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Effects of L-Carnitine Supplementation on Metabolic Utilization of Oxygen and Lipid Profile among Trained and Untrained Humans

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Abstract

Background: The effectiveness of L-carnitine supplementation has been met with conflicting findings when used by sedentary and athletic adults.
Objectives: This study aimed to investigate the acute effects of L-carnitine supplementation on aerobic metabolic efficiency and lipid profiles in sedentary and athletic men.
Methods: Fifteen sedentary (20.4 $\pm$ 1.5 years) and 15 athletic (21.5 $\pm$ 2.4 years) men were studied in durations of control, placebo intake and 2 g of L-carnitine supplementation. Lipid profiles, including triglyceride, cholesterol, high-density lipoprotein (HDL) and very-low density lipoprotein (VLDL), were determined before and 40 min after either the placebo or L-carnitine intake. Oxygen consumption (direct VO_2), ventilatory threshold (VT), and running time (RT) were recorded after a submaximal treadmill exercise test.
Results: Direct VO_2 increased significantly at 80% of maximal heart rate after L-carnitine supplementation in both athletic and sedentary men, whereas, a statistical increase in VT and RT occurred only after L-carnitine use in athletes, when compared to the control and placebo subjects. The sedentary group showed no changes in lipid parameters, but triglyceride levels reduced significantly in the athletes after consuming L-carnitine.
Conclusions: Acute L-carnitine supplementation possibly affects exercise performance and triglycerides in athletes rather than sedentary men.

Keywords: L-carnitine, VO_2, Running Time, Lipids, Athletics, Sedentary

1. Background

Dietary supplements are currently of interest worldwide for maintaining good health and treating sickness. L-Carnitine is one of many supplements that have been reported to possess beneficial protection of physical performance in various conditions such as advanced cancer (1), fatigue (2), inherited neuro-metabolic disorders (3), maple syrup urine disease (MSUD) (4), intermittent claudication (5), metabolic syndrome, and cardiovascular disease (6). L-Carnitine enhances physical performance by increasing fat oxidation during exercise and sparing glycogen (7). It is a natural component of mammalian tissue and possesses multiple physiological roles, for example, providing antioxidant protection, increasing nitric oxide production and/or maintaining circulating nitric oxide (8). It also enhances energy production from fatty acid oxidation (9), especially triglyceride from adipose tissue (10), and optimizes the use of adenosine triphosphate (ATP) fuel substrate in skeletal muscle during exercise (11). L-carnitine also plays a major role in regulating the mitochondrial acetyl-CoA/CoASH ratio (12) and activating carnitine acyltransferases (CAT), which transport long-chain fatty acid across the mitochondrial inner membrane (13). Prior study showed that carnitine supplementation for 3 weeks increases fatty acid oxidation in skeletal muscle by increasing total carnitine content in soleus muscle mitochondria and total content of acyl-carnitine (7). The majority of studies have reported an increase in maximal oxygen consumption (VO_{2max}) and reduced respiratory quotient (RQ) following carnitine ingestion. Carnitine is not only involved in the energy productive system, but also other beneficial aspects, for example cardiovascular function. Previous reports have discussed the metabolic effects of carnitine on the cardiac system and skeletal muscle, which indicates a high rate of fatty acid oxidation associated with lower rates of glucose oxidation relating to

myocardial ischemic injury (14). The study of Broderick et al. (15) showed that supra-physiological concentration of L-carnitine affects the normal working heart rate by activating the pyruvate dehydrogenase (PDH). Furthermore, carnitine also can decrease the fatty oxidation rate and enhance the rate of glucose oxidation and pyruvate oxidation for ATP generation (16). Therefore, these phenomena improve the efficiency of cardiac function (6, 17). Moreover, carnitine possesses more varied benefits such as insulin-sensitivity in skeletal muscle, and anti-steatotic and hypolipidemic effects on liver metabolism (17). Other works have shown that prolonged supplementation of orally administered carnitine at 1 g per day for 12 weeks could affect C-reactive protein, tumor necrosis factor-alpha (TNF-α), and interleukin-6 (IL-6) in patients with coronary artery disease (CAD), thus indicating the involvement of carnitine in inflammatory function, but exact mechanisms are unknown (18, 19).

