Clinical and microbiological periodontal aspects of treatment HIV patients

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Abstract:
Objective: This study aims to review the literature on periodontal disease and its clinical and microbiological peculiarities in patients with HIV.

Material and methods: A search was made from 2007 to 2018 of the scientific literature to evaluate the clinical and microbiological aspects of therapy periodontal in HIV patients.

Results: The studies shows periodontal status may predict the progression of HIV to Aids and periodontal treatment may be not complete effective in HIV-associated with oral manifestations. In respect to HIV infection, it is also associated with dysregulation of oral microbiota which may compromise the oral mucosal immunity of HIV-infected. Thus, the highly active antiretroviral therapy (HAART) regimens contributed to reduce plasma load of the virus and improvement the results of periodontal treatment in patients that has CD4 control.

Conclusion: The studies revealed periodontal status may predict the progression of HIV to Aids and periodontal treatment may be not complete effective in HIV-associated with oral manifestations. Further studies are needed to understand the complete dynamics of microbiomes and to establish new management of periodontal aspects.

Keywords: Periodontal disease; HIV; Microbiology.

Introduction

Human Immuno-deficiency Virus (HIV) is transmitted by sexual contact, infected blood or by blood-containing bodily fluids, and by infected mothers to infants. The level of viral load in the blood appears to be determinant of transmission risk. It is considered a global public health problem. Acquired Immunodeficiency Syndrome (AIDS) is a disease caused by the HIV. Characterized by a profound state of immunosuppression, resulting in opportunistic infections, secondary malignancies and neurological manifestations. In this condition, HIV targets and attacks T helper cells (CD4) resulting in immune response suppression. Diseases progression can be detected by monitoring HIV viral load and T helper cells (CD4+). Oral manifestations associated with AIDS may be the first symptoms of the disease, being evident in the clinical course of the syndrome, they are considered as possible markers of the disease. Several authors indicate periodontal diseases as one of the main lesions found in patients infected with HIV. Therefore, it can be a useful indicator for screening the immune condition of potential HIV positive individuals and can be easily recognized and detected by clinicians. Periodontal Disease are the most common infection diseases, which affect tooth-supporting bone structures. Includes conditions such as Gingivites and periodontitis.Biofilms enriched of Gram-negative anaerobic bacteria activates pro-inflammatory path-ways and promotes formation of periodontal pockets. However, HIV infection has been considered a modifier of periodontal disease.
The absence of oral lesions as a marker of the efficacy of HAART (Higher Active Antiretroviral Therapy) treatment. HIV depletes and/or dysregulates multiple arms of the human system defenses. Particularly at mucosal sites causes substantial irreversible damage. This leads to hyper-immune activation motivated for microbial products translocation. The goals of treatment are reduce HIV-related morbidity and mortality, improve the quality of life associated with increased life expectancy, restore and preserve immunologic function and suppress viral load in undetectable levels the population level, and prevent the transmission of HIV. Food and Drug Administration, USA approved twenty five drugs under this six classes drug categories (This six drug classes are: Nucleoside reverse transcriptase inhibitors, Non-nucleoside reverse transcriptase inhibitors, Integrase inhibitors, Protease inhibitors, Fusion inhibitors and Coreceptor antagonists) which are available for treatment of HIV-1 infection. Although, HIV drug resistance is an increasing problem. Based on this the aim of this study was to review the literature on clinical and microbiological periodontal aspects in HIV positive patients.

