The role of xylitol in patient caries management*

Xylitol has become a controversial issue in caries prevention. The aim of this paper was to examine and review the recent literature on the role of xylitol in the patient-centered management of dental caries. There is a good body of evidence suggesting that xylitol has antibacterial properties that may alter the oral ecology while the evidence for a caries-preventive effect still must be regarded as inconclusive. However, recent studies indicate that preventive programs should include as many complementary strategies as possible especially when directed towards caries-active patients. Therefore, xylitol should be considered as an adjunct to other measures such as fluoride exposure, fissure sealants and dental health education in individuals assessed as being at risk for future caries development or with a proven caries activity. A daily dose of at least 5 gram in fractioned doses is recommended. Chewing gums seem to be the best vehicle for administration but age-related and individual preferences must be considered in order to enhance compliance.

Keywords: caries prevention, mutans streptococci, oral ecology, xylitol

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1 Introduction

The five-carbon sugar alcohol xylitol has become a controversial issue in caries prevention and although positive results have been achieved worldwide in a number of field trials, the acceptance of its effectiveness is not universal. In fact, two systematic reviews of literature have concluded the evidence for a caries preventive effect as insufficient or inconclusive [3, 11]. It is however important to keep in mind that lack of evidence is not the same as lack of effect. Inconclusive or insufficient evidence is most often due to a low quality of the existing research or that the studies are assessed with a high probability of bias or confounders. Consequently, one important rationale of systematic reviews is to identify gaps of knowledge and to stimulate further and better research. Moreover, “best available evidence” is only one cornerstone in evidence-based medicine that should be weighed together with the clinician’s skill, experience and knowledge as well as the patients need and demands. The aim of this paper was to examine and review the recent literature on the role of xylitol in patient-centered management of dental caries.

2 Role of xylitol in the caries balance

Dental caries forms through a complex interaction over time between acid-producing bacteria, fermentable carbohydrates and host factors including teeth and saliva [22]. In the recent decade, the process has been explained by the “ecological plaque hypothesis” [18]. In a simple way, the theory can described as an ever ongoing battle between de- and re-mineralisation; if more minerals are lost than gained from the hard tissues over time, a lesion will occur (Figure 1). The reason for this imbalance is a broken homeostasis in the oral ecosystem driven by the pH. For example, frequent small eating or a reduced saliva flow will prolong the time with low pH conditions in the oral cavity and favour the growth of aciduric bacterial species that are normal inhabitants of the oral biofilm. The highly aciduric strains, such as mutants streptococci and lactobacilli, simply get an ecological advantage since they are able to withstand the low pH. These strains are also highly acidogenic which further promotes a down-going spiral resulting in an increased cariogenic environment and challenge. It is important to stress that there is no specific bacteria, for example Streptococcus mutans, that are directly causative for caries according to Koch’s classical postulate; instead a variety of bacteria with specific properties are linked to the initiation of the disease. This is important to understand and explains why caries-preventive actions directed to eliminate one specific bacterium seldom meet the expectations. It is also important to keep in mind that numerous trials with xylitol evaluate the selective effect on mutans streptococci and this “surrogate endpoint” does not necessarily has a direct impact on the caries development.

It is well known that xylitol may influence the oral ecology in four principal ways:

i) it hampers bacterial metabolism and diminishes the pH-drop in the dental plaque,
ii) it reduces the amount of supragingival plaque,
iii) it promotes the selection of xylitol-resistant mutants streptococci which are thought to be less virulent, and,
iv) it stimulates saliva secretion.

Collectively, these properties suggest that xylitol may have a unique and dual impact on the caries balance by decreasing acid challenge on the pathological side and by enhancing the antibacterial action on the protective side.

3 Does it work?

There are several reviews available on the caries-preventive efficacy of xylitol but the conclusions differ in substantial ways. While some conclude that xylitol is superior to other polyols and has an
important role in caries prevention [4, 16], other claim that the beneficial effects primarily are based on saliva stimulation [19]. The reason for the conflicting opinions can be found in discrepancies in the thinking how evidence from non-randomized or quasi-randomized investigations should be interpreted and graded. While the majority of the initial studies on xylitol were field projects based on cohorts and graded with low evidence, some of the more recent investigations are randomized on individual basis. Data from the major clinical trials published after year 2000 with caries as endpoint are compiled in Table 1 and Figure 2. Results in benefit for xylitol were reported in four out of eight papers and if no qualitative aspects were considered, the mean prevented fraction was 21 %. However, very few studies were placebo-controlled and comparisons between intervention and no-treatment groups have a tendency to overestimate the treatment effect so it is likely that the true caries preventive effect is somewhat lower. Nevertheless, a very cautious conclusion from the recent trials would be that a beneficial effect on xylitol on caries development in children and young adults cannot be excluded. Notable, no recent studies performed in adults or were designed to evaluate the ability of xylitol to control caries, which means to arrest or reverse existing caries lesions.

