HIV in the Brain Usually Matches Levels in the Blood

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People with undetectable HIV levels in the blood are also likely to have undetectable levels in the brain, according to a study presented February 19 at the 17th Conference on Retroviruses and Opportunistic Infections (CROI) in San Francisco. However, the study doesn't fully answer whether people living with HIV must be on antiretrovirals (ARV) that penetrate the central nervous system in order to prevent damage to the brain.

The study involved an analysis of data from the CNS HIV Antiretroviral Therapy Effects Research (CHARTER) study, which is following 1,562 people living with HIV who are at various stages of disease and who have different histories of ARV therapy use. CHARTER is exploring relationships between HIV and the central nervous system (CNS), and the study is being conducted at six research sites across the United States.

CHARTER researchers have also found that maintaining high CD4 cell counts is independently associated with a reduced risk of brain damage in people living with HIV. These results were also reported at CROI

Scott Letendre, MD, from the University of California in San Diego presented a study evaluating the relationship between HIV levels in the blood and in the cerebrospinal fluid (CSF), along with the effects of ARV therapy.

Previous studies have suggested that the higher a person's virus levels in the brain, the more likely he or she might be to suffer from problems with cognitive performance (for example, memory and concentration) and to have areas of visible brain damage on sophisticated scans. Because measuring virus levels in the CSF can be a complicated procedure, it is important to understand the relationship between what is happening with the virus in the blood and what is happening in the brain in order to rule out the need for more invasive testing. Exploring this relationship was a primary objective of Letendre's study.

Viral Load in Blood and CSF

Letendre's team analyzed data from 1,221 CHARTER participants who had viral load measurements in both blood and CSF. Roughly 31 percent of those participants were taking ARV therapy. The average age was 43, and 62 percent had a history of an AIDS diagnosis. The average

lowest-ever (nadir) CD4 count was 175. Most people on ARV therapy had been on their current regimen for about one year, and 55 percent had undetectable HIV levels in their blood.

The factors that predicted whether a person would have detectable virus in the brain included older age, a higher viral load in blood, a lower current CD4 count and a lower CD4 nadir.

When Letendre and his colleagues limited their analysis to include only those taking ARV therapy, other factors became associated with having detectable HIV in CSF. They include a higher blood viral load level, non-white ethnicity and a CD4 count less than 200.

In both cases, whether on or off ARVs, virus levels in blood were strongly associated with virus levels in the CSF.

The Effect of ARVs

Letendre and others have previously estimated the degree to which various ARVs penetrate into the brain, called a central nervous system penetration effectiveness (CPE) score. CPE scores have been given to the individual ARVs, with a high score (4) demonstrating better penetration than a lower score (1). The combined CPE score of a regimen comes from adding the CPE scores of the individual drugs included in the regimen.

In this study, Letendre and his colleagues found that people with a high combined CPE score maintained better control of virus in their cerebrospinal fluid. For instance, 91 percent of people whose regimen had a high CPE score (9 or higher) maintained an undetectable viral load in the CSF, compared with just 57 percent of people with a CPE of 3 or less.

Examples of drugs known to penetrate the CNS well include Kaletra (lopinavir plus ritonavir), Viramune (nevirapine) and abacavir (found in Ziagen and Epzicom). Examples of drugs that do not penetrate the CNS well include tenofovir (found in Viread, Truvada and Atripla) and Viracept (nelfinavir).

Viral Load and Mental Functioning

Finally, Letendre reported on the impact of CSF viral load on psychoneurological performance, which measures aspects such as memory and concentration. When Letendre's researchers looked at the contribution of CSF viral load, independent of anything else, they found that detectable virus in the CSF did not predict poorer psychoneurological performance.

This finding does not fully answer whether someone must be on an HIV treatment regimen containing CNS-penetrating ARVs to stave off potential brain damage caused by the virus. Other studies have questioned this theory.

If a person had detectable virus in the blood, however, and if HIV levels in the brain were as high as those in blood—or higher—he or she was more likely to see a decline in psychoneurological

performance.

Letendre concluded by saying that measuring HIV in the blood gives a very good indication of what is happening in the brain. In other words, people with undetectable HIV in blood are likely to have undetectable virus in the CSF—and be better protected against signs and symptoms of brain damage—especially if they have maintained higher CD4 counts.

In people not taking ARVs, older age and low CD4s (both current and nadir) were associated with poorer control of virus in the CSF. In people who were taking ARVs, poor adherence, lower ARV brain penetration and non-white ethnicity were associated with higher viral loads in CSF.

Letendre cautioned, however, that the findings about age and ethnicity might be due to overlapping risk factors. For example, older people had usually been living with the virus for longer, and non-white participants were more likely to also be infected with hepatitis C.
