Unexpected Finding: Penetration of ARVs Into Nervous System Doesn't Protect the Brain

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While antiretroviral (ARV) drugs known to penetrate into the cerebrospinal fluid (CSF)—and thus possibly the brain—do lower HIV levels in the brain, they do not appear to protect against detrimental changes in thinking, memory and physical coordination. This is the conclusion of a study published in the July 17 issue of *AIDS*.

Infectious disease and neurology experts have theorized that people who take ARVs with the greatest potential to reach the brain are less likely to have HIV replication there. Thus, they may be better protected against cognitive decline. Several small studies looking into this theory have produced affirmative results.

To test the theory in a large group of people with HIV, the AIDS Clinical Trials Group tested levels of HIV in the blood and CSF, along with cognitive abilities, in a study involving 79 HIV-positive patients taking different ARV regimens.

The patients' ARV regimens were scored based on the ability of each specific drug to penetrate into the CSF. ARVs with low penetration were given a score of 0, drugs with moderate penetration were given a score of 0.5, and drugs with good penetration were given a score of 1. After the scores were added up, patients were separated into two groups: those with a score of less than 2, and those with a score of 2 or more.

Seventy-five of the patients underwent testing of cognitive function, including physical coordination, hand-eye coordination and short-term memory. Slightly more than half were given an ARV regimen with a score of 2 or more, and slightly less than half were given a regimen with a score of less than 2.

The team, led by Christina Marra, MD, from the University of Washington in Seattle, reported that while a higher CSF penetration score translated into lower HIV levels in the brain, they were no more likely to protect against cognitive decline. In fact, people with higher CSF penetration scores were more likely to have a decline in cognitive dysfunction after a year of follow-up.

The authors admit they do not have sufficient data to fully explain their unexpected results. They

did not test for adherence, which may have been a factor. What's more, cognitive decline was no more likely to occur in people who had more advanced HIV disease or a longer history of treatment experience.

As for the greater likelihood of cognitive decline with ongoing treatment using ARVs with high CNS penetration, Marra's group theorized that drugs reaching the brain might actually have unknown toxic effects. The researchers stress, however, that the study was not designed to measure this, and they point out that previous studies came to a different conclusion. More study, they say, is needed in this area.

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