4 Does xylitol do any harm?

It is well established that very high doses (50-60 gram/day) of xylitol can result in osmotic diarrhea which can be prevented through a slow and step-wise introduction together with fractioned doses. Reports on adverse-effect in the recently published clinical trials are however very scarce indicating that xylitol is well accepted by the patients. There are anecdotal reports on tiredness in the tempo-mandibular joint after excessive chewing but this is not specific for xylitol. According to EU-regulations, xylitol should however be avoided in small children since bulk sweeteners, among them sugar alcohols, in food and drinks are not recommended for children under the age of three years.

5 How much xylitol is needed to control caries?

The pioneering studies with xylitol utilized daily dosed exceeding 10 gram but the trend has moved to lower amounts in the later investigations. From recent studies it has become evident that a dose-response relationship exists concerning the impact of xylitol on oral ecology and also that the frequency of administration could affect the outcome [13, 20]. The data clearly suggest that a range of 6 to 10 grams of xylitol, divided into three to four intakes per day, is necessary for xylitol chewing gums to be effective. The effect was declining with lower doses while no additional benefit was shown by increasing the daily dose. It should however be stressed that effects were evaluated with salivary mutans streptococci as endpoint measure. As mentioned before, this may be regarded as a surrogate measure for caries and thus, not immediately applicable for caries development. The suggested daily dose of 6 gram corresponds however fairly well with the findings of the clinical caries trials listed in Table 1 in which caries-preventive regimens with less than 3 grams per day with few exceptions were ineffective for caries prevention.

6 Is xylitol feasible from a cost-benefit perspective?

In evidence-based medicine it is common to calculate the “number needed to treat” from randomised controlled
### Table 1
Controlled clinical trials in children and adolescents with xylitol-containing products and caries as endpoint published between 2000 and 2008.

<table>
<thead>
<tr>
<th>First author, reference</th>
<th>n</th>
<th>type/duration</th>
<th>age</th>
<th>xylitol dose gram/day</th>
<th>outcome test/control</th>
<th>PF</th>
<th>sign²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alanen, [2]</td>
<td>261</td>
<td>CCT/3 yr</td>
<td>school</td>
<td>5.0, gum</td>
<td>1.9/4.4 DMFS</td>
<td>57%</td>
<td>S</td>
</tr>
<tr>
<td>Alanen, [2]</td>
<td>219</td>
<td>CCT/3 yr</td>
<td>school</td>
<td>5.0, tablet</td>
<td>1.7/4.4 DMFS</td>
<td>61%</td>
<td>S</td>
</tr>
<tr>
<td>Alanen, [1]</td>
<td>326</td>
<td>CCT/5 yr</td>
<td>school</td>
<td>5.0, gum</td>
<td>2.1/1.6 ΔDMFS</td>
<td>0%</td>
<td>NS</td>
</tr>
<tr>
<td>Honkala, [7]</td>
<td>145</td>
<td>CCT/18 m</td>
<td>disabled students</td>
<td>3.0*, tablet</td>
<td>-1.2/3.5 ΔDMFS</td>
<td>100%</td>
<td>S</td>
</tr>
<tr>
<td>Kovari, [9]</td>
<td>921</td>
<td>CCT/5 yr</td>
<td>preschool</td>
<td>2.5, gum</td>
<td>1.2/1.6 dmf</td>
<td>25%</td>
<td>NS</td>
</tr>
<tr>
<td>Machiulskiene, [15]</td>
<td>602</td>
<td>CCT/3 yr</td>
<td>school</td>
<td>3.0, gum</td>
<td>3.4/5.3 DMFS</td>
<td>36%</td>
<td>S</td>
</tr>
<tr>
<td>Oscarson, [21]</td>
<td>132</td>
<td>RCT/2 yr</td>
<td>preschool</td>
<td>0.5–1.0, tablet</td>
<td>0.4/0.8 dmf</td>
<td>50%</td>
<td>NS</td>
</tr>
<tr>
<td>Sintes, [25]</td>
<td>3,394</td>
<td>RCT/30 m</td>
<td>school</td>
<td>&lt;0.2, toothpaste</td>
<td>1.3/1.5 DFS</td>
<td>13%</td>
<td>S</td>
</tr>
<tr>
<td>Steckén-Blicks, [27]</td>
<td>115</td>
<td>CCT/2 yr</td>
<td>adolescents</td>
<td>2.5, tablet</td>
<td>2.7/2,7³ ΔDMFSa</td>
<td>0%</td>
<td>NS</td>
</tr>
</tbody>
</table>

PF = Prevented fraction; RCT = randomised controlled trial; CCT = cluster-randomised or non-randomised controlled trial; S = statistically significant difference; NS = not statistically significant

