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# Xylitol in preventing acute otitis media

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**Abstract**

Xylitol is a polyol sugar alcohol and is referred to as birch sugar, because it can be produced from birch. Natural sources of xylitol include plums, strawberries, raspberries and rowanberries. Xylitol inhibits the growth of *Streptococcus pneumoniae* and it inhibits the attachment of both pneumococci and *Haemophilus influenzae* on the nasopharyngeal cells. In two clinical trials xylitol was found efficient to prevent the development of acute otitis media with a daily dose of 8.4–10 g of xylitol given in five divided doses. The efficacy in these 2–3 months follow-up trials was ~40% when chewing gum was used and ~30% with xylitol syrup. The need to use antimicrobials reduced markedly when using xylitol. In a high-risk group of children with tympanostomy tubes xylitol was ineffective in preventing otitis. Xylitol appears to be an attractive alternative to prevent acute otitis media. A more practical frequency of doses should be found before its use can be widely recommended. 

*Keywords:* Xylitol; Sugar; Otitis

## 1. Development of acute otitis media

Acute otitis media is a local infection. Bacteria from nasopharynx have to be able to enter the middle ear trough the Eustachian tube. Basically the development of acute otitis media requires a respiratory infection, which impairs the function of the Eustachian tube so that effusion develops in the middle ear [1]. The orifice of the Eustachian tube is in the upper part of nasopharynx. Liquid substances as well as substances which are soluble in saliva will get in touch with the Eustachian tube orifice and could thus have an effect on the pathomechanism of the middle ear infection.

## 2. Xylitol and otopathogenic bacteria

Xylitol is a polyol sugar alcohol and is referred to as birch sugar, because it can be produced from birch. Natural sources of xylitol include plums, strawberries, raspberries and rowanberries [2]. Xylitol inhibits the growth of *Streptococcus pneumoniae*. In an experimental study where we added 1 and 5% of xylitol into the growth media xylitol almost totally blocked the logarithmic growth acceleration of pneumococci [3]. The effect was more marked with 5% of xylitol than with 1%. Xylitol had some inhibitory effect on other otopathogenic bacteria as well, but with a much smaller efficacy [3]. In the mouth it is easy to achieve concentrations of this amount by using chewing gum sweetened with xylitol. However the concentration falls rapidly in the saliva (Fig. 1).

It has been suggested that the mechanism of xylitol to inhibit the growth of the *S. mutans* bacteria is mediated via the fructose phosphotransferase system. When fructose is present bacteria will not take xylitol in them and there is no inhibition of growth. We cultured pneumococci in four different media where there was: (1) 5% xylitol; (2) 5% fructose; or (3) both 5% xylitol and 5% fructose added; and (4) regular growth medium without any extra sugar. Xylitol did not inhibit the bacterial growth when fructose was present suggesting that the growth inhibition is dependent on the fructose phosphotransferase system (Fig. 2).

One important part of the pathomechanism of acute otitis media is the attachment of bacteria on nasopharyngeal cells. We evaluated the attachment of *S. pneumonia*, *Haemophilus influenzae* and *Moraxella catarrhalis* on the nasopharyngeal cells. The attachment

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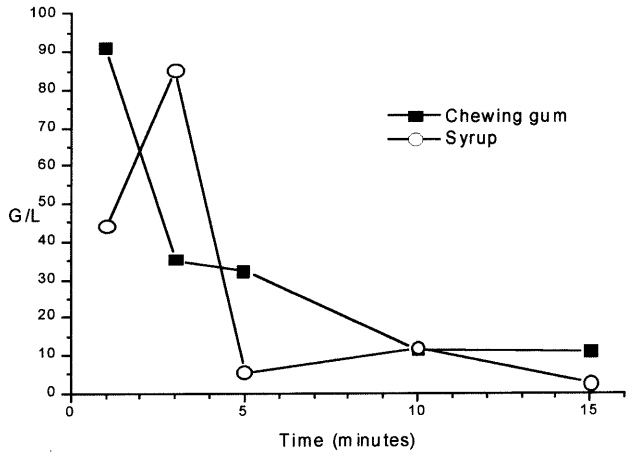


Fig. 1. The concentration of xylitol (g/l) in saliva in children after chewing two pieces of xylitol gum (1.68 g xylitol) or receiving 5 ml of xylitol syrup (2 g xylitol).

