L-CARNITINE AND L-ACETYLCARNITINE

What is carnitine?

L-carnitine is an amino acid found in red meat and acetyl-L-carnitine is another form of this nutrient. Carnitine can be made in small quantities by the brain, liver and kidneys. Among other things, this amino acid plays a role in helping to release energy from fat by moving fats to power plants within cells where fats can be burnt as fuel. These cellular power plants are called mitochondria and are responsible for making the energy a cell needs to survive and function.

Carnitine appears to have antioxidant properties and may also play a role in maintaining blood sugar levels. According to at least one study, people with HIV/AIDS (PHAs) can have normal levels of carnitine in their serum (the fluid part of the blood) while still having very low levels in the cells, where carnitine is needed.

In PHAs whose health has improved because of highly active antiretroviral therapy (HAART), carnitine levels may not return to normal.

When taken orally as a supplement, only a relatively small amount—between 5% and 18%—of carnitine is absorbed.

Why do PHAs use this supplement?

Carnitine has many potential uses, including the following:

1. helping to heal damaged nerves—peripheral neuropathy (PN)
2. helping to decrease levels of lactic acid in the blood
3. reducing higher-than-normal levels of cholesterol and/or triglycerides
4. helping to maintain muscle growth

1. To manage peripheral neuropathy (nerve damage causing tingling, numbness or burning in the hands, feet and legs)

Levels of carnitine in the blood are sometimes lower in PHAs with peripheral neuropathy, particularly under the following conditions:

- damage from viral infections such as HIV and CMV (cytomegalovirus)
- the use of “d” drugs such as d4T, ddI and ddC
- the use of some anti-cancer drugs and antibiotics
- alcohol abuse
- diabetes

What the medications in the above list have in common is that they can damage the energy-producing parts of nerve cells—the mitochondria. Injured mitochondria cannot supply sufficient energy and nerves begin to malfunction and can die. Nerves in the feet, legs and hands, particularly in the skin covering those body parts, appear to be especially susceptible to PN. Some researchers have noticed that PHAs with PN can develop abnormal sweating, suggesting that nerves in sweat glands can also be affected.

One formulation of carnitine, acetyl-L-carnitine...
(ALCAR), may play a role in the management of PN. This compound helps mitochondria function and also appears to enhance the effect of a chemical that helps nerves grow—nerve growth factor.

Researchers in England conducted an extensive study of ALCAR in PHAs with peripheral neuropathy. Their findings revealed that most PHAs showed some degree of recovery from nerve damage after taking ALCAR 1.5 grams twice daily for up to 2½ years.

Seventy-six percent of participants had significantly reduced pain. Because this was not a controlled clinical trial comparing ALCAR to a placebo or another substance, researchers cannot be certain that the reduction in pain was indeed caused by ALCAR. To clarify this issue, placebo-controlled studies of ALCAR are taking place in the European Union and in Vancouver, British Columbia.

In the British study, analyses of skin samples taken during the clinical trial found that after six months of ALCAR use, nerve fibres were undergoing re-growth. The longer participants took the supplement, the greater the re-growth. Nerve fibres are slow-growing so it clearly takes many months, perhaps even years, for the damage from PN to heal.

There were no significant changes to CD4+ and CD8+ cells or viral load measures during the study.

The research team speculates that ALCAR may have helped nerves for the following reasons:

- Carnitine has antioxidant properties, possibly protecting nerve cells from the toxicity of nucleoside analogues.
- By improving the transport of fats and sugar, carnitine may have helped cells become more energetic and active, perhaps stimulating their recovery.
- Carnitine could have helped nerve regrowth and repair by enhancing the effects of nerve growth factor.
- PHAs with PN have been found to have decreased levels of ALCAR in their blood and the supplement could have reversed this.

Overall, this study goes a long way toward helping researchers explore the role of carnitine, particularly ALCAR, as part of the management of PN.

Two randomized, placebo-controlled studies using ALCAR 500 mg/day or 1,000 mg/day have also found it to be beneficial in the management of PN in HIV negative people with diabetes.

2. To help reduce lactic acid levels in the blood

One of the complications that can occur in users of a class of anti-HIV drugs called nucleoside analogues, is the development of higher-than-normal levels of lactic acid. If levels become very high, the following signs/symptoms may occur as part of a condition called lactic acidosis:

- unexpected tiredness
- abdominal pain
- swollen, fatty liver
- shortness of breath
- nausea and/or vomiting

The following blood tests help identify lactic acidosis:

- lactate levels of 5 mmol/L or greater
- bicarbonate levels of 20 mmol/L or lower

Anecdotal reports suggest that L-carnitine may play a role in helping PHAs to recover from lactic acidosis. In a pilot study of six PHAs who were extremely ill and who had high levels of lactic acid in their blood from drug-related side effects, researchers gave them intravenous L-carnitine at doses between 50 mg and 100 mg/kg of body weight per day. Despite this treatment, only three of the participants survived and recovered from lactic acidosis. Other researchers have intervened at earlier stages of lactic acidosis with oral supplements of B vitamins and L-carnitine with successful results.
3. To reduce high levels of cholesterol and/or triglycerides in the blood

Having higher-than-normal levels of lipids—cholesterol and triglycerides—in the blood increases the risk of cardiovascular disease. In a small, controlled trial of HIV positive people, carnitine caused triglyceride levels to drop significantly after two weeks at a dose of six grams daily. However, this study was done in 1993, when AZT was the only antiretroviral drug being used.