Clinical status of HIV positive patients

The study of oral and periodontal lesions in HIV subjects shows a relationship between the oral manifestation of HIV infection and CD4 levels. High doses of viral load (greater than 3,000 copies/ml) were associated with the presence of oral lesions. Positive HIV patients demonstrate 70-90% of oral lesions during stages disease due to easy accessibility of the oral cavity because oral manifestations are sometimes the first and most important clinical indicators of HIV infection. The critical role in recognizing periodontal and oral manifestations may infer the HIV infection at different stages disease and refer patients for a strait follow up. This findings play an important role in predicting the progress of viral infection and detecting infection. It’s related that the type and percentage of oral lesions were found that sex, race, a transmission route, and stage of disease progression may affect development and a presence of oral findings. Oral lesions include progressive periodontal disease, hairy leukoplakia, necrotizing ulcerative gingivostomatitis, linear gingival erythema and necrotizing ulcerative periodontitis, aphthous ulcers, Kaposi’s sarcoma, non-Hodgkin’s lymphoma, herpes simplex and candidiasis. There is a correlation statistics between oral candidiasis and a decrease in the CD4+ count (less than 200 cells/mm3). More recently, after the introduction of HAART and its widespread use it promotes a stabilization of CD4+ counts and a reduction in viral load, resulting decreased considerably in the total oral lesions such as above-mentioned diseases. HAART is a combination of at least three antiviral drugs. Two nucleoside analogue reverse transcriptase inhibitors, a non-nucleoside reverse transcriptase inhibitor or a protease inhibitor may be in composition. Although other conditions such as oral warts and salivary gland disease have been described more prevalent in this population as part of immune reconstitution of therapy. Studies have shown that HAART has adverse effects on salivary flow, and yet there is no concrete evidence for over prolonged use of HAART therapy. Necrotizing ulcerative gingivitis can be treated by cleaning and debriding in areas with gauze soaked in a topical agent daily or on alternate days for about one week, the use of 0.12% chlorhexidinegluconate mouth rinses for 30 seconds twice daily is recomentade, for reducing the microbial load and bleeding, ensuring oral biofilm control and scaling and root planing after the patient has some improvement in symptomatology and healing. In the reevaluation of 4 weeks, healthy gingiva is expected. The non-response of linear gingival erythema to conventional therapy may be due in part to an invasion of Candida from the gingival tissues. In these cases, the use of an antifungal agent may be beneficial in reducing inflammatory changes. Evidences suggest that viral infections are involved in periodontal disease. Periodontitis is characterized by the destruction of the attachment apparatus by the interaction between the host and the host immune reaction to periodontal pathogenic microorganisms caused primarily by bacteria and bacterial products detected in dental plaque. Immunodepression causes reduction of CD4 + T cells, resulting in neutrophilic hyperactivity and consequently periodontal destruction. It is suggested that Interleukin (IL-18) is present in higher concentrations in HIV-positive patients, therefore it may influence the degree of HIV-positive periodontitis because it binds to higher levels of pro-cytokines with the contribution of the etiopathogenesis of periodontitis. However, the greatest damage in relation to insertion loss was attributed to the higher prevalence of smoking and poor oral hygiene, but the prevalence of chronic periodontitis reported in this study was similar between groups. Other research affirm that CD4 + has a moderate positive association with worse periodontal diagnosis that may be explaining that worse immunological conditions are associated with worse periodontal conditions. The prevalence of periodontitis was 64% in of HIV-positive patients, the data produced by the study state that all individuals showed some degree of periodontal disease, however none showed its severe form. The association between disease and CD4 + counts was negative. A South African study found no significant differences in clinical parameters (bleeding probing, pocket depth or insertion loss measures) between HIV-negative and HIV-positive controls. HIV-positive patients showed lower oral hygiene compared to HIV-negative controls, but the difference was not statistically significant. In this study, factors such as age and low CD4 + T cell count were not associated as a risk factor for greater severity of chronic periodontitis among HIV-positive individuals. In contrast, there are reports of gingival inflammation and loss of attachment and the association of its influence with HIV infection in chronic periodontitis.
compared with non-infected individuals. Conventional gingivitis and chronic periodontitis are also observed in HIV-positive patients but the damage in these patients is faster and greater developing than in HIV-negative individuals. However, variations in the prevalence of chronic periodontitis have been attributed to the racial differences of the studied population and to the methodological variations. Immune changes in the gingival sulcus of patients with HIV/AIDS were identified. A study reported lactoferrin an iron-binding glycoprotein stored in neutrophil secondary granules found in external secretions, it may modulate the inflammatory response. It has the ability to suppress IL-1β, IL-6, and TNF-a production in mononuclear cells in response to lipopolysaccharide activation, blocking the development of inflammation. The subgingival sites exhibit a tendency for decreasing of lactoferrin concentration in subjects with AIDS, but this relation is still unclear.

The oral environment after the introduction of HAART is not fully understood. It is suggested that patient within the HAART less propensity to present severe forms of periodontal disease when compared to seropositive individuals without HAART therapy.