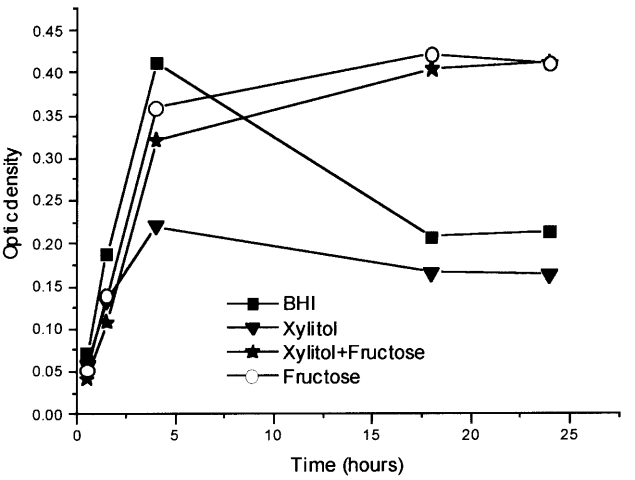


Fig. 2. Growth of pneumococci in a brain hearth infusion (BHI) medium without any sugar added, in the presence of 5% fructose, 5% xylitol or both xylitol and fructose. Growth is inhibited by xylitol and this inhibition does not occur in the presence of fructose.

of both pneumococci and haemophilus were significantly inhibited when the cells, bacteria or both were exposed to 5% xylitol (Fig. 3) [4].

## 3. Xylitol and acute otitis media in clinical trials

Three clinical trials have been performed to evaluate the use of xylitol to prevent acute otitis media. In the first randomised, double-blind trial performed in children recruited from 11 ordinary day care centres with healthy, normal children with a mean age of 4.9 years, xylitol chewing gum was found to be effective in preventing acute otitis media as compared to an ordinary sucrose chewing gum [5]. Each child was instructed to chew two pieces five times per day after meals or snacks, making a total dose of 8.4 g xylitol per day. The chewing lasted until there was no taste left or at least 5 min. The number of children with at least one episode of acute otitis media decreased by $\sim$42%. The occurrence of the first acute otitis media attack differed significantly between the groups and was associated with the amount of xylitol used: those who experienced acute otitis media had forgotten their xylitol chewing gums significantly more often than those who had not had any acute otitis media events. A similar dose dependence was not seen in the control group receiving sucrose chewing gum. The number of the children receiving at least one course of antimicrobials was $\sim$36% less among those who received xylitol chewing gum as compared to those who had sucrose chewing gum.

The pneumococcal carriage rates varied from 17.4 to 28.2% during the study, and there was no difference between the groups at any stage of the follow-up. The numbers of upper respiratory tract infections without acute otitis media, acute bronchitis, sinusitis and conjunctivitis leading to visit to a physician were nearly equal in the two groups [5].

Because the occurrence of acute otitis media is the highest among infants who are not able to chew gum, we planned a second trial where we gave syrup to those children [6]. In case the participating children were so young that they were unable to chew gum, they were randomized to receive either control syrup or xylitol mixture 5 ml five times per day after a meal. In the xylitol group the children received 10 g of xylitol daily. The control syrup was sweetened with xylitol only in a concentration of 20 g/l giving a daily dose of 0.5 g xylitol. The children who were able to chew gum were randomized to receive either a control chewing gum sweetened with sucrose and xylitol (control group) or xylitol chewing gum sweetened with xylitol only (xylitol group) or lozenges sweetened with xylitol and maltitol (lozenge group). Two pieces of gum and three lozenges were given five times a day after a meal. The children

