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Saliva A Revolutionary Approach In Diagnosis

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Abstract
Saliva offers an alternative to serum as a biologic fluid that can be analyzed for diagnostic purposes and has a number of advantages. The aim of this article is to emphasize the use of whole saliva as a diagnostic tool. Whole saliva can be collected non-invasively, and by individuals with limited training. No special equipment is needed for collection of the fluid. Diagnosis of disease via the analysis of saliva is potentially valuable for children and older adults. As a diagnostic fluid, saliva offers many advantages over serum.

Key Words
Saliva, Serum, salivary glands, diagnostic fluid.

INTRODUCTION

Saliva is a clear, slightly acidic mucoserous exocrine secretion. Whole saliva is a complex mix of fluids from major & minor salivary glands & gingival crevicular fluid, containing oral bacteria & food debris. It is a unique fluid and interest in it as a diagnostic medium has advanced exponentially in the last 10 years. The most commonly used laboratory diagnostic procedures involve the analyses of the cellular and chemical constituents of blood. Other biologic fluids like urine, sweat and saliva are also utilized for the diagnosis of disease, but saliva offers some distinctive advantages. Whole saliva can be collected non-invasively, and by individuals with limited training. No special equipment is needed for collection of the fluid. Diagnosis of disease via the analysis of saliva is potentially valuable for children and older adults.

DISCUSSION

Saliva can be considered as gland-specific saliva and whole saliva. Gland-specific saliva is secretions of individual salivary glands: parotid, submandibular, sublingual, and minor salivary glands whereas whole saliva is a mixture of oral fluids and includes secretions from both the major and minor salivary glands.

The collection and evaluation of the secretions from the individual salivary glands are primarily useful for the detection of gland-specific pathology, *i.e.*, infection and obstruction. However, whole saliva is most frequently studied when salivary analysis is used for the evaluation of systemic disorders. Saliva can be collected with or without stimulation. Stimulated saliva is collected by masticatory action (*i.e.*, from a subject chewing on paraffin) or by gustatory stimulation (*i.e.,* application of citric acid on the subject's tongue (1). Stimulation obviously affects the quantity of saliva; however, the concentrations of some constituents and the pH of the fluid are also affected. Unstimulated saliva is collected without exogenous gustatory, masticatory, or mechanical stimulation. Unstimulated salivary flow rate is most affected by the degree of hydration, but also by olfactory stimulation, exposure to light, body positioning, and seasonal and diurnal factors. The best two ways to collect whole saliva are the draining method, in which saliva is allowed to drip off the lower lip, and the spitting method, in which the subject expectorates saliva into a test tube (2).

Some systemic diseases affect salivary glands directly or indirectly, and may influence the quantity of saliva that is produced, as well as the composition of the fluid. These characteristic changes may contribute to the diagnosis and early detection of these diseases.

Analysis of saliva may be useful for the diagnosis of:

1.Systemic Diseases-
- a.hereditary disorders
- b.autoimmune diseases
- c.malignant diseases
- d.infectious diseases,

2.Viral diseases (including HIV)

3.Assessment of therapeutic levels of drugs and the monitoring of illicit drug use

4.The Monitoring of Hormone Levels

5.Diagnosis of Oral Disease with Relevance for systemic Diseases.

Hereditary disease like coeliac disease, cystic fibrosis show changes in salivary composition but because of the lower sensitivity saliva is not used for diagnosis.
Sialochemistry may also be used to assist in the diagnosis of *autoimmune diseases* such as Sjögren's syndrome (SS). A consistent finding is increased concentrations of sodium and chloride. This increase is evident in both whole and gland-specific saliva (3). In addition, elevated levels of IgA, IgG, lactoferrin, and albumin, and a decreased concentration of phosphate were reported in saliva of patients with SS (4). Other salivary changes associated with SS include an elevated concentration of β2 microglobulin, although differences exist

between patients. In addition, elevated lipid levels and increased concentrations of cystatin C and cystatin S have been observed. Increased salivary concentrations of inflammatory mediators-*i.e.*, eicosanoids, PGE_2, thromboxane B2, and interleukin-6-have also been reported. The most important aspect of salivary diagnosis for this disease is evaluation of the reduced quantity of saliva. Cut-off values of 0.1 mL/min for resting whole saliva and 0.5 mL/min for stimulated saliva may be considered as indicative of salivary gland hypofunction (5). But, this reduced salivary flow, although is not pathognomonic for SS.

Salivary analysis may aid in the early detection of certain *malignant tumors* such as squamous cell carcinoma, breast cancer etc. p53 is a tumor suppressor protein which is produced in cells exposed to various types of DNA-damaging stress. p53 antibody can also be detected in the saliva of patients diagnosed with oral squamous cell carcinoma (SCC), and can thus assist in the early detection of, and screening for, this tumor (6).

Elevated levels of recognized tumor markers c-erbB-2 (erb) and cancer antigen 15-3 (CA15-3) were found in the saliva of women diagnosed with breast carcinoma, as compared with patients with benign lesions and healthy controls (7). CA 125 is a tumor marker for epithelial ovarian cancer. Elevated salivary levels of CA 125 were detected in patients with epithelial ovarian cancer as compared with patients with benign pelvic masses and healthy controls (8). Tumor markers that can be identified in saliva may be potentially useful for screening for malignant diseases.

