REVIEW ARTICLE

Are herpes virus associated to aggressive periodontitis? A review of literature

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Received: 27-01-2013
Accepted: 23-11-2015

ABSTRACT

Periodontal Disease includes a wide variety of infectious entities with various clinical manifestations in the oral cavity and responses to treatment. The determinants of clinical manifestations of periodontal disease include the type of infectious agent, the host immune response and environmental factors. Aggressive periodontitis (AP) is defined as a type of inflammation with specific clinical and laboratory features, which distinguish it from other types of periodontitis, with high incidence rates in a sub-group of individuals. Bacteria have been frequently mentioned as the agent inciting gingival inflammation and tissue destruction that underlies the pathogenesis of periodontitis. However, recent studies, with some controversial results, have suggested that the herpes family of viruses, including CMV and EBV-1 as well as papillomaviruses, HIV, Human T-lymphotropic virus type 1, Torquetenovirus and hepatitis B and C occur with high frequency in active periodontal lesions. There is a lack of information about this disease and the role of herpesviruses in its pathophysiology. This review provides a critical analysis of the scientific evidence linking bacteria and viruses with AP and their potential impact on clinical characteristics, prognosis and therapy.

Key words: Aggressive periodontitis, herpes viruses, periodontal microorganisms

INTRODUCTION

Aggressive periodontitis (AP) with a prevalence between 0.1% and 1.0% in European Caucasians, affects a minority of patients but is consider as a severe disease regardless the serious damage that can lead to early tooth loss.[1,2] The AP is characterized by the quick loss of insertion and the bone destruction. It usually affects young people who do not have a significant medical history and can show a familial aggregation of cases.[1-3]

Clinical characteristics of aggressive periodontitis

The AP is less frequent than chronic periodontitis and mainly affects young patients, however, it can occur at any age.[3] This implies that the etiologic agents have been able to cause clinically detectable disease levels in a relatively short period of time. This is important for the current understanding of these diseases since it involves an infection with a highly virulent microflora and/or a high level of the individual susceptibility to the AP disease.[3-5]

The environmental factors play a key role in the expression of this type of periodontitis. These factors involve tobacco smoke (disturbs the relationship between host and parasite leading to the worst levels of clinical parameters and limits the success of treatment resulting in negative prognosis), oral hygiene (although in many cases, the quantity of microbiological

Access this article online

Quick Response Code:

Website: www.jomfp.in

DOI: 10.4103/0973-029X.174621

How to cite this article: Rodrigues PM, Teixeira AL, Kustner EC, Medeiros R. Are herpes virus associated to aggressive periodontitis? A review of literature. J Oral Maxillofac Pathol 2015;19:348-55.

deposits in the tooth surfaces is inconsistent with the severity of periodontal tissue destruction), stress (psychological stress appears to be a particularly important trigger of reactivation of herpesviruses in immunocompetent subjects),[2,6] systemic diseases (diabetes mellitus and obesity) modify the inflammatory tissue responses of the host changing the course of the AP, some genetic disorders are associated with severe periodontitis in children and adolescents, such as neutropenia, hypophosphatasia, leukemia, Chediak–Higashi syndrome, leukocyte adhesion deficiency, Papillon–Lefevre syndrome, trisomy 21, histiocytosis and agranulocytosis.[7-9]

The AP may be localized (LAP) or generalized (GAP) and there are common features to both [Table 1] or they can differ in many aspects, namely in relation to its etiology and pathogenesis.[3,7,10]

Regarding the clinical individual response, the LAP is not only a localized way of GAP. [Table 2].

