Early prevention of childhood caries with maternal xylitol consumption

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ABSTRACT

الأهداف: تقييم تأثير استخدام الأمهات للزيلتول على الوقاية المبكرة لانتقال العدوى من الأمهات للأطفال .

الطريقة: وقد أجريت الدراسة السريرية العشوائية في عيادات طب أسنان الأطفال وعيادات الأطفال الأصحاء بجامعة الملك عبدالعزيز، جدة، المملكة العربية السعودية. وقد شملت عينة الدراسة 60 طفل وأمهاتهم في خلال الفترة من2010م إلى 2012م. وقد تم اختيار المشاركين على أساس وجود ارتفاع في مستوى البكتريا اللعابية العقدية المتحورة. قسمت عينة البحث عشوائياً إلى مجموعة الدراسة ومجموعة الشاهد (30 زوج في كل منهما) وقد أعطيت الأمهات فقط في فترة الدراسة علكة الزيلتول 3 مرات في اليوم لمدة 3 أشهر. وتلقت المجموعتان تعليمات نظافة الفم والمشورة الغذائية وتنظيف الأسنان المهنية بينما تلقت الأمهات في مجموعة الشاهد Fluoride varnish. لم يعطى الأطفال أي علاج وتم فحصهم لتقييم التسوس واللويحة السنية ومستوى البكتريا اللعابية المتحورة بعد مرور 6،12،24 شهراً من بدء استخدام الزيلتول عند الأمهات.

النتائج: أظهرت النتائج زيادة في مستوى البكتريا اللعابية المتحورة في مجموعتي الدراسة والشاهد ولكن الزيادة كانت ذات دلالة إحصائية في مجموعة الشاهد فقط. وأظهرت الدراسة عدم وجود تغير في نشاط التسوس في الأطفال في مجموعة الدراسة بعد 24 شهر على عكس مجموعة الشاهد التي سجلت زيادة ذات دلالة إحصائية في حين لم يكن هناك فرق بين مجموعتين الدراسة في اللويحة السنية عند نهاية الدراسة.

الخاتمة: أن تناول الأمهات لعلكة الزيلتول أعطيت نتائج وقائية في مستوى البكتريا اللعابية المتحورة ونشاط التسوس في الأطفال.

Objectives: To evaluate the effect of maternal xylitol consumption on children's salivary *mutans streptococci* (MS) level, caries activity, and plaque accumulation in contrast with maternal fluoride varnish in a group of mother-child pairs.

Methods: In this randomized controlled trial, the study subjects were 60 mother-child pairs recruited from the pediatric dentistry clinic and the hospital well baby clinic at King Abdulaziz University, Jeddah, Kingdom of Saudi Arabia. The sample was recruited on the basis of maternal high salivary MS levels, and a child aged 10-36 months. The subjects were randomly assigned to experimental and control groups. Mothers in the experimental group chewed xylitol gum, 1.8 gram (66% xylitol by weight), 3 times/day for 3 months. Mothers in the control group received fluoride varnish. Both groups received oral hygiene instructions, dietary counseling, and restorative treatment. Children were examined after 6, 12, and 24 months from the initiation of the study to evaluate salivary MS levels, caries, and plaque accumulation.

Result: There was an increase in MS levels in the experimental and control children at 24 months, which was non-significant in the experimental group, and significantly higher in the control group when compared with the baseline (p=0.008). The decayed, missing, filled scores of the children in the experimental group showed no change after 24 months, contrary to the controls that showed a significant increase (p=0.001). Plaque scores revealed no differences over time or between the 2 groups.

Conclusion: Compared with fluoride varnish, maternal xylitol consumption provided preventive outcomes on salivary MS and caries levels in children.

