A review on saliva implication in caries development and consequences on primary canines and molars

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Abstract

Background: Caries are a multifactorial infectious disease in which many factors such as saliva, microbial flora, tooth morphology, general health condition, hormonal status, dietary habits, fluoride supply, and hygiene control are implicated. Salivary flow, acidity, and saliva composition are particularly the contributors in tooth decay both development and prevention. Consequences of dental caries can be dramatic not only on the patient’s well-being in the esthetic and functional aspects but also on the arch dimensions, a potential need for orthodontic intervention.

Aim: In this article, the etiology of caries is overviewed with a focus on the effects of saliva and its components in this process as well as salivary defence mechanisms for a better understanding of the role of saliva, and potentially the focus on preventive therapies in primary and mixed dentition children.

Conclusion: Saliva was found a major factor in decays formation and subsequently tooth loss, through its chemical components and physical properties.

Clinical Significance: Hygiene control and early caries removal combined with knowledge on saliva characteristics in children would help preventing the leeway space loss, thus decreasing the need for orthodontic treatment related to arch length discrepancy.

Introduction

Dental caries are the most frequent infectious disease among children worldwide,[1,2] and their development showed a strong relationship with hygiene habits and salivary factors.[3] Nevertheless, the severity of caries development varies among individuals and populations when consuming the same amount of sugar.[4] In fact, dental caries were first defined as a transmissible infectious disease in animals by Keyes in 1960,[5] and Streptococcus mutans and Lactobacillus were considered the major bacterial groups responsible of dental caries formation.[6] S. mutans can actually colonize and multiply on the dental surface, as soon as the tooth erupts into the oral cavity.[7] On the other hand, Lactobacillus is essentially related to the caries progression.[8] The plaque bacteria associated with dental caries is mostly Gram-positive and capable of breaking sugars, metabolizing glycans, and producing acids.[9]

Formation of dental caries

Caries develop from the bacterial acids present in the adherent dental biofilm (plaque), in the presence of carbohydrates, the major dietary components implicated in dental caries, particularly sucrose.[9] Carbohydrate fermentation in the presence of plaque cariogenic bacteria leads to organic acid production, mainly lactic, formic, and acetic acids.[10,11] This acidification decreases dental plaque pH, consequently, leading to tooth surface demineralization[12,13] and further growth of cariogenic bacteria.[14,15] In fact, the regulation of plaque pH is a major factor that affects caries development. In individuals who experience caries, the bacterial acids are less effectively neutralized than in caries-free individuals.[16]

Review of the Literature

The dental pellicle

The dental pellicle is a unique film covering tooth surface. It is mainly formed by salivary proteins selectively adsorbed onto the enamel tooth surfaces.[17,18] In fact, local ecological factors largely affect the composition of the biofilm, which can get widely assorted if it is not removed. The pellicle’s microflora may be
significantly different inter- and intra-individually. The major salivary proteins forming the pellicle include acidic proline-rich proteins (PRPs), secretory immunoglobulin A (sIgA), cystatin, mucin MG1, lactoferrin, and lysozyme. Alpha-amylase, statherins, muccins, acidic PRPs, salivary immunoglobulins (Igs), and some protein-like parotid agglutinins, all present in the pellicle, seem to mediate the adhesion of streptococci to the dental surfaces. Recent studies have shown that dental caries can be detected in the absence of streptococci and lactobacilli species favoring the ecological biofilm/plaque hypothesis. The main function of the dental pellicle is enamel protection from interdental friction and friction between teeth and the oral mucosa, a necessity during mastication and oral functions. The dental pellicle also serves as a surface for bacterial adhesion, through nonspecific electrostatic and Van der Waals forces as well as through the microbial interaction with some salivary proteins. Parotid agglutinins are the most important proteins involved in the S. mutans adhesion to teeth. Interestingly, these proteins, in addition to muccins, play a role in salivary clearance through bacterial adhesion, when they are in the liquid phase. Variations exist among individuals regarding the aggregation and adhesion activities of the salivary proteins toward S. mutans. In fact, MG1 mucin is mostly present in the saliva of caries-susceptible individuals, whereas MG2 mucin is predominant in the saliva of caries-resistant individuals.

Role of saliva

Saliva is an exocrine secretion of three pairs of salivary glands: The parotid, the submaxillary, and the sublingual glands. Saliva secretion is regulated by both the sympathetic and the parasympathetic systems, with a dominance of the parasympathetic nervous system. Saliva aids in the mechanism of the oral functions such as speaking, eating, and swallowing. While the resting saliva is responsible for the protection of the oral mucosa, the role of stimulated saliva is the elimination of the oral debris and noxious mediators.

