

Long-Term Oral Carnitine Ingestion Does Not Alter Fat Metabolism Substrates during Exercise

Eizadi Mojtaba, Khorshidi Davood, Seyedhoseini Mohammad Ali, Dooaly Hussein

Department of Physical Education and Sport Science, South Tehran Branch, Islamic Azad University, Iran

ABSTRACT

Background & Aims: Accumulating evidence has reported significant sparing of muscle glycogen during exercise with elevated free fatty acid concentration (FFA), although the mechanisms underlying this response are a matter of some debate. The purpose of this study was to determine whether a long-term L-carnitine ingestion is effect on some markers of fat metabolism in none-trained male students.

Methods: Subjects included in the study were 30 none-trained male students (BMI 25–35 kg/m²) that divided into experimental (L-carnitine, 3g orally, daily, 21 days) and control (Lactose) groups, matched for age. Each subject participated in two experimental trials. All participants completed submaximal ergometry Astrand protocol on bicycle for 20 minutes before and after this supplementation period. A venous blood sample was collected immediately after each exercise test for determine plasma free fatty acid (FFA), triglyceride (TG) and other metabolites from all the subjects. Statistical analysis was performed with the SPSS software version 15.00. A p-value < 0.05 was considered to be statistically significant. **Results:** The data showed that FFA levels were not affected by L-carnitine supplementation ($P < 0.05$). In addition, all other blood variables measured were not significantly changed as a result of L-carnitine supplementation in experimental group ($P < 0.05$). **Conclusion:** Based on this data, it was concluded that long-term oral carnitine ingestion can not induce favorable changes in fat metabolism substrates during submaximal exercise in people without carnitine deficiency.

Keywords: Submaximal exercise, Carnitine ingestion, Metabolism.

INTRODUCTION

Glycogen and triacylglycerol (triglyceride) are condensed fuel reserves (1) which provide the body's skeletal muscle cells or other tissues with the chemical energy in form of glucose and free fatty acids (FFA) when necessary; for instance for growth and restoration or during exercise when metabolic rate increases, and are known as the main fuel source of the body(1). Despite abundant and inexhaustible body triglyceride reserves, the hepatic and muscular glycogen reserves are limited and its depletion during exercise, especially during prolonged endurance activities is predictable (1,2). Since the depletion of muscular glycogen and blood glucose is regarded as the main cause of muscular fatigue during this type of activities (2), extensive studies have been conducted by the scholars of biochemistry and sports physiology in order to increase FFA consumption during such activities; because increased consumption of FFA is associated with decreased glucose consumption during endurance exercise and delayed depletion of glycogen resources the consequence of which is delay in the onset of fatigue, especially during endurance activities (2).

FFA released through lipolysis of adipose tissue constitutes a major part of fuel for active muscles especially when the exercise is prolonged and its intensity is low to moderate (3). FFA metabolism is a complex process that involves several phases including FFA transport in plasma and its entry into the mitochondrial matrix (4). Mitochondrial transport OF FFA depends on the availability of a carrier protein called L-carnitine (4). It is hypothesized that increased plasma L-carnitine is associated with higher FFA transport (6-4).

Various studies have been conducted on the effects of plasma L-carnitine on FFA consumption or endurance capacity, subsequent to oral or intravenous administration of L-carnitine. In this regard, some findings show that L-carnitine supplementation would lead to increased Lipid oxidation (5), reduced carbohydrate oxidation (6), improved endurance exercise (7) and shortened recovery time following exercise (8). However, some studies report carbohydrate oxidation (9), maximum oxygen consumption (VO₂max) (10), heart rate, oxygen consumption, respiratory exchange ratio and blood lactate concentration remaining unchanged (11) after consumption of L-carnitine.

Recent experimental studies have revealed that the main sources of body's carnitine reserves are skeletal muscles and plasma carnitine reserves are scarce (12). Some studies have shown that the amount of muscular carnitine becomes limited during sub-maximal exercise (13). Most studies have assessed acute or one-session L-carnitine supplementation on the said factors during exercise. On the other hand, L-carnitine L-tartrate is one derivative of L-carnitine the effects of supplementation of which on the variation of oxidation substrates used during exercise have been studied less. Therefore, long-term effect of L-Carnitine L-Tartrate supplementation on Lipid oxidation substrates during exercise is the main

*Correspondence Author: Eizadi Mojtaba, Department of physical education and sport science, South Tehran Branch, Islamic Azad University, Iran. E-mail: izadimojtaba2006@yahoo.com

objective of this study. This study intends to study the effect of 21 day L-Carnitine L-Tartrate (physiological active form of carnitine) supplementation (3 g daily), on certain components of Lipid oxidation such as FFA, triglyceride, lipase, and such physiological components as resting and exercise heart rate.

