Clinical Treatment Outcomes of Periodontal Therapy in HIV-seropositive Patients Undergoing Highly Active Antiretroviral Therapy

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Abstract

Introduction: Since the worldwide HIV/AIDS epidemic started, various oral manifestations have been described. However, scientific assessment of therapeutic outcomes of chronic periodontitis in HIV-seropositive patients, in particular undergoing highly active antiretroviral therapy (HAART), has not been addressed.

Materials and Methods: 22 patients divided into a HIV-1-seropositve test group and seronegative control group were studied for 12+ months after receiving periodontal therapy by conservative scaling and root planning and maintenance care.

Results and Conclusions: Periodontal inflammatory parameters improved significantly under the immune reconstituting influence of HAART without major statistical differences in both examination groups. According to this standardized interventional concept, HIV-1-seropositive patients with chronic periodontal disease can be treated successfully. The treatment outcome in maintaining the periodontal attachment is equally well represented in both clinically controlled groups.

Key words: HIV infection, periodontal disease, HAART, CCT

Introduction

Since the spreading of HIV infection and the AIDS epidemic worldwide in the early 1980's the annual incidence has grown exponentially [1]. Left untreated the viral infection often results in mortality of 90% within three years after an AIDS diagnosis by breakdown of the immune system. Since therapeutical intervention has become available, symptom-free intervals can be significantly prolonged, particularly in the so-called industrialized countries [2]. Due to the unique targeting of the HI virus and under an increased viral load, cellular immunity is weakened in cells with CD4 surface markers, such as CD4 T-helper cells and monocytes as well as macrophages [3]. Even in early infection this can become manifest in oral diseases [4], but under the influence of highly active antiretroviral therapy, especially acute periodontal diseases are successfully treated [5]. As survival rates in these patients continue to increase, however, chronic periodontal diseases gain clinical importance; a phenomenon also true for the general population. HIV infection with its specific immune alterations is generally recognized as a risk factor for chronic periodontitis [6], although epidemiological studies have failed to confirm a causal link [7, 8]. Nevertheless, the *American Academy of Periodontology* regards HIV infection as a risk factor for periodontitis. Basic research considerations stress four possible synergistic mechanisms for this inter-action: (1) limited chemotaxis of neutrophilic granulocytes in the initial phase of periodontal bacterial infection [9, 10]; (2) dysfunction of macrophages with CD4 surface markers in the succeeding phase of phagocyte activity [11], (3) disorganization of gingival B- and T-lymphocyte activity and their protective humoral products [12] and (4) direct toxicity of certain antiretrovirals on hematopoesis [13].

Clinically controlled data on therapeutic outcomes of chronic periodontitis in HIV-seropositive patients are sparse [14]. In particular, scientific studies addressing the immune-reconstitutive effects of various antiretroviral agents on treatment results of chronic periodontal diseases have not been documented.

Therefore, the purpose of this prospective controlled study was (i) to evaluate the outcome of non-surgical periodontal treatment influenced by established highly active anti-retroviral medication in HIV-seropositive patients, and (ii) to compare the treatment outcome with a matching control group of HIV-seronegative patients exhibiting chronic periodontitis.

Material and Methods

From December 2000 to September 2004 eleven test patients and the same number of control patients with mean age of 37.8 yrs received periodontal therapy for an average observation period of 15 months. Inclusion criteria were: ≤45 yrs of age, 20 remaining teeth and at least four teeth with probing pocket depths ≥4 mm. Additionally, subjects in the test group were HIV-1-seropositive receiving highly active antiretroviral therapy. Exclusion criteria were: further systemic diseases, other medication within three months of the start of the study and limited compliance. After initial oral hygiene procedures (baseline) and at the end of the study the following dental parameters were recorded: *gingi-*

val bleeding on probing (BOP), *probing periodontal pocket depth* (PPD) and number of teeth. Additionally, in the test group the *dental plaque index* was assessed, and composition of antiretroviral therapy, hemato-immunological values of CD4 counts, CD4/CD8 ratio and viral load was determined. The strategy of periodontal therapy adhered to standardized methods for conservative treatment with repeated appointments for professional tooth cleaning, oral hygiene instructions and motivation as well as instrumental removal of supra-gingival plaque deposits. Scaling and root planning of pockets greater than 3.5 mm in depth was executed under local anaesthesia by using the *Gracey* curette set at weekly intervals, one quadrant per session. Six weeks postoperatively the supportive phase of periodontal therapy followed with a four-month recall interval. The low level for the *plaque index* of 0.25 in the test group after completing the study exemplifies good patient motivation for prophylactic home care and plaque control. Statistical analysis of all included parameters was performed using the *Wilcoxon Rang-Sum* test to compare the two arms of the study. The *t* test was used for statistical analysis of interindividual group evaluation. Statistical significance was set with $p < 0.05$.

RESULTS

Comparison of hemato-immunological risk markers for HIV infection over the whole study period showed a high degree of stability. CD4 counts, the CD4/CD8 lymphocytes ratio and viral load as the number of HIV-RNA copies/ml plasma are illustrated in Figures 1-3.

