Management of Dyslipidemia in Patients With Human Immunodeficiency Virus

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Dyslipidemias are more common in the patient population with human immunodeficiency virus (HIV). Combination antiretroviral therapy (ART) has dramatically reduced HIV-associated morbidity and mortality and has transformed HIV disease into a chronic, manageable condition. As a result, non–AIDS-related illnesses, including cardiovascular diseases, are now the leading causes of death in the HIV-infected population. Optimizing fasting lipid parameters plays an important role in reducing cardiovascular risk in this population. This review focuses on the management of dyslipidemia in HIV-infected individuals treated with combination ART.

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KEY WORDS

Human immunodeficiency virus • Dyslipidemia • Antiretroviral therapy • Cardiovascular risk

Combination antiretroviral therapy (ART) has dramatically reduced human immunodeficiency virus (HIV)-associated morbidity and mortality and has transformed HIV disease into a chronic, manageable condition.[1-4] Non–AIDS-related illnesses, including cardiovascular diseases, are now the leading causes of death in the HIV-infected population.[5-14] The review by Triant on the epidemiology of coronary heart disease in this supplement summarizes a series of studies which show that HIV infection confers an increased risk for coronary heart disease (*Rev Cardiovasc Med.* 2014;15[suppl 1]:S1-S8). There is growing body of evidence that suggests that HIV-associated factors such as chronic inflammation and immune activation, coupled with a high burden of traditional coronary risk factors in HIV-infected people, contribute to this heightened risk. In addition, some

specific antiretroviral medications, as reviewed by Mallon in this supplement (*Rev Cardiovasc Med*. 2014;15[suppl 1]:S21-S29), have been associated with an increased risk of myocardial infarction (MI). Specific antiretroviral medications have been linked to insulin resistance, lipodystrophy syndrome, and dyslipidemia. The review by Guaraldi and colleagues (*Rev Cardiovasc Med*. 2014;15[suppl 1]:S30-S37) provides a nice summary of the impact of contemporary antiretroviral medications on fasting lipid parameters using evidence from randomized clinical trials. This review focuses on the management of dyslipidemia in HIV-infected individuals treated with combination ART.

It has long been known that dyslipidemias are more common in people with HIV infection. Prior to the era of highly active ART (HAART), untreated HIV infection was observed to produce a progressive lipid "signature," often with dramatic decreases in low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterols and increases in triglyceride levels.[12] With immune reconstitution and viral suppression with initiation of HIV therapy, patients have a "return to health," generally accompanied by increases in total cholesterol, LDL, and triglycerides. The magnitude of these increases depends on patient factors such as genetics, diet, active versus sedentary lifestyle, and choice of antiretroviral agents. It is well recognized that antiretroviral medication may alter lipid parameters, some with more impact than others. Therefore, in selecting initial antiretroviral medications, HIV clinicians may consider the existing comorbidities and cardiovascular risk factors of patients and the lipid profile of the drug, as well as its antiviral potency, safety, and tolerability.

A lipid profile consisting of elevated total and LDL cholesterols and low HDL cholesterol is a classic risk factor for coronary artery disease. Therefore, it makes sense to improve an unfavorable lipid profile, as one way to modify the risk for a future cardiovascular event. However, this strategy is theoretical. There is an incomplete understanding of how lipid changes associated with HIV and/or its treatment impact the risk for a future cardiovascular event. It is appealing to believe that we will reduce cardiovascular events in our HIV patients by optimizing their lipid profiles, but currently, there is a paucity of data from prospective studies that definitively show that lipid management will reduce the incidence of cardiovascular events in this population.

Guidelines

Lipid treatment guidelines for HIV-infected people have long reflected the National Cholesterol Education Program (NCEP) guidelines from 2003, referenced by the HIV Medicine Association (HIVMA)/Infectious Diseases Society of America and AIDS Clinical Trial Group recommendations from that era.[15] The recent HIVMA 2013 Primary Care Guidelines for HIV[16] also refer to the NCEP guidelines. These guidelines all emphasize treatment to achieve lipid parameter goals (lower total cholesterol, LDL, and triglycerides; raise HDL).

