The Effect of Non-Cariogenic Sweeteners on the Prevention of Dental Caries: A Review of the Evidence

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Abstract: The role of sugar substitutes such as xylitol and sorbitol in the prevention of dental caries has been investigated in several clinical studies. The purpose of this report is to review the current published evidence regarding the relationship between sugar substitutes and dental caries. A literature search was conducted using MEDLINE and EMBASE and included studies published from 1966 to 2001. Studies that included human subjects and were published in English were included in this review. A total of fourteen clinical studies were reviewed that evaluated the effect of sorbitol or xylitol or the combination of both sugar substitutes on the incidence of dental caries. Most of the reports were of studies conducted with children outside of the United States. These studies demonstrated a consistent decrease in dental caries, ranging from 30 to 60 percent, among subjects using sugar substitutes as compared to subjects in a control group. These caries rate reductions were observed in subjects using xylitol or sorbitol as the sugar substitute in chewing gum or toothpaste. The highest caries reductions were observed in subjects using xylitol. These findings suggest that the replacement of sucrose with sorbitol and xylitol may significantly decrease the incidence of dental caries.

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The role of sucrose and other fermentable carbohydrates in the etiology of dental caries has been well established. Since it is known that sugared chewing gums may increase the risk of dental caries, it has been proposed that the replacement of sucrose in chewing gum or candies with a sugar substitute such as xylitol may contribute to caries prevention**.** This relationship has been studied in situ and in several clinical studies[1-3] that will be the focus of this report.

It is believed that the benefits of sugar-free gums[4-6] may be twofold; 1) decreased lactic acid production and increased salivary flow potentially leading to an increased buffering of acids in plaque, and 2) increased supersaturation of saliva with the mineral ions as well as enhanced clearance of sugars from the mouth. Thus sugar substitution and salivary stimulation could, it has been argued, be equally responsible for the noncariogenicity of sugar-free chewing gum.[6]

Sorbitol and xylitol are the most commonly used sugar substitutes. Although sorbitol is metabolized at a slower rate than sucrose and not at all by most microorganisms, it can be fermented at a slow rate by all of the mutans streptococci including *S. mutans* while xylitol is considered to be non-acidogenic.[7-10]

Review of Published Studies

In a clinical trial in Puerto Rico, 2,601 schoolchildren were randomly assigned to two study groups.[11] One examiner evaluated caries in the permanent dentition at baseline and after two and three years of follow-up with the use of artificial light, mirror, explorer, and radiographs. After baseline exams, classrooms were randomly assigned to receive no gum or sugar-free chewing gum (Extra Orbit, Wrigley) with sorbitol (40-60 percent), mannitol (4-15 percent) and aspartame (<0.6 percent) sweeteners. Children were instructed to chew three times per day for twenty minutes. The change in DMFS index was evaluated adjusting for age, sex, baseline scores (DMFS), and baseline surfaces at risk, school, treatment by classroom, and within treatment by school. The mean age was 11.65 years in the control group and 11.72 years in the treatment group. Subjects in the chewing gum group had 6.4 percent fewer new DMF surfaces than controls. These differences were statistically significant. It is possible, however, that these results are biased since it is impossible to know how often the children in the "no gum" group actually chewed gum with or without sucrose outside of school. It is possible that they did use chewing gum outside of

the school, thus increasing their risk of developing caries.

In a study within the U.S. Veterans Affairs system, patients were enrolled in a double-blind randomized clinical trial as part of standard recall visits.[12] All inpatients with exposed root surfaces were invited to participate. One hundred and eighty-eight consented to participate and were systematically assigned to xylitol or sorbitol and followed for 1.8 years. There were forty subjects in each of the intervention groups and 105 in the nonparticipating group. There were thirty-six root surface caries among 2,632 person years of risk in the sorbitol group and six lesions among 2,349 person years of risk in the xylitol group resulting in a relative risk comparing the two types of gum of 0.19 (0.06,0.62) (p=0.0065), indicating a significant reduction in carious lesions on exposed root surfaces among those who chewed xylitol gum. An adjustment by age, gender, number of carious root surfaces at baseline, or caries-free root surfaces at baseline did not appreciably alter these results. The data were not analyzed against the nonparticipating group since the authors believed such an analysis to be "unjustified."

