RESEARCH PAPER | Medical Science | Volume : 5 | Issue : 3 | March 2015 | ISSN - 2249-555X

HERPES VIRUSES AND PERIODONTAL DISEASE- A SHORT REVIEW

KEYWORDS: herpes virus, chronic periodontitis, aggressive periodontitis, cytomegalovirus, periodontitis

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ABSTRACT *Periodontal diseases affect majority of adults worldwide. Conventional periodontal therapy is directed towards stabilization of disease followed by long term maintenance. However, clinical relapse is commonly seen and there is limited efficacy in resolving late-stage disease. These would amount to substantial expenses. A definite understanding of the etiology and pathogenesis of periodontal disease is critical for developing therapeutic strategies which are more effective and ensure long term disease control. Plaque bacteria along with host response have been implicated as the etiology for periodontal disease. However, they are not always able to justify the clinical condition. Some other etiologic agents might play a role in severe periodontal diseases. Research in the past two decades has implied the role of herpes viruses in the etiopathogenesis of destructive periodontal disease. Increased numbers of CMV and EBV have been reported in aggressive and chronic periodontitis. The probability that viruses would be innocuous bystanders in destructive periodontitis seems unlikely. They may be an active participant in the disease initiation and progression. This short review discusses the role of viruses in destructive periodontal disease and steers the areas of investigation towards cost effective preventive therapies for periodontitis which will benefit large population.*

INTRODUCTION:

Periodontitis is the most common form of oral disease in adults. It is associated with dental plaque and calculus. It progresses at a slow to moderate pace, with intermittent periods of rapid periodontal destruction. This destruction, at times, affects relatively few teeth despite the omnipresence of periodontopathic bacteria in the mouth. Sometimes the disease affects the teeth in a bilaterally symmetrical pattern and in mouths with minimal plaque deposits. Hence, a pure bacterial etiology for periodontitis seems unacceptable. It is assumed that periodontitis debuts in genetically or environmentally predisposed individuals, who are infected with virulent infectious agents and reveal persistent gingival inflammation and distinct immune responses.[1] Fitting this concept, various herpes viruses have been associated with severe types of periodontal diseases.[2] This short review summarizes the probable link between herpes viruses and severe types of periodontitis.

HERPES GROUP OF VIRUSES-

Herpes viruses are large, double stranded DNA viruses widely dispersed in nature and associated with many human diseases.[3] The term 'herpes' is derived from the Greek word meaning "to creep" reflecting clinical observations of latent recurring infections that progresses slowly.[4] The human herpes viruses share four significant biologic properties:

They encode specific enzymes involved in the biosynthesis of viral nucleic acids. These enzymes are genetically distinct from the host enzymes and provide unique therapeutic targets for inhibition by antiviral agents.[5,6]

The synthesis of viral DNA is initiated in the nucleus, and assembly of the capsid is also initiated in the nucleus.

Release of progeny virus from the infected cell is accompanied by cell death.

They establish latent infection within tissues that are distinct for each virus, and latency is established lifelong in the host.[7]

ROLE OF HERPES VIRUSES IN PERIODONTAL DISEASES-

Healthy gingiva harbours predominantly gram positive facultative bacteria, whereas periodontal lesions contain a large variety of gram negative anaerobic bacterial species. Human Herpes virus (HSV-1, -2, -6, -8), Varicella zoster (VZV) and Human Cytomegalovirus (HCMV) and Epstein Barr virus (EBV) are detected in biopsies from periodontal lesions.

They are known to infect inflammatory cells of the periodontium, thus affecting the host defense. Herpes virus may cause direct cytopathic effects on inflammatory cells like leukocytes, lymphocytes, macrophages and on fibroblasts, keratinocytes and endothelial cells.[8] They may include abnormalities in adherence, chemotaxis, phagocytosis and antibacterial activities of leukocytes. These may hamper tissue turnover and repair process. Herpes infection may increase the pathogenicity of the periodontal microbiota.

