Combination Antiretrovirals Double Risk of MI in Patients With HIV

ARTICLES BY
DIANA MAHONEY
New England Bureau

BOSTON — Patients receiving combination antiretroviral therapy to suppress HIV are at significantly increased risk for myocardial infarction, and the longer they take the drugs, the higher the risk, according to recent findings from an ongoing multicenter study.

Because the benefits of the so-called AIDS cocktails still far outweigh the associated cardiovascular risks, physicians should focus on convincing at-risk patients to modify lifestyle-related risk factors, rather than discontinuing the potent medications, Jens Lundgren, M.D., said during a symposium on the cardiovascular effects of antiretroviral therapy (ART) at a conference on retroviruses and opportunistic infections.

"In 1994, before we had combination antiretroviral therapy, the 1-year mortality of HIV-infected patients was 23%. Today, the mortality rate is about 1.5%-2%," said Dr. Lundgren of the University of Copenhagen. "Clearly, the drugs are working, and patients are living longer. Now we're starting to see some of the longer-term events that we wouldn't be seeing if the drugs were not effective."

Among 23,441 HIV-infected patients (median age 39 years) being treated with conventional or highly active ART (HAART) in the University of Copenhagen Data Collection on Adverse Events of Anti-HIV Drugs (DAD) trial, 277 myocardial infarctions were reported—about twice the number seen in the untreated population.

"Those are relatively small numbers, but this is a young population," Dr. Lundgren said. "You wouldn't expect that many myocardial infarcts in that young a population. Still, the overall risk of having a heart attack remains low." And even though there's no question that treatment with antiretroviral drugs is an independent risk factor for MI, he said, "we do not have enough events to look at the contribution of HIV drug classes."

In a separate analysis of the DAD data collected between 1999 and February 2004, Wafaa El-Sadr, M.D., of Columbia University, New York, and colleagues determined that patients' risk of MI rose 17% with each additional year of treatment after adjustment for other potential risk factors, and the increase was independent of both gender and age.

The risk increase was maintained when the investigators included repeat MIs in the analysis, and when they considered only patients who were treatment-naive when the study started. The risk increase was also stable when they included only those participants with definite MIs. Not surprisingly, Dr. El-Sadr said, the odds of having a heart attack were independently increased by male gender, family history, previous cardiovascular disease, smoking, and every 5-year increment in age.

'You wouldn't expect that many myocardial infarcts in that young a population. Still, the overall risk of having a heart attack remains low.'

Physicians should routinely evaluate HIV patients' risk of heart disease prior to initiating drug therapy by conducting thorough medical histories and checking cholesterol levels and blood pressure, Dr. Lundgren advised. At-risk patients should be advised to modify some of the conventional risk factors, such as diet, exercise, and smoking, in an effort to compensate for some of the effects of the HIV drugs.

For example, the increased MI risk seen with ART is comparable to that associated with smoking, "and a lot of HIV patients, particularly in Europe, are smokers," Dr. Lundgren said at the conference, sponsored by the Foundation for Retrovirology and Human Health. "Quit smoking, and your heart forgives you."

There may also be a role for lipid-lowering therapy. According to a multifactor analysis of the DAD findings, changes in total cholesterol, triglycerides, and high-density lipoproteins were linked to increases in MI risk. The correlation between some antiretroviral drugs—particularly protease inhibitors—and increased lipids might partly explain the relationship between increased MI risk and duration of therapy, "but it cannot explain the whole increase," Dr. El-Sadr said.

In the absence of definitive data on cause and effect, "it seems reasonable to evaluate lipid disorders in HIV-infected patients according to the same criteria used in the general population," added symposium participant Esteban Martinez, M.D., of the University Hospital Clinic in Barcelona, Spain. "The impact of individual antiretroviral drugs on lipid parameters should be included among the factors to be considered when prescribing combination antiretroviral therapy," he said.

Protease inhibitors in particular have been linked to increased lipid levels. Therefore, for treatment-naive patients with cardiovascular risk factors, Dr. Martinez advised avoiding drug regimens that include these agents and prescribing lipid-lowering therapy if necessary.

For at-risk patients already on HAART, lipid-lowering therapy should be tried first, followed by a change in the drug regimen if the desired effect is not achieved. For example, at-risk patients on a regimen that includes protease inhibitors should be switched to nonnucleoside reverse transcriptase inhibitors or to an ART agent that has been shown to have lesser effects on lipids, such as atazanavir (Reyataz), Dr. Martinez recommended. Patients who take stavudine (Zerit) should switch to tenofovir (Viread), he advised. ■

Fish Oil Can Improve Triglyceride Levels

BOSTON — Daily ingestion of fish oil tablets can decrease blood lipid levels in HIV-infected patients with hypertriglyceridemia associated with antiretroviral drug therapy, a French study has shown.

