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ORIGINAL

The relationship between saliva and the prevalence of tooth decay: A mini review

La relación entre la saliva y la prevalencia de la caries dental: Una mini revisión

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Abstract

Saliva plays a significant role in maintaining oral health, helping to build and maintain the health of soft and hard tissues. When saliva flow is reduced, oral health problems such as dental caries and oral infections can develop. As a biological fluid whose main constituents are proteins and electrolytes, saliva can be a suitable, inexpensive, affordable and non-invasive diagnostic tool in the diagnosis of oral infections. By conducting a proteomic study on saliva, one can accurately understand all salivary protein compounds, their role in human health, the function of each of the protein compounds, and the nature of different isomètres of enzymes in saliva. In this study, after classifying and presenting a summary of the results of research on the role of saliva in the diagnosis and evaluation of oral diseases, especially tooth decay, it has been attempted to discuss the importance of salivary secretion proteins so that the reader can find valuable information on the relationship between saliva and the prevalence of tooth decay.

Key words: Saliva, proteomics, biomarkers, salivary leak proteins, tooth decays.

Resumen

La saliva desempeña un papel importante en el mantenimiento de la salud bucodental, ya que ayuda a construir y mantener la salud de los tejidos blandos y duros. Cuando el flujo de saliva se reduce, pueden surgir problemas de salud bucal como la caries dental y las infecciones orales. Como fluido biológico cuyos principales constituyentes son las proteínas y los electrolitos, la saliva puede ser una herramienta de diagnóstico adecuada, barata, asequible y no invasiva en el diagnóstico de las infecciones orales. Al realizar un estudio proteómico de la saliva, se pueden comprender con precisión todos los compuestos proteicos salivales, su papel en la salud humana, la función de cada uno de los compuestos proteicos y la naturaleza de los diferentes isómeros de enzimas en la saliva. En este estudio, después de clasificar y presentar un resumen de los resultados de las investigaciones sobre el papel de la saliva en el diagnóstico y la evaluación de las enfermedades bucodentales, especialmente la caries, se ha intentado discutir la importancia de las proteínas de secreción salival para que el lector pueda encontrar información valiosa sobre la relación entre la saliva y la prevalencia de la caries.

Palabras clave: Saliva, proteómica, biomarcadores, proteínas de secreción salival, caries dentales.

Introduction

Dentists are looking for a suitable diagnostic tool that is preferably non-invasive so that they can diagnose caries, determine the status of periodontal disease, monitor patients' response to treatment, and estimate how sensitive individuals are to the progression of possible future dental disease. Thus, the role of saliva in the diagnosis of diseases was first introduced by the National Institute of Dental and Craniofacial Research (NIDCR)[1].

This complex oral fluid consists of the secretions of three pairs of main and secondary salivary glands of mucosa. In the second definition, saliva is an extracellular fluid produced and secreted by the salivary glands of the mouth. Salivary secretions are automatically controlled by mechanical and neurological factors. Parasympathetic nerves lead to watery salivary secretions and sympathetic nerves lead to salivary protein secretions[2].

Saliva is an exocrine solution consisting of 99% water. The remaining 1% consists of a variety of electrolytes and proteins. These components combined are responsible for the various functions attributed to saliva[3,4].

Saliva is formed primarily (approximately 90%) from the secretions of the three paired major salivary glands, the submandibular (around 65%), parotid (around 20%) and sublingual (around 5-7%)[5,6]. These glands are controlled by the autonomic nervous system, while minor glands (labial, lingual, buccal and palatine), distributed around the oral cavity, produce the remaining saliva (<10%)[7].

At rest, without exogenous or pharmacological stimulation, there is a small, continuous salivary flow, an unstimulated secretion, present in the form of a film that covers, moisturizes, and lubricates the oral tissues[8]. This flow of saliva at rest is in the region of 0.4–0.5mL/minute in healthy subjects[9].

Stimulated saliva is produced in response to a mechanical, gustatory, olfactory, or pharmacological stimulus, contributing to around 40-50% of daily salivary production[10]. The Salivary Flow (SF) index is a parameter allowing stimulated and unstimulated saliva flow to be classified as normal, low or very low (hyposalivation). In adults, normal total stimulated SF ranges 1-3 mL/minute, low ranges 0.7-1.0 mL/minute, while hyposalivation is characterized by a stimulated SF <0.7mL/minute[10,11].

Saliva also contains calcium and phosphate ions, which are useful for repairing damaged parts of the tooth and reversing the decay process.

Scientists' research indicates that mother's saliva boosts the baby's immune system, so that food pre-chewing acquaints the baby's body with pathogenic pathogens in the mother's saliva, causing the body to produce antibiotics and preparing the baby's immune system[12].

