The effect of alpha-lipoic acid supplementation and Electrical isotonic contraction on anthropometric measurements, body composition, angiogenesis factors, sirtuin-1, and PGC1- α in obese people undergoing a weight loss diet

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Research

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Abstract

Background: The anti-obesity effects of Alpha-lipoic acid (α -LA) and isotonic contraction has been reported. However, the underlying mechanism is not fully understood. This study aimed to investigate the effect of α -LA supplementation and Faradic (an electrical stimulating system) on anthropometric parameters, body composition, VEGF, Sirtuin-1, nitric oxide (NO), and PGC1- α in obese people undergoing a weight loss regime.

Methods: This randomized clinical trial was carried out on 100 obese adults. The subjects were randomly assigned to four groups of 25 subjects including Faradic, α -LA, α -LA+Faradic, and control. A Bio Impedance Analyzer (BIA) was used to estimate anthropometric measurements including weight, body mass index (BMI), fat mass, and fat free mass. The serum levels of Sirtuin-1, PGC1- α , VEGF, and NO levels were measured. All measurements were done at baseline and after 8 weeks of intervention.

Results: A significant weight reduction was observed in all four groups compared to baseline ($p < 0.01$). The placebo group had significantly higher weight, BMI, weight circumference (WC), and body fat (BF) compared with the other groups. The α -LA+Faradic group had significantly lower weight, BMI, BF, WC than control, faradic, and α -LA groups and higher, Sirtuin, and PGC than the control group (all $P < 0.05$).

Conclusions: The findings indicated that the α -LA and Faradic interventions may have a synergistic effect on weight, BMI, BF, WC, and SLM, possibly through changes in serum level of VEGF, NO, and PGC. Further researches are warranted to clarify the mutual effects of α -LA and Faradic on obesity and molecular biomarkers.

Name of the registry: Iranian Registry of Clinical Trials

Trial registration number: IRCT20131117015424N2

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Background

Obesity has been dramatically increasing worldwide, with a prevalence of 600 million obese adults (1–3). Numerous factors including genetics and lifestyle are strongly associated with obesity and overweight (4). Recent studies reported the anti-obesity effects of Alpha-lipoic acid (α -LA) (5–7). α -LA is naturally found in dietary sources such as meat, spinach, and broccoli and plays a key role of mitochondrial energy metabolism as a cofactor for mitochondrial enzymatic complexes such as pyruvate dehydrogenase and alpha-ketoglutarate dehydrogenase (6). Pyruvate dehydrogenase complex (PDC) is a multifunctional enzyme complex that converts pyruvate into acetyl-CoA (5, 6). α -LA supplementation can prevent weight gain with decreasing adipose tissue size and increasing energy expenditure (7). One study reported that supplementation by 1200 mg α -LA for 12 weeks reduced body weight and body mass index (BMI) (8).

Other studies have also reported α -LA supplementation reduced weight and body fat and decreased appetite (9–11). The possible mechanisms of anti-obesity effects of α -LA included decreased food intake and increased energy expenditure. α -LA decreases food intake via reduction of Hypothalamic AMP-activated protein kinase (AMPK) activity which has an important role in regulation of energy intake and consumption (10). α -LA also inhibits adipogenesis, improves glucose metabolism (11), and regulates adipokine production. It also affects lipid metabolism and reduces lipid accumulation not only in adipose tissue but also in other tissues (8, 12). α -LA treatment can increase the number of mitochondria, Sirtuin1 and brown adipose tissue (13).

In the other hand, multiple interactions are existed between diet, physical activity and obesity (14). Simultaneous diet and physical activity interventions are recommended to management of obesity (14, 12). Faradic is an electrical stimulating system that increased muscle contraction, physiological activity, blood flow and lymph evacuation and causes isotonic contraction (like the exercise isotonic contraction) to reduce body weight and size (12). One study reported that the Faradic and aerobic training affected the abdominal circumference and significant reduction of fat percentage of whole body and abdomen fat (12). Considering the potential therapeutic effects of α -LA on weight loss, as well as Effect the Faradic apparatus in weight loss, this study aimed to investigate the effect of α -LA acid supplementation and electrical isotonic contraction on anthropometric parameters, body composition and angiogenesis factors, sirtunin-1 and Peroxisome proliferator-activated receptor gamma co-activator 1-alpha (PGC-1 α) in obese people under weight loss regime.

