

Is an Ergogenic Effect Produced by L-Carnitine Supplementation in Healthy Adults?

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Introduction

L-carnitine (carnitine) is a vitamin-like, short chain carboxylic acid, synthesised in the liver and kidneys from methionine and lysine and is found mostly in meat and dairy products. Whilst short and medium chain fatty acids are able to traverse the inner mitochondrial membrane, long chain fatty acids require a transport mechanism in which carnitine plays an essential role. Within the muscle cell long chain free fatty acids are activated by coenzyme A (CoA) and bind to carnitine enabling transfer from the cytosol to the mitochondrial matrix. Thus carnitine is essential for long chain fatty acid oxidation. Once inside the mitochondrial matrix the fatty acid chain is released from carnitine and becomes available for energy metabolism. The free carnitine then binds with metabolic by-products (acyl-CoA) and returns to the cytoplasm via the translocase to repeat the cycle. Carnitine therefore not only shuttles fatty acids for energy production but also removes waste from the mitochondria.

The role of carnitine in fatty acid transportation has not gone unnoticed by manufacturers of nutritional supplements. They argue, with the support of some studies, (Kaats *et al.*, 1992) that supplemental carnitine helps in weight management by enhancing the rate at which the body utilises fat for energy production. The notion is that if fat is being metabolised it is not being stored as adipose tissue. Thus carnitine is being marketed as a 'fat burner' for those seeking a leaner body. Furthermore, as carnitine removes bi-products of metabolism from the mitochondria it

is suggested that a detoxification effect can be achieved by supplementation thus enhancing removal of waste from the mitochondria which would otherwise impair performance.

Successes in medical therapies have given further impetus to claims that carnitine may benefit healthy people which has opened a market aimed at athletes. Treatment with supplemental carnitine of disorders such as type II carnitine palmitoyltransferase deficiency, end stage renal disease and peripheral arterial disease appear to demonstrate beneficial effects. Indeed, treatment of patients with peripheral arterial disease has been shown to improve claudication limited exercise perhaps due to a vaso-dilatory effect. This has been seized upon by body builders and other athletes as a possible strategy for alleviating delayed onset muscle soreness.

Carnitine is being sold to athletes for its potential respiratory quotient lowering effect. It is suggested that with enhanced fatty acid metabolism glucose energy stores can be spared resulting in greater endurance and delayed onset of fatigue. Indeed, Gorostiaga *et al.*, (1989) reported a decreased respiratory quotient following administration of 2g of carnitine a day. They believed that this suggests increased fatty acid utilisation and probable glycogen sparing.

Some studies have suggested that endogenous carnitine is depleted by prolonged or high intensity aerobic exercise resulting in reduced mitochondrial fatty acid uptake. Naturally, this has led to the hypothesis that carnitine supplementation may be used to increase muscle fatty acid oxidation. It is well understood that the contribution of fat to energy production decreases with higher exercise intensities. A study by van Loon

et al., (2001) found that the relative contribution of fat energy to total energy expenditure did not change at exercise intensities ranging from rest to 55% of work max. However, at increased levels of up to 75% work max. body fat oxidation decreased by around 34%. It was noted that this was despite the fact that sufficient free fatty acids were available for metabolism. They suggest that at high exercise intensity free carnitine availability is reduced and hypothesise that this could be responsible for reduced fat oxidation by limiting entry of long chain fatty acids into the mitochondria.

Brass and Hiatt (table 1) reveal the key areas postulated for carnitine supplementation; however, they suggest that ‘While these rationales are attractive, varied assumptions have gone unchallenged and supportive data from clinical studies are frequently not available.’ (Brass & Hiatt, 1998).

Table 1. Postulated Biochemical or Physiological Effects of Carnitine Supplementation Relevant to Exercise Performance

Increase rate of fatty acid oxidation
Enhance efficiency of muscle oxidation
Preservation of muscle glycogen
Enhanced muscle acylcarnitine production, lowering acyl-CoA content
Maintain pyruvate dehydrogenase activity
Facilitate complete oxidation of substrate
Lower content of toxic acyl groups
Improve muscle fatigue resistance
Increase muscle blood flow secondary to vasodilatation
(Brass & Hiatt, 1998)

Literature Review

The theoretical case for carnitine as an ergogenic aid appears to be well established; however, studies in support of this do not appear to be convincing. Beltz & Doering, (1993) in their review into the efficacy of nutritional supplements used by athletes point out that the Food and Drug Administration (FDA) regard nutritional supplements as food and not drugs; therefore, 'dosage guidelines are inadequate, and quality control is poor.' They suggest that there is little evidence that nutritional supplements produce an ergogenic effect and 'some products have the potential for harm.' Indeed, Brass & Hiatt, (1998) say that the regulatory standards for traditional pharmacology provide objective evidence towards claims made; however, 'in the absence of such standards for dietary supplements, the scientific community must provide equivalent rigor in evaluating the available data.' (Brass & Hiatt, 1998). One of the key questions within current research is to establish whether or not supplemental carnitine can increase the size of the intracellular carnitine pool. The studies below appear to suggest that this is not possible and therefore raises doubt as to whether carnitine supplementation can enhance the transportation of long chain fatty acids into the cell.

