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L-carnitine ameliorated weight loss in fasting therapy: A propensity score-matched study

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ABSTRACT

L-carnitine infusion has been proven to reduce fasting-induced fatigue and hunger in patients with metabolic syndrome in our former study. However, the association between L-carnitine and clinical outcomes of fasting therapy is yet to be investigated. In this study, data from 192 patients who finished fasting therapy from September 2008 to July 2018 were reviewed, among which 142 patients received L-carnitine infusion in fasting regimen. Propensity matching was used to overcome retrospective bias. Patients' anthropometric measurements and metabolic markers were evaluated. After propensity matching, 40 patients were included in each group. Weight (-4.05 ± 1.65 kg vs -3.25 ± 1.68 kg, $P = 0.031$) and BMI (-1.51 ± 0.61 kg/m^2 vs -1.20 ± 0.62 kg/m^2, $P = 0.036$) decreased in both groups, but significantly more in L-carnitine group, while diastolic blood pressure (-1.67 ± 9.82 mmHg vs -6.21 ± 8.83 mmHg, $P = 0.043$) and triglycerides (-0.18 ± 0.63 mmol/L vs -1.05 ± 1.70 mmol/L, $P = 0.007$) decreased significantly more in non-L-carnitine group compared between groups, blood glucose did not differ significantly between groups. L-carnitine can boost the positive effects of fasting therapy on weight loss and maintain the stability of blood pressure.

1. Introduction

Fasting therapy is a regimen whereby juicy food intake is limited to 200–500 Kcal per day for 5–28 days. As a special form of very-low-calorie-diet (VLCD), it has been proven to reduce weight, blood pressure, lipid profiles, and glucose, applied for decades in Europe as a therapeutic method for overweight, obese, hyperlipidemia, hypertension, type 2 diabetes and other chronic and acute diseases.[1,2]

As we introduced fasting therapy from Germany in 2008, applied it to Chinese patients for the first time, we developed a Chinese protocol on fasting therapy. Unlike European patients, fatigue or weakness was the most common adverse reaction in Chinese people, and energy deficiency might be the main reason. In fasting period, the fuel of energy metabolic oxidation switch from glucose to fat tissues, while long-chain fatty acid cannot enter mitochondrion, transfer to ATP and supply energy in short of L-carnitine.[3] Besides, oral L-carnitine supplements have low absorptivity in the intestine,[4] while intravenous L-carnitine can be distributed in skeletal muscle and reduce perceived hungriness. Thus, we added intravenous L-carnitine into fasting therapy and discovered that the adverse reaction such as hunger and fatigue were ameliorated in patients with metabolic syndrome (MetS).[5]

However, this study was with a rather small sample size and the association between L-carnitine and clinical outcomes of fasting therapy is yet to be investigated. Therefore, in the present study, we aimed to explore the effects of L-carnitine on patients' weight, blood pressure, blood lipids profiles and glucose in fasting therapy using propensity score matched analysis.

2. Materials and methods

2.1. Patients

We screened all patients completed fasting therapy in the Seventh and First Affiliated Hospital of Sun Yat-Sen University between September 2008 and July 2018. There were 50 patients who completed fasting therapy without L-carnitine infusion before L-carnitine was applied in fasting regimen in November 2012, since then there were 142 patients received L-carnitine infusion in fasting regimen.

The clinical outcomes were compared after using 1:1 propensity score matching because this could effectively decrease bias and

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Table 1
Clinical characteristics of the patients.

