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ORIGINAL CONTRIBUTION

# The effect of L-carnitine supplementation on insulin resistance, sex hormone-binding globulin and lipid profile in overweight/obese women with polycystic ovary syndrome: a randomized clinical trial

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## Abstract

**Purpose** Polycystic ovary syndrome (PCOS) is a common endocrine disorder among reproductive-age women. Insulin resistance and dyslipidemia are linked to PCOS. L-Carnitine supplementation as a management strategy for women with PCOS has been proposed. The effect of L-carnitine supplementation on insulin resistance, sex hormone-binding globulin (SHBG) and lipid profile in overweight/obese women with PCOS was investigated.

**Methods** This randomized, double-blind, controlled clinical trial, was conducted on 62overweight/obese women with PCOS. Participants were randomly assigned into two groups to receive 1000 mg/day L-carnitine or placebo (1000 mg starch) for 12 weeks.

**Results** L-Carnitine supplementation compared to the placebo showed a significant improvement in insulin [− 0.7 (− 7.3 to 4.0) vs. 0.7 (− 3.0 to 5.2); $P=0.001$], homeostatic model assessment for insulin resistance [− 0.4 (− 1.7 to 1.1) vs. 0.0 (− 0.7 to 1.3); $P=0.002$], quantitative insulin sensitivity check index ($+0.01\pm0.02$ vs. $-0.01\pm0.01$; $P=0.02$) and a non-significant change toward improvement in SHBG ($+11.5\pm40.2$ vs. $-3.2\pm40.2$; $P=0.2$). However, there was no significant differences between the two groups in serum levels of fasting plasma glucose, total cholesterol, triglyceride, low density lipoprotein-cholesterol and high density lipoprotein cholesterol ($P>0.05$).

**Conclusion** 12-week L-carnitine supplementation in overweight or obese women with PCOS ameliorate insulin resistance, but has no effect on SHBG and lipid profile. Studies with higher dosages and duration of L-carnitine intake are required. The trial was registered on 30 December 2019 at Iranian Registry of Clinical Trials IRCT20191016045131N1.

**Trial registration** Registered on 30th December 2019 at Iranian Registry of Clinical Trials (IRCT20191016045131N1).

**Keywords** Polycystic ovary syndrome · L-Carnitine · Sex hormone-binding globulin · Insulin resistance · Lipid profile

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## Abbreviations

| | |
|---|---|
| Acyl-CoA | Acyl-coenzyme A |
| AES | Androgen Excess Society |
| ASRM | American Society for Reproductive Medicine |
| BMI | Body mass index |
| CVD | Cardiovascular disease |
| DHEA | Dehydroepiandrosterone |
| ESHRE | European Society of Human Reproduction and Embryology |
| FAI | Free androgen index |
| FPG | Fasting plasma glucose |
| HC | Hip circumference |
| HDL-c | High density lipoprotein-cholesterol |
| HOMA-IR | Homeostatic model assessment for insulin resistance |
| IPAQ | International physical activity questionnaire |

| | |
|---|---|
| LDL-c | Low-density lipoprotein-cholesterol |
| LH | Luteinizing hormone |
| MET-h | Metabolic equivalent task hours |
| NAFLD | Nonalcoholic fatty liver disease |
| NIH | National Institutes of Health |
| PCOS | Polycystic ovary syndrome |
| QUICKI | Quantitative insulin sensitivity check index |
| SHBG | Sex hormone-binding globulin |
| T2DM | Type 2 diabetes mellitus |
| TC | Total cholesterol |
| TG | Triglyceride |
| VLDL | Very low-density lipoprotein |
| WC | Waist circumference |

