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A Conservative Triple Antioxidant Approach to the Treatment of Hepatitis C

Combination of Alpha Lipoic Acid (Thioctic Acid), Silymarin, and Selenium: Three Case Histories

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ABSTRACT

❑ *Background:* There has been an increase in the number of adults seeking liver transplantation for hepatitis C in the last few years and the count is going up rapidly. There is no reliable and effective therapy for chronic hepatitis C since interferon and antivirals work no more than 30% of the time, and liver transplant surgery is uncertain and tentative over the long run. This is because, ultimately, residual hepatitis C viremia infects the new liver. Furthermore, liver transplantation can be painful, disabling and extremely costly.

❑ *Treatment Program:* The author describes a low cost and efficacious treatment program in 3 patients with cirrhosis, portal hypertension and esophageal varices secondary to chronic hepatitis C infection. This effective and conservative regimen combines 3 potent antioxidants (alpha-lipoic acid [thioctic acid], silymarin, and selenium) that possess antiviral, free radical quenching and immune boosting qualities.

❑ **Conclusion:** There are no remarkably effective treatments for chronic hepatits C in general use. Interferon and antivirals have less than a 30% response rate and because of the residual viremia, a newly transplanted liver usually becomes infected again. The triple antioxidant combination of alpha-lipoic acid, silymarin and selenium was chosen for a conservative treatment of hepatitis C because these substances protect the liver from free radical damage, increase the levels of other fundamental antioxidants, and interfere with viral proliferation. The 3 patients presented in this paper followed the triple antioxidant program and recovered quickly and their laboratory values remarkably improved. Furthermore, liver transplantation was avoided and the patients are back at work, carrying out their normal activities, and feeling healthy. The author offers a more conservative approach to the treatment of hepatitis C, that is exceedingly less expensive. One year of the triple antioxidant therapy described in this paper costs less than $ 2,000, as compared to mor than $300,000 a year for liver transplant surgery. It appears reasonable, that prior to liver transplant surgery evaluation, or during the transplant evaluation process, the conservative triple antioxidant treatment approach should be considered. If these is a significant betterment in the patient's condition, liver transplant surgery may be avoided.

Key Words: Hepatitis C · Treatment · Antioxidant · Alpha lipoic acid · thioctic acid · Silymarin · Selenium

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According to a recent article, the number of adults seeking liver transplants for hepatitis C infection will skyrocket in the next 20 years [11]. About 10,000 Americans die from this disease each year. Deaths are estimated to increase because of the increasing risk of infection, and the resulting cirrhosis, portal hypertension, thrombocytopenia, bleeding from varices, and liver cancer. Five years ago, 20% of these hepatitis C patients were candidates for liver transplantation and today the number has increased to about 50%.

An estimated 4 million Americans are infected with hepatitis C and many of them are being evaluated for liver transplant surgery. This expensive process costs roughly $ 300,000 during the first 3 months, and can be painful and incapacitating. Add to this the thousands of dollars for anti-rejection drugs and the costs of more frequent visits to health care facilities. Of course some people do require liver transplant surgery, however, the author believes that in many cases, an effective alternative therapy exists.

Often, patients with progressive hepatitis C, who seek a more conservative treatment, prior to surgery present to our facility. These patients are treated with a program that includes and combines alpha-lipoic acid, silymarin and selenium. Most patients recover quickly, however, a few find it difficult to follow a healthy nutritional and lifestyle program, or their condition is so far advanced that they go on to liver transplant surgery. In this paper, the case histories of 3 patients are presented.

BACKGROUND

More than 20 years ago, when the author was in medical and pathology training at 2 hospitals in Cleveland, Ohio, he was assigned to 6 critical patients who were suffering from acute hepatic

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necrosis secondary to hepatotoxic mushroom poisoning. He ordered thioctic acid (alpha-lipoic acid, ALA) from the National Institutes of Health and injected this antioxidant drug into the patients. In spite of their highly threatening condition the patients, as measured by laboratory values and clinical parameters, recovered quickly. Dr. Fred Bartter (then Chief of Hypertension and Endocrinology at the National Institutes of Health) and the author were astounded by their recoveries and went on to treat many more mushroom poisoning patients. Over the years, the author continued to treat additional patients with other medical conditions using ALA, and observed similar results. The author has recently added silymarin and selenium to the regimen. In this paper he will discuss the use of this triple antioxidant regimen in the management of 3 chronic hepatitis C patients.