Methods:

Sample characteristics

This study was a randomized clinical trial that carried out from April 2018 to September 2018 on 100 randomly selected adult people referred to dietary clinics in the city of Ahvaz, Iran. The Inclusion criteria was BMI between 30-40 kg/m², age from 18 to 50 years, participants' willingness to participate in the study and not participating in a weight loss programs or specific diet during last six months. We excluded participants with systemic inflammatory and chronic diseases (diabetes, hypertension, and kidney), women with pregnancy and lactation, people with skin problems and allergies and people who took anti-epilepsy, anti-Inflammatory, and hormonal drugs, or anti-oxidant and vitamin supplements. All measurements were done at baseline and after 8 weeks of intervention.

Anthropometric measurements

Height was measured using a measuring tape fastened to a wall and without shoes with a nearest 0.5 cm. A bio impedance analysis scale (BIA) (ioi353) was used to measure body weight, body mass index (BMI), body fat (BF), body fat percentage (PBF) and lean soft tissue mass (SLM). The waist circumference (WC) was measured between the lower borders of the rib cage and iliac crests with a measuring tape. Faradic (B333) is used for isotonic contraction.

Laboratory Measurement

Fasting blood samples (10ml) were collected of all participants for biochemical assessments. : Fasting blood samples (10 mL) were taken at baseline and end of each study phase in an early morning after an overnight fast. Blood samples were immediately centrifuged (Hettich D-78532, Tuttlingen, Germany) at 3500 rpm for 10 min to separate serum. Then, the samples were stored at -70°C before analysis at the laboratory. The level of serum angiogenesis factors including vascular endothelial growth factor (VEGF), Sirtuin, NO and PGC1- α were measured by a direct competitive enzyme-linked immunosorbent assay (ELISA) test (EASTBIOPHARM).(17)

Intervention

This study was a randomized placebo-controlled study. Eligible subjects were randomly divided into four groups. Group (1) received 2 capsules containing 600 mg α -LA 1 hour before lunch and dinner along with a calorie-restricted diet for weight loss; Group (2) performed Faradic exercise for 8 weeks and 3 sessions of 60 minutes per week. Electrical stimulation based on strength and endurance of abdomen muscles. (); Group (3) received both 2 capsules daily containing 600 mg and Faradic exercise along with a weight loss regimen, and Group (4) receive 2 placebo capsules containing 600 mg wheat flour with calorie-restricted diet for weight loss. A personalized diet for weight management was prescribed for each participant by a trained nutritionist.

Dietary and physical activity assessment

A 24-hour Dietary Questionnaire was used for two days at baseline and at the end of study to assess the calorie, macronutrients, and micronutrients intake of each participant through the face-to-face interview. Data were analyzed by the Nutritionist 4 software to calculate macronutrient and micronutrient intake of participants in each groups. Physical activity levels were also assessed through physical activity records at baseline and at the end of study. Data from physical activity records were expressed as MET-h/day.

Statistical analysis

Mean $\pm$ SD was used to represent continuous variables after checking for normality of the distribution. Differences between the variables at baseline were assessed using analysis of covariance (ANCOVA). To control the confounding variables, analysis of covariance (ANCOVA) test was used in order to determine the differences between the four groups.

Tukey's test was implemented for anthropometric and biochemical measurements in the interventions and the control groups at baseline and the end of intervention between groups. A p-value less than 0.05 was considered to be statistically significant.

Results

All measurement data were normally distributed, the seven subjects in the intervention group and three participant in the control group, were lost to follow. But all the analyses were performed using intention-to-treat.

Body fat was significantly different between the groups ($P=0.001$). No significant differences were found between the other variables. Details of subjects' characteristics are presented in Table 1.