However, recent American College of Cardiology/American Heart Association (ACC/AHA) guidelines[17] de-emphasize treatment to specific lipid goals. Instead, they recommend risk analysis to guide treatment (typically with a statin agent) based on 10-year risk of a cardiovascular event (MI or cerebrovascular accident). These new guidelines are accompanied by a risk calculator, which has been criticized for overestimating risk. Choice of a statin agent and dose depends on level of risk; titration of statin therapy to a particular lipid goal is not recommended. The approach of choosing statin therapy based on risk level rather than cholesterol goal is a new one that will require a change in treatment philosophy by providers.

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The ACC/AHA guidelines state they do not apply to HIV-positive populations or others with comorbidities that may impact risk. Therefore, it is challenging to apply these guidelines to HIV-infected populations. The risk calculator published by the ACC/AHA task force may not be accurate for HIV-infected patients. The investigators in the Data Collection on Adverse Events of Anti-HIV Drugs study have developed a risk calculator for HIV-infected patients,[18] but its application to the recommendations of the ACC/AHA task force is uncertain.

Approach to the HIV Patient With Dyslipidemia

Management of dyslipidemia in HIV-infected people involves a comprehensive approach that includes lifestyle counseling (diet, exercise, and appropriate weight), selection of antiretroviral drugs that do not exacerbate dyslipidemia, modification of antiretroviral regimen to improve dyslipidemia,

and (when necessary) utilization of lipid-lowering agents such as statin agents and fibrates.

Lifestyle

The HIV-infected patient with dyslipidemia should be counseled on the same lifestyle modification as discussed with the HIV-uninfected patient. Regular exercise is helpful in maintaining a healthy weight and general overall vigor, and has been shown to reduce triglycerides in HIV-infected people.[19] In addition, a low-fat diet and, more recently, a Mediterranean diet are recommended. Improvement in diet has been demonstrated to improve cardiovascular endpoints in the general population.[20] A diet high in fiber and/or use of a soluble fiber supplement (psyllium or oat bran) is also recommended. Studies showed that dietary changes improve lipid parameters in HIV-infected patients.[21,22] Because cigarette smoking is a major risk factor for cardiovascular disease, the smoker should be counseled to quit. Counseling, however, is time-consuming, and it is hard to change unhealthy habits such as smoking. For many people, it may be easier to take a pill than to change eating habits or engage in routine exercise. Despite these behavioral obstacles, the approach to reducing cardiac risk is not complete without counseling on lifestyle habits and choices that negatively impact cardiovascular health.

Studies showed that dietary changes improve lipid parameters in HIV-infected patients.

Choice of Initial HAART

The choice of initial HAART can have an impact on subsequent lipid parameters. There are differences in the lipid effect of guideline-preferred and commonly used initial antiretroviral regimens. The article by Guaraldi and associates in this supplement (*Rev Cardiovasc Med*. 2014;15[suppl 1]:S30-S37) provides a comparative analysis of guideline-preferred antiretroviral drugs on fasting lipid parameters. Older antiretroviral agents such as zidovudine, stavudine, and combination lopinavir/ritonavir tend to have a more deleterious effect on lipid levels and glucose metabolism. However, as drug therapy advances, newer antiretroviral agents with improved lipid profile are approved and become the standard of care.

Change of HAART

What are some common approaches to managing dyslipidemia in patients on HAART? Discontinuation of ART might improve lipid parameters, but it was shown in the Strategies for Management of Antiretroviral Therapy (SMART) study to actually increase the risk of cardiovascular events, likely due to an increase in inflammation and a clotting diathesis related to uncontrolled viremia.[23] This landmark study was designed to evaluate whether HIV patients might do better with intermittent "drug holidays" to spare the toxicities of ART, as long as their immune function is good. Instead, the study found that uncontrolled HIV viremia was associated with increased rates of cardiovascular, hepatic, and renal events.

Older antiretroviral agents such as zidovudine, stavudine, and combination lopinavir/ritonavir tend to have a more deleterious effect on lipid levels and glucose metabolism.