An introduction to Proteomics

Saliva consists of gingival cervical fluid, mucosal transudates, nasal and bronchial expectorated secretions, blood and serum derivatives of oral ulcers, bacteria, bacterial products, viruses and fungi, fallen epithelial cells and other cellular compounds and food leftovers[13].

By studying the proteomics of human saliva, we reach four types of salivary secretion proteins including proline-rich proteins, statins, cystatins, histatins[14].

The purpose of proteomic studies on human saliva are as follow:

Finding all salivary protein compounds, their role in human health, learning about the function of each protein compound and identification of different isomètres of enzymes in saliva[15-17].

Salivary secretion proteins play a significant role against tooth decay. Now, using Nano-proteomics, the concentration, quantity and quality of substances in saliva can be accurately determined. The term proteome was first coined and used in 1994 by Mark Wilkins. In his definition, a proteome refers to the complete set of proteins expressed at a particular moment in a cell. Today, however, the level of this definition has extended from the cell to the organ tissue of the organism. The study of proteomes is the subject of proteomics[18,19].

Biomarkers

Numerous researchers have attempted to show the relationship between saliva and the prevalence of caries, since the most important advantages of saliva is its being cheap, availability, and easy and non-invasive sampling.

In addition, various markers such as hormonal, microbiological, immunological, pharmacological and oncological markers can be found in saliva and compared with its serum concentration[20]. Since the concentration of these markers is lower in saliva than that of blood, it may distort clinical diagnosis through saliva. However, new methods of diagnosis have been designed to solve this problem[21].

Thus, salivary proteins and peptides are easily identified by biochemical methods such as liquid chromatography, gel electrophoresis, capillary electrophoresis, immunoassay and Lectin probe analysis, and they are used as diagnostic biomarkers[22].
Biomarkers play a diagnostic role in detecting oral infections in saliva.

Biomarkers are actually specific molecules that exist in the body and given their unique properties, they can be used by pharmacological or physiological assays as a tool to predict a complication and measure the progression of a disease and its treatment effects[23].

Tooth decay (caries)

Studies show that measuring the concentration of specific oligosaccharides in saliva and specific changes in salivary proteome are used to diagnose tooth decay[24]. As the amount of proline-rich proteins PRP3, PRPI histatin 1 and statins in saliva increases, tooth decay does not occur and a decrease in these proteins causes tooth decay[25]. Moreover, increasing the number of microorganisms

such as *Streptococcus mutanus* and lactobacilli in saliva causes tooth decay[26].

Studies show that healthy human saliva contains certain peptides, such as histatin, which help heal wounds and caries. In addition to its antibacterial properties, histatin protein increases cell contact and transport, as well as the angiogenesis process. The process of angiogenesis is a physiological process in which new blood vessels grow from existing blood vessels. Proline protein has a unique structure because it is the only protein-producing amino acid with a secondary amine. It not only helps make proteins but also acts as a catalyst in many organic reactions. The main properties and role of proline include helping collagen, regenerating cartilage, forming connective tissue, repairing skin damages and wounds, improving intestinal lining, and repairing joints[27].

Proline is converted to hydroxycine and hydroxyproline to help collagen. One of the reasons why proline is important in the body is that it, along with the amino acid glycine, is involved in collagen synthesis[28].

Collagen is the most abundant protein in the human body and is a major component of connective tissue in the body. Proline is an amino acid that is very similar to an amino acid. It is an unnecessary amino acid because the human body can synthesize it spontaneously, unlike certain amino acids that enter the body through the diet. However, glonamate can be used to produce proline. Foods high in proline protein include bone extract, source of proline for animal products such as meat, liver, chicken, fish and eggs[29].

Decreased salivary secretion, decreased salivary pH, decreased salivary buffering, increased total protein and total antioxidants in saliva, decreased total calcium in saliva cause tooth decay in children[30].

Tooth decay is one of the most common chronic infectious diseases in childhood, and various studies show that its effective factors are: *Streptococcus mutans* and Lactobacilli. *Streptococcus mutans* is an acidogenic and to some extent an aciduric bacterium and the main etiological factor in human dental caries, whose high accumulation in dental plaque is an important factor in caries[31].

Now, since the decrease in saliva flow, decrease in buffering capacity, and increase in the number of *Streptococcus mutans* and lactobacilli in saliva are usually associated with an increase in the incidence of tooth decay[32], in health conditions, there is no association between salivation and tooth decay[33]. But when the amount of salivary secretion drops below the minimum, the rate of tooth decay increases. The feeling of dryness in one's mouth, called xerostomia (dry mouth), is seen in salivary gland disorders, systemic disorders, pharmacotherapy, radiation therapy, and old age[34].

