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LEPTIN AND SOLUBLE LEPTIN RECEPTOR LEVELS IN PATIENTS WITH ABNORMAL FAT REDISTRIBUTION AND METABOLIC DISTURBANCES ASSOCIATED WITH HIV THERAPY.

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Treatment with HIV-1 protease inhibitors (PI) may induce lipodystrophy (LD), hyperlipidemia, and impaired glucose tolerance due to insulin resistance. Leptin is an adipocyte-derived hormone interacting with specific receptors located in the central nervous system and peripheral tissue. Its likely involvement in lipid abnormalities often seen with antiretroviral therapy has not been investigated. Here we evaluated bound leptin and soluble leptin receptor levels with specific radioimmunoassays in HIV patients treated with PI's in comparison to PI naïve and healthy control subjects. Soluble leptin receptor levels were significantly increased in PI treated patients with LD compared to PI naïve patients (3.92 ± 2.29 nmol/l versus 2.29 ± 0.81 nmol/l, $p=0.007$), as were fasting cholesterol, triglycerides, LDL, VLDL, fasting C-peptide, insulin, and proinsulin ($p<0.01$). Bound leptin levels were slightly elevated in the PI group compared to PI naïve patients but not statistically significant (0.41 ± 0.21 nmol/l versus 0.32 ± 0.17 nmol/l). PI therapy was associated with insulin resistance, hyperlipidemia, and increased soluble leptin receptor levels (3.57 ± 1.95 nmol/l versus 2.29 ± 0.80 nmol/l, $p<0.001$). Increased soluble leptin receptor and bound leptin concentrations were significantly correlated to increased 120 min glucose and insulin values during oral glucose tolerance test (0.48, $p=0.0002$ and 0.42, $p=0.001$), and increased fasting apolipoprotein B and E, LDL and VLDL ($p<0.001$). Neither soluble leptin receptor nor bound leptin levels were able to discriminate patients with and without LD receiving PI. Since insulin resistance and resulting hyperinsulinemia is a characteristic feature of PI treatment, elevated insulin values might be the reason for increased soluble leptin receptor levels in these subjects. Thus, elevated soluble leptin receptor levels may implicate leptin resistance, which inhibit energy expenditure and increase food intake.

Keywords: AEGIS, Leptin, Carrier Proteins, Proinsulin, Insulin, Glucose Tolerance Test, C-Peptide, Antiretroviral Therapy, Highly Active, Fasting, Blood Glucose, Insulin Resistance, HIV Protease Inhibitors, Lipodystrophy, Glucose, Hyperinsulinemia, Glucose Intolerance, Endocrine Diseases, Metabolism, Inborn Errors, Hyperlipidemia, leptin receptor, Human, AIDS

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