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ORIGINAL ARTICLE

The effect of alpha-lipoic acid (ALA) supplementation on cardiovascular risk factors in men with chronic spinal cord injury: a clinical trial

This article has been corrected since advance online pubilcation and a corrigendum is also printed in this issue

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Study design: A randomized, double-blind, placebo-controlled clinical trial.
Objective: To assess the effect of alpha-lipoic acid (ALA) supplementation on IL-6, hs-CRP, FBS, anthropometric indices, food intake and blood pressure in male patients with chronic spinal cord injury (SCI).
Setting: Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran.
Methods: Fifty-eight men with chronic SCI participated in the study. Participants were divided in two groups: one group received 600 mg of supplemental ALA ($n=28$) and the other group received placebo ($n=30$) for 12 weeks. At the beginning and end of the study, biochemical parameters, anthropometric indices, blood pressure and dietary intakes were measured. Dietary intake was measured using N4 software, and statistical analyses were carried out using SPSS16.
Results: No significant reduction was found in IL-6 ($P=0.97$) and hs-CRP levels ($P=0.23$). There was significant reduction in fasting blood sugar ($P=0.001$), body weight ($P=0.001$), BMI ($P=0.001$), waist circumference ($P=0.001$) and blood pressure ($P=0.001$). Dietary intake was significantly reduced, including fat ($P=0.001$), carbohydrate ($P=0.001$), protein ($P=0.002$) and energy intakes ($P=0.001$).
Conclusion: Lipoic acid supplementation had no significant effect on the measured inflammatory markers but it reduces fasting blood sugar, anthropometric parameters, food intake and blood pressure in men with chronic SCI.
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INTRODUCTION

Alpha-lipoic acid (ALA) or thiocitic acid is an eight-carbon, sulfur-containing compound. It functions as a cofactor in the multienzyme complexes that catalyze the oxidative decarboxylation of α-keto acids.[1] There is general agreement about the antioxidant properties of ALA, which is thought to work by scavenging free radicals directly, chelating metallic ions, increasing intracellular glutathione and activating endogenous antioxidant systems.[2,3] ALA's antioxidant properties are thought to inhibit the deleterious mechanisms associated with inflammation; however, a number of studies suggest contradictory effects for ALA on inflammatory markers such as IL-6 and C-reactive protein (CRP).[4–6] Apart from the antioxidant properties of ALA, it is found to increase nitric oxide synthesis through which endothelial function is probably improved.[7] In addition, ALA reduces body weight and changes other anthropometric indices by suppressing appetite and increasing metabolism.[8–12]

Spinal cord injury (SCI) is a devastating condition and entails considerable burden on the individual and society.[13,14] Persons with chronic SCI are at increased risk for obesity, cardiovascular disease, hypertension, diabetes, dyslipidemia and systemic inflammation[15–19] because of changes in their lifestyle, body composition and fat mass.[20] However, these complications may be preventable and treatable.[21]

Studying the effect of ALA on cardiovascular risk factors and dietary intake is not novel; however, the effects of ALA supplementation in persons with SCI have not been investigated yet. This study examined the effect of ALA supplementation on inflammation, energy balance and some chronic disease markers in males with chronic SCI.

MATERIALS AND METHODS

The protocol of this randomized, double-blind, placebo-controlled clinical trial was approved by the research Ethics Committee of Tehran University of Medical Sciences (TUMS) and was registered in the Iranian Registry of Clinical Trial (IRCT201106122602N6).