Saliva is involved in the first step of carbohydrate digestion due to its digestive and lubricating functions. In addition, it has a protective buffering role with a pH of 6.5-6.9. Saliva is also implicated in the maintenance of tooth integrity and antibacterial activity in the oral cavity. It provides host defensive mechanisms to maintain equilibrium between mineralization and demineralization. Oral clearance capacity refers to the flushing and neutralizing capacities of saliva. It increases with saliva flow rate increase, enhancing saliva buffer capacity, the latter being influenced by hormonal and metabolic changes such as pregnancy, gender, menopause, and contraception.

Composition of saliva

According to the gland that secretes it, saliva can be either serous, seromucous, or mucous. The three types of saliva contribute differently to the mixed saliva. Saliva content can be divided into organic substances, including enzymes and other proteins, and inorganic substances which include electrolytes, vitamins, and low-molecular-weight compounds. Moreover, the salivary bacterial profile can be different in individuals highly experiencing caries than in those with low caries experience. The salivary electrolytes and proteins are involved in the control of the oral microbiota and the protection of the dental enamel from dissolution. Each of the salivary glands secretes in variable amounts a wide range of molecules: Statherins favoring enamel remineralization, amylases, cystatins known for their proteolytic activity, PRPs, mucins, and sIgA. Other proteins are also found in saliva in smaller amounts: Antimicrobial and antifungal histatins, an antimicrobial peptide, beta (ß)-defensin-1, and proteases. Saliva is hypotonic relative to plasma, with higher concentrations of potassium (K+) and bicarbonate (HCO₃⁻), and lower concentrations of sodium (Na+) and chloride (Cl⁻).

Saliva as a buffer system

Three major buffer systems are involved in the buffer function of both the stimulated and unstimulated saliva: The bicarbonate (HCO₃⁻) system, the phosphate system, and the protein buffer system. The bicarbonate system has a pH of 6.1-6.3 and the phosphate system has a pH of 6.8-7.0. The contribution of the phosphate and the protein systems is minor to the total salivary buffer capacity, in comparison with the bicarbonate system.

The human saliva presents a homeostatic state of super saturation regarding calcium and phosphate. Salivary proteins such as cystatins, histatins, acidic PRPs, and statherins are implicated in maintaining this status of equilibrium and in the interaction of some microorganisms.

Reduced salivary secretion

Hyposalivation and reduced salivary flow were correlated to caries development and mucosal inflammation. A study reported that when low saliva flow rate is associated with low or moderate buffer capacity, resistance against bacterial agents is decreased.
Oral defence mechanisms

Saliva confers defence mechanisms to the mouth, and those can be divided into mechanisms related to the innate defence system and others related to specific defence factors.

In the innate defence mechanism, peroxidase, lysozyme, lactoferrin, and histatins represent the predominant defence molecules. In vitro studies of these proteins showed their implication in limiting bacterial or fungal growth, regulating bacterial glucose uptake or glucose metabolism, and promoting aggregation and clearance of bacteria. The levels of these proteins are age-related. All of these protein levels are lower during childhood and early teenage years compared to adult rates. With significant tooth loss, the protein levels are also decreased. Several studies attempted to correlate the level of peroxidase activity, lactoferrin, and other protein levels with dental, gingival, and mucosal health. The results remain controversial, mainly due to the variability in research design, saliva collection methods, saliva analysis techniques, statistical analysis, and presentation. It is unlikely to find a strong correlation between one salivary innate defence molecule and others related to specific defence factors.

In the specific defence system, Igs such as IgM, IgA, and mainly IgG and sIgA are the predominant actors. Secretory IgA is produced by local plasma cells in the salivary glands and transported through the secretory epithelia to the oral cavity. Most salivary IgG derive from the blood circulation through the gingival crevicular epithelium, yet some are the local production of the gingiva and the salivary glands. Salivary IgG is found at birth, whereas it takes salivary IgA 1 week after birth to be detected. IgG levels will decrease few months after birth and increase again with tooth eruption. A correlation between salivary IgA and bacterial colonization has been found. In children over 3 years of age, IgA against S. mutans was detected, in levels proportional to the duration of exposure to that bacterium.

