CHAPTER 20

HIV / HCV Coinfection

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SECTION 4

Naturopathic Treatment Options

Introduction

This section discusses the naturopathic treatment options available for people coinfected with the *hepatitis C virus* (*HCV*) and the *human immunodeficiency virus* (*HIV*). See *Chapter 14, Naturopathic Medicine* for more information about the naturopathic approach to treating viral *hepatitis*. See *Chapter 16, Nutritional Supplementation* for additional details on the nutritional supplements mentioned in this section.

Antioxidants

An important similarity between *chronic hepatitis* C and HIV/AIDS is that both infections appear to progress more rapidly in situations of increased oxidative stress. Oxidative stress refers to a state in which there is an overabundance of molecules called *free radicals*. Free radicals can damage cells and are involved in the processes of *inflammation* and scarring. Increased oxidative stress is indicated by low levels of the active form of *glutathione* in the *lymphocytes* and blood of people with HIV and/or HCV. Lack of glutathione can lead to immune suppression, decline of *immune system* function, and an increase in HIV *replication*.[1] While glutathione levels are low in those infected with HCV or HIV alone, they are lowest in those who are coinfected.[2]

Glutathione is produced by the liver. Low levels of glutathione are associated with active liver disease on *liver biopsy* and increased levels of the *liver enzyme ALT*.[2] Several studies have been done in both HCV and HIV to look at the role of *antioxidants* in raising glutathione levels. These studies show the use of antioxidants such as N-acetyl cysteine and *vitamin C* have a positive effect on glutathione levels in the blood and white blood cells of those infected with HIV. Antioxidants have also been shown to significantly lower HIV *viral load*.[3]

N-Acetyl Cysteine

Not all studies of N-acetyl cysteine (NAC) in HIV/AIDS and chronic hepatitis C have shown significant effects.[4] However, studies that showed no effect were generally small and lasted only a few weeks. In studies that have shown NAC has a glutathione elevating effect in people with HIV, this effect was seen only after eight weeks of therapy.[5]

A small study found HCV positive, HIV negative patients who were given 600 mg of NAC three times a day for four weeks experienced normalization of ALT levels. These normalized ALT levels may relate to increased glutathione levels.[6] Two additional randomized studies involving 147 and 77 patients with chronic hepatitis C evaluated the effects of adding NAC to *interferon monotherapy*. The study results were mixed, with one showing significant benefit and the other no evidence of benefit. Additional research with larger study populations and perhaps with higher doses of NAC are needed to determine a definitive role for NAC in the setting of HCV/HIV coinfection.[7, 8]

NAC has been shown to be safe in doses of 1,500 mg to 2,000 mg per day. Researchers in this field suggest this dose is sufficient to affect glutathione levels in people who are HIV infected (personal communication, Lenore A. Herzenberg, PhD,

Stanford University). In a 2007 review article on the topic of NAC, Dr. Herzenberg and her coauthors concluded, "Oral administration of NAC, a safe, well-tolerated drug with no clinically significant adverse effects, has been shown to be beneficial in settings where GSH [glutathione] deficiency occurs, for example, HIV infection..."[9]

Alfa-Lipoic Acid

Alfa-lipoic acid is an antioxidant that exists in small quantities in the food we eat. It has been shown to increase glutathione levels in those with HIV when given at doses of 450 mg per day. This dosage is considered moderate and has been shown to be safe. This dose was also effective at significantly raising the level of *CD4 cells* (a type of immune cell) after 14 days in the same study patients.[10] The findings of a small study published in 2008 showed that daily oral supplementation with alfa-lipoic acid (300 mg three times per day in the study) over a 6-month period resulted in significant elevation of blood glutathione and *CD4 counts*.[11]

Alfa-lipoic acid has positive antioxidant effects in mitochondrial *toxicity*, a common problem inside the cells in coinfected people. In addition, alfa lipoic acid has been shown to prevent damage that results from *free radical* production in both the nervous system and the liver.[12]

Oxidation or production of free radicals occurs in the white blood cells and liver of HCV/HIVcoinfected persons. This can lead to *neuropathy* (nerve damage) and liver damage. Although there have been no large scale studies on the effects of alfa-lipoic acid in HCV/HIVcoinfected individuals, it has been proven to be safe at dosages of up to1,200 mg daily in those who are HIV positive.[13]

Alfa-lipoic acid may be useful in decreasing the risk of kidney stones, a side effect of the protease inhibitor indinavir, an *antiviral* drug used to treat HIV infection.[14]

SAMe

S-adenosylmethionine (SAMe) is a protein made in the liver. It is also available as a nutritional supplement. SAMe has been found to be an effective treatment for certain types of *depression*. A recent study of 20 persons living with HIV and diagnosed with major depression found treatment with SAMe resulted in rapid and progressive decreases in depressive symptoms over the 8-week study period.[15]

SAMe is also used to treat liver disease. SAMe has been shown to be effective in raising glutathione levels in the liver cells of those with *cirrhosis*, and in the nervous systems of HIV positive patients.[16, 17] In addition, a recent animal model study of oxidative liver damage (which is believed to contribute to hepatitis C disease progression), found SAMe supplementation interrupted the experimentally induced liver damage.[18]

Dosages of 1,200 mg daily have been shown to increase liver glutathione levels in people with liver diseases. This dose has been used in other conditions and has been shown to be safe and free of side effects.

