THE ROLE OF XYLITOL IN THE THERAPEUTIC PREVENTIVE MANAGEMENT OF CARIOUS LESIONS: A NARRATIVE REVIEW

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ABSTRACT

Aim of the study Since a century ago, xylitol, a white, crystalline carbohydrate, has been known as a naturally occurring five-carbon sugar polyol. Its impact on dental caries has been extensively researched during the previous forty years. It can be derived from plant materials rich in xylan, like the wood of birch and beech trees, and is naturally present in fruits, vegetables, and berries. The amount of MS in dental plaque and saliva is reduced because xylitol interferes with the energy-producing processes of Mutans Streptococci (MS), causing their death. It also reduces the adhesion of these microorganisms to the surface of teeth and, as a result, decreases their acid-producing potential. **Conclusions** Despite all the information available on xylitol, further study is still required to fully understand its mechanisms of action, the clinical implications of xylitol resistance, and how it affects Streptococcus Mutans and the plaque-saliva complex. Properly planned randomised controlled clinical trials must be conducted in conjunction with research to show that xylitol prevention is feasible in a variety of groups with various dietary and dental hygiene practices. It is also necessary to thoroughly confirm the best delivery methods for xylitol and the degree to which it can be "diluted" with other polyols without losing its ability to prevent dental caries. It is necessary to calibrate the minimal daily dose and frequency required for xylitol's effects on MS, dental plaque, and caries.

Key words: antibacterial effect, caries, xylitol, saliva

INTRODUCTION

Current aetiopathological theories of dental caries view dental caries as the result of an intricate interplay between biological, social, and behavioral elements manifested in the host and environment, with dental biofilm serving as a crucial component (Bradshaw DJ,2013).

The primary catalyst for the growth of cariogenic biofilm is fermentable carbohydrates (Marsh PD, 2003).

It has long been acknowledged that diet plays a significant part in the aetiology of dental caries, and there is little question about the benefits of sufficient nutrition for enhancing public health (Jihan Turkistani, 2020).

Diet is one of the risk factors or can be regarded as a prognostic risk factor with major influence on the non-pathogenic bacterial plaque ecosystem. In case of wrong dietary habits, it is able to promote a local caries-inductive environment responsible for increasing individual caries activity and caries risk (Iovan G, 2011; Andrian S. 2019; Ghiorghe A. 2008).

The effects of nutrition on the etiopathogenesis of carious disease are exerted post-resorptively, systemically and pre-resorptively, locally. The latter are more important and mainly involve carbohydrates.

Carbohydrate-rich diet is the food substrate required for bacterial metabolism in biofilm. Carbohydrates can be directly fermented or after storage in the biofilm as extra- and intra-cellular polysaccharides. Anaerobic fermentation results in an increase in the concentration of organic acids especially lactic acid in dental plaque and carious lesions.

In this situation, a pH decrease (increase in H+ concentration) occurs after each intake of fermentable carbohydrates followed by the initiation of demineralisation phenomena.

A number of foods which actively reduce the effects of dietary sugars and which can be considered to have a therapeutic action (more correctly a neutral, non-cariogenic action) may act either by inhibiting demineralisation or by reducing or preventing acid formation and/or accumulation in the plaque.

Natural inhibitors of demineralisation (antisolubility agents) are present in many foods and include phytic acid and glycyrrhizinic acid from the sweet wood plant (Glycyrrhiza glabra) and an unidentified factor in chocolate.

Some of these factors are removed in the refining process. Orthophosphates (orthophosphoric acid in soft drinks) are included in some foods to delay demineralisation through a common ionic effect. Additives containing calcium and phosphate can support remineralization of incipient enamel lesions, an effect also attributed to cheeses and sugar-free chewing gums.

Xylitol is a natural sweetener (a non-cariogenic sugar alcohol with 5 carbon atoms) that can be found in birch sap, fruits and vegetables (berries, mushrooms, lettuce, hardwood, corn), as well as in certain foods and oral hygiene products. It tastes similar to sugar, but significantly differs in its effects on dental health.

German scientist Emil Fisher and colleagues discovered xylitol in 1891 (Washuttl J, 1973). In the 1960s, xylose that was taken from plants could be economically produced by adding hydrogen to create xylitol, which was then utilized as a sweetener in food manufacture (Hansom J, Mühlemann HR, 1970).

