Clinical Inertia in the Management of Low-Density Lipoprotein Abnormalities in an HIV Clinic

James H. Willig,[1] David A. Jackson,[1] Andrew O. Westfall,[3] Jeroan Allison,[2] Pei-Wen Chang,[1] James Raper,[1] Michael S. Saag,[1] and Michael J. Mugavero[1]

Divisions of [1]Infectious Diseases and [2]General Internal Medicine, Department of Medicine, and [3]Department of Biostatistics, University of Alabama at Birmingham, Birmingham

A retrospective cohort study evaluating the frequency of and factors related to clinical inertia in low-density lipoprotein (LDL) management was performed. Subjects were 90 patients that were not meeting National Cholesterol Education Program Adult Treatment Panel III LDL goals at the University of Alabama at Birmingham 1917 HIV/AIDS Clinic between 1 August 2004 and 1 August 2005. Clinical inertia was observed in 44% of cases. Patients with higher baseline LDL levels were less likely to experience inertia, whereas women and those in the highest coronary heart disease risk category were more likely to be affected.

HAART has revolutionized HIV care, transforming a uniformly lethal illness into a chronically managed condition in populations with access to treatment. The success of HAART has resulted in new challenges in HIV-related morbidity and mortality, including a high prevalence of cardiovascular risk factors and coronary artery disease [1, 2]. Dyslipidemias are important cardiovascular risk factors among HIV-infected patients, because both the disease and antiretroviral therapy contribute to lipid abnormalities [3, 4]. During outpatient clinic encounters, contemporary HIV providers must now increasingly treat dyslipidemias and other chronic comorbid medical conditions in addition to managing HIV infection with antiretroviral and associated medications (e.g., prophylactic medications).

In non-HIV primary care settings, clinical inertia, defined as failure to initiate or intensify therapy when indicated on the basis of evidence-based guidelines, has been recognized as a common problem that presents an important barrier in the successful management of dyslipidemias and other chronic disorders [5, 6]. The role of clinical inertia in the management of lipid abnormalities in HIV-infected populations has not yet been studied. Therefore, we investigated the prevalence of clinical inertia and the factors associated with its occurrence among dyslipidemic HIV-infected patients in our outpatient HIV cohort.

Methods. The University of Alabama at Birmingham (UAB) 1917 HIV/AIDS Clinic Cohort Observational Database Project is a prospective cohort study that contains detailed sociodemographic, psychosocial, and clinical information from clinic patients, including >1500 patients who are currently receiving care. The clinic uses a locally programmed electronic medical record that imports all laboratory values from the central UAB laboratory, requires electronic prescription for all medications, and contains detailed encounter notes. This retrospective cohort study was approved by the UAB Institutional Review Board.

For this analysis, patients with an initial lipid panel performed during July–December 2004 (LDL1), a second lipid panel 12 weeks to 9 months later (LDL2), and a final lipid panel 12 ± 3 months after the first (LDL3) were identified in our database. Individual low-density lipoprotein (LDL) goals were calculated for each patient meeting these criteria on the basis of the third report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults executive summary (NCEP-ATP III) [7]. LDL levels were directly measured, not calculated, at our reference laboratory. Patients with the following profiles were included in the analysis; (1) patients who did not meet their LDL goal at LDL1 and LDL2 measurements, and (2) patients with abnormal results at LDL1 who met their LDL goal at the LDL2 measurement because of a pharmacological intervention initiated after the LDL1 measurement.

Patients who met their NCEP-ATP III LDL goal at their LDL2 measurement in the absence of pharmacological interventions were excluded. This criterion was used to avoid the misclassification of clinical inertia for patients with isolated elevations in their LDL level for whom pharmacological intervention was not indicated or those who responded to lifestyle modification alone.

Clinical inertia was recorded as a dichotomous variable, defined as failure to initiate an appropriate pharmacological LDL-

Received 1 November 2007; accepted 18 December 2007; electronically published 13 March 2008.

Presented in part: 11th International Workshop on HIV Observational Databases, Monte Carlo, Monaco, 22–25 March 2007.

Reprints or correspondence: Dr. James H. Willig, CCB 174, 908 S. 20th St., Birmingham, AL 35294-2050 (jwillig@uab.edu).

Clinical Infectious Diseases 2008; 46:1315–8

1058-4838/2008/4608-0028$15.00
DOI: 10.1086/533466

lowering intervention (including fish oil, 3-hydroxy-3-methylglutaryl coenzyme A [HMG-CoA] reductase inhibitors, ezetimibe, or niacin) or failure to refer to another provider for lipid management during the 12-month study period for a patient with a persistently abnormal LDL level. Pharmacological interventions included recommendation, initiation, dose escalation, or change to a more potent lipid-lowering agent or the addition of a second LDL-lowering drug; adherence counseling directed at lipid therapy; or a change in HAART in response to an LDL abnormality. Interventions were determined by detailed review of all provider notes and medications prescribed during the study period. When rationale for avoidance of pharmacological interventions addressing LDL abnormalities was included in provider notes (e.g., past toxicity to HMG-CoA reductase inhibitor or interaction with concurrent medications), the encounter was exonerated from being classified as clinical inertia.