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Dental caries has been reported to be an infectious disease of the teeth, which involves the proliferation of opportunistic bacteria, mainly *mutans streptococci* (MS) and is also influenced by diet and other host factors.[1] Increasing consumption of high sucrose-containing dietary products among the Saudi population[2] and the high prevalence of dental caries warns of a potential economic burden and mandates the implementation of strategic health policies.[3] *Mutans streptococci* has been considered the main pathogen associated with the initiation of dental caries, inducing mineral loss as a result of strong adhesion to the tooth surface and the production of acid from fermentable carbohydrates, which keeps local pH at a low level.[4,5] Early colonization of children's teeth by MS leads to higher caries experience than in children with late or no MS colonization.[6] Several reports have described that the earlier the MS colonization, the greater the decay of children's teeth in later years. Various interventions to prevent MS transmission in pregnant women and nursing mothers have been effective.[7,8] The window of infectivity has been defined by Caulfield[9] as the period from 19-31 months of age, when the risk of *mutans streptococci* acquisition is high. Some investigators have shown that initial MS colonization can be suppressed by antimicrobial agents given to mothers before or during the window of infectivity of the child.[10] Xylitol is a sugar substitute, that occurs naturally and was shown to protect against caries. Studies have shown that xylitol has anti-caries abilities and hardens advanced carious lesions even in the presence of highly cariogenic diet.[11,12] Investigators have reported xylitol to enhance the remineralization of teeth, especially in incipient white spot lesions. They demonstrated that bacteria is unable to produce acid from xylitol resulting in a decrease in plaque pH values. Stable pH prevents demineralization and hardens the walls of the cavity making untreated cavities less sensitive.[13] It has been reported that xylitol changes the virulence of MS by affecting fructose pathway.[6] On the other hand, a recent study[15] demonstrated in vitro that xylitol could lower the production of polysaccharide; hence, the adhesion of MS and the plaque accumulation was contributed to a different mechanism.[14,15] Salivary MS levels have been shown to decline with the use of xylitol, as cariogenic micro-organisms do not metabolize it. Xylitol decreases the synthesis of insoluble extracellular polysaccharides in vitro. For that reason, consumption of xylitol might limit colonization of MS on the enamel surface inhibiting its transmission.[8] The fall in the incidence of dental caries is not accidental, but due to the application of effective preventive measures.[16] Xylitol containing chewing gums are being studied for caries prevention among mothers, and the reduction of MS acquisition in children during tooth eruption.[8] Xylitol is being promoted as a preventive measure and a cariostatic agent. Thus, the aim of this clinical study was to evaluate the effect of maternal xylitol consumption as a dental caries preventive measure on children's salivary MS level, caries activity, and plaque accumulation in contrast to maternal fluoride varnish in a group of mother-child pairs.

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Methods. This was a randomized controlled clinical study performed on a group of mother-child pairs. The study was conducted between 2010 and 2012. Sixty mothers and their children attending the pediatric dentistry clinic and the hospital well baby clinic of King Abdulaziz University, Jeddah, Kingdom of Saudi Arabia participated in the study. They were selected from 196 mothers who were screened for salivary MS count level. Inclusion criteria were healthy mothers with high salivary counts $\geq 10^5$ colony forming units, (CFU) and having a healthy child of at least 10 months of age (10-36 months) or a minimum of 8 intact primary teeth. Children with systemic disorders such as diabetes, hyperglycemia, sleeping disorders, or regular medications were excluded from the study.

The study was conducted after the approval of the King Abdulaziz University Ethics Committee. Mothers received written information on the study design and collected samples. Consent forms were signed by all participants after they were given verbal and written information concerning the study material, procedures, and purpose.

The random number table was used to allocate the study sample of mothers and their children into 2 study groups; experimental (n=30 pairs) and control (n=30 pairs). Each member in the study had an assigned number. Once a number was chosen, it was not used again. Both mothers in the experimental and control groups (active participants) received preventive measures that included oral hygiene, diet instructions, and professional tooth cleaning. Mothers in the experimental group were instructed to chew one pellet of xylitol chewing gum tablet (Fennobon Oy, Yrittäjäntie, Karkkila, Finland), 1.8g, containing 66% xylitol by weight, 3 times per day for a period of 3 months. The total dose of daily xylitol was 3.64g. Mothers were instructed to follow a

three 5 minutes chewing regimen; after breakfast (8:00 am), after lunch (1:00 pm), and after supper (6:00 pm). Mother compliance was checked by completing a form that was delivered weekly at the time of dispensing the xylitol chewing gum. Mothers in the control group received fluoride varnish application (Duraphat 5% Na F, Ultradent Products, Utah, USA) every 6 months from the clinic.