ART can have a deleterious effect on lipid parameters; therefore, modification of some or all drug component of an antiretroviral regimen can improve the lipid profile. However, this must be done with a careful eye toward maintaining viral suppression. The principle is to replace some or all of the antiretroviral drugs in the regimen with agents that have less (or no) effect on lipids, while maintaining viral suppression.

The lipid effect of various antiretroviral medications is based on findings from randomized, clinical trials comparing two (and sometimes three) HAART regimens, each differing by one, or at most two, drugs. As a rule, these studies are designed to compare the antiviral efficacy of two regimens, and lipid data are almost always collected and reported. In this way, it is possible to create a hierarchy of lipid effect among different antiretroviral drugs, ranging from agents with the most adverse lipid profile (certain protease inhibitors such as ritonavir-boosted lopinavir or fosamprenavir), to those with various intermediate degrees of lipid effect (ritonavir-boosted darunavir or atazanavir; the non-nucleoside agents efavirenz and nevirapine; the nucleoside fixed-dose combinations zidovudine/lamivudine and abacavir/lamivudine); to those with minimal or no adverse lipid effect (the non-nucleosides etravirine and rilpivirine; the integrase inhibitors raltegravir, dolutegravir, and possibly elvitegravir; the entry-inhibitor maraviroc; and the nucleoside/nucleotide fixed-dose combination tenofovir disoproxil fumarate/emtricitabine).

Based on this hierarchy of lipid effect, the HIV specialist can often modify a regimen by substituting one or more drug components of the regimen with more lipid-friendly or -neutral agents. Newer

TABLE 1

Examples of Antiretroviral Switch Studies Within and Between Antiretroviral Classes

Study	Classes	Drugs	TC	HDL	LDL	TG
Henry K et al[43]	NRTI to N(t)RTI	Abacavir/lamivudine to tenofovir disoproxil fumarate/emtricitabine	↓	No change	↓	↓
Mills AM et al[44]	NNRTI to NNRTI	Efavirenz to rilpivirine	↓	No change	↓	↓
Waters L et al[45]	NNRTI to NNRTI	Efavirenz to etravirine	↓	No change	↓	↓
Tebas P et al[46]	PI to NNRTI	Various PIs to rilpivirine	↓	No change	↓	↓
Martínez E et al[47]	PI to integrase strand transfer inhibitor	Various PIs to raltegravir	↓	↓	↓	↓

HDL, high-density lipoprotein; LDL, low-density lipoprotein; NNRTI, non-nucleoside reverse-transcriptase inhibitor; N(t)RTI, nucleoside and nucleotide reverse transcriptase inhibitor; PI, protease inhibitor; TC, total cholesterol; TG, triglycerides.

antiretroviral medications, in general, tend to have less effect on lipids than the older ones. A typical scenario might be that a patient was started on antiretroviral therapy years ago with agents that have more adverse lipid effects, causing or exacerbating dyslipidemia. It may be possible to improve lipid parameters by making changes in the antiretroviral regimen. Some prescribers frame this discussion to patients as "updating the regimen" as a way to explain to them that changing their antiretroviral medications may have a beneficial effect on their lipid levels.

A number of studies have validated the concept of switching antiretroviral drugs to reduce toxicities, including adverse lipid effects.

A number of studies have validated the concept of switching antiretroviral drugs to reduce toxicities, including adverse lipid effects. In most antiretroviral switch studies, maintenance of antiretroviral efficacy is the primary goal, with safety, including changes in lipid parameters, as a secondary endpoint. The least desirable outcome would be for the prescriber to change the patient's antiretroviral regimen in an effort to improve lipids, but in doing so induce virologic failure. Fortunately, there are many studies demonstrating that antiretroviral medications can be carefully switched while maintaining control of the virus.

