L-Carnitine Supplementation Combined With Aerobic Training Does Not Promote Weight Loss in Moderately Obese Women

Rudolph G. Villani, Jenelle Gannon, Megan Self, and Peter A. Rich

L-Carnitine (L-C) transports fatty acids into mitochondria for oxidation and is marketed as a weight loss supplement. In a double-blind investigation to test the weight loss efficacy of L-C, 36 moderately overweight premenopausal women were pair matched on Body Mass Index (BMI) and randomly assigned to two groups ($N = 18$). For 8 weeks the L-C group ingested 2 g twice daily of L-C, while the placebo (P) group ingested the same amount of lactose. All subjects walked for 30 min (60–70% maximum heart rate) 4 days/week. Body composition, resting energy expenditure (REE) and substrate utilization were estimated before and after treatment. For the subjects who completed the study (15 P, 13 L-C), no significant changes in mean total body mass (TBM), fat mass FM, and resting lipid utilization occurred over time, nor were there any significant differences between groups for any variable. Conversely REE increased significantly for all subjects, but no between group differences existed. Five of the L-C group experienced nausea or diarrhea and consequently did not complete the study. Eight weeks of L-C ingestion and walking did not significantly alter the TBM or FM of overweight women, thereby casting doubt on the efficacy of L-C supplementation for weight loss.

Key Words: L-carnitine supplementation, weight loss, overweight women

Introduction

In recent years L-Carnitine (L-C), an essential cofactor for the oxidation of long chain fatty acids by mitochondria, has been widely marketed in health food products as a nutritional supplement useful in the management of obesity. However, to our knowledge, the present investigation is the first reported scientific evaluation of L-C as a weight loss supplement. Carnitine (3-hydroxy-4-trimethylaminobutyrate) is a quaternary amine that facilitates the transport of activated long chain fatty acids (acyl CoA) across the inner mitochondrial membrane of skeletal muscle to the site of beta-oxidation in the mitochondrial matrix (8).

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The amount of free muscle carnitine is considered to be a limiting factor in energy production from lipids (1, 7) in vitro, since the extent of in vitro fat oxidation has been shown to be directly related to muscle carnitine concentration (16, 25). An increase in muscle carnitine has been clearly demonstrated with oral L-C supplementation in rats (22) and horses (11). The results of human supplementation studies have varied. In a study where patients with intermittent claudication took 2 g/day for 15 days, total muscle carnitine content significantly increased from 19.3 to 24.6 nmol/g of non-collagenous protein (6). However, in more recent studies where endurance trained individuals ingested 6 g/day for 14 days (27) or 4 g/day for 14 days (3), there were no significant changes in muscle carnitine content. In contrast, 2g/day of L-C taken by patients with mitochondrial myopathy for four weeks (7) and 1g/day of L-C taken by sprint and endurance trained athletes for 120 days significantly increased muscle carnitine content (1). Such findings suggest that long periods of supplementation (greater than four weeks) may be required to increase human muscle carnitine levels.

Generally in L-C deficient populations, supplementation has led to improved oxidation of long chain fatty acids in vivo (26) and in vitro (2), and to reduced blood free fatty acid (23) and triglyceride concentrations (4). However a different picture has emerged with trained subjects who did not have an L-C deficiency, with some studies finding slight improvements in lipid oxidation after L-C supplementation (21), but the majority finding no changes in lipid oxidation (3, 27).

Both oral L-C supplements and L-C based rub-on creams are advertised and sold throughout Australia, America, and Europe. The manufacturers make unsubstantiated claims that L-C supplementation alone, without dietary caloric reduction or exercise intervention, leads to significant body fat losses. Others claim that L-C enhances the fat reduction that often accompanies regular aerobic exercise. The purpose of this study was to determine if L-C supplementation for 8 weeks, combined with regular and prolonged walking exercise (60–70% of HR_max), could augment lipid utilization and energy consumption and reduce the adiposity of moderately overweight women.

Methods

Subjects

Thirty-six female subjects volunteered to participate in the study after answering advertisements circulated on the Bundoora Campus of the Royal Melbourne Institute of Technology (RMIT) in Victoria, Australia. They had a mean (±SD) age of 27.2 ± 9.6 years (range, 19–48 years), body weight of 70.1 ± 9.9 kg (range, 56–96 kg), body mass index (BMI) of 24.7 ± 0.66 and percentage body fat of 35.2 (range, 24.3–42.9%) estimated by bioelectrical impedance and skinfold data. While obesity was not a criterion for inclusion, 33 of the 36 women had a percentage body fat over 30%, which based on commonly accepted definition meant that overall the group was moderately obese or overweight (29), even though their mean BMI was within “normal” range. The criteria for acceptance were premenopausal, non-smokers who had not been on a weight loss program for the previous 6 months and were not taking any medication that would confound the results of the study. All subjects had medical clearance to participate, and none had diabetes mellitus, heart disease, or
metabolic disorders that would otherwise interfere with the study. They maintained their habitual dietary (no reduction in caloric intake) and physical activity levels, except for the supplements and exercise prescribed in the study. All were fully informed about the testing procedures and nature of the investigation prior to giving their informed consent to participate. The protocol was approved by the Human Research Ethics Committee of RMIT.