After a 12-week trial of therapeutic lifestyle changes, guidelines recommend the initiation of lipid-lowering drug therapy if LDL goals are not achieved [7]. Study inclusion criteria requiring a second lipid measurement (LDL2) at least 12 weeks after the first (LDL1) ensured that all study patients both had an adequate time period to respond to lifestyle changes and met criteria for advancement to pharmacological LDL-lowering interventions.

Analytically, univariate logistic regression analyses were performed to evaluate the relationship between clinical inertia and a priori–selected independent variables. Next, a multivariable logistic regression model was used to evaluate factors associated with clinical inertia while adjusting for covariates. Variable selection for the multivariable model was based on univariate results and clinical judgment. All analyses were performed using SAS software, version 9.1.3 (SAS Institute).

Results. A total of 640 patients had lipid panels performed during July–December 2004 (LDL1) and again 12 months later (LDL3). Of these, 138 patients (22%) did not meet their NCEP-ATP III LDL goal at their LDL1 measurement. Ninety (65%) of the 138 patients met study inclusion criteria; 10 were excluded because they lacked an intermediate LDL (LDL2) measurement, and 38 were excluded because they achieved their LDL goal in subsequent lipid measurements (LDL2) in the absence of pharmacological intervention or in response to lifestyle modification alone. Demographic and medical characteristics of study participants included the following: median age, 46 years; white race, 61%; and male sex, 80%. Fifty-two percent were men who have sex with men, 36% were heterosexual, 47% received protease inhibitors during the observation period, 46% were active smokers, and 30% were known to have diabetes (table 1). Clinical inertia in lipid management was observed for 40 (44%) of 90 patients during a median observation time of 365 days. No pharmacological interventions occurred for these patients despite persistently abnormal LDL values over a median of 4 visits (interquartile range, 3–4 visits) and 4.5 LDL measurements (interquartile range, 4–5 LDL measurements).

In multivariable logistic regression analysis, patients with baseline LDL elevations greater than their NCEP-ATP III LDL goal (OR, 0.56 per 20 mg/dL; 95% CI, 0.32–0.99) and those belonging to the 2 NCEP-ATP III lower risk categories (0–1 risk factor with LDL goal of <130 mg/dL or ⩾2 risk factors with LDL goal of <160 mg/dL) for cardiovascular disease (OR, 0.32; 95% CI, 0.10–0.99) were less likely to experience clinical inertia. Female patients had an increased risk of experiencing clinical inertia (OR, 6.59; 95% CI, 1.54–28.2). Baseline liver function tests (measurements of serum aspartate and alanine aminotransferase, alkaline phosphatase, indirect and direct bilirubin levels) and hepatitis C virus infection status had no statistically significant association with clinical inertia on univariate analysis (data not shown). No other study variables achieved statistical significance (table 1).

Discussion. In our cohort, clinical inertia or failure to initiate or adjust lipid management was observed for 44% of patients with persistently abnormal LDL levels in our outpatient cohort, despite a median of 4 clinical visits during a 12-month study period. Although clinical inertia in lipid management has been well studied in other patient populations, this is the first study, to our knowledge, to evaluate clinical inertia in HIV-infected patients. Previous studies of non–HIV-infected persons have documented rates of provider intensification of pharmacotherapy for elevated lipids in 16%–56% of provider visits [8, 9]. Because patients with HIV infection are living longer and becoming increasingly affected by dyslipidemia and other cardiovascular risk factors, this area of research is critical for improving long-term clinical outcomes.

In our study, lipid abnormalities in patients further from their NCEP-ATP III LDL goal at baseline were more aggressively managed—that is, these patients were significantly less likely to experience clinical inertia. However, patients in the highest risk category (LDL level goal, <100 mg/dL) for cardiovascular disease were more likely to experience inertia in their lipid management. This may relate to providers focusing more on absolute LDL levels than on individualized LDL goals (e.g., <100 , <130, or <160 mg/dL) based on coronary heart disease risk category as defined by the NCEP-ATP III guidelines.

Consistent with studies of non–HIV-infected patients [10], women were disproportionately affected by clinical inertia. Sex bias in provider attitudes ascribing greater importance to control of cardiovascular disease risk factors among men has been reported in other patient populations [11]. Further sex disparities in the care of HIV-infected women have been documented, including lower rates of HAART initiation and use of prophylaxis against opportunistic infections [12]. Understanding the underlying causes of clinical inertia and therapeutic sex

Table 1. Characteristics of 90 HIV-infected patients with initial LDL levels above NCEP-ATP III goals at the University of Alabama at Birmingham 1917 HIV/AIDS Clinic from August 2004 to August 2005.