Children in this study were passive participants (received no intervention) and were followed up for a period of 24 months after the initiation of xylitol regimen for the mothers. Baseline clinical examination for the children was performed after 6 months from the initiation of maternal xylitol consumption, which coincides with the MS window of infectivity.[17] Examination was carried out by one calibrated examiner (who was blinded to the mothers' study group) to assess salivary MS levels, decayed, missing and filled teeth (dmft) scores and plaque accumulation. Examinations were conducted in the clinic in optimal light using mouth mirror and explorer. The diagnosis of dental caries was based on the World Health Organization (WHO) criteria, 1997.[18] Dental caries level was assessed using the dmft index for deciduous teeth. Plaque levels were assessed using the debris component of the simplified oral hygiene index by Greene and Vermillion.[19] The re-examination was carried out after 12 and 24 months from initiation of the study to assess longitudinal changes in salivary MS levels, dmft, and plaque scores.

Unstimulated saliva samples were collected from children for microbiological screening after 6, 12, and 24 months from the initiation of maternal xylitol treatment. Saliva sampling was performed before conducting the clinical examination, between 9-11 am for a period of 15 minutes. On the sample collection day, mothers were instructed to refrain their children from morning tooth brushing, and to not allow them to eat or drink for 2 hours before sampling. Saliva was collected with the pipette supplied by the dentocult (CRT) kit (Ivoclar Vivadent, Lichtenstein, Germany). Saliva was not taken if the child had received antibiotics within one month prior to the examination. The agar surface was wetted with saliva, and then placed in the test vial that was incubated at 37°C for 48 hours. The density of the MS colonies was compared with the enclosed corresponding evaluation model chart. According to the manufacturer criteria, findings of $\geq 10^5$ CFU of MS indicate a high caries risk, whereas findings $<10^5$ CFU were considered as low caries risk.

Intra-examiner reliability was conducted prior to the baseline registration. Ten children were examined for caries, plaque, and salivary MS levels. The re-examination of the subjects was conducted after 2 days, and the level of agreement was determined between the 2 corresponding readings from the Kappa method. The intra-examiner result from the Kappa test for primary teeth was 1.00, which represented an excellent agreement.

Statistical analysis. In this study, the primary outcome was MS level, while dmft scores, and plaque scores were considered secondary outcomes. Statistical analysis was carried out using the Statistical Package for Social Sciences version 16 (SPSS, Inc., Chicago, Il, USA).[20] Measures of central tendency (mean and standard deviation) were used to describe quantitative variables, while frequencies, and percentages were used to describe qualitative variables. Student t test and paired t test were used to evaluate differences between experimental and control groups, and differences throughout the study period for dmft and plaque scores. Pearson Chi-square test and McNemar test was used to detect differences in MS levels between experimental and control groups and throughout the study period. Significance level was set at <0.05.

Results. The initial study sample comprised of 60 mother and child pairs divided into 2 groups; experimental (n=30 pairs) and control (n=30 pairs). After 6 months from initiation of the study (child baseline examination), only 24 pairs from the experimental group (drop-out rate of 20%) and 12 pairs from the control group (drop-out rate of 50%) were reached for examination. Subjects were lost to follow up due to the family travel and moving, or loss of interest in completing the study. No statistical difference was detected between the lost to follow up and the examined groups in their initial oral health indicators (MS count, dmft score, and plaque score).

Table 1 shows the distribution of children with high MS count at 6, 12, and 24 months. At 6 months (baseline) and 12 months follow up there was no significant difference between the experimental group with high MS count and their controls (p=1.00 and p=0.378). While at 24 months, the control group showed a significant increase in the proportion of children with high MS count (p=0.011) when compared with the experimental group. Applying the McNemar test to study the longitudinal changes in MS count within each study group from baseline to 24 months, showed an increase in the proportion of children with high MS count. This increase was significant in the control group (p=0.008), but not for the experimental group (p=0.500). Also, calculating the odds ratio of

acquiring high MS levels in the study groups revealed that at baseline (6 month of the initiation of maternal xylitol consumption) the odds of the experimental group for having a high MS level was less than that in the control group (0.71). This protective relationship increased gradually to record a decreasing odds of the experimental group acquiring a high MS level (0.43 at 12 months and 0.13 at 24 months).