Covariate	Before PS match			After PS match		
	L-carnitine (n = 142)	Non-L-carnitine (n = 50)	*P* value	L-carnitine (n = 40)	Non-L-carnitine (n = 40)	*P* value
Age (years)	44.32 ± 12.16	46.20 ± 13.64	0.513	45.23 ± 13.17	44.30 ± 13.45	0.563
Gender			0.140			0.171
Male	46(67.6%)	22(32.4%)		13(40.6%)	19(59.4%)	
Female	96(77.4%)	28(22.6%)		27(56.3%)	21(43.7%)	
Diagnoses						
Overweight	42(29.6%)	15(30.0%)	0.955	15(37.5%)	13(32.5%)	0.639
Obesity	85(59.9%)	26(52.0%)	0.333	20(50.0%)	21(52.5%)	0.823
Hypertension	50(35.2%)	24(48.0%)	0.111	20(50.0%)	13(32.5%)	0.112
Type 2 diabetes	36(25.4%)	14(28.0%)	0.714	8(20.0%)	12(30.0%)	0.302
Hyperlipidemia	90(63.4%)	36(72.0%)	0.270	25(62.5%)	31(77.5%)	0.143
Fatty liver	109(76.8%)	31(62.0%)	0.043	30(60.0%)	26(65.0%)	0.329
Body mass (kg)	80.17 ± 15.48	76.13 ± 16.10	0.145	78.73 ± 16.53	77.15 ± 14.66	0.962
BMI (kg/m^2)	29.64 ± 4.35	28.36 ± 4.75	0.144	29.04 ± 4.72	28.39 ± 4.59	0.784
SBP (mmHg)	128.86 ± 17.29	134.63 ± 18.01	0.029	129.58 ± 19.36	131.70 ± 17.87	0.513
DBP (mmHg)	81.51 ± 12.27	80.80 ± 11.55	0.946	77.78 ± 9.99	81.00 ± 12.30	0.161
TC (mmol/L)	5.30 ± 1.19	5.75 ± 1.37	0.073	5.42 ± 1.22	5.67 ± 1.51	0.064
TG (mmol/L)	1.72 ± 0.83	2.28 ± 2.27	0.344	1.86 ± 2.63	2.26 ± 2.18	0.780
HDL-c (mmol/L)	1.21 ± 0.26	1.20 ± 0.31	0.717	1.17 ± 0.28	1.17 ± 0.28	0.821
LDL-c (mmol/L)	3.33 ± 0.79	3.75 ± 1.02	0.029	3.24 ± 0.87	3.63 ± 0.90	0.634
FPG (mmol/L)	5.28 ± 1.26	5.54 ± 1.98	0.934	5.54 ± 1.69	5.39 ± 1.97	0.836

Abbreviation: BMI = body mass index, SBP = systolic blood pressure, DBP = diastolic blood pressure, TC = total cholesterol, TG = triglycerides, HDL-c = high density lipoprotein cholesterol, LDL-c = low density lipoprotein cholesterol, FPG = fasting plasma glucose. Variables are expressed as mean ± SD.

improve control for confounding variables.[6] Matching was based on age, gender, weight, body mass index, blood pressure, lipid profiles (total cholesterol, triglycerides, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol), and fasting glucose.

2.2. Intervention

Patients in the L-carnitine group received 4 g/d L-carnitine infusion (2 g, twice a day) (Lanling Pharmaceutical CO., LTD, Changzhou, China) from the beginning of the pre-fasting day at 9 a.m. and 4 pm to the last day of fasting. 2 g L-carnitine was dissolved into 20 ml saline for intravenous injection. Other than that, patients in both groups had no different interventions.

During the initial baseline week, patients were encouraged to maintain their normal dietary intake. The fasting treatment consisted of 2 days with moderate calorie restriction (700–800 Kcal/day), 5 days of intense calorie restriction (200 Kcal/day), followed by 3 days with the stepwise reintroduction of a normal diet. Fasting was initiated with the intake of 10–20 g of thenardite powder on the first fasting day for bowel-cleansing. During the 5-day fasting period, patients were asked to drink at least 2 L of mineral water and were prescribed a diet of 200 Kcal/d that consist of one serving of the liquid meal replacement and two cups of light vegetable soup. Each serving of the liquid diet provided approximately 150 Kcal: 7.9 g protein, 2.8 g fat, and 22 g carbohydrate. The liquid diet was prepared by mixing the powdered product with 250 ml water and was to be consumed at dinner. Two bowls of vegetable soup provided about 50 Kcal and were given at breakfast and lunch. All patients were required to engage in low-level physical activity consisting of 2 h of slow walking per day. Furthermore, patients were recommended to avoid alcohol, coffee or tea during the study. All participants were compulsorily hospitalized during 2-days pre-fasting and during 5-days fasting period.

