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Saliva as A Diagnostic Fluid - A Review

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ABSTRACT

In the last 10 years, the use of saliva as a diagnostic fluid has become somewhat of a translational research success story. Technologies are now available enabling saliva to be used to diagnose disease and predict disease progression. This review describes some important recent advances in salivary diagnostics and its application in various systemic diseases .This review will also stimulate future research activity.

Key word: Saliva, sjogren syndrome.

INTRODUCTION

Saliva is a unique fluid and interest in it as a diagnostic medium has advanced exponentially in the last 10 years.The literature is replete with articles,2500+ since 1982, describing the use of saliva, gingival crevicular fluid, and mucosal transudates for drug monitoring and for the detection of various oral and systemic malignancies.

Advances in the use of saliva as a diagnostic fluid have been tremendously affected by current technological developments. For example, the ability to measure and monitor a wide range of molecular components in saliva and compare them to serum components has made it feasible to study microbes, chemicals and immunologic markers (Slavkin, 1998). As a consequence, these advances in technology have helped to move saliva beyond measuring oral health characteristics to where it now may be used to measure essential features of overall health. The primary purpose of this review is to summarize some important recent applications of saliva-based diagnostics.

Considerations in the development of salivary diagnostic testing

The major advantages for using saliva in diagnosis rather than blood (easy access, non-invasive collection) have been described in depth earlier (e.g. Ferguson, 1987;Mandel, 1990,1993a, 1993b Malamud, 1992;Slavkin,1998). Similarly, considerations for selecting the type of saliva, i.e. mixed vs individual glandular (Mandel, 1980; Sreebny and Zhu, 1996), the specific collection methodology to be used (Navazesh, 1993) and the physiological factors affecting salivary collection (Dawes, 1993) have also been reviewed in depth. Consequently, more attention will be given here to fundamental issues involved in the development of a saliva-based diagnostic test, with examples as well as possibilities.

Autoimmune disorders

Sjogren's syndrome is a chronic, autoimmune disorder characterized by salivary and lacrimal gland dysfunction, serologic abnormalities, and multiple organ system changes.

Attempts have been made to use saliva for the conclusive diagnosis of Sjogren's syndrome (Fox and Spreight,1996;Sreebny and Zhu,1996; Rhodus *et al*, 1998; Streckfus *et al*, 2001). With the exception of sialometry (salivary flow rate determination), most salivary function tests must be conducted in special laboratories or clinics. Included among these tests are sialography, salivary scintigraphy, biopsies, and sero- logical tests. While these tests are helpful, they are invasive, expensive, and not always conclusive (Daniels, 1996). Sreebny and Zhu (1996) proposed a panel of salivary determinants that could be used clinically for the diagnosis of Sjogren's syndrome. These include flow rate, pH, buffer capacity, lactobacillus, and yeast concentration.

Cardiovascular diseases

Cardiovascular disease is a major cause of death world-wide. Markers in saliva may be useful in postoperative follow up among patients undergoing cardiovascular surgery. For example, determinations of total serum amylase and salivary amylase activity have been made before and 6 h after cardiovascular surgery. The results indicated that if salivary amylase levels were low in preoperative patients with ruptured aortic aneurysm, there was an associated increase in mortality (Adam *et al*, 1999). Furthermore, salivary a-amylase appears to be a more direct and simple end point of catecholamine activity than changes in heart rate when evaluating patients under a variety of stressful conditions (Chatter- ton *et al*, 1996). Such assessments are in the initial stages of development and require considerable further research to determine their clinical utility

Endocrinology

Saliva levels of steroid hormones reflect the free, and thus active, level of these hormones while most blood measurements reflect the total level, i.e. free and bound. Consequently, the use of saliva for monitoring of steroid hormone levels has increased (Read, 1989).