Vitamin E

Vitamin E deficiency is common in HIV infection.[19, 20] While vitamin E has not been shown to raise glutathione levels, it does play an important role as an antioxidant in coinfection. Increased intake may be related to slower HIV disease progression. A study of HIV positive men who were followed for over six years showed a decreased risk of disease progression to AIDS in those who took twice the amount of vitamin E as those in the study who did not have HIV.[21] At a moderate dose of 200 IU to 400 IU per day, vitamin E has also been shown to protect against the bone marrow toxicity that is a well-established side effect of the HIV drug zidovudine (AZT).[22,23] As an antioxidant, vitamin E has been shown to protect cell membranes from *lipid* peroxidation, a specific type of free radical damage. This is one of the reasons vitamin E is particularly helpful in preventing liver damage. As explained in *Chapter 16, Nutritional Supplementation*, vitamin E interrupts the biochemical pathways that lead to liver *fibrosis*. However, this does not mean that vitamin E can completely stop the damage caused by HCV, or that it is okay to continue drinking *alcohol* if you take vitamin E.

Research indicates that vitamin E is protective against liver fibrosis and plays a role in preventing the free radical activity that can lead to HIV replication. Vitamin E is nontoxic in doses up to 2,000 IU per day, unless there are blood clotting problems. In this case, vitamin E should only be used with guidance from a doctor. The most beneficial forms of vitamin E are d-alfa-tocopherol, d-alfa tocopherol succinate, and mixed tocopherols.

Selenium

Selenium is probably one of the most important nutrients for HIV positive people. A 1997 research study of HIV-infected people showed that those with the lowest levels of selenium had a 10-fold greater risk of dying from the disease than those with normal levels of selenium. This risk was independent of the *CD4 count* at the time of the study (often an important marker of HIV prognosis), the use of antiviral treatment, and levels of other important nutrients.[24] A more recent 2007 study confirmed the protective effects of selenium supplementation for those with HIV. Investigators found that those receiving daily selenium had decreased HIV viral load, and higher CD4 counts.[25] This held true even for those in the study who were coinfected with HCV.

Studies have found selenium levels in people with HCV/HIVcoinfection are even lower than in those with HIV only, even in people without symptoms.[26] Selenium has been shown to raise blood levels of the active form of glutathione in HIV positive persons.[27]

Clinical trials involving HIV/AIDS patients have shown that 400 mcg of selenium per day resulted in significant increases in blood selenium levels, improved appetite, better digestion, and fewer recurrent infections.[28]

Amino Acids

L-Glutamine

L-glutamine is an *amino acid* found in large quantities in muscle, intestine, and immune cells. L-glutamine and the amino acid cysteine are both required by the body to make glutathione.

L-glutamine is particularly important in people with HIV. L-glutamine is one of the nutrients the body loses because of HIV infection. This loss is compounded by the body's demand for additional L-glutamine resulting from the rapid turnover of immune cells and the stress of infections (including coinfection with HCV and other viruses). This added demand usually results in an L-glutamine deficiency. Glutamine deficiency appears to be one of the causes of wasting (weight loss and muscle loss) that occurs in people with AIDS.[29]

L-glutamine is a primary fuel source for intestinal cells. An L-glutamine deficiency can lead to problems absorbing nutrients from the intestine. About 20% of people with AIDS have abnormal intestinal absorption. This problem has been treated successfully with L-glutamine.[30] Supplemental L-glutamine has been shown to be beneficial in regaining lost muscle and lean body mass (body weight that is not fat) among people with HIV-related wasting. In one study, the daily doses of L-glutamine supplementation ranged from 8 grams to 40 grams. The people who gained the most lean body mass took daily doses of 40 grams per day (divided into four equal doses of 10 grams) for a period of 12 weeks.[30-32] See *Chapter 16, Nutritional Supplementation* for more information.

L-Carnitine

L-carnitine is an amino acid that is particularly important for muscle and immune cells. L-carnitine is another nutrient that can become deficient in certain groups of HIV-infected individuals. One study found carnitine deficiencies in 72% of a group of AIDS patients on AZT.[33] HIV positive patients are at risk for L-carnitine deficiency as a result of *malabsorption*, kidney problems, specific antibiotic and *antiviral* medications, and lipoatrophy (weight loss that is mostly fat tissue).[34] Preliminary studies have shown that people with chronic hepatitis C have a deficiency of acylcarnitine, a specific form of L-carnitine.[35] It is not fully understood why this deficiency occurs; but we know that HCV damages the mitochondria (the powerhouses of cells) in the liver, and that mitochondrial function uses acylcarnitine. Therefore, by causing mitochondrial damage, HCV may cause a need for more L-carnitine in people with chronic hepatitis C. More studies are needed to clarify this issue.

Studies in people with HIV have shown that L-carnitine has a positive effect on the immune system, normalizes high *triglycerides* (blood fats), reduces muscle wasting from AZT, and improves neuropathy symptoms associated with NRTI antiviral medications.[36-41] Carnitine and acetyl-L-carnitine (a specific form used to treat mitochondrial toxicity) are used in Europe to treat the peripheral neuropathy (nerve damage) that often occurs in HIV patients as a side effect of some antiviral drugs. Dosages of 3 grams to 6 grams per day of L-carnitine are used to treat elevated blood fats and muscle wasting in people with HIV. Carnitine is available both as a prescription drug and over-the-counter as a nutritional supplement.

Summary

The biological effects of HIV and HCV on antioxidants in the body make it necessary to restore these nutrients with nutritional supplements. Research has shown that taking N-acetyl cysteine, alfa lipoic acid, SAMe, vitamin E, selenium, L-glutamine, and L-carnitine is safe when appropriate doses are used. These supplements can also be used safely in combination with western therapies and/or traditional Chinese medicine. A healthcare provider who is trained in clinical nutrition and the treatment of coinfection should be consulted for optimal benefit from an antioxidant protocol. It is important to discuss your nutritional supplementation with all of your healthcare providers to make sure your protocol is both safe and effective.

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