The control group had significantly higher weight than subjects received α -LA+Faradic (1.92 ± 0.59), α -LA than α -LA+Faradic (1.26 ± 0.62) and Faradic than α -LA+Faradic (1.98 ± 0.59). BMI in the control group was significantly higher than α -LA+Faradic (0.56 ± 0.27), and in Faradic group was higher than α -LA+Faradic (0.72 ± 0.27). The control group had significantly higher WC than α -LA+Faradic (1.42 ± 0.62), α -LA than α -LA+Faradic (1.34 ± 0.65) and Faradic group than α -LA+Faradic (1.27 ± 0.62). The control group had significantly higher BF than α -LA+Faradic (1.37 ± 0.41), Faradic than α -LA (-0.73 ± 0.37) and Faradic than α -LA+Faradic (1.46 ± 0.41). The Faradic group had significantly higher SLM than control (-490 ± 0.23), α -LA than α -LA+Faradic (0.55 ± 0.24) and Faradic than α -LA+Faradic (0.49 ± 0.23).

VEGF and NO were not significant in α -LA+Faradic compare with other groups.

Sirtuin in control is higher than α -LA (4.30 ± 1.70), Faradic than control (-4.11 ± 1.56) and α -LA than Faradic (4.68 ± 1.40). The α -LA group had significantly higher PGC than the control group (-3.26 ± 1.45), α -LA+Faradic than control (-4.59 ± 1.33), α -LA than the Faradic group (2.65 ± 1.19).

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Jondishapour University of Medical Sciences, Ahvaz, Iran (IR.AJUMS.REC.1396.860). No severe side effects were reported in studies for doses of 600 mg α -LA supplementation for 4 years (15) and 1800 mg dose for 12 weeks (16). Consequently, α -LA supplementation at the prescribed dose (1200 mg) is supposed to have no adverse effect on human health. The details of the study were explained to participants with an explanatory letter and written informed consent was obtained from subjects prior to joining the project.

Discussion

Body fat was significantly different between the groups ($P = 0.001$). Weight was significantly decreased between the groups at the end of intervention ($p = < 0.01$). A significant weight reduction was also observed in four groups compared to baseline ($p = < 0.01$). The control group had significantly higher weight, BMI, WC, BF than subjects received α -LA + Faradic. The α -LA + Faradic group had significantly lower weight, BMI, BF, WC, SLM than faradic and α -LA group. VEGF and NO were not significant in α -LA + Faradic than control.

Sirtuin in control, faradic + α -LA groups was higher than α -LA, placebo and faradic group (respectively). PGC in α -LA was higher than control, faradic and in α -LA + Faradic was higher than the control group.

Effect of dietary supplementation to enhance the effects of weight-loss diets has been reported (18, 19).

In line with this study, Huerta et al, found that α -LA supplementation alone or together with EPA lead to weight loss in healthy obese subjects (19). Another study reported that α -LA supplementation in combination with calorie-restricted diet reduced weight, BMI and WC (20). Carbonelli et al. (8) reported that α -LA reduced weight, fat mass and WC only in overweight and obese participants, but not in normal-weight participants. Some Studies found that α -LA reduced weight by decreasing food intake and stimulating energy expenditure (8, 21,22) α -LA could inhibit lipogenesis and adipogenesis, increase lipolysis (23, 24).In contrast with this study, Manning et al, found that a -LA supplementation did not change WC, BMI, Wight compared with placebo (25). Some studies did not report any significant association between weight loss and a -LA supplementation (26, 27). Thereby, the difference between studies could be associated with specific features of the subjects, variety in diet and the duration of treatment.

In our study, Sitruin in α -LA supplementation higher than placebo and α -LA group had higher Sitruin than faradic. These observations are consistent with some studies. Chen et al reported that, α -LA supplementation activated Sitruin and regulated lipid profile (28). α -LA supplementation decreased the acetylation levels of PGC1 β by the stimulation of Sitruin (29).

α -LA regulates intrahepatic and serum triglyceride level via the SIRT1 and AMPK signaling pathway (30). α -LA increased NAD⁺/NADH ratio and activated SIRT1. The SIRT1 is regulated by NAD⁺, nicotinamide (NA) and the nicotinamide phosphoribosyltransferase (NAMPT). α -LA is converted into dihydrolipoatein by lipoamide dehydrogenase or the thioredoxin reductase enzymes that regulated the NAD⁺/ NADH ratio. NA can be inhibited SIRT1 and converted to NAD⁺ by NAMPT that it is regulated with deprivation, physical activity and AMPK activation (31).