Following the discovery of xylitol's ability to prevent tooth decay by a group of researchers headed by Professor Mäkinen of Turku University in Finland (Scheinin A, 1975), xylitol was recognized globally as a functional food that lowers the risk of tooth decay.

At the moment, xylitol is produced and sold in a variety of products, such as gum, candies, snacks, syrups, tablets, and more (Gupta M, 2018). For the purpose of preventing dental caries in infants, kids, teens, and people with special needs, the American Academy of Pediatric Dentistry (AAPD) acknowledges the advantages of sugar substitutes, especially xylitol (American

Academy on Pediatric Dentistry Council on Clinical Affairs, 2016).

Consequently, a policy on the use of xylitol-based products in caries prevention has been intended by the AAPD (Jihan Turkistani, 2020).

The following are a few consequences of xylitol in the mouth: decreases the amount of bacterial biofilm, causes the bacterial biofilm to become less adherent, neutralizes plaque acids by reducing the production of lactic acid, reduces Streptococcus mutans levels, significantly reduces long-term caries (88-93%), reduces cavity lesion formation by up to 80%, helps remineralize enamel by repairing the surface defect and maintaining the newly obtained crystallization system, reduces gum inflammation, reduces symptoms of "dry mouth" syndrome and halitosis.

Additionally, xylitol increases salivary flow rate, which protects both hard and soft oral tissues and increases the mobility and accessibility of calcium ions (Tyagi et al., 2013).

This product has been shown to possess passive and active anticariogenic properties (Andrian S, 2019). One of its advantages is that it does not increase blood pressure or blood glucose levels as most sugar substitutes do (Tyagi et al., 2013).

The mechanisms involved in these phenomena are extremely diverse and complex and can take several directions:

1. Inhibits the growth of cariogenic bacteria. It acts on bacteria that cause dental caries, such as Mutans Streptococcus. Regular consumption of xylitol can inhibit the growth of these bacteria, thereby reducing the risk of caries formation.

2. Xylitol stimulates the production of saliva, which plays an essential role in protecting teeth. Saliva helps to neutralise acids produced by bacteria, wash away food debris and remineralise enamel.

3. An important aspect of xylitol is that it is not fermented by bacteria in the mouth. These bacteria metabolise sugar and other carbohydrates, producing acids that erode enamel and lead to caries formation. Xylitol cannot be metabolised by bacteria, which makes it less cariogenic and more beneficial for dental health.

4. Xylitol promotes remineralization of tooth enamel. This is because xylitol stimulates the secretion of saliva, which contains essential minerals for tooth structure. By increasing the concentration of minerals in saliva, xylitol can help to repair enamel weakened by acids and strengthen teeth.

Many in vitro and in vivo studies have demonstrated the efficiency of xylitol in reducing the risk of dental caries (Gupta M, 2018 ; Tyagi et al., 2013; Hansom J, Mühlemann HR, 1970 ; Marsh PD, 2003).

A study published in the Journal of Dental Research found that consumption of xylitol products reduced tooth decay in children by up to 70%. Clinical studies have also shown that xylitol products, such as chewing gum or xylitol-sweetened foods and drinks, can reduce dental plaque formation and inhibit the growth of cariogenic bacteria.

It is important to note that xylitol should be used appropriately and in moderation. Excessive consumption of xylitol can have side effects such as diarrhea or other digestive disorders. It is recommended to consult a dentist or specialist before introducing xylitol into an individual's oral hygiene programme or diet.

There are a lot of studies and research that have evaluated the effects of xylitol on dental health and have linked xylitol consumption to a reduced risk of dental caries, particularly in smokers.

An example of a study published in the journal Caries Research in 2016 showed that the use of xylitol in oral hygiene products, such as toothpaste and chewing gum, induced a significant reduction in the number of Mutans Streptococcus in dental plaque, particularly in patients who smoke.

Another study published in the International Journal of Dentistry in 2019 evaluated the effects of xylitol in reducing dental plaque formation and tooth decay in smokers. The results showed that regular use of xylitol-containing products, such as chewing gum or xylitol-sweetened foods, not only reduced dental plaque formation, but also decreased the number and severity of cavities among smoking patients.

These are just some examples but a wide variety of studies are investigating the effects of xylitol on dental health. One widely cited study related to xylitol and cariogenesis is called "The Turku Sugar Studies". These extensive studies have been conducted in the city of Turku in Finland since the 1970s and investigate the effects of sugar consumption and alternative sweeteners, including xylitol, on dental health.

