ORIGINAL ARTICLE

The effect of alpha-lipoic acid supplementation on anthropometric indices and food intake in patients who experienced stroke: A randomized, double-blind, placebo-controlled clinical trial

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Background: Stroke as a devastating condition is a major cause of death worldwide. It is accountable for long-term disability with high personal and social cost in adults. Alpha-lipoic acid (ALA) is an eight-carbon, sulfur-containing compound with antioxidant properties which reduces body weight, changes other anthropometric indices, and regulates food intake by suppressing appetite and increasing metabolism This study was designed to evaluate the possible effects of ALA supplementation on anthropometric indices and dietary intake in patients with stroke. **Materials and Methods:** In this randomized, double-blind, placebo-controlled clinical trial, 67 patients with stroke were randomly allocated to two groups (taking a 600 mg ALA supplement or placebo daily for 12 weeks). Weight, waist circumference, energy, carbohydrate, protein, and fat intake were measured, and body mass index (BMI) was calculated before and after intervention. Dietary intake and statistical analyses were carried out using Nutritionist IV and SPSS (version 16; SPSS Inc., Chicago, IL, USA) software, respectively. **Results:** Primary features were similar in the intervention and placebo groups ($P > 0.05$). Waist circumference ($P < 0.001$), energy, carbohydrate, protein, and fat intake ($P < 0.001$) decreased significantly, after the intervention period, in ALA group compared with placebo. While no significant change was observed in weight ($P = 0.26$) and BMI ($P = 0.56$) in ALA supplementation group compared with placebo. **Conclusion:** Results of this trial indicated that 12-week supplementation with 600 mg ALA can decrease waist circumference and food intake (energy, carbohydrate, protein, and fat) in patients with stroke.

Key words: Alpha-lipoic acid, body mass index, food intake, weight

How to cite this article: Mohammadi V, Khorvash F, Feizi A, Askari G. The effect of alpha-lipoic acid supplementation on anthropometric indices and food intake in patients who experienced stroke: A randomized, double-blind, placebo-controlled clinical trial. J Res Med Sci 2017;22:98.

INTRODUCTION

Alpha-lipoic acid (ALA) or thioctic acid is an eight-carbon, sulfur-containing compound. Traditionally, it is recognized as a cofactor in the multienzyme complexes that are responsible for the oxidative decarboxylation of α-ketoacids.[1] A general agreement exists about the antioxidant properties of ALA, which is thought to function by clearing free radicals directly, chelating metallic ions, enhancing intracellular glutathione, and activating endogenous antioxidant systems.[2,3] Being a strong antioxidant is not the only property of ALA. Studies reported different properties for this cofactor including modulating blood pressure,[4,5] lipid profile,[6,7] blood glucose,[5,8] and being a neuroprotective agent.[3,9] In addition, there is a large body of growing evidence showing that ALA reduces body weight, changes other anthropometric indices, and regulates food intake by suppressing appetite and increasing metabolism.[6,10-13]

Clinical studies have shown that ALA intake up to 1800 mg/day did not show any side effect in humans. It is reported that taking 300–600 mg ALA daily is safe for humans.[14,15]

Access this article online

Quick Response Code:

Website: www.jmsjournal.net

DOI: 10.4103/jrms.JRMS_1_17

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Received: 14-01-2017; **Revised:** 26-04-2017; **Accepted:** 12-05-2017

Stroke as a devastating condition is a major cause of death worldwide. It is accountable for long-term disability with high personal and social cost in adults.[16,17] The 2012 BRFSS (Centers for Disease Control and Prevention) data indicated that history of stroke was seen in 2.9% of people ≥18 years of age. In addition, projections show that, by 2030, stroke will be experienced by more people and a 20.5% increase will be observed in prevalence from 2012.[18] Metabolic syndrome and obesity are well-known risk factors of coronary artery disease, stroke, and mortality. In addition, metabolic syndrome has been identified as an independent risk factor for acute ischemic noncardioembolic stroke and stroke risk increases along increment in the number of metabolic syndrome components. Two prospective cohort studies confirmed these associations.[19-22] As we explained that metabolic syndrome components are risk factors of stroke and ALA can modify this component, it can be useful for patients with stroke.