The diagnosis of one of these ways of AP excludes the presence of systemic diseases that can severely damage the host's defenses and lead to premature loss of teeth.[9]

The recommended anti-infective treatment for quite some time (nonsurgical periodontal treatment/conventional or the surgical treatment) is effective in controlling the disease progress and the subsequent attempts to regenerate some of the lost periodontal tissue are usually successful.[11-13] The periodontal support phase designed to maximize the effectiveness of the patient's oral hygiene and for the disruption/removal of sub-gingival biofilms at regular intervals is absolutely essential to prevent long-time disease recurrence.[13]

Table 1: Common manifestations of aggressive periodontitis in localized and generalized forms

Primary manifestations
Medical history not significant
Quick attachment loss and bone destruction
Concentration of family cases
Secondary manifestations
Amounts of microbial deposits inconsistent with the severity of periodontal tissue destruction
High proportions of *Aggregatibacter actinomycetemcomitans* and in some populations of the Far East *Porphyromonas gingivalis*
Phagocytic abnormalities
Phenotypes of hyper-reactive macrophages, including increased production of PGE and IL-1β in response to bacterial endotoxin
Progression of attachment loss and bone loss can be stopped

IL-1β: Interleukin-1 beta, PGE: Prostaglandin E

Table 2: Specific manifestations in localized aggressive periodontitis and generalized aggressive periodontitis

LAP
Starts peri-pubertal
Intense serum antibody response to infectious agents
Located on the first molar/incisor with interproximal attachment loss on at least two permanent teeth, one of the first molar and involving no more than two teeth other than first molars and incisors
GAP
It affects people under 30 years, but can occur in older patients
Loss of adhesion interproximal affecting at least three permanent teeth than the first molars and incisors
Episodic nature with pronounced destruction of the gum insertion and alveolar bone
Insufficient serum antibody response to infectious agents

LAP: Localized aggressive periodontitis, GAP: Generalized aggressive periodontitis

Pathogens involved in aggressive periodontitis

The current periodontal therapy strongly recommends the suppression or eradication of specific pathogens. However, it has been difficult to determine the precise role of various pathogens involved in the immune response of this disease. It is not fully understood why, but in hosts with comparable risk factors, some periodontal infections result in loss of periodontal attachment and alveolar bone, while in other infections, they are limited to gingival inflammation with little or no discernible clinical consequences. A low level of traditional risk factors is also observed in many aggressive periodontal patients.[9,11] It remains an enigma why most patients show periodontitis in relatively few teeth despite an omnipresence of periodontopathic bacteria in saliva.[14,15] Furthermore, many periodontal lesions are self-limiting with short-duration morbidity despite a persistent presence of periodontopathic bacteria in the periodontal pocket.[14,15] Moreover, as clearly evidenced in LAP, periodontal tissue destruction tends to occur in a bilaterally symmetrical pattern around the midline of the mouth and may almost reach the apex in one tooth while barely affecting a neighboring tooth sharing the same interproximal space.[14]

Healthy gingival sites harbor a scant microbiota of mainly facultative, fermentative, Gram-positive bacteria, whereas periodontitis lesions contain predominantly anaerobic, proteolytic, Gram-negative species.[15-17] Microbiological culture and culture-independent molecular studies have identified more than 1200 bacterial species and 18,000 phylotypes in the oral cavity and at least 400 bacterial species in subgingival sites, but despite the long list of different bacteria in periodontitis, <20 species are designated major periodontal pathogens.[18] The detection and quantification of periodontal bacterial species are useful to identify people with high-risk periodontitis development, but not consistently predict possible future events.[15,17,18]

Even if it is considered that specific infectious agents are significantly important in the development of periodontitis, it is not likely that a single agent or even a small group of pathogens are the unique cause or the modulators of these

heterogeneous diseases.[15,17,18] Currently, it is being accepted that AP infections are caused by a diverse microbiota and is not caused only by anaerobic Gram-negative bacteria. Because of the many puzzling clinical features of periodontitis mostly an indirect evidence exists for a bacterial etiology of the disease, it is our contention that pure bacterial cause of periodontitis has been overemphasized.

Recent studies, with some controversial results, have suggested that the herpes family of viruses, including human cytomegalovirus (HCMV) and Epstein–Barr virus type 1 (EBV-1), papillomavirus, human immunodeficiency virus, human T-lymphotropic virus type 1 Torquetenovírus and hepatitis B and C occur with high frequency in active periodontal lesions.