ZUSAMMENFASSUNG

Eine konservative dreifache antioxidante Methode zur Behandlung von Hepatitis C. Eine Kombination von Alpha-Liponsäure (thioctic acid), Silymarin und Selenium: Drei Krankenberichte

❑ *Hintergrund:* Es gibt im Allgemeingebrauch keine bemerkenswert erfolgreiche Behandlung von chronischer Hepatitis C. Interferon und Virostatika haben weniger als eine 30prozentige Ansprechsquote, und wegen der zurückbleibenden Virämia wird meistens eine neu transplantierte Leber wieder infiziert.

❑ *Behandlungsprogramm:* Die dreifache antioxidante Kombination von Alpha-Liponsäure, Silymarin und Selenium wurde für eine konservative Behandlung von Hepatitis C gewählt, denn diese Stoffe schützen die Leber vor freier radikaler Beschädigung, erhöhten das Niveau anderer fundamentaler Antioxidanzien und hindern virale Fortpflanzung. Die drei Patienten, die in dieser Abhandlung geschildert werden, folgten dem dreifachen antioxidanten Programm, sie erholten sich rasch, und ihre Laborwerte verbesserten sich beachtlich. Außerdem wurden Lebertransplantationen vermieden, die Patienten arbeiten wieder, führen ein normales Leben und fühlen sich gesund.

❑ **Schlußfolgerung:** Der Autor bietet eine konservativere Methode zur Behandlung von Hepatitis C, die wesentlich billiger ist. Ein Jahr der dreifachen antioxidanten Behandlung, die in dieser Abhandlung beschrieben wird, kostet weniger als $ 2000, eine Lebertransplantation kostet im Vergleich mehr als $ 300.000 im Jahr. Es scheint vernünftig zu sein, bevor eine Lebertransplantationsoperation in Erwägung gezogen wird oder während der Bewertung einer Lebertransplantationsoperation die konservative dreifache Behandlung zu erwägen. Wenn es eine beachtliche Verbesserung im Befinden des Patienten gibt, kann eine Lebertransplantationsoperation vermieden werden.

Schlüsselwörter: Hepatitis C · Behandlung · Antioxidant · Alpha-Liponsäure · Thiotic acid · Silymarin · Selenium

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Patients and Method

The 3 basic antioxidants that were used in this report are alpha-lipoic acid (thioctic acid), silymarin and selenium (selenomethionine). The alpha-lipoic acid product was manufactured by Asta Medica at Frankfurt am Main, Germany. The silymarin was a product distributed by Now Foods of Bloomingdale, Illinois, and the selenium was encapsulated by Metabolic Maintenance Products Inc. of Sisters, Oregon.

The 3 patients were selected at random from a group of approximately 50 chronic hepatitis C charts at the Integrative Medical Center of New Mexico in Las Cruces. Each patient was maintained on a dose of 600 mg of alpha-lipoic acid a day in 2 divided portions of 300 mg. The silymarin dose was 900 mg per day in 3 divided portions of 300 mg. The selenomethionine dose was 400 μg in 2 divided portions of 200 μg.

Because alpha-lipoic acid depletes some of the B vitamins, the patients were prescribed 2 B-100 capsules a day. In addition, each patient also took between 1,000 and 6,000 mg of vitamin C, 400 IU of vitamin E, and a mineral supplement. The patients were also requested to eat a daily diet that included at least 6 servings of fresh vegetables and fruits, only 4 oz or less of meat per meal, and 8 glasses of fresh water.

