Care of Diabetes in Patients Infected with Human Immunodeficiency Virus: a comparison of HIV specialists and general medicine providers' compliance with ADA/AHA guidelines.

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Specific Aims:

(1)The purpose of this study is to evaluate the care HIV specialists provide their HIV/AIDS patients with Type II Diabetes Mellitus based on the standards of care of the American Diabetes Association(ADA)/American Heart Association (AHA)[1].

Exploratory Aims:

(1) Determine the percentage of patients with both HIV and Diabetes/Insulin Resistance who have diabetic risk factors including family history of diabetes, obesity, history of steroid use, sedentary lifestyle, hypertension, history of gestational diabetes, hypercholesterolemia, and African/Asian/Hispanic ethnicity.

(2) Determine the percentage of patients with both HIV and Diabetes/Insulin Resistance who have been exposed to Protease Inhibitors.

(3) Determine the temporal relationships among the diagnoses of Diabetes/Insulin Resistance, the diagnoses of HIV, the diagnoses of AIDS, treatment with protease inhibitors, and changes in weight and fat distribution.

A. Study Purpose and Rationale

Since the introduction of HAART therapy, the care of HIV/AIDS patients has moved dramatically from the inpatient, acute-care setting to the outpatient, chronic care arena. Death among HIV/AIDS patients in the United States is increasingly attributable to non-HIV related causes including

cardiovascular disease, substance abuse, and non-HIV related cancers[2-4]. The prolongation of life through good HIV/AIDS control now leaves these patients to face the epidemics of diabetes, cardiovascular disease, and obesity along with their HIV non-infected counterparts[3, 5-9].

Soon after the advent of protease inhibitors, reports of increase insulin resistance arose among patients receiving HAART[10, 11]. Similarly, the phenomenon of HIV-associated lipodystrophy was increasingly attributed the use of protease inhibitors[12]. Nearly a decade later, there remains controversy over whether insulin resistance and lipodystrophy are attributable to HIV itself, recovery from AIDS, intrinsic side-effects of the drugs, or a combination of these factors[7, 13-18]. Likewise, there exists no consensus among HIV specialists as to how to best manage diabetes and insulin-resistance in HIV/AIDS patients[14].

HIV/AIDS research in the form of large clinical trials and bench science is attempting now to determine the clinical significance and mechanisms of the metabolic derangements associated with HIV and HAART therapy. A review of published literature reveals very little, however, of how well HIV/AIDS providers are managing diabetes. This study seeks to evaluate the care HIV specialists are providing to their HIV/AIDS and Diabetes co-affected patients based on the standards of care of the American Diabetes Association (ADA)/American Heart Association (AHA)[1].

B. Study Design and Statistical Analysis

This study is designed as a cross-sectional study of patients with diabetes followed in either an HIV/AIDS or a general medicine clinic. Both clinics share the same geographic, ethnic and socioeconomic catchment area. Patients with diabetes will be identified in both clinics by IC9 coding (250.0-250.9) and will be considered for inclusion if they have the diagnosis of diabetes for at least six months prior to the initiation of the study and have been followed at least twice within the study year. Patients with Type I diabetes will be excluded.

A retrospective chart review will be conducted of 150 randomly-selected patients with diabetes from each clinic. Using standardized forms based on ADA/AHA guidelines, laboratory data and information about physician management practice will be extracted from patient charts. The primary end-

point will be assessed by percentage of patients with HgAIC less than 7%. Based on the chi-square test for 80% power and testing at P=0.05, this study should allow detection of an effect size of 10%. Secondary end-points will be percentage of patients at goal in terms of the following variables; frequency of HgAIC testing, urine microalbumin/creatinine ratio, LDL cholesterol, HDL cholesterol, Triglycerides, Blood pressure, BMI, ASA therapy, ACE/ARB therapy, annual foot exam, annual dilated retinal exam, flu vaccine, pneumonia vaccine, smoking cessation counseling, nutrition/exercise counseling. In addition, the following variables will be assessed in determining risk factors for diabetes including family history of diabetes, obesity, history of steroid use, sedentary lifestyle, hypertension, history of gestational diabetes, hypercholesterolemia, African/Asian/Hispanic ethnicity, and protease inhibitor exposure.

C. Study Procedure

Study subjects will be enrolled based on results of a planned retrospective chart review of patients followed in the outpatient Infectious Diseases Clinic and in the outpatient general medicine clinic at CUMC. Patients with diabetes from both clinics will be identified via WebCIS data warehouse inquiry by ICD-9 coding for diabetes (250.0- 250.9). Data for standards-of-care measures and diabetes risk factors will be assessed by chart review.

D. Study Drugs: N/A

E. Medical Devices: N/A

F. Study Questionnaires: N/A

G. Study Subjects:

Eligible subjects will be recruited from the CUMC Infectious Diseases clinic (HP6) and general medicine clinic at CUMC (AIM). Subjects will have diabetes based on ICD-9 coding and will be excluded for known Type I diabetes. All patients recruited from the Infectious Disease clinic will have a known diagnosis of HIV with past HIV-1/HIV-2 antibody testing with confirmatory enzyme immunoassay (EIA) present in their medical records.