METHODS

To determine the effects of 21 days (3g, daily) oral L-carnitine supplementation on some fat metabolism substrates physiological indexes such as resting and exercise heart during submaximal exercise, a total 30 none-trained male students matched ages (20-25 years) and BMI (20-25 kg/m²) were divided into experimental and control groups by randomly. This protocol was approved by ethics committee of Azad university of Iran. Each participant received written and verbal explanations about the nature of the study before signing an informed consent form. Subjects with a history or clinical evidence of impaired fasting glucose or diabetes, orthopedic abnormalities, neuroendocrine tumor, anemia, or who were on medications known to alter insulin sensitivity were excluded. Subjects had neither used any medication 6 weeks prior to the study nor participated in any regular physical exercise. Body weight and height were measured with a standard physician's scale and a stadiometer, respectively when subjects were in a fasting state when the participant had thin clothes on and was wearing no shoes. Before and after of supplementation periods, the all subjects completed an ergometry cycling test according to Astrand submaximal protocol on cycle for twenty minute (14). The subjects were advised to avoid any physical activity or exercise 48 hours before the blood sampling. Blood samples were drawn immediately followed up exercise. The blood samples were immediately centrifuged and serum was stored at -80°C. Blood samplings were performed in order to measuring of FFA, Lipase, triglyceride (TG), total cholesterol (TC), and low-density lipoprotein (LDL) and high-density lipoprotein (HDL). Rest and submaximal heart rate monitored by polar telemetry.

Statistical analysis:

We used the SPSS for Windows software (version 15:00; SPSS) for statistical analysis. The statistical significance of divergences between the means in the test and control groups were evaluated using the unpaired Student's t-tests in the case of normal distribution of data sets, and using the Kolmogorov-Smirnov's test when at least in one of the data sets the normal distribution was excluded. A paired T-test used to compare significant differences in each variable between two blood samplings (pre and post-test) in each group. A p-value < 0.05 was considered to be statistically significant.

RESULTS

Descriptive anthropometric and biochemical marker indicatives of the participants in pre and post-test are presented in Table 1. All values are represented as mean ± SD. At baseline (pretest) there were no differences in the age, weight, biochemical and physiological markers between the two groups (see Table 1). The data of paired T-test showed that long term L-carnitine ingestion had no significant preferential effect compared to placebo on rest and sub-maximal heart rate during cycling test in experimental group ($P < 0.05$). Additionally, L-carnitine supplementation had no significant effect on FFA concentration and thus could not alter other fat metabolism marker indicatives such as TG, TC, LDL, HDL and lipase during cycling exercise ($P < 0.05$). All variables remained without in placebo group.

Table 1: Mean and standard deviation of biomedical and physiological variables in studied groups during exercise test

variables	Experimental group		Control groups	
	Pretest	Post-test	Pretest	Post-test
Age (year)	22 ± 3	22 ± 3	21 ± 3	21 ± 3
Weight (kg)	71 ± 11	71 ± 9	72 ± 11	71 ± 12
Height (cm)	175 ± 8	175 ± 8	176 ± 7	176 ± 7
Heart rate (rest)	69 ± 8	70 ± 9	70 ± 9	72 ± 10
Heart rate (exercise)	158 ± 15	163 ± 14	153 ± 19	157 ± 21
FFA (mm/L)	0.71 ± 0.15	0.73 ± 0.19	0.68 ± 0.15	0.72 ± 0.12
TG (mg/dL)	168 ± 43	175 ± 48	171 ± 29	173 ± 28
TC (mg/dL)	214 ± 31	206 ± 29	209 ± 39	216 ± 38
Lipase (U/L)	147 ± 28	142 ± 33	151 ± 42	155 ± 24
LDL (mg/dL)	98 ± 11	100 ± 19	103 ± 14	100 ± 15
HDL (mg/dL)	47 ± 4	48 ± 5	48 ± 6	47 ± 5

DISCUSSION

Carnitine has a key role in lipid metabolism due to the transport of FFA into the mitochondria for energy generation (15). Free fatty acid can not penetrate into the mitochondria by itself, however once combined with carnitine; it turns into acylcarnitines and easily passes through the mitochondrial membrane. Inside the mitochondria carnitine acylcarnitine again turns into Acyl-CoA and carnitine molecules and Acyl-CoA is converted to acetyl CoA in the process of Beta-oxidation and carnitine returns back to the cytoplasm (15). Exercise training enhances skeletal muscle capacity for fatty acid oxidation, which in turn requires increased transfer of free fatty acids into the mitochondria (15).