It was also suggested that the patients reduce their stress levels, and take part in an exercise program that included at least a 1-mile walk 3 times a week. The patients followed the nutritional supplement program carefully, however, it is not clearly known whether the other regimens were correctly followed.

Case Studies

❑ Patient 1

Mrs. M. P. is a 57-year-old woman who aquired hepatitis C after a blood transfusion during surgery about 10 years ago. She did not eat a nutritious diet and did not live a very healthy life style at that time. About 5 years ago, she became very fatigued and nauseous, and was diagnosed with non-A, non-B hepatitis. She was treated with conventional therapies and continued to degenerate into a poorer state of health. About 3 years ago she was diagnosed with chronic hepatitis C, cirrhosis, portal hypertension, esophageal varices, and thrombocytopenia, and treated with steroids and interferon. She did not improve. Her AFP (alpha-fetoprotein) level became elevated (16.1) and a mass was located in her liver. Mrs. M. P. was told that the mass was probably cancer and that there was no hope.

Mrs. M. P. presented at our office last year appearing fatigued, weak, pale, and her abdomen was grossly enlarged. The abdominal distention was due to ascites. She was administered oral furosamide (40 mg) and potassium chloride (10 meq) with a balanced diet and wholesome life style. She lost almost 50 lb of fluid in 1 month. Mrs. M. P. was treated with 600 mg of oral alpha-lipoic acid in 2 divided doses (300 mg), 900 mg of silymarin in 3 divided doses (300 mg), and 400 μg of selenium a day. A premium B complex vitamin was added to her regimen because alpha-lipoic acid depletes the body of

thiamin, biotin and other B vitamins. Adequate amounts of vitamin C (2,000 mg), vitamin E (800 IU), Coenzyme Q10 (300 mg), and basic mineral supplements were also prescribed. Figures 1 and 2 track the favorable changes in her ALT levels and her AFP levels. Today, Mrs. M. P. is working 8 hours a day, feels healthy, looks good, and is not tired. She is free of the signs and symptoms of a serious chronic hepatitis C infection.

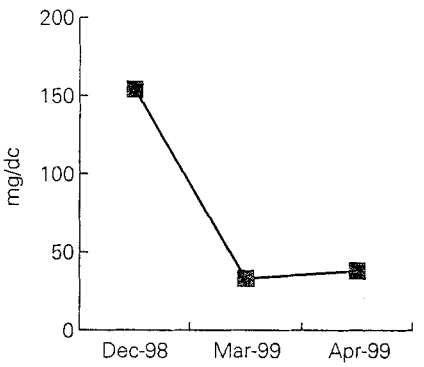

Figure 1. SGPT (ALT) levels in patient 1.

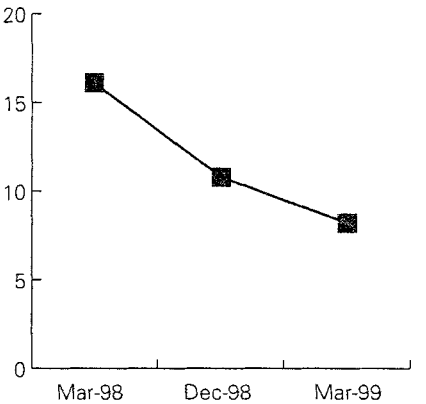

Figure 2. AFP levels in patient 1.

❑ Patient 2

Mrs. P. P. is a 49-year-old woman who was infected with hepatitis C following a blood transfusion prior to trauma surgery more than 10 years ago. During surgery, her spleen was excised because it was lacerated.

About 3 years ago, a liver biopsy was performed that showed moderate cirrhosis with active inflammation. As a result of this pathology, Mrs. P. P. went on to develop portal hypertension with esophageal varices. She never acquired thrombocytopenia because of the splenectomy, and did not show an elevated AFP. Mrs. P. P. was treated with interferon therapy without any satisfactory results. She was told that her condition was hopeless and that a liver transplant was her only option. Her health continued to decline and she presented at our office with fatigue, anxiety, and insomnia.