Brass *et al.*, (1994) undertook a study aimed at challenging the hypothesis that carnitine supplementation by intravenous administration during exercise can modify muscle carnitine homeostasis. Healthy volunteers were administered 185 μ mol/Kg of carnitine and undertook a bicycle ergometer exercise session. Compared to controls results revealed that, despite elevated carnitine levels in blood plasma, supplemental carnitine had no effect on muscle carnitine content, respiratory exchange ratio, muscle

lactate accumulation, plasma lactate concentration or muscle glycogen utilisation during exercise.

In a field study involving seven male endurance-trained athletes, during a marathon run, Colombani *et al.*, (1996) administered 2g carnitine supplements 2 hours prior and at the 20km stage of the event in an attempt to study the effects of carnitine supplementation on physical performance and energy metabolism. Plasma concentrations of metabolites and hormones were measured prior to and following the event. Further measurements for respiratory exchange were also collected. Results suggested that although there was an increase in plasma carnitine concentrations there were no improvements in performance or any effect on metabolism. Furthermore, there was no evidence of improved recovery.

In another study aimed at athletes Trappe *et al.*, (1994) considered the effects of carnitine supplementation on short high intensity exercise. Twenty male swimmers took part in this study and were subjected to two trials separated by a seven day period. After the first trial the swimmers were placed in either a carnitine or control group. During the trials each swimmer was asked to undertake five short distance (91.4m) swims with a 2 minute rest interval separating each bout of maximal exercise. Post exercise they were administered either 2g carnitine by means of a citrus drink or just a citrus drink twice a day for seven days. Blood serum carnitine levels in the treated group were found to be significantly elevated whilst the control group remained unchanged. However, no differences in performance times were recorded and it was concluded that supplementary carnitine has no ergogenic benefits.

Similarly, Barnett *et al.*, (1994) undertook a study aimed at determining the effects of supplementary carnitine on muscle carnitine, blood carnitine and lactate accumulation in high intensity exercise. They involved eight subjects in a series of high intensity sprint cycling exercises involving a 4 minute cycle at 90% VO_2 max with a 20 minute rest period with a further five 1 minute cycles at 115% VO_2 max each followed by a short rest. The subjects received dietary supplementation of 4g/day carnitine for 14 days. As with the previously reported studies plasma carnitine was significantly elevated, however, there was no effect on muscle pool carnitine and it was therefore concluded that supplemental carnitine could not alter lactate accumulation.

Preservation of muscle glycogen is of great interest to endurance athletes as enhanced economy would increase endurance and lengthen the time taken to reach fatigue. Carnitine has been linked with a lowering effect of the respiratory-quotient by increasing the availability of fatty acids. Decombaz *et al.*, (1993) carried out a study considering the effect of carnitine supplementation on sub maximal exercise after depletion of muscle glycogen. Nine healthy males were given either carnitine or a placebo for seven days. Following an overnight fast they were engaged in a series of cycle exercises aimed at depleting glycogen. Their results concluded that carnitine supplementation has no effect on substrate metabolism following glycogen depletion and therefore it seems unlikely that a glycogen sparing effect can be achieved.

In another study Vukovich *et al.*, (1994) measured the effects of supplemental carnitine on muscle carnitine and muscle glycogen levels during exercise by means of biopsy and serum analysis of subjects taking 6g a day of carnitine. Subjects were fed a fatty meal (90g of fat) 3 hours before undertaking exercise involving cycling for 1

hour at 70% VO_2 max. Blood and biopsies were taken pre exercise and at regular intervals. Random subjects then undertook further trials at 7 and 14 days following continued supplementation with carnitine. One group received 2000 units of heparin 15 minutes before exercise to increase levels of free fatty acids. The other group received none. They reported that there was no difference in VO_2 , respiratory exchange ratio, heart rate, or the amount of carbohydrate or fat oxidized in any of the trials. It was concluded that carnitine supplementation does not increase muscle carnitine concentrations nor does it affect lipid or carbohydrate oxidation during exercise. They suggest that a sufficient amount of carnitine exists within the mitochondria to facilitate lipid oxidation.

