Epilepsy Drug Doesn’t Reduce HIV Reservoir

June 18, 2008

Long-term use of a drug commonly used to treat bipolar disorder and epilepsy does not reduce the reservoir of long-lived HIV-infected CD4 cells, say the authors of a study published in the June 19 issue of *AIDS*. These new data seriously challenge the results of a preliminary study suggesting that valproic acid, also known as Depakote, could work in tandem with antiretrovirals (ARVs) to eradicate HIV from the human body.

Researchers learned in the late 1990s that eradication of HIV infection is an unlikely possibility, due to the existence of a population of HIV-infected CD4 cells that remain inactive for many years and thus are not affected by ARVs. In 2002, a research team led by David Margolis, MD, at the University of North Carolina, began to study valproic acid because of its potential to force HIV DNA out of these long-lived cells, thereby making the virus susceptible to ARV therapy. Margolis’s initial research was promising, with the addition of valproic acid resulting in a reduction in the number of resting cells infected with HIV DNA. More recent studies have called these results into question.

To study the effect of long-term use of valproic acid on the otherwise unreachable HIV reservoir, Nathalie Sagot-Lerolle, MD, from the Paris Descarte Laboratory of Virology, and her colleagues conducted a series of tests involving blood samples collected from 24 HIV-positive patients. All of the patients had to have been on ARV treatment for at least two years and maintained viral loads below 50 copies for the duration of treatment. Eleven of them had also been on valproic acid treatment for two years—five because of brain infections and six because of epilepsy. Their blood samples were compared with the 13 who had not taken valproic acid, but who were similar in other characteristics such as age, gender and CD4 counts.

Sagot-Lerolle’s team found that the patients on valproic acid had the same number of inactive HIV-infected cells as those who’d never taken valproic acid. Moreover, when the researchers looked at the ability of the infected cells to reproduce infectious virus, known as replication competency, both groups looked the same. These results suggest that even after two years of valproic acid treatment, the size of the reservoir of HIV-infected cells does not decrease.

The authors suggest that valproic acid be studied in combination with other promising treatments that target the HIV reservoir.

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