## Background

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder among reproductive-age women, and is associated with increased risk of infertility, type 2 diabetes mellitus (T2DM), nonalcoholic fatty liver disease (NAFLD), and cardiovascular disease (CVD) [1–3]. The prevalence of PCOS in the general population has been estimated to be 3–10% [4, 5]. There are three different sets of diagnostic criteria for PCOS as follows: 1; the National Institutes of Health (NIH), 2; the European Society of Human Reproduction and Embryology and the American Society for Reproductive Medicine (ESHRE/ASRM), which is also known as the Rotterdam criteria, and 3; the Androgen Excess Society and PCOS Society (AES-PCOS) [6–9]. Anovulation, hyperandrogenism, amenorrhea or oligomenorrhea, hirsutism, acne, and obesity are the most common clinical features of PCOS [10]. Moreover, dyslipidemia is a common disorder among women with PCOS [11]. Insulin resistance is closely linked to the PCOS pathogenesis [12, 13]. Insulin resistance by mechanisms such as suppressing the hepatic sex hormone-binding globulin (SHBG) production, and subsequently increasing free testosterone, increasing the luteinizing hormone (LH) pulse amplitude, stimulating the adrenal P450c17α activity and inducing hyperandrogenism is involved in the pathogenesis of PCOS [13]. Currently, diet modification and weight loss are the important strategies in the management of PCOS [14].

L-Carnitine as a conditionally essential amino acid synthesized from lysine (diaminohexanoic acid-26) and methionine (amino-4-(methylthio) butanoic acid-2), is found in almost every cell in the body (specially muscles) and plays a critical role in the energy production, lipid and glucose metabolism [15–18]. Carnitine is obtained from endogenous synthesis or diet [16, 19]. Meat products, fishes, and dairy foods are rich sources, and most fruits and vegetables are poor sources of carnitine [15, 19]. Several studies have investigated the effects of L-carnitine on osteoarthritis, CVD, hypothyroidism, obesity and T2DM [20–25]. In addition, the evidence demonstrated the therapeutic effects of L-carnitine on insulin resistance and dyslipidemia [26, 27]. L-Carnitine by increasing the glucose transporter GLUT4 expression, and the serum levels of adiponectin improved insulin resistance in metabolic syndrome-induced rats [28]. Moreover, oral administration of L-carnitine led to a decrease in the levels of cholesterol, triglyceride (TG), low-density lipoprotein-cholesterol (LDL-c) and very low density lipoprotein-cholesterol (VLDL-c) as well as an increase in the levels of high-density lipoprotein-cholesterol (HDL-c) in metabolic syndrome-induced rats [28]. The benefits of L-carnitine in the management of infertility have been demonstrated [29, 30]. L-Carnitine can attenuate the effect of high LDL and oxidized LDL on spermatogenesis and improve the serum testosterone and LH levels in rats [31]. The studies reported a direct relationship between serum carnitine and SHBG, which is a transporter of sex hormones [32–34]. Moreover, a negative correlation between serum carnitine and free androgen index (FAI) was found [34]. To date, there is no clinical trial evaluating the effect of L-carnitine on SHBG. In addition, there are limited number of clinical trials (with contradictory findings) investigating the effects of L-carnitine on insulin resistance and dyslipidemia in women with PCOS [35, 36]. According to the current evidence, the present clinical trial was designed to investigate the effect of 1000 mg/day oral L-carnitine intake on insulin resistance, SHBG and lipid profile in overweight/obese women with PCOS.

## Methods

### Recruitment and eligibility screening

From May 2019 to August 2019, 75women with PCOS referred to diabetes research center in Yazd, Iran were screened. The diagnose of PCOS was performed based on the Rotterdam criteria by an endocrinologist. In the PCOS defined by Rotterdam criteria, the women must represent symptoms in two out of three categories, which include oligo/anovulation, hyperandrogenism, and the presence of polycystic ovaries [9, 10]. A total of 62women diagnosed with PCOS met the inclusion criteria, which is defined as follows: aged 18–45 years, and body mass index (BMI) $\geq$ 25. The exclusion criteria included T2DM, thyroid diseases, psychiatric diseases, smoking, pregnancy, taking letrazole, glucose-lowering drugs (metformin, rosiglitazone, pioglitazone, glimepiride, nateglinide), and lipid lowering medications, insulin infusion, adherence to a specific diet, and unwillingness to continue the study. In addition, the

participants were excluded if their L-carnitine and placebo capsules consumption (the compliance rate) was less than 80%.

## Study design

We conducted a double-blind, randomized, controlled clinical trial. The registration of the protocol was performed at Iranian clinical trials website (http://www.irct.ir) with code number: IRCT20191016045131N1. After a detailed description of the potential benefits and side effects of study participation, the participants signed a written informed consent. At the baseline, the participants were randomly assigned into the treatment and control groups by a trained person, using a simple randomization sampling method. Randomization list was prepared using a computer-generated random number table. The follow-up was done for 12 weeks from September 2019 to December 2019. The participants, and investigators remained blinded for the randomization and intervention assignment until the end of the study.

