Saliva - A Non Invasive Diagnostic Tool for Aging Population

D K Gupta*, V Singh**, A Singh***, R K Dubey****, G B Gupta*****

Abstract

Ours is a vast country with second largest elderly population of the world. Along with this, there is an exponential increase in disability, mental and physical morbidity of the elderly population needing special health services. Thereby, interest has been increasing in non-invasive diagnostic testing which will be convenient for the aged and handicapped population. Saliva offers an alternative to serum as a biologic fluid and is particularly appealing for diagnostic purpose. 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 where compliance is a problem. This is of particular relevance in the developing world, where many health risks and illnesses remain poorly defined and health care resources are insufficient.

Keywords: Saliva, non invasive, diagnostic tool, aging population

Introduction

India is a vast country with second largest elderly population of the world. The elderly population has grown from 12.06 million in 1901 to 75.93 million in 2001 and within the next half century the aged population is likely to touch the 300 million mark, thereby challenges to dental and medical profession in the coming years will be greater in providing oral and medical care to people in older age group. 1,2 As health care providers attempt to create new approaches to handle increased elderly patient loads with limited resources, the ability to diagnose a condition on site and make clinical decisions at the convenience of the patient is an attractive goal.

Oral fluids mirror the status of the body and their examination may permit monitoring of the health and disease. Saliva offers an alternative to serum as a biologic fluid and is particularly appealing as a diagnostic aid. 3 Whole saliva contains locally produced as well as serum-derived markers that have been found to be useful in the diagnosis of a variety of systemic disorders. Whole saliva can be collected in a non-invasive manner by individuals with modest training. This facilitates the development and introduction of screening tests that can be performed by patients at home. 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.

This review suggests that certain diagnostic uses of saliva hold considerable promise. The article focuses on how upcoming technologies and new diagnostic tests can reliably confirm the presence of clinical disease and it is hoped to help clinicians diagnose it at an earlier stage than is currently possible.

Vision and challenges

The phenomenal growth of geriatric population is the result of improved life expectancy. Along with this, there is an exponential increase in disability, mental and physical morbidity of the...
elderly population needing special health and social services. Due to decrease reserves, elderly people develop symptoms at an early stage of the disease and if treated actively the outcome is much better. Unfortunately, this advantage is set off by the patient’s indifferent attitude towards these early symptoms.

The novel technologies create the possibility of developing radically new ways of detecting and diagnosing health and disease states in a person even in remote or impoverished settings. This is of particular relevance in the developing world like India where many health risks and illnesses remain poorly defined and are economically dependent. As a result, most geriatric patients are unable to receive treatment in time. Inherent in this vision are the establishment of scientific and diagnostic biomarkers in saliva and development of robust, simple-to-use biosensor technologies for reliable and valid clinical applications.

Saliva as a diagnostic fluid

Diagnostic tests based on fluid generally use blood, urine and less frequently the esoteric fluids such as saliva, sweat and tears. Sweat and tears, however, are difficult to obtain in sufficient quantities for routine testing and urine will always lack the charisma of the other fluids. Saliva, by default, therefore becomes the most favored alternative to blood to assess and monitor health and disease state.³

Advantages of saliva as a diagnostic fluid in elderly ⁴, ⁵

1. Noninvasive diagnosis of disease and monitoring of general health.
2. Painless, patient suffers no discomfort and little anxiety in the collection process.
3. Simple in collection with a modest trained assistant and applicable in remote areas.
4. Relatively cheap technology as compared to other tests.
5. Cost effective applicability for screening large population.
6. Can be used to study special population where blood sampling is a problem eg children, anxious/handicap/elderly patients.
7. Convenient for multisampling.
8. Safer for health professionals than blood tests.
9. Compared to blood and urine, saliva is also cheaper to store and ship.
10. In addition saliva does not clot and can be manipulated more easily than blood.

Limitations ⁴, ⁵, ⁶

1. Levels of certain markers in saliva are not always a reliable reflection of the levels of these markers in serum.
2. Salivary composition can be influenced by the method of collection and degree of stimulation of salivary flow.
3. Changes in salivary flow rate may affect the concentration of salivary markers and also their availability due to changes in salivary pH.
4. Variability in salivary flow rate is expected between individuals and in the same individual under different conditions.
5. In addition, many serum markers can reach whole saliva in an unpredictable way (i.e. gingival crevicular fluid flow and through oral wounds). These parameters will affect the diagnostic usefulness of many salivary constituents.
6. Furthermore, certain systemic disorders, numerous medications and radiation may affect salivary gland function and consequently the quantity and composition of saliva.
7. Whole saliva also contains proteolytic enzymes derived from the host and from oral microorganisms. These enzymes can affect the stability of certain diagnostic markers. Some molecules are also degraded during intracellular diffusion into saliva.

