Influence of Highly Active Anti-Retroviral Therapy (HAART) on the Subgingival Biofilm in HIV-infected Patients

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Introduction

Microbiological studies in HIV-infected patients have been conducted since the beginning of the epidemic, but less is known about anti-retroviral drug influences on periodontal pathogens. Findings indicate an influence of HAART in the development of HIV-related oral lesions. Microbiological investigations of the subgingival biofilm composition in HIV-infected patients undergoing HAART demonstrated clearly differences as compared to a HIV-seronegative control group.

Aim

It was the aim of this investigation to analyze differences in the subgingival profile of HIV-infected patients with chronic periodontitis on supportive periodontal therapy (SPT) undergoing different HAART regimens to generate a working hypothesis for a prospective clinical study.

Patients and Methods

Study design	Prospective clinical series
Place of study	Outpatient HIV oral health care centre, Berlin (Germany)
Intra-examiner reliability	Ƙ = 0.91
Inclusion criteria	HIV-1 infection, chronic periodontitis in ≥ 4 teeth with PPD ≥4mm, HAART ≥6 mths, <45 yrs of age
Exclusion criteria	Other systemic disorders associated with periodontitis, antibiotics 3 mths prior to study
Periodontal treatment	Scaling and root planing (S/RP) followed by supportive periodontal treatment at 3 mths interval
Pathogen recordings	Before (t_0) and mean 10.6 mths after (t_1) S/RP with ParoCheck® 10 DNA chip microarray (Greiner Bio-One GmbH, Frickenhausen, Germany) according to Haffajee and Socransky technique (1992)
Periodontal pathogens	***Red complex*** *Tannerella forsythia (T. f.), Porphyromonas gingivalis (P. g.), Treponema denticola (T. d.)* ***Orange complex*** *Campylobacter rectus (C. r.), Fusobacterium nucleatum (F. n.), Peptostreptococcus micros (P. m.), Prevotella intermedia (P. i.)* ***Green complex****: Eikenella corrodens (E. c.)* ***NOS:*** *Aggregatibacter actinomycetemcomitans (A. a.), Actinomyces viscosus (A. v.)*
Participant study flow	see Fig. 1
Statistical analysis	OR for HAART using contingency tables and Fisher's exact test, inter group comparison with Mann Whitney test, paired observations with Wilcoxon signed rank test
Ethics	IRB Witten/Herdecke University No. 16/2009

