

# L-Carnitine

## The effect of L-carnitine supplementation on plasma carnitine levels and various performance parameters of male marathon athletes

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*Nutrition Research Volume 17, Issue 3, March 1997, Pages 405-414*

### **Abstract**

The effect of L-carnitine supplementation on the plasma carnitine levels and various performance parameters of seven male marathon athletes was investigated. Each athlete completed two progressive treadmill tests to exhaustion, separated by a six week supplementation period (2g L-carnitine/day). During the treadmill tests peak treadmill running speed, oxygen consumption, cardiovascular responses, respiratory exchange ratio and plasma carnitine levels were monitored. After supplementation peak treadmill running speed increased by 5.68%, average oxygen consumption (VO<sub>2</sub>) and heart rate decreased, and respiratory exchange ratio values showed a declining tendency. After supplementation plasma acyl-, total- and percentage bound carnitine levels increased significantly, whereas free carnitine levels increased but remained below the normal range. Findings from this study suggest that L-carnitine supplementation could positively influence aerobic capacity.

# **Efficacy of L-CARNITINE administration on fatigue, nutritional status, oxidative stress, and related quality of life in 12 advanced cancer patients undergoing anticancer therapy**

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## **Abstract**

### **Objective**

Fatigue is a multidimensional symptom that is described in terms of perceived energy, mental capacity, and psychological status: it can impair daily functioning and lead to negative effects on quality of life. It is one of the most common side effects of chemotherapy and radiotherapy. In recent studies, L-CARNITINE (LC) supplementation has been demonstrated to be able to improve fatigue symptoms in patients with cancer.

### **Results**

Fatigue, as measured by the Multidimensional Fatigue Symptom Inventory—Short Form, decreased significantly, particularly for the General and Physical scales, and for quality of life in each subscale of quality of life in relation to oxidative stress. Nutritional variables (lean body mass and appetite) increased significantly after LC supplementation. Levels of reactive oxygen species decreased and glutathione peroxidase increased but not significantly. Proinflammatory cytokines did not change significantly.

### **Conclusion**

Improvement of symptoms with respect to fatigue and quality of life in relation to oxidative stress may be explained mainly by an increase in lean body mass, which may be considered the most important nutritional or functional parameter in assessing the cachectic state of patients. In this view, fatigue with related symptoms can well be considered an important constituent of cancer-related anorexia cachexia syndrome.

## **Antioxidant and antiradical activities of L-CARNITINE**

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*Life Sciences, Volume 78, Issue 8, 18 January 2006, Pages 803-811*

### **Abstract**

L-CARNITINE plays an important regulatory role in the mitochondrial transport of long-chain free fatty acids. In this study, the antioxidant activity of L-CARNITINE was investigated as in vitro. The antioxidant properties of the L-CARNITINE were evaluated by using different antioxidant assays such as 1, 1-diphenyl-2-picryl-hydrazyl free radical (DPPH<sup>•</sup>) scavenging, total antioxidant activity, reducing power, superoxide anion radical scavenging, hydrogen peroxide scavenging and metal chelating activities. Total antioxidant activity was measured according to ferric thiocyanate method.  $\alpha$ -tocopherol and trolox, a water-soluble analogue of tocopherol, were used as the reference antioxidant compounds. At the concentrations of 15, 30 and 45  $\mu\text{g/mL}$ , L-CARNITINE showed 94.6%, 95.4% and 97.1% inhibition on lipid peroxidation of linoleic acid emulsion, respectively. On the other hand, 45  $\mu\text{g/mL}$  of standard antioxidant such as  $\alpha$ -tocopherol and trolox indicated an inhibition of 88.8% and 86.2% on peroxidation of linoleic acid emulsion, respectively. In addition, L-CARNITINE had an effective DPPH<sup>•</sup> scavenging, superoxide anion radical scavenging, hydrogen peroxide scavenging, total reducing power and metal chelating on ferrous ions activities. Also, those various antioxidant activities were compared to  $\alpha$ -tocopherol and trolox as references antioxidants.

## **Oxidative stress on mitochondrial antioxidant defense system in the aging process: Role of DL- $\alpha$ -lipoic acid and L-CARNITINE**

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*Clinica Chimica Acta, Volume 355, Issues 1-2, May 2005, Pages 173-180*

### **Abstract**

#### **Background**

Oxidative damage is hypothesized to accumulate throughout the lifetime of an organism, eventually giving rise to aging. The mitochondria may be the primary cellular source and target of endogenous ROS as they are produced as a normal byproduct of the electron transport system.