**Testing**

In the 24 hr prior to laboratory tests, subjects collected 24-hr urine samples in 4-L pre-sterilized flasks, which they brought to the laboratory on each testing day. These were subsequently analyzed for total nitrogen and creatinine excretion (15, 24). Twenty-four hour urinary nitrogen excretion, normalized for urinary volume changes using creatinine output, is used to provide an accurate assessment of protein utilization for calculation of the non-protein respiratory quotient (NP-RQ), and this can then be used to estimate lipid and carbohydrate utilization.

The pretests were performed in the week before the intervention period, while post-tests were carried out in the week after it. On each testing day, subjects came to the laboratory in the morning between 7 AM and 11 AM (same time for each subject in the pre and post tests) after a 12-hr overnight fast. The subjects had been encouraged to sleep at least 8 hr, they had the same diet in the 24 hr before the pre and post tests, and they did not exercise in this period. The subjects were driven to the laboratory and, on arrival, their unclothed weight and height were recorded, after which they dressed and rested supine on a padded bench for half an hour in a quiet temperature controlled room (20 °C). While resting supine, the subject placed her head in a ventilated canopy (24) connected to a metabolic cart (Medgraphics Metabolic Cart, St. Paul, MN). After a 10-min washout period, respiratory gases were sampled for estimation of steady state resting energy expenditure (REE) and respiratory quotient (RQ). The most stable (steady state) 20-min period, when oxygen uptake (VO2) did not vary more than ± 5% of the mean and the RQ did not vary more than ± 2.5% of the mean, was employed to estimate resting RQ and REE (24). Respiratory quotients were reported unchanged and also subsequently modified to non-protein RQ using the nitrogen excretion data obtained from the 24-hr urine collections. Oxygen consumption values obtained using this system were converted to REE using standard tables (13), and expressed as absolute REE and REE/kg body weight.

Body composition, that is fat mass (FM) and fat free mass (FFM), was estimated using bioelectrical impedance (SEAC multiple frequency, model SFB3, v. 1, Uniquest) and a four site skinfold test with Harpenden calipers (10). For the bioelectrical impedance measurements, two electrodes were placed on the dorsal surfaces of the subjects' hand and foot (dominant side) while they lay supine. A very mild current was introduced via the distal electrodes, and the voltage attenuation detected in the proximal electrodes was used to estimate the body's resistance to current flow (20). Measurements were taken in triplicate, averaged, and used in the Lukaski equation to estimate FFM and FM (20). Skinfold measurements were taken from the anterior surface of the biceps, middle triceps, subscapular, and suprailliac regions. A minimum of two measurements were taken at each site and repeated until consecutive measurements varied by less than 1 mm. The skinfold results were reported as the average skinfold over the four sites.
L-Carnitine Supplementation and Aerobic Training Program

After all the pretests were carried out, subjects were pair matched using the Body Mass Index (BMI) due to its strong correlation with many of the variables being tested. These pairs were then randomly assigned to one of two groups (N = 18), placebo (P) that ingested lactose powder and a supplement (L-C) that ingested L-Carnitine (powder supplied by Amcor, NSW Australia), in a double-blind protocol. The subjects took either 2 g of the supplement or placebo mixed in a drink twice daily, once in the morning and once in the evening. The 4 g per day dose was used on the recommendation of the manufacturers of the L-C supplement and from the results of previous human studies. On a day when they performed the exercise session, they took one dose 20 min before the activity. Both groups also walked for 30 min per day, 4 days per week at an intensity of 60–70% of their estimated (220–age) maximal heart rate. They were taught how to monitor their own exercise heart rates, which they checked regularly during each 30-min walk, to make sure they kept within the target heart rate and exercise intensity. The supplementation and walking regime continued for 8 weeks before the post tests. While training and supplementation were not directly supervised, participants were regularly reminded (by phone) of their commitment. Additionally, a diary was completed by all subjects to record their exercise and supplementation compliance.

