Salivary Biomarkers of Chronic Periodontitis

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Chronic periodontitis is a slow progressing disease of oral tissue that causes inflammation and bleeding of gingiva. If it is untreated, it leads to periodontal pockets, loosening of teeth and ultimate tooth loss. Saliva is a hypertonic fluid present in the oral cavity that is now used as a diagnostic tool. Saliva contains water, organic and inorganic molecules that can act as biomarkers for systemic and oral diseases. Presence of these biomarkers in saliva can help in the early detection of chronic periodontitis disease for therapeutic purpose. This review summarizes the salivary biomarkers that can help in early detection and diagnosis of chronic periodontitis disease.

KEY WORDS: Chronic periodontitis, salivary biomarkers, systemic diseases, oral diseases.

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INTRODUCTION

Saliva is a complex hypertonic solution which is an exudate from salivary acini, gingival crevicular fluid and oral mucosa. Major salivary glands include parotid, submandibular and sublingual glands which secrete approximately 90% of saliva and the rest 10% of saliva is produced by minor salivary glands.[1] Saliva contains 99% of water and 1% consist of organic molecules and inorganic component (e.g., proteins, carbohydrates and lipids). A healthy person secretes 600ml of saliva in the whole day.[2] The function of saliva is to maintain the oral cavity health by means of their antibacterial and antiviral activity. It also helps in lubrication, taste, digestion and provides tooth integrity and repair of oral mucosa[3] (Figure 1). "The term, biomarker, refers to measurable and quantifiable biological parameters than can serve as indicators for health and physiology-related assessments, such as pathogenic processes, environmental exposure, disease diagnosis and prognosis or pharmacologic responses to a therapeutic intervention".[4] According to the National Institutes of Health (NIH), a biomarker is a characteristic that is objectively measured and evaluated as an indicator of a normal biological process, pathogenic process, or pharmaceutical response to therapeutic intervention.[5]

BIOMARKERS IN SALIVA

In comparison to the blood sample collection, saliva
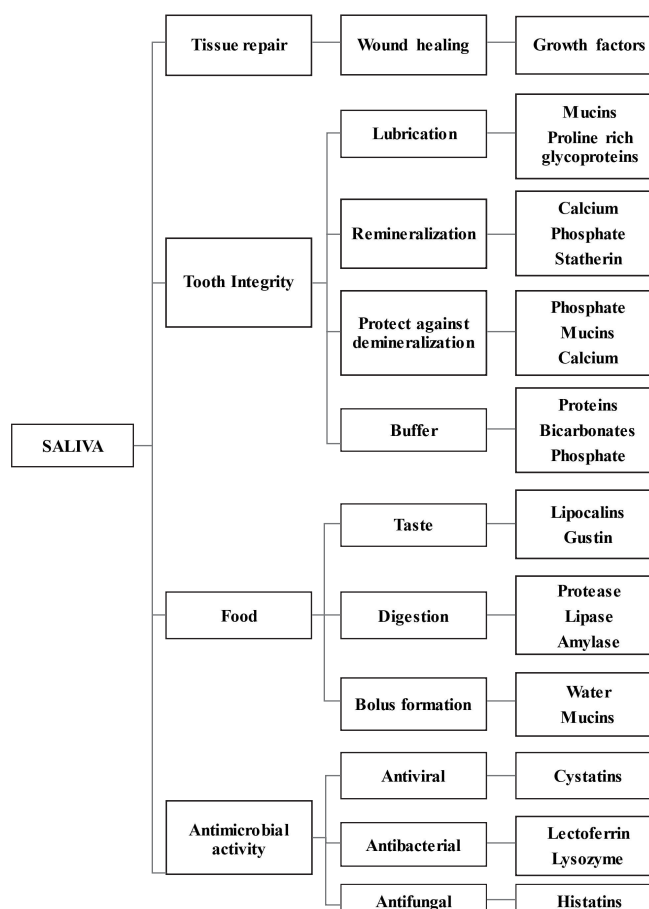
Figure 1: Physiological functions and active constituents of human saliva

collection is non invasive, patient compliant and convenient for clinician. Saliva consists of different types of hormones, enzymes, antibodies, antimicrobial components and

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cytokines .[4] Saliva contains numerous defense proteins such as salivary immunoglobulins and salivary chaperokine 70kDa heat shock proteins (HSP70/HSPA), which are related to both innate and acquired immune system.[6] The secretory immunoglobulin A (IgA) is the major salivary immunoglobulin that produces adherence of specific microorganisms, avoiding their cohesion to oral mucosa and making clusters. Recent study has shown that saliva also contains surfactant proteins, which are the members of the immune defense system.[7]

Saliva consists of many systemic markers such as antibodies, interleukins and neoplastic markers which can be used in diagnosis and analyzing various systemic diseases such as diabetes mellitus[8], cancers such as breast cancer[9], oral diseases such as oral squamous cell carcinoma[10] and cardiovascular diseases such as acute myocardial infarction.[11] This can help in the early detection and progression of disease and monitoring of the therapeutic drugs.[12] Salivary biomarkers of systemic and oral diseases are listed in table 1.

