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Original Article

Obesity control via carnitine drink in obese adults: A randomized, double-blind placebo-controlled human trial

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Background and Purpose: A randomized, double-blind, placebo-controlled human trial was conducted to investigate the effects of carnitine drink on obesity in obese subjects in Taiwan.
Methods: Fifty subjects with simple obesity and body mass index (BMI)≧27 (or >30% body fat) who engaged in aerobic exercise for 2–4h weekly were recruited. The subjects were randomly assigned to receive either carnitine drink or placebo, once daily, for 6 consecutive weeks. Body weight, body fat, and biochemical indicators (i.e., blood glucose, blood lipids, albumin, serum creatinine, blood urea nitrogen, glutamic oxalacetic transaminase (GOT), and glutamic-pyruvate transaminase (GPT)) were measured every 3 weeks. Subsequently, magnetic resonance imaging was conducted to examine the distribution and thickness of abdominal fat and the results were used to determine the effects of carnitine drink on body fat.
Results: A total of 28 subjects completed the study. Six weeks of consumption of carnitine drink led to 0.7% and 2.1 kg reductions in body fat and body weight, respectively, compared with the placebo group. In addition, cholesterol level was reduced by 3.8%. No severe adverse effects were observed.
Conclusions: Intake of carnitine drink is effective for reducing body weight and cholesterol in obese subjects.

Keywords: exercise prescriptions, frailty, heart rate reserve, intervention effects, Rating of Perceived Exertion

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Introduction

Obesity was classified as a chronic disease by the World Health Organization (WHO) and Food and Drug Administration of the US in 1996. Obesity is a medical condition in which changes

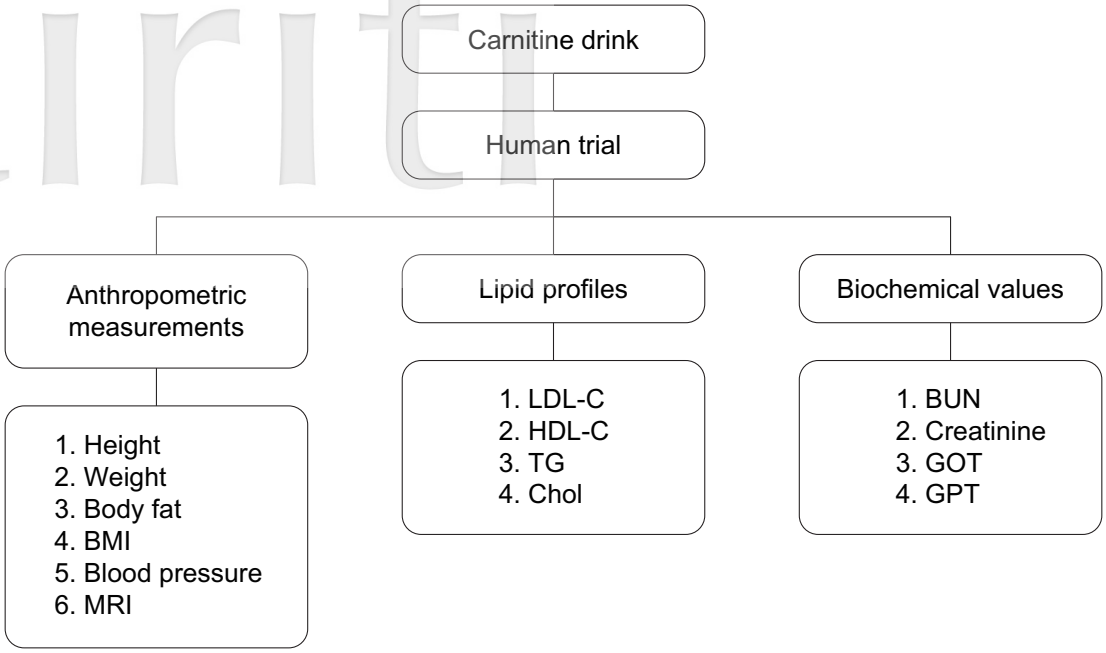


Fig. 1 Schematic representation of the study protocol.