#### **Result**

There was a significant reduction in the levels of antioxidants in both middle-aged and aged rats whereas the thiobarbituric acid reactive substances were found to be increased. Co-supplementation of carnitine and lipoic acid improved the antioxidant status and brought down the levels of TBARS.

#### **Conclusion**

Co-supplementation of lipoic acid with carnitine has a beneficial effect in reversing the age-related abnormalities seen in aging. This effect was associated with the decrease in free radical production and rise in antioxidant levels by carnitine and lipoic acid, thereby lowering oxidative stress.

**Oral carnitine supplementation increases sperm motility in asthenozoospermic men with normal sperm phospholipid hydroperoxide glutathione peroxidase levels**

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*Fertility and Sterility, Volume 83, Issue 2, February 2005, Pages 355-361*

**Abstract**

**Objective**

To clarify the role of carnitine supplementation in idiopathic asthenozoospermia and to look for a rationale for its use in asthenozoospermic patients.

**Result(s)**

When asthenozoospermic subjects were divided in two groups on the basis of PHGPx levels, we observed an improvement of mean sperm motility only in the group of patients with normal PHGPx levels.

**Conclusion(s)**

Phospholipid hydroperoxide glutathione peroxidase has an important role in male infertility, and carnitine treatment might improve sperm motility in the presence of normal mitochondrial function.

## **Primary carnitine deficiency: adult onset lipid storage myopathy with a mild clinical course**

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*Journal of Clinical Neuroscience, Volume 11, Issue 8, November 2004, Pages 919-924*

### **Abstract**

We studied two adult patients with myalgia and muscular fatigability during prolonged physical exercise. Serum creatine kinase was increased and muscle biopsy revealed a lipid storage myopathy affecting predominantly the type I fibres. Skeletal muscle carnitine content was reduced to 15% and 21% of the normal mean values, while serum carnitine levels were either normal or decreased. Four months of oral therapy with L-CARNITINE (3 g per day) resolved the clinical symptoms completely in both patients, and a subsequent muscle biopsy confirmed a marked reduction of lipid storage, along with increased muscle carnitine levels. The analysis of renal carnitine excretion and the exclusion of possible secondary carnitine deficiencies in both patients are compatible with mild defects of the carnitine transporter in one patient and of carnitine biosynthesis in the other. Since myalgia and muscular fatigue are frequent but unspecified complaints of otherwise clinically unremarkable adult patients, it is important to identify myopathies associated with primary carnitine deficiency because they may be amenable to treatment.

**Abbreviations:** CK, creatine kinase; COX, cytochrome *c* oxidase; OCTN, organic cation transporter; s, seconds

## **L-CARNITINE and acetyl-L-CARNITINE in the treatment of complications associated with HIV infection and antiretroviral therapy**

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***Mitochondrion, Volume 4, Issues 2-3 July 2004, Pages 163-168  
Mitochondria, HIV and Antiretroviral Therapy***

### **Abstract**

L-CARNITINE (LC) and acetyl-L-CARNITINE (ALC) play major roles in cell energy and lipid metabolism. Supplementation with these nutrients, which are highly popular in USA, has been associated with favorable effects, including anti-oxidant action, neuro- and cardioprotection, immunomodulation, and cognitive enhancement. Patients with HIV infection and undergoing highly active antiretroviral therapy (HAART) often develop complications, such as polyneuropathy, skeletal myopathy, dyslipidemia and lipodystrophy, which have been linked to mitochondrial dysfunction. Moreover, these patients are often LC-deficient. Thus, they may benefit from LC and ALC supplementation. Indeed, oral, i.v., or i.m. administration of large doses of LC and/or ALC to HIV positive subjects untreated/treated with HAART was shown to: (1) increase the number of CD4 cells and reduce lymphocyte apoptosis; (2) improve symptoms of polyneuropathy; (3) prevent cardiovascular damage from wasting and diarrhea syndromes; (4) decrease serum levels of triglycerides and TNF $\alpha$ . No significant toxicities were associated with LC and ALC treatment. Although promising, most of these findings derive from small uncontrolled clinical trials. Further research is warranted to prove the efficacy and safety of LC and ALC supplementation in patients with complications of HIV infection and HAART.

