

## Periodontal Management of HIV-infected Patients : An Overview

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### ABSTRACT

Recognition and diagnosis of the general oral manifestations and specific periodontal manifestations of HIV infection will continue to be a major responsibility of the dental practitioner. By combining local and systemic therapy aimed at both preventing and treating oral lesions and periodontal diseases, combined with new systemic antiviral and vaccine therapies, dental and medical practitioners may together help reduce both the dental morbidity and the overall patient morbidity in the HIV infected patient. With the advent of newer pharmacological approaches to the treatment of human immunodeficiency virus (HIV) infection, the incidence and progression of both atypical and conventional periodontal diseases are changing. While the accepted approaches to treating the spectrum of periodontal diseases in HIV patients remain essentially unchanged over the past 15 years, the impact of newer systemic therapies on patient immunocompetence may influence treatment decisions.

**Key words:** HIV, periodontitis, immunocompetence,  
systemic antiviral and vaccine therapies ,highly active antiretroviral therapy.

### INTRODUCTION

HIV infection remains a global health problem of unprecedented dimensions. Unknown 27 years ago, HIV has already caused an estimated 25 million deaths worldwide and has generated profound demographic changes in the most heavily affected countries. While the percentage of people living with HIV has stabilized since 2000, the overall number of people living with HIV has steadily increased, as new infections occur each year, HIV treatments extend life and in addition, new infections still outnumber AIDS deaths. Eradication of HIV infection cannot be achieved with available antiretroviral regimens. This is mainly attributed to

the fact that the pool of latently infected CD4 + T-cells is established during the earliest stages of acute HIV infection and persists with a long half-life, even with prolonged suppression of plasma viraemia<sup>1</sup>

Human immunodeficiency virus (HIV) is a lent virus (a member of the retrovirus family) that causes acquired immunodeficiency syndrome (AIDS), a condition in humans in which the immune system begins to fail, leading to life-threatening opportunistic infections.

Discovered first by *Luc Montagnie & Françoise Barre-Sinoussi*.<sup>2</sup>

There are two strains of HIV

HIV-1: M (major) – clades A-K, O (outlier), N (neither M/N) HIV-2.

#### **Oral lesions associated with hiv infection**

The first report linking periodontal disease and HIV infection was published in 1985<sup>3</sup>

EC-Clearinghouse on Oral Problems Related to HIV Infection and WHO Collaborating Centre on Oral Manifestations of the Immunodeficiency Virus. Classification and diagnostic criteria for oral lesions in HIV infection. 1993 revised

#### **Group I—Lesions strongly associated with HIV infection**

Candidiasis, Erythematous, Pseudomembranous, Hairy leukoplakia, Kaposi's sarcoma, Non-Hodgkin's lymphoma, Periodontal disease, Linear gingival leavage, Necrotizing (ulcerative) gingivitis, Necrotizing (ulcerative) periodontitis

#### **Group II – Lesions less commonly associated with HIV infection:**

Mycobacterium avium– in trancellulare Mycobacterium tuberculosis, Melanotic hyperpigmentation, Necrotizing (ulcerative) stomatitis, Salivary gland disease, Thrombocytopenic purpura, Ulceration not otherwise specified, Viral infections, Dry mouth due to decreased salivary flow rate, Unilateral or bilateral swelling of major salivary glands, Herpes simplex virus, Human papillomavirus, Condyloma acuminatum, Focal epithelial hyperplasia, Verruca vulgaris, Varicella-zoster virus, Herpes zoster, Varicella

#### **Group III - Lesions seen in HIV infection**

Bacterial infections Actinomyces israelii *Escherichia coli* Klebsiella leavage Cat-scratch disease Drug reactions (ulcerative, erythema multiforme, lichenoid, toxic epidermolysis) Epithelioid (bacillary) angiomatosis

#### **Fungal infection other than candidiasis**

Cryptococcus neoformans Geotrichum candidum *Histoplasma capsulatum* Mucoraceae (mucormycosis / zygomycosis) *Aspergillus flavus*

#### **Nervous system disturbances**

Facial palsy, Trigeminal neuralgia, Recurrent aphthous stomatitis

#### **Viral infections**

Cytomegalovirus, Molluscum contagiosum, Linear gingival erythema

Two types of gingival/periodontal disease associated with HIV infection have been widely reported in the literature. In the past, these have been called HIV-associated gingivitis (HIV-G) and HIV-associated periodontitis (HIV-P). There is now evidence that these diseases also occur in HIV-negative immunocompromised individuals and are not specific to HIV infection, thus making the original terms inappropriate. Therefore, HIV-associated gingivitis has been renamed linear gingival erythema (LGE) and HIV-associated periodontitis has been renamed necrotizing ulcerative periodontitis (NUP). The prevalence of these two diseases remains unclear, with estimates of occurrence among HIV-infected individuals ranging from 5% to 50%.<sup>4-6</sup>

It is not yet clear where in the spectrum of HIV disease these conditions occur or which patients are at greatest risk for developing them. There is some evidence that NUP is associated with a low CD4 count (<200 cells/mm<sup>3</sup>)<sup>7</sup>

#### **Periodontal considerations**

Periodontal diseases form an important part of the constellation of oral manifestations of HIV infection<sup>8</sup> as lesions strongly associated with the infection. As a microbial disease affecting the hard and the soft tissues of the oral cavity, periodontal diseases acquire a unique status in the diversity of their manifestations, having implications not only for oral health but also on systemic health.