Carnitine supplementation has also been used to treat those who are overweight or obese. It has been claimed to reduce fat mass and is often portrayed as a "fat burner", despite little direct evidence in support of this (13). Some reports indicated that a high dose of L-carnitine modulates glucocorticoid receptor function and might mimic some glucocorticoid functions, which stimulate lipolysis in adipose tissue (20). Previous knowledge of carnitine function involves beta-oxidation of free fatty acid by being carried through the mitochondria membrane for energy production.

Carnitine might not only impact energy metabolism but may also have an effect on lipoprotein metabolism such as triglyceride, very low density lipoprotein (VLDL), low density lipoprotein (LDL), and high density lipoprotein (HDL). Previous study showed that 14 weeks of carnitine supplementation decreased serum free fatty acid and triglyceride in obese and insulin-resistant ponies (21). Furthermore, some reports in animal studies indicated that supra-physiological carnitine levels in the liver would be reduced to a lower rate of secretion in VLDL, triglyceride, and cholesterol. Therefore, minimized VLDL secretion is expected to increase plasma HDL (22). However, no studies have confirmed this event in humans. Athletes have had a longstanding interest in carnitine administration for purposes of increasing physical performance from ATP generation, with various forms of carnitine used. Previous evidence proposed that during intensive physical activity, muscle carnitine is redistributed in muscle and increases fatty acid oxidation in healthy subjects under normal conditions (23). Thus, previous data reviewed the dose and duration of L-carnitine supplementation in both trained and untrained people, showing controversial results. The supplement dose of 2 g/d taken orally for 14 or 28 days was studied in untrained subjects, and it had no effect on VO_{2max} (24), which correlated with 7 healthy males taking 3 g/d of L-carnitine orally for 7 days (25). Whereas, a single dose of L-carnitine supplementation at 2 g taken orally increased VO_{2max} and decreased lactate in 10 moderately trained males (26). The study of Natali et al. (27) reported that 40 minutes after 12 active males had received 3 g of L-carnitine intravenously, oxygen consumption (VO_2) did not change significantly, but increased fatty acid oxidation occurred during recovery from bicycling exercise.

Therefore, the present study aimed to evaluate the efficiency of single dose of carnitine supplementation on metabolic utilization, running capacity, and lipid profiles (cholesterol, triglyceride, VLDL and HDL) in sedentary, and athletic people.

2. Methods

The protocol in this study was approved by the Human Ethics Committee (Declaration of Helsinki, 2001) at the faculty of associated medical sciences, Chiang Mai University, Thailand (ethical registered number 028E55).

2.1. Subjects

Thirty athletic and sedentary volunteers participated in this study. Fifteen athletic participants were non-smoking healthy males, who comprised university athletes or men exercising more than 3 days per week. They were football players (n = 5), basketball players (n = 4), and shotgun shooters (n = 3), as well as people who exercised regularly (n = 2). In addition, their body mass index (BMI) was within the normal range (18.5 - 24.9 kg/m^2), according to the world health organization (WHO) and international obesity task force. Fifteen sedentary males, who exercised for less than 3 days per week (28), were included in this study for comparison with the 15 athletic participants. No intake of drugs or nutrient supplements 6 months prior to the start of this study was allowed. Individual health status was obtained from interviews, and screening for hospital admission, drug administration, medical treatment, and basic complete blood count (CBC). A physician screened all of the participants for esophageal reflux, hemoptysis, rib fracture, coagulopathy, cardiac arrhythmias, recent surgery and any pulmonary or neurological disorders taken from the interview and hospital records that dated back at least 6 months prior to the study. Moreover, re-assessment on health status, with repeated screening was confirmed by a physician at the AMS clinical service center, faculty of associated medical sciences, Chiang Mai University, Chiang Mai, Thailand. Finally, the participants agreed with the policy of this study, and signed a consent

form, in that during the study period their regular activities such as diet and behavioral aspects must be controlled, including avoidance of taking extra-supplementary multivitamins.

