Section: Research Paper

An Affiliation of Cytokines and Periodontal Diseases: A Review

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ABSTRACT
In the medicinal world genes play a pivotal role where genomic medicine has set a new shaft in research. Moreover; genetic factors are carrying major position in the progression of periodontal diseases and this inflammation begins as an acute inflammatory response after host-bacterial interaction; proceed into advanced stage which is dominated by B lymphocytes and macrophages, following intense T lymphocytes stage. In the entire process cytokines plays a prevailing role in the transition between these stages. This review narrates the role of cytokines in the inflammation of periodontal disease patterns.
Keywords: periodontitis, cytokines, inflammation, gene

INTRODUCTION

Periodontal disease is one of the most ubiquitous diseases which occur as a result of multifaceted connections between plaque microorganisms and host immune system. Even though periodontal diseases are initially caused by bacteria but the host response is supposed to play an indispensable role in the breakdown of connective tissue and bone. [1] As innate and adaptive immune responses are concerned where microbial antigens and virulence factors bring forth an inflammatory and immune reaction. [2] In the topical date human genome in the biological sciences has given a novel dimension in various chronic inflammatory disease, including periodontal disease. Genomic medicine has further created new scope of research in the field of medical world. In the periodontal diseases, genetic factors play a key role in inflammatory and immune responses. [1, 3] Even genes act as significant factor in the pathogenesis of periodontitis such as in predisposition and progression of periodontal diseases. Thereafter, researchers have concerted through their studies on the recognition of genetic polymorphisms in numerous aspects of immunity. Allelic variants at multiple gene loci perhaps sway the susceptibility of periodontitis. [4]

Few of the genetic variants are having large and clinically significant effects whereas fewer are probably having minor and not clinically significant. If the receptiveness of the genetic basis of periodontal disease can be understood then such information can be utilized in diagnostic and therapeutic purposes. [3, 5] It has been said through various reports there is an association between genes, genetic polymorphisms, and progression of periodontal disease which is really important to understand that how the different genes contribute to disease in various ways.

Inflammation of periodontal diseases begins as an acute inflammatory response after host-bacterial interaction; proceed into advanced stage which is dominated by B lymphocytes and macrophages, following intense T lymphocytes stage. [5] Here cytokines plays a dominant role in the transition between these stages. Cytokines are one of the soluble mediators supporting many biologic processes such as hematopoiesis, wound healing, systemic and local inflammatory responses. They are having pleiotropic effects on diverse target cells by regulating cell activation, proliferation and function. While in the initiation, progression and the host modulation of periodontal disease cytokines are considered to having pivotal role. [6]

It has been said through fewer studies that these T cell derived cytokines are having immunoregulatory properties which can further develop or assuage the succession of periodontal disease.[5] Hence an attempt has made through this review in order to comprehend the potential clinical relevance of genetic variability on periodontitis and role of cytokines in the host inflammatory response.

CYTOKINES AND PERIODONTAL HEALTH

Tissue homeostasis plays a significant role in periodontal tissue which is a fragile equilibrium between anabolic and catabolic activities. Periodontal tissue homeostasis contributes in the regulations of migration, proliferation, and differentiation of resident cells and of the production of tissue matrix. [7]It has been said through various reports that cytokines which are secreted by fibroblasts endothelial cells are having main role in tissue homeostasis and two pathways are used to control the periodontal bone loss and balance of gingival tissue and bone remodeling.

In the first pathway interface of osteoblasts and stroma is connect between bone formation and resorption throughout physiological bone remodeling processes. Whereas inflammatory or osteoclastogenic cytokines are produced in the second pathway during local tissue inflammation or trauma or systemic issues which are accountable for bone loss under pathological conditions where bone remodeling is difficult. [1,5,6]

CYTOKINE'S ROLE IN PERIODONTAL INFLAMMATION

Cytokines are a biologically active molecule that is released by precise cells which further bring out a meticulous response from other acting cells locally and effective in very low concentrations. [8] There are few cytokines induced during an inflammatory response which are known as an inflammatory cytokine and among them IL-1α, IL-1β, IL-6, IL-8 and TNF-α, are classified as pro inflammatory cytokines that boost the bactericidal capacity of phagocytes. Although cytokines are having key role in various physiological processes, but they can induce pathology too if secretion is done in inappropriate manner.[9,10] IL-1, IL-6, and TNF-α cytokines causes periodontal tissue destruction which are secreted by a various cells comprises of monocytes, macrophages, dentritic cells, epithelial cells, keratinocytes and fibroblasts. IL-1 stimulates the production of keratinocytes, fibroblasts and endothelial cells of the periodontal tissues and also increases the fibroblast synthesis of type I procollagen, collagenase, hyaluronate and fibronectin. [11,12]Hence IL-1 is a vital component in the tissues homeostasis whereas unhampered fabrication may show the way to tissue damage. IL-1β is an effective stimulator of bone resorption as it used to upregulates matrix metalloproteinases and downregulates tissue inhibitors of metalloproteinase production. Even it has been reported through various studies that PGE2 and IL-1β are significant mediators in the periodontal inflammation and bone destruction. [11,13]They are also concerned in tissue response regulation.