Parra B *et al.*, 1996, stated that Human viruses have been identified in GCF from periodontal pockets.<sup>9</sup> Some investigations done by Barr *et al.* 1996 have assessed HIV viral burden in oral fluids by means of HIV RNA quantification.<sup>10</sup>

Shugars *et al.*,<sup>11</sup> who quantified HIV-1 RNA in saliva and plasma of 40 HIV seropositive adults.

Many (42%) of their subjects had detectable salivary HIV-1 RNA, which highly correlated with plasma viral levels, and HIV-associated periodontal disease.

Patel *et al.*, 2003 concluded from his research works that, many species of the periodontal microflora found in sites with diseases associated with HIV are also found in non-HIV infected individuals with classic periodontitis in particular, *Porphyromonas gingivalis*, *Prevotellai ntermedia*, *Fusobacterium nucleatum*, *A.Actinomyces comitans*, *Eikenella corrodens*, and *Campylobacter rectus*. A combination of certain periodontal pathogens may be responsible for chronic periodontitis seen in HIV-infected patients .three combinations of periodontal pathogens (*P. nigrescens* and *C. rectus*; *P. nigrescens* and *P. gingivalis*; and *P. nigrescens* and *T. denticola*) were significantly associated with HIV-positive compared with HIV-negative patients.<sup>12</sup>

In GCF of HIV-positive patients, the levels of IL-1, IL-6, and TNF were higher than thenon-HIV infected individuals. The levels were higher in deeper pockets than in shallow pockets.<sup>13</sup>This may explain the increased rate of attachment loss and tissue destruction seen in HIV-positive patients in the GCF of HIV-negative patients.

### Management

The most important components in the management of HIV-associated gingival and periodontal disease should be the removal of local irritants from the root surfaces, debridement of necrotic tissues, and appropriate use of antibiotics.

Systemic antibiotics, such as metronidazole, tetracycline, clindamycin, amoxicillin, and amoxicillin-clavulanate potassium, should be combined with debridement of necrotic tissues. As systemic antibiotics increase the patient's risk of developing candidiasis, concurrent, empiric administration of an antifungal agent should be considered.

Frequent appointments are appropriate and recommended in the acute and healing stages of NUP to perform the necessary periodontal therapies, to assess tissue response, and to monitor

the patient's oral hygiene performance.

### Linear gingival erythema

There is, on the other hand, little information based on controlled studies of linear gingival erythema.

Conventional therapy plus rinsing with 0.12% chlorhexidine gluconate twice daily has shown significant improvement after 3 months<sup>14</sup> However, HIV-associated free gingival erythema did not respond to removal of plaque by intense scaling and root leavage and improved plaque control measures alone or supplemented with povidone-iodine irrigation 3-5 times daily.

No significant improvement in clinical features or indices was obtained after 1 or 3 months of treatment. However, povidine-iodine substantially reduced pain associated with the lesions.<sup>15</sup>

### Necrotizing Gingivitis

Necrotizing gingivitis in HIV-infected patients does not always respond to conventional treatment with scaling and improved oral hygiene.<sup>15</sup> However, the adjunctive use of metronidazole in these patients is reported to be extremely effective in reducing acute pain and promoting rapid healing.<sup>16</sup>

Due to the susceptibility of HIV-infected patients to leavag infections simultaneous treatment with appropriate antimycotic agents may be necessary. Sometimes healing is delayed in HIV-infected patients and pain may be prolonged.

Necrotizing periodontitis in HIV-infected patients does not always respond to conventional treatment with scaling and improved oral hygiene.<sup>15</sup> However, the adjunctive use of metronidazole in these patients is reported to be extremely effective in reducing acute pain and promoting rapid healing.<sup>16</sup> Due to the susceptibility of HIV-infected patients to leavag infections simultaneous treatment with appropriate antimycotic agents may be necessary. Sometimes healing is delayed in HIV-infected patients and pain may be prolonged.