2.3. Data collection

Data were obtained by reviewing medical records of the patients completed fasting therapy in the Seventh and First Affiliated Hospital of Sun Yat-Sen University during September 2008 and July 2018. As a retrospective study, no ethics approval is required in our institute. Informed consent regarding data storage and publication was obtained from each patient who were recorded in the database during their hospitalization. All of the data records were de-identified and analyzed pseudonymously. Collected variables included demographics, medical history, etiology, laboratory tests (blood routine examination and blood biochemistry).

2.4. Statistical analysis

All data are presented as means and standard deviation or numbers and percent. After propensity matching, variables and outcomes between the two groups were compared by Mann-Whitney *U* test and $\chi 2$ tests for continuous and categorical variables, respectively. All statistical tests were two-tailed, and the statistical significance was considered as $P < 0.05$. All analyses were performed using the SPSS 24.0 software package (SPSS, Inc., Chicago, IL, USA).

3. Results

3.1. Baseline clinical characteristics

192 participants completed the fasting therapy, L-carnitine group and non-L-carnitine group were administered to 142 and 50 patients, respectively. Before PS-matching, we found the systolic blood pressure ($P = 0.029$) and LDL cholesterol ($P = 0.029$) were higher in the group without L-carnitine than that in the group received L-carnitine. The age, gender, weight, BMI, diastolic blood pressure, total cholesterol, triglyceride, HDL cholesterol, and fasting glucose between the groups had no significant difference. Also, the proportion of patients with fatty liver was significantly higher in L-carnitine group ($P = 0.043$) (Table 1).

After propensity matching, 40 patients were selected from each group, there were no significant differences between the two matched group, all variables were sufficiently balanced (Table 1).

3.2. Changes in clinical outcomes

The changes in body mass, BMI, systolic and diastolic blood pressure, lipid profiles, and fasting glucose between baseline and post-fasting are presented in Table 2. In comparison of changes between baseline and post-fasting between the two matched groups, there was an average loss of 4.05 kg of weight in L-carnitine group and 3.25 kg in

Table 2
Clinical outcomes after propensity matching.

Changes	L-carnitine (n = 40)	Non-L-carnitine (n = 40)	*P* value
Body mass (kg)	−4.05 ± 1.65	−3.25 ± 1.68	0.031
BMI (Kg/m^2)	−1.51 ± 0.61	−1.20 ± 0.62	0.036
SBP (mmHg)	−8.55 ± 16.43	−12.74 ± 15.82	0.325
DBP (mmHg)	−1.67 ± 9.82	−6.21 ± 8.83	0.043
TC (mmol/L)	0.32 ± 0.48	−0.12 ± 0.93	0.061
TG (mmol/L)	−0.18 ± 0.63	−1.05 ± 1.70	0.007
HDL-c (mmol/L)	−0.13 ± 0.14	−0.15 ± 0.22	0.729
LDL-c (mmol/L)	0.37 ± 0.42	0.33 ± 0.98	0.686
FPG (mmol/L)	−1.27 ± 1.51	−0.67 ± 1.26	0.068

Abbreviation: BMI = body mass index, SBP = systolic blood pressure, DBP = diastolic blood pressure, TC = total cholesterol, TG = triglycerides, HDL-c = high density lipoprotein cholesterol, LDL-c = low density lipoprotein cholesterol, FPG = fasting plasma glucose. Variables are expressed as mean ± SD.

non-L-carnitine group ($P = 0.031$ between groups).

Diastolic blood pressure decreased significantly more during fasting in the non-L-carnitine group ($P = 0.043$ between groups), while there was a tendency in the decrease of systolic blood pressure compared between the two groups but there was no statistical difference.

Triglyceride decreased significantly more during fasting in the non-L-carnitine group ($P = 0.007$ between groups). Changes in total cholesterol, HDL cholesterol, LDL cholesterol, and fasting blood glucose showed no significant difference between the two groups.

4. Discussion

In the present study, our findings demonstrated that L-carnitine could boost the weight loss during fasting therapy, maintain the stability of blood pressure, and have no negative effects on other metabolic markers.

