Antivirals May Affect Brain Pathology in HIV

BY NANCY WALSH
New York Bureau

BOSTON — HIV-infected patients treated with an antiretroviral regimen that included a nonnucleoside reverse transcriptase inhibitor are less likely to develop primary HIV brain pathology than are those who never received one of these agents, according to an autopsy study.

Before the era of highly active antiretroviral therapy (HAART), the incidence of inflammatory HIV brain pathology (HBP) was approximately 20%, and it is not yet clear whether antiretroviral drugs enter the brain in sufficient concentration to suppress HIV replication and prevent the development of leukoencephalopathy or microglial nodular encephalitis, Dr. Ian P. Everall said at the 15th Conference on Retroviruses and Opportunistic Infections.

In the first large-scale autopsy study, 392 brains were analyzed to assess the influence of a class of antiretrovirals on the risk of developing HBP.

To address this question, researchers performed an autopsy study on patients enrolled in the National NeuroAIDS Tissue Consortium, which was formed in 1998 to aid in research efforts to understand the effects of HIV infection on the brain. The consortium is funded by the National Institute of Mental Health and the National Institute of Neurological Disorders and Stroke.

To date, more than 2,000 patients have enrolled in the consortium; these patients provide demographic, medical, and psychological data, as well as information on medications used, and they allow access to their tissues after death.

A total of 392 brains were analyzed in the first large-scale autopsy study to assess the potential influence of a class of antiretrovirals on the risk of developing HBP, said Dr. Everall, a professor of psychiatry at the University of California, San Diego.

Currently, the primary classes of HIV drugs are protease inhibitors (PIs), nucleoside reverse transcriptase inhibitors (NRTIs), and nonnucleoside reverse transcriptase inhibitors (NNRTIs). A total of 76 patients were found to have had HBP on autopsy. When this group was compared with the non-HBP group, no differences were found in median age (45 years), sex (primarily male), or race and ethnicity. Mean disease duration was 11 years in both groups.

There also were no differences in mode of disease transmission, which was important because previous studies had suggested that certain groups such as intravenous drug users had higher rates of HBP, Dr. Everall said at the meeting, which was sponsored by the Foundation for Retrovirology and Human Health and the CDC.

The prevalence of HBP was 28% among the 123 patients who had not received a HAART regimen during the study. Among patients whose regimens included a PI plus an NRTI, the prevalence was 22%. Among those who had received an NRTI alone, the prevalence was 17%.

The prevalence was lower, at 12%, among patients whose exposure included an NNRTI plus an NRTI or all three classes of drugs.

Multivariate analysis controlling for demographic and clinical variables, including CD4 count nadir and degree of recovery, found that the only significant predictor of HBP by drug class was the last HIV viral load measurement, which was 5.3 $\log_{10}$ copies/mL in the HBP group and 4.2 $\log_{10}$ copies/mL in the non-HBP group.

After controlling for viral load, the class of drug exposure was no longer significant. "It's slightly confusing," Dr. Everall said.

"We think an explanation for this is that the last viral load assessment was done within 6 months of death, but exposure to classes of antiretrovirals was cumulative over the study, with the effect of drug exposure being partly negated by the viral load," he said.

These results cannot offer a final conclusion, Dr. Everall cautioned, but it would appear that the class of drugs and viral load together may influence the risk of HBP. ■