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Aerobic Capacity and Glucose Metabolism in Response to Oral Carnitine Ingestion in Healthy People

Short Running title
L-carnitine, metabolism and physical performance

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ABSTRACT

Background and objective: Carnitine plays an important role in regulation of fat and carbohydrate oxidation in skeletal muscle. The objective of present study evaluated the effects of an acute L-carnitine supplementation on carbohydrate metabolism and aerobic capacity during aerobic exercise test. **Method**: Forty two untrained males divided into experimental and control groups and cycled on two separate occasions. 1). Exercise protocol without L-carnitine or placebo supplementation. 2). Exercise protocol with acute L-carnitine or placebo supplementation (3g, 90 minute before exercise). Venous blood samplings were taken immediately after exercise protocol in order to measuring glucose and lactate concentration, lactate dehydrogenase activity (LDH), heart rate and VO2max. **Result**: There was no significant change in glucose and lactate concentration, VO2max and the other variables during exercise test by carnitine supplementation in experimental subjects ($p<0.05$). All variables remained without changes in the control trial. **Conclusion**: Our study finding demonstrated that carnitine supplementation does not affect exercise capacity and glucose metabolism in healthy people.
KEYWORD: Glucose, Lactate, Carbohydrate Metabolism, exercise.

INTRODUCTION

Free fatty acid transport into mitochondria is of considerable importance in energy generation and fat oxidation [1]. L-Carnitine is a naturally occurring compound available in skeletal muscle and heart, liver, kidney tissues and plasma [2]. Its biological function is to transport the long-chain of free fatty acids into the mitochondrial matrix to produce energy in beta-oxidation process. Therefore, athletes use L-Carnitine to increase free fatty acid transport into mitochondria as an ergogenic aids in endurance activities [3]. The main reason for supplementation of this amino compound is to increase fat oxidation and to decrease carbohydrate oxidation and finally to maintaining carbohydrate reserves to continue endurance activities and delay fatigue threshold. Scientific evidence about the benefits of L-Carnitine energy yield during sports activities is often heterogeneous. Some findings confirm the beneficial effects of L-Carnitine supplementation, especially in endurance activities and some reject its energizing effect [3, 4, 5, 6, and 7].

In this area, Bacura et collegous (2003) states that L-carnitine supplementation increases endurance time, reduces the rate of carbohydrate oxidation, accelerates fat oxidation process during exercise in rats [4]. On the other hand, Matera (2003) states that reducing lactate formation during exercise is yet another function of L-Carnitine [5]. Also Stephens (2007) alludes to his findings and suggests that increasing muscle carnitine content following its supplementation leads to maintaining glycogen reserves; reduces glucose consumption and increases fat oxidation and leads to improved exercise capacity [3]. But despite these findings, the Eroglu study (2008) showed that acute L-carnitine supplementation has no effect on lactate concentration, anaerobic threshold, VO2 max and other metabolic factors during exercise [6]. The study by Wyss et collegous (1990) noted that no change occurs in minute ventilation, oxygen uptake, carbon dioxide excretion, heart rate, systolic blood pressure, lactate, and glycerol and plasma glucose during exercise after supplementation of L-Carnitine [7].

In this area, research evidence indicates that findings on the effects of acute L-Carnitine supplementation on metabolic factors and sports performance in athletic and non-athletic populations often represent inconsistent and contradictory results. Some emphasize the beneficial effects while others suggest this supplement has no effect on endurance performance. Hence, the aim of this study is to evaluate the effect an acute L-carnitine supplementation (3g) on some carbohydrate metabolism determinatives and physiological indexes during submaximal exercise test in young boy students.

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MATERIALS AND METHODS

Statistical Society of this control trail study was none-trained boy students. The study was conducted with the approval of the Ethics Committee of Islamic Azad University, Saveh Branch (IAU). In this study, forty two none- trained boy students were divided to experimental and control groups, matched for age and BMI. The purpose of this study was to determine whether a acute oral L-carnitine supplementation affect the response of glucose and lactate concentration, lactate dehydrogenase activity (LDH), heart rate and VO2max to a standard cycling test in these subjects.

Participants were included if they had not been involved in regular physical activity or diet in the previous 6 months. Nutritional status of two groups was similar during the time before the study. The participants of two groups were asked to remain their diet during the study. Written consent was obtained from each subject after the experimental procedures and possible risks and benefits were clearly explained. Subjects included individuals with no cardiovascular diseases, gastrointestinal diseases, kidney and liver disorders or diabetes. In addition, if any of the people had been participating in regular exercise or diet program during the past 6 months, they were excluded study. All subjects were non-smokers. In addition, exclusion criteria included inability to exercise and supplementations that alter carbohydrate-fat metabolism. Height was measured with Seca height rod (0.5 accuracy), without shoes, and weight with Seca weight scale (100 g accuracy), with light clothes and without shoes. Body mass index (BMI) was calculated using weight divided by squared height. Resting heart rate (HR) was measured after a 15-min rest in a sitting position and in a quiet environment. Blood pressure was measured using the left arm after the subject had been sitting comfortably for 5 min, using an oscillometric device (Alpikado, Japan). Three readings were taken and the lowest one recorded.