Fasting therapy has been approved effective for several metabolic diseases such as overweight/obese, hypertension, type 2 diabetes, metabolic syndrome.[1] However, it has been reported fatigue or weakness, especially in Chinese participants due to the different diet based on grain and vegetables. As we introduced intravenous L-carnitine into fasting regimen in 2012 and conducted a randomized controlled study on patients with metabolic syndrome, we found that perceived hunger scores, physical fatigue, and fatigue severity were significantly reduced in L-carnitine group but were aggravated in control group, plus weight loss was significantly different between the two groups.[5] However, this previous clinical trial was with small sample size of 15 patients in each group. In consistent with the previous study in MetS patients, we demonstrated that L-carnitine could promote the weight loss effect of fasting therapy. However, other results in present study were seemingly at variance with the previous study that a significant reduction in diastolic blood pressure was found in patients without L-carnitine, which might be related to the different spectrum of diseases. Thus, with a relatively larger sample size, these data show that L-carnitine can be a promising candidate for weight management and reduce the risk of postural hypotension during fasting regimen.

Weight reduction is seemed to be the major outcome of fasting therapy, for it can lead to other clinical benefits. Some studies proved the association between weight loss and improved health outcomes such as cardiometabolic disease risk and functional status in calorie restriction.[7] In the present study, we concluded that fasting therapy with L-carnitine could boost the effect of weight loss so that adding L-carnitine to the fasting regimen was an improvement in patients' clinical benefits.

The reason for this might be the increase in energy expenditure.[8] In experimental models, L-carnitine administration led to an increase in total energy expenditure in obese rats with insulin resistance.[9] Supplementing carnitine are likely to activate fat oxidation and reduce body fat. A meta-analysis including 9 studies showed that receiving carnitine resulted in weight loss,[10] as well as another clinical trial proved the same effect on PCOS women who received oral carnitine supplementation.[11] However, other clinical studies have reported different results that L-carnitine does not improve weight loss in bipolar patients consuming an energy-restricted diet[12] or impaired glucose metabolic patients in calorie restriction.[13] The contradiction between our results and those may, therefore, be due to the use of different study cohorts in these two studies.

A significantly larger degree of diastolic blood pressure decrease was found in non-L-carnitine group. It can be explained by the report which suggested elevated blood pressure was significantly associated with higher physiological L-carnitine levels.[14] In former studies, participants might suffer postural hypotension due to dehydration during the fasting period,[15] thus, L-carnitine could maintain a stability of blood pressure and reduce the risk of postural hypotension in fasting therapy. However, the increase of blood pressure because of L-carnitine infusion might weaken the effect of fasting therapy on blood pressure reduction, therefore, we suggested that physicians should choose whether to add L-carnitine into the fasting therapy according to patients' condition.

Triglyceride was reduced in both groups during the fasting period, but there was a significantly larger degree of reduction in non-L-carnitine group. Also, L-carnitine administration exerted no obvious effect on total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol in fasting therapy. The possible increase effect of L-carnitine in triglycerides is in accordance with one study where Gollestan et al. found that L-carnitine significantly increased triglyceride in type II diabetic patients.[16] The reason might be the concentration of Apo B100 and fatty acids were increased significantly in the L-carnitine group, which produced more VLDL in liver and consequently the increase in TG concentration.[17] However, the results did not agree to another previous study. Motta et al. proved that L-carnitine-treated diabetes patients showed significant improvements compared with the placebo group in LDL cholesterol and triglycerides.[18] Considering these studies did not combine L-carnitine with calorie restriction or fasting, when L-carnitine supplementation is associated with fasting or caloric restriction, the resulting increased expression of OCTN2 may favor and increase the uptake of carnitine and its rapid accumulation in tissues.[19] Thus, the association of L-carnitine supplementation and lipid profiles in calorie restriction or fasting therapy requires further study.

Certain limitations of this study need to be addressed. First, this was a nonrandomized and retrospective study with a relatively small number of patients, the statistical power of the analyses could be relatively weak and some of the findings may be not significant in a larger sample. Second, there was a lack of follow-up data. Therefore, the interpretation of these findings is restricted to shorter-term outcomes, the long-term outcomes of the fasting therapy are yet to be evaluated.

5. Conclusions

L-carnitine can boost the positive effects of fasting therapy on weight loss and maintain the stability of blood pressure.

Data availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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