Characteristic	Overall (n = 90)	Inertia		OR (95% CI)	
		No (n = 50)	Yes (n = 40)	Crude	Adjusted
Age,[a] years	46.0 (40.3–52.7)	45.5 (40.0–49.5)	47.3 (41.7–56.2)	1.72[b] (1.07–2.79)	1.65[b] (0.95–2.85)
Sex					
Female	18 (20)	6 (12.0)	12 (30.0)	3.14 (1.06–9.33)	6.59 (1.54–28.2)
Male	72 (80)	44 (88.0)	28 (70.0)	R	R
Race					
African American	35 (38.9)	16 (32.0)	19 (47.5)	1.92 (0.81–4.54)	0.70 (0.22–2.21)
White	55 (61.1)	34 (68.0)	21 (52.5)	R	R
Body mass index[a]	26.1 (23.9–30.2)	27.0 (23.1–30.2)	25.4 (24.1–30.5)	1.02 (0.96–1.08)	…
Protease inhibitor use[c]					
Yes	42 (46.7)	26 (52.0)	16 (40.0)	0.62 (0.27–1.43)	0.54 (0.20–1.45)
No	48 (53.3)	24 (48.0)	24 (60.0)	R	R
Active smoking[c]					
Yes	41 (45.6)	23 (46.0)	18 (45.0)	0.96 (0.42–2.21)	…
No	49 (54.4)	27 (54.0)	22 (55.0)	R	…
Diabetes mellitus					
Yes	27 (30.0)	15 (30.0)	12 (30.0)	1.00 (0.40–2.48)	…
No	63 (70.0)	35 (70.0)	28 (70.0)	R	…
CD4 cell count,[a] cells/mm^3	457 (267–616)	520 (281–662)	389 (220–547)	0.94[d] (0.86–1.02)	0.91[d] (0.82–1.01)
Plasma HIV load,[a] $1og_{10}$ copies/mL	1.69 (1.69–2.86)	1.69 (1.69–2.10)	2.00 (1.69–3.47)	1.07 (0.96–1.18)[e]	…
CHD					
Yes	7 (7.8)	2 (4.00)	5 (12.5)	3.43 (0.63–18.7)	…
No	83 (92.2)	48 (96.0)	35 (87.5)	R	…
No. of visits[f]	4.00 (3.00–4.00)	4.00 (3.00–4.00)	4.00 (3.00–4.50)	0.95 (0.73–1.26)	…
No. of LDL measurements	4.50 (4.00–5.00)	5.00 (4.00–5.00)	4.00 (4.00–5.00)	1.01 (0.75–1.35)	…
NCEP-ATP III LDL cholesterol goal, mg/dL					
<100 (CHD and CHD risk equivalents)	43 (47.8)	21 (42.0)	22 (55.0)	R	R
<130 and <160 (0–1 or ⩾2 risk factors)	47 (52.2)	29 (58.0)	18 (45.0)	0.59 (0.26–1.37)	0.32 (0.10–0.99)
Elevation in LDL above goal,[a] mg/dL	24.0 (16.0–42.0)	27.5 (19.0–42.0)	21.0 (14.0–37.5)	0.78[g] (0.53–1.15)	0.56[g] (0.32–0.99)
Primary provider					
MD	32 (35.6)	15 (30.0)	17 (42.5)	1.72 (0.72–4.12)	…
Other (PA/CRNP)	58 (64.4)	35 (70.0)	23 (57.5)	R	…
Lipids managed by outside provider					
Yes	18 (20.0)	9 (18.0)	9 (22.5)	1.32 (0.47–3.72)	…
No	72 (80.0)	41 (82.0)	31 (77.5)	R	…

NOTE. Data are no. (%) or median (interquartile range), unless otherwise indicated. CHD, coronary heart disease; CRNP, certified registered nurse-practitioner; LDL, low-density lipoprotein; MD, medical doctor; NCEP ATP III, National Cholesterol Education Program Adult Treatment Panel III [7]; PA, physician's assistant; R, reference.

[a] At time of initial LDL measurement.
[b] OR per 10 years.
[c] At any time during 1 year study period.
[d] OR per 50 cells/mm^3.
[e] OR per 5000 copies/mL.
[f] Any visit to the UAB 1917 Clinic throughout the year for the purpose of laboratory measurements, sick call, and/or regularly scheduled follow-up.
[g] OR per 20 mg/dL.

disparities for HIV-infected women are important areas for future research.