## Intervention

The treatment group received one L-carnitine capsule (1000 mg L-carnitine) daily and the control group received daily one placebo capsule containing 1000 mg starch. All subjects received clomiphene citrate, and were advised to the common healthy dietary recommendations during follow-up. L-carnitine and placebo capsules were prepared by Karen Pharmaceuticals Co., Yazd, Iran. The odor, shape and color of the L-carnitine and the placebo capsules were similar. L-Carnitine and placebo capsules were given to participants every 2 weeks, and the compliance rate was monitored.

## Physical activity and dietary intake measurement

Using the international physical activity questionnaire (IPAQ), the level of physical activity was measured at the baseline and the end of the study. In addition, using a 3-day (1 weekend day and 2 nonconsecutive weekdays) 24-h recall questionnaire, evaluating energy intake and diet composition was performed at the baseline and the end of the study.

## Blood sampling and biochemical measurements

At the baseline and the end of the trial, 5 cc blood was taken from each participant after 12 h fasting, and the blood samples were centrifuged for 10 min at a speed of 3600 rpm. The microtubes containing serum samples were stored at − 80 °C. Insulin and SHBG were measured by ELISA method using the Q-1-DiaPlus, USA kits. Fasting plasma glucose (FPG), total cholesterol (TC), TG, LDL-c, and HDL-c were measured using Pars Azmoon, Iran kits by an autoanalyzer. The laboratory measurements were done in the diabetes research center laboratory, based on the standard protocols.

## Glucose homeostasis

To determine insulin resistance, the homeostatic model assessment for insulin resistance (HOMA-IR) was calculated using the following formula: HOMA-IR = [fasting insulin (mU/L) × fasting plasma glucose (mg/dL)]/405. In addition, the quantitative insulin sensitivity check index (QUICKI) was calculated based on the following formula:1/[log (fasting insulin (mU/L)) + log (fasting plasma glucose (mg/dL))].

## Anthropometric measurements

Height, weight, waist circumference (WC), and hip circumference (HC) were measured under the standard protocols at the baseline and the end of the trial. Height, WC and HC were assessed using a measuring tape. Measuring weight was performed by a portable digital scale (Omeron BF511, Japan) with an accuracy of 100 g. The participants' height, WC, HC and weight were measured in standing position without shoes. To measure weight, participants had light clothes. Using the following formula, body mass index (BMI) was calculated: weight (kg)/height squared ($m^2$).

## Sample size and statistical analysis

The sample size was calculated based on insulin, as the main variable of the study of Samimi et al. [36], with $\alpha = 0.05$, power = 80%. The minimum sample size was 28 participants in each group. The sample size increased to 31 participants per group, after considering ~10% dropout. The normal distribution of variables was assessed using Kolmogorov–Smirnov test. An independent t-test was used to compare the means of normal variables at the baseline and the end of the study, as well as comparing mean changes of normal data between two groups. To compare the abnormal data between the two groups at the baseline and after the intervention as well as the mean changes of abnormal data between two groups Mann–Whitney U test was used. We used paired t test to compare the mean of normal variables in each group, and if the distribution of data was not normal,

Wilcoxon test was utilized. ANCOVA was also carried out to control the covariates. Data were analyzed using SPSS version 24 (SPSS, Inc.). $P < 0.05$ was considered as significance level.

## Results

### Characteristics of the participants

Sixty-two women who met inclusion criteria were enrolled in the trial. During follow-up, three women due to pregnancy, and three women due to refuse to continue were excluded. 28 participants in the control group and 28 participants in the treatment group completed the trial (Fig. 1).

### Baseline and anthropometric variables

At the baseline, no significant differences were found between the two groups in terms of age, physical activity, energy intake, anthropometric indices, glycemic variables, SHBG and lipid profile (except for HDL-c with $P$-value = 0.007) (Table 1). There was no significant difference between the two groups in the levels of energy intake, diet composition and physical activity during follow-up ($P > 0.05$) (Table 2). In addition, we found no significant difference between the two groups in terms of weight, BMI, and HC during follow-up; but, a significant change in WC ($P = 0.001$) was observed (Table 3). There was no serious side effect related to consuming supplements during follow-up.