Male volunteers with SCI were referred to Imam Khomeini Hospital and upon meeting the study criteria were enrolled into this study (from June 2012 to December 2013) after obtaining their consent. The inclusion criteria

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included complete SCI since at least 1 year with a maximum of 10 years, body mass index (BMI) $\geqslant 18.5$, age 30–50 years, no self-reported specific diseases and malignancies, no vitamin and antioxidant supplementation and no smoking and drinking. Study volunteers were excluded for failure to follow trial guidelines ($<80\%$ compliance). Participants were randomly allocated to two numerically equal groups from a double-blind, 70-person list, using a table of random digits and given either 600 mg ALA or a placebo wheat flour capsule. Study participants, as well as the placebo group, ingested those pills once daily before breakfast for 12 weeks. Twelve participants were excluded during the study (because of unwillingness, infection, ulcer, diarrhea and rash), which left 28 volunteers in the ALA group and 30 in the placebo group.

At the beginning of the study, written consent was obtained. Trained personnel performed all data collection and measurements. Body weight for the study participants was measured to the nearest 0.1 kg with minimal clothing by means of a digital wheelchair balance. To measure height, knee height was determined and the following formula[22] was used: height in cm (for men) = $64.19-(0.04\times \text{Age})+(2.02\times \text{knee height in cm})$.

BMI was calculated for each patient (BMI = weight in kg/height^2 in m). Waist circumference was measured at the level of the iliac crest using an Ergonomic Circumference Measuring Tape (model 201; Seca GmbH & Co., KG, Hamburg, Germany). Blood pressure was measured with a mercury sphygmomanometer after 5 min of sitting rest. The average of three readings was used for the waist circumference and blood pressure measurements. Food intake was collected by 24-hour food recall (3-day recall before, and the same after intervention). A nutritionist completed questionnaires during face-to-face interviews. To assess energy and macronutrient intake, dietary data were analyzed using Nutritionist IV software (Version 4.1, First Databank Division, The Hearst Corporation, San Bruno, CA, USA).

After a 12 -h overnight fast, venous blood samples were collected. After centrifugation, the serum samples were frozen and stored at $-70\,^{\circ}C$.

All biochemical measurements were recorded in the Laboratory of Biochemistry, School of Public Health, Tehran University of Medical Sciences. IL-6 was measured with ELISA (using a kit from Orgenium Company, Finland). The method of measurement of hs-CRP was turbidimetry using Roche kits on the Cobas Auto analyzer. Fasting blood sugar (FBS) was measured by means of an enzymatic method (using a Hitachi 750 instrument, Elitech kit from Feppim Company, French).

SPSS (version 16; SPSS Inc, Chicago, IL, USA) was used for all statistical analyses. Descriptive statistics are presented as mean $\pm$ s.d. The normality of data was checked by the Kolmogorov–Smirnov test (K–S test). A paired *t*-test (in case of normal distribiution) or a nonparametric statistical test, Wilcoxon (in case of non-normal distribiution), was used for comparing data within groups. An independent *t*-test (in case of normal distribution) or a nonparametric statistical test, Mann–Whitney (in case of non-normal distribiution), was used for comparing data between two groups. Adjustment for differences in baseline covariates and changes in variables during the study were studied by means of analysis of covariance (ANCOVA). All tests were two-sided and *P*-values <0.05 were considered statistically significant.

RESULTS

Baseline characteristics were similar in the ALA and placebo groups (Table 1). No statistically significant differences were found for age, weight, height and disease duration between the two groups.

After the intervention period no significant reduction was found in IL-6 and hs-CRP levels. There was significant reduction in FBS, body weight, BMI, waist circumference, blood pressure, carbohydrate, protein, fat and energy intake (Table 2).

DISCUSSION

The present study shows that a 12-week supplementation with 600 mg ALA in chronic SCI male patients does not change IL-6 and hs-CRP levels but decreases fasting blood sugar, anthropometric indices, food intake and blood pressure. To our knowledge, this is the first study to investigate the effect of ALA supplementation on cardiovascular risk factors in men with chronic SCI.