According to Slots,[19] periodontal destruction may be associated with the coexistence of periodontal herpes viruses, especially HCMV and EBV, periodontopathogenic bacteria and the local impaired host-immune response. AP sites presenting HCMV, EBV-1 or herpes simplex virus type 1 (HSV-1) had a higher occurrence of *Porphyromonas gingivalis* and *Dialister pneumosintes* than sites without the viruses.[20] Furthermore, AP sites infected with active HCMV harbored more *Aggregatibacter actinomycetemcomitans* than sites with latent HCMV infection.[20] Saygun *et al*.[17] reported that HCMV, EBV-1 and HSV-1 were positively associated *with P. gingivalis*, *Prevotella intermedia*, *Tannerella forsythia* and *Campylobacter rectus* but not with *A. actinomycetemcomitans* in young adults with advanced periodontitis. The herpes viral infection can stimulate the release of cytokines and chemokines from inflammatory and noninflammatory cells and impair the periodontal immune defense, resulting in more virulent resident bacteria.[15,18,19]

The recognition that periodontitis is a multifactorial disease that involves the herpes viruses, bacteria and host defense reactions may explain why the AP is relatively uncommon in the great number of the population despite the high prevalence of persons with herpes viruses and periodontal bacteria.

The periodontal pockets infected with herpes viruses tend to present greater tissue destruction than the pockets non- infected with this virus.[21,22] The active viral herpetic infection is also associated with a high risk of progressive periodontal disease.[21]

Viruses reside in high levels within gingival tissue. Saliva can contain several additional viruses of medical importance, but their relationship to periodontitis has still to be determined.[23,24]

HERPESVIRUSES IN AGGRESSIVE PERIODONTITIS

The occurrence of herpesviruses in this specific type of periodontal disease has been studied by qualitative and quantitative identification techniques. Table 3 summarizes the studies that have been performed until October 2015 for the presence of human herpes virus (HHV) family, as per the tissues/fluids of the oral cavity from where the samples were collected, the laboratory method used by the authors, the country of origin of the population under study and the percentage of positive samples for each herpesvirus.

According to this table, we see that individual lesions of AP may yield subgingival herpes viruses as high as 89% for EBV, 78% for cytomegalovirus, 87% for HSV-1 and 64% for herpes virus type 7. The remarkably high copy counts of pathogenic viruses in AP lesions make it unlikely that these infectious agents are acting merely as harmless bystanders present in proportion to the severity of the underlying periodontal pathosis.

In Turkey, Saygun *et al*.[36] detect subgingival HCMV and EBV-1 in 72% of AP lesions. In 62 Chinese patients, Ling *et al*.[35] found EBV in 58% of disease-active periodontitis sites, but only in 23% of quiescent periodontitis sites. In India, Das *et al*.[26] and Bilichodmath *et al*.,[28] in 2009 and 2012 found similar results for detection of EBV. In Italy,[31] EBV-1 and HHV-7 have been related to periodontal disease. Even though herpesvirus carriage varies by age, country, region within country and population subgroups (e.g., Nibali *et al*.,[27] in UK, and Stein *et al*.,[25] in Germany, did not detect considerable percentage of cytomegalovirus or EBV-1 in their AP patients), studies from the various countries report high prevalence of this type of viral DNA in AP, attesting to the robustness of the herpes-virus-periodontitis association. Kamma *et al*.[37] investigated the occurrence of DNA of HCMV, EBV-1 and selected pathogenic bacteria in 16 patients with AP from Greece. In each patient, subgingival samples were collected from two progressing and two stable periodontitis sites with similar depth and gingival inflammation. The study revealed that herpesviruses can be detected in some but not in other periodontitis lesions of the same individual and even if no difference was observed in the level of gingival inflammation, herpesviruses occurred more frequently in actively progressing than in stable periodontitis sites. Kubar *et al*.[34] found increased periodontal pocket depth and attachment loss in AP sites with HCMV presence, compared to periodontitis sites with a similar degree of clinical inflammation but with no detectable HCMV. Ting *et al*.[38] studied the relationship between HCMV activation and disease-active versus disease-stable AP in 11 patients between the ages of 10 and 23 years. The presence of messenger RNA of the HCMV major capsid protein, which is an indication of an active HCMV infection, was detected in deep pockets of all five HCMV-positive patients with early disease (aged 10–14 years), but only in one of three HCMV-positive patients older than 14 years and not in any shallow test sites. The study found HCMV reactivation in some and HCMV latency in other periodontal sites of the same patient, pointing to site-specificity in oral HCMV transcription state. Gingiva of AP lesions tends to show high levels of T-suppressor cells and Langerhans cells which are potential carriers of the HCMV genome.[41]