2.2. Study Design

The study protocol was designed with three visiting time periods: the control, placebo intake (starch) and L-carnitine supplementation. Pure L-carnitine at 500 mg per capsule was purchased from the Pharmaceutical Shop, Chiang Mai, Thailand (Acetyl L-carnitine (HCL) (100%), Vitacost®, USA), whereas the placebo capsules were produced at the Faculty of Pharmacology, Chiang Mai University, Thailand, by encapsulating 500 mg of pure starch in the same sized capsule as that for L-carnitine. Each experiment was carried out three times every other week and all of the subjects had to be controlled strictly regarding their basic daily activities and all dietary intakes. In addition, they were required to refrain from taking supplementary multi-vitamins or extra food. A pilot experiment on the treadmill exercise was carried out, as supervised by a physician, in order to familiarize the subjects with the equipment, according to the submaximal Bruce protocol (29) and ACSM guideline of 2004 (30). Consequently, no abnormal signs or symptoms that were contraindicated to the criteria, such as severe dyspnea, leg fatigue, angina chest pain, dizziness, vertigo, or abnormal response of heart rate or blood pressure, was shown during or after the exercise. During the experimental period, all of the volunteers could not consume food for at least 1.5 hour and slept for at least 8 hours before each experiment. The participants were blinded to the experiments and selected randomly for 2 g of L-carnitine supplementation taken orally at 2 g of placebo (starch) intake for the second or third time in a one-week interval period. Lipid profiles were evaluated before and 40 minutes after supplementation. Metabolic utilization was measured by the treadmill exercise test 20 minutes later.

2.3. Physical Fitness Test

Direct VO_2, running time (RT), and ventilator threshold (VT) were analyzed automatically with a CPX Ultima Gas exchange from MedGraphics® (St.Paul, Minnesota, USA). Before testing, all of the subjects were requested to rest for 30 minutes in the laboratory and 5 minutes of large muscle stretching took place, especially on the quadriceps and gastrocnemius muscles. All of the participants were asked to wear a mouthpiece held with a mask connected to a pneumatic sensor, which could detect bi-directional differential pressure; and the heart rate was monitored at the middle finger by a Nonin® pulse oximeter (USA). Each breath passing through the system was controlled with a nose clip. A modified submaximal Bruce protocol (29) was started automatically after 60 minutes of L-carnitine supplementation or placebo intake using the GE's CASE® exercise testing system (USA) connecting to the treadmill (Margarete® USA). Warm up started with treadmill walking for 3 minutes at a comfortable speed of 1.4 miles per hour on a 0% slope before the program progressed with changing speed and degrees of slope every three minutes, according to the Bruce protocol. The participants were asked to relate to their common experience of leg discomfort while running on the treadmill. Ratings of perceived leg fatigue were made throughout the exercise, using a 0 - 10 scale, with "0" meaning no discomfort in the leg and "10" meaning severe or strong discomfort (31). Reasons for stopping the exercise in this protocol test followed the American College of Sport Medicine (ACSM, 2004) (30) criteria. The subjects were required to run on the treadmill continuously until 80% of their theoretical maximal heart rate (MHR), whilst breathing through the system. When the exercise test stopped, direct VO_2, VT, and RT at 80% of MHR were recorded automatically by the BreezeSuit Software program. Finally, all of the subjects were cooled down with walking slowly at a comfortable speed of 1.4 miles per hour on a 0% slope, and stretching their leg muscles as same as in the warm up stage 5 - 10 minutes before stopping the experiment.