Table 2 demonstrates the impact of maternal xylitol use on the dmft score. Children in the experimental group had lower mean dmft score than the controls. This difference was only significant at the twenty-fourth month(p=0.043). Longitudinal analysis of the difference within each study group showed statistically significant increase in the control group (p=0.001). Calculating the percentage increase in the mean dmft scores at the end of the twenty-fourth month demonstrated more than 60% increase in the control dmft, (4.08-6.67) compared with less than 20% increase in the experimental group (3.08-3.67).

There was no statistical difference in the mean plaque scores when comparing the experimental and control groups at baseline, 12, as well as at 24 months (**Table 3**). Longitudinal analysis of the difference in plaque scores within each study group showed no statistically significant difference in both groups (p=0.770 and p=0.723).

Discussion. Vertical transmission of MS in mother-child pairs facilities early acquisition of MS by their infants.[9,21] Mothers with high levels of MS are more likely to have children with high MS.[22] *Mutans*

Table 1 - Distribution of children with high mutans streptococci (MS) level (≥10^5) at different study phases.

Study phases	Children with high MS level		Experimental /control group	
	Experimental n (%)	Control n (%)	*P*-value	Odds ratio (95% CI)
6 months (baseline)	3/24 (12.5)	2/12 (16.7)	1.000†	0.71 (0.08-7.43)
12 months	3/24 (12.5)	3/12 (25.0)	0.378†	0.43 (0.05-3.41)
24 months	5/24 (20.5)	8/12 (66.7)	0.011*,†	0.13 (0.02-0.77)
Baseline/24 months (McNemar; *p*-value)	0.500	0.008*		

*significant difference at <0.05, †Chi-square test, 95% CI - 95% confidence intervals

Table 2 - Comparison of decayed, missing, and filled teeth score of children in the experimental and controls groups at the different study phases.

Study phases	Study groups				Experimental/ control group *P* value
	Experimental		Control		
	Mean±SD	(95% CI)	Mean±SD	(95% CI)	
6 months (baseline)	3.08±4.96	(0.99-5.18)	4.08±3.70	(1.73-6.44)	0.542‡
12 months	3.38±4.6	(1.34-5.32)	4.58±4.27	(1.87-7.30)	0.450‡
24 months	3.67±3.94	(2.0-5.33)	6.67±4.21	(3.99-9.34)	0.043*,‡
Baseline/24 months (paired t test; *p*-value)	0.395	0.395	0.001*	0.001*	

*significant difference at <0.05, 95% CI - 95% confidence intervals, ‡t test

Table 3 - Plaque scores of children in the experimental and control groups at different study phases.

Study phases	Study groups				Experimental/ control group *P*-value
	Experimental		Control		
	Mean±SD	(95% CI)	Mean±SD	(95% CI)	
6 months (baseline)	0.96±0.55	(0.73-1.19)	0.83±0.72	(0.38-1.29)	0.566‡
12 months	1.04±0.81	(0.70-1.38)	0.83±0.72	(0.38-1.29)	0.453‡
24 months	0.92±0.58	(0.67-1.16)	0.92±0.79	(0.41-1.42)	1.000‡
Baseline/24 months (paired t test; *p*-value)	0.770	0.770	0.723	0.723	

significant difference at <0.05, 95% CI - 95% confidence intervals, ‡t test

streptococci does not appear in the oral cavity of infant until after tooth eruption and is transmitted to the infants from the mothers. This period is called the "window of infectivity". The danger of the child's mouth becoming infected is increasing when the mother have high MS levels. Xylitol consumption affects the flora composition by a decrease in MS. Xylitol inhibits the growth of bacteria via the stimulation of the fructose phosphptrasnferase system and formation of xylitol-5-phosphate. As a consequence, this will lead to the accumulation of xylitol-5-phosphate, which interferes with bacteria carbohydrate metabolism. In addition, it can disturb the protein synthesis and cause ultrastructure changes in the bacteria.[23,24]

In this study, maternal xylitol consumption started when children were below the age of the window of infectivity, and had not more than 8 anterior teeth. Baseline examination was implemented when children had just entered the window of infectivity. The study revealed that after 6 months of initiation of the study, the experimental and control groups showed comparable levels of MS colonization.