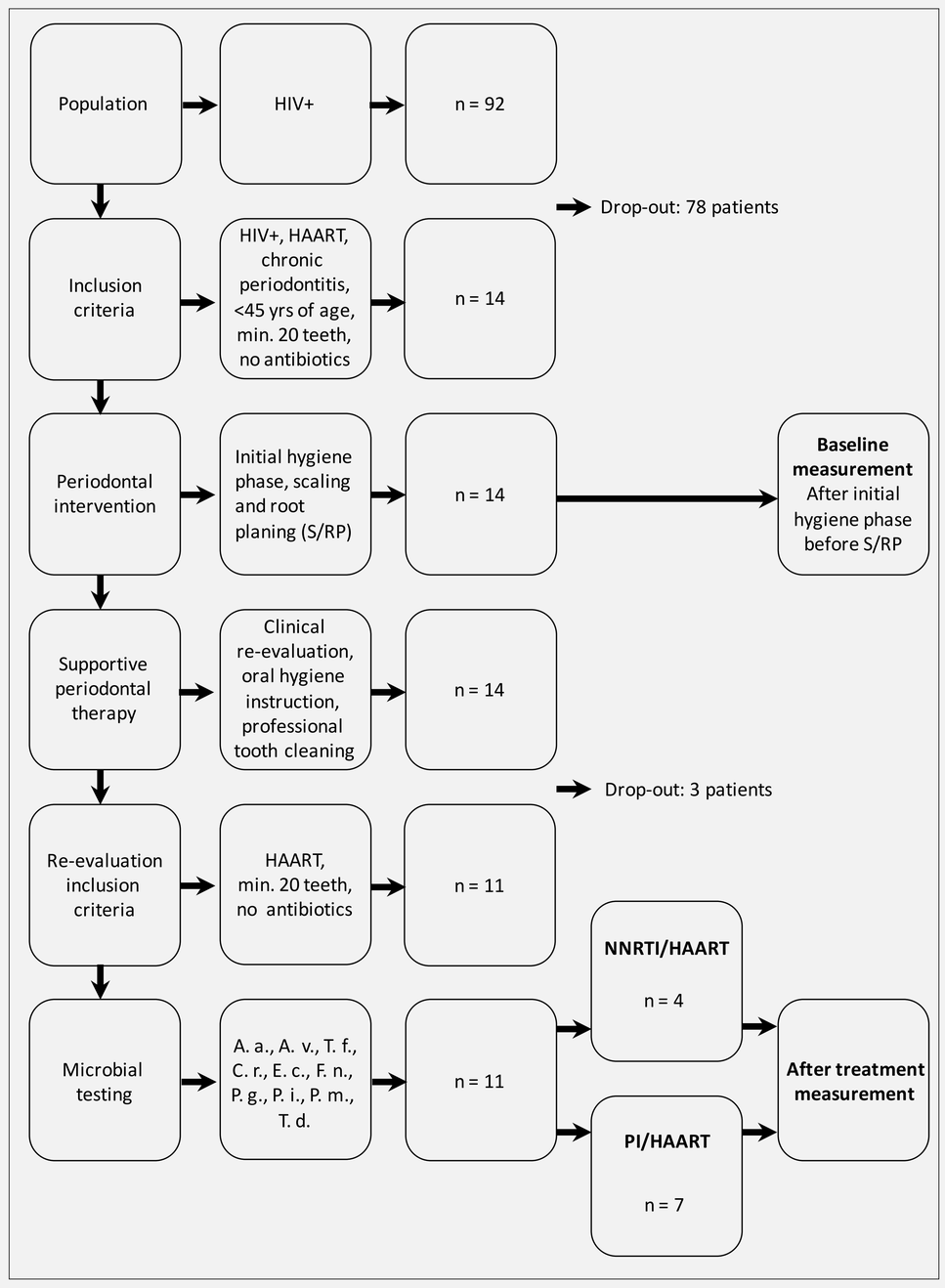

Figure 1: Study design and flow of patients

Results

Table 1: Clinical characteristics of the subjects with Non-nucleoside reverse transcriptase inhibitor highly actice anti-retroviral therapy (NNRTI/HAART) and protease inhibitor highly actice anti-retroviral therapy (PI/HAART) at baseline (t_0) and after treatment (t_1)

Time	Group of patients	Age (95%-CI)	Gender	No. of samples	Smoking habits	Median Months of SPT (95%-CI)	Median No. of teeth (95%-CI)	Median No. of pockets 4-6mm (95%-CI)	Median No. of pockets >6mm (95%-CI)	Median CD4 counts (95%-CI)	Median Viral load (95%-CI)
Baseline	NNRTI/ HAART	40.0 (33.8; 42.8)	Male	28	57%	11.0 (2.8; 23.0)	27.0 (23.3; 28.4)	8.0 (5.1; 12.3)	0.0 (0.0; 1.2)	360 (0; 943)	28060 (0; 89246)
After treatment							27.0 (23.3; 28.4)	2.0 0.0; 4.6)	–	396 (166; 666)	0 (0; 141158)
Intra group comparison (p value)							1.0	0.01*	1.0	1.1	0.9
Baseline	PI/ HAART	35.0 (30.8; 40.7)	Male	16	50%	10.0 (2.3; 17.8)	27.5 (24.8; 29.3)	7.5 (3.6; 10.4)	–	518 (38; 1178)	0 (0; 152009)
After treatment							27.5 (23.7; 29.8)	2.0 (0.0; 4.6)	0.0 (0.0; 1.0)	615 (137; 950)	0 (0; 0)
Intra group comparison (p value)							1.0	0.1	1.0	0.8	0.8
Inter group comparison (p value) Baseline/ After treatment		0.4	1.0		0.9	0.9	0.6/ 0.6	0.6/ 0.9	1.0/ 1.0	0.4/ 0.2	0.6/ 1.0

All data presented as median except for gender and smoking habits; CD4 counts in cells per µl blood; Viral load in RNA copies per ml blood; No. = number; SPT = Supportive periodontal therapy; * intra group comparison statistically significant difference (p <0.05); first p value: NNRTI/HAART vs. PI/HAART at baseline, second p value: NNRTI /HAART vs. PI/HAART after treatment

Table 2: Odds ratios (OR) for periodontal pathogens associated with non-nucleoside reverse transcriptase inhibitor highly actice anti-retroviral therapy (NNRTI/HAART) and protease inhibitor highly actice anti-retroviral therapy (PI/HAART)

Periodontal pathogens and complexes	NNRTI/HAART				PI/HAART				Odds ratio of positive number of subjects with PI as reference HAART and NNRTI as HAART at risk	Odds ratio of positive number of subjects with NNRTI as reference HAART and PI as HAART at risk	p value
	No. of samples	Positive tested subjects	Median SNR	95%-CI	No. of samples	Positive tested subjects	Median SNR	95%-CI			
A. actinomycetemcomitans	24 (n = 7 subjects)	1	0.0	0.0; 19.2	16 (n = 4 subjects)	1	0.0	0.0; 381.1	0.6	1.7	1.0
A. viscosus		–	–	–		3	22.7	0.0; 80.3	0.003	303.3	0.03
T. forsythia		5	133.4	9.7; 281.9		3	235.5	0.0; 505.0	1.7	0.6	1.0
C. rectus		3	8.1	0.0; 29.4		4	35.9	9.2; 56.8	0.01	90.0	0.2
E. corrodens		1	0.0	0.0; 12.1		–	–	–	24.5	0.04	1.0
F. nucleatum		6	184.2	40.4; 371.9		3	163.0	0.0; 528.7	55.7	0.01	0.4
P. gingivalis		3	7.3	0.0; 152.2		2	47.4	0.0; 556.6	1.0	1.0	1.0
P. intermedia		3	8.4	0.0; 193.8		3	38.5	0.0; 358.8	0.3	3.0	0.6
P. micros		5	34.8	11.3; 59.2		2	8.0	0.0; 56.1	5.0	0.2	0.5
T. denticola		5	0.0	0.0; 248.9		4	190.9	105.4; 320.8	0.04	24.5	1.0
Red complex		2	336.5	84.2; 565.4		2	446.4	0.0; 1326	0.5	2.0	1.0
Orange complex		1	296.4	77.6; 556.6		2	248.7	0.0; 947	0.2	5.0	0.5
Green complex		1	0.0	0.0; 12.1		0	0	0; 0	24.5	0.04	1.0

CI = Confidence interval; No. = number; SNR = Signal-to-noise ratio

Conclusion

The results demonstrated statistical associations between subgingival bacteria and anti-retroviral drug therapies. These preliminary results support the generation of a working hypothesis that different anti-retroviral therapies might have an influence on subgingival bacteria. Further investigation on the clinical significance and underlying mechanisms are needed to lighten these findings.

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Literature: Haffajee AD, Socransky SS: Effect of sampling strategy on the false-negative rate for detection of selected subgingival species. Oral Microbiol Immunol. 1992;7:57-9.

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