AIDS Cocktails Drive Up Risk of Heart Disease

BY DIANA MAHONEY
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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, 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—approximately twice the number seen in the untreated HIV-infected 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.

For at-risk patients already on HAART, lipid-lowering therapy should be tried first, followed by a change in drug regimen if the desired effect is not achieved.

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.

HIV patients' risk of heart disease should be evaluated 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. ■

Daily Fish Oil Supplement Tamed ART-Related Triglyceride Rise

BY DIANA MAHONEY
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BOSTON — Daily ingestion of fish oil tablets can decrease blood lipid levels in HIV-infected patients with hypertriglyceridemia associated with antiretroviral drug therapy, according to the results of a French study.

The prospective investigation 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 experienced 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 experienced 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 of the 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 experienced 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, Dr. de Truchis said. 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. "Reducing blood lipid increases may lower the increased risk of cardiovascular disease associated with HIV infection and with antiretroviral therapy," he said.

The fish oil supplementation in this 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, according to Dr. De Truchis. ■

When to Start HAART? Take Key Steps First Before Beginning Tx

SAN FRANCISCO — The debate continues to rage on over when to initiate highly active antiretroviral therapy for patients with HIV disease.

At a meeting on HIV management, sponsored by the University of California, San Francisco, Paul A. Volberding, M.D., joked that the answer is obvious: before it's too late, but after it's too early.

There is a series of steps that must be taken before antiretroviral therapy begins.

But whatever the clinician decides, there is a series of steps that must be taken before antiretroviral therapy begins, said Dr. Volberding of the Veterans Affairs Medical Center in San Francisco:

► Confirm the HIV results. "We [recently] had in the Bay Area yet another case of a person who had been followed for HIV infection without anyone noticing that his HIV test was negative," Dr. Volberding said.

► Take a detailed health history and conduct a thorough physical exam.

► Get a CBC and a chemistry profile.

► Order a CD4 cell count and a plasma HIV RNA measurement, Dr. Volberding said.

► Consider doing resistance testing. "I think we're at the point where baseline resistance testing should be recommended in all cases," Dr. Volberding said, noting that this step is not yet part of official practice guidelines.

► Assess the patient's readiness for treatment and the likelihood that he or she will be adherent.

► Refer the patient for an ophthalmology exam if the CD4 count is below 100 cells/ L.

► Make sure female patients get a gynecologic exam with a Pap smear.

► Test for syphilis with a rapid plasma reagin test or a Venereal Disease Research Laboratory test.

► Test for tuberculin with a purified protein derivative test.

► Order a chest x-ray.

► Order hepatitis A, B, and C serology.

► Order a toxoplasma IgG test.

► Order a fasting glucose and a lipid panel.

—Robert Finn