Dworacka et al reported that α -LA significantly increased VEGF serum levels in diabetic patients (32). α -LA treatment may decrease VEGF serum level. α -LA Supplementation suppressed the VEGF and angiopoietin 2 expression (33, 11).

Another study found that a-lipoic acid combined with exercise significantly decrease BF, WC and hip circumference (34) But α -LA supplementation alone or together with moderate intensity exercise was not change glycemic regulation (34). Razavi et al reported that faradic significantly decreased the abdomen circumference and fat percentage (12).

Chitrav et al reported that faradic stimulated abdominal muscles and reduced abdominal obesity than Interferential Therapy with a supervised exercise program (35). The precise mechanisms of how the faradic stimulation reduced fat mass are unclear. However, Faradic Stimulation breaks down fat molecules and converts them into free fatty acids, which can then enter the Krebs cycle, increasing the muscle atrophy and strength, stimulating the excretion of fluid collected in the organs (34–35).

α -LA affected AMPK hypothalamic, AMPK has a key role in sensing energy and energy balance. α -LA has anti-obesity effects by reducing AMPK hypothalamic activity (5). α -LA supplementation by suppressing hypothalamic AMPK may reduce appetite by atypical antipsychotics (5). We found that α -LA by activating AMPK expanded glucose uptake and oxidation of fatty acid in skeletal muscle (5, 6). α -LA is absorbed from the diet and it has anti-obesity properties. α -LA could suppress hypothalamic AMPK activity, decrease food intake, lipoprotein lipase activity and increased energy expenditure, lipolysis (36).

However, there are some limitations in this study. First, small sample size may affect the generalizability of the results. Weight, body composition, and biochemical indices are influenced by genetic profile. It is possible that differences between the groups were partially induced by gene variations (37, 38). Second, short period of intervention may not be enough to detect the effects of α -LA and Faradic on obesity markers. Third, obesity is a multi-factorial phenotype influenced by many psychological (39) and environmental factors (40). More adjustments should be done in further studies to make a comprehensive conclusion.

Conclusion

This study found that Body fat and Weight was significantly different between the groups. A significant weight reduction was also observed in four groups at the end of intervention. The placebo group had significantly higher weight, BMI, WC, BF than subjects received α -LA + Faradic. The α -LA + Faradic group had significantly lower weight, BMI, BF, WC, SLM than faradic and α -LA group. Sirtuin in placebo, faradic and alpha higher than alpha, control and faradic group, respectively. PGC in α -LA was higher than control, faradic and α -LA + Faradic was higher than control.

At the end of study the mean serum levels of sirtuin and PGC increased significantly in the alpha and alpha + faradic group compared to the control group but the mean of VEGF and nitric oxide concentration in the intervention group was not significantly different from the control group.

Abbreviations

α -LA: Alpha-lipoic acid

NO: nitric oxide

BMI: body mass index

WC: weight circumference

BF: body fat

PDC: Pyruvate dehydrogenase complex

AMPK: AMP-activated protein kinase

PGC-1 α : proliferator-activated receptor gamma co-activator 1-alpha

VEGF: vascular endothelial growth factor

Declarations

Ethics Approval and Consent to Participate

This protocol, approved by Medical Ethics Committee of Ahvaz Jundishapur University of Medical Sciences, was in accordance with the Declaration of Helsinki (approval number: IR.AJUMS.REC.1396.860). Each subject also signed an informed consent form. Moreover, this investigation was registered on Iranian Registry of Clinical Trials (IRCT registration number: IRCT20131117015424N2)

Consent for publication

Not applicable.

Availability of Data and Materials

The data could be available on request to the authors.

Conflict of Interests

The authors declared no conflict of interests.

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Authors' Contributions

All the authors were involved in designing the study and drafting the protocol. All the authors also read and approved the final protocol.