### Outcomes

In the treatment group compared to the control group, a significant improvement was seen in the terms of insulin (changes: − 0.7 (− 7.3 to 4.0) vs. 0.7 (− 3.0 to 5.2); $P = 0.001$), HOMA-IR (changes: − 0.4 (− 1.7 to 1.1) vs. 0.0 (− 0.7 to 1.3); $P = 0.002$) and QUICKI (mean changes: $+0.01 \pm 0.02$ vs. $-0.01 \pm 0.01$; $P = 0.02$), after adjusting for changes of WC and baseline values. However, FPG remained without significant change (changes: − 6.0 (− 9.4 to 5.0) vs. − 1.0 (− 4.0 to 1.0); $P = 0.44$) (Table 4).

No significant improvement was found in the treatment group compared to the control group in serum SHBG (mean changes: $+11.5 \pm 40.2$ vs. $-3.2 \pm 40.2$; $P = 0.2$) (Table 4). In addition, serum levels of TC (mean changes: $-3.0 \pm 29.5$ vs. $-6.7 \pm 15.5$; $P = 0.54$), TG (changes: − 3.0 (− 20.1 to 22.0) vs. 0.0 (− 20.8 to 3.5); $P = 0.72$), LDL-c (mean changes: $-6.4 \pm 30.0$ vs. $-10.7 \pm 13.6$; $P = 0.48$) and HDL-c (changes: 3.0 (− 6.1 to 9.2) vs. 5.0 (0.8–9.8); $P = 0.44$) remained without significant change (Table 4).

## Discussion

In the present study that conducted among overweight/obese women with PCOS, 12-week L-carnitine intake can reduce insulin resistance; however, SHBG and lipid profile without significant change. The study of Samimi et al. [34] found a significant reduction in insulin, FPG and HOMA-IR among women with PCOS consuming 250 mg/day L-carnitine for 12 weeks. In addition, the study of Ismail et al. [33] reported that L-carnitine intake (3 g/day) can reduce levels of insulin and FPG in women with PCOS. We demonstrated

