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Saliva as a Diagnostic Tool

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ABSTRACT

This review examines the diagnostic application of saliva for systemic diseases. As a diagnostic fluid, saliva offers distinctive advantages over serum because it can be collected non-invasively by individuals with modest training. And also saliva may provide a cost-effective approach for screening of large populations. Analysis of saliva may be useful for the diagnosis of hereditary disorders, autoimmune diseases, malignant and infectious diseases, and endocrine disorders, as well as in the assessment of therapeutic levels of drugs and the monitoring of illicit drug use.

Keywords: Saliva, Endocrine, Bacterial Infection, hereditary disorders.

INTRODUCTION

Saliva is a clear, slightly acidic and complex biological fluid composed of secretions from the major salivary glands which include parotid, submandibular and sublingual glands as well as minor salivary glands includes buccal, lingual and palatal glands. In general human salivary glands produce about 1 to 1.5 liters of serous and mucinous saliva daily by combining water, salts and an abundance of molecules from the blood and salivary protein in the oral cavity to give rise to the multi constituent whole saliva.

The advantages of saliva is a diagnostic tool are surveillance of disease, diagnosis of the disease, prognosis and research purposes. Like blood, saliva is a complex fluid containing a variety of harmones, antibodies, antimicrobial constituents and growth factors. Many of these enter saliva from the blood by passing through the spaces between the cells by transcellular and paracellular routes[1]. Therefore, most compounds found in blood are also present in saliva, thus saliva is functionally equivalent to serum in reflecting the physiological state of the body including hormonal, nutritional, and metabolic variations.

One of the main advantages of saliva as a diagnostic tool is that sample collection is easy and non-invasive, thus dramatically diminishing discomfort associated with blood collection and privacy issues associated with urine collection. Saliva has many advantages in terms of collection, storage, shipping, and voluminous sampling, all of these processes can be carried out very economically compared with serum or urine. Saliva is also easier to handle during diagnostic procedures than blood because it does not clot, thus reducing manipulation techniques for the patient or examinees. The non-invasive collection approach could dramatically reduce anxiety and discomfort and increase their willingness to undergo health check up routinely that will greatly increase the opportunity to monitor their general health over time and to diagnose morbidities.

Collection methods

The different methods for collecting saliva can be classified according to whether they use stimuli. Stimulated saliva is commonly collected by inducing masticatory action on chewing gum to increase the salivary flow rate. This method will affects the quantity and PH of saliva, and generally this method is used in patients who have difficulty producing enough saliva. Unstimulated saliva is collected without exogenous facilitation, and its flow rate is mostly affected by the degree of hydration. The three most common approaches for collection of unstimulated saliva are draining, spitting and suctioning. Before collecting the saliva, subject should be instructed to clean the oral cavity by rinsing the mouth thoroughly with water to avoid contamination .

The following sections review representative and important about saliva-based diagnostics according to disease category.

Autoimmune disorder

Sjogren syndrome is a chronic autoimmune disorder characterized by salivary and lacrimal gland dysfunction, serological abnormalities and multiple organ system changes[2]. Most salivary function test conducted are sialometry, sialography, sialosyntiography, salivary synitiography, biopsies and serological test. These tests are helpful but invasive method, expensive and not always conclusive. With help of saliva investigation are measured specific cytokine concentrations in the saliva in sjogren's syndrome[3]. Studies suggested that salivary IL-2 and IL-6 concentrations are significantly elevated in sjogren syndrome patient. Thus, alteration in salivary cytokine profiles may be useful for both sjogren syndrome diagnosis and prognosis.

Cardiovascular system

Cardiovascular disease is a major cause of death world wide. Determination of total serum amylase and salivary amylase activity[4] have been made before and after cardiovascular surgery. In ruptured aortic aneurysm salivary alpha amylase level is increased.

Endocrinology

Currently, the following steroids can be accurately assessed in saliva; they are cortisol, dehydroepiandrosterone, estradiol, estriol, and testosterone[5]. These assays can be useful in evaluations of mood and cognitive emotional behaviour, to predict sexual activity in adolescent males, to study child health and development, in considerations of premenstrual depression and to screen for cushing's syndrome and also salivary steroid hormone levels can also be used to assess ovarian function, to monitor full-term and pre-term neonates and also to evaluate risk for preterm labour and delivary[6].

Infectious diseases

Viral diseases

Testing for the human immunodeficiency virus is an excellent example of the potential usefulness of saliva in infectious disease diagnosis. The development of antibodies directed toward specific viral protein epitopes, and also measuring of these proteins, has facilitated the use of testing for HIV infection. When testing saliva for HIV using an enzyme-linked fluorescence technique in combination with western blot assays, saliva was superior to serum regards to sensitivity and specificity[7]. This method is highly useful in mass screening of population study and also does not require trained laboratory individual. PCR is used to measure many viruses herpes virus 6,7and 8, cytomegalovirus and Epstein bar virus[8]. Saliva also been used for the measurement of hepatitis C, virus a leading cause of cirrhosis.

Bacterial Infections

Saliva is used for the diagnosis of Helicobacter Pylori infection, which is the critical pathogen associated with peptic ulcer[9]. H. Pylori antibodies in saliva may be valuable for predicting risk for gastric adenocarcinoma. Saliva also used for detection of dental caries, gingivitis and periodontal diseases.