2.4. Sample Collection and Analysis

Ten mL of blood was taken from the anterior cubital vein by a medical technologist and separated into two 5 mL tubes; one non-heparinized tube for evaluating the lipid profiles in serum, and one heparinized tube for evaluating the completed blood count (CBC) in plasma by centrifuged 3,000 rpm for 10 minutes. Both samples were analyzed at the AMS Clinical service center, faculty of associated medical sciences, Chiang Mai University, Chiang Mai, Thailand. Triglyceride, cholesterol, HDL and VLDL were determined by a fully automated Olympus AU400 Analyzer (Olympus Diagnostics GmB, Umkirch, Germany) with the specific standard Olympus reagent Kits (Catalog Number: HDL3-30, LDL3-30 and TRI2-125).

2.5. Statistical Analysis

Normal distribution of all parameters was tested with a Kolmogorov-Smirnov test. Characteristics between groups were analyzed statistically by the independent paired t-test. CBC and lipid profiles before and after L-carnitine supplementation or placebo intake were analyzed by the dependent paired t-test. Whereas, all utilized energy parameters: VO_2 (80% MHR), VT and RT between

each duration of control, placebo intake, and L-carnitine supplementation, were analyzed using repeated measurement ANOVA, and least significant difference (LSD) with the SPSS program (Version 10) (SPSS Inc, Chicago, IL, USA). Data showed the mean ± SD. A P value < 0.05 was considered significant. Moreover, the G*Power (3.1.9.2) was calculated for the size of effect in significant outcomes in this study period.

3. Results

The characteristics such as age, height, weight and BMI of sedentary and athletic men in this study showed no statistical difference between each group (P > 0.05) (Table 1). Furthermore, all parameters in the CBC results presented non-statistical differences between pre and post supplementation in either the placebo or L-carnitine group (Table 2).

3.1. Energy Utilization

Table 3 shows the changes of energy utilization in sedentary subjects, which found a significant increase of VO_2 level at 80% of MHR after L-carnitine supplementation, when compared to the control (P = 0.029) and placebo (P = 0.006) intake. The VO_2 levels between the control and placebo intake were not statistically different (P = 0.581). The results were similar in the athletes, in that the VO_2 level after L-carnitine supplementation was statistically different, when compared to the control (P = 0.002) and placebo (P = 0.001) intake. Whereas, the VO_2 level between the control and placebo intake had no statistical difference (P = 0.11).

Results from the VT in the athletic men showed a significant increase after L-carnitine supplementation, when compared to the control (P = 0.000) and placebo intake (P = 0.000). However, VT between the control and placebo intake did not differ (P = 0.14). The VT was not statistically different (P = 0.17) between the control, placebo and L-carnitine supplementation in the sedentary subjects.

The total RT on the treadmill exercise was recorded when it reached the target heart rate of 80% of MHR. The RT result in athletic subjects increased significantly after supplementation with L-carnitine, when compared to the control (P = 0.000) and placebo intake (P = 0.001), whereas, no statistical difference was seen in RT between the control and placebo intake (P = 0.87). All data for the sedentary subjects showed no statistical difference between the control, placebo intake, or L-carnitine supplementation (P = 0.84). Moreover, RT after L-carnitine supplementation in the athletes was significantly higher than that during all periods in the sedentary subjects (P = 0.001).

Furthermore, the fatigue score for sedentary men after the exercise running test on the treadmill showed no statistical difference between the control, placebo or L-carnitine intake (P = 0.65), but it decreased significantly in athletes after L-carnitine supplementation when compared to the control (P = 0.002) and placebo intake (P = 0.000).

3.2. Lipid Profiles

The results of lipid profiles showed no statistical difference in cholesterol, triglyceride, HDL or VLDL before and after either the placebo intake or L-carnitine supplementation in the sedentary subjects (P > 0.05) (Table 4). These results were similar to those in athletes after placebo intake. After L-carnitine administration, cholesterol, HDL and VLDL showed no statistical difference when compared to before consumption (P > 0.05), but the level of triglyceride decreased statistically (P = 0.02).

4. Discussion

In this study, the results on the characteristics between groups showed non-significant data, the same as those in basic CBC data. This study protocol was designed to evaluate lipids in the blood at 40 min after supplementation, and approximately 60 min after supplementation when having exercised on the treadmill. This is because the maximal absorption in blood circulation affects the oxygen uptake within 40 to 60 minutes, as described in a previous study (26).

