Tenofovir Might Reduce Inflammation, Boost Immune System

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The antiretroviral (ARV) drug tenofovir (found in Viread, Truvada and Atripla) might calm the immune system in people with HIV and make them less susceptible to other infections, according to a study published online April 5 in the *Journal of Acquired Immune Deficiency Syndromes*.

HIV directly harms the immune system by infecting, and ultimately destroying, key immune cells. Such direct killing, however, doesn't fully explain how or why the immune systems of people with HIV become so damaged over time, as only a small proportion of cells ever become infected.

Since the introduction of potent ARV therapy in the late 1990s, scientists have been able to study other ways that the presence of HIV can cause harm to those infected with the virus. Inflammation is believed to be a primary culprit. When the body is under threat—either from infection, cell damage or cancer—it produces dozens of different chemicals that place the immune system on high alert. This is a good thing, as it allows the body to respond to those threats, but if the immune system never fully calms down—which appears to be the case in people living with HIV—it can lead to serious problems, such as cardiovascular disease.

Another problem with HIV is that is it can, ironically, put the brakes on some components of the immune system while also revving up inflammation. In particular, by reducing a chemical messenger called interleukin-12 (IL-12) and increasing another called interleukin-10 (IL-10), the immune system becomes suppressed and less able to fight off other serious infections.

HIV drugs significantly reduce inflammation by shutting down HIV replication, but even when virus levels are diminished almost completely, inflammation remains. However, one ARV drug, Selzentry (maraviroc), has been found to calm down inflammation in addition to shutting down the virus. This has sparked researchers' attention and led them to begin studying other ARVs.

Jesper Melchjorsen, PhD, from the Aarhus University Hospital Skejby, in Aarhus, Denmark, and his colleagues set out to understand the anti-inflammatory properties of tenofovir, Retrovir (zidovudine) and Ziagen (abacavir). The team incubated non-HIV-infected cells, treated them with the drugs, and then stimulated them with a variety of other types of pathogens, including the cytomegalovirus (CMV), Escherichia coli and Streptococcus pneumoniae.

Meclchjorsen and his colleagues found that tenofovir offered two types of protection to the cells.

First, it suppressed the production of inflammatory messengers, such as Interleukin-8 (IL-8). The authors note that other studies of tenofovir have not found an inflammatory effect, and so caution is warranted in interpreting the results. They stress, however, that because they used both tenofovir in its commercial form Viread, which is actually a modified version of the active drug tenofovir, and purified tenofovir, they feel their results are valid and deserve further testing.

Tenofovir also appeared to keep the balance of IL-12 and IL-10 stable. The drug enhanced the IL-12 levels, thus increasing their ability to respond to other infectious pathogens, and it kept IL-10 levels low, thus keeping the body from putting the brakes on the immune response.

Retrovir, on the other hand, had detrimental effects in both directions. Not only did it increase the production of IL-8 and other inflammatory chemicals, but it also reversed the balance of IL-12 and IL-10, thus making the cells more susceptible to infection.

Lastly, the team found that Ziagen had a neutral effect on cells. It neither increased nor decreased inflammation. It also had no effect on the balance of IL-12 and IL-10, neither increasing nor decreasing the cells' susceptibility to other infections.

Further research will be needed to determine whether these findings actually translate into a clinical benefit in people's bodies. Nevertheless, the authors conclude that the findings are intriguing enough to warrant such research.
