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Metabolic Complications and Simplification

Death rates and sickness from HIV/AIDS have dropped in the developed world since the arrival of effective combination treatments, or HAART (for Highly Active Antiretroviral Therapy). Sometimes called "the cocktail" it has helped many HIV+ people lead active lives.[1] But these highly effective treatments may cause unwanted side effects. These changes are called "metabolic complications" and there is growing concern that some of the changes that happen to HIV+ patients on HAART, like high cholesterol, high blood pressure, diabetes and body fat changes (lipodystrophy) may lead to increased risk for heart problems (coronary artery disease). [See box].

What can be done to treat lipodystrophy? Changes in diet (less fat) and exercise might help. Switching to a different class of drugs or taking medication to reduce levels of blood fat and blood sugar are medical possibilities. Taking a growth hormone or cosmetic surgery might restore one's appearance. There is still no agreement on what the best treatment for lipodystrophy in HIV+ patients might be. Ideally the goal would be to prevent it or slow it down.

Increased blood fats (both cholesterol and triglycerides) are most often associated with the protease inhibitor class of antiretrovirals, but they have been reported with efavirenz (Sustiva), a drug in the NNRTI class. Change of diet and exercise should be tried first. Second, a person could take drugs called "statins" or "fibrates" which may normalize blood fat levels, although they can interfere with HIV medications. Smoking also increases the risk of heart disease.

Studies have been done to see if body fat changes improve when patients switch to a non-protease inhibitor combination treatment. Generally studies show that switching to NNTRI or NRTI based combination treatments improves the diabetes-like condition and blood fat levels, but without substantial improvement in the more visible body fat.

One study was done to see if replacing stavudine (d4T) or zidovudine (AZT) in combination therapy with abacavir (Ziagen) could improve fat loss (lipoatrophy).[2] The major finding was that patients who switched to abacavir had an average increase in arm and leg fat of 400 grams or 10% after 24 weeks whereas those who remained on d4T had no change. The change in body fat was small, but statistically significant. Unfortunately neither the patients nor their doctors could see the difference. The study author suggested a longer study might get more significant reversals. Patients who had switched treatment retained viral load suppression and had few other side effects. The rate of suspected abacavir hypersensitivity reaction in this study was 10%.

What is Lipodystrophy and why does it affect HIV+ people?

"Lipodystrophy" refers to the visible changes in body fat that can include fat gain on the breasts, abdomen or back of the neck. Fat loss (or "lipoatrophy") occurs on the face, arms, legs and buttocks. Changes in appearance, as well as the mental and emotional impact of them can vary a lot, but can be very significant. An HIV+ person stressed out by these changes may not take medications on schedule or may even stop taking them, thus increasing the risk of HIV progression.

The change in body fat can occur by itself, but often there are other changes taking place too. These can include a type of diabetes, high blood pressure, and high blood fats, like cholesterol. The reported frequency of lipodystrophy varies because there is no standardized diagnosing or reporting method, but estimates range from one out of five to as many as four out of every five HIV+ patients on long-term HAART.

Lipodystrophy is more common among patients whose therapy includes a protease inhibitor for more than 18 months. It is less common among patients whose treatment did not include a protease inhibitor, and occurs occasionally in persons who never took any treatment for HIV/AIDS.[4]

Studies have shown that being white, older, having HIV infection longer, having more severe immune suppression, and being on antiretroviral treatments longer may be more important factors leading to lipodystrophy than taking protease inhibitors.[5] Fat loss (also called "lipoatrophy") has been found to be associated with the use of the NRTI drug class, most specifically stavudine (d4T). It is thought that the treatment interferes with energy production by the mitochondria of the fat cells. (Mitochondria are the energy source within all human cells).

In February 2002 the week 48 results from a 96 week long study on blood fat (hyperlipidemia) were presented.[3] Patients who had never been on antiretroviral treatments were randomly placed in one of three therapy groups: 1) zidovudine (AZT)/ lamivudine (3TC)/ abacavir (Ziagen); 2) zidovudine (AZT)/ lamivudine (3TC)/ nelfinavir (Viracept); or 3) stavudine (d4T) /lamivudine (AZT)/ nelfinavir (Viracept). The primary purpose of the study was to measure changes in the levels of so called "bad cholesterol" in the blood. Both of the nelfinavir groups had increases in all blood fats, including "bad cholesterol" and triglycerides. The increase was more pronounced in the group on stavudine/ lamivudine/ nelfinavir. The group on zidovudine/ lamivudine/ abacavir (Trizivir) did not have the increases in blood fats experienced by the other two groups. The study showed positive blood fat (lipids) effects in HIV+ patients taking the triple NRTI treatment as compared to a combination of two NRTIs and a protease inhibitor, while still maintaining similar beneficial effects on viral loads and CD4 counts.

Combination therapies for HIV are beneficial but they may increase the risk of blood fats, high blood pressure, diabetes and abdominal fat, which can lead to heart disease. A healthy diet, exercise and non-smoking are important in the treatment of HIV/AIDS, but may be hard to maintain. HIV+ patients with increased risk factors for heart disease may benefit by using combination therapies that do not contain protease inhibitors to delay or prevent metabolic complications.

Simplifying treatment may not only lead to HIV+ patients being better able to stick to their "cocktail" to insure continued treatment success but may also reduce their need to take additional medications often prescribed to treat associated metabolic complications.

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