

Hyperglycemia in HIV infected patients

Lydia Concept ion

A. Purpose and Rationale

a. Main Goals

To determine the prevalence of hyperglycemia in a cohort of minority HIV infected patients evaluate the known risk factors for the development of impaired glucose tolerance in this urban setting.

Patients with HIV infection are believed to be at risk for the development of several metabolic abnormalities including impaired glucose tolerance, diabetes mellitus, and dyslipidemia. An entity has been described as part of a novel syndrome called lipodystrophy. It is also associated with peripheral fat wasting, with central and visceral fat accumulation. The cause is unknown a recent hypothesis suggests deranged retinoic acid metabolism leads to dysregulation of fat metabolism (1). Highly active antiretroviral therapy (HAART) has been closely associated with DM and lipodystrophy, especially the protease inhibitors (PI). However, the syndrome has also been seen in HIV infected pts on no treatment (2,3,4). Diabetes is an important part of this syndrome. It has been reported with a prevalence of 1 to 7% in pts with lipodystrophy (1,5). Another study (6) demonstrated insulin resistance or frank DM in over half of HIV infected men on PI therapy. Fisher et al, in a predominately white male population, showed that HIV pts did seem predisposed to the development of impaired glucose tolerance. But, Kilby et al, who studied preexisting diabetic traits vs. drug associated DM found hyperglycemia to be uncommon (2%) in HIV infected pts (8). Of this 2%, half had preexisting DM conditions, and most of the other were clearly associated with corticosteroid or megestrol acetate use. The question of increased prevalence of impaired glucose tolerance in minority HIV infected patients due to drug associated DM or simply preexisting factors remains unclear.

B. Study design

This prospective study will follow specific outcomes in a cohort of HIV infected subjects at the Harkness 6 clinic using a longitudinal design, then apply a logistics regression for the analysis of increased prevalence of abnormal glucose tolerance.

Eligibility requirements:

- age 21-55 at time of enrollment
- newly dx HIV infection

HAART naïve Demographic data will be obtained and recorded using a standardized form. All pts will get an initial comprehensive evaluation including complete history and physical. Known risk factors for the development of impaired glucose tolerance such as age, family hx, report of lipodystrophy, height, weight, and waist/ hip ratio, onset of HAART therapy, and treatment of acute illness will be clearly documented. The following lab tests: chem7, cbc, Ifts, lipids , gly hgb, ogtt, c-peptide, serum insulin, CD4, and VL will be obtained at baseline and every six months for an anticipated 3 years. Patients found to have diabetes will be referred to NBDC for treatment.

C. Study Procedure

There will be approximately 75cc of blood drawn for the above mentioned analysis at baseline, then q6 months for 3 years. Participation in the study will not affect the treatment at H6 clinic. History and physical will be performed by the H6 clinic provider.

D. Potential Benefits:

This study would provide preliminary data to support a larger longitudinal clinical trial aimed at determining the potential risks and benefits of the treatment of hyperglycemia in HIV infected, minority population.

E. References

1. Carr A, Samaras K, Thorisdottir A et al. Diagnosis, prediction, and natural course of HIV-1 protease-inhibitor-associated lipodystrophy, hyperlipidaemia, and diabetes mellitus: a cohort study, *Lancet* 1999;353:2093-2099.
2. Saint-Marc T, Partisani M et al. A syndrome of peripheral fat wasting (lipodystrophy) in patients receiving long-term nucleoside analogue therapy. *AIDS* 1999, 13:1659-1667.
3. Hadigan C, Miller K et al. Fasting hyperinsulinemia and changes in regional body composition in human immunodeficiency virus-infected women. *J Clin Endocrinol Metab* 1999, 84:1932-1937.
4. Carr A, Samaras K, Burton S et al. A syndrome of peripheral lipodystrophy, hyperlipidaemia, and insulin resistance in patients receiving ZDV protease inhibitors. *AIDS* 1998;12:F51-F58.
5. Deeks SG, Smith M, Holodny M, Kahn MO. HIV protease inhibitors: a review for clinicians, *JAMA* 1997;277:145-153.
6. Walli R, Herfort O, Michl GM et al Treatment with protease inhibitors associated with peripheral insulin resistance and impaired oral glucose tolerance in HIV-1 infected patients. *AIDS* 1998,12:F167-173.