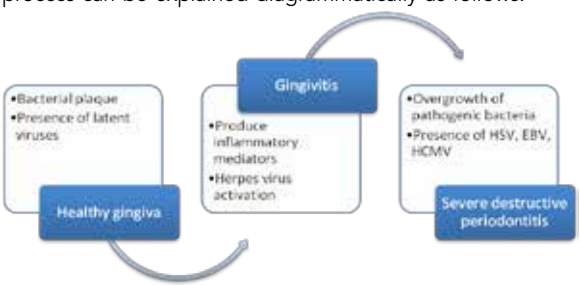
HSV and HCMV can induce cell mediated immunosuppression by reducing the cell surface expression of MHC Class 1 molecule, which will interfere with T-lymphocytes recognition. HCMV infections can upregulate IL-1β and TNF-α. [9] They suppress antigen specific cytotoxic T- lymphocyte functions, resulting in decrease in circulatory CD4+ cells and increase in CD8 suppressor cells which leads to impairment of cell mediated immunity.[9] HCMV even enhances the adherence of A.actinomycetemcomitans to primary periodontal pocket epithelial cells and HeLa cells. [10]

EBV infection can activate polyclonal B lymphocytes and generate anti- neutrophil antibodies. The EBV infected B lymphocytes may shed viral structural antigens that result in production of blocking antibodies, immune complex function and T- suppressor cell activation.[11] The mechanism of herpes virus is to exacerbate the severity of periodontitis. Hence, a dual infection with HCMV and EBV or HCMV with HSV is seen in severe periodontitis.

Volume : 5 | Issue : 3 | March 2015 | ISSN - 2249-555X

HERPES VIRUSES AND BACTERIAL INTERACTION IN PERIODONTITIS-

The interaction between herpes viruses and bacteria can be bidirectional. The progress of periodontitis proceeds from bacteria to herpes virus and again to bacteria. This process can be explained diagrammatically as follows:



The activation of herpes virus leads to increased inflammatory mediator response triggering a cytokine or chemokine of IL-1β, TNF-α, IL-6, prostaglandins, interferons and other mediators which have a potential to propagate bone resorption.[12]

Conteras and Slots reported that herpes viruses may cause direct cytopathic effects on fibroblasts, keratinocytes, endothelial cells and on leukocytes.[13] Klein reported that herpes infection may promote subgingival attachment and colonization of periodontopathic bacteria, similar to the enhanced bacterial adherence to virus- infected cells observed in medical infections.[14] HCMV can cause metabolic abnormalities in lymphocytes and monocytes.[15]

THERAPEUTIC IMPLICATIONS

The bacteria-herpes virus model of periodontitis provides a reason for consideration of new therapeutic approaches to disease prevention and treatment. Conventional periodontal therapy can reduce the periodontal load of herpes viruses. Mechanical debridement has showed suppressed subgingival EBV.[10] Repeated debridement in periodontitis patients showed no CMV but few EBV and Herpes virus-7, suggesting that CMV is particularly susceptible to the effects of periodontal therapy.[16] The probable reason for the decrease in the viral load post-treatment could be due to reduction in the inflammation and virally-infected inflammatory cells.[17]

Drugs such as acyclovir and valacyclovir have been studied for their potential use in limiting the virus infections. It has been reported that prolonged treatment with valacyclovir at dosages of 500-1000 mg/day is well tolerated, perhaps except in immunosuppressed individuals, and the adverse effects are infrequent and generally mild, with headache being reported most often.[18] Miller et al. reported that a short course of valacyclovir, 2g twice on the day of treatment and 1g twice the following day resulted in a significant decrease in the salivary occurrence of EBV compared with controls.[19]

FUTURE DIRECTIONS AND CONCLUSIONS

The role of Herpes virus in the pathogenesis of periodontal disease is still in its infancy. Herpes viruses may play a role as an activator in the disease process as shown in various studies in the literature. The current information justifies addition of EBV, HCMV and herpes viruses as a likely contributing etiological agent for human periodontitis. The scope of development of herpes virus vaccines in the future will open up new therapeutic modality for treatment of periodontitis. It would over-shadow the current periodontal therapeutic methods of surgery and use of antibiotics and may also provide a low-cost prevention of periodontitis. Further research in the identification of viruses in different severity of periodontitis and use of antiviral therapy and vaccines can certainly benefit large groups of individuals suffering from periodontitis.

Acknowledgement – Nil
Ethical clearance - NA-
Source of funding - NA-
Conflict of Interest – Nil

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