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CHANGES IN BODY FAT DISTRIBUTION IN 154 HIV-INFECTED MALE PATIENTS TREATED WITH COMBINED ANTIRETROVIRAL THERAPY

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BACKGROUND: Inter-LIPOCO study is a French prospective observational cohort study of risk factors for the development of changes in body fat distribution (BFD) in unselected patients receiving antiretroviral (ARV) therapy currently being performed in five AIDS clinical centres.

OBJECTIVES: To assess the pattern of subcutaneous and visceral fat distribution as well as metabolic abnormalities in HIV-infected males treated with combined ARV therapy.

DESIGN: Cross-sectional and longitudinal study.

PATIENTS AND METHODS: 154 male patients treated with two or more ARV drugs, observed between July 1998 and February 1999. Changes in BFD were assessed by means of a physical examination, BIA skinfold thickness at four sites, and CT scan performed at two body levels to measure abdominal and mid-thigh subcutaneous (SQAT) fat areas as well as intra-abdominal (VAT) fat area. Fasting triglyceride (TG), cholesterol, HDL and LDL cholesterol, Apo A1, B, free fatty acid (FFA), cortisol, testosterone, FSH, LH levels, CD4 cells and HIV RNA load were determined. An oral glucose tolerance test was used to assess glucose tolerance and to measure the insulin response to 75 g of oral glucose.

RESULTS: As of 10 February 1999, 154 male patients have been consecutively evaluated (mean age 40.24 ± 0.67 years). 27.4% had an AIDS-defining disease. Mean baseline plasma HIV RNA and CD4 cells were $3.15 \pm 0.11 \log_{10}$ copies/ml and 429 ± 17.62

cells/mm³, respectively. 15 patients were therapy naïve, 39 on long-term NRTI therapy and 100 were receiving at least one PI. Three clinical types were identified: Purely lipotrophic (LA) in 34 (22%) patients, mixed (M) in 39 (25.3%), pseudo-obese in 9 (5.9%). Seventy-two (46.8%) were clinically normal (N). Body fat as determined using both skinfolds and BIA as well as abdominal and mid-thigh SQAT were significantly lower in the purely LA patients as compared with M, O and N patients. VAT was significantly higher in the M and O patients ($P<0.001$) but it did not differ between LA and N patients. Within the M patients ($n=39$) there were significant differences in percentage of body fat, SQAT and TG levels between those taking stavudine-containing regimens and those taking combination including zidovudine. Fasting insulin and the sums of the insulin (T0, T60, T120) levels were significantly higher in the M and O patients ($P<0.01$) and were within the normal range in the LA and N patients. TG levels were significantly higher in the LA patients ($P<0.01$) whereas FFA were significantly higher in the M and O patients ($P<0.01$). VAT measured by CT scan was positively correlated with fasting insulin and the sum of insulin levels ($P<0.0001$). Fasting insulin as well as the sum of insulin levels were negatively correlated with the change in HIV RNA (\log_{10}). The use of stavudine significantly correlated with LA in both NRTI (odds ratio 413; 95% CI 5.2-999; $P=0.0068$) and PI (odds ratio 4.01; 95% CI 1.2-12.7; $P=0.018$) patients whereas the risk was significantly lower in patients taking zidovudine.

CONCLUSIONS: Three different syndromes must be distinguished: (i) a syndrome of fat depletion characterized by a decrease in abdominal and mid-thigh SQAT which could be related to the use of stavudine; (ii) a syndrome of fat redistribution combining loss of SQAT and increase in VAT related to an unusual side-product of effective virus control; and (iii) a syndrome of subcutaneous fat disposition reflecting increase in caloric intake after HAART was begun.

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