Malaria Drug Plaquenil Calms Immune Activation

March 9, 2011 By David Evans

Plaquenil (hydrochloroquine), a drug used to treat malaria, lupus and rheumatoid arthritis, was able to significantly reduce immune activation in a small group of HIV-positive people. These data, reported Tuesday, March 1, at the 18th Conference on Retroviruses and Opportunistic Infections (CROI) in Boston, offer hope of finding drugs that can reduce HIV-related immune activation, which is thought to contribute to poorer health, even in people whose virus is well controlled by antiretroviral (ARV) therapy.

The cells in our bodies—particularly our immune cells—have the capacity to respond to threats, be they injury or infection from the outside, or internal biological emergencies, such as wild fluctuations in blood sugar or even cancer. When faced with these threats, the cells become "activated" or "inflamed" and they don't usually calm down again until the threat is gone.

One example is how our body responds to the influenza virus. We usually become feverish and achy and our throats hurt. We may also have respiratory problems. It's not the flu bug that directly makes us feel this way. Rather, it is our body's response to the flu. These responses are desirable, in that they help us get well again, but it is also desirable that the activation calms down once the flu virus is conquered. With viruses that our immune systems can't eliminate or control well, such as HIV, the activation never calms down, and that can take a toll on the body.

Many scientists believe that immune cell activation lies behind not only HIV disease progression, but also many of the non-AIDS-related diseases that strike HIV-positive people more frequently than their HIV-negative counterparts: health problems that include cardiovascular disease, liver disease and kidney disease.

The current crop of ARV drugs, when used in the most potent combinations, significantly reduces immune activation, but not completely. Some researchers have speculated that residual immune activation could lead people who are otherwise healthy and doing well on ARVs to have shorter life spans than HIV negative people.

Of particular concern are people who waited to start ARVs until their CD4 counts had plunged below 200, and who fail to see their CD4 cells increase after starting treatment. Some studies have suggested that chronic immune activation might be a partial cause of blunted CD4 cell recovery in these individuals, whom researchers refer to as immunologic non-responders.

Currently, other than ARVS, there are no well studied, U.S. Food and Drug Administration (FDA)–approved medications to deal with immune activation, but research is moving forward. One drug that has sparked interest is Plaquenil, and researchers in Italy reported at CROI on a small study of the drug in immunologic non-responders.

In that study, Stefania Piconi, MD, from the Hospital Luigi Sacco in Milan, and her colleagues gave 20 HIV-positive immunologic non-responders who were on ARV therapy 400 milligrams (mg) per day of Plaquenil for six months, and measured the impact on markers of immune activation and the levels of gut bacteria in the blood that are thought to contribute to immune activation over and above HIV.

The average age of the participants was 50, about three quarters were men, and the average time since testing HIV positive was just over five years. Twenty percent were also infected with hepatitis C virus (HCV).

Piconi's team found that Plaquenil significantly reduced immune activation in the 20 study participants. Levels of activated CD4 and CD8 cells were reduced, as were the expression of a particular cell receptor (Toll-like receptors, or TLR) on the surface of immune cells known as dendritic cells. Levels of the cell-signaling molecule interleukin-6 (IL-6) also went down, as did levels of the gut bacteria lipopolysaccharide (LPS) circulating in blood.

While these data are preliminary, and further researcher will be needed to confirm and expand on these results, the authors conclude: "[Plaquenil] could be considered to be a useful immunomodulating drug in particular groups of HIV-infected patients."

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