



Protease inhibitors and changes in lipid profiles

by Anne Drummond

The association between highly active antiretroviral therapy (HAART) and abnormalities in glucose and lipid metabolism was observed soon after protease inhibitors (PI) were included in antiretroviral regimens. In recent years there have been increasing reports of HIV-related lipodystrophy syndrome—a combination of metabolic disorders and morphological changes—among patients treated with PIs. The syndrome has assumed considerable importance because dyslipidemia and other metabolic disorders increase the risk of coronary heart disease in PI-treated persons. In addition, patients experience significant distress and isolation as a result of changes in their body image.

It is well known that nearly half of all patients on PIs show elevated levels of triglycerides, total cholesterol, low-density lipoprotein (LDL, or “bad” cholesterol), insulin, and fasting glucose. These changes begin soon after initiating treatment with PIs, often within a few weeks. The extent of the changes in lipoproteins and triglycerides, however, has not been quantified in an observational setting.

Dr. Adrian Levy and his co-workers at the BC Centre for Excellence in HIV/AIDS set out to explore the direction and magnitude of change in lipid profiles over 12 months in a large group of patients receiving PIs. They conducted the study between August 1996 and January 2002. There were 679 patients; 91 percent of them were male, the median age was 38 years old, and the median baseline CD4 count was 210 cell/mm³. All patients initiated HAART that included a nucleoside analog and a protease inhibitor. Investigators followed patients for a median of 47 months, and patients had at least three blood lipid measurements during this time.

Twelve months after initiation of PI treatment, researchers found statistically significant increases of 20 percent and 22 percent in total cholesterol and triglycerides, respectively.

These, and other results, suggest that persons on HAART including PIs are at an increased risk for cardiovascular disease. This growing body of evidence implicating PIs in metabolic abnormalities also creates a significant clinical dilemma. Protease inhibitor-based HAART is very effective in achieving and maintaining undetectable viral loads, therefore discontinuing PI treatment, even in patients with dyslipidemia is undesirable; yet the effects of PIs on lipid levels are of considerable consequence. A possible solution is to initiate treatment with drugs that lower cholesterol in the blood, such as statins and/or fibrates. Statins have proven effective in preventing cardiovascular disease in HIV-negative patients, but as yet their effectiveness for PI-induced dyslipidemia has not been confirmed.

The demonstrated lipid abnormalities in combination with the predominance of men, high rates of smoking, and aging in the HIV-positive population means the future occurrence of cardiovascular disease in this group is likely to be high. ⊕

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