in physiological or biochemical functions cause the accumulation of excess body fat, resulting in increased body weight [1]. Obesity is a critical public health concern. In 2016, WHO noted that the 2014 worldwide obesity rate was more than double that reported in 1980 [2]. Obesity can be classified into two types: simple obesity and secondary obesity. Simple obesity makes up more than 95% of obesity. Secondary obesity, also referred to as symptomatic obesity, is caused by endocrine disorders or metabolic diseases. Carnitine (or Vitamin Bt) is a compound that occurs naturally in human cells. Its chemical nomenclature is β-hydroxy-γ-N-trimethylaminobutyric acid. Sources of carnitine include synthesis in the human body and food (mainly red meat). Carnitine promotes conversion of fat into energy [3]. Supplemental carnitine upregulates expressions of carnitine palmitoyltransferase-I (CPT-I) to exert anti-obesity effects, probably by modulating peroxisome proliferator-activated receptor-associated genes [4-6]. Carnitine deficiency is a rare condition caused by congenital metabolic disorder (e.g., diabetes mellitus) or excessive physical activity [7]. Carnitine deficiency leads to reduced mobility, in addition to myasthenia gravis, hyperlipidemia, and obesity in severe cases [8]. However, taking carnitine alone cannot reduce body fat. Carnitine supplementation is effective only when accompanied by adequate aerobic exercise and suitable diet. Moreover, carnitine regulates lipid metabolism in the body by activating hormone-sensitive lipase to achieve reduction in body fat [9]. Carnitine drink has been shown to reduce fat level in animals [10, 11]. The aim of this study was to evaluate the efficacy of carnitine drink in lowering body fat in obese human subjects.

Materials and Methods

Study Samples

Carnitine drink (Goslim™) and placebo were provided by TCI Co., Ltd. (Taipei, Taiwan). One bottle of carnitine drink (50 mL, 4% carnitine) was administered daily. The placebo was a similar aromatic beverage packaged in a bottle that was identical to that of the carnitine drink in weight and appearance.

Human Trial

(1) Study Design

The function of the carnitine drink in reducing

body fat was verified using the assessment approach prescribed in the Health Food Control Act. Subjects were recruited to partake in this 8-week, randomized, double-blind, and placebo-controlled trial. They were randomized into the study group or the placebo group and required to drink one bottle of the carnitine drink or the placebo daily for 6 weeks, respectively. They were then followed up for 2 weeks after discontinuing the study product. The placebo used in this study was an aromatic beverage that was similar to the carnitine drink in color, appearance, and taste. This clinical trial was carried out at Chung Shan Medical University Hospital, following the guidelines of the Declaration of Helsinki. All procedures involving human subjects were approved by the ethical review board of Chung Shan Medical University Hospital, Taiwan (Protocol No. CS12039). The subjects were informed of the study content and goals and signed an informed consent form before the intervention.

(2) Inclusion Criteria

The inclusion criteria were adults aged 20 years and above who participated in the trial voluntarily and exhibited either of the following conditions: body mass index (BMI)≧27 or body fat≧30% for two consecutive weeks, as well as engaged in aerobic exercise 2–4h weekly. Subjects in the placebo group and carnitine drink group had no other severe diseases, were examined by a physician, and were able to comply with the requirements of this study.

(3) Exclusion Criteria

Subjects with chronic disease (cardiovascular disease, liver disease, cancer, uncontrolled diabetes mellitus), a habit of smoking, alcoholism, BMI>35 or who were pregnant or lactating were excluded.

(4) Withdrawal Criteria

Subjects participated in this study at their own discretion. They were informed that they could retract their consent at any time and withdraw from this study without providing a specific reason. Their withdrawal would not result in unpleasant event, punishment or infringement on their interests or rights. In addition, the subjects fully understood that the principal investigator or sponsor could terminate this study if necessary.