SALIVARY BIOMARKERS IN CHRONIC PERIODONTITIS

Chronic periodontitis is a slow progressing inflammatory disease which can lead to the destruction of the periodontal ligament, alveolar bone loss, pocket formation and gingival recession.[13,14] It mostly occurs in adults. Clinical features include plaque and calculus deposition, when untreated leads to inflammation and bleeding of gingiva, periodontal pockets and periodontal tissue attachment loss. It is classified according to the clinical conditions as localized and generalized periodontitis.[15,16] It is also categorized by severity of periodontal tissue breakdown that includes mild, moderate and severe chronic periodontitis. It determines the health of the periodontal tissue that can be recorded as clinical attachment level (CAL) and that is measured with a periodontal probe. CAL is the distance between cemento-enamel junction (CEJ) and the base of the periodontal pocket.[17] Various local and systemic factors are associated with chronic periodontitis such as poor oral hygiene, poor nutrition, malocclusion, overhanging restorations, smoking, obesity, alcohol consumption, psychological factors and metabolic disorders.[13]

Pathogenesis of chronic periodontitis involved the gram negative anaerobic bacteria such as Porphyromonas gingivalis, Bacteroides forsythus, and Prevotella intermedia.[18,19] These microorganisms present in calculus, may exert pathogenic effect either directly by tissue destruction or indirectly by activating host response. Substances released from bacteria reach gingival tissue and results in chronic inflammation

that leads to activation of B-lymphocytes, T-lymphocytes, neutrophils, monocytes, and macrophages that release inflammatory mediators such as chemokines, proteolytic enzymes, and cytokines. Therefore, local variation and damage of host tissue may manifest as periodontal disease.[13]

Many molecules have been analysed as potential biomarkers for periodontal diseases such as enzymes {for example matrix metalloproteinases-8 (MMP-8)}, cytokines {for example interleukin-1β (IL-1β)}, receptors (for example collectins) and other proteins (for example high sensitive c-reactive protein (hs-CRP) and osteocalcin). These biomarkers can also be present in several biological fluids (such as serum, blood, plasma and gingival crevicular fluids) in higher concentration in compare with healthy individuals. d High sensitivity c-reactive protein (hs-CRP) is member of an innate immune system, it has higher levels in serum of chronic periodontitis patients and used as a systemic biomarker.[20] Osteocalcin is non-collagenous calcium binding protein present in mineralized tissue which take part in bone destruction. Salivary levels of osteocalcin are raised in chronic periodontitis patients in compare with healthy individuals.[21]

Anaerobic gram negative bacteria such as Prevotella porphyromonas (mainly P.gingivalis) and Tannerella forsythia in saliva have pathogenic potential in chronic periodontitis. These organisms contain 3-hydroxy fatty acid (3-OH-FA). 3-OH FA analysis in saliva help in determining the early detection of chronic periodontitis.[22] There is the number of enzymes that are released by inflammatory cells during the pathophysiology of chronic periodontitis which caused the connective tissue degradation and bone loss. Matrix metalloproteinase (MMP-8), alanine aminotransferase (ALT), aspartate aminotransferase (AST) and lactate dehydrogenase (LDH) are some of the enzymes that are used as a salivary biomarker of chronic periodontitis.[23]

Oral epithelial cells secretes a large number of cytokines such as granulocyte-macrophage colony stimulating factor (m-CSF), interleukin-1β (IL-1β), interferon-ɣ (IFN-ɣ) and tumour necrosis factor-α (TNF-α) which can cause inflammation and destruction of periodontal tissue. The levels of these cytokines in saliva are influenced by the salivary mucins whose presence can limit the absolute concentration of these cytokines for detection.[24,25] Salivary nitric oxide (NO) metabolite and toll- like receptors (TLR-2 and TLR-4) are used as biomarkers which are predictive indicator of periodontal inflammatory condition.[26,27] Protein carbonyl (PO) causes oxidative damage may leads to decline of protein function. Higher levels of PO and salivary cortisol present in Chronic periodontitis are used as salivary biomarkers.[28,29]

CONCLUSION

The early detection or diagnosis of chronic periodontitis can resist the disease progression. This can positively affect the health of the individual as untreated chronic periodontitis causes pain, swelling and bleeding of gingiva, loosening of teeth and tooth loss. Numerous salivary biomarkers of chronic periodontitis can help in the early diagnosis and monitoring of this disease. Furthermore, there are still chances of unidentified biomarkers in the saliva of chronic periodontitis that can be explored.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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