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ACUTE INHIBITION OF LIPOLYSIS IMPROVES INSULIN SENSITIVITY IN PATIENTS WITH HIV LIPODYSTROPHY AND INSULIN RESISTANCE

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HIV lipodystrophy is associated with significant fat redistribution, dyslipidemia and insulin resistance, however, the mechanism of insulin resistance remains unknown in this large patient population. Patients with HIV infection and lipodystrophy have elevated free fatty acids (FFA). We hypothesized that increased FFA levels resulting from visceral obesity contribute to insulin resistance in HIV-infected patients with lipodystrophy. In order to determine the role of FFA in insulin resistance among these patients, we performed frequent sampled intravenous glucose tolerance tests (FSIGTT) following administration of acipimox, a potent inhibitor of lipolysis (1000 mg in two divided doses) compared with placebo in seven HIV-infected men with lipodystrophy and hyperinsulinaemia. Each patient completed two FSIGTTs separated by 3-7 days, and acipimox and placebo were administered in a double-blind randomized order. Patients were 45±2 years (mean±SEM), had a body-mass index of 28.8±1.9 kg/m², a waist-to-hip ratio of 0.99±0.01, and the duration of HIV was 8±1 year. All patients were on a protease inhibitor with a mean duration of 3.6±years. Patients were markedly insulin resistant [insulin sensitivity (SI) 0.88±0.3 10⁻⁴ per µU/ml/min compared with normative values of 7.56 10⁻⁴ µU/ml/min for healthy men). FFA levels were significantly reduced after administration of acipimox compared to placebo (FFA area under the curve: acipimox 73±8 versus placebo 122±12 mmol/l/270 min, *P*=0.002). Acipimox resulted in a significant increase in insulin sensitivity (SI 1.63±0.5 10⁻⁴ per µU/ml/min, *P*=0.015). Acute inhibition of lipolysis and a reduction in FFA levels were associated with improved insulin sensitivity in patients with HIV lipodystrophy and insulin resistance. Long-term strategies to reduce FFA concentrations may be useful in the treatment of the metabolic disturbances associated with HIV lipodystrophy.

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