This might be explained by the fact that during this period saliva washes out bacteria resulting in comparable levels of MS. With the progression in time and eruption of more teeth, bacteria started to adhere to the erupted teeth leading to the significantly higher salivary MS levels detected in the control group compared with the experimental group of children and indicated a positive impact of the maternal xylitol gum consumption on their children's salivary MS level in the experimental group. Also, comparing longitudinal changes in MS count within each study group from baseline to 24 month, showed an increase in the proportion of children with high MS count in the control group (p=0.008), while in the experimental group, the increase was not significant (p=0.500). This was confirmed as the children's odds of MS colonization decreased in the experimental group gradually from 0.7 at 6 months from initiation of the study to 0.13 at the end of the study (24 months). This denotes the protective effect of the xylitol ingestion by the mother. Regarding the dmft score, the results showed that the dmft score was higher in the control group than in the experimental group through the follow up interval. This difference was only significant at the twenty-fourth month. Also, longitudinal analysis of the difference within each study group showed statistically significant increase only in the control group, which denotes the positive impact of maternal xylitol on the dental caries activity. Simple calculation of the percentage increase of the dmft score throughout the study period showed an increase of more than 60% in the control group, while the increase in the experimental group was less than 20%.

These results agree with the findings of other studies,[9,11] where they found a 5-fold and a 3-fold risk of MS colonization in children using bi-annual fluoride varnish and chlorhexidine treatment in the mothers compared with habitual daily xylitol consumption throughout the study period (2 years). The findings suggested that maternal use of xylitol may lead to caries prevention even when used for a short period. Previous studies have shown that the suppression of MS level would result in a long standing effect on MS colonization and caries activity in children.[22] These results agree with the our findings. However, a 10-year study revealed no difference in caries experience in children after one year of maternal consumption of combinations of xylitol, sorbitol, and chlorohexidine chewing gum.[25] Further studies are needed to define the possible long-term protective effect of xylitol in dental caries. Clinical studies[26,27] reported that xylitol would reduce the adherence and the acidogenic property of the dental plaque. In the current study, plaque accumulation in children showed no difference between the 2 groups. The difference between the baseline and 24 months were also non-significant in both groups. The finding suggests that maternal xylitol consumption was less effective on plaque levels in children when compared with its anticariogenic effect. In contrast, Holgerson et al,[28] concluded that children consuming xylitol showed reduction in dental plaque. It might be argued that the positive effect of xylitol on plaque formation would have been noted if children had personally consumed xylitol.

Several difficulties were encountered during the implementation of the study such as high dropout rate especially in the control group, despite all efforts made to motivate them to continue the study. Also, a strict follow up was needed to assure compliance of the mother to the xylitol regimen. The high cost of the xylitol medicinal preparation was another limitation of the study.

The selection of appropriate preventive measures should take into account practical aspects. The application of most preventive measures requires equipment, material, timing, and above all, the identification of high risk mother-child pairs. In contrast, the maternal use of xylitol can be recommended as part of pre and post natal care that will only require the mother is compliance for the consumption regularity.

Study findings suggest that the maternal use of xylitol as a caries prevention strategy could be beneficial to Saudi children at high risk for caries. The present results,

although promising, should not be misinterpreted as a substitution for the conventional preventive practices such as fluoride, oral hygiene measures, and regular dental visits offered to children.

It is believed that, when caries occurrence is high and affects the majority of the population, even modest prevention procedures lead to substantial reductions in dental decay. This study adds to the confirmation of the preventive xylitol effect on the children with MS levels and caries experience when given to mothers for a short period of time within the window of infectivity.

Further longitudinal studies are needed to confirm the impact of the xylitol on pregnant women and the continuation of this regimen in their offspring and the effect of xylitol on the MS strains

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