Table 3: Studies concerning prevalence of herpesviruses in aggressive periodontitis, according to locations of sampling, study populations and laboratory methods

Authors/country	Collection site of the samples	Laboratorial methods	Herpesvirus (% prevalence)
Stein *et al.* (2012)/Germany[25]	Sub-gingival plaque	PCR real time	HSV-1 (1.5) EBV (10.8) Cytomegalovirus (1.5)
Das *et al.*/India[26]	Sub-gingival plaque	PCR multiplex	HSV-1 (80) EBV (32)
Saygun *et al.*/Turkey[24]	Saliva	PCR real time	EBV (60)
Nibali *et al.*/UK[27]	Sub-gingival plaque	PCR real time	EBV (9) Cytomegalovirus (0)
Bilichodmath *et al.*/India[28]	Sub-gingival plaque	PCR multiplex	HSV-1 (57) EBV (29) Cytomegalovirus (7)
Imbronito *et al.*/Brazil[29]	Sub-gingival plaque	Nested PCR	HSV-1 (87) EBV (33) Cytomegalovirus (47)
Botero *et al.*/Colombia[30]	Gingival crevicular fluid	Nested PCR PCR real time Viral culture	Cytomegalovirus (48)
Rotola *et al.*/Italy[31]	Biopsy of the gingival periodontal pocket	Nested PCR	EBV (55) Herpes virus type 7 (64)
Saygun *et al.*/Turkey[17]	Sub-gingival plaque	PCR real time	EBV (60) Cytomegalovirus (53)
Ding *et al.*/China[32]	Sub-gingival plaque	Nested PCR	Cytomegalovirus (44)
Botero *et al.*/Colombia[21]	Sub-gingival plaque	Nested PCR	Cytomegalovirus (40)
Watanabe *et al.*/Brazil[33]	Gingival crevicular fluid	PCR	EBV (57) Cytomegalovirus (7)
Kubar *et al.*/Turkey[34]	Biopsy of the gingival periodontal pocket	PCR real time	EBV (89) Cytomegalovirus (78)
Ling *et al.*/Taiwan[35]	Sub-gingival plaque	Nested PCR	EBV (58)
Saygun *et al.*/Turkey[36]	Sub-gingival plaque	PCR	HSV-1 (78) HSV-2 (17) EBV (72) Cytomegalovirus (72)
Kamma *et al.*/Greece[37]	Sub-gingival plaque	Nested PCR	HSV-1 (34) EBV (44) Cytomegalovirus (59)
Ting *et al.*/USA[38]	Gingival crevicular fluid	Nested PCR	HSV-1 (54) EBV (63) Cytomegalovirus (72)
Dani *et al.*/India[39]	Gingival biopsies	PCR real time	HSV-1 (47) EBV (67) Cytomegalovirus (53)
Grigoras *et al.*/Romania[40]	Sub-gingival plaque	PCR real time	HSV-1 (78) EBV (72) Cytomegalovirus (72)

