Indian Journal of Clinical Biochemistry, 2003, 18 (1) 5-7

GINGIVAL CREVICULAR FLUID A MARKER OF THE PERIODONTAL DISEASE ACTIVITY

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ABSTRACT

Gingival crevicular fluid (GCF) is an inflammatory exudate that can be collected at the gingival margin or within the gingival crevice. The biochemical analysis of the fluid offers a non invasive means of assessing the host response in periodontal disease. Active phase of periodontal disease process can be measured or assessed by the constituents of gingival fluid. Bacterial enzymes, bacterial degradation products, connective tissue degradation products, host mediated enzymes, inflammatory mediators, extracellular matrix proteins either together or individually can be detected in higher levels in gingival crevicular fluid during active phase of periodontitis.

INTRODUCTION

Periodontal diseases encompasses everything from the earliest stage of marginal gingivitis to the most advanced destructive periodontitis, with loss of connective tissue, loss of epithelium, loss of attachment, loss of bone and resultant tooth mobility and exfoliation of teeth if not treated.

Inflammatory periodontal diseases are characterized by periods of disease activity followed by periods of remission (inactivity).

Traditional methods of assessing the periodontal status involve probing measurements and reactions to probing, supplemented by radiography. These methods show the resultant destruction of periodontal tissues due to past activity of periodontal disease. Conventional parameters fail to detect sites of present destructive periodontal disease activity and its manifestations leading to subsequent further loss of supporting tissues.

Much recent research into potential clinical markers of periodontal disease activity aims to meet the need of the clinician for a diagnostic aid. A range of biomarkers implicated in the development and progression of periodontal disease have been investigated. Gingival crevicular fluid has been particularly attracted as a marker of the periodontal disease activity. Gingival crevicular fluid contains elevated levels of a vast array of biochemical factors which offer us proper diagnosis of disease activity. Usage of micropipettes have more advantage than other methods because we can collect gingival crevicular fluid more precisely at a given site in fixed volume micropipettes (1-10 µl in volume). The collected fluid can be stored until required and it can also be applied directly for analysis such as electrophoretic procedures without any problems.

GCF AS DIAGNOSTIC MARKER

1. Prostaglandin E_2
2. β-glucuronidase
3. Neutrophil Elastase
4. Aspartate Aminotransferase
5. Collagen in gingival crevicular fluid
6. Proteoglycans in GCF
7. Glycoproteins in GCF

Prostaglandin E_2: Prostaglandin E_2 (PGE_2) is formed as a result of the metabolism of arachidonic acid. With cellular perturbation, the action of the enzyme cytooxygenase upon arachidonic acid yields a series of fatty acids that participate in the inflammatory response.

Proinflammatory effects of PGE_2

Increased vasodilation

Enhanced responsiveness of receptors to painful stimuli

Release of collagenase by inflammatory cells

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Activation of osteoclasts thereby causing resorption of bone.

The relationship of PGE2 concentration in GCF has been studied by several scientists and has been found significantly and statistically high during active phase of periodontitis.

β-glucuronidase: It is a lysosomal enzyme involved in the degradation of the connective tissue ground substance. This acid glycohydrolase is used as a marker for primary granule release from polymorphonuclear leukocytes (PMN) and β-glucuronidase in GCF has been correlated with the number of PMN in gingival crevice. During active phase of periodontal disease there is influx of PMN cells into the gingival crevice. This denotes the body's self defence against bacterial products and bacteriae. PMN cells release lysosomal enzymes. 6 fold increase of β-glucuronidase has been found in periodontal diseases. Many cross sectional studies and longitudinal studies have confirmed the increased levels of β-glucuronidase in GCF. The data suggested that activity of the enzyme in GCF was related to but was a different measure of inflammation than standard clinical indices.

Neutrophil Elastase: The assessment of neutrophil elastase (NE) in GCF provides another marker of the intracrevicular PMN activity. NE is a serine endopeptidase found in primary granules and is a powerful proteolytic enzyme that can attack many substrates. The relationship of NE to the severity of periodontal disease has been well documented. The activity of NE in periodontitis is much higher compared to gingivitis. This has been proved both in animal and human studies. There is a profound correlation between increase levels of NE in gingival crevicular fluid and periodontal disease progression. Alveolar bone loss has been correlated with increased levels of NE in gingival fluid.

Aspartate Aminotransferase: Aspartate aminotransferase (AST) is a cytoplasmic enzyme present in many body tissues with especially pronounced distribution in heart, liver and skeletal muscle. The extracellular release of AST and other cytoplasmic enzymes is associated with cell damage and cell death. Changes in AST levels in GCF has been found in experimental periodontitis in beagle clogs.

Recently a series of studies examined the relationship of AST activity in GCF to both existing periodontal disease and the progression of periodontal disease in humans. Chaubers *et al* found relationship of increased levels of AST gingival fluid to that of increased activity of periodontitis. In gingivitis increased levels of AST has been found 5 to 0 where as in periodontitis AST levels ranged from 2-12. Longitudinal studies cross sectional studies and multi-centre trials all have established definite correlation between increased levels of AST and increased activity of periodontal disease process.

Collagen in Gingival Crevicular Fluid: Collagens are responsible for main tenance of the framework and tone of tissues and exhibit a wide range of diversity. There are at least 19 recognized collagen species encoded by at least 25 separate genes, dispersed among at least 12 chromosomes. Collagen is by far the most commonly found structural protein in the body and in the periodontum where it occurs primarily in the form of type 1.

Increased levels of hydroxyproline were evident in gingival crevicular fluid in patients suffering from periodontitis. Meug *et al* indicated that pyridinoline and dexoypyridinoline are only present in mature collagen and are detectable in gingival crevicular fluid obtained from disease active sites. In contrast, no detectable amounts were evident in gingival crevicular fluid from healthy sites.

Variations in collagen product levels resulting from disease states will be reflected in gingival crevicular fluid shows the activity status of the periodontal disease process.

Proteoglycans in GCF: Increased levels of proteoglycans in GCF have been found in active phase of periodontitis. Chondroitin 4 and 6 sulfate isomers and hyaluronan in increased amounts in GCF indicate the increased periodontal disease activity. Many scientists detected parent proteoglycans in gingival crevicular fluid.

Glycoproteins in GCF: A variety of glycoproteins have now been identified as important extracellular matrix components which differ in their molecular size, structured functions and distribution. The glycoproteins of the extracellular matrix have a number of important functions, which are implicated in the development and pathological changes. Many glycoproteins are rich in the acidic aminoacids (glutamic acid and aspartic acid). These glycoproteins concentration will increase in GCF along with increased disease process and decrease

in concentration when healing process takes place in periodontium.

CONCLUSION

This review represents an update account of knowledge on the potential usefulness of various components of gingival crevicular fluid as biomarkers of periodontal disease activity. It may well be that the future for biochemical diagnosis may also rest in assay "packages" which combine a variety of assays for a number of gingival crevicular fluid constituents to variety gold standard baselines.

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