama University Hospital, and ^bDepartment of Pediatric Dentistry, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan; ^cDepartment of Dental Public Health Sciences, Northwest/Alaska Center to Reduce Oral Health Disparities, University of Washington, Seattle, Wash., USA; ^dInstitute of Dentistry, University of Turku, Turku, Finland

Key Words

Chewing gum · Mutans streptococci · Pregnant women · Saliva · Xylitol

Abstract

To assess mutans streptococci (MS) during xylitol gum chewing (mean 3.8 g/day, 2.9 times/day) for 13 months and then for 15 months after the intervention, Japanese mothers with high salivary MS were randomized into two groups: xylitol gum (n = 56) and no gum (n = 51). The proportion of low MS levels was highest at 3 months of consumption (48.8%), but was significantly lower compared to baseline at the end of the intervention ($p < 0.001$). MS levels did not change during the postintervention period. The data suggest that in the xylitol group 23.3% showed persistent carryover effects by xylitol gum chewing in the postintervention period.

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In a previous paper we reported the results of a randomized controlled trial that confirmed the effect of xylitol gum on mutans streptococci (MS) colonization in infants when the mother chewed gum during pregnancy

and 9 months after childbirth [Nakai et al., 2010]. The group of children whose mothers chewed the xylitol gum were less likely to show MS colonization than the group of children whose mothers did not chew gum. The children in the control group acquired MS 8.8 months earlier than the children in the xylitol group. Studies by other investigators found similar results [Söderling et al., 2000; Thorild et al., 2003], except in the case of Fontana et al. [2009], where unplanned attrition compromised validity.

In this paper, we present a secondary analysis of our original clinical trial in order to assess MS levels of the mothers during habitual xylitol gum chewing for 13 months as well as for 15 months after cessation of any intervention. Longitudinal analyses of MS levels during xylitol consumption with a follow-up after the cessation of the consumption have never been published before.

Subjects and Methods

Study Setting and Participants

The study was conducted at the Miyake Obstetrics and Gynecology Clinic in central Okayama, Japan. A total of 400 pregnant women at months 3–5 of pregnancy were screened. Individuals reporting either xylitol or antibiotic use during the prior

month or gastrointestinal problems were excluded. Salivary MS levels were estimated using Dentocult® SM Strip Mutans (Orion Diagnostica, Espoo, Finland) and individuals with scores ≥ 2 (equivalent to $\geq 10^5$ CFU/ml SM) were sent an informational letter describing the study and were invited to participate ($n = 255$). Of these individuals 107 agreed to participate (mean 30.2, range 19–40 years). The women completed a baseline questionnaire. It included questions about age, estimated delivery date, whether or not this is the first birth, current dental visit, what kind of dental treatment received if any, whether or not xylitol chewing gum is consumed daily, and smoking history. The Okayama University Institutional Review Board approved this study (trial registration: <http://www.umin.ac.jp/ctr/index/htm>, UMIN000001690).

Study Design and Intervention

Participants were assigned to one of two groups – xylitol gum (xylitol) or no gum (control) – using a block randomization procedure with various block sizes unknown to the investigators. Computer-generated random numbers were used to prepare the assignment schedule in advance.

The study procedures were carried out at the Hello Dental Clinic associated with the Miyake Clinic. Both groups received equal basic prevention measures including oral hygiene instruction and professional tooth cleaning at baseline. In the control group, only basic prevention measures were given at the 6th month of pregnancy. In the xylitol group, maternal gum chewing was started in addition to basic prevention measures at the 6th month of pregnancy and terminated 13 months later. As an incentive, both groups received toothbrushes at every visit, and for the xylitol group, the results and interpretation of the Dentocult® SM Strip Mutans testing were mailed to each participant with encouragement to continue participation in this program and a reminder of the next study visit.

Gum and Adherence

Each gum pellet contained 1.32 g xylitol as the only sweetener (Shika-Sen-Yoh XYLITOL®; Lotte Co. Ltd., Tokyo, Japan). The gum was dispensed every 3 months. Participants were instructed to chew one gum pellet for ≥ 5 min at least 4 times/day. Participants recorded the quantities of gum used daily on a calendar provided for that purpose and returned the calendar at each 3-month follow-up. This particular chewing gum was only distributed by health professionals. Participants were interviewed at each follow-up appointment and stated that they had not purchased the gum. No topical antimicrobials were available to the participants. Chlorhexidine digluconate is not prescribed by dental professionals in Japan.

Saliva and Plaque Sampling and Cultivation

Sampling was undertaken at 9.30–11.30 a.m. at 3, 7, 10 and 13 months of the intervention period, and at 3, 9 and 15 months after cessation. Participants were asked to refrain from eating, drinking or brushing their teeth for at least 1 h before their visit. Prior to sampling, participants chewed a piece of paraffin for 1 min and swallowed the secreted saliva. Then, the roughened side of the strip was gently pressed against the tongue. The inoculated strip was inserted into the culturing vial of the Dentocult® SM Strip Mutans kit. Vials were transported at room temperature to the university for incubation.

