

REVIEW ARTICLE



Saliva: A mirror to health

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Abstract

Salivary composition enables it to fulfill multiple tasks, which is based both on components that originate in the oral, oropharyngeal mucosa and as secretions from the salivary glands themselves, as well as serum derivatives. Accordingly, salivary analysis facilitates the evaluation of both local and systemic changes in the body. Salivary analysis may also be used in order to examine specific disease-related alterations such as epithelial tumor markers, which is shown to be significantly increased in the saliva of oral squamous cell carcinoma. Similarly, patient's salivary components are representative of its composition under physiological or pathological conditions, and these components that may be altered in several oral and systemic conditions, aid in the further understanding of the relationship between saliva and the disease pathogenesis, as well as its contribution to its diagnosis.

Keywords: Antimicrobial, tumor marker, stimulated saliva, whole saliva

Introduction

Saliva, a unique body fluid presents in the oral cavity and is composed of a complex mixture of secretory products. Water forms, the major component of saliva comprising up to 99% of its composition. In the oral cavity, saliva has a major role in oral functions such as mastication, speech, and tissue lubrication. Saliva also exhibits several biological activities such as antifungal, antibacterial, and antiviral.^[1]

The diagnostic applications of saliva was observed by Lamster and Kaufman, 2002 who concluded that saliva offers an alternative to serum as a biologic fluid that can be analyzed for diagnostic purposes. Whole saliva or the oral fluid comprises of both secretions that are locally produced as well as serum-derivatives that have been found to be useful in the diagnosis of various systemic disorders. Whole saliva collection thus represents a non-invasive technique that can be performed even by individuals with minimal training, including patients.^[2]

Salivary analysis offers an inexpensive approach for screening of large populations, and may thus represent an alternative for patients in whom blood drawing is difficult, and in non-compliant individuals.^[3]

Salivary Constituents and its Diagnostic Application

Saliva, a dilute fluid consists of 99% of water and 1% of molecules and electrolytes. It is a hypotonic solution that allows taste buds to perceive different tastes without being masked

by normal plasma sodium level and allows for expansion and hydration of mucin glycoprotein that form a protective layer over the oral mucosa. Lower levels of glucose, bicarbonate, and urea augment this hypotonic environment enhancing taste.

Albumin, immunoglobulin (Ig) IgG, IgA, IgM, vitamins, drugs, hormones, water, and ionic constituents of saliva are derived from blood plasma. Most of the organic molecules are produced by acinar cells such as major proteins like histatins and cystatins and minor proteins like epidermal growth factor and lactoferrin. Duct cells produce lysozyme. Components of saliva occur in small amounts and vary with changes in flow. But, saliva is a unique biological fluid and must be considered as a whole that is greater than the sum of its parts.

Organic Components

Proteins

Salivary proteins comprise approximately 200 mg/100 ml (about 3% of the protein concentration in serum). Meurman *et al.*, 2002 evaluated salivary albumin concentrations in the elderly with a mean age of 77 years.

Albumin was analyzed spectrophotometrically from the saliva specimens collected, and values so obtained were statistically analyzed. A significant increase in the salivary albumin concentrations in the elderly was reported. An increase in the albumin was not related to any mucosal pathologic condition in these individuals and thus was not a contributing

factor for the raise in albumin levels. More studies are called for to find out how salivary diagnosis could be developed for aiding the clinical decision making in future oral health assessments of the individuals.^[4]

Alpha amylase

It is a major digestive enzyme of saliva found in highest concentration that metabolizes starch and other polysaccharides, and is produced by serous acinar cells of major salivary glands. It is present at concentration of 60-120 mg/100 ml in parotid saliva and 25 mg/100 ml in submandibular saliva.

Lipase

It is secreted by the lingual (Von Ebner) salivary glands and is responsible for the initial step in fat digestion. It is particularly important when pancreatic levels of lipases are low as in newborn and in diseases like cystic fibrosis.

Immunoglobulins

Secretory IgA is the predominant Ig at approximately 20 mg/100 ml with IgG (1.5 mg/100 ml) and IgM (0.2 mg/100 ml) arising from the gingival crevice. IgA aggregates oral bacteria and make it difficult for the cells to bind to oral epithelial and hard tissue surfaces.

Antibacterial proteins

Lysozyme, lactoferrin and sialoperoxidase are antibacterial proteins.

Lysozyme (muramidase) cleaves the linkage between N-acetyl muramic acid and N-acetyl glucosamine of the peptidoglycan component of the bacterial cell wall. But the oral bacteria are resistant to this action, lysozyme increases its antibacterial effects by synergizing with IgA, H_2O_2 , peroxidase and certain complement components.

Lactoferrin is a product of the serous cells. Lactoferrin can directly interact with the bacterial surface through a carboxyl anion interaction thus causing antibacterial effects. Lactoferrin is an iron-binding protein which removes free iron from saliva depleting iron supply needed for bacterial growth. Lactoferrin plays a significant role in its activity on actinobacillus organisms that induced aggressive periodontitis.