Although studying the effect of ALA on cardiovascular risk factors such as anthropometric indices and dietary intake is not novel, to the best of our knowledge, the beneficial effects of ALA supplementation in patients who experienced stroke have not been investigated by far. Thus, we designed this study to assay the possible effect of ALA supplementation on anthropometric indices and dietary intake in patients with stroke.

METHODS

Research Ethics Committee of Isfahan University of Medical Sciences (IUMS) approved the protocol of this randomized, double-blind, placebo-controlled, parallel-designed clinical trial (code: IR.MUI.REC.1395.3.068). In addition, we registered this trial protocol in the Iranian Registry of Clinical Trial (IRCT2016051811763N23).

Study design and participants

Eighty patients with stroke who referred to Al Zahra Hospital and met the study criteria were enrolled in this trial. The inclusion criteria included filling out informed consent, thrombotic and embolic stroke, body mass index (BMI) = 18.5–35, age 30–70 years, no specific diseases, and malignancies such as liver disease, kidney disease, and cancer based on self-reports, no vitamin, antioxidant, and omega-3 supplementation. Exclusion criteria included no collaboration, failure to follow the program of trial (compliance <80%), death, experienced gastrointestinal side effects, dizziness, amnesia and eating problems, and recurrent stroke.

We calculate sample size with power 80% and α = 5% with the following formula. Thirty-three participants were required for each group, which after considering 20% sample loss, forty patients in each group were enrolled.

$$N = \left[\frac{1+\varphi}{\varphi}\right]\frac{Z_1 - \alpha/2 + Z_1 - \beta)^2}{\Delta^2} + \frac{Z_1^2 - \alpha/2}{1(1+\varphi)}$$

Intervention

We allocated participants randomly into two quantitatively equal groups (in a double-blind parallel manner from randomized number in an eighty-person list): ALA and placebo groups that were taking a 600 mg ALA supplement and similar placebo capsule (containing wheat flour) every day for 12 weeks, respectively. We prepared ALA supplement from Caren company and capsulated it in the School of Pharmacy, IUMS. Thirteen participants were excluded from the study because of different reasons; finally, with 33 and 34 patients remaining in ALA and placebo groups, respectively [Figure 1].

Measurements

At the beginning of the study, we obtained written consent from all volunteers. All data collection and measurements were performed by trained personnel. Body weight was measured by a digital balance to the nearest 0.1 kg with minimal clothing. To measure height, a seca stadiometer was used, and in case of not being able to stand up for measuring height, we determined knee height and the following formula was used:

Height in centimeters (for men) = 64.19 − (0.04 × age) + (2.02 × knee height in centimeters)

We calculated BMI for each patient (BMI = weight in kg/ht^2 in meters). We measured waist circumference at the level of the iliac crest by an ergonomic circumference measuring tape (model 201; Seca GmbH and Co, KG, Hamburg, Germany). Food intakes were collected by 24-h food recall during face-to-face interviews by a nutritionist (three 24-h food recalls including two midweek days and one weekend day). To assess energy and macronutrient

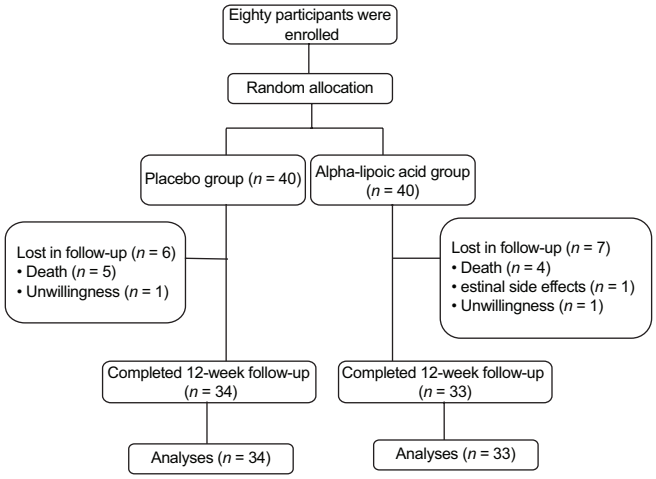

Figure 1: Flowchart of participants throughout the intervention

intakes, dietary data were analyzed by Nutritionist IV software (Version 4.1, First Databank Division, The Hearst Corporation, San Bruno, CA, USA). We measured blood pressure by a mercury sphygmomanometer after 5 min of sitting rest.