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

Characteristics	*α-lipoic acid group*	*Placebo group*	P-*value*
Age (years)[a]	39 ± 6.44	36.8 ± 7.48	0.22
Disease duration (years)[a]	6.51 ± 2.73	6.31 ± 2.92	0.78
Weight (kg)[a]	77.11 ± 14.58	75.72 ± 15.15	0.72
Height (cm)[a]	165.68 ± 8.95	165.23 ± 9.29	0.85
BMI (kg m^{-2})[a]	27.77 ± 4.33	28.02 ± 5.09	0.84
Waist circumference (cm)[a]	101.79 ± 10.93	96.70 ± 13.48	0.12
Systolic blood pressure (mmHg)[b]	26.43 ± 9.98	123.50 ± 10.26	0.14
Diastolic blood pressure (mmHg)[b]	87.85 ± 9.94	82.50 ± 10.31	0.05
Energy intake (kcal per day)[a]	1574.1 ± 294.61	1527.4 ± 241.27	0.51
Carbohydrate intake (g per day)[a]	207.14 ± 50.40	206 ± 38.01	0.61
Protein intake (g per day)[a]	51.14 ± 13.38	50.86 ± 16.43	0.76
Fat intake (g per day)[a]	0.28 ± 10.86	54.36 ± 10.86	0.74
L-6 (pg ml^{-1})[a]	25.65 ± 15.84	23.51 ± 27.50	0.23
Hs-CRP (mg l^{-1})[a]	22.05 ± 26.96	26.72 ± 31.68	0.92
FBS (mg dl^{-1})[a]	102.43 ± 20.18	92.73 ± 16.76	0.05

Abbreviations: CRP, C-reactive protein; FBS, fasting blood sugar.
[a]Independent *t*-test.
[b]Mann–Whitney.

Our results indicate no significant effect of ALA supplementation on serum levels of IL-6 and hs-CRP. Consistent with the present study, in a randomized, placebo-controlled clinical trial, Ramos *et al.*[6] studied the effect of tocopherol (666 IU) and lipoic acid (LA; 600 mg) combination in patients with chronic renal failure for 2 months but found no significant change in IL-6 and hs-CRP. In contrast, in two studies by Sola *et al.*[4] (Clinical trial, 300 mg LA, 4 weeks, in subjects with metabolic syndrome) and Khabbazi *et al.*[5] (Clinical trial, 600 mg ALA, 8 weeks, in patients with ESRD on hemodialysis) ALA supplementation reduced IL-6 and CRP (%18.7) levels, respectively. As mentioned, there are major differences between our study participants and those in other studies, such as changes in lifestyle, body composition and fat mass,[20] that predispose them to show different responses to the same interventions.

We found significant effect of ALA supplementation on FBS in SCI patients. Evidence suggests that this effect of ALA may be mediated by increasing GLUT-4 transportation to muscle and fat cell membranes and increasing glucose uptake.[23] An intravenous injection of 1000 mg LA improves insulin sensitivity and insulin-stimulated metabolic clearance rate in patients with type II diabetes.[24] Another study reported a positive effect of oral administration of supplemental LA on insulin sensitivity and metabolic clearance rate in patients with type II diabetes.[25] In a randomized, double-blind, placebo-controlled clinical trial, Ansar *et al.*[26] noted that ALA supplementation (300 mg, 8 weeks) could improve FBS and insulin resistance in patients with type II diabetes.

Our result shows that a 12-week ALA supplementation has beneficial effects on anthropometric indices (body weight, BMI and waist circumference) and food intake in SCI patients. There is a large body of growing evidence showing that LA can have a substantial role in the regulation of food intake and anthropometric indices by suppressing appetite and elevating energy metabolism.[8,9,11,12] In agreement with our study there are two human studies; in a randomized, double-blind, placebo-controlled, 20-week trial, 1800 mg LA reduced body weight significantly more than did 1200 mg LA and placebo in 360 obese individuals.[10] In a case series study by Kim *et al.*,[9] the effect of LA on body weight gain induced by antipsychotics in schizophrenic patients was studied ($N=7$, 1200 mg

