

3rd International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV



23-26 October 2001, Athens, Greece

Both insulin resistance and relative β -cell insensitivity are characteristics of HIV-associated glucose intolerance

Antiviral Therapy 2001; 6(Suppl. 4):6 (abstract no. 6)

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BACKGROUND AND OBJECTIVES: We examined the metabolic mechanisms that contribute to HIV-associated impaired glucose tolerance (GT) using the insulin-modified (0.02 U/kg over 5 min) intravenous 6,6-d₂-glucose tolerance test (300 mg/kg; iv GTI) with minimal modelling.

METHODS: We evaluated insulin sensitivity, β -cell sensitivity to glucose and hepatic insulin extraction in 12 HIV-infected men [42 \pm 9 years (mean \pm SD); bodymass index (BMI)=28 \pm 4 kg/m²; VL=4.4 \pm 2.5 \times 10⁴ copies/ml; CD4=534 \pm 98 copies/ μ l]; four with normal GT (NGT), six with impaired GT (IGT) and two with NIDDM. Results from the HIV-infected men were also compared (ANOVA) to those from seven healthy young (25 \pm 4 year; BMI=27 \pm 2 kg/m²) and nine healthy older (69 \pm 5 year; BMI=28 \pm 3 kg/m²) men.

RESULTS: Insulin sensitivity (10⁴ min⁻¹ per μ U/ml) was lower in the IGT+NIDDM HIV-infected men (1.0 \pm 0.8) than the NGT (6.9 \pm 0.4), young (6.2 \pm 3.9) and older men (4.6 \pm 2.3; P <0.0007), and was inversely correlated with exposure time (weeks) to protease inhibitors and nucleoside reverse transcriptase inhibitors (r^2 =0.3; P <0.04). Baseline insulin secretion rate normalized to fasting glucose concentration (10⁹ min⁻¹) was higher in the IGT+NIDDM HIV-infected men (14.3 \pm 3.3) than in the NGT (5.9 \pm 2.7), young (4.9 \pm 1.4) and older men (6.2 \pm 1.3; P <0.0001). β -cell sensitivity to glucose did not differ among groups during the initial portion of the ivGTI (first phase), while it was higher in IGT+NIDDM (17.8 \pm 9.6 10⁹ min⁻¹) than in NGT (8.1 \pm 4.2), young (9.9 \pm 4.3) and older men (11.4 \pm 5.2; P =0.052) during the latter portion of the ivGTI (second phase). β -

cell sensitivity to glucose in IGT +NIDDM HIV-infected men was not adequate to compensate for their degree of insulin resistance, in either the basal, first or second phases, as reflected by significantly lower disposition indices (β -cell sensitivity \times insulin sensitivity) when compared with NGT, young and older men. Baseline hepatic insulin extraction (%) was lower in both the NGT (40 ± 30) and the IGT+NIDDM HIV-infected men (52 ± 18) than in the young (67 ± 10) and older men (75 ± 7 ; $P=0.002$).

CONCLUSIONS: HIV-associated glucose intolerance is characterized by: (a) insulin resistance (b) insufficient β -cell insulin secretion given the fasting and ivGTI glucose levels and the degree of insulin resistance (that is, relative insulin deficiency) (c) a greater exposure to antiretroviral medications, and (d) an impaired ability of the liver to extract insulin.

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