(5) Blood collection

In addition to conducting clinical evaluations, we collected blood samples 4 times (Weeks 0, 3, 6, and 8) during the trial period. Blood samples (20 mL) were collected in the morning after the subjects had fasted for 8h. They were tested for serum adiponectin, albumin, glutamic oxalacetic transaminase (GOT), glutamic-pyruvate transaminase (GPT), blood glucose, blood urea nitrogen (BUN), and blood lipids. Blood pressure, BMI, waist circumference, and body fat levels were also measured at weeks 0, 3, 6, and 8. Two vacutainer tubes, one containing no anticoagulant and the other containing anticoagulant ethylenediaminetetraacetic acid (EDTA), were used to collect the blood samples, which were immediately refrigerated at 4 ºC, and centrifuged within 4 h of collection (3000 rpm, 10 min, 4 ºC) to obtain serum, plasma and blood cells.

(6) Instruments

The instruments adopted in this study included body fat analyzer (Model NO.TBF-410-GS, Tanita, Japan); spectrophotometer (U-2001, Hitachi, Japan); centrifuge (CR-21, Hitachi, Japan); water bath (OD320, YIH DER, Taiwan); ELISA reader (BO2153, Versamax, USA); and MRI (Siemens Sonata1.5T, Erlangen, Germany).

Statistical Analysis

Analysis of data was carried out with software Statistical Package for the Social Sciences (SPSS version 18.0 for Windows; SPSS Inc., Chicago). Paired t-test was used to compare the results of each group at various time points before and after consumption of the study product. Comparisons between the groups were conducted using Student's t-test. Statistical results were considered significant at $p<0.05$ and expressed as mean ± standard deviation.

Results and Discussion

Table 1. Subject demographic characteristics

Age (y)	Male	Female
Placebo		
20-40	1	3
41-61	3	7
Total	4	10
Carnitine drink		
20-40	3	8
41-60	0	3
Total	3	11

Demographic Characteristics

Fifty subjects were recruited in three phases. Eleven subjects were excluded due to noncompliance (including product administration, exercise duration, and substantial difference). In total, 14 subjects in the placebo group (4 men and 10 women; average age 44.57±11.63 years) and 14 subjects in the carnitine drink group (3 men and 11 women; average age 35.36±10.68 years) completed this study. Table 1 summarizes the demographic characteristics of the enrolled subjects.

Effects of carnitine drink on body weight and body fat

Table 2 shows the changes in body weight and body fat of the subjects before and after the study. The placebo group demonstrated increased body weight at week 3 and week 6, but the carnitine drink group demonstrated significant reduction in body weight after six weeks ($p<0.05$). Compared with the placebo group, the carnitine drink group showed significantly reduced body weight of approximately 2.1 kg between Week 0 and Week

Table 2. Effects of carnitine drink or placebo on body weight and body fat

	Weight (Kg)	Body Fat (%)
	Placebo	
Initial	70.5±13.4 ^{a}	32.9±6.6 ^{a}
3rd wk	71.0±13.4 ^{b}	33.1±7.2 ^{a}
6th wk	71.2±13.6 ^{b}	33.3±7.1 ^{a}
Fu	71.4±13.3 ^{b}	33.5±7.2 ^{a}
(Difference 0-3rd) wk	0.5±0.5	0.2±2.3
(Difference 0-6th) wk	0.8±0.6	0.4±2.0
(Difference 0-fu) wk	0.9±0.7	1.1±2.0
	Carnitine drink	
Initial	73.7±15.1 ^{a}	35.5±5.5 ^{a}
3rd wk	73.2±15.0 ^{a}	35.3±5.5 ^{a}
6th wk	72.4±14.4 ^{b}	35.2±5.8 ^{a}
Fu	72.7±13.9 ^{a}	35.5±5.1 ^{a}
(Difference 0-3rd) wk	-0.5±1.0	-0.2±1.8
(Difference 0-6th) wk	-1.3±1.6	-0.3±1.7
(Difference 0-fu) wk	-1.0±1.9	-0.0±1.6

Values are means± SD. (Placebo, n=14; Carnitine drink, n=14)
Data within the same column bearing different superscript letters are significantly different ($\rho<0.05$). Student's *t* –test was used to compare differences between the two groups.