Salivary peroxidase is derived mainly from submandibular and parotid glands and a small percentage from the leukocyte and gingival crevicular fluid. It adds to the synergistic effect of antibacterial activity along with lysozyme and IgA.

The most important functions of salivary peroxidase is to control oral bacteria that form dental plaque which imbalances the oral ecology promoting dental caries and chronic periodontal disease. Salivary peroxidase catalyzes the peroxidation of the thiocyanate ion (SCN^-) to generate oxidation products (O_2SCN , O_3SCN , SCN_2 , $HOSCN$ and the more stable $OSCN$) that inhibit the growth and metabolism of many micro-organisms.

Mucin

It is high molecular weight glycoprotein produced by mucus secreting cells located primarily in the submandibular, sublingual, and minor salivary gland. It lubricates the oral surfaces and forms a protective barrier. Mucin complexes with IgA enhancing the binding capacity of the antibody to the pathogen. Mucin being a part of enamel pellicle help initiate bacterial colonization by promoting growth of normal commensals and forms a protective barrier and lubrication against excessive wear, it also forms a diffuse barrier against acid penetration and limits mineral egress from tooth surface regulating intercellular calcium levels.

Glycoprotein

Two major groups of salivary glycoprotein include (a) mucous glycoprotein found in submandibular and sublingual saliva. (b) Proline-rich glycoprotein found in parotid saliva.

These glycoproteins promote the colonization of oral microbiota like actinomyces viscosus.

Organic Compounds

Urea - many bacteria hydrolyze urea with the release of ammonia leading to a rise in pH.

Glucose concentration is minimal thus minimizing growth of pathogenic bacteria.

Inorganic Constituents

It includes ions such as sodium, potassium, chloride, and bicarbonates adding to the molarity of saliva. Bicarbonates are the principle buffer in saliva. Fluoride content is similar to that of plasma. These small amounts aid in the anti-cariogenic activity of saliva.

Calcium and phosphates are the chief inorganic constituent of saliva. part of calcium is bound to protein and a part of it complexes with carbonate, phosphate, and lactate, which plays a very important role in buffering saliva thereby maintaining the pH of saliva at 6.47 (resting) 7.62 (stimulated).

Saliva in Diagnosis

Saliva provides an easily available now increasing diagnostic medium for a rapidly widening range of diseases and clinical situations. Within the past 20 years, more than 2500 citations have focused on the diagnostic value of oral fluids particularly saliva.^[5]

It is used in the diagnosis of oral and systemic viral diseases such as measles, mumps, rubella, hepatitis A, B, and C, HIV-1 and -2 through the detection of antibodies.

Saliva also aids in diagnosis of sarcoidosis, tuberculosis, lymphoma and Sjogren's syndrome. In addition, saliva is used to monitor the levels of endogenous molecules in the body including polypeptides, steroid hormones, and antibodies.

Saliva also is being used to monitor the level of selected chemicals introduced into the body like alcohol, drugs and addictive substances among them.^[6]

Salivary diagnosis is a late bloomer. In the first half of the 20th century relatively little research was conducted in this field when salivary use was limited to a yes/no answer. The earliest “sialochemical” studies on oral fluids was conducted by Michaels and Kirk who established and studied several specific components in saliva that could contribute to its diagnostic applications in various systemic conditions, including gout and rheumatism.^[7]

Advantages

Saliva has clinical advantages over other body fluids like blood, serum/urine in diagnosis. It is easy to collect (very young and very old) store and ship. Easy sample collection allows patient to collect samples at home when clinically relevant or in other places, including the workplace were collecting blood or urine may be difficult. It can be obtained at low cost and sufficient quantities for analysis. The non-invasive nature of saliva sample collection reduces patient discomfort and anxiety and is safer for health care workers than serum analysis with its associated exposure to needles and possibly AIDS or hepatitis virus.

Conclusion

Most molecules found in blood and urine is also found in saliva, although their concentrations is negligible compared to those in blood. Studies to compare the concentrations in blood and saliva have found excellent correlations and the results greatly extrapolate that of serum (ethanol, cortisol, theophylline, antibodies to HIV, and lactate dehydrogenase in oral cancers) and poor concordance (thyroxine, dehydroepiandrosterone,

prolactin, and adrenocorticotrophic hormone). Expecterated whole saliva (stimulated/unstimulated) is most commonly used for diagnostic purposes. When volume measurement is not needed, collecting devices can be used as well as specific kits that use cotton/cellulose swab, pads, rolls, dipsticks for sampling.

As we enter the era of genomic medicine, salivary diagnostics will emerge as an increasingly important tool in the early detection of disease, monitoring of disease progression and the evaluation of patient behavior.

This will allow a shift of health care system from a panel of disease diagnosis to health surveillance. With this advancement in technology an additional obligation to ensure privacy and rights of patients becomes mandated.^[7]

With a revolution in biomedical and molecularly based diagnostics, it is now possible to quantitate saliva, thus increasing its significance as a diagnostic, as well as prognostic indicator.

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