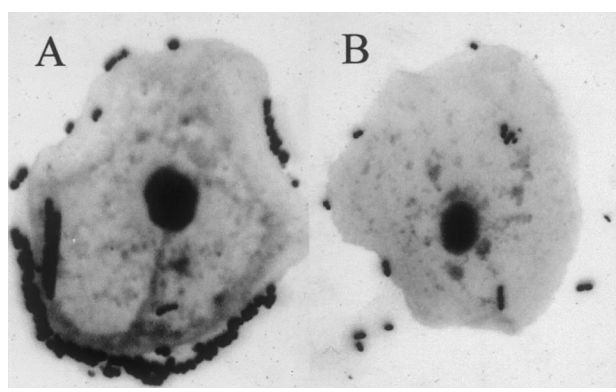


Fig. 3. The attachment of pneumococci to the nasopharyngeal cells is inhibited by exposing the cells, bacteria or both to 5% xylitol before mixing them together. Control cell (A), cell (B) when both the cell and bacteria were exposed to xylitol.

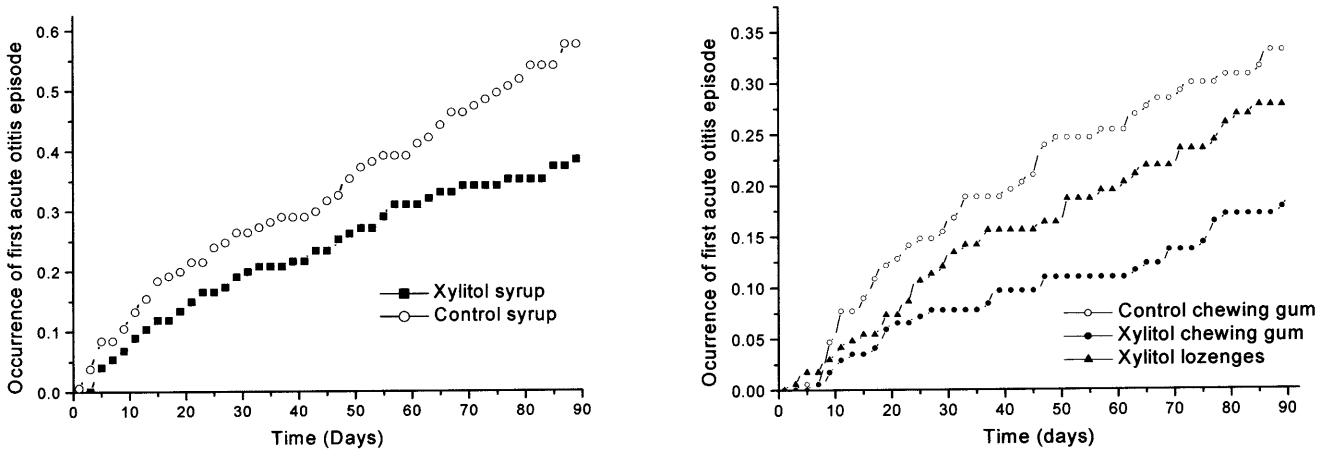


Fig. 4. The cumulative occurrence of first acute otitis media episode during the follow-up among children who received control or xylitol syrup (left) and among children who received either xylitol chewing gum, xylitol lozenges or control chewing gum (right). The occurrence of otitis was 30–40% less among those who received xylitol syrup or chewing gum.

chewed the gum and the lozenges at least for 5 min or as long as it tasted sweet. In the control chewing gum group the daily xylitol dose was 0.5 g per day and in the xylitol chewing gum group 8.4 g. Dosages of xylitol varied from 10 g/day in the syrup and lozenge groups to 8.4 g/day in the xylitol chewing gum group. Because after our first trial we were criticized for regularly giving sucrose chewing gum to children we added a small amount of xylitol to the control preparations as well. This was done to prevent the development of dental caries, but the dosage chosen was so low that it should have had no effect on the development of acute otitis media.