## **L-carnitine and its possible role in red cell and platelet storage\***

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*Transfusion Medicine Reviews, Volume 18, Issue 1, January 2004, Pages 58-65*

### **Abstract**

The storage of red cells or platelets in the liquid state results in changes in quality over time. These changes are collectively known as the storage lesion and are associated with decreased in vivo viability and functionality. Modification of the components of the liquid milieu could favorably influence these changes. ◀L-carnitine▶ is a naturally occurring compound, which is best known for its role in facilitating the transport of long chain fatty acids across the mitochondrial membrane. An additional role for this compound may also exist as a reservoir of acylcarnitines to replace oxidized fatty acids in membrane phospholipids. In experimental studies, ◀L-carnitine▶ has been shown to reduce hemolysis and to improve in vivo survival in nonleukoreduced red cells. This effect on hemolysis appears to be attenuated by prestorage leukoreduction, but the practical benefit of this effect to transfusion recipients is unclear. ◀L-carnitine▶ has also been shown to reduce glycolysis and maintain a better pH in liquid stored platelets. This effect could result in extended platelet storage to 7 or 10 days. Based on such results, a role for ◀L-carnitine▶ as an additive to improve platelet quality in extended platelet storage is suggested.

\* Supported by a grant from Sigma-tau Corporation, Pomezia, Italy.



## **blind crossover trial\***

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*Fertility and Sterility Volume 79, Issue 2, February 2003, Pages 292-300*

### **Abstract**

#### **Objective**

To determine the efficacy of **L-carnitine** therapy in selected cases of male factor infertility.

#### **Result(s)**

Excluding outliers, a statistically significant improvement in semen quality, greater than after the placebo cycle, was seen after the **L-carnitine** therapy for sperm concentration and total and forward sperm motility. The increase in forward sperm motility was more significant in those patients with lower initial values, i.e.,  $<5 \times 10^6$  or  $<2 \times 10^6$  of forward motile sperm/ejaculate or sperm/mL.

#### **Conclusion(s)**

Based on a controlled study of efficacy, **L-carnitine** therapy was effective in increasing semen quality, especially in groups with lower baseline levels. However, these results need to be confirmed by larger clinical trials and in vitro studies.

\* Supported by the Italian Ministry of University and Research, the University of Rome "La Sapienza," and the Rome University Hospital of the Faculty of Medicine through grants from Sigma Tau srl (Pomezia, Italy).

## **Effects of carnitine on cardiac function after cardioplegic ischemia in neonatal rabbit hearts**

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*The Annals of Thoracic Surgery, January 2001, Pages 254-259*

### **Abstract**

#### **Background.**

Ischemia immediately impairs myocardial fatty acid metabolism and reduces the concentration of carnitine which is an essential cofactor for fatty acid metabolism in the mitochondria. The purpose of this study was to investigate the effects of carnitine administration on recovery of cardiac function after cardioplegic ischemia in the neonatal heart where fatty acid metabolism is not a predominant source of adenosine triphosphate.

#### **Results.**

Carnitine significantly improved not only LV systolic function but also LV diastolic function ( $p < 0.05$ ) as well as LV compliance after ischemia. Coronary blood flow and myocardial oxygen consumption were significantly improved after ischemia in the carnitine group compared with the control group ( $p < 0.05$ ).

#### **Conclusions.**

These results suggest that carnitine strikingly improves LV functional recovery and aerobic metabolism after cold cardioplegic arrest, and may improve cardiac performance in neonates after open heart surgery.

## **Three-year survival of patients with heart failure caused by dilated cardiomyopathy and L-carnitine administration**

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*American Heart Journal, Volume 139, Issue 2, Supplement 2, February 2000, Pages s120-s123*

### **Abstract**

We examined the efficacy of long-term L-carnitine administration for the treatment of heart failure caused by dilated cardiomyopathy in adult patients. To accomplish this, we studied 80 patients with moderate to severe heart failure (New York Heart Association classification III to IV) caused by dilated cardiomyopathy. This article reports on the nearly 3 years of follow-up data on patient mortality. Primary results will be published in the future. After a period of stable cardiac function up to 3 months, patients were randomly assigned to receive either L-carnitine (2 g/d orally) or placebo. There were no statistical differences between the 2 groups at baseline examination in clinical and hemodynamic parameters, such as ejection fraction, Weber classification, maximal time of cardiopulmonary exercise test, peak  $VO_2$  consumption, arterial and pulmonary blood pressure, and cardiac output. After a mean of  $33.7 \pm 11.8$  months of follow-up (range 10 to 54 months), 70 patients were in the study: 33 in the placebo group and 37 in the L-carnitine group. At the time of analysis, 63 patients were alive. There were 6 deaths in the placebo group and 1 death in the L-carnitine group. Survival analysis with the Kaplan-Meier method showed that patients' survival was statistically significant ( $P < .04$ ) in favor of the L-carnitine group. L-carnitine appears to possess considerable potential for the long-term treatment of patients with heart failure attributable to dilated cardiomyopathy. (Am Heart J 2000;139:S120-S123.)