In 2001, results of a pilot study in Montreal were released. L-carnitine at a dose of 3 grams daily was used by 16 PHAs who were also taking HAART. Triglyceride levels decreased significantly within the first month and by the end of the study had deceased by about 35%. By the end of the study, 70% of participants had their triglyceride levels return to the normal range.

In the same year, a German study found that L-carnitine at a dose of 1 gram twice daily for three months lowered cholesterol but not triglyceride levels in 12 PHAs.

4. To avoid muscle wasting and fatigue

Some HIV positive people use carnitine supplements to treat muscle wasting and fatigue due to anti-HIV drugs. A 1994 study of 21 men with AZT-related myopathy (muscle wasting) showed that the men’s muscle tissue had been damaged and that lipids (fats) had built up in the tissue. The study also showed that the most badly damaged muscle had the lowest levels of carnitine. A test-tube study done the same year suggested that carnitine supplements might improve AZT-related myopathy, although no trials in HIV positive people have been done to assess this compound’s impact on muscle wasting and fatigue.

5. To delay or minimize fat wasting

L-carnitine has been tested in Germany as a potential treatment to stop the loss of fat that can occur with the HIV lipodystrophy syndrome. Twelve PHAs were given 1 gram of L-carnitine twice daily for three months. However, this supplement did not prevent fat loss, though cholesterol but not triglyceride levels fell significantly. Researchers at the University of Modena in Italy are planning a clinical trial of acetyl-l-carnitine at a dose of 3 grams daily to assess any impact on the HIV lipodystrophy syndrome. They have decided to do this because they have previously conducted lab experiments with cells, nukes and ALCAR. In doing those experiments, they found that this supplement was able to partially prevent some of the damage caused by d4T and AZT (Giovanni Guaraldi MD, personal communication).


Availability

Carnitine is made by the Sigma-Tau company, in Italy, in two formulations:

- L-carnitine
- acetyl-L-carnitine

L-carnitine is sold under the brand name Carnitor and is available by prescription in North America. Acetyl-L-carnitine (ALCAR) is sold under the brand name Nicetile in Italy and some countries of the European Union. Sigma-Tau does not appear to market ALCAR in North America. In Canada and the United States, some health food stores also sell different brands and formulations of carnitine. All formulations of carnitine are expensive. ALCAR is more often used in studies of neuropathy and may be most useful for this condition. Both formulations of carnitine have been used in trials related to HIV, although some HIV nutritional experts have suggested the acetyl form may be more useful.

The dose usually recommended for PHAs varies between 500 mg and 3,000 mg (3 grams) a day. This can be divided into several doses and taken with food.
Side effects

1. Gastrointestinal
Nausea, vomiting and diarrhea may occur, especially in people who take more than 4 grams per day.

2. Neurological
Seizures have been reported in some people taking carnitine supplements, regardless of whether or not these people had seizures in the past.

3. Thyroid hormones
The hormones produced by the thyroid gland are called T3 (triiodothyronine) and T4 (thyroxine). Thyroid hormones help control the body's ability to produce energy and regulate its temperature. In lab experiments, L-carnitine blocks the ability of cells to respond to these hormones. In studies in HIV negative people, L-carnitine, at doses of 2 or 4 grams per day, reduced thyroid hormone levels. We are not sure what effect lower doses of carnitine might have on thyroid hormone levels. If thyroid hormone levels fall below normal, a range of symptoms may develop, including the following:
   - unexpected tiredness
   - feeling cold
   - dry skin
   - muscle weakness
   - forgetfulness and difficulty concentrating
   - impaired hearing
If you are taking carnitine supplements, your doctor may wish to regularly monitor the health of your thyroid gland.

4. Pregnancy
Carnitine has not been studied in pregnant women. Therefore, the manufacturer suggests that carnitine only be used in this population if it is clearly needed.

Drug interactions
Always tell your doctor and other members of your health care team about all the medications—prescription and non-prescription—herbs and supplements that you are taking. Carnitine may interfere with the following drugs:
   - drugs to treat or prevent blood clots—acenocoumarol/nicoumalone (Sintrom)
   - thyroid hormones

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Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV-related illness and the treatments in question.

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