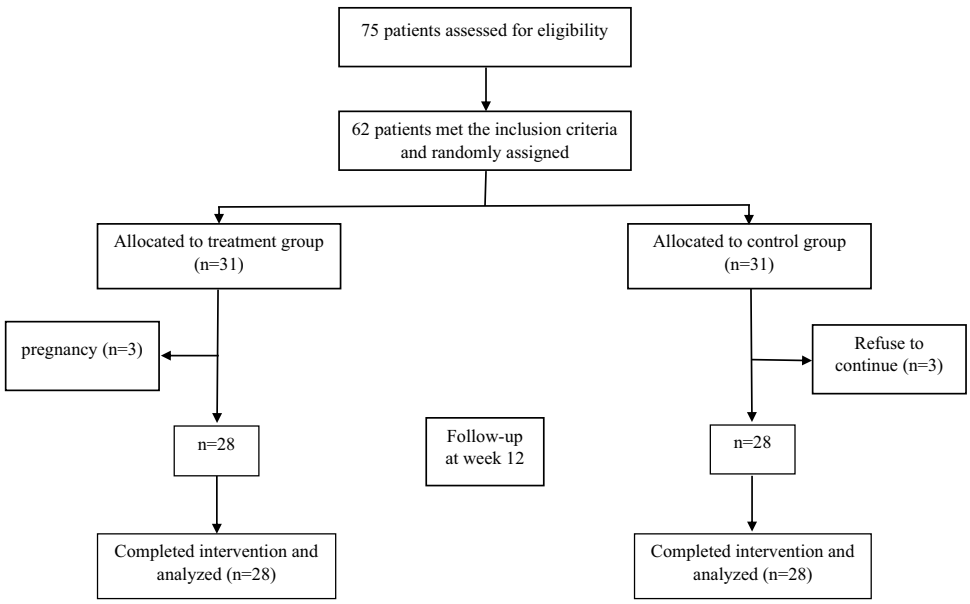


**Fig. 1** Participant eligibility, screening, and follow-up

**Table 1** Demographic characteristics in women with PCOS

| | L-Carnitine ($n=31$) | Placebo ($n=31$) | $P$ |
|---|---|---|---|
| Age, year | 30.7 ± 6.7 | 30.8 ± 6.6 | 0.68 |
| Height, cm | 162.0 ± 4.9 | 163.2 ± 4.8 | 0.33 |
| Weight, kg | 81.4 ± 13.0 | 82.2 ± 12.0 | 0.79 |
| MET-h/day | 27.6 ± 3.6 | 28.2 ± 3.4 | 0.28 |
| Energy intake, kcal/day | 1930.4 ± 103 | 1912.8 ± 96 | 0.88 |
| BMI, kg/m$^2$ | 31.0 ± 4.7 | 30.8 ± 3.6 | 0.84 |
| WC, cm | 99.0 (93.2–103.8) | 99.1 (92.2–102.9) | 0.72* |
| HC, cm | 113.3 ± 11.2 | 115.3 ± 9.4 | 0.45 |
| SHBG, nmol/L | 98.5 ± 40.6 | 113.5 ± 40.8 | 0.23 |
| Lipid profile | | | |
| TC, mg/dL | 186.9 ± 35.4 | 188.7 ± 30.7 | 0.83 |
| TG, mg/dL | 109.8 (74.4–156.4) | 136.0 (108.2–197.4) | 0.05* |
| LDL-c, mg/dL | 113.6 ± 30.9 | 118.8 ± 24.7 | 0.47 |
| HDL-c, mg/dL | 46.9 (40.1–55.0) | 39.0 (36.2–45.1) | 0.007* |
| Glycemic indices | | | |
| FPG, mg/dL | 96.0 (88.1–99.2) | 98.4 (93.1–102.0) | 0.30* |
| Insulin, mU/L | 17.4 (12.4–27.2) | 19.2 (12.6–26.4) | 0.25* |
| HOMA-IR | 4.1 (3.0–6.6) | 4.9 (3.1–6.1) | 0.90* |
| QUICKI | 0.30 ± 0.02 | 0.31 ± 0.02 | 0.71 |

Values for QUICKI, SHBG, TC and LDL-c were presented as mean ± standard deviation (SD), except for WC, FPG, insulin, HOMA-IR, TG and HDL-c that the values were presented as median and quartile range

Using independent *t*-test *P* values are computed and data are expressed as mean ± standard deviation (SD)

**P* values were computed by Mann–Whitney *U* test

*PCOS* polycystic ovary syndrome, *MET-h* metabolic equivalent task hours, *BMI* body mass index, *WC* waist circumference, *HC* hip circumference, *SHBG* sex hormone-binding globulin, *TC* total cholesterol, *TG* triglyceride, *HDL-c* high-density lipoprotein-cholesterol, *LDL-c* low-density lipoprotein-cholesterol, *FPG* fasting plasma glucose, *HOMA-IR* homeostatic model assessment for insulin resistance, *QUICKI* quantitative insulin sensitivity check index

a non-significant change toward improvement in the term of FPG. It seems, higher doses of L-carnitine and longer duration of supplementation with L-carnitine could improve the levels of FPG. L-Carnitine by stimulating glucose metabolism via increasing mitochondrial oxidation of acyl-coenzyme A (Acyl-CoA), modulating pyruvate dehydrogenase complex activity, stimulating insulin and insulin like growth factor-1 cascade, as well as regulating glycolytic and gluconeogenic enzymes gene expression, can improve insulin resistance [26, 37].

For the first time, we investigated the effect of L-carnitine on SHBG in women with PCOS. Evidence suggested a direct correlation of serum total L-carnitine with SHBG, but a negative correlation of serum L-carnitine with FAI [34]. Furthermore, SHBG as a strong predictor of serum total L-carnitine level, is inversely correlated with insulin resistance [34]. We found a non-significant change toward improvement in SHBG, and if the intervention duration was longer, we could probably see a significant improvement. A study revealed that after 12-week L-carnitine intake, levels of free testosterone and dehydroepiandrosterone (DHEA) remained without significant change in women with PCOS [38]. In addition, a clinical trial demonstrated that L-carnitine intake (250 mg/day) for 12 weeks has no effect on levels of free testosterone, but can significantly reduce DHEA [36].