PCR: Polymerase chain reaction, HSV-1: Herpes simplex virus type 1, EBV: Epstein-Barr virus

Concerning the present results, we have observed important differences in the percentage of prevalence of genomic viral DNA, among the papers analyzed. The sampling methods are similar and standardized. The polymerase chain reaction (PCR) analysis is the method of choice for the detection of viral DNA. However, because of high assay sensitivity, PCR may detect herpesviruses at copy counts too low to be of clinical significance.[42] As low herpesvirus counts occur more frequently in healthy or slightly inflamed periodontal sites[42] than in periodontitis lesions, PCR-based studies may disproportionately overestimate the significance of herpesviruses in normal periodontal sites. False negative PCR results may be caused by failure to sample gingival epithelial cells rich in EBV[43] or by an inhibitory effect of components of the amplification process. Dissimilar inclusion criteria for the study of individuals and sample sites are probably the main reasons for differences in the detection rate of periodontal herpesviruses.[42] It is important to investigate

periodontitis lesions that are actively progressing or, at very least, have not recently received professional treatment. The characteristic latency between the herpes virus may also explain some more discrepant results since it is not known if the disease is active at the time of sampling or if the herpes virus family were present at an earlier stage of the disease.

For the study populations, most studies have been performed in South America, China, Turkey, or African Americans (those populations have many ethnic groups) and there are few studies to be performed in Caucasians. In those, periodontal cytomegalovirus and EBV have been found at low prevalences in some, but not in all European countries with a predominantly Caucasian population.[42] In terms of number of persons with AP disease which have been the samples, there have been studies that used from 11 persons to 140 persons.

The main purpose of studies on periodontal herpesviruses is eventually to prevent or cure periodontitis by controlling the viruses. Further progress in delineating the periodonto-pathogenicity of herpesviruses depends on the use of well-defined periodontal disease and control populations, sufficiently large study groups, validated molecular detection methods.

Pathways of interaction between herpes virus and bacteria in the development of aggressive periodontitis

The evidence supports the hypothesis of co-infection in which the development and progress of periodontal disease are associated with the infection of active herpesviruses, in conjunction with opportunistic pathogenic bacteria living in the endogenous sub-gingival microbiota.[18,19] The theorized events for this association could now have several scenarios.

One is that the herpes virus infection results in increased local pro-inflammatory cytokines that subsequently break the homeostatic balance between the existing periodontal microbiota and the host. Members of this sub-gingival microbiota that take advantage of the inflammatory conditions (e.g. *P. gingivalis, T. forsythia* and *Treponema* spp.) proliferate and help in the development and progress of periodontitis.[19,41] Another interesting hypothesis is that the proposed primary cytomegalovirus infection acting during the formation of the tooth root and then when there is reactivation during puberty, this virus may be involved in the pathogenesis of LAP. This may lead to malformation of the initial periodontal attachment apparatus and may partially explain why there is a minimum amount of bacterial plaque in the early stages of LAP.[15,19,41]

Herpesviruses target various cells of the immune system and subvert host immune functions to their own advantage. It is known that cytomegalovirus infects periodontal monocytes/macrophages and T lymphocytes and EBV infects periodontal B lymphocytes. These infected inflammatory cells stimulate tissue destructive cytokines and decrease the defensibility against periodontal bacteria.[16,19,41]

The host immune response attempts to control both viruses and bacteria in periodontal pockets. However, it is not clear whether some inflammatory mediators such as cytokines and some chemokines play a primary role of protection or destruction in periodontal disease.[9,14] On the other hand, some immune mechanisms that are active against viruses may decrease the antibacterial immune response and vice versa. It may be possible that periodontitis is the result of extensive or partial responses opposite against combined viral-bacterial infections.[15,18-20]

The discovery of abundant herpesviruses in periodontal lesions redefines the pathogenic paradigm and inflammatory periodontal disease. In Figure 1, we can observe a potential model of development of periodontitis by a sequential infectious process, adapted from Slots.[19]