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Tables

Table 1: Characteristics of the sample at baseline (n=100) (mean $\pm$ SD)

		α -LA (n=25)	Faradic (n=25)	α -LA + faradic (n=25)	Control (n=25)	P
Sex	Female	15 (60)	17(68)	16(64)	17(68)	0.92
	Male	10(40)	8(32)	9(36)	8(32)	
Age(year)		34.88 ($\pm$ 10.05)	36.04 ($\pm$ 8.99)	35.28 ($\pm$ 9.48)	36.04 ($\pm$ 8.83)	0.96
MET-h/day		32.75 ($\pm$ 3.20)	31.91 ($\pm$ 2.80)	32.69 ($\pm$ 2.10)	31.05 ($\pm$ 2.07)	0.07
Kilocalories (kcal)		2020.86 ($\pm$ 393.87)	2073.93 ($\pm$ 551.42)	2041.25 ($\pm$ 416.85)	2034.67 ($\pm$ 465.13)	0.98
Protein (gr/day)		79.49 ($\pm$ 21.23)	79.89 ($\pm$ 24.37)	79.50 ($\pm$ 22.74)	84.51 ($\pm$ 27.42)	0.85
Carbohydrate (gr/day)		311.93 ($\pm$ 76.98)	318.84 ($\pm$ 98.90)	313.70 ($\pm$ 59.84)	303.79 ($\pm$ 76.74)	0.92
Fat(gr/day)		53.90 ($\pm$ 16.39)	57.18 ($\pm$ 19.79)	56.12 ($\pm$ 20.20)	54.65 ($\pm$ 27.78)	0.85
Cholesterol (mg/dl)		191.04 ($\pm$ 198.47)	171.97 ($\pm$ 104.07)	186.49 ($\pm$ 139.49)	205.98 ($\pm$ 121.17)	0.87
Saturated (mg/dl)		16.25 ($\pm$ 5.12)	18.01 ($\pm$ 6.28)	16.22 ($\pm$ 4.96)	16.05 ($\pm$ 7.83)	0.64
Mono fat (mg/dl)		13.86 ($\pm$ 4.48)	14.79 ($\pm$ 6.68)	13.72 ($\pm$ 5.19)	15.43 ($\pm$ 8.84)	0.76
Poly fat (mg/dl)		17.16 ($\pm$ 9.71)	17.49 ($\pm$ 8.50)	17.16 ($\pm$ 9.25)	19.44 ($\pm$ 12.43)	0.82
Zinc (umol/L)		8.53 ($\pm$ 2.22)	8.78 ($\pm$ 2.90)	7.96 ($\pm$ 1.86)	9.12 ($\pm$ 0.04)	0.51
Selenium (umol/L)		0.08 ($\pm$ 0.04)	0.08 ($\pm$ 0.04)	0.07 ($\pm$ 0.04)	0.09 ($\pm$ 0.04)	0.35
Vitamin A (mcg/day)		622.4 ($\pm$ 370.24)	539.62 ($\pm$ 556.92)	377.37 ($\pm$ 195.60)	538.79 ($\pm$ 564.27)	0.27
Beta carotene (mcg/day)		195.27 ($\pm$ 266.96)	216.43 ($\pm$ 536.62)	106.38 ($\pm$ 184.68)	131.61 ($\pm$ 174.78)	0.64
Vitamin E(mcg/day)		3.79 ($\pm$ 1.80)	3.78 ($\pm$ 3.45)	3.22 ($\pm$ 2.30)	4.83 ($\pm$ 2.51)	0.17
Alpha tocopherol (mcg/day)		7.84 ($\pm$ 5.75)	6.31 ($\pm$ 2.42)	6.78 ($\pm$ 3.98)	7.33 ($\pm$ 4.47)	0.62

Vitamin C (mcg/day)	154.38 (±107.82)	192.99 (±140.33)	133.46 (±89.45)	191.25 (±154.74)	0.26
Dietary fiber(gr/day)	18.22 (±6.26)	19.27 (±9.09)	15.77 (±5.99)	19.46 (±8.84)	0.30