The present study did not find any change in lipid profile after L-carnitine intake. The study of Samimi et al. [36] reported that 12-week L-carnitine supplementation (250 mg/day) has no effect on lipid profile of women with PCOS. A study revealed that L-carnitine supplementation cannot improve TC, TG and HDL-c in hemodialysis patients [39]. In addition, Lee et al. [40] showed that L-carnitine

**Table 2** Dietary intakes and physical activity in women with PCOS

| variables | Week 0 | Week 12 | $p^{\dagger\dagger}$ | Change | $P^{\dagger\dagger\dagger}$ |
|---|---|---|---|---|---|
| Energy intake, kcal/day | | | | | 0.36 |
| L-Carnitine | 1930.4 ± 103 | 1905.5 ± 98 | 0.49 | − 24.9 ± 46 | |
| Placebo | 1912.8 ± 96 | 1933.5 ± 97 | 0.56 | 20.7 ± 41 | |
| $P^{\dagger}$ | 0.88 | 0.74 | | | |
| Carbohydrates, (% of total energy) | | | | | 0.60 |
| L-Carnitine | 52.08 ± 6.3 | 51.16 ± 6.1 | 0.84 | − 0.92 ± 2.2 | |
| Placebo | 51.30 ± 5.8 | 50.12 ± 6.2 | 0.52 | − 1.18 ± 2.3 | |
| $P^{\dagger}$ | 0.70 | 0.55 | | | |
| Proteins, (% of total energy) | | | | | 0.38 |
| L-Carnitine | 14.15 ± 2.8 | 13.47 ± 3.1 | | − 0.68 ± 1.5 | |
| Placebo | 13.98 ± 3.0 | 14.52 ± 2.9 | | 0.54 ± 1.7 | |
| $P^{\dagger}$ | 0.81 | 0.43 | | | |
| Fats, (% of total energy) | | | | | 0.42 |
| L-Carnitine | 33.77 ± 4.7 | 35.37 ± 4.3 | | 1.6 ± 2.1 | |
| Placebo | 34.72 ± 5.1 | 35.36 ± 5.2 | | 0.64 ± 2.0 | |
| $P^{\dagger}$ | 0.65 | 0.87 | | | |
| Physical activity, (MET-h/day) | | | | | 0.42 |
| L-Carnitine | 27.6 ± 3.6 | 28.3 ± 3.5 | 0.32 | 0.7 ± 1.2 | |
| Placebo | 28.2 ± 3.4 | 28.5 ± 3.7 | 0.51 | 0.3 ± 1.20 | |
| $P^{\dagger}$ | 0.28 | 0.46 | | | |

Values were presented as mean ± standard deviation (SD)

$P^{\dagger}$: resulted from comparisons between groups

$P^{\dagger\dagger}$: resulted from comparisons within groups

*PCOS* polycystic ovary syndrome

supplementation (1 g/day) has no significant effect on TC, TG and LDL-c in coronary artery disease. In addition, the study of Malaguarnera et al. [41] reported that supplementation with L-carnitine (2 g/day) has a beneficial effect on lipid profile in patients with T2DM. A logical reason for this discrepancy can be the differences in dosage of L-carnitine. It seems, higher dosages of L-carnitine can improve lipid profile. A recent meta-analysis showed that L-carnitine less than 2 g/day has no effect on TC, TG and LDL-c [42]. Previously, some studies suggested that L-carnitine by stimulating the production of apolipoprotein-A1, modulating the TG synthesis and esterification toward the formation of acetylcarnitines, can decrease the TG and VLDL-c plasma concentration [43–46].

Our study has some strengths. The present study was the first clinical trial evaluating SHBG in women with PCOS. In addition, we considered the significant changes of anthropometric variables from baseline as covariates. However, we used the low dose of L-carnitine as well as small sample size, which are the important limitations of the present study. In addition, use of instruments to measure body composition that are not the gold standard tools was another limitation of the present study.