Saliva may be used in the detection of *infectious diseases* like Helicobacter pylori and Shigella infection. Furthermore, the detection of pneumococcal C polysaccharide in saliva by ELISA may offer a valuable complement to conventional diagnostic methods for pneumococcal pneumonia.

The antibody response to infection is the basis for many diagnostic tests in virology. Saliva contains immunoglobulins that originate from two sources: the salivary glands and serum. The predominant immunoglobulin in saliva is secretory IgA (sIgA), which is derived from plasma cells in the salivary glands, and constitutes the main specific immune defense mechanism in saliva. In contrast, salivary IgM and IgG are primarily derived from serum via GCF, and are present in lower concentrations in saliva than is IgA. Antibodies against viruses and viral components can be detected in saliva and can aid in the diagnosis of acute viral infections, congenital infections, and reactivation of infection.

Saliva was found to be a useful alternative to serum for the diagnosis of viral hepatitis. Saliva may also be used for determining immunization and detecting infection with measles, mumps, and rubella (9). The detection of antibodies in oral fluid samples produced sensitivity and specificity of 97% and 100% for measles, 94% and 94% for mumps, and 98% and 98% for rubella, respectively, in comparison with detection of serum antibodies for these viruses (10).
For newborn infants, the salivary IgA response was found to be a better marker of rotavirus (RV) infection than the serum antibody response. Salivary levels of anti-dengue IgM and IgG demonstrated sensitivity of 92% and specificity of 100% in the diagnosis of primary and secondary infection, and salivary levels of IgG proved useful in differentiating between primary and secondary infection (11).

Studies have demonstrated that the diagnosis of infection with the human immunodeficiency virus (HIV) based on specific antibody in saliva is equivalent to serum in accuracy, and therefore applicable for both clinical use and epidemiological surveillance. As compared with serum, the sensitivity and specificity of antibody to HIV in saliva for detection of infection are between 95% and 100%. Analysis of antibody in saliva as a diagnostic test for HIV (or other infections) offers several distinctive advantages when compared with serum. Saliva can be collected non-invasively, which eliminates the risk of infection for the health care worker who collects the blood sample. Furthermore, viral transmission via saliva is unlikely, since infectious virus is rarely isolated from saliva. Saliva collection also simplifies the diagnostic process in special populations in whom blood drawing is difficult, *i.e.*, individuals with compromised venous access (*e.g.*, injecting drug users), patients with hemophilia, and children. Several salivary and oral fluid tests have been developed for HIV diagnosis (12).

Saliva has been proposed for the *monitoring of systemic levels of drugs.* A fundamental prerequisite for this diagnostic application of saliva is a definable relationship between the concentration of a therapeutic drug in blood (serum) and the concentration in saliva. For a drug to appear in saliva, drug molecules in serum must pass through the salivary glands and into the oral cavity. Saliva is useful for the monitoring of drugs such as anti-epileptic drugs, amphetamines, anti-cancer drugs, barbiturates, benzodiazepines, cocaine, phencyclidine (PCP), and opiods (13).

Measurements of *salivary hormone levels* are of clinical importance if they accurately reflect the serum hormone levels or if a constant correlation exists between salivary and serum hormone levels. More recent studies supported the use of salivary diagnosis for the evaluation of clinical problems associated with progesterone, estradiol, insulin, cortisol, aldosterone, and testosterone hormones.

The monitoring of gland-specific secretions is important for the differential diagnosis of diseases that may have an effect on specific salivary glands, like obstruction or infection.

It has been suggested that salivary nitrate, nitrite, and nitrosamine may be related to the development of oral and gastric cancer. Increased consumption of dietary nitrate and nitrite is associated with elevated levels of salivary nitrite. Higher levels of Saliva can be used for the detection of oral candidiasis, and salivary fungal counts may reflect mucosal colonization. Saliva may also be used for the monitoring of oral bacteria. Increased numbers of Streptococcus mutans and Lactobacilli in saliva were associated with increased caries prevalence and with the presence of root caries. Saliva can serve as a vector for bacterial transmission, and also as a reservoir for bacterial colonization. Detection of certain bacterial species in saliva can reflect their presence in dental plaque and periodontal pockets (14). Saliva may also be used for periodontal diagnosis, due in large part to contributions from GCF.

Human saliva contains proteins that can be informative for disease detection and surveillance of oral health.

CONCLUSION

Saliva offers an alternative to serum as a biologic fluid that can be analyzed for diagnostic purposes. Analysis of saliva can offer a cost-effective approach for the screening of large populations, and may

represent an alternative for patients in whom blood drawing is difficult, or when compliance is a problem. Due to its many potential advantages, salivary diagnosis provides an attractive alternative to more invasive, time-consuming, complicated, and expensive diagnostic approaches. Several diagnostic tests are commercially available and are currently used by patients, researchers, and clinicians.

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