Table2: Anthropometric measurements in the interventions and the control groups at the end of intervention

variable		α -LA (n=25)	Faradic (n=25)	α -LA + faradic (n=25)	control (n=25)	P
Weight(Kg)	before	90.51 (± 11.22)	89.10 (± 13.62)	91.14 (± 11.86)	91.48 (± 13.94)	0.91
	after	87.04 (± 11.48)	86.31 (± 14.20)	87.09 (± 11.72)	89.01(± 13.80)	<0.01
	MD CI95(%)	(2.76,4.17) 3.47	(2.18,3.41) 2.80	(3.26,4.85) 4.06	(1.93,3) 2.47	
	p-value	<0.01	<0.01	<0.01	<0.01	
BMI(kg/m2)	before	33.56 (± 2.61)	33.19 (± 2.31)	33.63 (± 2.99)	34.35 (± 3.18)	0.52
	after	32.26 (± 2.70)	32.12) (± 2.67)	32.15 (± 2.87)	33.30 (± 3.10)	0.04
	MD) CI 95(%)	(1.01,1.6) 1.30	1.07 (0.82,1.31)	(1.15,1.81)1.48	(0.68,1.41) 1.04	
	p-value	<0.01	<0.01	<0.01	<0.01	
WC(cm)	before	93.6 (± 6.49)	94.6 (± 8.74)	96.22 (± 6.32)	97.36 (± 9.48)	0.34
	after	90.74 (± 7.01)	91.42 (± 9.50)	92.52 (± 5.73)	94.82 (± 9.40)	0.08
	MD) CI 95(%)	(2.20,3.52) 2.86	3.18 (2.46,3.90)	3.70 (2.83,4.56)	(1.90,3.8) 1.56	
	p-value	<0.01	<0.01	<0.01	<0.01	
BF%	before	33.24 (± 5.88)	34.48 (± 5.30)	38.18 (± 5.04)	39.88 (± 4.46)	0.001
	after	30.79 6.01 $\pm$ ()	32.66 (± 5.92)	35.36 (± 4.78)	38.31 (± 4.45)	<0.01
	MD) CI 95(%)	(1.97,2.93) 2.45	1.82 (1.32,2.32)	2.82 (2.28,3.36)	1.56 (1.19,1.94)	
	p-value	<0.01	<0.01	<0.01	<0.01	
SLM%	before	51.82 (± 8.64)	48.90 (± 11.97)	47.28 (± 12.06)	46.20 (± 11.67)	0.31
	after	50.84 (± 8.66)	47.88 (± 12.05)	46.06 (± 12.08)	45.32 (± 11.69)	0.126
	(%95 CI) MD	(0.7,1.28) 0.99	1.02 (0.78,1.25)	1.24 (0.93,1.56)	0.89 (0.67,1.10)	
	p-value	<0.01	<0.01	<0.01	<0.01	

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BMI: body mass index, WC: waist circumference, BF: body fat, SLM: soft lean mass, weight was significantly different between the groups at the end of intervention ($p < 0.01$). A significant weight reduction was also observed in four groups compared to baseline ($p < 0.01$).

Table 3: Biochemical measurements in the interventions and the control groups at the end of intervention