The prospective study included 122 HIV-infected patients taking antiretroviral therapy (ART); 58 were randomized to receive two 1-g capsules of a fish oil supplement t.i.d. This group had a median 26% reduction in triglyceride levels from baseline. In contrast, the median triglyceride levels of patients given a placebo increased 1%, Pierre de Truchis, M.D., reported at a conference on retroviruses and opportunistic infections.

"Triglyceride levels normalized in 22% of the [fish oil] recipients, but in only 7% of the placebo group," said Dr. de Truchis of Hôpital Raymond Poincaré, Garches, France. Neither total nor HDL cholesterol levels changed over the course of the study in either group.

During a subsequent 8-week open-label phase of the study, patients in the original fish oil group maintained their triglyceride reductions while continuing fish oil supplementation, and patients originally given placebo had a median 21% decrease with the switch to fish oil tablets, he said at the conference, sponsored by the Foundation for Retrovirology and Human Health.

At baseline, all patients in the study had triglyceride levels greater than 2 g/L with a mean triglyceride level of 4.5 g/L after 4 weeks of following an appropriate diet. Patients with baseline levels greater than 10 g/L were not randomized in the initial trial, but 10 such patients were included in the open-label phase. After 8 weeks of supplementation, this group had a 44% reduction in triglycerides, said Dr. de Truchis, suggesting that there was a benefit in patients with severe blood lipid elevation.

The fish oil supplements were well tolerated, and there were no significant differences in adverse events between groups. Because of their efficacy and tolerability and the absence of drug interactions, fish oil supplements represent a potential first-line therapy for ART-associated hypertriglyceridemia, he said.

"Reducing blood lipid increases may lower the increased risk of cardiovascular disease associated with HIV infection and with antiretroviral therapy," he added.

The fish oil supplementation in the study included a total of about 1 g/day each of the omega-3 fatty acids eicosapentaenoic acid and docosahexaenoic acid—the equivalent of two meals containing oily fish per day. This formulation has been shown to reduce LDL cholesterol and triglyceride levels in adults without infection, Dr. De Truchis said. ■

Markers for Cardiovascular Risk Assessed in HIV Infection

BOSTON — The concurrent presence of metabolic syndrome and subclinical atherosclerosis in HIV infection may help identify individuals at increased risk for cardiovascular disease, a study has shown.

The findings, reported by Alexandra Mangili, M.D., in a poster presentation at a conference on retroviruses and opportunistic infections, could be used to guide therapy designed to prevent cardiovascular events in people with AIDS or HIV infection.

In a longitudinal study examining nutritional and metabolic parameters in HIV infection, Dr. Mangili and colleagues at Tufts University in Boston measured common carotid and internal carotid intima-medial thickness (IMT) by B-mode ultrasonography in 327 HIV-infected patients. Coronary calcium score was also measured by high-resolution ECG-synchronized computed tomography.

The investigators compared these parameters in patients with and without signs of metabolic syndrome, defined as the presence of at least three of the following: abdominal obesity, hypertriglyceridemia, low HDL cholesterol, hypertension, and elevated fasting glucose.

After adjustment for sex, age, race, and smoking, individuals with metabolic syndrome had significantly higher common carotid IMT values than did patients without metabolic syndrome. The metabolic syndrome patients were also more likely to have abnormal coronary calcium scores, but not internal carotid IMT values, Dr. Mangili said at the conference, which was sponsored by the Foundation for Retrovirology and Human Health.

CD4 cell counts, viral load values, and use of highly active antiretroviral regimens, protease inhibitors, and nonnucleoside reverse transcriptase inhibitors were similar between patients with and without metabolic syndrome, she noted.

Subclinical carotid and coronary atherosclerosis are independent predictors of adverse cardiac events, and there is increasing evidence that metabolic syndrome is predictive of cardiovascular disease. The association seen in this study population between metabolic syndrome and subclinical atherosclerosis as determined by elevated IMT and coronary calcium adds to the growing body of knowledge linking HIV infection and/or treatment to an increased risk of cardiovascular events, Dr. Mangili noted.

The increased cardiovascular risks for HIV patients with both metabolic syndrome and subclinical atherosclerosis should be considered when planning their treatment, she said. ■

Pages 62a—62b◊