This study showed different results between sedentary and athletic subjects, and that supplementation of L-carnitine significantly improved VO_2 consumption. L-carnitine involves metabolic utilization when VO_2 increases during exercise, as confirmed in this study by both sedentary and athletic subjects who showed a significant VO_2 increase when compared to the control or placebo intake. The basic function of L-carnitine involves the beta-oxidation of lipid metabolism in the mitochondria muscles (7). Thus, extra-consumption of L-carnitine has been suggested as potentially improving energy production by protecting tissues from oxidative damages during exercise or the inflammation process, including enhancement of various metabolic pathways such as fat oxidation (3). Previous evidence showed that the high oxidative stress from exhaustive exercise related to some inflammatory cytokines such as IL-6, interleukin-Iβ, and TNF-α (32). An increase in TNF-alpha has been proposed to be associated with nitric oxide (NO) bioavailability and affects endothelial dysfunction (33). Reports confirm that high oxidant production and low antioxidant buffering factors reduce muscle

Table 1. Complete Blood Count Before and After L-Carnitine Supplementation in Sedentary and Athletic Subjects[a]

	Sedentary (n = 15)	Athletic (n = 15)	P Value[b]
Age, y	20.4 ± 1.5	21.5 ± 2.4	0.63
Range	(18 - 22)	(18 - 23)	
Height, cm	170.5 ± 5.0	175.5 ± 5.8	0.64
Range	(160 - 180)	(167 - 185)	
Weight, kg	65.5 ± 11.6	66.5 ± 8.7	0.46
Range	(55 - 69)	(54 - 78)	
BMI, kg•m^{-2}	21.6 ± 3.3	21.8 ± 2.4	0.91
Range	(18.3 - 29.2)	(18.5 - 25.5)	

[a] Values are expressed as mean ± SD.
[b] P value was the statistical analysis from the independent paired t-test.

Table 2. Complete Blood Count (CBC) at Before and After Supplementations Between Groups[a]

	Sedentary Subjects (n = 15)				Athletic Subjects (n = 15)			
	Placebo		L-Carnitine		Placebo		L- Carnitine	
	Before	After	Before	After	Before	After	Before	After
WBC	5.9 ± 0.3	6.6 ± 0.5	5.7 ± 0.3	5.7 ± 0.3	5.2 ± 0.2	5.3 ± 0.2	5.3 ± 0.1	4.9 ± 0.1
Range	(4.5 - 8.5)	(4.4 - 9.7)	(4.1 - 7.4)	(4.7 - 7.1)	(3.1 - 7.5)	(4.2 - 8.5)	(3.8 - 7.1)	(4.1 -6.5)
RBC	5.2 ± 0.1	5.3 ± 0.2	5.3 ± 0.2	5.4 ± 0.2	5.3 ± 0.3	5.1 ± 0.2	5.7 ± 0.2	5.3 ± 0.8
Range	(4.6 - 6.0)	(4.5 - 6.4)	(4.8 - 6.4)	(4.8 - 6.5)	(4.1 - 6.3)	(4.1 - 5.9)	(4.1 - 6.8)	(4.4 - 6.3)
Hb	14.2 ± 0.4	14.4 ± 0.3	14.4 ± 0.4	14.7 ± 0.3	13. 9 ± 0.1	12.1 ± 0.2	13.1 ± 0.4	14.1 ± 0.3
Range	(12.0 - 6.6)	(12.7 - 5.9)	(12.6 - 17.5)	(12.7 - 17.0)	(13.2 - 15.3)	(11.3 - 15.2)	(11.7 - 16.3)	(11.1 - 18.0)
Hct	43.9 ± 1.0	44.5 ± 0.8	45.0 ± 0.9	45.4 ± 0.8	41.2 ± 1.1	40.5 ± 0.3	39.1 ± 0.4	42.2 ± 0.7
Range	(38.1 - 51.2)	(40.2 - 49.3)	(41.5 - 52.3)	(41.5 - 52.6)	(33.1 - 50.5)	(38.2 - 41.5)	(39.3 - 51.7)	(42.4 - 51.3)
Lym	22.4 ± 1.6	22.4 ± 1.6	24.7 ± 2.2	26.2 ± 2.7	20.1 ± 1.2	21.3 ± 1.4	23.7 ± 2.1	25.3 ± 1.9
Range	(14.7 -30.3)	(14.8 -29.4)	(17.3 - 38.2)	(15.9 - 41.2)	(13.2 - 29.4	(14.2 - 34.4)	(13.7 - 36.2)	(12.6 - 43.8
PLT	232.6 ± 11.2	240.7 ± 14.3	241.5 ± 15.0	241.3 ± 11.8	212.3 ± 10. 1	242.1 ± 11.3	232.1 ± 11.2	211.7 ± 10.1.
Range	(196 - 297)	(204 - 348)	(178 - 331)	(184 - 314)	(126 - 287)	(211 - 329)	(165 - 321)	(176 - 326)

