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Significance of salivary biomarkers as a drug monitoring aid

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Introduction

Current statistics pertaining to Illegal Drug-related morbidity and mortality, in the span of a decade, highlight an alarming underlying deficiency in the failed implementation of Drug Control Policies. Although alcohol levels are efficiently measured using simple devices such as Breathalyzers, there is a dire need for the development of a similar safe, accurate, inexpensive and time-efficient methodology that can be applied for illegal drug abuse such as Fentanyl, Cocaine, Methamphetamines, Codiene etc. Saliva is a unique biological fluid and it has been described as the "mirror of the body". Saliva is composed mainly of water (98%) and about 2% other compounds, such as minerals, electrolytes, hormones, antibacterial compounds, mucins, various enzymes, immunoglobulins and cytokines.[1] Salivary biomarkers have been gaining credibility and acceptance since the past several years. Current researches have been able to show significant associations of salivary biomarkers with existing disease conditions of Auto-immune, Cardiac, Endocrine, Genetic, Dental and Periodontal origins.[2] According to the National Institute of Health (NIH), a biomarker is an objectively measured and evaluated indicator of normal biologic processes, pathogenic processes, or pharmacologic responses to therapeutic intervention.[3]Amongst these, the presence of various drug metabolites in saliva in correspondence with serum concentrations generates significant interest. Salivary Biomarkers, not only provide information regarding the patient's current prescribed medications, but can also effectively detect the presence and abuse of illegal substances.[4,5]

Why saliva over blood?

Current substance-abuse evaluation methods involve extraction of a blood sample, done by a registered medical auxiliary, which then needs to be stored in controlled conditions followed by laboratory analysis using expensive equipment. These requirements incur high costs in skilled collection, handling and assessment. Saliva provides the following advantages over Serum Analysis:

1. Collection is simple enough that it requires no specific skills and can be self-collected.[6]
2. The procedure is non-invasive; it eliminates an important hurdle of sample collection through the use of a needle to extract blood. Saliva collection is, therefore, patient-friendly. The subject will not only be comfortable in providing repeated samples, but this will also encourage others to readily participate in sampling procedures for research purposes.[7]
3. Prevention of cross-contamination of high-risk blood-borne diseases such as HIV. Salivary enzymes have an inhibitory effect on HIV infectivity and chances of transmission are negligible.[8]
4. Logistical requirements for shipping and storage are significantly less since salivary samples do not clot and require less manipulation techniques when compared with serum.
5. More economical in comparison to blood. This works to the benefit of the patients as well as their health-care providers.
6. Saliva metabolomics provide the added advantage of being safe for the licensed health-care professional as well, since normal blood collection methods can include needle-stick injuries resulting in possible exposure to HIV and Hepatitis Viruses.[9,10]

Although the aforementioned attributes indicate saliva as a more favorable diagnostic fluid, saliva has still not attained a mainstream status. This may partly be due to diminished concentrations of various analytes in saliva when compared with serum.[11] It was reported that IgG and IgM levels are exponentially higher in serum when compared with saliva.[12] However, this does not hold true for prescription and illegal drug metabolites.

Saliva: a "window" into a patient's general health history

Along with the long established purpose of saliva being maintenance and protection of oral tissue integrity, salivary components have emerged as a 'window' into a patient's local and systemic disease conditions as well.[13,14] After more than two decades, the advent of sensitive ELISA and Protein Chain Reaction techniques have tapped into the fundamental core of diagnostic information regarding a patient's current general health status. These techniques can not only help in detecting systemic diseases such as Sarcoidosis, Cystic Fibrosis, Sjogren's Syndrome, Liver Cirrhosis and Diabetes Mellitus, it can also serve a valuable purpose in the detection of microorganisms such as Herpes Virus (associated with Kaposi's Sarcoma), Helicobacter Pylori (in condition of gastritis, peptic ulcers and is also associated with stomach cancer) and even HIV.[9] Many inflammatory biomarkers associated with oral and periodontal lesions may be present in the saliva.[15–18] The early detection of breast cancer was made possible through genetic protein biomarkers and this revolutionary development resulted in the application of salivary biomarkers for early detection of oro-pharyngeal and ovarian cancers as well.[19]

Correlation of drug metabolites in saliva and blood serum levels

Drug metabolites in saliva correlate with blood serum levels. It was demonstrated that salivary metabolites are the preferred method for GHB analysis since it provides an easy, drug-stable, non-invasive procedure for sample collection.[20]

Saliva: an illegal drug-monitoring aid

Saliva has now established itself as a diagnostic fluid for the presence of nicotine, cannabis, cocaine, phencyclidine, opioids, barbiturates, diazepines, amphetamines, and ethanol. Their salivary biomarkers are made available for detection through the transport of unbound fractions of the drug in the serum diffusing into saliva. According to a landmark research by Drummer, these biomarkers are detected in saliva as long as they are present in the blood serum.[21] Furthermore, the mere presence of these salivary biomarkers is satisfactory for the detection of illegal substance abuse.[22] Other common illicit drugs that result in serious complications as well as higher mortality rates, such as methamphetamines and cocaine, can be rapidly and accurately detected in saliva through hydrophobic porous silicon array.[22,23] The accuracy in contraband drug usage, such as opiates, alcohol and cocaine, when correlated between Blood Serum and Saliva was reported as >90%.[22] Police and other law enforcement officers can see great value in the rapid detection of these drugs to avoid possible harm to self and others. These highlight the significance of salivary fluid as an alternative diagnostic tool.

Conclusion

Today more than ever, Saliva has emerged as a prominent diagnostic tool with a wide variety of applications. Current advancements, such as Oral Fluidic NanoSensor Test (OFNASET) by the UCLA Collaborative Oral Fluid Diagnostic Research Center, in salivary metabolomics are increasingly making an impact. It can be safely said that the discovery of salivary diagnostics has revealed that saliva may be a better alternate to blood serum analytical techniques. However, Salivary Biomarkers require more research in order to be established as a standard protocol for illegal drug abuse. With all of its favorable attributes such as its painless non-demanding technique, inexpensive and skill-free approach, the time is not too far that saliva will be the first choice for patients and health-care providers alike for timely monitoring of illegal substance-abuse for routine and emergency situations.

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Conflict of interest

None.

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