Early researches have been reported that total muscular carnitine decreases by 20% during 40 minutes of exercise at 55% VO_{2max}, (16). However, one study suggests that intense physical exercise decreases muscle carnitine (17). These findings gave rise to the notion that the decrease of carnitine reserves in muscle or plasma is associated with reduced FFA transport and increasing muscular carnitine reserves by long-term supplementation would prevent that phenomenon. Shortage of carnitine in skeletal muscle is associated with impaired muscular function (18). Increase in muscular carnitine content decreases glycolysis and increases muscular glycogen reserves and increases lipid oxidation (13). It is also maintained that increase in muscular carnitine content leads to a reduction in carbohydrate oxidation, which is probably due to increased lipid oxidation (6). Another study shows that although instantaneous L-carnitine supplementation does not affect the components of carbohydrate and lipid oxidation, its long-term supplementation leads to lower glucose consumption and carbohydrate oxidation (9).

However, according to one study, the use of L-carnitine for 6 weeks would have no effect on the consumption of plasma free fatty acids fat and Beta oxidation and it does not seem to be associated with improved exercise performance (19). Another study shows that daily consumption of 4 grams of L-carnitine for 3 months would not lead to increased muscular carnitine and enhanced athletic performance (20). The study of Brad et al shows that a daily intake of 3 grams of L-carnitine for 3 months would have no effect on carbohydrate oxidation and substrates consumption and endurance performance (21).

Our study finding showed that a 21-day L-carnitine supplementation would not lead to any changes in plasma concentration of FFA, triglycerides, total cholesterol and lipase activity. In other words, none of the said components which somehow influence Lipid oxidation would change by this type of supplementation. Meanwhile the physiological parameters like resting and sub-maximal heart rate also remain unaffected by this supplementation.

Some experimental studies have shown that very low amounts of carnitine are required for optimal muscular function (18). Improved athletic performance caused by carnitine supplementation in subjects whose disease is somehow associated with carnitine deficiency has repeatedly been demonstrated (22-24, 11). However, the effect of carnitine supplementation on enhancing muscular function in healthy individuals has always been challenged. It is known that the possibility of carnitine deficiency in skeletal muscle of healthy subjects is low after any level of exercise (15). A review study states that healthy yet sedentary subjects and non-athletes do not benefit from carnitine supplementation (17). However, another study on animal species has shown that the benefits of L-carnitine supplementation in the athletic rabbits are far more than those of non-athletic rabbits (25). Following high-intensity exercise, although the concentration of free muscular carnitine decreases it is compensated due to proportionate increase of acylcarnitine. As a result the total muscular carnitine remains unchanged during intense exercise or endurance training (15).

Conclusion

In spite of 20 years of study, there is still no conclusive evidence based demonstrating the effect of carnitine supplementation on improving or enhancing exercise performance in healthy subjects. In this regard, most studies have failed to describe how exercise performance is improved in healthy subjects due to supplementation. The findings of the study also indicate that chronic carnitine supplementation does not influence substrate consumption and lipid oxidative capacity in healthy subjects. This evidence is probably associated with carbohydrate oxidation and glycogen reserves of the body remaining unchanged.

REFERENCES

1. Robergs, R.A., Roberts S. Fundamental Principles of Exercise Physiology: For Fitness, Performance and Health. USA, McGraw Hill, 2000; pp 237-42.
2. Maughan R, Gleeson M, Greenhaff P.L. Biochemistry of exercise & Training. USA, Oxford Medical Publications, 1997; 131-3.
3. Felig P, Wahren J. Fuel homeostasis in exercise. *N Engl J Med* 1975; 239 (21): 1078-84.
4. Heinonen OJ. Carnitine and physical exercise; a review article. *Sport Med* 1996; 22(2): 109-35.
5. Ibrahim WH, Bailey N, Sunvold GD, Bruckner GG. Effects of carnitine and taurine on fatty acid metabolism and lipid accumulation in the liver of cats during weight gain and weight loss. *Am J Vet Res* 2003; 64(10):1265-77.
6. Stephens FB, Constantin-Teodosiu D, Laithwaite D, Simpson EJ, Greenhaff PL. An acute increase in skeletal muscle carnitine content alters fuel metabolism in resting human skeletal muscle. *J Clin Endocrinol Metab* 2006; 91(12):5013-8.
7. Guarnieri G, Biolo G, Vinci P, Massolino B, Barazzoni R. Advances in carnitine in chronic uremia. *J Ren Nutr* 2007; 17(1):23-9.
8. Karlic H, Lohninger A. Supplementation of L-carnitine in athletes: does it make sense? *Nutrition* 2004; 20(7):709-15.
9. Abramowicz WN, Galloway SD. Effects of acute versus chronic L-carnitine L-tartrate supplementation on metabolic responses to steady state exercise in males and females. *Int J Sport Nutr Exerc Metab* 2005; 15(4):386-400.