One of the studies in this project, published in the Journal of Dental Research in 2002, examined the effects of xylitol on school populations in a caries prevention programme. The results showed that regular use of xylitol in chewing gum significantly reduced the incidence of caries among children.

Another important study in the area of xylitol and smoking is "Effects of xylitol on salivary mutans streptococci, plaque pH, and caries prevalence in cigarette smokers" published in Caries Research in 2011. This study evaluated how xylitol consumption influences salivary Streptococcus mutans levels, plaque pH levels, and caries prevalence in smokers. The results indicated that regular use of xylitol reduced the number of cariogenic bacteria and helped maintain a more alkaline pH in the oral cavity, leading to a decrease in the prevalence of dental caries in smokers.

The use of xylitol in foods, medications, and oral health products—mostly chewing gum, toothpaste, syrups, and pastries—has been approved in more than 35 countries.

The best time is right after meals and after the patient has rinsed their mouth with plain water. Recommended dosages vary depending on the purpose. For maximum protection against caries, 7–20 g/day divided into several doses of lollipops or chewing gums is indicated (Milgrom et al., 2009).

Chewing gum should not be used for people with temporomandibular joint dysfunction who have trouble chewing; instead, xylitol candies should be used. When taken in large quantities, xylitol can induce diarrhea in children at 45 g/day and in adults at 100 g/day.

The amount that can be tolerated varies depending on body weight and individual susceptibility. Adults can typically handle 40 g per day.

The frequency of administration, dose response, and minimum salivary concentration are crucial factors to consider when administering xylitol. Only a small number of studies, with inconsistent findings, have measured the concentration of saliva polyol following consumption of xylitol-containing products (Riedy, C.A 2008).

In the early 1990s, US dental literature started to publish the first meaningful recommendations for the use of xylitol. Chewing gum, toothpaste, drops, and mouth rinse solutions can all contain xylitol.

The medical model approach to dental caries, which included xylitol, fluorides, antimicrobials, and sealants, was introduced by Anderson et al. in 1993 (Anderson MH, 1993).

Research has demonstrated the necessity of recommended preventive strategies to control caries risk factors. These strategies are primarily based on dietary modifications, such as cutting back on sugar intake and enhancing host resistance with fluoride product administration twice daily (Milgrom P 2012, Petersen PE 2004).

But the distribution of caries prevalence, which is skewed toward high levels, indicates that novel and efficient preventive strategies are required, particularly for high-risk populations (Bagramian R 2009, Marcenes W, 2013). Chewing gum without sugar has the potential to prevent dental caries (Deshpande A, 2008). Enhanced salivary flow stimulates oral clearance and enhances the ability of the saliva to act as a buffer against the pH of acidic plaque (Dodds MW, 2012).

According to published research, taking xylitol may result in less plaque buildup, fewer SM, and a decreased risk of caries (Söderling EM 2009, Campus G 2013).

While xylitol's exact mechanisms of action are unknown, a number of studies have highlighted its advantages, and clinical trials have revealed that xylitol has both cariostatic and noncariogenic qualities (Splieth CH, 2009).

The optimal dosage is up for debate, but for clinical effect, a daily total dose of 3 to 8 g of xylitol is typically recommended. Low doses of xylitol have been suggested to be effective in preventing dental caries in children (Riley P, 2015); however, the results are not significant for long-term caries reduction efficacy.

The main ways that xylitol is administered are through toothpaste, mouthwash, and chewing gum.

Chewing gum increases saliva secretion and speeds up the body's natural cleansing and acid neutralization processes. This helps the body absorb calcium phosphate molecules, which help to remineralize tooth enamel (Honkala E, 2006). After a meal, chewing should be done for about twenty minutes. Chewing gum containing xylitol for at least three weeks reduces S. mutans levels in saliva and plaque over a long term (Mäkinen KK,2009). Children exposed to daily xylitol use for 12–40 months have been shown to have a lower incidence of dental caries (Kandelman D, 1988).

Benefits have been seen for up to five years following xylitol use interruption (Isokangas P, 1993). The reduction of plaque MS levels with increasing exposure to xylitol was confirmed by a prospective, double-blind, controlled clinical trial. Nonetheless, an ongoing impact was noted within the 6.88 g/day and 10.32 g/day range. During the xylitol use period, a long-term relationship between tooth eruption and the caries prevention effect was observed (Scheie AA,1998).

Children who chewed xylitol gum had considerably less decay progression after 24 months than those who did not use it, according to a Montreal study on children.