Mrs. P. P. was prescribed 600 mg of alpha-lipoic acid each day in 2 divided doses (300 mg each). To that, was added silymarin (900 mg/day) and selenium (400 µg/day). To combat the anxiety and insomnia, 0.5 mg of aprazolam was prescribed, as needed at bedtime. Mrs. P. P. was put on our balanced health and lifestyle program, and within 7 months regained her health. Figures 3 to 5 trace the favorable changes in her ALT levels, viral load and platelet levels. She is doing very well today and is working at a arduous job and playing at sports without any fatigue or other symptoms of serious disease.

❑ Patient 3

Mrs. L. M. is a 35-year-old mother of 3 children who developed hepatitis C secondary to a blood transfusion during the birth of her baby girl 15 years ago. Three years ago she became ill and was diagnosed with cirrhosis of the liver, portal hypertension, and esophageal varices. As a result of the portal hypertension, she developed splenomegaly and thrombocytopenia. Mrs. L. M.'s hepatologist sent her to the university hospital for liver transplant evaluation. When she presented to our office, she was anxious, tired, and pale, and complained of constant pain in the regions of her liver and spleen. Mrs. L. M.'s fasting blood sugars were in the 300 mg/dc range. She did not have hyperglycemia prior to the hepatitis C infection. Mrs. L. M. decided that prior to the liver transplant surgery, she wanted to investigate a more conservative treatment regimen.

Mrs. L. M. was prescribed alpha-lipoic acid (600 mg), silymarin (900 mg), and selenium (400 µg) per day with supportive supplements. She was encouraged to follow a healthy life style program with a 2,000-calorie diabetes diet. Within 2 weeks she began to feel much better and recovered quickly. Her blood sugar fell into the normal range and the pain in her liver and spleen ended. She became energized and was able to do her normal work as a housewife. She returned to college the next semester earning

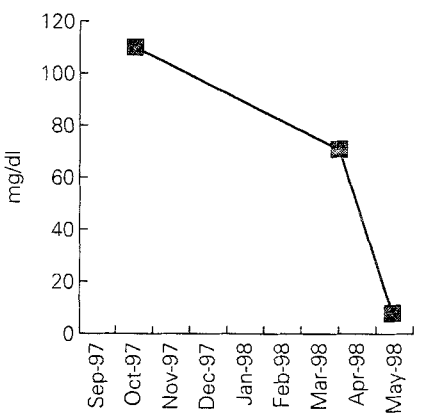

Figure 3. SGPT (ALT) levels in patient 2.

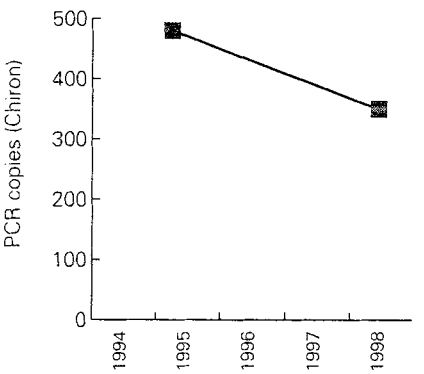

Figure 4. Viral load in patient 2.

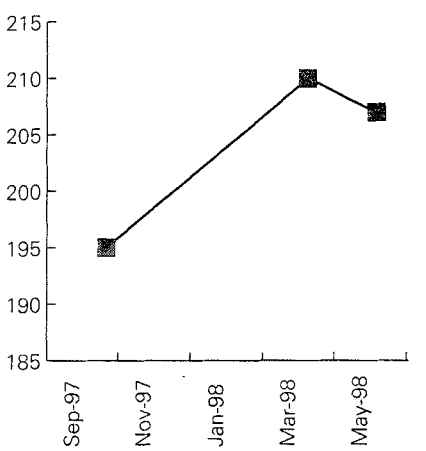

Figure 5. Platelet levels in patient 2.