After anthropometrical measuring, all participants of experimental and control groups completed a cycling ergometery test according by Astrand protocol guidelines [8] on two separate occasions. 1). Exercise protocol without L-carnitine or placebo supplementation (Pretest). 2). Exercise protocol with acute L-carnitine or placebo supplementation (3g, 90 minute before exercise) (Post-test). Each exercise test lased 20 minutes. Daily food records were kept for 48 h preceding each test session, and subjects were instructed to refrain from caffeine consumption and intense physical activity for 24 h before testing. No difference was observed in the subjects' diets 48 h before each trial. Exercise heart rate and VO2max also calculated by Astrand protocol guideline. Venous blood was immediately taken after exercise test from subjects. Blood sampling performed in order to measuring glucose and lactate concentration, lactate dehydrogenase activity. Blood glucose was measured by glucose oxidase using Calorimetric method (Pars Azmoun, Tehran, Iran). Lactate and lactate d hydrogenise were measured by enzymatic method by Cobas Mira AutoAnalyzer (German).

Statistical analysis: All values are represented as mean ± SD. Statistical analysis was performed with the SPSS software version 15.0 An Independent sample T-test was used to compare the variables between experimental and placebo groups. Paired T-test used to determine significant differences in each variable between first and second cycling test. When a signigcant F ratio was obtained, the Tukey post hoc test was used to compare means. A probability level of $p<0.05$ was used to indicate statistical significance.

RESULTS

Table 2 presents anthropometric, physiological and biochemical features of the study groups. The characteristics such as age, BMI, weight, glucose, Lactate and LDL did not differ between the experimental and control subjects. VO2max and heart rate did not differ among the groups ($p<0.05$). Glucose levels were not significant affected in response to cycling protocol by carnitine supplementation in experimental group ($p<0.05$). In addition, blood lactate concentration did not change significantly during exercise test in these subjects. All other variables measured such as VO2max and heart rate were not significantly changed as a result of carnitine supplementation ($p<0.05$). All variables remained without change in control subject ($p<0.05$).

Table 1: Anthropometric, physiological and biochemical features of two studied groups

Variables	**Control group**		**Experimental group**	
	Pretest	**Post-test**	**Pretest**	**Post-test**
Age (year)	22 ± 3	-------	21 ± 3	-------
Height (cm)	174 ± 9	-------	175 ± 11	-------
Weight (kg)	74 ± 7	-------	75 ± 6	-------
BMI (kg/m2)	24.44 ± 2.14	-------	24.48 ± 3.11	-------
Glucose (mg/dl)	98 ± 11	96 ± 13	95 ± 10	97 ± 14
Lactate (mmol/L)	5.41 ± 1.14	5.84 ± 1.02	5.98 ± 0.95	5.48 ± 0.87
LDH (IU/L)	311 ± 65	324 ± 38	324 ± 61	317 ± 52
VO2max (L/min)	2.35 ± 0.32	2.41 ± 0.32	2.29 ± 0.65	2.40 ± 0.51
Resting heart rate (bpm)	75 ± 11	77 ± 9	78 ± 12	75 ± 11
Exercise heart rate (bpm)	**168 ± 23**	**159 ± 19**	**165 ± 16**	**161 ± 21**

DISCUSSION

Athletes are often vulnerable to the temptation of taking various supplements to improve athletic performance and usually use different methods of nutritional supplements such as carbohydrate loading and use of other medicinal supplement [9]. Although carnitine is synthesized in the body and absorbed from the diet as well, in some circumstances, supplementation of L-carnitine is beneficial in competitive athletes and in intense endurance activities in which muscle carnitine deficiency is possible [10].

The main role of carnitine is focused on lipid metabolism; however, scientific evidence corroborates its other role in the metabolism of carbohydrate. Indeed, there is a strong correlation between muscle carnitine and Krebs cycle. Fat oxidation is stimulated after consumption of L-Carnitine by mices [4]. Muscle carnitine concentration is directly proportional to muscle glycogen reserves [10, 11]. Due to its storage effect and saving muscle glycogen due to its higher energy yield than beta-oxidation process, carnitine acts as a glycogen anti-catabolic agent that effectively reduces the need to burn glycogen [10, 11]. The study of Panjwano (2007) showed that L-Carnitine supplementation has no effect on plasma glucose concentration during exercise [12]. There are other studies supporting the ineffectiveness of L-carnitine on blood glucose levels [7]. The distinction of our study from the said studies is the amount consumption and duration of the consumption of L-Carnitine. The findings of this study also suggest that acute L-Carnitine supplementation (3g) is ineffective on blood glucose. It must be emphasized that one of the limitations of this study is failure to measure plasma concentrations of carnitine before and after its supplementation in the said samples.