Table 2 Anthropometric, hypertension, dietary, and serum variables of subjects of study before and after α-lipoic acid supplementation and changes in variables during the intervention

Characteristics	*α-lipoic acid group*				*Placebo group*				P-*value*[b]
	Before intervention	*After intervention*	P-*value*[a]	*Changes*	*Before intervention*	*After intervention*	P-*value*[a]	*Changes*	
Weight (kg)[c,d]	77.11 ± 14.58	73.3 ± 13.7	0.001	−3.7 ± 4.4	75.72 ± 15.15	76.1 ± 14.7	0.14	0.38 ± 1.4	0.001
BMI (kg m^{-2})[c,d]	27.77 ± 4.33	26.6 ± 4.1	0.001	−1.0 ± 0.6	28.02 ± 5.09	28.1 ± 5.1	0.44	0.09 ± 0.6	0.001
Waist circumference (cm)[c,d]	101.79 ± 10.93	98.0 ± 10.4	0.001	−3.7 ± 2.7	96.70 ± 13.48	97.1 ± 13.8	0.13	0.4 ± 1.4	0.001
Systolic blood pressure (mm Hg)[e,f]	126.43 ± 9.98	116.9 ± 11.7	0.001	−9.4 ± 9.3	123.50 ± 10.26	125.3 ± 10.4	0.22	1.8 ± 7.3	0.001
Diastolic blood pressure (mmHg)[e,f]	87.85 ± 9.94	78.7 ± 10.5	0.001	−9.1 ± 10.7	82.50 ± 10.31	84.6 ± 9.9	0.11	2.1 ± 6.9	0.001
Energy intake (kcal per day)[c,d]	1574.1 ± 294.61	1415.6 ± 222.7	0.001	−158.4 ± 119.3	1527.4 ± 241.27	1559.2 ± 313.6	0.33	31.8 ± 177.8	0.001
Carbohydrate intake (g per day)[c,d]	200.14 ± 50.40	182.7 ± 38.2	0.001	−17.4 ± 17.0	206 ± 38.01	205.2 ± 43.0	0.84	−0.73 ± 19.8	0.001
Protein intake (g per day)[c,d]	48.14 ± 13.38	41.4 ± 13.0	0.001	−6.7 ± 7.4	9.86 ± 16.43	51.0 ± 13.0	0.57	1.13 ± 10.9	0.002
Fat intake (gr per day)[c,d]	55.28 ± 10.86	45.2 ± 6.8	0.001	10.0 ± 7.6	54.36 ± 10.86	57.3 ± 12.0	0.11	2.9 ± 9.7	0.001
IL-6 (pg per ml)[e,g]	25.65 ± 15.84	24.0 ± 16.8	0.17	−1.6 ± 6.5	23.51 ± 27.50	22.4 ± 27.1	0.08	1.0 ± 4.3	0.97
Hs-CRP (mg l^{-1})[e,g]	22.05 ± 26.96	7.8 ± 19.9	0.24	4.2 ± 25.6	26.72 ± 31.68	27.9 ± 30.2	0.57	1.2 ± 24.2	0.23
BS (mg dl^{-1})[c,g]	102.43 ± 20.18	80.8 ± 13.6	0.001	−21.5 ± 15.1	92.73 ± 16.76	2.4 ± 15.9	0.93	0.3 ± 20.5	0.001

[a]*P*-value for comparisons within groups.
[b]*P*-value for comparisons between groups changes.
[c]Paird *t*-test.
[d]Independent *t*-test.
[e]Wilcoxon.
[f]Mann–Whitney.
[g]ANCOVA adjusted for weight changes.

LA, 12 weeks). Mean weight loss was 3.2 kg and a remarkable reduction in BMI was observed. Neither of the aforementioned studies measured food intake and only the latter assessed BMI changes with a small sample size. These limitations make it difficult to compare our results with those of other studies. ALA-induced appetite suppression is likely the major cause of changes in anthropometric indices in our study.