Switch strategy may involve replacing one drug component with another in the same or different antiretroviral class by mechanism of action. A number of switch studies have demonstrated improvements in lipids on the new drug component or regimen. Tables 1 and 2 identify switch studies conducted to assess the changes in lipid parameters with antiretroviral drug substitution. In each of the five studies shown in Table 1, virologic control was maintained and lipid parameters improved. Table 2 shows the relative change (usually improvement) in various lipid parameters after a switch of ART. These and other studies guide our initial strategy when confronted with patients experiencing dyslipidemia on suppressive ART.

Some switch studies have provided important lessons with their less-than-positive results. In the SWITCHMRK study,[24] patients who had virologic suppression on a regimen containing lopinavir/ritonavir were switched to raltegravir. Their lipid levels improved, but there was an excess of virologic failure in the group that switched from lopinavir/ritonavir to raltegravir. It appears that, in this case, not enough attention was paid to creating a new regimen that would adequately suppress resistant viruses harbored by some of the study volunteers. This is a lesson that antiretroviral switches need to be performed by an expert HIV provider, with the primary goal of maintaining viral suppression, while seeking a secondary goal of improvement in lipids and perhaps other parameters.

It is well-recognized that protease inhibitors such as ritonavir, used either as an antiviral agent or a pharmacokinetic booster, can adversely affect lipid parameters. In the Atazanavir Ritonavir Induction with Epzicom Study (ARIES) study,[25] patients virologically suppressed on a regimen of abacavir/

TABLE 2

Relative Change From Baseline in Fasting Lipid Parameters in Antiretroviral Switch Studies

Antiretroviral Switch Trials	SWIFT[a] ABC/3TC to TDF/FTC		SWITCHMRK 1[b] LPV/RTV to RAL		SWITCHMRK 2[b] LPV/RTV to RAL		SPIRIT[a] PI+RTV to RPV/TDF/FTC	
	ABC/3TC (n = 156)	TDF/FTC (n = 155)	LPV/RTV (n = 174)	RAL (n = 174)	LPV/RTV (n = 178)	RAL (n = 176)	PI + RTV (n = 156)	RPV (n = 155)
Other agent(s)	PI + RTV	PI + RTV					TDF/FTC	TDF/FTC
Change at	Week 48	Week 48	Week 12	Week 12	Week 12	Week 12	Week 24	Week 48
Total cholesterol (fasted)	−3	−21	0 (+0.7%)	−31 (−12.8%)	0 (+1.3%)	−35 (−12.4%)	−1	−24
HDL cholesterol (fasted)	0	−1	0 (+0.8%)	4 (−0.9%)	0 (−2.5%)	0 (−0.6%)	−1	−2
LDL cholesterol (fasted)	+2	−7	0 (+2.1%)	−8 (−2.4%)	0 (−0.6%)	0 (+4.0%)	0	−16
Triglycerides (fasted)	−9	−18	+4 (+3.6%)	−31 (−41.5%)	+8 (+8.2%)	−39 (−42.8%)	+3	−64

[a]Median change from baseline in fasting lipid parameters (mg/dL).
[b]Percentage change in parentheses.
3TC, lamivudine; ABC, abacavir; LPV/RTV, lopinavir/ritonavir; PI, protease inhibitor, RAL, raltegravir; RTV, ritonavir; SPIRIT, Switching Boosted PI to Rilpivirine in Combination With Truvada as a Single-Tablet Regimen; SWIFT, Switching From Lamivudine/Abacavir (3TC/ABC) to Emtricitabine/Tenofovir DF (FTC/TDF); TDF/FTC, tenofovir disoproxil fumarate/emtricitabine.
Data from Eron JJ et al,[24] Campo R et al,[48] and Fisher M et al.[49]