In severe cases of xerostomia, saliva is observed with low pH and low buffering capacity, increased concentration of total protein, albumin and sodium, decreased ratio of amylase to protein, increased concentration of lactulose bacilli[35].

Carbonic acid buffer, bicarbonate, acts when saliva flow rate increases.

Phosphate buffer plays an important role when saliva flow is very low.

At pHs above 6, saliva reaches its highest phosphate saturation due to hydroxyapatite. When the pH drops below the critical level of 5.5, hydroxyapatite begins to dissolve, releasing phosphates in an attempt to restore the pH balance.

The mouth is often exposed to foods whose pH is lower than that of saliva and can cause tooth enamel to dissolve[36].

In addition, it has been indicated that the formation of heterotype complexes between salivary molecules, such as high molecular weight mucin glycoprotein, amylase, histatin one, protein one rich in acidic proline and statin are associated with plaque formation and dental caries[37].

Table I: Methods for identifying proteins in saliva.

Proteins	Methods of detection
Cystatins	HPLC-ESIMS
Proline	RP-HPLC-ESIMS-MALDI-TOFMS
AStatrine	Proteomic method
Histatin	Mass fingerprinting method

Proteins involved in salivary defense function are[38]:

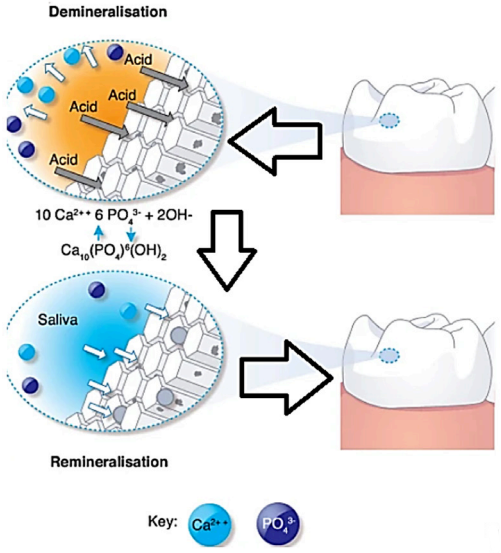
- Immunoglobulins include: IgA, lysozyme, mucins
- Antimicrobial peptides or alarmins
- Catalysidin
- Defensins
- Adrenomedullin
- Histatin: secreted by parotid and submandibular glands.
- Lactoferrin Calprotectin: A protein containing calcium and zinc.

In addition to moderating microbial factors and encouraging preventive dietary behaviors a core goal in caries prevention is promoting the natural protective mechanisms of saliva[39].

The pH of dental plaque is a key factor in the balance between acid demineralization of the teeth and the remineralization of the initial caries lesion. Plaque pH falls each time acid accumulates in the plaque due to bacterial acid production following the consumption of fermentable carbohydrates –mainly sugars– in foods and drinks. Conversely, plaque pH rises when the acids are washed away or neutralized by saliva, which contains the important buffer, bicarbonate[40].

In healthy teeth, the loss of minerals is balanced by the reparative mechanisms of saliva. This equilibrium can be depicted chemically by the equation overleaf opposite (**Figure 1**)[41].

Figure 1: The process of tooth remineralization[41].



When the saliva pH or the plaque pH is below a 'critical value' of about 5.5, the saliva or plaque becomes unsaturated with respect to tooth mineral[42]. As a result, tooth enamel can begin to dissolve. However, when the pH is above this value, the saliva and plaque are supersaturated with respect to tooth mineral. The calcium and phosphate ions in saliva then start to repair any damaged mineral crystals in the enamel – the process of remineralization[43].

Thus, acidic conditions contribute to bringing phosphate and hydroxyl ions below saturation levels, allowing the solid hydroxyapatite crystals of the tooth mineral to dissolve. If above saturation levels, the chemical reaction will move towards remineralization and any damaged crystals will be repaired by the acquisition of ions from the solution[44].

Stimulation of saliva flow results in an increase in the washing out of acids (and sugars), and also an increase in the amount and concentration of bicarbonate buffer and of remineralising ions[45].

Conclusion

From what stated above, one can understand the importance of salivary secretion proteins as methods for identifying and examining oral diseases, especially tooth decay. This calls for conductin further studies in this area. Therefore, since the introduction of liposomes as carriers of proteins in the 1960s and their proposal for the treatment of diseases, it is recommended to use nanotechnology and biocompatible nanomaterials with optimal mechanical properties as restorers and pharmacists in dentistry.

Conflict of Interest

The authors declare that they have no conflict of interest.

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