## **Carnitine Deficiency in Diabetes Mellitus Complications**

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*Journal of Diabetes and its Complications, Volume 13, Issues 5-6, September-December 1999, Pages 251-253*

### **Abstract**

In this study, the serum total, free and ester carnitine levels in 24 type II diabetes mellitus (DM) patients with complications and 15 type II DM patients with no complications were investigated. The patients were investigated in four groups; the control group included the patients with no complications (group 1), the groups including the patients with retinopathy (group 2), hyperlipidemia (group 3), and neuropathy (group 4). In addition, patients were grouped into two. The first group included 10 patients who took insulin by injection (group 5), and the second group included 29 patients using antidiabetic drugs orally (OAD) (group 6). Free and ester carnitine levels were determined by using Boehringer Manheim UV-enzymatic **L-carnitine** kit. Statistical analysis results showed that both the plasma total and free carnitine levels of groups 2, 3, and 4 were found to be low when compared to the levels of group 1 ( $p < 0.05$ ). It was observed that the plasma total and free carnitine levels of group 5 were lower when compared to group 6. No significant difference was observed between the plasma ester carnitine levels of all the groups investigated. As a result of this study, it has been thought that carnitine plays an important role in diabetes mellitus complications.

## **Carnitine and its derivatives in cardiovascular disease**

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*Progress in Cardiovascular Diseases, Volume 40, Issue 3, November-December 1997, Pages 265-286*

### **Abstract**

Carnitine and its derivative propionyl-**L-carnitine** are endogenous cofactors which enhance carbohydrate metabolism and reduce the intracellular buildup of toxic metabolites in ischemic conditions. The carnitines have been, and are being used in a spectrum of diseases including multiple cardiovascular conditions. These include angina, acute myocardial infarction, postmyocardial infarction, congestive heart failure, peripheral vascular disease, dyslipidemia, and diabetes. Most published data on carnitine, propionyl-**L-carnitine**, and other carnitine congeners are favorable but the clinical trials have been relatively small. In currently used doses, these substances are virtually devoid of significant side effects.

## **A new era for carnitine?\***

Giuseppe Famularo and Claudio De Simone

*Immunology Today, Volume 16, Issue 5, May 1995, Pages 211-213*

### **Abstract**

*Early in vitro experiments demonstrated the immunomodulating and anti-apoptotic properties of **L-carnitine**. More-recent studies have shown that the depletion of this compound plays a role in the pathogenesis of immune-mediated disorders, such as AIDS, septic shock and chronic fatigue syndrome. These data, combined with the safety of **L-carnitine**, have highlighted the potential for using this compound as an additional therapy to treat such disorders.*

## **Clinical and neurochemical effects of acetyl-L-carnitine in Alzheimer's disease**

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*Neurobiology of Aging, Volume 16, Issue 1, January-February 1995, Pages 1-4*

### **Abstract**

In a double-blind, placebo study, acetyl-L-carnitine was administered to 7 probable Alzheimer's disease patients who were then compared by clinical and  $^{31}\text{P}$  magnetic resonance spectroscopic measures to 5 placebo-treated probable AD patients and 21 age-matched healthy controls over the course of 1 year. Compared to AD patients on placebo, acetyl-L-carnitine-treated patients showed significantly less deterioration in their Mini-Mental Status and Alzheimer's Disease Assessment Scale test scores. Furthermore, the decrease in phosphomonoester levels observed in both the acetyl-L-carnitine and placebo AD groups at entry was normalized in the acetyl-L-carnitine-treated but not in the placebo-treated patients. Similar normalization of high-energy phosphate levels was observed in the acetyl-L-carnitine-treated but not in the placebo-treated patients. This is the first direct in vivo demonstration of a beneficial effect of a drug on both clinical and CNS neurochemical parameters in AD.