Bacterial translocation into systemic circulation from the periodontal pocket is a common event, supported by detection of bacteremia subsequent to relatively minor periodontal events and procedures. If antibiotics are required, the narrow-spectrum antibiotic should be considered because of the minimal effect on the gram-positive anaerobic bacterial flora. Antibiotics such as clindamycin, metronidazole, and amoxicillin may be useful for treatment. For treatment of Necrotising ulcerative disease the recommendation is Metronidazole (250 mg orally 4 times daily for 10 days), or other systemic antibiotics (such as tetracycline, clindamycin, amoxicillin, and amoxicillin-clavulanate potassium). The gain of 2 mm was reported with the use of tetracycline in a persistent pocket after the local administration of the drug.

Antibiotics should be used with caution because of the risk of excessive growth of C. albicans. To avoid such overgrowth, the generally accepted approach is to use a topical antifungal agent Nystatin pastilles 100,000 units, dissolve 1 in mouth 4 times a day for 14 days or Nystatin oral suspension 500,000 units: Swish 5 mL in mouth as long as possible, 4 times a day for 14 days) and systemic fluconazole (Fluconazole 100 mg, 15 tablets for 2 tablets on day 1, followed by 1 tablet a day for the remainder of the 14-day treatment period) in cases of more severe immunosuppression.

Usually the scaling and root planing (SRP) as a method of periodontal treatment has satisfactory results. However, in complex cases, it is necessary a adjunct therapy. A recent study reported an additional benefit of the photodynamic therapy (PDT), which was used as an adjunct to scaling and root planing in the treatment of HIV-associated periodontitis.

On PDT, the photosensitising agent is used to apply light therapy selectively. It is useful for sensitizing bacterial cells leading to an effective antimicrobial activity. Experienced results with the use of green malachite in adjuvant therapies led to the reduction of significant pathogen levels. However, there is not benefits on clinical results compared to SRP alone. The dental treatment and adequate oral hygiene results in a periodontal profile similar to healthy population. There are no restrictions on the dental treatment of stable patients on regular HAART. A mean increase in CD4 count of over 100 cells/ml was detected after the dental intervention.

**Microbiological aspects**

The mouth may harbor viruses, fungi and over 700 different bacterial species, billions of bacteria. Teeth connect two environments that are separated by a junctional epithelium. During chronic periodontal disease, the junctional epithelial seal is widened, leading translocation of bacteria and bacterial by-products to underlying connective tissue and bone. Known periodontal pathogens like Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis, Tannerella forsythia and Treponema denticola are able to induce inflammatory responses that induce attachment loss and periodontal destruction, and other species as well.

Studies about the microbiota suggest that a considerable number of same bacteria contribute to periodontitis in healthy individuals also contribute to periodontitis on HIV-positive patients. The composition of the periodontal microbiota in HIV infected individuals still motivates several researches. The role of oral microbiome in HIV-infected individuals requires attention, disease or treatment can affect the diversity and composition of the microbiota oral. High plasma HIV viral loads were associated with severe periodontal disease and associated with the presence of oral pathogens.

The decline in host defense due to HIV-related changes makes oral tissues more susceptible to the effects of various pathogens, as well as to side-effects of antiretroviral therapy and ageing. HIV infection considerably augments the bacterial burden in the oral cavity and alters patterns of microbiota composition in the process of aging. HIV-associated gingivitis and periodontitis were significantly more frequent in patients over 50 years old. However, periodontal status of younger HIV+ and HIV- patients appeared rather similar. Highly significant increase in bacteria of the “red complex”- P. gingivalis and T. forsythia in HIV+ compared to HIV- patients we related.

Interestingly, it was reported a higher prevalence of periodontal pathogens was found in non-HIV infected individuals. In contrast, the presence of oral pathogens such as Prevotella nigrescens, Tannerella forsythia, and Eikenellacorrodens was related in the case of Detectable viral load. Elevated viremia in untreated patients were associated with significantly higher proportions of potentially pathogenic as Veillonella, Prevotella, Megathra and Campylobacter species than in healthy controls.