**Table 3** Anthropometric variables in women with PCOS*

| | Week 0 | Week 12 | $P^{\dagger\dagger}$ | *Change* | $P^{\dagger\dagger\dagger}$ |
|---|---|---|---|---|---|
| Weight, kg | | | | | 0.1 |
| L-Carnitine | 81.4 ± 13.0 | 79.5 ± 12.0 | 0.03 | − 1.9 ± 4.6 | |
| Placebo | 82.2 ± 12.0 | 81.9 ± 12.6 | 0.33 | − 0.3 ± 1.8 | |
| $P^{\dagger}$ | 0.79 | 0.45 | | | |
| BMI, kg/m$^2$ | | | | | 0.16 |
| L-Carnitine | 31.0 ± 4.7 | 30.4 ± 4.4 | 0.06 | − 0.6 ± 1.8 | |
| Placebo | 30.8 ± 3.6 | 30.6 ± 3.9 | 0.34 | − 0.2 ± 0.7 | |
| $P^{\dagger}$ | 0.84 | 0.79 | | | |
| WC, cm | | | | | 0.001* |
| L-Carnitine | 99.0 (93.2–103.8) | 97.0 (91.3–102.0) | 0.002** | − 1.0 (− 3.1 to 0.0) | |
| Placebo | 99.1 (92.2–102.9) | 99.1 (91.8–103.1) | 0.66** | 0.0 (− 0.6 to 0.8) | |
| $P^{\dagger}$ | 0.72* | 0.56* | | | |
| HC, cm | | | | | 0.07 |
| L-Carnitine | 113.3 ± 11.2 | 112.1 ± 10.5 | 0.01 | − 1.2 ± 2.5 | |
| Placebo | 115.3 ± 9.4 | 115.0 ± 9.5 | 0.11 | − 0.3 ± 1.1 | |
| $P^{\dagger}$ | 0.45 | 0.25 | | | |

Values for weight, BMI and HC were presented as mean ± standard deviation (SD), while for WC were presented as median and quartile range

**P* values are computed by Mann–Whitney U test

***P* values are computed by Wilcoxon test

$P^{\dagger}$: resulted from comparisons between groups

$P^{\dagger\dagger}$: resulted from comparisons within groups

$P^{\dagger\dagger\dagger}$: resulted from comparing changes from baseline between groups

*PCOS* polycystic ovary syndrome, *BMI* body mass index, *WC* waist circumference, *HC* hip circumference

**Table 4** Effect of L-carnitine on insulin resistance, SHBG and lipid profile in women with PCOS*

| | Week 0 | Week 12 | $P^{\dagger\dagger}$ | *Change* | $P^{\dagger\dagger\dagger}$ | $P^{\dagger\dagger\dagger\dagger}$ |
|---|---|---|---|---|---|---|
| FPG, mg/dL | | | | | 0.31* | 0.44 |
| L-Carnitine | 96.0 (88.1–99.2) | 90.0 (88.0–96.4) | 0.14** | − 6.0 (− 9.4 to 5.0) | | |
| Placebo | 98.4 (93.1–102.0) | 95.4 (88.2–100.2) | 0.09** | − 1.0 (− 4.0 to 1.0) | | |
| $P^{\dagger}$ | 0.30* | 0.19* | | | | |
| Insulin, mU/L | | | | | 0.21* | 0.001 |
| L-Carnitine | 17.4 (12.4–27.2) | 15.2 (12.0–23.3) | 0.26** | − 0.7 (− 7.3 to 4.0) | | |
| Placebo | 19.2 (12.6–26.4) | 18.6 (13.6–26.9) | 0.65** | 0.7 (− 3.0 to 5.2) | | |
| $P^{\dagger}$ | 0.25* | 0.13* | | | | |
| HOMA-IR | | | | | 0.21* | 0.002 |
| L-Carnitine | 4.1 (3.0–6.6) | 3.3 (2.6–5.1) | 0.36** | − 0.4 (− 1.7 to 1.1) | | |
| Placebo | 4.9 (3.1–6.1) | 4.5 (2.9–6.2) | 0.55** | 0.0 (− 0.7 to 1.3) | | |
| $P^{\dagger}$ | 0.90* | 0.10* | | | | |
| QUICKI | | | | | 0.10 | 0.02 |
| L-Carnitine | 0.30 ± 0.02 | 0.31 ± 0.02 | 0.10 | 0.01 ± 0.02 | | |
| Placebo | 0.31 ± 0.02 | 0.30 ± 0.01 | 0.50 | − 0.01 ± 0.01 | | |
| $P^{\dagger}$ | 0.71 | 0.36 | | | | |
| SHBG, nmol/L | | | | | 0.20 | 0.20 |
| L-Carnitine | 98.5 ± 40.6 | 110.0 ± 43.4 | 0.19 | 11.5 ± 40.2 | | |
| Placebo | 113.5 ± 40.8 | 110.3 ± 40.4 | 0.67 | − 3.2 ± 40.2 | | |
| $P^{\dagger}$ | 0.23 | 0.97 | | | | |
| TC, mg/dL | | | | | 0.54 | 0.54 |
| L-Carnitine | 186.9 ± 35.4 | 183.9 ± 39.1 | 0.57 | − 3.0 ± 29.5 | | |
| Placebo | 188.7 ± 30.7 | 182.0 ± 25.9 | 0.22 | − 6.7 ± 15.5 | | |
| $P^{\dagger}$ | 0.83 | 0.81 | | | | |
| TG, mg/dL | | | | | 0.31* | 0.72 |
| L-Carnitine | 109.8 (74.4–156.4) | 119.9 (83.1–160.1) | 0.70** | − 3.0 (− 20.1 to 22.0) | | |
| Placebo | 136.0 (108.2–197.4) | 131.9 (102.1–184.6) | 0.19** | 0.0 (− 20.8 to 3.5) | | |
| $P^{\dagger}$ | 0.05* | 0.46* | | | | |
| LDL-c, mg/dL | | | | | 0.52 | 0.48 |
| L-Carnitine | 113.6 ± 30.9 | 107.2 ± 30.6 | 0.30 | − 6.4 ± 30.0 | | |
| Placebo | 118.8 ± 24.7 | 108.1 ± 24.6 | 0.001 | − 10.7 ± 13.6 | | |
| $P^{\dagger}$ | 0.47 | 0.89 | | | | |
| HDL-c, mg/dL | | | | | 0.19* | 0.79 |
| L-Carnitine | 46.9 (40.1–55.0) | 49.9 (39.6–60.0) | 0.22** | 3.0 (− 6.1 to 9.2) | | |
| Placebo | 39.0 (36.2–45.1) | 45.2 (40.4–53.0) | 0.01** | 5.0 (0.8–9.8) | | |
| $P^{\dagger}$ | **0.007*** | 0.21* | | | | |