In the oral cavity, Igs are implicated in the neutralization of some virulence factors, limiting bacterial adherence, bacterial aggregation, and protection of the oral mucosa from foreign antigen penetration. They can also opsonize bacteria for subsequent phagocytosis. Conflicting results were found related to the direct effect of Igs on dental caries. In fact, methodologies of caries evaluation were different from one study to another, some correlating Ig levels with DMFT/DMFS (D=Decayed, M=Missing, F=Filled, T=Teeth, and S=Surfaces) scores, others with the presence of active carious lesions or with the salivary levels of S. mutans.

The consequences of decays on the primary teeth

The permanent premolars being smaller than the primary molars, the sum of the mesiodistal width of primary canines and premolars is then greater than that of their permanent successors. An extra space, called the leeway space, will be available in both arches after the shedding of the primary molars. This space is on average 2.5 mm in the mandible and 1.5 mm in the maxilla.

The leeway space will be used for permanent teeth alignment by a forward movement of permanent molars. Consequently, between the ages of 8 and 13 years, the mandibular arch length decreases by 2-3 mm on average, and the mandibular arch circumference decreases by 3.5-4.5 mm. Alignment in the leeway space depends on “the sequence of shedding and eruption of maxillary and mandibular posterior teeth and molar occlusion.” In the presence of dental crowding and when this space is needed for tooth alignment, the timing of space maintenance to preserve the leeway space is of great importance for the relief of crowding. Indeed, a study found that the preservation of the leeway space in the mixed dentition could relieve moderate (average of 4.8 mm) mandibular incisor crowding after the use of lingual arches in 60% of the patients.

Loss of the leeway space

Caries are the major contributory fact, leading to the early loss of primary teeth in children, and saliva is considered a major factor in decays pathogenesis. Many studies reported space loss as a consequence affecting the mandible more than the maxilla, especially after the early loss of second primary molars. More space loss occurs usually during the first year following deciduous tooth extraction. The rate of space loss differs according to the arch: In the maxilla, more loss was reported when the extractions were done at younger ages, whereas in the mandible, the rate of space loss was similar at all ages. Space maintenance is thus recommended to prevent any subsequent space loss.

According to the literature, the prevalence of space loss following the premature loss of primary molars ranges from 11% to 83%. Literature agrees on the fact that the premature loss of primary molars can be considered a contributory factor to the development of malocclusion, mainly due to a decrease in arch dimension after a primary molar loss.

Clinical consequence of leeway space loss

After the loss of mandibular first primary molars, it is more probable to see the primary canine drifting distally impeding the...
space of the underlying first premolar.\textsuperscript{61-63} The erupting incisors push the primary canine distally more than the erupting primary molar does on the primary second molar mesially.\textsuperscript{66} In the maxilla, with a similar tooth loss, the primary second premolars tend to fill the space of the lost deciduous first molar.\textsuperscript{61,67-69} In children aged <11 years, the first permanent molar and the second primary molar tend to shift mesially, leading to an ectopic/blocked-out eruption of the permanent canine, and a more mesial eruption of the first premolar.\textsuperscript{66}

Following early tooth loss, the available space is unlikely to accommodate for the entire permanent dentition; the severity of the consequences of such decrease in arch perimeter depends on the duration of tooth absence, the location of tooth loss in the arch, and on the sequence of deciduous tooth extraction or loss. In the maxillary arch, impaction or ectopic eruption of permanent canines is more likely to occur after the loss of primary first molars, whereas impaction of second premolars is almost predictable following the early extraction of a primary second molar. In the mandible, the impaction of second premolars tends to be the consequence of primary molars loss.\textsuperscript{66}

The unilateral early loss of primary canines usually leads to a midline shift due to the migration of the incisors toward the extraction site.\textsuperscript{64,70} On the other hand, bilateral loss of deciduous canines would affect the midline to a lesser extent but would cause a reduction in arch perimeter due to the lingual tipping of mandibular incisors.\textsuperscript{64,70} Following the early loss of a primary canine, space maintenance is required to prevent the subsequent lingual movement of the incisors.\textsuperscript{65}

**Conclusion**

Preventing decay formation is commonly seen through the optimization of dietary habits and plaque accumulation control. On the other hand, the adequate salivary examination would also help in controlling caries formation, and thus decreasing tooth loss. Particularly in children, an optimal oral health condition should be maintained to keep the integrity of the arch. This applies especially in individuals where the leeway spaces are needed for permanent teeth alignment and/or correction of permanent molars relationship. Future research focusing on salivary functions and salivary components would help in a comprehensive prevention of dental caries, and consequently, the need for orthodontic intervention especially in children at risk.

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