TABLE 3

Pros and Cons of Classes of Lipid-lowering Agents for HIV-infected Patients

Class	Pro	Con
Statins	Effective at lowering LDL/non-HDL; may lower TG, raise HDL	Some have adverse interactions with some antiretroviral agents
	Best (only?) endpoint data	Risk of diabetes
	Anti-inflammatory effect may theoretically have additional benefit in HIV	Risk of myalgias/rhabdomyolysis
	Strongly supported in new ACC/AHA guidelines	Cost issues with nongeneric statins
Ezetimibe	Lowers LDL	Endpoint data not encouraging in HIV-negative studies
		Little support in new guidelines
Fibrates	Raise HDL, lower TG marker data in HIV	Little support in new guidelines except for hypertriglyceridemia
Fish oil/omega-3 fatty acid	Lowers TG	Little support in new guidelines except for hypertriglyceridemia
	Useful if TG > 500 mg/dL to prevent pancreatitis	
Niacin	Raises HDL	Risk of hepatotoxicity
		Endpoint data not encouraging
		Little support in new guidelines

ACC/AHA, American College of Cardiology/American Heart Association; HDL, high-density lipoprotein; HIV, human immunodeficiency virus; LDL, low-density lipoprotein; TG, triglycerides.

lamivudine plus ritonavir-boosted atazanavir were randomized to discontinue versus continue ritonavir to evaluate changes in lipid parameters. In the study, virologic suppression was maintained and the regimen was simplified by this strategy, which is arguably a benefit to the patient. However, lipid changes were minimal, other than a decrease in triglycerides apparently related to the elimination of ritonavir. Here the lesson is that "deboosting" a protease inhibitor regimen does not necessarily have a dramatic beneficial effect on lipids and should not be done with that sole goal.

Lipid-lowering Agents

The cornerstone of dyslipidemia management involves the use of lipid-lowering medications. There are several classes of drug approved for this purpose (Table 3). Statins have by far the best endpoint data. For some nonstatin agents, it has been difficult to show an impact on cardiovascular endpoints, despite salutary lipid changes. The 2013 ACC/AHA guidelines[17] place great emphasis on statin therapy to reduce cardiovascular risk while de-emphasizing both the use of other lipid-lowering agents and the concept of treating to a goal LDL level. In addition to their lipid-lowering effect, statins may also reduce cardiovascular events via an anti-inflammatory effect that other classes of lipid-lowering agents do not have. This may be particularly relevant for the HIV-positive population, in whom chronic inflammation is an issue and a likely contributor to excess risk of cardiovascular disease.

In the following section, the term *favorable* to refers to reductions in total cholesterol, LDL and/or non-HDL cholesterol, total cholesterol to HDL ratio, and triglycerides; and/or elevations in HDL. *Unfavorable* lipid changes are elevations of these parameters.

Statin drugs lower total and LDL cholesterol, but have a lesser effect on HDL and triglycerides. Interactions with HIV medications are an issue with statin drugs. Some (simvastatin, for example) are metabolized by hepatic cytochrome P450 3A (CYP3A).[26] This enzyme is inhibited by the pharmacokinetic booster ritonavir and cobicistat used in some HIV regimens.[27,28] Lovastatin and simvastatin should not be used with boosted HIV regimens as this may result in excess toxicity from high levels of the statin. Other antiretroviral agents such as nevirapine and efavirenz induce CYP3A4, potentially reducing the efficacy of lovastatin and simvastatin by hastening their metabolism and increasing their systemic clearance.[29] Other statins, such as pravastatin, have fewer interactions, but their potency is low.[30] In a high-risk population such as those with HIV infection, it makes sense to choose a higher potency statin.

The statins of choice for people with HIV appear to be atorvastatin

and rosuvastatin. The former has some CYP3A metabolism, and levels can be increased by boosting agents, so the recommendation is to start at a low dose and titrate carefully. Rosuvastatin theoretically does not interact with HIV drugs; however, levels do seem to be increased by coadministration with ritonavir-boosted darunavir, and its lipid effect is paradoxically blunted.[28,31] Pitavastatin, the newest statin agent, seems to be relatively free of interactions with HIV medications.[32,33] A study in an HIV-positive population has shown better efficacy with pitavastatin than pravastatin.[32]