We found significant reduction in systolic and diastolic blood pressure after 12 weeks of LA supplementation in SCI patients. It has been suggested that LA affects blood pressure by increasing reduced glutathione (GSH) levels in tissues. It is thought to work by affecting glutathione peroxidase activity and elevating nitric oxide production in endothelial cells.[3,7,27] Several animal studies introduced LA as a blood pressure regulator.[28–32] In a randomized clinical trial, Mazloom and Ansar[33] reported that systolic and diastolic blood pressure significantly improved following 8 weeks of 300 mg LA supplementation in type II diabetes patients. Noori *et al.*[34] observed significant reduction in systolic blood pressure but no change in diastolic blood pressure after 12 weeks of combined administration of LA (800 mg) and pyridoxine (80 mg) in patients with diabetic nephropathy. Two prior studies showed contrasting result to our findings. In one study, Sola *et al.*[4] examined the effect of LA, Irbesartan and their combination vs placebo in patients with metabolic syndrome, but found no significant effect on blood pressure. In the second study, the impact of LA on endothelial function and proteinuria in quinapril-treated diabetic patients with stage I hypertension was assessed and found to not have a significant effect on blood pressure.[35] A possible contributing factor to the difference found between our clinical trial and the two aforementioned contrasting studies could be the inherent physical differences associated with our patients with SCI.

Several limitations must be considered in the interpretation of our findings, including limited duration of the clinical trial and the sample size. Furthermore, because of budget limitation we were not able to include healthy individuals and compare the results of SCI patients with them, and measure other inflammatory markers or total antioxidant capacity. It seems to be a need for further studies.

In conclusion, on the basis of the present study results, it can be concluded that ALA supplementation (600 mg, 12 weeks) improves FBS, anthropometric indices, food intake and blood pressure but has no effect on measured inflammatory markers in men with chronic SCI.

DATA ARCHIVING

There were no data to deposit.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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1 Packer L, Witt EH, Tritschler HJ. Alpha-lipoic acid as a biological antioxidant. *Free Radic Biol Med* 1995; **19**: 227–250.
2 Packer L, Roy S, Sen CK. α-Lipoic acid: a metabolic antioxidant and potential redox modulator of transcription. *Adv Pharmacol* 1996; **38**: 79–101.
3 Packer L. alpha-Lipoic acid: a metabolic antioxidant which regulates NF-kappa B signal transduction and protects against oxidative injury. *Drug Metab Rev* 1998; **30**: 245–275.