Microorganisms not usually associated with periodontitis were also been detected in subgingival sites of HIV-positive
patients, including Candida albicans, Staphylococcus epidermidis, Clostridium diffili, Enterococcus faecalis, Mycoplasma salivarium, Klebsiellapneumonialae, Pseudomonas aeruginosalEntameobaginivalis, and Acinetobacterbaumannii. HIV-positive patients often have a larger number of atypical microorganisms that are strongly present or non-existent in HIV negative patients.\textsuperscript{24-27} The increase of prevalence of these potential pathogens results in a decrease in presence of commensal Streptococcus and Veillonellasp. A comparison from HIV positive and negative patients with periodontal disease, the periodontal pathogens, including Campylobacter rectus, Capnocytophagaochaecraeae, Porphyromonasgingivalivalis, and Prevotellaintermediawere highly prevalent in plaques removed from both groups. The only difference between the groups was a slight but significantly higher proportion of Porphyromonasgingivalivisin the HIV positive subjects, which was attributed to a subgroup of HIV-positive subjects with widespread attachment loss.\textsuperscript{21} Research has shown greater diversity in the bacterial communities of the subgingival biofilm of HIV patients compared to non-HIV infected individuals. The presence of a larger number of species that make up individual subgingival communities in the HIV-infected group suggests a complex microbiota.\textsuperscript{24} A number of microbiological studies test the composition of subgingivalflora of periodontal lesions in HIV-positive patients show that it is different from the microbiome composition of the plaque of HIV-negative patients with gingivitis and periodontitis.\textsuperscript{25} In contrast, some others pathogens were associated with periodontitis were founded more commonly in the setting of HIV infection, including Staphylococcus aureus.\textsuperscript{28} Enterococcus faecalis has been described most prevalent in the subgingivalmicrobiota of HIV-infected patients with reduced CD4 + T lymphocytes (<200 cells / mm3), suggesting that HIV-related immunodeficiency may help to provide adequate conditions for the growth and colonization of opportunistic pathogens in the oral microbiota.\textsuperscript{24} Another research demonstrated that sites colonized with Fusobacteriumnucleatum, Prevotellaintermedia, and Actinobacillusactinomycetemcomitanswere most likely to be found in sites with progressive periodontal disease in HIV subjects beyond to finding the typical periodontal pathogens in HIV-infected subjects, a number of studies have demonstrated the presence of opportunistic bacteria and Candida species.\textsuperscript{29} Before the HAART the data showed an elevated prevalence of periodontal diseases, especially acute forms such as necrotizing ulcerative periodontitis and gingivitis and periodontitis followed by high levels of atypical periodontal microbiota. Microbiological investigations of subgerival biofilm composition in HIV-infected patients undergoing HAART demonstrated clear differences compared to a HIV seronegative individuals. Under HAART bacterial and fungal infections significantly decreased.\textsuperscript{30} About individuals treated with HAART, they demonstrate lower colonization on oral cavity by Neisseria flavescens compared to healthy controls. The increased prevalence of potential pathogens results in a reductioned presence of commensal Streptococcus and Veillonellasp. The studies reported a microbial diversity in the oral cavity on HIV-infected individuals was lower than healthy controls, and this diversity was further reduced following HAART treatment. Analysing the bacterial community composition of oral wash the specimens was unchanged in HIV-infected compared to healthy controls. In contrast, a difference of fungal communities was observed using a deeper approach analysis. Significant difference in the prevalence and distribution of the saliva bacterial communities on HIV-infected individuals before and after initiation of HAART were reported principallyActinomyces, Atopobium, and Aggregatibacter genera were significantly different from the baseline after HAART. These evidences suggest an alteration in the oral microbiome and the association with HIV infection and/or HIV-treatment.\textsuperscript{8} Recently study statistically correlated the presence of subgingival bacteria and antiretroviral therapies. These preliminary results indicate that antiretroviral therapies may influence subgingival bacteria.\textsuperscript{30} The increased bacterial diversity and different community patterns in the periodontal microbiota of HIV-infected patients compared with non-HIV infected individuals may be related to the HIV infection status, as well as the prolonged use of HAART and several other drugs that affect oral immunity.\textsuperscript{24} In addition, these changes in the oral microbiome can impact other opportunistic pathogens in the oral cavity. Candida species (majorly C. albicans) are commonly found in the normal oral flora, but they can become opportunistic pathogens, especially immunocompromised conditions.\textsuperscript{21} However, the description of the oral microbiota associated with HIV is controversial.\textsuperscript{31} One of the main limitations of these studies seems to be the limited number of subjects. Therefore, additional studies on larger cohorts are required to better understand the potential role of HIV infection and HIV treatment of oral of microbiome.

Conclusion

The studies revealed periodontal status may predict the progression of HIV to Aids and periodontal treatment may be not complete effective in HIV- associated with oral manifestations. Further studies are needed to understand the complete dynamics of microbiomes and to establish new management of periodontal aspects. The authors declare no conflict of interest.

Referências


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