10. Eroğlu H, Senel O, Güzel NA. Effects of acute L-carnitine intake on metabolic and blood lactate levels of elite badminton players. *Neuro Endocrinol Lett* 2008; 29(2):261-6.
11. Stuessi C, Hofer P, Meier C, Bouteiller U. L -Carnitine and the recovery from exhaustive endurance exercise: a randomised, double-blind, placebo-controlled trial. *Eur J Appl Physiol* 2005; 95(5-6):431-5.
12. Kraemer WJ, Volek JS, Dunn-Lewis C. L-carnitine supplementation: influence upon physiological function. *Curr Sports Med Rep* 2008; 7(4):218-23.
13. Stephens FB, Constantin-Teodosiu D, Greenhaff PL. New insights concerning the role of carnitine in the regulation of fuel metabolism in skeletal muscle. *J Physiol* 2007; 581(Pt 2):431-44.
14. Siconolfi SF, Cullinane EM, Carleton RA, Thompson PD. Assessing VO₂max in epidemiological studies: Modification of the Astrand- Ryhming test. *Med Sci Sports Exerc* 1982; 14(5): 335-8.
15. Villani RG, Cannon J, Self M, Rich PA. L- carnitine Supplementation Combined with aerobic training does not promote weight loss in moderately obese women. *Int J Sport Nutr Exers Metab* 2000; 10 (2): 199-207.
16. Lennon DL, Stratman Fw, Shrago E, Nagle Fj, Madden M, Hanson P.A, et al. Effects of acute moderate-intensity exercise on carnitine metabolism in men and women. *J Appl Physiol* 1983(55): 489-95.
17. Benvenga S. Effects of L-carnitine on thyroid hormone metabolism and on physical exercise tolerance. *Horm Metab Res* 2005; 37(9):566-71.
18. Brass EP. Carnitine and sports medicine: use or abuse? *Ann N Y Acad Sci* 2004; 1033:67-78.
19. Lee JK, Lee JS, Park H, Cha YS, Yoon CS, Kim CK. Effect of L-carnitine supplementation and aerobic training on FABPc content and beta-HAD activity in human skeletal muscle. *Eur J Appl Physiol* 2007; 99(2):193-9.
20. Wachter S, Vog M, Kreis R, Boesch C, Bigler P, Hoppeler H, Kerahenbuhl S. Long-term administration of L-carnitine to humans: effect on skeletal muscle carnitine content and physical performance. *Clin chim Acta* 2002; 318(1-2): 51-61.
21. Broad EM, Maughan RJ, Galloway SD. Effects of four weeks L-carnitine L-tartrate ingestion on substrate utilization during prolonged exercise. *Int J Sport Nutr Exerc Metab* 2005; 15(6):665-79.
22. Rajasekar P, Anuradha CV. Effect of L-carnitine on skeletal muscle lipids and oxidative stress in rats fed high-fructose diet. *Exp Diabetes Res* 2007; 727-41.
23. Borghi-Silva A, Baldissera V, Sampaio LM, Pires-DiLorenzo VA, Jamami M, Demonte A et al. L-carnitine as an ergogenic aid for patients with chronic obstructive pulmonary disease submitted to whole-body and respiratory muscle training programs. *Braz J Med Biol Res* 2006; 39(4):465-74.
24. Kosan C, Sever L, Arisoy N, Caliskan S, Kasapcopur O. Carnitine supplementation improves apolipoprotein B levels in pediatric peritoneal dialysis patients. *Peditr Nephrol* 2003; 18(11): 1184-8.
25. Bacurau RF, Navarro F, Bassit RA, Meneguello MO, Santos RV, Almeida AL, Costa Rosa LF. Does exercise training interfere with the effects of L-carnitine supplementation? *Nutrition* 2003; 19(4): 337-41.