Table 3. Effects of carnitine drink or placebo on blood lipid profiles

	Chol (mg/dl)	HDL-C(mg/dl)	LDL-C(mg/dl)	TG(mg/dl)
		Placebo		
Initial	212.43±23.99 [a]	49.21±11.22 [a]	134.67±28.14 [a]	157.29±115.08 [a]
3rd wk	198.14±16.22 [b]	47.66±12.18 [a]	124.36±20.53 [a]	153.14±96.65 [a]
6th wk	202.71±22.36 [b]	46.16±11.62 [b]	127.14±22.89 [a]	157.79±106.85 [a]
(Diff 0-3rd) wk	-14.29±21.13	-1.60±5.52	-10.31±21.02	-4.14±32.90
(Diff 0-6th) wk	-9.71±16.49	-3.06±4.45	-7.53±13.94	0.50±56.70
		Carnitine drink		
Initial	192.14±28.69 [a]	49.05±10.44 [a]	121.17±22.75 [a]	117.71±77.73 [a]
3rd wk	189.93±33.21 [a]	47.50±10.79 [a]	120.96±27.56 [a]	120.93±62.88 [a]
6th wk	187.43±33.97 [b]	47.50±10.79 [a]	118.19±27.02 [a]	106.93±58.39 [a]
(Diff 0-3rd) wk	-2.21±13.13	-1.55±2.85	-0.21±14.9	3.21±40.84
(Diff 0-6th) wk	-2.21±13.13	-1.55±2.85	-2.98±11.82	-10.79±52.78

Values are means ± SD. (Placebo, n=14; Carnitine drink, n=14)
Data within the same column bearing different superscript letters are significantly different (ρ< 0.05). Student's *t* –test was used to compare differences between the two groups.

6 (p<0.05). After 6 weeks of carnitine drink consumption, the level of body fat was reduced by 0.7% (+0.4%; -0.3%), compared with the placebo group. Carnitine drink has been shown to lower fat level in animals [12]. L-Carnitine (LC) supplementation has been used to reduce obesity caused by high-fat diet (HFD) and has been shown to be beneficial for lowering blood and hepatic lipid levels and ameliorating fatty liver [13, 14]. Jang et al. (2014) demonstrated that LC at a dose of 300 mg/kg BW is most effective for reducing fat accumulation in mice fed HFD during a 9-week study [9]. In addition, exercise should be carried out in combination with LC supplementation to

Table 4. Effects of carnitine drink or placebo on liver and renal functions

	GOT(IU/L)	GPT(IU/L)	Creatinine(mg/dl)	BUN(mg/dl)
		Placebo		
Initial	27.57±16.99 [a]	34.29±34.32 [a]	0.77±0.15 [a]	10.71±3.05 [a]
3rd wk	25.50±12.6 [a]	30.71±28.86 [a]	0.74±0.16 [a]	10.14±1.83 [a]
6th wk	26.21±11.52 [a]	32.07±26.98 [a]	0.77±0.13 [a]	11.14±3.18 [a]
		Carnitine drink		
Initial	27.29±25.23 [a]	39.07±60.87 [a]	0.74±0.18 [a]	11.00±2.25 [a]
3rd wk	22.93±10.24 [a]	29.00±29.82 [a]	0.74±0.16 [a]	10.14±2.54 [a]
6th wk	22.07±6.89 [a]	29.57±19.34 [a]	0.72±0.16 [a]	10.36±2.87 [a]

Values are means ± SD. (Placebo, n=14; Carnitine drink, n=14)
Data within the same column bearing different superscript letters are significantly different (ρ< 0.05). Student's *t* –test was used to compare differences between the two groups.