Nephrology

Salivary creatinine concentrations show a high sensitivity and specificity for determining the presence of renal diseases[10].

Oncology

Molecular markers for the diagnosis of oral squamous cell carcinoma can be identified in 3 levels. 1. Changes in cellular DNA 2.Altered rnRNA transcripts 3.altered protein levels.

Changes in cellular DNA

Allelic loss on chromosome 9p has been observed in Oral squamous cell carcinoma. Mitochondrial DNA mutations have also been useful targets to detect exfoliated oral squamous cell carcinoma cells in saliva. Using plaque hybridization, tumor specific p53 mutation aare identified from patient with head and neck cancer

Cyclin D1 gene amplification has been found to be associated with poor prognosis in OSCC. Microsatellite alterations of DNA were also observed in the saliva of patients with small cell lung cancer. The presence of HPV (human papilloma virus) and Epstein Barr virus genomic sequences have been identified as possible DNA molecular markers in detecting OSCC and tumor progression.

Altered mRNA transcripts

Various mRNA molecules were found up-regulated in the saliva of patients suffering from OSCC they are 1.IL-8 playing a role in angiogenesis, replication, calcium mediated signalling pathway, cell adhesion, chemotaxis, cell cycle arrest and immune response. 2.IL1B -which take part in signal transduction, proliferation, inflammation, and apoptosis. 3.DUSP1 (dual specificity phosphate 1) with a role in protein modification, signal transduction, and oxidative stress. 4. H3F3A (h3 histone, family 3A) – DNA binding activity 5.OAZ1 (ornithine decarboxylase anti enzyme 1) taking part in polyamine biosynthesis. 6. S100P (S100 calcium binding protein) with a role in protein binding and calcium ion binding. 7. SAT – Which take part in enzyme and transferase activity were found significantly elevated in OSCC patient than healthy controls.

Altered Protein Markers

Interleukin -8 was detected at higher concentrations in saliva[11]. Salivary kallikrein shows higher level in malignant tumor compare with benign diagnosed patient.

Drug monitoring

Saliva can be used to detect and monitor cotinine, cocaine, phencyclidine, opioids, barbiturates, diazepines, amphetamines, and ethanol[12].

Psychiatry

Saliva has been used to monitor therapeutic responses in the treatment of anxiety by measuring salivary level of 3-methoxy-4-hydroxy phenyl glycol and also it has been used to measure post – traumatic stress disorder associated with wartime[13].

Barriers to the development of salivary diagnostics

First barrier is the need to design and develop micro sensors capable of accurate measurements in small volumes. This type of research requires a long term investment, which may not be attractive to the private sector. Secondly, cost of development is expensive and may produce significant barrier. Third, medical insurance companies will have to be convinced that saliva-based tests are highly accurate as well as cost – effective.

CONCLUSION

Saliva offers an alternative to serum as a biological fluid that can be analysed. This review suggest that certain diagnostic uses of saliva hold considerable promise in future. Monitoring of immune responses to viral infection including hepatitis, HIV, may prove valuable in the identification of infected individual, non-synptomatic carriers and immune individuals. Saliva can also be used in monitoring of therapeutic drug levels due to it many potential advantages, salivary diagnosis provides an attractive alternative to more invasive, time consuming, complicated and expensive diagnostic approaches. Hence the salivary diagnostic test can replace the serum diagnostic procedure in near future.

REFERENCES

1. Aguirre A, Testa-Weintraub LA et al, *oral biomedical* **4**:343-350 (1993).
2. Daniels TE; Sjogren's syndrome: Clinical spectrum and current diagnostic and controversies. *Adv dent res* **10**: 3-8 ((1996)).
3. Sreebny LM, Zhu WX: The use of whole saliva in the differential diagnosis of Sjogren's syndrome. *Adv dent res* 17-24 (1996).
4. Adam et al: Serum amylase isoenzyme in patients undergoing operation for ruptured and nonruptured abdominal aortic aneurysm. *J Vasc Surg* **30**; 229-235 (1999).
5. Aardal E et al; Cortisol in saliva-reference ranges in relation to serum; *J Clin Chem-Biochem*; **33**: 900-932 (1995).
6. Lu et al; Salivary progesterone level in conception and nonconception cycles in women; *J Fertil Steril* **71**: 863-868 (1999).
7. Scully C ; HIV salivary testing for antibodies. *Oral Dis* **3**: 200-215 (1997).
8. Lucht E et al; Herpes virus in saliva of Human Immunodeficient virus in HIV patients and healthy controls; *Clin Infect Dis* **27**:137-141 (1998).
9. Kountorar; Diagnostic test for Helicobacter pyroli; *Gut* **42**: 900-901 (1988).
10. Lloyd et al ; Salivary creatinine assay as a potential screen for renal disease; *Ann Clin Biochem* **33**:428-431 (1996).
11. St John M et al; Interleukin 6 and Interleukin 8 as a potential biomarker in Oral cavity squamous cell carcinoma; *J Head Neck Surg*, **130**: 929-935 (2004).
12. Schramm; Drug of abuse in saliva: *J Anal Tox* **16**:1-9 (1992).
13. Yamada et al; Saliva level in psychiatric outpatient with anxiety; *Int Clin Psychopharmacol* **13**:213-217 (1998).