In a double-blind cohort study in Belize, 1,277 schoolchildren (mean age 10.2 years) were randomly assigned (by school) into nine treatment groups: four xylitol groups (4.3-9.0g/day); two xylitol-sorbitol groups (8.0-9.7g/day); one sucrose group (9.0g/day); one sorbitol group (9.0g/day); and one sucrose group.[13] All participants were fourth grade pupils attending nineteen public schools. The gums used in the study were packed in number coded blank wraps to ensure that students were blinded as to the type of gum. During each of the approximately 200 schooldays per year, there were five-minute periods of gum use supervised by teachers with timers. Verbal and written instructions were provided during school vacations.

The onset of a carious lesion on a previously sound or unerupted tooth was evaluated as the outcome. A total of four blinded and calibrated dentist examiners carried out the exams at baseline and sixteen, twenty-eight, and forty months, applying the WHO criteria for caries detection. A carious lesion was recorded if physical discontinuity and softness of the enamel in either pits or smooth surfaces were evident. Radiographs were not used to assess caries incidence, and enamel-only caries were scored as D_0. The overall loss to follow-up was 32 percent with an uneven distribution between groups. The largest reduction in caries rates occurred in xylitol groups that was significant when compared with sorbitol or sucrose. Relative risks for caries rates were adjusted for age, gender, DMFS, and number of sound surfaces at baseline. The most significant caries reduction was observed in the group assigned to the highest xylitol concentration (RR = 0.27) (0.20, 0.36). The protective effect of xylitol increased with increasing xylitol composition. The group assigned to the sucrose chewing gum exhibited a slight increase in caries rate (RR = 1.20) (0.96-1.49) that was not statistically significant. Sorbitol decreased caries rates significantly (RR= 0.74) (0.60-0.92) as did the sorbitol/xylitol groups.

Another study in Belize evaluated the effect of xylitol and sorbitol chewing gums on caries rates in primary teeth with six-year-old subjects. This study demonstrated a lower rate of caries in subjects in the xylitol or sorbitol pellet groups compared to a group of children who were not assigned to a chewing group, with relative risks reported as 0.35 (.21-.59) and .44 (.30-.63) respectively.[14]

Subjects from the two cohort studies in Belize were evaluated to determine the effect of xylitol on rehardening or nonprogression of carious lesions.[15] The rehardening of dentinal caries was examined by blinded examiners with explorers and fiber optic lights, using the same criteria as in the original studies. Radiographs were not used. The number of lesions that went from D_3 to D_0 or D_4 to D_0 were recorded for each of the nine groups. The following formula was used to assess the rate of caries arrest and nonprogression:

$$\frac{\textit{\# surfaces that were diagnosed to reharden or nonprogressed}}{\textit{carious surfaces with a caries diagnosis of } D_3 \textit{ or } D_4 \textit{ at baseline}}$$

Arrest or nonprogression of caries was seen more frequently in subjects using the xylitol gum. The group with the highest percentage of xylitol exhibited a higher percent of arrested carious lesions (27 percent), than the no gum group (9 percent) or the sorbitol group (7 percent) ($p < 0.05$). A five-year follow-up study of the effect of xylitol candies or gums was conducted with 740 ten-year-old children in twelve schools in four towns in Estonia.[16] The candies were used for two years and the gum for three years. Two examiners conducted blinded exams at a local school dentist's office with mirror and explorer using the WHO criteria. After three years, 75 percent of the original group was reexamined. Both xylitol groups had significantly reduced caries rates compared to controls. The mean DMFS scores after three years, adjusted for age, gender, examiner, and baseline DMFS, were: 4.42 ($\pm$4.36) in the control group, 1.87 ($\pm$2.55) in the chewing gum group, and 2.77 ($\pm$3.05) and 1.72 ($\pm$ 2.04) in the two candy groups. The overall reduction in caries rates compared to controls was 53.5 percent in the chewing gum group and 33-59 percent in the two candy groups compared to controls. These results were statistically significant ($p < 0.005$).