Table 5. Effects of carnitine drink or placebo on blood plasma Na, K, Cl, Ca levels

	Na(mmol/L)	K(mmol/L)	Cl(mmol/L)	Ca(mg/dl)
		Placebo		
Initial	138.79±1.93 [a]	4.36±0.87 [a]	105.36±2.95 [a]	9.10±0.38 [a]
3rd wk	139.00±2.08 [a]	4.29±0.79 [a]	104.50±1.70 [a]	9.10±0.29 [a]
6th wk	138.00±1.92 [a]	4.01±0.33 [a]	103.57±2.47 [b]	9.10±0.32 [a]
		Carnitine drink		
Initial	137.86±1.51 [a]	4.27±0.44 [a]	104.50±2.93 [a]	9.18±0.24 [a]
3rd wk	138.21±1.53 [a]	4.44±0.80 [a]	104.29±2.13 [a]	9.26±0.33 [a]
6th wk	138.14±1.51 [a]	4.26±0.33 [a]	104.36±1.95 [a]	9.31±0.30 [b]

Values are means± SD. (Placebo, n=14; Carnitine drink, n=14)
Data within the same column bearing different superscript letters are significantly different (p< 0.05). Student's *t* –test was used to compare differences between the two groups.

enhance reductions in body weight and body fat.

Effects of carnitine drink on blood lipids

Table 3 presents the changes in lipid profiles, including triglycerides (TG), total cholesterol, high-density lipoprotein (HDL-C), and low-density lipoprotein (LDL-C). The results indicated that after 6 weeks of carnitine drink consumption, blood plasma cholesterol level is significantly reduced by 4.7 mg/dL (3.8%, p<0.05), and TG level is slightly reduced. These results were similar to those of Lee et al. (2016)[15] who found that LC supplementation at a dose of 1000 mg/d results in significantly increased HDL-C and slightly decreased TG. However, the placebo group also demonstrated significant change (p<0.05) possibly due to reduced intake of high-cholesterol foods during the study period.

Biochemical markers

Table 4 shows GOT, GPT, creatinine and BUN values before and after the trial. These indicators of liver and renal function were unaffected by either the carnitine drink or placebo. Table 5 shows that the levels of electrolytes (Na, K, and Cl) also remained unchanged in both study groups. Although the Ca level increased after 6 weeks of carnitine drink consumption, values were within the acceptable range. These results suggested that consuming carnitine drink or placebo does not affect liver or renal functions. In addition, it does not influence electrolyte values. No adverse effects were noted during the study period.

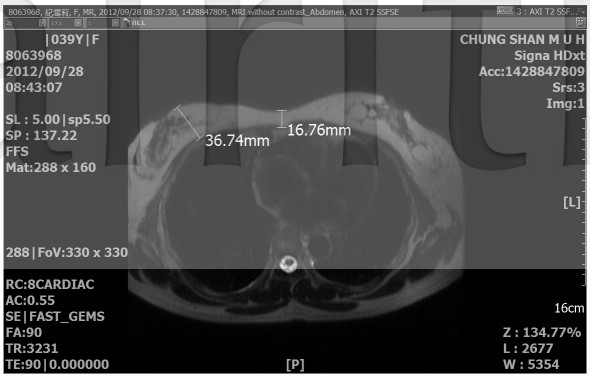
Magnetic Resonance Imaging (MRI)

The subjects were randomized to undergo MRI before and after taking carnitine drink (Table 6 and Fig. 2,3) to examine changes in the thickness (mm) of the abdominal fat layer. MRI results are presented in Table 6. In Case Study 1, at two

Table 6. MRI results

(Unit: mm)			
Case Study 1	Before consumption	After consumption	Difference
Measurement Point 1	36.74	33.27	-3.47
Measurement Point 2	16.76	15.47	-1.29
Case Study 2			
Measurement Point 1	18.98	16.17	-2.81
Measurement Point 2	14.06	15.94	-1.88

Case Study 1 (Week 0, before consumption)



Case Study 1 (Week 6, after consumption)