* a p-value less than 0.05 was considered statistically significant

² not given by authors but calculated from the product used

³ control group was fissure sealed

₃ xylitol lozenges were compared with xylitol-fluoride lozenges

### Table 2
Suggested guidelines for patient-based caries management with xylitol-containing products.

- Patients at caries risk could be recommended to use xylitol-containing products as a complement to the daily fluoride exposure
- At least 5 gram of xylitol per day is needed to optimize the beneficial effects on oral ecology in schoolchildren and adolescents
- The daily intake should be divided into 3–4 occasions, for example morning, noon and evening. The exposure time should not be shorter than 5–10 minutes
- Xylitol products that actively stimulates saliva secretion should be advocated
- Recommended products should contain as much xylitol per unit as possible and with xylitol as the single sweetener
trials in order to compare observed differences between test and intervention groups in various studies. The value is a measure that indicates how many patients that need to undergo a defined intervention over a period of time in order to gain one caries-free patient but unfortunately such figures are seldom available from xylitol trials due to incomplete data presentation. Instead, the number of chewing gums needed to avoid one cavity can be estimated. Such a calculation based on the 3-year chewing gum trial published by Machiakiewicz et al. [11] revealed that approximately 3000 pieces of chewing gums would be needed to avoid one cavitated lesion. The direct cost only for the gums would therefore exceed 250 Euro according to average chewing gum prices. Other studies that have reported a less favourable outcome would of course exhibit even higher costs and whether or not the price is affordable can only be decided by the individual patient. Interestingly, one study has equalled the costs for xylitol-based prevention with fissure sealants [1], a treatment that is commonly questioned from a health-economical point of view.

7 Which patients benefit from xylitol?

A common recommendation is that xylitol-containing oral products such should be included in the armamentarium for preventing caries in patients with high risk or in caries active patients [12]. However, there are few studies of acceptable quality available on selected risk patients and it should be stressed that findings from previous trials in high-caries populations, such as the Belize project, cannot readily be generalised into today’s caries situation in low-caries communities. One recent randomised controlled trial included xylitol among other preventive measures in a 3-year very intensive targeted program for caries active adolescents [6]. The program resulted in significantly less decay but the relative impact of the various components of the program was unclear. Interestingly, no differences were found in the self-reported dietary habits between the test and the control group except for the use of xylitol products. Another recent trial tested xylitol-containing lozenges vs. similar tablets containing xylitol and fluoride in teenagers at risk and compared the results after two years [27]. The findings did not disclose any significant difference between the experimental groups and the caries increment was similar to a control group with a conventional risk management. However, the study suffered from a high drop out rate and less that 50 % of the adolescents showed a good compliance. The fact that the “compliers” exhibited less caries than those with poor adherence to the program illustrates some of the obstacles involved with the high risk strategy. Individuals lacking confidence and motivation, neglecting health messages and self-care, are probably unlikely to comply with any treatment regimen and in this aspect, xylitol lozenges were no exception.

Other suggested target groups for xylitol-based interventions include frail elderly as well as mentally retarded and physically disabled patients [7, 17, 24]. In such vulnerable groups, the daily oral care may be difficult to perform adequately and the saliva-enhancing and plaque-reducing properties of xylitol can be a valuable adjunct to other preventive measures. Studies have also indicated that adolescents undergoing treatment with fixed orthodontic appliances may benefit from habitual intake of xylitol-containing lozenges or gums in order to reduce risk for white spot lesion development adjacent to the fixed appliances [23, 26]. Xylitol-based interventions have also proven successful in clinical trials with the aim to diminish and delay the early transmission of mutants streptococci from highly colonised mothers to their off springs [8, 28].

8 Are some products better than others?

Xylitol are available in a wide range of commercial products such as toothpaste, chewing gums, slow-melting tablets and candy in various forms. Although there are no direct head-to-head comparisons available, the current concept seem to favor chewing gums because of its superior saliva-stimulating capacity. As all self-administered interventions are heavily depending on compliance, the clinicians’ challenge is to advocate a convenient way to administer xylitol in sufficient amounts, adjusted to age but also realistic from an economical point of view. As a high intake frequency may be a barrier for patients to follow a given recommendation, products with a high amount of xylitol and with xylitol as the single sweetener should be preferred. Unfortunately, there are numerous low-xylitol products with mixed sweeteners out on the consumer’s market that are less suitable for clinical use. One should also keep in mind that chewing gums, tablets or candies are not accepted by all patients. In parallel with the use of fluoride in public health, school-based xylitol-rinses in immigrant and low-income communities could be an interesting approach. Likewise, xylitol-containing rinses could be an option for elderly with active root caries. A “rinse-and-spit out” procedure would allow high topical concentrations of xylitol in the oral environment over an extended period of time without the risk of side-effects [10]. In fact, a recent study has shown that xylitol solutions were well-tolerated by infants and toddlers when given for otitis media prophylaxis [29]. Other delivery options with good compliance for low-aged children could be syrup, milk or gummy bears [14].

9 Conclusions and clinical recommendations

There is a good body of evidence that xylitol has antibacterial properties that may alter the oral ecology while the evidence for a caries-preventive effect is inconclusive. However, recent studies indicate that preventive programs should include as many complementary strategies as possible especially when directed towards caries-active patients. Therefore, xylitol should be considered as an adjunct to other measures such as fluoride exposure, fissure sealants and dental health education in individuals assessed as being at risk for future caries development or with a proven caries activity. A daily dose of at least 5 grams in fractioned doses is recommended and chewing gums seem to be the preferred vehicle for administration. The evidence-based clinical guidelines are summarised in Table 2.
References


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