Abbreviations: Hb, hemoglobin; Hct, hematocrit; PLt, platelet; RBC, red blood cells; WBC, white blood cells.
[a] Values are expressed as mean ± SD.

strength, endurance, and functional capacity (34). Previous study in vitro has claimed that L-carnitine scavenges radicals (8), in accordance with the study of Ho et al. (2010), which showed an improvement in physical performance and recovery from exercise exertion after administering 2,000 mg/d of carnitine to middle-aged men (35). Also, inflammatory cytokines were inhibited in patients with CAD (19). Therefore, it is possible that this mechanism reduces free radicals or cytokine release, which supports why the running time increased slightly in sedentary subjects and had a significant result in the athletes. However, this study did not evaluate the oxidative stress status or any cytokine markers, and this should be done for confirmation in future research.

The experiment for this study was designed to evaluate physical fitness using the submaximal Bruce treadmill exercise test, and report the times of running time and ventilatory threshold. VT in the noninvasive reflection of anaerobic threshold increased disproportionately at ventilation, when compared to the whole-body oxygen uptake (36), and related to increasing blood lactate (37). A previous study revealed a high correlation between VT and endurance (38). Therefore, evaluation of VT and RT in this study was designed to find the efficacy of L-carnitine sup-

Table 3. Metabolic Utilization and Running Capacity Before and After L-Carnitine Supplementation in Sedentary and Athletic Subjects[a]

	Sedentary Subjects (n = 15)						Athletic Subjects (n = 15)					
	Control	Placebo	L-carnitine	P Value[b]	P Value[c]	Effect Size[d]	Control	Placebo	L-carnitine	P Value[b]	P Value[c]	Effect Size[d]
VO_2 (80% MHR), mL/kg/min	28.6 ± 1.2	29.4 ± 1.5	32.8 ± 1.9	0.029	0.006	8.5	29.7 ± 1.6	27.1 ± 1.4	36.0 ± 1.9[c]	0.002	0.001	17.8
Range	(23.4 - 35.1)	(21.2 -38.1)	(25.8 - 49.9)				(26.4 - 34.4)	(27.1 - 38.1)	(29.7 - 44.2)			
VT, min	3.2 ± 0.5	3.1 ± 0.5	3.4 ± 0.7	0.17[e]	0.17[e]	N/A	3.4 ± 0.5	3.5 ± 1.3	5.3 ± 0.6[c]	0.000	0.000	4.6
Range	(1.2 -7.5)	(2.1 - 9.5)	(2.7 - 9.7)				(1.0 - 4.3)	(1.4 - 6.1)	(2.4 - 9.0)			
RT, min	9.4 ± 1.4	9.3 ± 1.7	9.4 ± 1.7	0.84[e]	0.84[e]	N/A	8.9 ± 1.1	9.4 ± 1.1	11.1 ± 1.2[c]	0.000	0.001	17.0
Range	(5.9 -11.9)	(4.3 - 14.4)	(6.1 - 15.9)				(7.4 - 11.0)	(7.4 - 11.2)	(10.3 - 13.4)			
Fatigue (80% MHR)	4.2 ± 1.6	4.1 ± 1.4	3.8 ± 1.0	0.65[e]	0.65[e]	N/A	4.5 ± 1.8	4.1 ± 1.0	3.4 ± 1.0	0.002	0.000	7.0
Range	(3 - 7)	(2 - 7)	(2 - 5)				(2 - 7)	(2 - 5)	(1 - 4)			