Statistical Analysis

The data were analyzed using the Statview 512+ software program (Brainpower, Calabasas, CA). A 2 × 2 (treatment by time) analysis of variance (ANOVA), with repeated measures across time, was used to analyze the dependent variables at the completion of the study, while unpaired t tests were carried out to compare the groups at baseline. The significance level was set at .05. The results (Table 1) are given as mean and standard error.

Results

Compliance and Withdrawal From the Study

The compliance to the aerobic training, reported in the training diaries, for the L-C group was 84% and for the placebo group was 80%. Supplementation compliance

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Body Composition Before and After Treatment Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
<td>L-Carnitine</td>
</tr>
<tr>
<td></td>
<td>Pre</td>
</tr>
<tr>
<td>Body mass (kg)</td>
<td>71.29 ± 2.25</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>25.52 ± 1.48</td>
</tr>
<tr>
<td>Fat free mass (kg)</td>
<td>45.77 ± 1.41</td>
</tr>
<tr>
<td>Average skinfold (mm)</td>
<td>21.1 ± 1.5</td>
</tr>
</tbody>
</table>

Note. Values are expressed as mean ± SE.
Table 2  Resting Metabolic Indicators Before and After Treatment Period

<table>
<thead>
<tr>
<th>Variable</th>
<th>L-carnitine</th>
<th></th>
<th>Placebo</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>Pre</td>
<td>Post</td>
</tr>
<tr>
<td>RQ</td>
<td>0.84 ± 0.02</td>
<td>0.83 ± 0.02</td>
<td>0.84 ± 0.02</td>
<td>0.86 ± 0.01</td>
</tr>
<tr>
<td>NPRQ</td>
<td>0.86 ± 0.03</td>
<td>0.85 ± 0.02</td>
<td>0.84 ± 0.02</td>
<td>0.86 ± 0.02</td>
</tr>
<tr>
<td>REE (kJ/hr)*</td>
<td>240.73 ± 9.71</td>
<td>251.65 ± 14.46</td>
<td>227.33 ± 13.01</td>
<td>246.4 ± 9.14</td>
</tr>
<tr>
<td>REE/TBM (kJ/kg hr)*</td>
<td>3.38 ± 0.14</td>
<td>3.53 ± 0.2</td>
<td>3.30 ± 0.19</td>
<td>3.55 ± 0.13</td>
</tr>
</tbody>
</table>

Note. Values expressed as mean ± SE. RQ = respiratory quotient, NPRQ = non-protein respiratory quotient, REE = absolute resting energy expenditure, RMR/TBM = resting energy expenditure per kg total body mass.

* Pretreatment means significantly smaller (p < .05) than posttreatment means. There were no significant differences between treatments or interactions.

for the L-C group was 82% and for the placebo group was 86%. Twenty-eight women completed the study and were used in the data analysis. Three withdrew from the placebo group due to other commitments and five from the L-C group due to the side effects of the supplement.

**Body Composition**

The body composition data are summarized in Table 1. There were no significant differences between the L-C and P groups on any of the dependent variables prior to the intervention, indicating that the groups were well matched. There were no significant differences between the groups (treatment effects) for TBM, FM, or FFM (estimated from bioelectrical impedance) at the completion of intervention, nor were there any significant changes over time. There was no significant difference between the groups for average skinfold thickness before or after the intervention, but there was a significant increase for both groups over the intervention period. Intra-test and inter-test coefficients of variation (CV) for body composition measurement by bioelectrical impedance were 0.38% and 0.45%, respectively, while for skinfold thickness, they were 5% and 6%, respectively.

**Resting Metabolism**

Results of the metabolic measures are presented in Table 2. There were no significant differences between the groups for REE, REE/kg (Total Body Mass, TBM), RQ, or NPRQ. However, both groups significantly increased their REE and REE/kg TBM over time. Intra-test CV for steady state REE was 3.9%, while for RQ, it was 1.8%.

**Discussion**

The results of this study indicate that 8 weeks of L-C supplementation at 4 g/day combined with regular walking, does not significantly alter body weight, fat mass,
percentage body fat, or lean body mass in a group of premenopausal, moderately obese women. There were no significant differences between the two groups for any of the body composition (bioelectrical impedance or skinfold thickness) variables measured over the intervention period. These results suggest that L-C supplementation does not change either total body or fat mass. Consequently, this study casts doubt on the claims made in the “health food industry” about the fat reducing properties of L-C. To the knowledge of the authors, this is the first reported investigation on the effectiveness of L-C as a weight loss agent.