After incubation at 37°C for 48 h, bacterial growth on the strip was assessed blind by a single trained examiner using the density chart provided by the manufacturer as a reference. Intraexaminer reliability was $\kappa > 0.8$. Dentocult® SM Strip Mutans scores 0–1, 2, 3 correspond to $<10^5$, 10^5 – 10^6 , and $>10^6$ CFU/ml of saliva, respectively.

Statistical Procedures

Contingency table analysis was used to assess the proportion of participants with each score by group at each time point. Cochran Q test was performed for changes over time within each group. Alpha was set at 0.05 for a two-tailed test. Dropout analysis was performed with the χ^2 and t tests.

Results

Based on the adherence calendars, mean ($\pm$ SD) actual xylitol consumption was 2.9 ± 0.9 times/day or 3.8 ± 1.2 g/day total during the intervention period. All participants completed the trial, but not all participants attended all visits. The primary problems were change of residence and scheduling conflicts. No side effects of the gum chewing caused any dropouts. Those who attended all sampling times during the entire study did not differ significantly from those who did not, with respect to age, month of pregnancy at screening, untreated decay or distribution of low versus high MS levels at baseline. Participants were questioned and did not use chewing gums except for those provided by the study organizers. No topical antimicrobials, such as chlorhexidine, were prescribed or used.

Effects of Xylitol on Salivary MS

At baseline, the distribution of subjects with high versus low Dentocult® SM Strip Mutans scores was not different between groups (χ^2 ; $p = 0.22$). Initially, 56 and 51 subjects showed scores ≥ 2 in the xylitol and control groups, respectively. For ease of interpretation, scores were dichotomized (low: 0–1, high: 2–3) corresponding to clinically meaningful levels. An analysis was carried out among participants in the xylitol group with complete data from all sampling points to examine the distribution of the MS levels in the group over time (table 1). For the xylitol group, the percentage of participants with low MS levels was highest (48.8%) at the 3-month examination during the intervention period, and the distribution of MS levels differed significantly from baseline to the end of the intervention (13 months) (Cochran; $p < 0.001$). The distribution of MS levels measured at the end of the intervention (13 months) was not different from that of the postintervention period (Cochran; $p < 0.759$).

Table 1. Distribution of MS levels among xylitol group subjects with complete data from all periods (n = 43)

	Intervention period, months					Postintervention period, months		
	0	3	7	10	13	3	9	15
Low	0 (0%)	21 (48.8%)	17 (39.5%)	17 (39.5%)	10 (23.3%)	13 (30.2%)	12 (27.9%)	10 (23.3%)
High	43 (100%)	22 (51.2%)	26 (60.5%)	26 (60.5%)	33 (76.7%)	30 (69.8%)	31 (72.1%)	33 (76.7%)
Within-group comparison	p < 0.001					p = 0.678		
	p < 0.001							

Nevertheless, at the end of the postintervention period 76.7% of subjects showed high Strip Mutans scores in the xylitol group, suggesting that 23.3% had shown persistent carryover effects of xylitol chewing. No significant changes were observed in the proportion of control subjects in each group during the study (data not shown, Cochran; $p = 0.206$).

Discussion

This study adds to our understanding of xylitol by demonstrating the reduction of MS levels longitudinally in women with high levels of MS when the women started chewing xylitol gum during pregnancy. The uniformly high MS levels of the xylitol group mothers first decreased during gum use. By the end of the intervention, 23% had low MS scores and this distribution did not significantly change during the 15-month postintervention period. Most long-term xylitol studies, lasting from 6 months to 3 years, demonstrated several-fold decreases in MS levels of plaque and saliva, which stayed low during xylitol consumption [Mäkinen et al., 1989; Ly et al., 2006; Milgrom et al., 2006].

A few studies assessed MS after the cessation of a xylitol intervention. Chewing xylitol gum for 4 weeks reduced MS levels significantly, but 4 weeks [Loesche et al., 1984] and 6 months [Holgerson et al., 2007] after the intervention the MS levels had returned to baseline values. Campus et al. [2009] reported a reduction of salivary MS counts at the end of a 6-month intervention in which the children used high doses of xylitol gum (5 times/day, 11.6 g xylitol/day). After a 3-month postintervention period there was still a trend for lower MS counts. Our results showed that long-term xylitol consumption had car-

ryover effects on MS levels in 10 out of the 43 subjects consuming xylitol. The effect was not large and may be of limited clinical importance. However, the small 'xylitol effects' on MS seen in a Finnish study carried out with university students and including a 6-week washout period may be a result of this carryover effect [Söderling et al., 2011].

Conclusion

Xylitol gum chewing decreased MS levels during a 13-month intervention, while no changes were detected in the control group. A subgroup of subjects within the xylitol group (10/43) showed low MS levels also during the postintervention period, demonstrating a carryover effect of long-term xylitol use.

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Disclosure Statement

No conflict of interest exists for any of the authors.

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