The best time to introduce chewing gum for caries prevention is at least a year before the eruption of permanent teeth, according to a long-term study that found that using xylitol chewing gum can reduce the risk of caries by 59% (Hujoel PP, 1999).

For smokers, xylitol-sweetened chewing gum can be a great alternative. Chewing xylitol gum after smoking has the potential to enhance salivation and counteract acidity in the mouth.

Since young children who have early childhood caries are more likely than those who do not to develop dental caries in their permanent teeth, **xylitol syrup** is recommended for them, beeing the most appropriate and secure approach. Oral xylitol syrup, administered twice daily at a total daily dose of 8 g, has been found to be beneficial in preventing dental cavities.

Research validates that xylitol's antibacterial properties are due to the substance itself, rather than the chewing and digestion processes of the food ingested.

For the syrup to be effective, should be consumed two times a day, which will improve both compliance and the therapeutic effect. Since retail xylitol syrup is not yet accessible, substitutes can be made with commercially available products like pudding, jam, and syrup.

Mouthwash with xylitol. In comparison to xylitol and chlorhexidine alone, the impact of a combination of the two on the viability of Sanguis Streptococcus or Mutans Streptococcus during the early phases of biofilm generation has been investigated (Decker EM,2008).

Compared to xylitol or chlorhexidine used alone, the combination of xylitol and chlorhexidine inhibited streptococci more. This recently identified synergistic activity may be beneficial for patients at high risk of dental caries or for lowering the risk of mother to child transmission of Mutans streptococcus.

Chlorhexidine monotherapy and solutions including xylitol and chlorhexidine are efficient against both Mutans Streptococcus and Sanguis Streptococcus. Mutans Streptococcus colonies were more susceptible to the xylitol/chlorhexidine solution, whereas Sanguis Streptococcus was more sensitive to the antiseptic effects of chlorhexidine alone.

Mouth sprays. In addition, there exist mouth sprays or mouthwashes with xylitol that can be used to rinse the oral cavity after smoking or between toothbrushing sessions. These oral care products help maintain a clean mouth and reduce the risk of cavities.

Toothpaste with xylitol. Research has demonstrated that the utilization of toothpaste containing xylitol leads to a reduction in the number of Mutans Streptococcus colonies present in saliva, a decrease in salivary flow rate and an increase in pH levels. According to Surdacka (2005), the introduction of it into preventive programs could have a beneficial impact on the overall quality of the oral environment.

According to a study conducted by Makinen KK in 1985, it has been demonstrated that the presence of xylitol in fluoride toothpastes at a reduced quantity can enhance the protective effects against tooth enamel decay.

The combined utilization of xylitol in conjunction with small concentrations of fluoride ions has been found to effectively manage dental cavities and prevent direct exposure of tooth enamel to fluoride throughout the mineralization stages (Petersson LG, 1991).

Chewing gum has emerged as the predominant xylitol product in terms of usage. It has been established that sustained and prolonged exposure of teeth to xylitol is necessary, regardless of the specific product employed, such as chewing gum, toothpaste, mouthwash, pills, or confectionery.

In a given scenario, a clinician possesses the ability to select from a variety of possible solutions. For instance, those afflicted with temporomandibular joint disease may abstain from consuming xylitol gum during the mastication process.

Furthermore, the use of xylitol is advised, particularly for youngsters or those who have limited physical dexterity and lack supervision during brushing (Kovari H, 2003).

According to Shyama M (2006), the consistent utilization of xylitol candies three times daily in children with mental disorders demonstrates a significant reduction in plaque scores and gingival index. This finding provides evidence for the beneficial impact of incorporating xylitol candies into oral hygiene practices for this specific population.

There are few studies in the existing literature regarding the combined impacts of xylitol and other dental health-enhancing products, including fluoride, chlorhexidine, and probiotics.

According to a study conducted by Taipale et al. (2007), the combination of xylitol with probiotics has demonstrated a positive impact on the composition of intestinal microbiota. According to Twetman (2008), the efficacy of probiotics, specifically L. reuteri and L. rhamnosus GG, has been demonstrated in reducing the abundance of oral infections. Additionally, these probiotics exhibit positive effects when combined with xylitol.