Statistical analysis

All statistical analyses were performed by SPSS (version 16; SPSS Inc., Chicago, IL, USA). Quantitative data are presented as mean ± standard deviation. The normality of data was evaluated by Kolmogorov–Smirnov test. In case of normal distribution of data, paired *t*-test was used to compare variables before and after the intervention within groups. Comparing the variables after intervention, adjusting for baseline values and in some cases energy intake were performed by analysis of covariance (ANCOVA). All tests were two sided and $P < 0.05$ was considered statistically significant.

RESULTS

Baseline characteristics were similar in the ALA and placebo groups [Table 1]. We found no statistically significant differences in age, weight, height, BMI, waist circumference, blood pressure, energy and macronutrient intake, and fasting blood sugar between two groups before the intervention ($P > 0.05$).

Based on within-group analysis, no significant changes were observed in placebo group for all studied variables ($P > 0.05$), while body weight, BMI, waist circumference, energy, carbohydrate, protein, and fat intake decreased significantly within ALA group ($P < 0.001$).

Based on ANCOVA results, statistically significant reductions were observed for waist circumference ($P < 0.001$), energy, carbohydrate, protein, and fat intake ($P < 0.001$), and there were no differences for weight ($P = 0.26$) and BMI ($P = 0.56$) in ALA supplementation group compared with placebo group [Table 2].

Table 1: Baseline characteristics of the study participants who received α-lipoic acid (600 mg) or placebo before the intervention

Characteristics	α-lipoic acid group	Placebo group	*P**
Age (years)	62.33±6.19	64.23±8.01	0.28
Weight (kg)	73.09±13.93	68.49±9.04	0.11
Height (cm)	162.03±8.72	161.88±5.06	0.93
BMI (kg/m^2)	27.68±3.92	26.14±3.32	0.08
Waist circumference (cm)	110.08±15.53	106.71±15.44	0.28
Systolic blood pressure (mmHg)	133.18±9.90	132.94±11.62	0.92
Diastolic blood pressure (mmHg)	84.24±6.13	86.02±7.66	0.29
Energy intake (kcal/day)	2182.3±367.37	2061.5±333.61	0.16
Carbohydrate intake (g/day)	335.2±56.66	316.21±58.46	0.18
Protein intake (g/day)	55.87±13.15	52.33±8.82	0.19
Fat intake (g/day)	68.74±12.52	65.57±10.34	0.26
FBS (mg/dL)	109.39±20.17	105.68±20.81	0.46

*Independent *t*-test. FBS = Fasting blood sugar; BMI = Body mass index

DISCUSSION

This study results indicate that 12-week consumption of 600 mg ALA has no effect on body weight and BMI, but can reduce waist circumference, energy, carbohydrate, protein, and fat intake in patients with stroke. According to our knowledge, the present trial is the first study, which investigated the effect of ALA consumption on anthropometric indices and food intake in patients with stroke.

Our results indicate that ALA could change weight and BMI within group, but this change was not significant between groups after eliminating the confounding effect of energy intake. It means that these changes were because of reduction in food intake. However, changes in waist circumference (confounding effect of energy intake eliminated), energy, carbohydrate, protein, and fat intake were significant.

There is a large body of growing evidence indicating that ALA supplementation can play an important role in the regulation of food intake and anthropometric indices by suppressing appetite and elevating energy metabolism.[5,6,10-13,23] In agreement with our study, there are four human studies; Mohammadi *et al*.[5] evaluated the effects of ALA supplementation in men with spinal cord injury. In a randomized, double-blind, placebo-controlled, 12-week trial, they demonstrated that 600 mg ALA could reduce body weight, BMI, waist circumference, energy, and macronutrients significantly. Based on our search, this is the only study which measured energy intake, but they did not control the effect of changes in energy intake in their result analysis. It seems that if they would have taken the energy intake component into account, different results would have been reported.