Abbreviations: Fatigue (80% MHR), fatigue at 80% of maximal heart rate; RT, running time; VO_2 (80% MHR), oxygen consumption at 80% of maximal heart rate; VT, ventilatory threshold.
[a] Values are expressed as mean ± SD.
[b] Compared to the control.
[c] Compared to Placebo group from a post-hoc Significant Difference (LSD) after Repeated measurement ANOVA when $P < 0.05$.
[d] Effect of size was calculated by G*Power (3.1.9.2) between placebo and L-carnitine, and N/A is non-analyzed.
[e] From repeated measurement ANOVA analysis.

Table 4. Lipid Profile Before and After L-Carnitine Supplementation in Sedentary and Athletic Subjects[a]

		Placebo			L-Carnitine		
		Before	After	P Value	Before	After	P Value
Sedentary subjects (n = 15)	Cholesterol, mg/dL	171.9 ± 25.8	170.3 ± 24.9	0.57	169.9 ± 30.9	171.5 ± 21.5	0.77
		(129 - 208)	(128 - 207)		(137 - 236)	(137 - 238)	
	Triglyceride, mg/dL	86.5 ± 59.5	97.6 ± 63.8	0.87	84.3 ± 36.1	101.1 ± 52.4	0.11
		(20 - 224)	(34 - 240)		(23 - 136)	(44 - 194)	
	HDL, mg/dL	64.1 ± 12.3	63.2 ± 10.5	0.75	59.9 ± 11.3	62.2 ± 10.6	0.84
		(44 - 89)	(48 - 79)		(38 - 78)	(44 - 97)	
	VLDL, mg/dL	19.8 ± 6.7	21.8 ± 5.2	0.64	20.4 ± 9.1	22.6 ± 7.7	0.77
		(11.5 - 26.5)	(10.8 - 33.7)		(10.6 - 32.5)	(11.4 - 31.8)	
Athletic subjects (n = 15)	Cholesterol, mg/dL	179.2 ± 27.6	178.7 ± 27.1	0.91	181.2 ± 28.5	180.9 ± 26.3	0.93
		(152 - 227)	(154 - 225)		(146 - 214)	(158 - 213)	
	Triglyceride, mg/dL	83.3 ± 44.4	97.2 ± 46.1	0.33	91.7 ± 40.7	80.9 ± 32.9	0.02[b]
		(50 - 122)	(63 - 133)		(48 - 189)	(38 - 133)	1.38[c]
	HDL, mg/dL	62.2 ± 13.5	61.6 ± 11.6	0.97	63.2 ± 10.8	61.1 ± 10.2	0.43
		(49 - 95)	(48 - 81)		(47 - 86)	(49 - 95)	
	VLDL, mg/dL	17.1 ± 4.9	21.9 ± 6.5	0.72	22.4 ± 9.4	17.3 ± 5.5	0.77
		(10.0 - 24.4)	(12.6 - 32.6)		(9.6 - 31.8)	(11.6 - 26.6)	

Abbreviations: HDL, high-density lipoprotein; VLDL, very-low density lipoprotein.
[a] Values are expressed as mean ± SD and range.
[b] $P < 0.05$ from dependent pair t-test within group.
[c] Effect of size result from analysis with the G*Power (3.1.9.2) program.