CYTOKINES ROLE IN DIAGNOSIS

Various biochemical agents are secreted or released from the cells located around vascularized tissues during the inflammation and further they defend the host organisms against infection, helps in tissue healing and refurbish. It has been reported through studies that circulating inflammatory markers are getting increased among those individuals who are having periodontal infections. [13,14] Among the periodontitis patients, cytokines used to be detected in the gingival crevicular fluid (GCF) and their exudates can get collected at the gingival margin, and in gingival tissue. Even IL-6 is present in enlarged way in GCF of those individuals who are having periodontitis or in gingival diseased conditions whereas after nonsurgical periodontal therapy IL-6 got decreased that depicts the clinical improvement of the periodontal status.[15] In the similar way TNFα and IL-1β are also seen in higher concentrations in GCF and gingival tissue of periodontitis related patients and they got decreased after treatment of periodontal disease. In context to bone loss, it was also reported that IL-1 has pivotal role in periodontal pathogens and IL-1β was detected in elevated level in the GCF at sites of bone or attachment loss among periodontitis patients. [16,17]

CYTOKINES AS THERAPEUTICS IN PERIODONTAL DISEASE

During the periodontal diseases treatment measures inhibition of pro-inflammatory cytokines causes the modification of destructive host response against periodontal pathogens and NSAIDs may diminish the host modulation bone resorption too among patients with chronic periodontitis.[18]Even it has been found through various studies that treatment effect used to get improved with additional use of non-steroidal anti-inflammatory drugs (NSAID) while giving the nonsurgical periodontal therapy as they are having suppressing effect of prostaglandin synthesis via COX- 1 and COX- 2. They may proceed as inhibitor of gingival inflammation and bone destruction in periodontitis conditions. [18,19] Even cytokines are helpful indicators for the diseases activity or treatment prognosis as elevated levels of PGE2 and IL-1β in gingival tissue depicts the recurrence and progression of disease whereas reduced amount of PGE2 and IL-1β after management act as positive indicator for successful periodontal therapy. [17,20]

DISCUSSION

Human genome project with advanced technological facilities have altered the face of biological investigations as various diseased conditions or treatment modalities are highly influenced by genetic prediction which further changes the health care delivery system. [1] Human genome carries important information that lead to an

enhanced understanding of the inflammatory mediators or therapeutic targets. There should be the proper knowledge of the gene complement or metabolic pathways that are involved in periodontal destruction and regeneration as many cases of periodontitis are result of interactions between the genome, behavior and environment.[12]Progression of periodontitis depends upon both environmental and genetic factors at one point of time and if genetic factors are inherited more, then greater the genetic predisposition and there will more chances of development of periodontitis at early age. [10]

Since the last 20 years a considerable paradigm has occurred during the perception of periodontal disease and the emphasis for risk is being placed on host genetic and other non-microbial environmental factors. There are sequences of immune regulatory molecules which are known as anti-inflammatory cytokines that control the response of proinflammatory cytokines. They assist the inflammation through physiologic role as well as pathologic role in systemic inflammation and such foremost anti-inflammatory cytokines include interleukin (IL)-1 receptor antagonist, IL-4, IL-6, IL-10, IL-11, and IL-13. [21]

In the periodontal research, IL- 6 is an significant parameter due to its role in inflammation and bone resorption through stimulating activity of the osteoclasts. Even many studies reported that IL-4 was significantly higher in the periodontally healthy group than periodontal diseases population. [22,23]Human genome sequencing with advanced achievements in genomics provides an incomparable opportunity to move forward for better understanding of the genetic factors and their role in diseased or healthy conditions. [12] Even this helps in more specific prevention, diagnosis and treatment of the diseases by detecting the susceptible patients at earlier stage. But the existing knowledge of genetic factors in periodontitis is narrow. Thus faultless collaborations among clinicians, epidemiologists, geneticists, and periodontists will be desirable to solve the genetic underpinnings of complex disease that affects the quality of lives of millions worldwide.

CONCLUSION

Cytokines have a persuasive blow on periodontal pathogenesis through both destructive and protective perspectives. Apart from destructive effects, Th1/Th17 mediated cytokines play vital role to spawn an efficient immune response to shield the host against periodontal infection.

Although "Human Genome Project", is the factual pledge of genomics research for benefitting mankind but we are still far away from the determination of genetic basis among both aggressive and chronic periodontitis. Hence there is requisite of further studies to elucidate the mechanisms of cytokines regulation for better host modulation interventions for resolving the inflammation in various periodontal conditions or diseases.

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