### Necrotizing Periodontitis

In Initial visit, Prescribe narrow spectrum

antibiotics such as metronidazole 500 mg, dispense 14 to 20 tablets, take 1 tablet twice daily for 7 to 10 days. Other antibiotic options include clindamycin and amoxicillin. Pain management is extremely important, Nutritional supplementation or counseling may be necessary. Detailed periodontal

care, such as scaling and root planning as a follow-up visits.<sup>17</sup>

### **Necrotizing stomatitis**

The treatment aspects for necrotizing stomatitis are similar to those mentioned for necrotizing periodontitis.

## **Fungal Infections Systemic Antifungal Medications<sup>18</sup>:**

<b>Anti Fungal medications</b>	<b>Dosage</b>
Ketoconazole (an imidazole), fluconazole (a triazole), itraconazole (a triazole)	Common dosage: ketoconazole 200 mg once daily; fluconazole 100 mg once daily; and itraconazole 200 mg once daily.
Amphotericin B (a polyene antifungal agent)	Used as an intravenous medication that may be used for candidiasis resistant to other medications. (Note: Amphotericin B is also available as a topical preparation.)

<b>Anti Fungal medications</b>	<b>Dispense</b>	<b>Dosage</b>
Clotrimazole troches (an imidazole)	2- to 4-week supply	Slowly dissolve one 10-mg troche in mouth 5 times/day for treatment. Slowly dissolve 1 troche in mouth 3 times/day for maintenance therapy.
Nystatin oral suspension (a polyene antifungal agent)*	2- to 4-week supply	Hold 1 teaspoonful (500,000 u) in mouth for 5 minutes, 4 times/day.
Amphotericin B oral suspension (a polyene antifungal agent)†	2- to 4-week supply	Place 1 mL (100 mg) on tongue and swish in mouth for as long as possible before swallowing.

### **Anti-retroviral drugs**

#### **Act at different stages of life cycle of HIV**

1. One that blocks binding of HIV to target cells
2. One that blocks viral RNA leakage.
3. One that inhibits enzyme reverse transcriptase.

#### **Classification**

##### **Inhibitors of viral attachment**

Recombinant soluble CD4 or immunoglobulins

##### **Nucleoside analogue RT inhibitors**

Zidovudine, Didanosine, Zalcitabine, Adenosine, Stavudine, Lamivudine

##### **Non-nucleoside analogue RT inhibitors**

Nevirapine, Delaviridine, Thiobenzimidazole derivatives.

##### **Protease Inhibitors**

Saquinavir, Ritonavir, Indinavir, Nelfinavir

##### **Integrase Inhibitors**

##### **Agents that block virus assembly and budding:**

Interferons

##### **Antiretroviral Therapy Regimens**

Antiretroviral therapy (ART) is the combination of several antiretroviral medicines used to slow the rate at which HIV makes copies of

itself (multiplies) in the body. A combination of three or more antiretroviral medicines is more effective than using just one medicine (Monotherapy) to treat HIV. Currently, the national programme provides the following combinations for first-line regimens.

The development of highly active antiretroviral therapy (HAART) especially after 1995, has significantly modified the course of HIV disease, at least in the industrialized world, into a manageable chronic disease. With longer survival and improved quality of life in HIV-infected. HAART generally consists of a dual nucleoside analogue reverse transcriptase inhibitor (NRTI) backbone and a third drug, such as a non-nucleoside reverse transcriptase inhibitor (NNRTI) or a protease inhibitor (PI), usually a "boosted" one. The use of a NNRTI as a third drug is less potent and therefore, in most settings not a preferred option and it is recommended that baseline resistance testing should guide the specific regimen design. HAART increases CD4 + cell count, decreases levels of HIV RNA and extends AIDS-free survival, at least in the short-term. Moreover, HIV suppression with antiretroviral therapy may decrease inflammation and immune activation

thought to contribute to higher rates of cardiovascular and other co-morbidities reported in HIV-infected cohorts. Cannot be achieved with available antiretroviral regimens. This is mainly attributed to the fact that the pool of latently infected CD4 + T-cells is established during the earliest stages of acute HIV infection and persists with a long half-life, even with prolonged suppression of plasma viraemia.<sup>19,20</sup>(i) Stavudine (30 mg) + Lamivudine (150 mg) (ii) Zidovudine (300 mg) + Lamivudine (150 mg) (iii) Stavudine (30 mg) + Lamivudine (150 mg) + Nevirapine (200 mg) (iv) Zidovudine (300 mg) + Lamivudine (150 mg) + Nevirapine (200 mg) (v) Efavirenz (600 mg) (vi) Nevirapine (200 mg)

### CONCLUSION

By combining local and systemic therapy aimed at both preventing and treating oral lesions and periodontal diseases, combined with new systemic antiviral and vaccine therapies, dental and medical practitioners may together help reduce both the dental morbidity and the overall patient morbidity in the HIV infected patient.

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