It appears conclusive that supplemental carnitine will not increase uptake in the muscle. Hawley *et al.*, (1998) point out that this might be due to the significant concentration gradient working against the plasma pool (plasma 40 to 60 $\mu\text{mol/L}$ – muscle 3 to 4 mmol/L). They suggest that even substantial oral doses of carnitine would not overcome such a large gradient. Furthermore, they report that although small quantities of carnitine are lost each day in the urine the turnover between synthesis and loss in healthy adults is balanced and that there is no evidence that heavy exercise contributes to depletion. They conclude that current data, from well controlled studies, do not suggest any benefits from carnitine supplementation on oxidation of fatty acids. This appears to be supported by Heinonen, (1996) who sums up a review of current scientific based knowledge by stating ‘carnitine supplementation neither enhances FA oxidation in vivo nor spares glycogen or postpones fatigue during exercise...does not unequivocally improve performance of

athletes...does not reduce body fat or help to lose weight...does not affect the maximal oxygen uptake ($VO_2\text{max}$).’ ((Heinonen, 1996)

Conclusions

There is a theoretical argument favoring the ergogenic potential for carnitine supplementation which is supported by some successes in the treatment of certain medical conditions. Aspects of the theory are based on the notion that exogenous consumption can increase the availability of intra cellular carnitine and therefore enhance the transportation of long chain fatty acids into the mitochondria. However, a number of studies have been reviewed with supplemental dosages of carnitine ranging from 2-6g per day. Furthermore, experimental studies have employed a broad variety of exercise conditions ranging from glycogen depletion to fat saturation and from short high intensity to extended duration marathon running. Results have repeatedly shown that whilst plasma carnitine is increased with supplementation there is no effect on the levels within the cell. This is believed to be due to a significant concentration gradient between the plasma and muscle.

Current data from well controlled studies do not support the use of carnitine supplementation to improve performance in healthy individuals. It is accepted that during exercise there is a redistribution of free carnitine but there is no loss of total carnitine. It appears evident that there is no risk of athletes becoming deficient in carnitine or that there is an increased need brought about by activity. It is generally accepted that further studies are needed to fully understand potential ergogenic uses. However, based on current data, the ergogenic efficacy of carnitine is questionable.

References

- BARNETT, C., COSTILL, D. L., VUKOVICH, M. D., COLE, M. D., GOODPASTER, B. H., TRAPPE, S. W. & FINK, W. J. (1994). Effect of L-carnitine supplementation on muscle and blood carnitine content and lactate accumulation during high-intensity sprint cycling. *International journal of sport nutrition* **4**, 280-288.
- BELTZ, S. D. & DOERING, P. L. (1993). Efficacy of Nutritional Supplements Used by Athletes. *Clinical pharmacy* **12**, 900-908.
- BRASS, E. P. & HIATT, W. R. (1998). The role of carnitine and carnitine supplementation during exercise in man and in individuals with special needs. *American College of Nutrition* **17**, 207-215.
- BRASS, E. P., HOPPEL, C. L. & HIATT, W. R. (1994). Effect of Intravenous L-Carnitine on Carnitine Homeostasis and Fuel Metabolism During Exercise in Humans. *Clinical Pharmacology & Therapeutics* **55**, 681-692.
- COLOMBANI, P., WENK, C., KUNZ, I., KRAHENBUHL, S., KUHNT, M., ARNOLD, M., FREYRINDOVA, P., FREY, W. & LANGHANS, W. (1996). Effects of L-carnitine supplementation on physical performance and energy metabolism of endurance-trained athletes: A double-blind crossover field study. *European journal of applied physiology and occupational physiology* **73**, 434-439.
- DECOMBAZ, J., DERIAZ, O., ACHESON, K., GMUENDER, B. & JEQUIER, E. (1993). Effect of L-carnitine on submaximal exercise metabolism after depletion of muscle glycogen. *Medicine and science in sports and exercise* **25**, 733-740.
- GOROSTIAGA, E. M., MAURER, C. A. & ECLACHE, J. P. (1989). Decrease in Respiratory Quotient During Exercise Following L-Carnitine Supplementation. *International journal of sports medicine* **10**, 169-174.
- HAWLEY, J. A., BROUNS, F. & JEUKENDRUP, A. (1998). Strategies to enhance fat utilisation during exercise. *Sports Medicine* **25**, 241-257.
- HEINONEN, O. J. (1996). Carnitine and physical exercise. *Sports Medicine* **22**, 109-132.
- KAATS, G. R., WISE, J. A., BLUM, K., MORIN, R. J., ADELMAN, J. A., CRAIG, J. & CROFT, H. A. (1992). The Short-Term Therapeutic Efficacy of Treating Obesity with a Plan of Improved Nutrition and Moderate Caloric Restriction. *Current Therapeutic Research-Clinical and Experimental* **51**, 261-274.
- TRAPPE, S. W., COSTILL, D. L., GOODPASTER, B., VUKOVICH, M. D. & FINK, W. J. (1994). The Effects of L-Carnitine Supplementation on Performance During Interval Swimming. *International journal of sports medicine* **15**, 181-185.

- VAN LOON, L. J. C., GREENHAFF, P. L., TEODOSIU, D. C., SARIS, W. H. M. & WAGENMAKERS, A. J. M. (2001). The effects of increasing exercise intensity on muscle fuel utilisation in humans. *Journal of Physiology-London* **536**, 295-304.
- VUKOVICH, M. D., COSTILL, D. L. & FINK, W. J. (1994). Carnitine Supplementation - Effect on Muscle Carnitine and Glycogen-Content During Exercise. *Medicine and science in sports and exercise* **26**, 1122-1129.