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EFFECT OF INITIATING INDINAVIR THERAPY ON GLUCOSE METABOLISM IN HIV-INFECTED PATIENTS: RESULTS OF MINIMAL MODEL ANALYSIS

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MP Dubé¹, R Aqeel², H Edmondson-Melançon¹, D Johnson¹ and TA Buchanan²

¹Department of Medicine and the Divisions of Infectious Diseases and ²Endocrinology, University of Southern California School of Medicine and the Los Angeles County-USC Medical Center, Los Angeles, California, USA

BACKGROUND: Hyperglycaemia is a recognized complication of treatment with HIV-1 PIs. Cross-sectional studies suggest that PI use is associated with insulin resistance, but prospective, longitudinal studies with serial evaluations have not been published.

DESIGN: Non-diabetic, non-wasted, HIV-infected patients were prospectively evaluated by 75 g oral and 22 sample intravenous (IV) glucose tolerance testing (GTT) at baseline, then 2 and 8 weeks after starting indinavir-based therapy. Patients with wasting, acute opportunistic infections, or who were receiving drugs known to alter insulin secretion or sensitivity were excluded. Results were compared among baseline, 2 week and 8 week tests by a two-tailed *t*-test.

RESULTS: Nine men and one woman were studied. Mean CD4 count at entry was 305 cells/mm³ and mean HIV RNA was 68,267 copies/ml; all experienced a virological response. Fasting glucose increased from 85.3±10.5 mg/dl at baseline to 93.3±10.8 at week 8 (*P*=0.04). Insulin sensitivity by minimal model analysis of the IV GTT decreased by 30% over 8 weeks, from 3.83±2.0 min⁻¹ per μU/ml × 10⁴ to 2.66±1.12 (*P*=0.05). Insulin secretion measured as the acute insulin response to IV glucose did not increase significantly (baseline 822±893 μU/ml • min, week 8 880±915, *P*=0.5), and the response to oral glucose (30 min Δinsulin/Δglucose) fell slightly but not significantly from 227±242 pmol/mmol at baseline to 156±153 at week 8 (*P*=0.09).

CONCLUSIONS: During 8 weeks of indinavir-based therapy, fasting glucose increased and insulin sensitivity decreased. Pancreatic B cell responsiveness did not manifest a normal increase in insulin release to compensate for the insulin resistance. This combination of insulin resistance and inadequate B cell response may explain the hyperglycemia and other metabolic abnormalities seen in some PI-treated patients.

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