Not all patients tolerate statin drugs. Side effects may be treatment limiting or at least dose limiting. Myalgias are the most common cause of statin discontinuation. Statin-related myalgias may be diffuse or localized to a particular muscle group.[34] HIV-infected individuals may be especially prone to this complication of statin therapy, both because of preexisting myalgias related to chronic inflammation, and potentially because of drug interactions between statins and antiretroviral agents. Creatine phosphokinase (CPK) elevations may or may not accompany statin-related myalgias, so a normal CPK level does not rule out whether a patient's complaint of muscle pain is related to statin therapy. It is often necessary to discontinue the statin to see if the myalgias improve. If they do, rechallenge may be attempted with a lower dose of the same statin or the lowest dose of a more potent statin. Frank rhabdomyolysis is a rare but feared adverse effect of statins.[35] In this case, CPK will uniformly be elevated and the statin must be discontinued. Coadministration of a CYP3A-metabolized statin with ritonavir or cobicistat can result in excessive statin levels, increasing the risk of this complication.

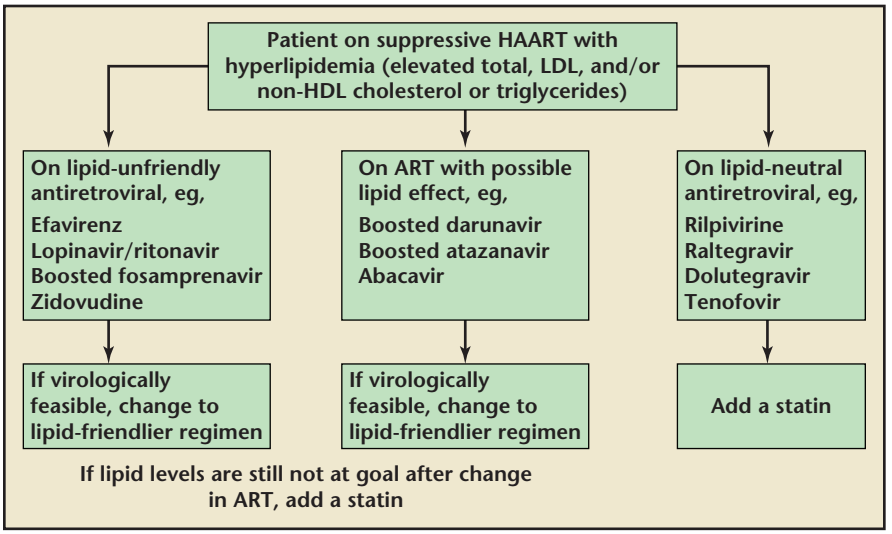

Figure 1. Pharmacologic approach to lipid levels in the HIV-infected patient. If triglyceride levels are not optimized with a statin, fish oil or fenofibrates should be considered. ART, antiretroviral therapy; HAART, highly active antiretroviral therapy; HDL, high-density lipoprotein; HIV, human immunodeficiency virus; LDL, low-density lipoprotein; lipid friendly, lowering total cholesterol and LDL and/or raising HDL and/or lowering triglycerides; lipid neutral, not associated with significant changes in lipid parameters; lipid unfriendly, associated with lipid changes in the opposite direction of lipid friendly.

There has been some suggestion that statins can impair cognitive function.[36] This is a particular concern for people living with HIV, because there is evidence of subtle cognitive decline over time in some individuals with even well-controlled HIV. However, a recent meta-analysis[37] finds no evidence of an association between statins and cognitive decline. There is also some evidence of increased risk of diabetes in people taking certain statin drugs, but the risk is small.[38]

For HIV-positive patients with elevated triglyceride levels and/or low HDL cholesterol, fish oil and fibrates (fenofibrate in particular) have shown efficacy.[39,40] The impetus to lower triglyceride levels becomes more urgent when they exceed 500 mg/dL, as there is a risk of pancreatitis; in addition, lowering triglyceride levels may also reduce the risk of cardiovascular events.[22,39-41]

For HIV-positive patients with hypercholesterolemia who cannot tolerate a statin drug, or who do not achieve lipid goals with statin therapy, ezetimibe has been shown to produce significant favorable improvements in lipid levels.[42] However, in HIV-negative individuals it has yet to be proven that ezetimibe therapy can alter cardiovascular outcomes, even with improvement in lipid markers. As with other lipid-lowering agents, there are no cardiovascular outcomes data for ezetimibe in the HIV population.