H. Recruitment of Subjects: Patients will be recruited at the CUMC Infectious Diseases (HP6) and the CUMC General Internal Medicine Clinics (AIM).

I. Confidentiality of Study Data: All study data will be strictly confidential. Subjects will be identified by a unique code, and all patient identifying information corresponding to the subject's code will be stored on computerized databases which will be accessible by password only.

J. Potential Conflict of Interest: There are no conflicts of interest in this study.

K. Location of the Study: CUMC

L. Potential Risks: There are no foreseeable risks for patients assessed in this study.

M. Potential Benefits: Potential benefits of this study to individual subjects will be indirect through provider's increased awareness of strengths and weaknesses in diabetes care at this CUMC clinic.

N. Alternative Therapies: N/A

O. Compensation to Subjects: N/A

P. Costs to Subjects: N/A

Q. Minors as Research Subjects: No minors will be involved as research subjects in this study.

R. Radiation or Radioactive Substances: N/A

S. Tables and Figures

REFERENCES

1. Buse JB, Ginsberg HN, Bakris GL, et al. Primary prevention of cardiovascular diseases in people with diabetes mellitus: a scientific statement from the American Heart Association and the American Diabetes Association. Diabetes Care 2007;30(1):162-72.

2. Sackoff JE, Hanna DB, Pfeiffer MR, Torian LV. Causes of death among persons with AIDS in the era of highly active antiretroviral therapy: New York City. Ann Intern Med 2006;145(6):397-406.

3. Friis-Moller N, Sabin CA, Weber R, et al. Combination antiretroviral therapy and the risk of myocardial infarction. N Engl J Med 2003;349(21):1993-2003.

4. Friis-Moller N, Weber R, Reiss P, et al. Cardiovascular disease risk factors in HIV patients--association with antiretroviral therapy. Results from the DAD study. Aids 2003;17(8):1179-93.

5. Gazzaruso C, Bruno R, Garzaniti A, et al. Hypertension among HIV patients: prevalence and relationships to insulin resistance and metabolic syndrome. J Hypertens 2003;21(7):1377-82.

6. Grinspoon SK. Metabolic syndrome and cardiovascular disease in patients with human immunodeficiency virus. Am J Med 2005;118 Suppl 2:23S-8S.

7. Grinspoon S, Carr A. Cardiovascular risk and body-fat abnormalities in HIV-infected adults. N Engl J Med 2005;352(1):48-62.

8. Behrens GM, Meyer-Olson D, Stoll M, Schmidt RE. Clinical impact of HIV-related lipodystrophy and metabolic abnormalities on cardiovascular disease. Aids 2003;17 Suppl 1:S149-54.

9. Morse CG, Kovacs JA. Metabolic and skeletal complications of HIV infection: the price of success. Jama 2006;296(7):844-54.

10. 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(15):F167-73.

11. Behrens G, Dejam A, Schmidt H, et al. Impaired glucose tolerance, beta cell function and lipid metabolism in HIV patients under treatment with protease inhibitors. Aids 1999;13(10):F63-70.

12. Vigouroux C, Gharakhanian S, Salhi Y, et al. Diabetes, insulin resistance and dyslipidaemia in lipodystrophic HIV-infected patients on highly active antiretroviral therapy (HAART). Diabetes Metab 1999;25(3):225-32.

13. Danoff A, Shi Q, Justman J, et al. Oral glucose tolerance and insulin sensitivity are unaffected by HIV infection or antiretroviral therapy in overweight women. J Acquir Immune Defic Syndr 2005;39(1):55-62.

14. Justman JE, Benning L, Danoff A, et al. Protease inhibitor use and the incidence of diabetes mellitus in a large cohort of HIV-infected women. J Acquir Immune Defic Syndr 2003;32(3):298-302.

15. Bitnun A, Sochett E, Dick PT, et al. Insulin sensitivity and beta-cell function in protease inhibitor-treated and -naive human immunodeficiency virus-infected children. J Clin Endocrinol Metab 2005;90(1):168-74.

16. Grinspoon S. Mechanisms and strategies for insulin resistance in acquired immune deficiency syndrome. Clin Infect Dis 2003;37 Suppl 2:S85-90.

17. Nolte LA, Yarasheski KE, Kawanaka K, Fisher J, Le N, Holloszy JO. The HIV protease inhibitor indinavir decreases insulin- and contraction-stimulated glucose transport in skeletal muscle. Diabetes 2001;50(6):1397-401.

18. Woerle HJ, Mariuz PR, Meyer C, et al. Mechanisms for the deterioration in glucose tolerance associated with HIV protease inhibitor regimens. Diabetes 2003;52(4):918-25.