The theoretical basis for using L-C supplementation to treat obesity is the assumption that obese individuals may have a deficiency of L-C (18), but this has not been substantiated by research. However, morbidly obese individuals have been found to have significantly higher L-C concentrations in the liver and skeletal muscle than nonobese controls (14). The authors hypothesized that increased L-C concentrations in these tissues may indicate an increased need for L-C in the obese, though whether a functional L-C deficiency existed cannot be answered by this (14), nor to our knowledge, by any other paper to date. This would seem to be a key question for future investigation. In the present study, most of the women had a preintervention percentage body fat close to or above 32% (bioimpedence mean = 35.2%), based on both bioelectrical impedance and skinfold estimations, and would therefore generally be categorized as overweight to obese (29). The majority of women who did not lose fat with the L-C supplement may have been consuming sufficient dietary L-C and/or endogenously producing enough L-C before the intervention to maximize muscle requirements. In these women, supplemental L-C may not have had any further influence over muscle L-C concentration and hence fatty acid transport. Previous short-term supplementation studies have shown that while serum L-C concentration is increased by supplementation, muscle L-C content is not (3, 27). Alternately, it has been suggested that for most people, the exchange capacity of carnitine acylcarnitine translocase far exceeds the fatty acid oxidation rate of the mitochondria (3). Therefore, even if muscle content does rise with supplementation, as shown in studies where L-C was taken for greater than 4 weeks (1, 7), it may not increase fat utilization.

In addition to ingesting either the L-C or placebo, the subjects in the present study also walked four times per week (30 min/day at 60–70% HRmax). Therefore, the results indicate that this walking regimen did not significantly induce fat or weight loss. Since the training was not directly supervised, it could be suggested that the participants may not have completed sufficient exercise to induce fat loss, although the exercise compliance rate reported in the training diaries was about 80% for both groups. These findings concur with those of some other studies in which women trained with aerobic exercise and did not lose weight. Despres et al. (9) trained women with 20 weeks of cycle ergometry 4 to 5 days per week, 40 min per day, at 80% of HRmax and found no changes in body weight, percentage body fat, or fat cell number. In another aerobic exercise training study with obese men and women, it was found that only the men significantly reduced their body fat (17).

One of the common features of these studies and the present work was that dietary intake was not directly controlled and therefore, had the women increased their energy consumption, the increased energy expenditure associated with exercise could have been negated. However this seems unlikely, as the women were highly motivated to lose weight and specifically agreed not to alter their habitual
food intake throughout the study. In investigations where aerobic training alone has resulted in weight loss, women trained for over a year (12), trained at high intensity (over 80% HR_{max}; ref. 19) or at high volumes (800 min per week; ref. 12). In a relatively recent review on the effectiveness of exercise alone to produce weight loss, it was concluded that women may need to train regularly and intensely for over 3 months before weight loss or body composition changes occur (30). This may explain why most of the subjects in the present study did not lose weight, since they only trained for 8 weeks at a moderate intensity (60-70% HR_{max}) and low volume (120 min per week).

While manufacturers of products containing L-C suggest that these supplements will induce weight loss without the need to exercise or diet, they often recommend that the supplement be taken 30 min prior to aerobic exercise, presumably to enhance fatty acid utilization during prolonged exercise. Although fatty acid utilization during exercise was not measured in the present study, estimated resting steady state lipid utilization, based on steady state RQ changes, in the L-C group was not significantly higher than in the placebo group. These data suggest that 8 weeks of L-C administration does not significantly enhance the use of fats for energy in the post absorptive state. Wagenmakers (28) concluded from an extensive review that it has been unambiguously shown that L-C supplementation does not increase fatty acid oxidation during exercise. The present study suggests that for a moderately obese group of females, it does not increase resting fatty acid utilization either.

There wasn’t a significant difference between the two groups for mean REE before or after the treatments. This finding does not support the suggestion by some manufacturers that L-C supplements “boost” basal metabolism. Both groups had an increase in REE of similar magnitude over the 8 weeks compared with pretreatment levels. Regular aerobic exercise has been shown to increase both REE and thyroid secretion (5); therefore, the present results are likely to be attributable to the walking program.

While L-C did not have any significant effects on body composition, half of the subjects in the L-C group did report feeling nausea and having diarrhea. Four subjects dropped out of the study because of chronic diarrhea, which began with L-C supplementation and persisted until they finished taking L-C. A further 5 subjects in the L-C group also reported these symptoms for only a few days, which then subsequently subsided as they continued to take the supplement. To our knowledge, only subjects in one previous study have reported similar side effects of L-C supplementation (7).

In summary, the findings of the present study indicate that L-C supplementation (4 g/day, for 8 weeks) combined with regular aerobic exercise does not significantly alter the body weight or fat mass of moderately obese premenopausal women. Therefore, L-C supplements do not appear to be suitable as part of any weight loss therapy, despite claims to the contrary on a wide range of health food products sold in Australia and other countries.

References


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