During the 3-month follow-up a study nurse examined all the children with any respiratory infections with tympanometry within three days from the beginning of the symptoms. The children were examined even without any suspicion of acute otitis media by the parents. The diagnoses of acute otitis media were based on the findings in tympanometry and verified by a qualified otoscopist.

Both chewing gum and xylitol syrup appeared to be effective in preventing acute otitis media (Fig. 4). The efficacy of chewing gum was almost identical to our first trial, being $\sim$40%. In the syrup groups there were more than one third less children with at least one acute otitis media episode in the group receiving xylitol syrup [6]. There were about one fifth less children with at least one episode of acute otitis media among those who received xylitol lozenges than in the control chewing gum group. This difference was not statistically significant.

The use of antimicrobials was significantly lower among those receiving xylitol mixture as compared to the control group. Similarly the prescriptions of antimicrobials decreased significantly in the xylitol chewing gum group but not in the lozenge group as compared to the control chewing gum group. The number of days on antimicrobials was significantly lower in each treatment group as compared to the controls.

In a randomized, controlled trial of 270 children who had tympanostomy tubes placed because of chronic middle ear effusion or recurrent otitis media, 90 children got hygienic instructions and xylitol in order to prevent the recurrences of otitis media. Their experiences were compared to one group receiving only hygienic instructions and to the third group who served as an open control. The cumulative occurrence of otitis media was similar in all three groups, possibly because of poor compliance in the intervention groups.

## 4. Other applications of xylitol — prevention of dental caries

As sucrose appeared to be the most important risk factor for dental caries, substitutes for it were systematically searched for. In experimental trials xylitol seemed to be a promising sweetener by being a non-cariogenic sweetener [7]. Xylitol has the same relative sweetness as sucrose. It inhibits the growth and acid production of *S. mutans*, which is the most important bacterium taking part in the pathomechanism of dental caries as is the acidity in mouth [8,9]. Regular consumption of xylitol has been shown to reduce the incidence of dental caries [10–12]. Based on these findings xylitol has been used as a sugar substitute in various sweets and especially in chewing gums. The use of xylitol chewing gums in order to prevent den-

tal caries has been widely accepted in Scandinavia and some other European countries.

## 5. Side effects of xylitol

Being a polyol, xylitol is slowly absorbed by the gut wall and may cause loose stools when ingested in large amounts. This was no problem in our trials, probably because of the dose we used. Children can tolerate daily doses up to 45 g of xylitol without gastrointestinal symptoms [13]. In addition to loose stools large amounts of xylitol may cause abdominal discomfort. This was found in our trial among those who received either lozenges or syrup. Up to 5% of these subjects did not want to take the product regularly because of some abdominal discomfort [6].

## 6. Importance of the use of xylitol

Acute otitis media is the most important indication for antimicrobial treatment in children especially at the age children are attending child day care centers. Bacterial resistance to antimicrobial agents is a rapidly growing problem worldwide with a direct association to the use of antimicrobials [14,15]. Especially young children attending day care centers contribute to the spread of resistant bacteria. Xylitol, a commonly used food sweetener seems to offer a possibility to prevent AOM in children and thus reduce the need for the antimicrobials. The dose of xylitol used in our trials is significantly higher than that which has been shown to be effective in preventing dental caries. We gave xylitol five times per day, but we do not actually know, whether a less frequent dosing could be as effective.

We recruited children in our trial from day care centers because these children have the greatest risk to develop AOM. On the other hand preventive trials are easy to organize at day care centers since the children and parents can be contacted with reasonable efforts. Yet we believe that our results are applicable to all children independent of their place of care. Xylitol seems to be ineffective when given immediately after the placement of tympanostomy tubes.

With the increasing appearance of antimicrobial resistance new alternatives are needed to prevent bacterial diseases. We found xylitol to be a promising new product, effective in mixture and chewing gums to prevent acute otitis media in children.

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