Values for QUICKI, SHBG, TC and LDL-c were presented as mean ± standard deviation (SD), while for FPG, insulin, HOMA-IR, TG and HDL-c were presented as median and quartile range

**P* values are computed by Mann–Whitney *U* test

***P* values are computed by Wilcoxon test

$P^{\dagger}$: resulted from comparisons between groups

$P^{\dagger\dagger}$: resulted from comparisons within groups

$P^{\dagger\dagger\dagger}$: resulted from comparing changes from baseline between groups

$P^{\dagger\dagger\dagger\dagger}$: resulted from comparing changes between groups after adjusting for changes of WC and baseline values

*PCOS* polycystic ovary syndrome, *FPG* fasting plasma glucose, *HOMA-IR* homeostatic model assessment for insulin resistance, *QUICKI* quantitative insulin sensitivity check index, *SHBG* sex hormone-binding globulin, *TC* total cholesterol, *TG* triglyceride, *HDL-c* high-density lipoprotein-cholesterol, *LDL-c* low-density lipoprotein-cholesterol

## Conclusions

Overall, 1000 mg/day oral L-carnitine supplementation ameliorated insulin resistance, however, has no effect on SHBG and lipid profile. Further clinical trials with higher dosages of L-carnitine and longer intervention durations are required.

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**Author contributions** FP and MH: conducted the study; AG: provided material and technical support, AS: interpreted the finding and drafted the manuscript; MH and AN: critically revised the manuscript; HF: carried out the statistical analysis; and MH: supervised the study. The final version of the manuscript was approved by all authors.

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## Declarations

**Conflict of interests** The authors have declared no competing interests.

**Ethical approval** The research council of Nutrition and Food Security Research Center, Shahid Sadoughi University of Medical Sciences and Health Services approved the study protocol. The ethical committee of Shahid Sadoughi University of Medical Sciences and Health Services in Yazd approved the written informed consent (code number: IR.SSU.SPH.REC.1397.014).

**Informed consent** Written informed consent was obtained from all participants before the data collection.

**Consent for publication** Not applicable.

**Data availability** The data and materials of the current study is available from the corresponding author on reasonable request.

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