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DECREASE OF MITOCHONDRIAL DNA CONTENT IN ADIPOSE TISSUE OF HIV-1-INFECTED PATIENTS TREATED WITH NRTIS

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BACKGROUND: It has been shown that the use of NRTIs can result in a clinically relevant depletion of mitochondrial DNA (mtDNA) by inhibiting polymerase- γ . It has been hypothesized that mtDNA depletion may be the pathophysiological link between the use of NRTIs and lipoatrophy.

OBJECTIVES: To evaluate if lipoatrophy is associated with mtDNA-depletion in subcutaneous fat tissue.

DESIGN: Subcutaneous fat biopsies were taken from the buttocks of 24 HIV-positive patients (19 patients treated with NRTIs plus PI, four patients with NNRTI plus PI and one naïve). Eleven patients under antiretroviral therapy had clinical evidence of lipoatrophy at the biopsy-site and 12 patients had not. In addition, eight HIV-negative controls were biopsied. MtDNA-content in each fat biopsy sample was quantified using a Southern blot technique and normalized to the content of nuclear DNA.

RESULTS: The age of the subjects was not different between all groups. MtDNA-content did not differ between HIV-negative controls ($n=8$) and HIV-patients never exposed to NRTIs ($n=4$; $P=0.9$). MtDNA content was significantly decreased in HIV-patients treated with NRTIs ($n=19$) compared to HIV-positive patients never exposed to NRTIs ($n=4$; $P=0.009$). MtDNA-content in patients under antiretroviral therapy with clinical evidence of lipoatrophy ($n=11$) was reduced by 38% compared with patients without lipoatrophy ($n=12$; $P=0.04$).

CONCLUSIONS: Treatment with NRTIs is associated with decreased mtDNA-levels in subcutaneous fat. Patients with lipoatrophy had significantly lower mtDNA content than patients without. This suggests a link between mitochondrial damage due to NRTIs and the presence of lipoatrophy in HIV infected patients.

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