The proposal suggests a recently developed approach for the release of remineralizing ions, in conjunction with xylitol, through the utilization of a NaF varnish known as Embrace Varnish (Pulpdent). The use of a xylitol coating serves to inhibit premature reactivity and promote controlled release of these ions. According to Goldstep (2012), when saliva comes into contact with xylitol, it causes the xylitol to dissolve. This dissolution leads to the release of calcium and phosphate ions. These ions then have the ability to react with the fluoride present in the varnish.

The resulting reaction forms a protective layer of fluorapatite on the surface of the enamel.

According to Rochel et al. (2011), the incorporation of xylitol at a concentration of 10% into toothpastes containing fluoride resulted in an enhanced protective effect on enamel, leading to higher resistance against erosion and abrasion.

According to Ibrahim-Auerkari et al. (2010), in vitro tests shown that the application of 20% and 50% xylitol solutions on demineralized enamel samples for a duration of 2 weeks at a temperature of 37 °C resulted in a considerable enhancement in enamel hardness and improvement in surface condition.

Research studies have demonstrated that xylitol exhibits clinical efficacy in reducing dental plaque and gingivitis among individuals in the pediatric and young adult age groups. In a study conducted by Shinga-Ishiharaa in vivo, it was observed that xylitol chewing gum had the ability to reduce levels of Mutans Streptococcus. On the other hand, in vitro experiments have demonstrated that xylitol exhibits inhibitory effects on the growth of various bacterial strains including Mutans Streptococcus, Streptococcus Sobrinus, Lactobacillus Rhamnosus, Actinomyces Viscosus, Porphyromonas Gingivalis, and Fusobacterium Nucleatum. However, it should be noted that the effects of xylitol on these strains vary.

According to Park (2014), xylitol has the capacity to impede the synthesis of inflammatory and proinflammatory cytokines originating from periodontal bacteria, including Porphyromonas Gingivalis and Aggregatibacter Actinomycetemcomitans.

Adverse consequences. The utilization of xylitol products as a sweetener is more costly in relation to sucrose, mostly due to the intricate production and purifying procedures involved. Furthermore, because to its inadequate hydrolysis and limited absorption inside the small intestine, excessive consumption of this substance might lead to the occurrence of osmotic diarrhea and flatulence. Excessive intake may also result in the development of intestinal problems, such as chronic osmotic diarrhea.

In order to mitigate the occurrence of gas and diarrhea, it is advisable to gradually introduce xylitol into the diet over a period of at least one week. This gradual introduction allows the body, particularly in the case of young children, to acclimate to the polyol.

Xylitol possesses potential applications in the field of medicine, such as its utilization in the treatment of acute medium otitis (AMO). This is attributed to its antibacterial capabilities against Streptococcus Pneumoniae, as well as its ability to aid in stomach emptying following surgical interventions. Xylitol solutions have been found to be effective in regulating blood glucose levels and addressing malnutrition in post-operative patients within the field of nutrition.

One notable benefit of incorporating xylitol into caries prevention initiatives is its accessibility, since it may be readily administered by parents at home and by teachers at school, without necessitating specialized people. This advantage holds particular significance in socioeconomically disadvantaged regions across the globe.

CONCLUSIONS

The real benefits and advantages of using xylitol for dental caries prevention have not yet been fully clarified. Additional well-designed randomized controlled studies are required to complete the current evidence on the effectiveness of xylitol in preventing dental caries, particularly in individuals who are at a high risk of developing caries.

Further studies following a research design are needed to refine the concepts of dose response, frequency of use, delivery vehicles, mechanisms of action, immediate and late effects, and at-risk groups that would be targeted for routine use of xylitol. Hence, it is imperative that the development of products and the implementation of therapeutic protocols to be based on scientific evidence in order to establish the viability of utilizing xylitol as a preventive measure across diverse populations with varying dietary and oral hygiene practices.

Although there exists an abundant literature regarding xylitol, further investigation is needed for underlying mechanisms by which xylitol exerts its effects, the clinical implications of xylitol resistance, and the impact of xylitol on the distribution of MS within plaque and saliva. In addition, it is necessary to systematically verify the appropriate delivery mechanisms for xylitol and determine the degree to which xylitol can be blended with other polyols without compromising its caries-preventive properties.

It is imperative to establish the appropriate minimum daily dosage and frequency required to observe the effects of xylitol on Mutans Sterptococci, plaque formation, and dental caries. It is recommended that additional research to be undertaken to determine the optimal age for initiating xylitol consumption, the appropriate frequency of consumption, the most efficient method of providing xylitol, and the ideal concentration of fluoride to be incorporated.

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