In another randomized, double-blind, placebo-controlled, 20-week trial by Koh *et al*.,[12] 1800 mg LA reduced body weight significantly more than did 1200 mg LA and placebo in 360 obese individuals. In addition, 20-week supplementation with 600 mg ALA decreased BMI in obese patients with diabetes mellitus and signs of peripheral polyneuropathia.[23]

Kim *et al*.[11] in a case series studied the effect of ALA on antipsychotics-induced weight gain in schizophrenic patients (n = 7, 1200 mg LA, 12 weeks). A remarkable reduction in weight (3.2 kg mean weight loss) and BMI was observed. Except the study of Mohammadi *et al*.,

Table 2: Anthropometric indices and food intake of the the study participants before and after supplementation in both groups

Variables	α-lipoic acid group			*P**	Placebo group			*P**	*P***
	Before intervention	After intervention	Change		Before intervention	After intervention	Change		
Weight (kg)	73.09±13.9323 (2-5)	69.89±14.87	−3.2±0.94	<0.001	68.94±9.04	68.32±8.82	−0.62±1.43	0.42	0.26†
BMI (kg/m^2)	27.68±3.92	26.38±3.74	−1.3±0.18	<0.001	26.14±3.32	26.08±3.27	−0.06±0.14	0.43	0.56†
Waist circumference (cm)	110.08±15.53	103.02±22.72	−7.06±7.26	<0.001	106.71±15.44	106.44±15.95	−0.27±0.44	0.21	<0.001†
Energy intake (kcal/day)	2182.3±367.37	1959.9±347.79	−222.1±22.41	<0.001	2061.5±333.61	2053.5±329.86	−8±43.91	0.39	<0.001
Carbohydrate intake (g/day)	335.2±56.66	300.06±56.63	−35.14±4.32	<0.001	316.21±58.46	315.51±57.41	−0.7±1.32	0.63	<0.001
Protein intake (g/day)	55.87±13.15	50.15±12.01	−5.72±1.78	<0.001	52.33±8.82	51.91±7.49	−0.42±2.09	0.48	<0.001
Fat intake (g/day)	68.74±12.52	62.43±12.65	−6.34±21	<0.001	65.57±10.35	65.36±10.31	−0.21±0.02	0.48	<0.001

*Paired *t*-test, **ANCOVA adjusted for the baseline value of the variable, †Adjusted for the baseline value of the variable and energy intake. Values are expressed as mean±SD. SD = Standard deviation; BMI = Body mass index; ANCOVA = Analysis of covariance

none of the aforementioned studies considered energy and macronutrient intake and neither of them took the confounding effect of energy intake into account.

Several animal[6,10] and human studies[5,12] have shown that ALA supplementation reduces appetite, weight, fat tissue, and restricts weight gain. Studies have shown that the effect of LA is not because of its toxicity.[10] Uncoupling protein-1 (UCP-1), located in the inner mitochondrial membrane, is the main regulator of energy metabolism in rodents. ALA supplementation increases UCP-1-messenger RNA expression.[10] On the other hand, ALA supplementation reduces appetite by suppressing hypothalamic adenosine5′-monophosphate-activated protein kinase.[24,25] It has been well known that the hypothalamus is the appetite center in the brain.[10]

Being a strong antioxidant is not the only property of ALA. Studies reported different properties for this cofactor including modulating blood pressure,[4,5] lipid profile,[6,7] blood glucose,[5,8] and being a neuroprotective agent.[3,9] Metabolic syndrome and obesity are well-known risk factors of coronary artery disease and stroke.[19,20] Therefore, it seems ALA can modify risk factors of stroke.

There are several limitations for this trial, which is better to be counted in the interpretation of our results, including sample size and restricted duration of the study. In addition, we were not able to measure body composition and metabolism.

CONCLUSION

Based on this randomized, double-blind, placebo-controlled, parallel-designed clinical trial results, supplementation with 600 mg ALA for 12 weeks can decrease some anthropometric parameters (waist circumference) and food intake in patients with stroke. Therefore, ALA could be a risk modifier for patients with stroke.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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