Initially, the biofilm bacteria induce gingivitis which allows latent herpes virus, embedded in DNA of macrophages, T lymphocytes and B lymphocytes to infiltrate the periodontium. Cytomegalovirus, for example, can be replicated in the gum tissue which may help to keep the periodontal infection. The reactivation of latent herpes virus may occur spontaneously or during periods of decreased host defenses, through immunosuppression induced by drugs, concomitant infection, prolonged emotional stress, hormonal changes, trauma, etc. Some of the factors involved in herpes virus activations are also risk indicators for the periodontitis.[19,41]

In response to the active herpes virus infection, the host starts a strong immune response mediated by T cells, namely $CD8^+$ T cells. To counteract this hostile environment created by the host, the herpes virus try strategies to reduce anti-viral

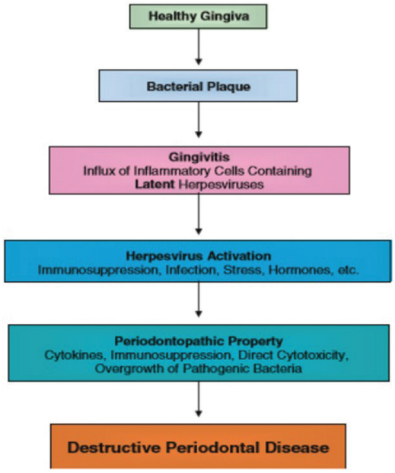

Figure 1: Infection model for the development of periodontitis (Modified from Slots J. Herpesviruses in periodontal diseases. Periodontol 2000 2005;38:33-62)

defense: They disintegrate major histocompatibility complex components and interfere with antigen presentation, silencing natural killer cells expressing a viral homolog of interleukin-10 and inhibiting the apoptosis. This clash between the host antiviral defense and anti-viral host response results in a great release of pro-inflammatory cytokines that have the potential to activate osteoclasts and inhibit the action of antibodies against bacteria such as *P. gingivalis* and *A. actinomycetemcomitans*. Then, the activation of known mechanisms involved in periodontal destruction, inflammation, collagen degradation and osseous resorption can be observed.[19,41]

Cytomegalovirus and other herpes viruses can promote pathological effects on fibroblasts, epithelial cells, keratinocytes, endothelial cells, inflammatory cells and bone cells. They can take part in the degradation of collagen and interfere with the cell turnover and the healing process in periodontal guided tissue regeneration.[19,41]

The propensity for local tropism of herpes virus may explain the pattern of periodontal tissue destruction which may differ from tooth to tooth in the same patient or from surface to surface in one tooth.[19,41]

The destruction of periodontal tissue may be depending on the simultaneous occurrence of a number of infectious pathological events that include a sufficient existence of herpes virus in periodontal tissue, activation of herpes virus in the periodontium, inadequate protective antiviral response of cytotoxic T lymphocytes, the presence of specific periodontal pathogenic bacteria and inadequate antibodies that are a protective response to the presence of certain bacteria.[19,41]

The interactions between herpes virus and bacteria may explain some characteristics of the destructive periodontal disease. The alternation between periods with long latency with periods of activation of viral infections may be partially responsible for episodes of disease exacerbation. The absence of herpes virus infection or viral reactivation may clarify why some persons are carriers of periodontal bacteria and present minimal signs of periodontal inflammation.

