

Issue 101

In a nutshell

Carnitine plays a major role in energy production at the mitochondrial level. It has the potential to limit anoxic damage, whilst reducing peripheral arterial resistance.

The main clinical application benefit for which there is reasonable trial evidence is claudication. Other potential applications (e.g. renal dialysis, Alzheimer's disease) lack consistent trial evidence.

Carnitine

Arbor Clinical Nutrition Updates 2001 (Sept.);101:1-2
ISSN 1446-5450

ARCHIVES

The full list of archived issues can be found at www.arborcom.com/archives/. Some issues of our translated language editions are also available in archive, for Spanish, Portuguese and French.

COPYRIGHT, disclaimer and terms of use

This copy from our archives is for your private use only, and is NOT to be forwarded to any other party. Your use of these Updates constitutes your agreement to our disclaimer and terms of use: see section at the end of this publication.

NUTRITION RESEARCH REVIEW

Study one: Leg claudication

Carnitine supplementation improves exercise performance in patients with leg claudication, according to results from a new study from the USA and Russia.

Subjects: 155 patients with disabling leg claudication.

Method: Randomised, double-blind, placebo-controlled trial in which subjects took either propionyl-L-carnitine (2 g/day orally) or placebo for 6 months.

Results: The carnitine group had a significantly greater increase in peak walking time compared to the placebo group (54% increase in walking time compared with 25% increase for placebo $p < 0.001$). Similar results were seen in relation to time to onset of pain. The carnitine supplemented group did better than the placebo group in relation to walking distance, walking speed and a self-reported measure of general health.

Reference: Hiatt WR et al. Propionyl-L-carnitine improves exercise performance and functional status in patients with claudication. *Am J Med* 2001;110:616-622

Study two : Angina

Carnitine supplementation moderately improves exercise tolerance in patients with chronic stable angina, according to results from Indian research.

Subjects: 47 patients with chronic stable angina.

Method: Randomised, placebo-controlled trial using L-carnitine (2 g/day) for 3 months. Stress testing was carried out at the beginning and end of the treatment period.

Results: The carnitine group had a statistically significant improvement in the exercise duration (7.8 pre-treatment, 8.6 minutes after treatment, $p = 0.006$) and in time needed for the ST changes to revert to baseline (7.2 pre-treatment, 5.7 min after treatment, $p = 0.019$). There were no benefits seen in time to onset for ST depression or ST score. The placebo treated group showed no significant changes in any parameter after placebo treatment.

Reference: Iyer RN et al. L-carnitine moderately improves the exercise tolerance in chronic stable angina. *J Assoc Physicians India* 2000;48:1050-1052

Study three: Hyperthyroidism

Carnitine may be useful in treating symptoms of iatrogenic hyperthyroidism, according to results of a clinical trial from Italy.

Subjects: 50 women already taking a fixed TSH-suppressive dose of L-thyroxine.

Method: Cross-over randomised, placebo-controlled, double-blind trial in which the women were given, in addition to the thyroxine, carnitine (either 2 or 4 g/day) or placebo for 2 month periods.

Results: Symptoms of hyperthyroidism as well as a number of thyroid hormone-sensitive biochemical parameters decreased during carnitine treatment

and increased during placebo treatment. There was no difference in outcome between the two carnitine doses.

Reference: Benvenga S et al. Usefulness of L-carnitine, a naturally occurring peripheral antagonist of thyroid hormone action, in iatrogenic hyperthyroidism: a randomized, double-blind, placebo-controlled clinical trial. *J Clin Endocrinol Metab* 2001;86:3579-3594

Study four: Alzhiemers Disease

Carnitine had no effect in slowing the development of probable early stage Alzheimer's disease in an American study.

Subjects: 229 patients with a diagnosis of probable early Alzheimer's disease.

Method: Multi-centre randomised, placebo-controlled, double-blind trial in which the patients were given one year of acetyl-L-carnitine (3g/day) or placebo.

Results: Carnitine treatment was not associated with any significant slowing in the progress of disease symptoms.

Reference: Thal LJ et al. A 1-year controlled trial of acetyl-L-carnitine in early-onset AD. *Neurology* 2000;55:805-10

Comments

Carnitine is a very interesting substance. It is a small amino acid derivative. Although the richest source of carnitine in the diet is meat, it can be synthesised from the amino acids lysine and sulphur-containing methionine. Hence a dietary deficiency is only likely to occur as part of more general protein-energy malnutrition.

Carnitine plays a major role in energy production at the mitochondrial level via stimulation of fatty acid metabolism. It helps the transport of fatty acids into muscle cells. It improves glucose disposal and may reduce insulin resistance. It has a particularly important function in energy production in muscle.

It has the potential to limit anoxic damage, whilst reducing peripheral arterial resistance. This makes it a particularly interesting substance in ischaemic disease. It inhibits entry of thyroid hormone into certain cells. It may inhibit platelet-activating factor.

At the same time, various disease states can alter carnitine status. For example, renal failure and certain medications (e.g. some anti-epileptic and some anti-viral drugs) can increase carnitine excretion, whilst arterial insufficiency can decrease carnitine content of heart muscle cells.

The four studies we have summarised above are just a small sample of a large number of clinical and laboratory studies published on carnitine in the last two years. Clinical settings for these studies include: hyperlipidaemia, male infertility and Peyronie's

disease, peripheral neuropathy, overweight, cardiomyopathy, cerebellar ataxia, HIV infection, cancer, diabetes, acne, and patients on chronic haemodialysis!

Of these studies, the largest number have been concerned with arterial insufficiency (e.g. angina, myocardial insufficiency, peripheral claudication).

What conclusions can we draw from all this research? Firstly, the majority of trials have had small to moderate numbers of subjects. Secondly, whilst there have been an encouraging number of moderately positive outcomes, at the same time many studies have failed to show a benefit. So even the positive results should be regarded as preliminary findings of interest, requiring larger follow-up studies to confirm them.

We believe that reasonable conclusions regarding some of the main potential clinical uses for carnitine are:

- Claudication: there seems to be significant clinical benefit, particularly in more severe cases
- Alzheimer's disease: carnitine supplementation has generally not produced significant benefits.
- Myocardial insufficiency (e.g. congestive heart failure or cardiomyopathy): any benefit is still not clear.
- Renal dialysis: any benefit (e.g. in quality of life or reduced need for erythropoietin) is still not clear.

Side-effects in the doses reported so far have tended to be minor (e.g. nausea).

Disclaimer, copyright and terms of use

Your use of these Updates constitutes your agreement to our disclaimer and terms of use which can be found on our web site at: <http://arborcom.com/disclaim3.htm>. You can also obtain the disclaimer and terms of use by emailing us at: upD@arborcom.com.

© Copyright Arbor Communications PTL 1999. All rights reserved. This publication may NOT be forwarded onto others without our written permission.

If you want to receive the Clinical Nutrition Updates on an ongoing basis, please send us a request email to upD@arborcom.com. This is a FREE service to health professionals and students. Include details of your name, email address, which country you live in, institution you are associated with (if relevant) and professional background. The Updates are available in English, Spanish, Portuguese, Italian, French, Korean and Russian