Regarding the periodontal inflammation index BOP improvement was seen in both groups from > 50% bleeding sites at baseline to approximately 20% bleeding sites postoperatively (Figs. 4 and 5).

In the test group an average of 8.1 (range: 4 – 19 teeth, SD 4.0) teeth and in the control group 8.3 (range: 4 – 18 teeth, SD 4.0) teeth exhibited chronic periodontitis. According to the current classification of periodontal diseases this quantity conformed criteria for a generalized affection of periodontitis. The mean probing pocket depth of periodontitis teeth in the test group decreased from 4.2 mm (range: 3.8 – 4.8
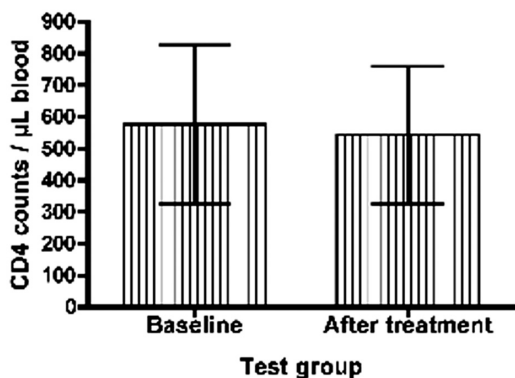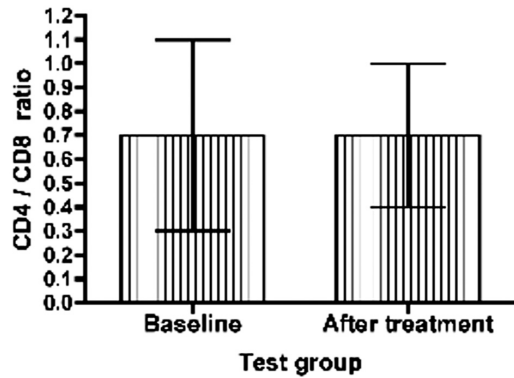

Fig. 2. Mean CD4/CD8 ratio in the test group at baseline and 15 month postoperatively.
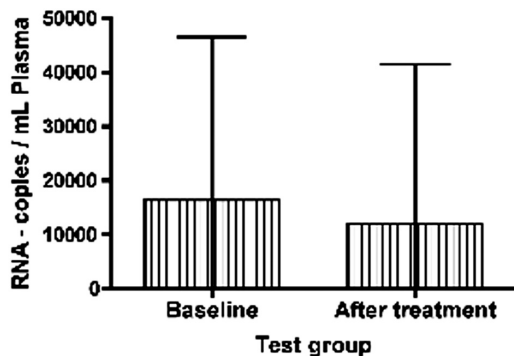

Fig. 3. Mean viral load in the test group at baseline and 15 month postoperatively.
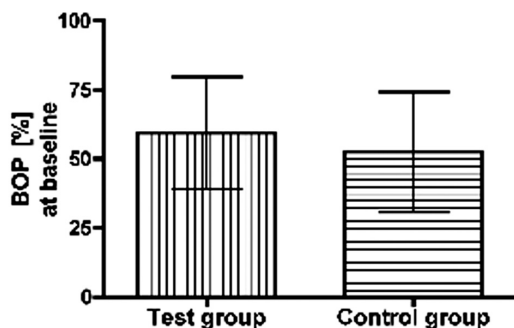

Fig. 4. Mean Bleeding on Probing index values (% of sites) in the test group and control group at baseline.
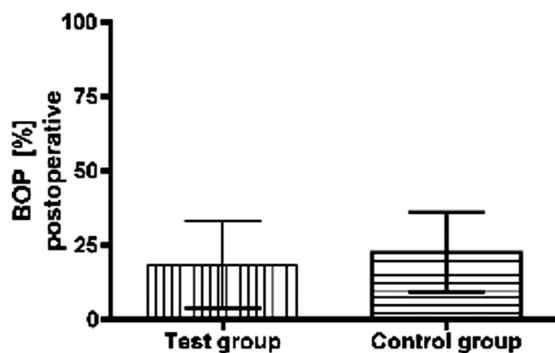

Fig. 1. Mean CD4 counts in the test group at baseline and 15 month postoperatively.

Fig. 5. Mean Bleeding on Probing index values (% of sites) in the test group and control group 15 month postoperatively.
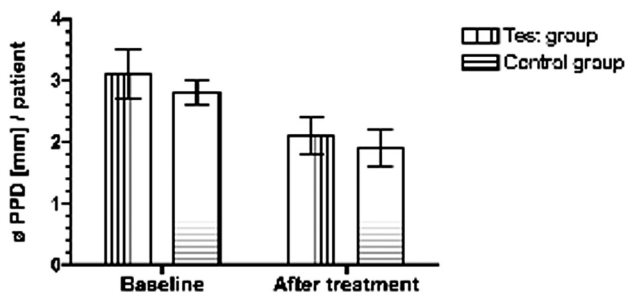
Fig. 6. Mean pocket reduction of individual average probing depth of periodontitis teeth in the test group and control group.

mm, SD 0.3 mm) at baseline to 2.6 mm (range: 2.0 – 3.4 mm, SD 0.4 mm) at the end of the study. The same reduction of periodontal pocket depth was documented for the control group from 4.3 mm (range: 4.0 – 4.8 mm, SD 0.3) at baseline to 2.6 mm (range: 2.0 – 3.4 mm, SD 0.4 mm) postoperatively. Pocket depth reduction within the groups was statistically highly significant (p = 0.0005); the statistical comparison of the two groups showed no significant differences (p > 0.3) (Fig. 6).