Despite these limitations, the use of saliva for diagnostic purposes is gaining popularity. Several diagnostic tests are commercially available and are currently used by patients, researchers and clinicians. Saliva is particularly useful for qualitative (detection of the presence or absence of a marker) rather than quantitative diagnosis which makes it an important means for the detection of viral infection (especially HIV due to the non-invasive method of collection), past exposure and immunity and the detection of illicit drug use. Saliva is also useful for the monitoring of hormone levels especially steroids and facilitates repeated sampling in short time intervals, which may be particularly important for hormone monitoring and avoiding compliance problems. Due to its many potential advantages, salivary diagnosis provides an attractive alternative to more invasive, time-consuming, complicated and expensive diagnostic approaches.
Saliva-based diagnostics

With increasing recognition of the link between oral and general health, attention has turned to saliva as a diagnostic fluid for a diverse array of health conditions. Dental healthcare professionals have been assessing patient risk for tooth decay for decades by measuring the buffering capacity and bacterial content of saliva. Recently advances in biochemistry, microbiology and immunology have given rise to new tools for diagnosing systemic illnesses that are reflected in the composition of saliva (Table 1 & 2). Nevertheless, the recent focus on the potential role of periodontal disease as a risk factor for cardiovascular and cerebrovascular diseases and the occurrence of pre-term low birth weight babies bring new importance to this aspect of salivary analysis.  

Table 1. Salivary diagnostic for diagnosis and monitoring of systemic and oral disease.

<table>
<thead>
<tr>
<th>Marker(s)</th>
<th>Test purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococcus mutans, Lactobacillus acidophilus, Porphyromonas gingivalis.</td>
<td>Dental caries, periodontal diseases.</td>
</tr>
<tr>
<td>Increased level of albumin in whole saliva.</td>
<td>Stomatitis</td>
</tr>
<tr>
<td>Reduced Salivary Epidermal Growth Factor levels in patients undergoing radiation therapy</td>
<td>Radiation induced mucositis</td>
</tr>
<tr>
<td>Higher levels of salivary nitrate, nitrosamine, nitrite and increased activity of nitrate reductase</td>
<td>Oral and gastric cancer</td>
</tr>
<tr>
<td>Glutamic acid decarboxylase autoantibody</td>
<td>Type I diabetes</td>
</tr>
<tr>
<td>Detection of infectious diseases using specific antibodies</td>
<td>Helicobacter pylori infection associated with peptic ulcer disease, chronic gastritis monitoring immune response in shigellosis / Pigeon breeder’s disease (PBD) / Lyme disease</td>
</tr>
<tr>
<td>Specific antibody to Taenia solium larvae</td>
<td>Neurocysticercosis</td>
</tr>
<tr>
<td>Salivary amylase level</td>
<td>Aortic aneurysm, catecholamine activity in stressful patients</td>
</tr>
</tbody>
</table>

Table 2. Salivary diagnostic for diagnosis and monitoring of malignant/hereditary/viral diseases.

<table>
<thead>
<tr>
<th>Detection of determinants.</th>
<th>Malignancy</th>
<th>Marker(s)</th>
<th>Test purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral squamous cell carcinoma (SCC)</td>
<td>p53 antibody</td>
<td>Oral cancer screening chip – for diagnosis</td>
<td></td>
</tr>
<tr>
<td>Epithelial ovarian cancer.</td>
<td>CA-125</td>
<td>Breast cancer biomarkers</td>
<td></td>
</tr>
<tr>
<td>Oral cancer screening chip – for diagnosis</td>
<td>CA-15; epidermal growth factor; receptor c-erbB-2 (erb); cathepsin-D and Waf 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cystic fibrosis biomarker</td>
<td>Zinc-binding antigen, increased calcium levels in saliva</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coeliac disease and Dermatitis herpetiformis</td>
<td>Serum IgA antigliadin antibodies (AGA)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral squamous cell carcinoma (SCC)</td>
<td>CA-15; epidermal growth factor; receptor c-erbB-2 (erb); cathepsin-D and Waf 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast cancer biomarkers</td>
<td>Diagnostic kit</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cystic fibrosis biomarker</td>
<td>Oral cancer screening chip – for diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OraQuick ADVANCE/Rapid HIV-1/2</td>
<td>For rational and appropriate drug use in elderly</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Due to multiple drug therapies, more geriatric adults are on multiple drugs. Monitoring levels of such drugs to prevent overuse and minimize risk of iatrogenic harms is very critical. At present commonly used monitoring tools are invasive in nature. In such geriatric population use of noninvasive salivary diagnostic can prove to be a boon in resource deprived developing country like India. Similar to other body fluids (i.e., serum, urine and sweat), saliva has been proposed for the monitoring of systemic levels of drugs and other compounds (Table 3). It can also be used in variety of situations e.g. for monitoring patient compliance with psychiatric medication, lithium levels in patients under lithium therapy, for the monitoring of anti-epileptic drugs and for monitoring levels of anti-cancer drugs.
Table 3. Saliva diagnostic for evaluation of illicit drug use and hormonal diseases.