Currently, the following steroids can be accurately assessed in saliva: cortisol (Aardal and Holm, 1995), dehydroepiandrosterone (Filaire and Lac, 2000), estradiol (Choe, Khan-Dawood and Dawood, 1983), estriol (Heine, McGregor and Dullien, 1999), progesterone (Schramm *et al*, 1990), and testosterone (Schramm *et al*,1992a). These assays can be useful in evaluations of mood and cognitive emotional behavior (Van Honk *et al*, 1999), to predict sexual activity in adolescent males (Halpern, Udry and Suchindran, 1998), to study child health and development (Granger *et al*, 1999), in considerations of premenstrual depression (Odber, Cawood and Bancroft, 1998), and to screen for Cushing's syndrome (Barrou *et al*, 1996; Raff, Raff and Findling, 1998; Castro *et al*, 1999). Further, salivary steroid hormone levels can also be used to assess ovarian function (Lu *et al*, 1999), to monitor full-term and preterm neonates (Bettendorf *et al*, 1998), and to evaluate risk for preterm labor and delivery (McGregor *et al*, 1995; Heine *et al*, 1999; Voss, 1999).

Infectious diseases

Viral diseases

Testing for the human immunodeficiency virus (HIV) 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 the development of technologies capable of measuring these proteins, have facilitated the use of testing for HIV infection (Scully, 1997; Emmons, 1997; Malamud, 1997). For example, when testing saliva for HIV using an enzyme-linked fluorescence technique in combination with Western blot assays, saliva was superior to serum and urine with regard to both sensitivity and specificity

Bacterial infections

Recently, there has been interest in using saliva for the diagnosis of Helicobacter pylori infection, which is the critical pathogen associated with peptic ulcer (Reilly *et al*, 1997; Kountoruras, 1998). For example, a nested PCR assay is available to detect H. pylori DNA in saliva and confirm the presence of H. pylori infection in patients (Jiang *et al*, 1998). Also, a relatively new immunologic assay that reportedly can detect H. Pylori antibodies in saliva may be valuable for

predicting risk for gastric adenocarcinoma (Vaira *et al*, 1999).

Nephrology

There are few reports that employ saliva to screen for renal disease. However, there are some. For example, salivary creatinine concentrations show a high sensitivity and specificity for determining the presence of renal disease (Lloyd, Broughton and Selby, 1996). Much more research is required before any role for saliva-based diagnosis can be assigned in nephrology.

Oncology

Because of the anatomical proximity of saliva to both premalignant and malignant oral neoplasms, saliva seemingly would be ideal for the screening of these lesions. Several investigators have tested this hypothesis. For example, a study by Boyle *et al* (1994) examined the possible value of p53 in saliva as a marker for squamous cell carcinoma. Interestingly, they detected and identified tumor-specific mutations in p53 in preoperative salivary samples of individuals suffering from head and neck squamous cell carcinoma. Positive findings were observed in 71% of the patients studied. A somewhat related study found salivary antibodies to p53 elevated among patients with oral carcinomas (Tavassoli *et al*,1998).

Drug monitoring

The use of saliva for drug monitoring, and the detection of illicit drugs, has grown remarkably (Slavkin, 1998). Currently, saliva can be used to detect and/or monitor cotinine, cannabinoids, cocaine, phencyclidine, opioids, barbiturates, diazepines, amphetamines, and ethanol (e.g. Schramm *et al*, 1992b, 1992c; Schramm, Smith and Craig, 1993; Smolle *et al*, 1999).

Psychiatry

Saliva may also be useful in providing objective outcome measures during psychiatric therapy. For example, saliva has been used to monitor therapeutic responses in the treatment of anxiety by measuring salivary levels of 3-methoxy-4-hydroxyphenylglycol (MHPG) (Yamada *et al*, 1998). Saliva also has been used to measure post-traumatic stress disorder associated with wartime (Aura *et al*, 1999). It would seem that potential applications of salivary monitoring in psychiatry are worthy of further exploration.

CONCLUSION

The study and use of saliva-based diagnostics have increased exponentially during the past 10 years. Saliva- based clinical testing shows much promise. There is, however, a pressing need for much additional research in this area before the true clinical value of saliva as a diagnostic fiuid can be determined.

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