DISCUSSION

Periodontal therapy aims to achieve a biologically adapted condition of periodontal repair, usually executed by a phylogenetically older replacement tissue [15]. Clinical parameters include indices of inflammation like BOP and metric values such as periodontal attachment level and probing depth of periodontal pockets. In an epidemiological study of in 796 non-selected and untreated HIV-seropositive subjects a BOP of 97% of gingival sites was reported [6]. In contrast to these results, the present study documented only an initial BOP of > 50% sites in both groups indicating that initial oral hygiene procedures before the start of the study were successful. In a long-term controlled study of supportive periodontal therapy Hofer demonstrated no gain of periodontal attachment in a HIV-seropositive cohort, while in HIV-seronegative control subjects improvement occurred [14]. Many studies have analyzed the reduction of pocket depth and gain of attachment after periodontal therapy. Notable differences are reported depending on the methods used, the person performing the procedure and the severity of the disease depending on bacterial virulence and local immunological response of the host.

In the present study mean pocket depth of periodontitis teeth was significantly reduced in both groups (1.6 and 1.7 mm). The mean periodontal pocket depth of these teeth after treatment was on average 2.6 mm in all subjects. A meta-analysis by Renvert and Persson regarding postoperative depths of periodontal pockets as a predictor for further loss of attachment revealed a critical depth of ≥6 mm [16]. The maximum pocket depth after treatment in our study was 5.0 mm. This does not need to be considered as refractory. Comparative studies of chronic periodontitis by Badersten et al. described changes in probing pocket

depth as related to different stages of therapy [17]: following professional dental cleaning a reduced depth of 0.3 to 0.7 mm was noticed, after pocket curettage depth reduction of 0.8 to 1.4 mm was achieved and as a result of wound healing an over-all reduction of 1.3 to 1.7 mm was obtained. The main changes were documented within the first six months of follow-up.

Although meticulous supragingival plaque control might be helpful in limiting subgingival biofilm development and inhibiting nascent infections, a bacterial subgingival recolonisation does not necessarily pose a problem for further disease progression *a priori*. However, current theories of biology are suggesting that periodontal diseases tend to correspond like most other chronic inflammatory diseases to the theory of punctuated equilibrium [18] with long periods of stagnation and short changes of progression. This biologically unique disease progression was recently explained as an *avalanche model* [19]: many risk factors are contributing for a rather long time to the snow accumulation before the "spontaneous" avalanche is developing. Therefore periodontal disease is depending from many factors of bacterial pathogenicity and the host response.

Axelsson and Lindhe [20] demonstrated that a continuous annual attachment loss of 0.1 mm could be reduced by regular professional prophylaxis [21]. The dynamic concept of the most common oral manifestations, dental caries and periodontal disease [22], implicates postoperative phases of stagnation and the lower risk of further progression [23]. Even in patients with periodontitis and associated systemic diseases like primary immune defects or diabetes therapy led to stable periodontal conditions [24].

Individual reports on conservative, i.e. non-surgically periodontal measures in AIDS patients as well as encouraging notices on periodontal supportive therapy in patients undergoing highly active antiretroviral therapy underscore our observation that the likelihood of recurrence of periodontal breakdown in motivated patients under immune reconstitution or stabilizing therapy is low. During the course of this study we were impressed by the over-all immune-stabilizing effects of anti-retroviral regimes with its different routing substance classes NNRTI and PI: only minimal shifts occurred in CD4 counts, CD4/CD8 ratio and viral load. Anti-retroviral combination therapy again demonstrated their long-term effectiveness in treating HIV infection while requiring few adjustments during our study. Risk-associated adjustment in treatment concepts of periodontal diseases is of major importance for therapeutical efficiency as the host response can be influenced by altered cellular immunity [25].

CONCLUSIONS

During the *13th International AIDS Conference* in Durban in 2000 a Workshop on the Oral Manifestations in HIV Infection left several open questions on chronic periodontal diseases which are, in part, addressed in the present study with useful results for clinical practice [26]: *Which therapeutic concepts in periodontal disease in HIV-seropositive patients are most effective?*

Chronic periodontal disease in HIV-seropositive patients undergoing highly active antiretroviral therapy can be successfully treated by scaling and root planning of affected teeth. Our study demonstrates that a clinical medium-term therapeutic success is likely if a strict recall programme is followed. At no point during the course of this study there was a need for therapeutic medication of antibiotics for patients on continuous immune reconstituting antiretroviral therapy.

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