

Hepatitis C: Choices

Part Three: Special Issues

Chapter 18:

HCV/HIV COINFECTION

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Section 4:

NATUROPATHIC TREATMENT OPTIONS

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INTRODUCTION

This section is a discussion of the naturopathic treatment options available for people who are coinfecting with the hepatitis C virus (HCV) and the *human immunodeficiency virus (HIV)*. See *Chapter 13: Naturopathic Medicine* for more information about the naturopathic approach to treating viral hepatitis. See *Chapter 14: 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 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 evidenced by low levels of the active form of *glutathione* in the *lymphocytes* and blood of people who have 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 coinfecting.²

Glutathione is produced by the liver. Low levels of glutathione are associated with more active liver disease on *liver biopsy*, and increased levels of the *liver enzyme ALT*.² Researchers have suggested that low glutathione is a factor in resistance to treatment that is seen with both *interferon treatment* for HCV and *antiviral* therapy for HIV.

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 has 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. However, the studies that showed no effect were small and lasted only a few weeks. In the major studies that showed NAC has a glutathione elevating effect in people with HIV, this effect was seen only after eight weeks of therapy.⁴ A small study found HCV positive, HIV negative patients who were given 600 mg of NAC three times a day for four weeks experienced a normalization of ALT levels. These normalized ALT levels may relate to increased glutathione levels.⁵ There are several drugs called cysteine pro-drugs that are currently in *clinical trials*. These drugs increase glutathione levels in people who are HIV infected. They may be useful in coinfection, but we need more information about them before that determination can be made.⁶ NAC has been shown to be safe in doses of 1,500-2,000 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 Herzenberg, Stanford University).

Alpha-Lipoic Acid

Alpha-lipoic acid (ALA) 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 dosage was also effective at significantly raising the level of *CD4 cells* (a type of immune cell) after 14 days in the same study patients.⁷

ALA has positive antioxidant effects in mitochondrial *toxicity*, a common problem in coinfecting people. In addition, ALA has been shown to prevent damage that results from free radical production in both the nervous system and the liver.⁸ Oxidation or production of free radicals occurs in the white blood cells and liver of coinfecting persons. This can lead to neuropathy (nerve damage) and liver damage. Although there have been no large scale studies on the effects of ALA in coinfecting individuals, it has been proven to be safe at dosages of up to 1200 mg daily in those who are HIV positive.⁹

ALA 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.¹⁰

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*. 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.^{11,12} Dosages of 1,200 mg daily raised 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.^{13,14} 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 vitamin E.¹⁵

At a moderate dose of 200-400 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).^{16, 17}

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 why vitamin E is particularly helpful in preventing liver damage. As explained in *Chapter 14: Nutritional Supplementation*, vitamin E has been found to interrupt 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. The research **does** indicate 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-alpha tocopherol, d-alpha tocopherol succinate, and mixed tocopherols.

Selenium

Selenium is probably one of the most important nutrients for people who are HIV positive. One 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 the levels of other important nutrients.¹⁸ Studies have found that selenium levels in people with coinfection are even lower than in those with HIV only, even in people without *symptoms*.¹⁹ Selenium has been shown to raise blood levels of the active form of glutathione in people who are HIV positive.²⁰

Clinical trials involving HIV/AIDS patients have shown that taking 400 mcg of selenium per day resulted in significant increases in blood selenium levels, improved appetite, better digestion, and fewer recurrent infections.²¹

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 for 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.²²

L-glutamine is a main source of fuel for the cells in the intestines. 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.²³ Giving supplemental L-glutamine to people with HIV-related wasting has been shown to be beneficial in regaining lost muscle and lean body mass (body weight that is not fat). In one study, the daily doses of L-glutamine supplementation ranged from 8-40 grams. The patients 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.^{23, 24, 25} See *Chapter 14: Nutritional Supplementation* for more information.

L-Carnitine

L-carnitine is an amino acid that is particularly important for muscle and immune cells. L-carnitine appears to be 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.²⁶ 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).^{27, 28}

There are preliminary studies that show chronic hepatitis C patients have a deficiency of acylcarnitine, a specific form of L-carnitine.²⁹ It is not fully understood why this deficiency occurs, but we know that HCV damages the mitochondria (the powerhouses of cells) of the liver. We also know 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 HIV patients have shown that L-carnitine has a positive effect on the immune system, normalizes high *triglycerides* (blood fats), reduces muscle wasting that results from taking AZT, and improves symptoms of neuropathy (nerve damage) that result from taking any of the NRTI class of antiviral medications.^{30, 31, 32, 33, 34} Carnitine and acetyl-L-carnitine (a specific form used to treat mitochondrial toxicity) are used in Europe to treat the peripheral neuropathy that often occurs in HIV patients as a side effect of some antiviral drugs. Dosages of 3-6 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, alpha lipoic acid, SAME, vitamin E, selenium, L-glutamine, and L-carnitine is safe when the appropriate doses are used. These supplements can also be used safely in combination with western therapies and/or traditional Chinese medicine. A health care 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 health care providers to make sure your protocol is safe and effective.

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