plementation on metabolic energy production and muscle fitness. Surprising results in this study found a significant increase of VT and RT in the athletic group, while no significant difference was seen in the sedentary one. This result is similar to that in previous data on trained cyclists (39), which showed a correlation between prolonged time of VT and better velocity of muscle fiber conduction. This study did not evaluate any difference in muscle structure or metabolic status between groups, but possible muscle fibers or some difference in metabolic capacity, cardiopul-

monary fitness, or neurohormoral or autonomic regulatory systems in athletic people should be greater than in untrained people, as proposed in previous study (40, 41). In addition, these results also found a significantly lower fatigue score in athletic subjects after L-carnitine supplementation, whereas no significant decrease was seen in the sedentary group. Decreased fatigue score has suggested the efficacy of L-carnitine supplementation on oxidative stress, as possibly shown in a previous study of advanced cancer patients, who took L-carnitine supplementation at a higher dose (6 g/d) for 4 weeks (1). However, this study used a lower single dose of L-carnitine (2 g/d) with no statistical difference, therefore, this dosage cannot claim the benefit of lowering fatigue score until it is confirmed in the future.

This study detected different lipoproteins such as cholesterol, triglycerides, VLDL, and HDL. The results in this study showed no statistical differences in any lipid parameters, including cholesterol, HDL, and VLDL, in the sedentary subjects during either placebo intake or L-carnitine supplementation, which was similar in the athletic subjects. It is interesting that triglyceride levels remained unchanged in the sedentary subjects after L-carnitine supplementation, whereas it significantly decreased in the athletic subjects. The possible mechanism of this result is similar to that in a previous report, in which athletes had more oxidation and capacity to oxidize fat or triglyceride related to endurance capacity and exercise performance (42), with more significant function of carnitine palmitoyl transferase (CPT)-1 activity in trained subjects than in untrained subjects (6, 43). Unfortunately, this study did not evaluate this enzyme activity. On the other hand, why cholesterol, HDL, and VLDL did not change statistically is still unclear and this needs more study or confirmation in the future.

In addition, the single dosage used in this study was 2 g/d orally, which is safe and non-toxic for humans, as confirmed in a previous report (44). However, the recommended dose for weight control and balance in the cardiovascular system is low at 0.5 to 1.0 g/d, whereas higher doses of 1.0 to 4.0 g/d twice daily can be used during regular exercise (45).

All significant data were analyzed for the overall effect of sample size, which confirmed the significance of the small sample size (n = 15) in this study. A previous report strongly suggested that a p value may be not standardized in the case of a small sample size, as the effect of sample size or Cohen (d) calculations from each result should be confirmed. Cohen calculations classify the effect of sample sizes, i.e. small (d = 0.2), moderate (d = 0.5), and large (d > 0.8) (46). If results present a significant difference from a small sample size, that parameter should be studied further. On the other hand, a significant result with a large sample size presents better validity and reliable results. Tables 3 and 4 show an effective size. Therefore, it can be concluded that all significant changes are reliable, even though this study used 15 subjects in each group.

5. Conclusions and Limitation

In this study, the administration of oral L-carnitine at 2 g/d before exercise appears to have no benefit in oxygen uptake, fatigue, or lipid profiles in sedentary subjects, but a distinct change in running time, ventilatory threshold, VO_2 consumption, and triglyceride utilization occurred in athletic subjects. Therefore, oral supplementation of a single dose of L-carnitine should be considered to have efficacy in terms of energy utilization and lipid change in this population. However, the limitations of this study were the small sample size of exclusively males, different sport specialties of the athletes, training level of athletes, and motion and nutrition monitoring between sedentary and athletic subjects that should be of concern and controlled in future study. These findings cannot necessarily be extrapolated to other populations or patients that use a single dose of L-carnitine, as well as other parameters related to oxidative stress, inflammation, or other biochemical measures thought to be influenced by L-carnitine supplementation.

Footnotes

Authors' Contribution: The study concept, design, acquisition of data, analysis and interpretation of data, including manuscript preparation: Jirakrit Leelarungrayub and Decha Pinkaew; critical revision of the manuscript for important content: Jakkrit Klaphajone and Wichai Eungpinichpong: and final manuscript preparation before submission: Richard J. Bloomer.

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