Intense physical activity or progressive exercise leads to accumulation of lactate together with decreased serum PH. High levels of lactic acid increases the acidity in the blood and tissues and triggers fatigue and decreased ATP production. L-Carnitine is an inhibitor of Phosphofructokinase key enzyme and reduces the rate of glycolysis. An Italian researcher in 1990 suggested that the carnitine supplementation reduces lactic acid accumulation during exercise [10]. L-Carnitine reduces the ratio acetyl-CoA to CoA and this factor activates the pyruvate dehydrogenase. It is generally held that the conversion of pyruvate to acyl-CoA and acetyl-carnitine synthesis escalates due to increased activity of pyruvate dehydrogenase after the loading of L-Carnitine. On the other hand, carnitine supplementation reduces lactate dehydrogenase activity which returns pyruvate to lactate as a result of which formation of lactic acid during sporting activities is reduced [13]. Consumption of 2 g of L-Carnitine just an hour before progressive cycling to exhaustion has led to a significant decrease in lactate accumulation [9]. L-Carnitine Supplementation improves exercise tolerance and strength of respiratory muscles in chronic obstructive pulmonary patients as well as decrease blood lactate [14]. But in Barent's study (1994), L-Carnitine consumption caused no changes in lactate accumulation during maximal exercise test [15]. The study of Stuessi (2005) showed that blood lactate concentration and conducting an exercise test the subsequent to supplementation of 2 g L-Carnitine and placebo were similar. However, our findings showed that acute L-Carnitine supplementation would have no effect on blood lactate and lactate dehydrogenase activity during sub-maximal aerobic cycling.

Increased level of VO 2max is considered a sign of improved cardiovascular fitness in athletes as well as untrained individuals or patients [1]. In addition, reduced frequency of heart rate during rest or exercise is yet another outstanding physiological sign of increased aerobic fitness. Many studies have been performed on the effect of carnitine loading on maximum oxygen uptake (VO 2max) in athletes and non athletes. Most of these researches have more or less reported improved VO 2max and enhanced exercise performance in privileged athletes as well as non-professional ones following supplementation of L-carnitine, especially after taking high doses in longer terms [16, 17]. Daily intake of 2 g carnitine brings about substantial increases in maximum oxygen uptake [16]. But Brass (2001) points out that consumption of L-Carnitine in renal patients, despite increasing plasma carnitine concentrations has no significant effect on VO2max [18]. These findings have also been confirmed by Eroglu (2008) [6].

Nattiali's et collegous (1993) showed that oral carnitine supplementation would slightly reduce exercise heart rate during submaximal exercise which is suggestive of improved functioning of the circulatory system during sub-maximal exercise [19]. Some findings have, however, reported no change in exercise heart rate as a result of L-Carnitine supplementation. The findings of our study confirm some of those findings signifying that L-Carnitine supplementation does not lead to significant changes in VO 2max and heart rate during exercise. It is also likely that L-Carnitine supplementation somehow increases glucose oxidation; as this phenomenon has been reported in the findings of animal models [20] In fact, this theory does not explain the increase in glucose consumption, but the mechanism of the boosting effect of carnitine on glucose oxidation means that by increasing the activity of pyruvate dehydrogenase, L-Carnitine supplementation increases converting pyruvate to acetyl-CoA on the one hand resulting in increased carbohydrate oxidation and decreases conversion of pyruvate to lactate and accumulation of it on the other hand [21, 22].

In summary, Considering the role of L-Carnitine in mitochondrial transport of free fatty acids, especially during sports activities, its increased plasma concentrations due to supplementation is expected to be associated with increased entry of free fatty acid into mitochondria the most important achievement of which is preservation of muscular and hepatic

glycogen reserves to sustain carbohydrate oxidation especially in the later stages of endurance activities and the delayed onset of fatigue. These benefits have been confirmed by a great deal of scientific evidence. But along with many recent studies our findings do not support these emerging benefits of L-Carnitine. In this regard Metin (2003) states that according to his findings, although intense or prolonged exercise is associated with decreased plasma carnitine levels but this reduction does not lead to a negative impact on their athletic performance [23].

However, the dosage of carnitine intake, intensity or volume of work and activity are the influencing factors on carnitine. It also is possible that although no change occurs at the level of metabolic factors or VO 2max, the benefits of carnitine are linked with final stages of prolonged endurance activities that require further studies with longer exercise tests.

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