In practice, the pharmacologic approach to lipid levels in the HIV-infected patient is a hybrid strategy of (1) minimizing the lipid effect of ART and (2) using lipid-lowering agents where appropriate. Figure 1 is a flow diagram outlining this approach. Table 4 illustrates an example of a patient in the author's practice in whom this approach was successfully followed.

Conclusions

Dyslipidemias are more common in the HIV patient population. Cardiovascular events are also more common and may occur at a younger age in those with HIV. Optimizing fasting lipid parameters plays an important role in reducing cardiovascular risk in this population. The means to achieve this goal include lifestyle changes,

TABLE 4

Example of Modifications in ART Regimen and Addition of Statin to Bring Lipid Levels to Goal

Visit	ART Regimen	Statin Regimen	Total Cholesterol (mg/dL)	HDL (mg/dL)	Triglycerides (mg/dL)	LDL (mg/dL)
Initial visit	Efavirenz/TDF/ emtricitabine FDC	—	268	46	237	175
Follow-up	Rilpivirine/TDF/ emtricitabine FDC	—	217	46	148	141
Subsequent follow-up	Rilpivirine/TDF/ emtricitabine FDC	Atorvastatin, 20 mg	163	42	90	103

Actual laboratory values from a real patient. Time between visits was approximately 8 months.
This patient presented on efavirenz/TDF/emtricitabine FDC with undetectable HIV RNA but unfavorable lipid profile in the setting of additional cardiovascular risk factors. After discussion, his regimen was changed to rilpivirine/emtricitabine/TDF with the hope of improving his lipid parameters without adding additional medication. This change resulted in improvement of lipid levels, although short of goal ranges. Ultimately, the patient agreed to start atorvastatin, resulting in a satisfactory lipid profile. Viral load remained undetectable throughout.
ART, antiretroviral therapy; FDC, fixed-dose combination; HDL, high-density lipoprotein; HIV, human immunodeficiency virus; LDL, low-density lipoprotein; TDF, tenofovir disoproxil fumarate.

optimization of ART for minimal adverse lipid effect, and prescription of lipid-lowering agents. Some important needs remain unmet; we need to improve our ability to predict cardiovascular risk in HIV-infected patients in order to guide lipid-lowering efforts, and we need outcomes studies to determine whether lipid-lowering efforts result in a reduction of cardiovascular events in this population. ■

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MAIN POINTS

- Combination antiretroviral therapy (ART) has dramatically reduced HIV-associated morbidity and mortality and has transformed HIV disease into a chronic, manageable condition. As a result, non–AIDS-related illnesses, including cardiovascular diseases, are now the leading causes of death in the human immunodeficiency virus (HIV)-infected population. Dyslipidemias are more common in the patient population with HIV. Optimizing fasting lipid parameters plays an important role in reducing cardiovascular risk in this population.
- Recent American College of Cardiology/American Heart Association (ACC/AHA) guidelines de-emphasize treatment to specific lipid goals; instead, they recommend risk analysis to guide treatment (typically with a statin agent) based on 10-year risk of a cardiovascular event (myocardial infarction or cerebrovascular accident). However, the ACC/AHA guidelines state they do not apply to HIV-positive populations or others with comorbidities that may impact risk; therefore, it is challenging to apply these guidelines to HIV-infected populations because the risk calculator published by the ACC/AHA task force may not be accurate for HIV-infected patients.
- The choice of initial antiretroviral therapy can have an impact on subsequent lipid parameters; older antiretroviral agents such as zidovudine, stavudine, and combination lopinavir/ritonavir tend to have a more deleterious effect on lipid levels and glucose metabolism.
- The cornerstone of dyslipidemia management involves the use of lipid-lowering medications. There are several classes of drug approved for this purpose; statin drugs have by far the best endpoint data. For some nonstatin agents, it has been difficult to show an impact on cardiovascular endpoints, despite salutary lipid changes.

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