<table>
<thead>
<tr>
<th>Saliva for evaluation of illicit drug use</th>
<th>Drugs / diagnostic kit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol level- Ethanol</td>
<td>Q.E.D. Saliva Alcohol Test</td>
</tr>
<tr>
<td>Recreational drugs</td>
<td>Amphetamines , barbiturates, benzodiazepines, cocaine, phencyclidine (PCP), opioids, marijuana</td>
</tr>
<tr>
<td></td>
<td>Diagnostic Kit-Micro-Plate</td>
</tr>
<tr>
<td></td>
<td>EIA Assays</td>
</tr>
<tr>
<td>Tobacco smoking/ exposure</td>
<td>Nicotine metabolite cotinine, Salivary thiocyanate</td>
</tr>
<tr>
<td>Hormones- Estradiol, progesterone, testosterone, DHEA, cortisol</td>
<td>feto-placental function, pre-term delivery, Cushing's syndrome, in hormonal replacement therapy</td>
</tr>
<tr>
<td></td>
<td>diagnostic tool- ZRT Saliva Test</td>
</tr>
</tbody>
</table>

Salivary cortisol levels, aldosterone

|ходдопд |
|ходдопд |

The future of salivary diagnostics

Still in its early stages, salivary diagnostics is rapidly increasing its range of applications. Saliva tests may soon become commercially available for the detection of breast cancer, viral and bacterial diseases, presence of hormones, drugs and toxins and for general nutritional deficiencies. Oral and general healthcare should benefit greatly as new salivary diagnostic techniques are developed and improved.

Regarding diagnostic capability, the gap between saliva and other bodily fluids such as blood, urine and cerebrospinal fluid is closing. It is primarily due to rapid technology development, scientific validation of diagnostic analytes and advocacy by the National institute of Dental and Craniofacial Research. Salivary diagnostics would enable clinicians to monitor diseases frequently and easily and would have impact on the future medical research and therapy. Scientific data to establish a benchmark for the diagnostic value of saliva in comparison with that of other biomedia will be necessary to assess the disease discriminatory value of saliva. It may well turn out that similar to the UCLA (University of California, Los Angeles) finding that saliva is more accurate than blood in detecting oral cancer and will outperform other biomedia in the diagnosis of other diseases as well.

We foresee that more products to be commercialized either as new inventions or based on products. With the current rate of progression, salivary diagnostics can become a key player in routine health monitoring in the near future and enable the early detection of disease using a simple and effective assay. Miniaturized saliva based diagnostic technologies will enable the use of minute amounts of body fluids to yield critical patient information that reflects health and disease status. Such technologies will allow clinicians to achieve real-time and simultaneous assessment of multiple diseases. Thus salivary diagnostics will not only save lives but also preserve the quality of lives that have been saved.

Conclusion

Due to non invasive nature, salivary diagnoses provides an attractive alternative to more invasive, time consuming, complicated and expensive diagnostic approaches in geriatric population. However, before a salivary diagnostic test can replace a more conventional one, the diagnostic value of a new salivary test has to be compared with accepted diagnostic methods. Considerable advancements have been made in the field of salivary diagnostics in the past decade. The identification of appropriate biomarkers and the validation of various testing methods will go a long way towards making salivary diagnostics an important tool for all health care practitioners.

References

7. Klock B, Svanberg M, Petersson LG. Dental caries, mutans streptococci, lactobacilli and saliva secretion