variable		α -LA (n=25)	Faradic (n=25)	α -LA + faradic (n=25)	control (n=25)	P
VEGF(ng/l)	before	125.40 (± 43.29)	120.76 (± 36.88)	122.84 (± 51.14)	126.32(± 56.14)	0.97
	after	121.40 (± 36.12)	88/128)42/39 $\pm$ ((± 36.63)	125.72)13/ ± 43 ((± 6.65)	130.28(± 51.58)	0.52
	(%95 CI) MD	4 (-,17.659.64)	(-,3.9820.21) -8.12	-2.88 (-13 $\square$ 7/24)	-3.96 (-,8.6516.57)	
	p-value	0.55	0.17	0.56	0.52	
NO(μ M)	before	18.81 (± 7.96)	17.80 (± 6.59)	17.52 (± 7.76)	16.82 (± 7.19)	0.81
	after	18.32 (± 6.7)	19.44 (± 6.63)	18.95 (± 6.65)	16.52 (± 6.75)	0.31
	(%95 CI) MD	0.49 (-,2.871.89)	-1.64 (-3.73, 0.46)	-1.44 (-,0.863.74)	(-,2.812.21) 0.3	
	p-value	0.67	0.12	0.21	0.80	
Sirtuin(ng/ml)	before	9.40 (± 5.19)	10.64 (± 5.51)	10.48 (± 7.04)	10.93 (± 5.34)	0.80
	after	15.26 (± 7.07)	11.82 (± 6.13)	15.31 (± 8.28)	10.50 (± 5.14)	<0.01
	(%95 CI) MD	(-7.89 $\square$ -3.81) -5.85	-1.18 (-3.10,0.74)	-4.82 (-,6.58 -3.06)	0.43(-,1.42 2.28)	
	p-value	<0.01	0.216	<0.01	0.63	
PGC (ng/ml)	before	7.88 (± 3.58)	7.81 (± 3.63)	6.68 (± 2.36)	7.25 (± 3.23)	0.52
	after	10.65 (± 4.64)	8.41 (± 3.94)	11.09 (± 5.57)	6.84 (± 2.63)	<0.01
	(%95 CI) MD	(-4.56 $\square$ -0.96) -2.76	(-2.16 $\square$ 0.95) -0.6	(-6.26 $\square$ -2.55) -4.41	(-0.52 $\square$ 1.34) 0.41	
	p-value	<0.01	0.43	<0.01	0.37	

No: nitric oxide, VEGF: Vascular endothelial growth factor, PGC: peroxisome proliferator-activated receptor- γ coactivator-1 α .

Table 4: Tukey's test for anthropometric and biochemical measurements in the interventions and the control groups at baseline and the end of intervention between groups

	Control vs α -LA(mean $\pm$ SD)	Control vs Faradic (mean $\pm$ SD)	Control vs α -LA + faradic (mean $\pm$ SD)	α -LA vs Faradic (mean $\pm$ SD)	α -LA vs α -LA + faradic (mean $\pm$ SD)	Faradic vs α -LA + faradic (mean $\pm$ SD)
Weight(kg)	0.36 (0.64)	-0.36 (0.61)	1.92 ** (0.59)	-0.72 (0.52)	1.26 *(0.62)	1.98 *** (0.59)
BMI(kg/m2)	0.11 (0.29)	-0.16 (0.28)	0.56 (0.27)*	-0.26 (0.24)	0.45 (0.28)	0.72 (0.27) **
WC(cm)	0.08 (0.68)	0.15 (0.65)	1.42 (0.62)*	0.07 (0.56)	1.34 *(0.65)	1.27 (0.62)*
BF (%)	0.64 (0.45)	-0.09 (0.43)	1.37 (0.41)***	-0.73 (0.37)*	0.73 (0.43)	1.46 (0.41)***
SLM (%)	-0.3 (0.25)	-490 (0.23)*	-0.26 (0.23)	0.08 (0.21)	0.55 (0.24)*	0.49 (0.23)*
VEGF(ng/l)	8.21 (7.55)	-2.58 (7.52)	2.06 (7.51)	-10.80 (7.52)	-6.14 (7.52)	4.65 (7.51)
NO (μM)	-0.56 (1.41)	-2.30 (1.40)	-1.97 (1.40)	-1.70 (1.40)	-1.41 (1.40)	-0.29 (1.40)
Sirtuin (ng/ml)	4.30 (1.70) **	0.38 1.62	-4.11 (1.56)**	4.68 (1.40) ***	0.19 (1.64)	-4.49 (1.57) **
PGC (ng/ml)	-3.26 (1.45)*	(1.38) -0.61	-4.59 (1.33)***	2.65 (1.19) *	(1.40) -1.32	-3.98 **(1.34)

BMI: body mass index, WC: waist circumference, BF: body fat, SLM: soft lean mass, No: nitric oxide, VEGF: Vascular endothelial growth factor, PGC: peroxisome proliferator-activated receptor- γ coactivator-1 α , *: $p < 0.05$, **: $p < 0.01$, *** $p < 0.001$