A demonstration project in Madagascar in which school children were randomly assigned to polyol chewing gum or control group included children in grades one and four in six schools.[17] All children received a school-based oral health education program that included daily supervised toothbrushing. The test group also received a chewing gum that contained 55.5 percent sorbitol, 4.3 percent xylitol, and 2.3 percent carbamide that they received three to five times per day. Dental examinations were performed by three calibrated dentists at baseline and after three years of follow-up using a standard explorer, mouth mirror, and daylight. After three years of follow-up, the overall DMFS scores did not differ significantly among any of the study groups. The only statistically significant finding was a decrease in occlusal caries in children in grade one in the xylitol group. It is interesting to note that the findings were different from the other studies cited in this review. The daily supervised toothbrushing that all children participated in may have made the groups more similar in terms of oral hygiene status, thus reducing the detectable difference in caries rates.

The discussed studies evaluated the use of chewing gum or candies with sugar substitutes on caries rates. One study evaluated the caries inhibitory effect of xylitol in a dentifrice.[18] This study was conducted in Costa Rica beginning in 1987 with 2,630 school children aged eight to ten. A calibrated dentist conducted clinical evaluations on all children at three time points throughout the study. The children were divided into two groups: 10.243 percent NaF/silica dentifrice or a dentifrice containing 0.243 percent NaF/silica plus 10 percent xylitol, and stratified by age and sex. They brushed twice daily with the study toothpaste: once daily at school and home on weekdays, and twice daily on the weekends.

The DFS incremental change was 3.3 in the control dentifrice and 3.1 in the dentifrice containing xylitol, representing a 9.1 percent difference in caries incremental change ($p<0.01$). After three years, the loss to follow-up was 36 percent that was consistent between the two groups. The mean DFS changes from baseline were 5.7 for the control group and 5.0 for the test group ($p < 0.001$).

Long-Term Effects

The long-term effects of sugar-free gum chewing have been reported in a single study in which children were re-examined five years after a two-year gum chewing study ended. Comparisons were made between sorbitol, xylitol, and no gum chewing. The sorbitol gum did not have a significant long-term effect on caries reduction. The xylitol and xylitol/sorbitol groups demonstrated significant long-term caries reductions with relative risks of 0.41 (0.23,0.75) and 0.56 (.36,.89) respectively. The protective effect of xylitol depended on when teeth erupted. Teeth erupting after one year of gum chewing or after the two-year period had ended demonstrated the most significant long-term caries reductions (93 percent and 88 percent respectively).[19]

The effect of sugar substitutes on changes in *S. mutans* levels also have been investigated. All studies have consistently demonstrated that xylitol use did significantly reduce the levels of *S. mutans*.[20-23]

Summary

The effect of sugar substitutes on changes in caries rates has been evaluated in several observational studies as well as clinical trials, with results consistently demonstrating a protective effect of xylitol on caries incidence. Sorbitol also was shown to decrease caries rates compared to controls; however, the reductions in caries rates were greatest when xylitol was the sugar substitute. Some limitations of previous studies include the lack of radiographs in caries diagnosis, high loss to follow-up, and potential confounding and bias due to the nature of long-term community intervention studies.

The criteria for causality—consistency, strength association, biologic plausibility, temporal sequence, and dose response relationship—should be considered. First, these studies are remarkably consistent, in terms of the magnitude of the effect observed as well as the consistent demonstration of the superiority of xylitol compared to sorbitol in decreasing the risk of dental caries. Second, the relative risks observed, 0.19-0.4, are considered strong evidence of a protective effect. Third, it is biologically plausible that xylitol can reduce dental caries since the pH of plaque is not lowered to the range that would increase caries risk with xylitol compared to sucrose. Fourth, a dose response trend was observed in the two studies that evaluated different concentrations of xylitol with the greatest effect observed in the subjects using the strongest xylitol preparations. Although several of these studies were flawed, it is unlikely that future studies can improve on what has been done to date. Furthermore, since the evidence suggests a strong caries protective effect of xylitol, it would be unethical to deprive subjects of its potential benefits. Given that several of the criteria for causality are met, it is concluded that xylitol can significantly decrease the incidence of dental caries.

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