Clinical inertia is believed to result from a combination of patient, system, and provider factors. Patient factors include low health literacy, polypharmacy, adverse effects of medication, costs, and denial of having an illness or of its severity. System factors encompass a lack of decision support and poor communication between physicians and staff. Provider factors include overestimation of care provided and a lack of awareness of recommended guidelines [6]. For HIV-infected patients, an additional factor contributing to clinical inertia may be decreased comfort in the management of chronic comorbid medical conditions among infectious disease specialists, compared with general medicine practitioners [13].

This study has limitations. Because the results were obtained in a single center, they may not be generalizable to other regions

of the country or other HIV clinics. This analysis was underpowered to gauge the impact of clinical inertia on biological outcomes—namely, achievement of LDL goals. This study focused on patient factors associated with clinical inertia and did not assess system and provider factors.

Clinical inertia is a well-chronicled obstacle to achieving success in treatment of dyslipidemia in non–HIV-infected populations. It is not surprising that our study found that clinical inertia plays an important role in the management of dyslipidemia in HIV-infected patients as well; 44% of patients with persistently elevated LDL levels were not prescribed a pharmacological intervention during a 12-month study period. Systems-based interventions to reduce clinical inertia have improved lipid management in other patient populations [8]. Future studies should further evaluate provider and system factors associated with clinical inertia of lipid management for HIV-infected patients. Such studies will be vital to the development of multilevel interventions that may lead to improved lipid management and ultimately to reduced cardiovascular morbidity and mortality for people living with HIV/AIDS.

Acknowledgments

We thank the UAB 1917 Clinic HIV/AIDS Clinic Cohort management team for their assistance with this project.

Financial support. UAB Center for AIDS Research (P30-AI27767 to UAB 1917 Clinic Cohort) and the Mary Fisher CARE Fund (UAB 1917 Clinic Cohort); Ruth L. Kirschstein National Research Service Award (5T32AI52069 to J.H.W.); American Medical Association Seed Grant (D.A.J.).

Potential conflicts of interest. J.H.W. has received recent research funding from Bristol-Myers Squibb Virology Fellows Research Program. W.O.W. has received recent research funding from Novartis. J.R. has served as a consultant and on the speakers' bureau for GlaxoSmithKline. M.S.S. has received recent research funding and done consulting for Achillion Pharmaceuticals, Avexa, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead, GlaxoSmithKline, Merck, Monogram Biosciences, Panacos, Pfizer, Progencis, Roche, Serono, Tanox, Tibotec, Trimeris, and Vertex. M.J.M. has received recent research funding from Tibotec. All other authors: no conflicts.

References

1. Friis-Møller 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**; 17:1179–93.
2. Glass TR, Ungsedhapand C, Wolbers M, et al. Prevalence of risk factors for cardiovascular disease in HIV-infected patients over time: the Swiss HIV Cohort Study. HIV Med **2006**; 7:404–10.
3. DAD Study Group, Friis-Møller N, Reiss P, et al. Class of antiretroviral drugs and the risk of myocardial infarction. N Engl J Med **2007**; 356: 1723–35.
4. Grinspoon S, Carr A. Cardiovascular risk and body-fat abnormalities in HIV-infected adults. N Engl J Med **2005**; 352:48–62.
5. Phillips LS, Branch WT, Cook CB, et al. Clinical inertia. Ann Intern Med **2001**; 135:825–34.
6. O'Connor PJ, Sperl-Hillen JM, Johnson PE, Rush WA, Biltz G. Clinical inertia and outpatient medical errors. In: Henriksen K, Battles JB, Marks ES, Lewin DI, eds. Advances in patient safety: from research to implementation. Vol 2. Concepts and methodology. Rockville, MD: Agency for Healthcare Research and Quality, **2005**:293–308.
7. Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). JAMA **2001**; 285:2486–97.
8. Goldberg KC, Melnyk SD, Simel DL. Overcoming inertia: improvement in achieving target low-density lipoprotein cholesterol. Am J Manag Care **2007**; 13:530–4.
9. Rodondi N, Peng T, Karter AJ, et al. Therapy modifications in response to poorly controlled hypertension, dyslipidemia and diabetes mellitus. Ann Intern Med **2006**; 144:475–84.
10. Kim C, Hofer TP, Kerr EA. Review of evidence and explanations for suboptimal screening and treatment of dyslipidemia in women: a conceptual model. J Gen Intern Med **2003**; 18:854–63.
11. Abuful A, Gidron Y, Henkin Y. Physicians' attitudes toward preventive therapy for coronary artery disease: is there a gender bias? Clin Cardiol **2005**; 28:389–93.
12. Hirschhorn LR, McInnes K, Landon BE, et al. Gender differences in quality of HIV care in Ryan White CARE Act-funded clinics. Womens Health Issues **2006**; 16:104–12.
13. Fultz SL, Goulet JL, Weissman S, et al. Differences between infectious diseases–certified physicians and general medicine–certified physicians in the level of comfort with providing primary care to patients. Clin Infect Dis **2005**; 41:738–43.