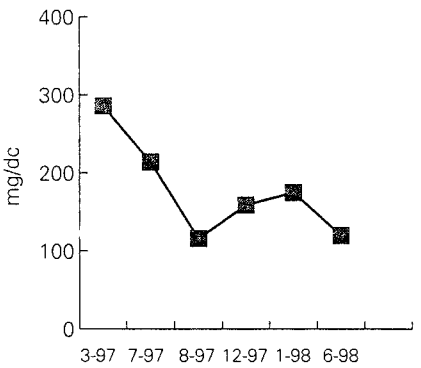

Figure 6. Fasting blood sugar levels in patient 3.

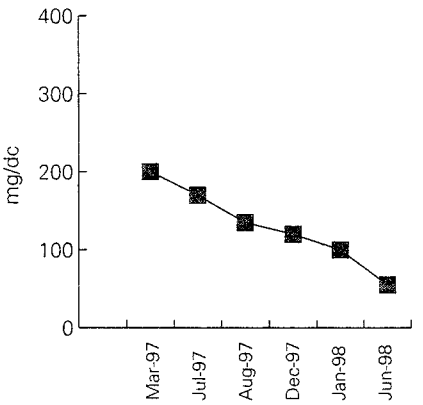

Figure 7. SGPT (ALT) levels in patient 3.

a 3.8 grade point average (A). Figures 6 and 7) trace her favorable progress.

Discussion

Alpha-Lipoic Acid

Alpha-lipoic acid (ALA) is a small organic molecule with a disulfide bond. It is a superb antioxidant that is soluble in both water and fat. ALA is an imposant coenzyme for the production of acetyl coenzyme A. Dihydrolipoic acid (DHLA), it's reduced form, is an electron donor that recycles other fundamental antioxidants (vitamin C, vitamin E, and glutathione). ALA and DHLA are superb free radical scavengers themselves because they neutralize peroxyl radicals [36], hydroxyl radicals [39] and singlet oxygen [38].

ALA is also a metal chelator that removes mercury from tissues [17], prevents calcium oxalate crystals from forming in the kidneys [21], chelates copper [28], and removes arsenic [18].

Lately, there has been a great explosion in ALA research. The lipoic acid/dihydrolipoic acid redox couple inhibits viral replication by stabilizing the NFκB transcription factor [4], blocks the development of cataracts [24], protects the kidney from aminoglycoside damage [35], insulates the pancreatic islet cells from inflammatory assault [7], inhibits thymocyte apoptosis [8], and stimulates the production of helper T cells [15]. In addition, the toxic side effects of cancer chemotherapy can be attenuated with the use of ALA [5] and it protects bone marrow from free-radical damage secondary to ionizing radiation [33].

Numerous other studies show that ALA is useful for the treatment of diabetes mellitus and syndrome X because it increases cellular glucose utilization [19] and significantly reduces insulin resistance [12, 20].

Diabetic neuropathy originates from a decrease in blood flow to various organs. This results in an accumulation of free radicals that can destroy nerve function. In one study, ALA brought about a significant reduction of neuropathic symptoms in 23 patients [46]. This was accomplished by abolishing the products of lipid peroxidation and increasing the entrance of glucose into the cell [27].

Due to ALA's lipophilic characteristics, it can cross the blood-brain barrier quite easily and can scavenge free radical toxins in the central nervous system. Both ALA and DHLA protect animals from neuronal death following laboratory-induced cerebral ischemia and reperfusion experiments [9, 16, 32]. This effect is explained by the fact that ALA greatly increases glutathione levels in nervous tissue, thus protecting the nerves from the toxic products of oxidation.

For many years, ALA was used as a treatment for liver disease. As of yet, however, there are not many papers on this subject, and some studies used entirely sub-therapeutic doses [25].

Ethyl alcohol (ETOH) damages the liver by several mechanisms that ultimately lead to the proliferation of innumerable free radicals. These toxins damage the cell membranes by lipid peroxidation. It has been reported that ALA lowers the levels of ETOH metabolic breakdown products, and in consideration of this ALA may be an effective treatment for alcohol induced hepatitis, early cirrhosis, and alcoholic coma [23, 37].