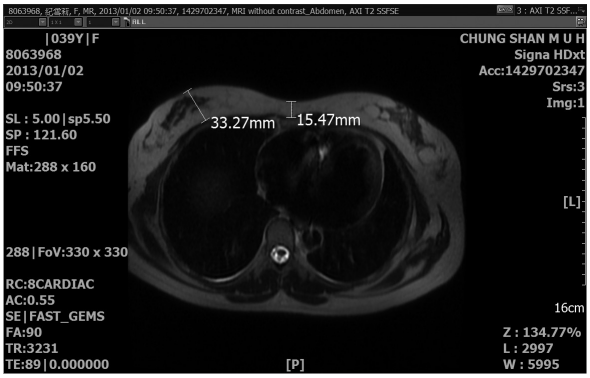
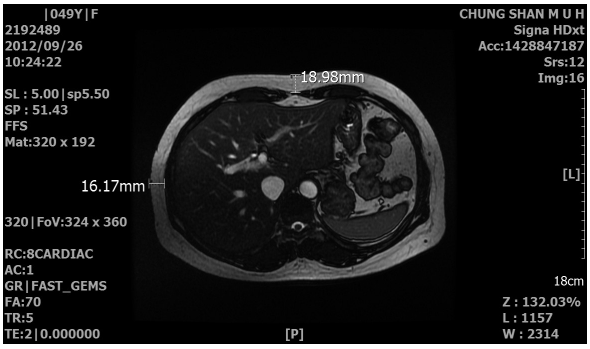


Fig 3 Case Study 2 (Week 0, before consumption)



Case Study 2 (Week 6, after consumption)

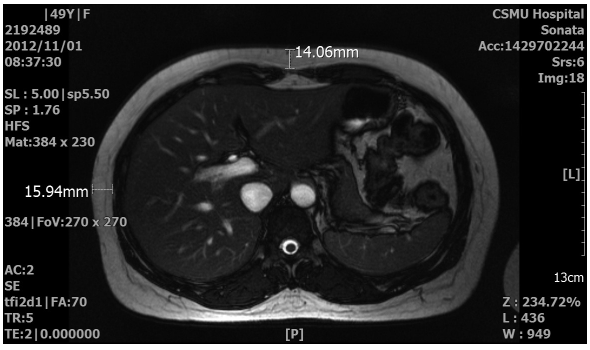


Fig. 2 Abdominal MRI scans from 2 different subjects. Carnitine drink effectively reduced the thickness of abdominal fat layer by 1.29– 3.47 mm after 6 weeks.

measurement points, there were reductions of 3.47 mm and 1.29 mm in abdominal fat thickness, respectively. In Case Study 2, at two measurement points, there were reductions of 2.81 mm and 1.88 mm, respectively. These MRI results directly manifested the effects of carnitine drink.

It was difficult to ask all subjects to maintain the same level of food consumption during the study period. However, they were asked to maintain their dietary habits during the study period. We expected that the randomized design would balance out the bias. The biochemical markers in both groups, such as cholesterol level, differed after intervention. Whether this was due to the intake of product or the change in eating habits of the subjects during the study period merits further exploration. There were some interesting observations in this study, including the loss of body weight in carnitine drink group but not in the placebo group and decreases in abdominal fat thickness (two subjects in the carnitine drink group). These results should be verified by future studies with larger samples and longer study periods.

Conclusion

In conclusion, after 6 weeks of carnitine drink consumption, body fat level was reduced by 0.3% and was 0.7% lower than that of the placebo group. The body weight of the carnitine drink group was significantly reduced by 1.3 kg, with 2.1 kg reduction in body weight when compared with the placebo group. Level of plasma cholesterol was significantly reduced by 3.8% after 6 weeks of carnitine drink consumption. Hence, we conclude that consumption of drink containing carnitine influences body weight loss and hypocholesterolemia. A short intervention can result in reduced body fat. Further studies of longer duration are warranted.

Conflict of Interests

The authors declare no conflicts of interest regarding the publication of this paper.

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