THERAPEUTIC IMPLICATIONS

The conventional nonsurgical periodontal therapy reduces the viral existence of herpes viruses.[13] The scaling and root planning remove genomic copies of cytomegalovirus, EBV and herpes virus type 7 until none detectable in sub gingiva and saliva.[12,13] The decrease posttreatment of the herpes virus counting is probably due to the reduction of gingivitis and consequently to the number of infected inflammatory cells.[19] Similarly, the low counting of herpes virus in periodontal healthy areas may be the result of the absence of inflammatory cells infected on them.[19]

The treatment of AP includes regular systemic antibiotics; not only because of the mechanical limitations that conventional treatment presents (some specific bacteria can be reduced but not all, negative consequences such as recession gum and tooth hypersensitivity after scaling and root planing and difficulty in reaching microbiological niche) but also by the specific characteristics of this kind of periodontitis. Thus, antibiotics should be used as helpers to conservative mechanical treatment, never as monotherapy and the best results are obtained when the taking is immediately after the last root planning. The dose demonstrated to be more effective refers to amoxicillin/metronidazole (375 mg ± 250 mg/8–8 h) or clindamycin (300–600 mg/6–6 h).[44]

The saliva may contain a high number of herpesviruses (EBV, cytomegalovirus and herpes virus 6 and 7) and conventional periodontal treatment can reduce the number of genomic copies in this fluid.[23,24] Some studies suggest that periodontal pockets are the major source of salivary herpes.[23,24] This potential of the conventional periodontal therapy in reducing the salivary viral levels may be helpful in reducing the risk of viral transmission and disease related to these micro-organisms.[42]

Marked reduction or eradication of herpesviruses in periodontal sites may improve not only the periodontal health status, but also decrease the frequency of herpesvirus viremia and salivary transmission and perhaps lower the risk of serious medial diseases and disabilities.[42]

Microbiological tests may be repeated 1–3 months after the completion of the therapy to verify the elimination or marked suppression of pathogens. After resolution of the periodontal infection, the patient should be placed on a periodontal maintenance program, which shall include the continuous evaluation of the occurrence and risk of disease progress, every 3 months.[12,13]

The infectious model of bacteria/viruses of the AP allows new considerations in the prevention and treatment of the disease, for example, treatment with anti-viral drugs, namely with valacyclovir 500 mg, 2 times daily for 10 days (anti-herpes drug).[45]

CONCLUSIONS

We intend with this work to summarize the evidence linking herpes viruses to the development of AP and elucidate the potential mechanisms, through which herpes viruses contribute to the breaking of periodontal tissue defenses. It has been suggested that the coexistence of these viruses and possibly of other viruses with periodontal bacteria and host immune responses can be seen as a precarious balance that has the potential to lead to periodontal destruction.

Nevertheless, despite a large body of compelling research data, definitive proof is still lacking that periodontal herpesviruses

play a causal role in periodontitis development and do not occur merely as an epiphenomenon to the periodontal disease process.

The etiopathogenesis of AP includes virulent factors of herpes virus and bacteria, host immune responses against viruses and bacteria and manipulation of host cellular processes by the infectious agents. Herpes viruses can induce periodontitis by activating channels of the specific destructive immune system and by placing the person in the hands of increased bacterial existence. However, the molecular contribution of the herpes virus versus bacteria in AP is still poorly understood. Potential factors of immunosuppression are trigger points for the viral reactivation and perhaps a risk factor for the periodontal disease. Herpes viruses are strong inducers of pro-inflammatory cytokines that have the capacity to activate osteoclasts and matrix metalloproteinases. Some periodontal bacteria can reactivate a latent herpes virus. The synergy between these viruses and bacteria in the periodontal tissue may play an important role in the advance and progress of AP.

Understanding the pathophysiology of periodontal herpes viruses may help to outline the molecular determinants that cause gum disease that progresses to periodontitis or stable periodontitis which become a progressive disease. Evidence of a causal role of herpes viruses in periodontitis could be the basis of new strategies for diagnosis, prevention and treatment of this disease.

The development of vaccines for herpes virus in the medium term would likely be an important victory for the maintenance of conditions favorable/stable to the aggressive periodontal disease that does not allow the disease to advance, reducing the role of conventional periodontal therapy or surgery and antibiotics. Conclusive evidence of an etiologic role for herpesviruses in periodontitis will probably have to await the development of effective herpesvirus vaccines.

Increased research into periodontal virology is encouraged given the remarkable preventive and curative possibilities it may offer.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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