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Salivary Diagnostics in Pediatrics and the Status of Saliva-Based Biosensors

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Abstract

Because of their ease of use, on-site application, non-invasiveness, and most likely improved patient compliance, salivary biomarkers are increasingly being used as an alternative to diagnose and monitor the progression of various diseases. The role of salivary biosensors in the general population is highlighted here, followed by the use of saliva as a diagnostic tool in the paediatric population. We looked in the literature for paediatric applications of salivary biomarkers, specifically in children aged 0 to 18. These biomarkers are used in the treatment of autoimmune diseases, developmental disorders, oncology, neuropsychiatry, respiratory illnesses, gastrointestinal disorders, and oral diseases. Salivary proteins have four major applications as biomarkers: dental health, gastrointestinal conditions, metabolic conditions, and respiratory conditions. Other classifications for biosensing based on the type of biomarkers used include genomics, metabolomics, microbiomics, proteomics, and transcriptomics.

Keywords: Biosensors • Biomaterials • Oral diagnostics • Pediatric population

Introduction

Blood and urine tests are now commonly used to assess an individual's immune status, neuropsychiatric state, and developmental status. Invasive screening, diagnostic, and prognostic tests, on the other hand, cause a high level of stress in the paediatric population and their parents. Salivary biomarkers have been shown in recent research to be an alternative non-invasive test, particularly useful in reducing stress in children aged 0 to 18. The purpose of this study is to review current research on the use of salivary biomarkers in the diagnosis of autoimmune diseases, developmental disorders, cancer, as well as neuropsychiatric, pulmonary, gastrointestinal, and oral diseases. It is an attempt to highlight the importance of saliva as a sample for use in biosensing applications.

Prospects for saliva-based biosensors: autoimmune disorders, developmental conditions, neuropsychiatric conditions, metabolic disorders, gastrointestinal disorders, pulmonary diseases, and oral diseases have all been identified as having biomarkers. For biosensing applications, they should be evaluated for the following characteristics: reproducibility at different time points, locations, and populations; specificity towards the marker and disease; sensitivity, which means they should be able to detect as low a concentration of the markers as possible, ideally lower than a clinically available test; assay response time, which should be as short as possible for faster results; and validation in clinical conditions in larger population sizes [1].

Literature Review

Several studies have found a significant increase in CRP and insulin concentrations in the saliva of obese children. An observational study in Spain followed a group of children aged 8 to 12 and measured levels of circulating inflammatory cytokines to look for signs of obesity-related inflammation and glucose intolerance, a risk factor for diabetes and metabolic syndrome. A large cohort study designed and tested a continuous approach to a scoring system for metabolic syndrome risk factors in children. Shi, et al diagnostic's tool incorporates a number of clinical parameters, including waist circumference and systolic blood pressure.

In the case of dental caries, Alqaderi, et al. found that a later bedtime in Kuwaiti children was associated with an increased incidence of caries. To explain this association, the authors point out that sleeping later causes changes in hormonal levels, specifically a lower leptin level and a higher ghrelin level. This hormonal change causes children to snack more frequently on carbohydrate-rich foods, predisposing them to caries. This finding paves the way for low-cost, easy-to-implement sleep interventions in vulnerable children to reduce their caries risk. Furthermore, these hormonal changes in saliva can be detected relatively easily and non-invasively. Syed, et al. found that a lower level of salivary nitric oxide and its metabolites was associated with an increased risk of caries in children.

Discussion

Collin, et al. compared salivary levels of several cytokines in children with JIA to those in healthy children in a study. While IL-8 levels appeared to be higher in JIA children, the authors eventually concluded that there was no significant difference in the levels of any investigated cytokines between the two groups. To explain this finding, the authors point out that the children with JIA received immunosuppressive therapy throughout the study, which could have kept their immune activity, and thus salivary cytokine levels, under control. Despite this, salivary cytokine levels may be used to develop a prognostic tool for children with JIA. Increased levels of salivary proinflammatory markers such as interleukin-6 and c-reactive protein have been linked to child maltreatment. IL-6 secretions have been found to have a distinct circadian rhythm, implying that a disrupted rhythm indicates a dysfunctional inflammatory system. These findings suggest that a disrupted IL-6 rhythm, and thus a disrupted inflammatory system, may be linked to childhood traumas. Mucosal secretory immunoglobulin A is important in the immune system. Acute psychosocial stress has been shown to increase s-IgA secretion in maltreated adults and children. This suggests that child maltreatment is prematurely ageing their immune system [2-4].

A large body of evidence suggests that salivary cortisol and alpha-amylase levels can be used as stress biomarkers. Salivary stress biomarkers have

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applications ranging from paediatric dental anxiety to internalising or externalising disorders. The partial hypofunction of the hypothalamus-pituitary-adrenal axis was discovered to be associated with paediatric ADHD patients by assessing cortisol levels to induced stress, which were found to be lower in positive patients. Furthermore, the salivary immune biomarker secretory immunoglobin is frequently measured in conjunction with HPA biomarkers to investigate the interactions between stress, the HPA axis, and the immune system. In the paediatric population, collecting samples via saliva is a great alternative to blood collection, especially for children with cerebral palsy. The sympathetic nervous system predominates in patients with cerebral palsy, causing vasoconstriction and peripheral neuropathy [5].

While using salivary stress biomarkers like cortisol and alpha-amylase as a diagnostic tool is generally beneficial, it is far from perfect. They, for example, are unable to distinguish between acute fear and chronic anxiety. Furthermore, salivary cortisol levels reflect free serum cortisol levels, which are the unbound and biologically active 5% of total cortisol under basal conditions. Measurement of plasma cortisol concentration, on the other hand, yields total cortisol. In other words, salivary cortisol can only be used as a proxy for free serum cortisol levels. Another study found that assessing manganese exposure through saliva samples requires more research. Manganese exposure in water and salivary levels have the weakest correlation of the candidate biomarkers, including saliva, hair, and toes.

Conclusion

We reviewed several methodologies that performed well in terms of sensitivity and specificity, as well as additional benefits that addressed some of the major limitations of standard diagnostic tests used in the paediatric population today. Recognizing its non-invasiveness and widespread applications, saliva as a probing biofluid sample remains very appealing. More research with larger samples, as well as better analytical and comparative evidence, is required. Further research into these biomarkers could have a significant impact. Indeed, salivary diagnostic/prognostic tools are less invasive and less harmful than current tools, allowing physicians to intervene earlier, changing the course of the disease and significantly reducing patient suffering and disability.

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Conflict of Interest

There are no conflicts of interest by author.

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