In the late 1960's and 1970's, there were several studies describing the successful treatment of hepatotoxic mushroom poisoning with intravenous ALA [22, 47]. National Institutes of Health studies reported the survival of 73 out of 79 seriously poisoned patients [3, 6]. In America, interest in the use of ALA for hepatotoxic mushroom poisoning, and liver disease in general, was in the main lost, because of the growing fascination with liver transplantation as a proposed "standard of care" treatment for serious liver disease.

Silymarin

Silymarin is the mixed extract of the milk thistle plant (Silibum marianum) and has been used for hundreds of years as a treatment for liver disease. In the late 1960's and 1970's it was extensively used for serious hepatotoxic mushroom poisoning with excellent results [43]. It has been demonstrated to be a proficient antioxidant, protecting the liver by neutralizing dangerous hydroxyl radicals, superoxide ions and hypochlorous acid. In this way silymarin neutralizes the toxins that destroy the cellular membrane systems and the hepatocyte's genetic material [10, 26, 41]. Silymarin, like ALA, increases cellular glutathione levels and decreases tumor promoter activity [1, 30].

Human viral hepatitis studies with silymarin demonstrate quicker normalization of liver enzymes, expeditious reduction of bilirubin levels, and shorter hospital stays [31]. In addition, silymarin has been shown to be an effective antidote for toluene and xylene toxicity, and drug overdoses [14, 29, 40]. Alcoholic and other chronic liver disease patients lowered their liver enzymes, decreased their levels of procollagen III, and improved the histology of their livers with daily oral administration of silymarin [2, 13, 34]. Taking this intelligent reasoning into account, silymarin offers another effective treatment choice for serious liver disease.

Selenium

Selenium (Se) is an essential metal that is required for normal antioxidant metabolism, reproduction and thyroid function. It is also an important coenzyme for the glutathione peroxidase detoxification system. Because of this, selenium

neutralizes peroxides that proliferate under oxidative stress and consequently protects cell membranes from free radical damage.

Selenium often combines with amino acids and forms selenoproteins. Viruses might benefit from being directly involved in this selenoprotein encoding process by monitoring selenium levels in the cell. Consequently, this viral behavior could act as a barometer for increasing or decreasing viral reproduction. If cellular selenoprotein levels fall, the virus might become more active and produce more viruses that attack new cells. If selenoprotein levels rise, the virus may remain in a dormant state for longer periods of time or remain permanently dormant.

Research papers have reported that RNA viruses, including hepatitis C virus, encode selenium-dependent glutathione peroxidase genes. In view of this concept, it is entirely possible that a specific viral gene could generate a selenium shortage in the host. And in this way, a selenium deficiency could stimulate viral proliferation and thus promote the progression of hepatitis C. To continue, in that case, the addition of selenium might act as a "birth control pill" for the virus, and thus slow down it reproductive mechanisms. According to several investigators this could give the immune system a chance to control the hepatitis C, or HIV disease process [42, 45].

Conclusion

There are no remarkably effective treatments for chronic hepatitis C in general use. Interferon and antivirals have less than a 30% response rates and liver transplantation is uncertain and tentative. This is partially due to the residual viremia; the newly transplanted liver ultimately becomes infected again [44].

The triple antioxidant combination of alpha-lipoic acid, silymarin and selenium were chosen for a conservative treatment of hepatitis C because these substances protect the liver from free radical damage, increase the levels of other fundamental antioxidants, and interfere with virus proliferation. The 3 patients presented in this paper followed the triple antioxidant program and recovered quickly from this potentially devastating viral infection. Furthermore, liver transplantation can be painful, disabling, and extremely costly.

The author offers a more conservative approach to the treatment of hepatitis C, that is exceedingly less expensive. One year of the triple antioxidant therapy described in this paper costs less than $ 2,000, as compared to more than $ 300,000 a year for liver transplant surgery. It appears reasonable, that prior to liver transplant surgery evaluation, or during the transplant evaluation process, this conservative triple antioxidant treatment approach should be considered. If there is a significant betterment in the patient's condition, liver transplant surgery may be avoided.

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