

5th International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV



8–11 July 2003, Le Meridien Montparnasse, Paris, France

INCREASED EXPRESSION OF 11 β -HYDROXYSTEROID DEHYDROGENASE TYPE 1 IN SUBCUTANEOUS ADIPOSE TISSUE IN HIV-ASSOCIATED LIPODYSTROPHY

Antiviral Therapy 2003; 8:L8 (abstract 5)

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BACKGROUND/AIMS: Highly active antiretroviral therapy (HAART) has dramatically improved the prognosis of HIV-infection, but is also associated with severe adverse events, such as lipodystrophy and insulin resistance. Patients with HAART-associated lipodystrophy do not have systemic hypercortisolism, although their phenotype shares some similarities with Cushing's syndrome. 11 β -hydroxysteroid dehydrogenase type 1 (11 β HSD1) converts inactive cortisone to active cortisol. Mice overexpressing 11 β HSD1 selectively in adipose tissue are centrally obese, hyperglycaemic and dyslipidaemic. In obese humans, 11 β HSD1 activity is increased in adipose tissue. We determined whether 11 β HSD1 expression is increased in adipose tissue of patients with HAART-associated lipodystrophy.

METHODS: A group of HIV-positive patients with HAART-associated lipodystrophy (LD+, $n=30$) was compared with a group of HIV-positive patients receiving HAART but without lipodystrophy (LD-, $n=13$). The mRNA levels of 11 β HSD1 and β 2-microglobulin (housekeeping gene) in subcutaneous adipose tissue biopsies were measured using real-time polymerase chain reaction (PCR). Liver fat (LFAT) was measured using proton spectroscopy and intra-abdominal (i.a.) and subcutaneous (s.c.) fat by magnetic resonance imaging.

RESULTS: Body mass indices (BMIs) were comparable (23.6 ± 0.5 vs 22.4 ± 1.1 kg/m², LD+ vs LD-, NS), but the LD+ group had significantly more intra-abdominal (1900 ± 200 vs 900 ± 300 cm³, $P < 0.01$) and less subcutaneous (1100 ± 200 vs 1800 ± 300 cm³, $P < 0.05$) fat than the LD- group. LFAT (8 ± 2 vs 2 ± 1 %, $P < 0.001$) and fasting serum insulin concentrations (11 ± 1 vs 7 ± 1 mU/l, $P < 0.01$) were significantly higher in the LD+ than the LD- group. The mRNA concentration of 11 β HSD1 relative to β 2-microglobulin was significantly higher in the LD+ than the LD- group (0.29 ± 0.20 vs 0.09 ± 0.07 , $P < 0.001$). In all HAART-treated patients, 11 β HSD1 mRNA levels correlated with features of insulin resistance: fasting serum triglycerides ($r = 0.56$, $P < 0.001$), insulin ($r = 0.49$, $P = 0.001$) and high-density lipoprotein (HDL)-cholesterol ($r = -0.48$, $P < 0.01$) and intra-abdominal fat ($r = 0.54$, $P < 0.001$) and LFAT ($r = 0.45$, $P < 0.01$), but not with subcutaneous fat ($r = -0.1$, not significant).

CONCLUSIONS: Increased expression of 11 β HSD1 in adipose may contribute to insulin resistance in patients with HAART-associated lipodystrophy.

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2003-07-08
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