4 Sola S, Mir MQS, Cheema FA, Khan-Merchant N, Menon RG, Parthasarathy S *et al.* Irbesartan and lipoic acid improve endothelial function and reduce markers of inflammation in the metabolic syndrome. *Circulation* 2005; **111**: 343–348.
5 Khabbazi T, Mahdavi R, Safa J, Pour-Abdollahi P. Effects of alpha-lipoic acid supplementation on inflammation, oxidative stress, and serum lipid profile levels in patients with end-stage renal disease on hemodialysis. *J Ren Nutr* 2011; **10**: 10.
6 Ramos LF, Kane J, McMonagle E, Le P, Wu P, Shintani A *et al.* Effects of combination tocopherols and alpha lipoic acid therapy on oxidative stress and inflammatory biomarkers in chronic kidney disease. *J Ren Nutr* 2011; **21**: 211–218.
7 Heitzer T, Finckh B, Albers S, Krohn K, Kohlschutter A, Meinertz T. Beneficial effects of alpha-lipoic acid and ascorbic acid on endothelium-dependent, nitric oxide-mediated vasodilation in diabetic patients: relation to parameters of oxidative stress. *Free Radic Biol Med* 2001; **31**: 53–61.
8 Kim MS, Park JY, Namkoong C, Jang PG, Ryu JW, Song HS *et al.* Anti-obesity effects of α-lipoic acid mediated by suppression of hypothalamic AMP-activated protein kinase. *Nat Med* 2004; **10**: 727–733.
9 Kim E, Park DW, Choi SH, Kim JJ, Cho HS. A preliminary investigation of alpha-lipoic acid treatment of antipsychotic drug-induced weight gain in patients with schizophrenia. *J Clin Psychopharmacol* 2008; **28**: 138–146.
10 Koh EH, Lee WJ, Lee SA, Kim EH, Cho EH, Jeong E *et al.* Effects of alpha-lipoic Acid on body weight in obese subjects. *Am J Med* 2011; **124**: e1–e8.
11 Seo EY, Ha AW, Kim WK. alpha-Lipoic acid reduced weight gain and improved the lipid profile in rats fed with high fat diet. *Nutr Res Pract* 2012; **6**: 195–200.
12 Prieto-Hontoria PL, Perez-Matute P, Fernandez-Galilea M, Barber A, Martinez JA, Moreno-Aliaga MJ. Lipoic acid prevents body weight gain induced by a high fat diet in rats: effects on intestinal sugar transport. *J Physiol Biochem* 2009; **65**: 43–50.
13 Johnson RL, Brooks C, Whiteneck GG. Cost of traumatic spinal cord injury in a population-based registry. *Spinal Cord* 1996; **34**: 470–480.
14 DeVivo MJ. Causes and costs of spinal cord injury in the United States. *Spinal Cord* 1997; **35**: 12.
15 Frost F, Roach MJ, Kushner I, Schreiber P. Inflammatory C-reactive protein and cytokine levels in asymptomatic people with chronic spinal cord injury. *Arch Phys Med Rehabil* 2005; **86**: 312–317.
16 Yekutiel M, Brooks M, Ohry A, Yarom J, Carel R. The prevalence of hypertension, ischaemic heart disease and diabetes in traumatic spinal cord injured patients and amputees. *Spinal Cord* 1989; **27**: 58–62.
17 McDonald CM, Abresch-Meyer AL, Nelson MD, Widman LM. Body mass index and body composition measures by dual x-ray absorptiometry in patients aged 10 to 21 years with spinal cord injury. *J Spinal Cord Med* 2007; **30**: S97.
18 Gupta N, White K, Sandford P. Body mass index in spinal cord injury–a retrospective study. *Spinal Cord* 2005; **44**: 92–94.
19 Guadalupe B, Gabriel G-S, Antonio I, David C, Villalon CM. Cardiovascular alterations after spinal cord injury: an overview. *Curr Med Chem Cardiovasc Hematol Agents* 2004; **2**: 133–148.
20 Buchholz AC, Bugaresti JM. A review of body mass index and waist circumference as markers of obesity and coronary heart disease risk in persons with chronic spinal cord injury. *Spinal Cord* 2005; **43**: 513–518.
21 Garshick E, Kelley A, Cohen S, Garrison A, Tun C, Gagnon D *et al.* A prospective assessment of mortality in chronic spinal cord injury. *Spinal Cord* 2005; **43**: 408–416.
22 Mahan LK, Escott-Stump S, Raymond JL, Krause MV Krause's food & the nutrition care process: Elsevier Health Sciences; 2012, Appendix 20, Indirect methods for measuring hight, page 1065.
23 Singh U, Jialal I. Alpha-lipoic acid supplementation and diabetes. *Nutr Rev* 2008; **66**: 646–657.
24 Jacob S, Henriksen E, Schiemann A, Simon I, Clancy D, Tritschler H *et al.* Enhancement of glucose disposal in patients with type 2 diabetes by alpha-lipoic acid. *Arzneimittelforschung* 1995; **45**: 872.
25 Jacob S, Ruus P, Hermann R, Tritschler HJ, Maerker E, Renn W *et al.* Oral administration of RAC-alpha-lipoic acid modulates insulin sensitivity in patients with type-2 diabetes mellitus: a placebo-controlled pilot trial. *Free Radic Biol Med* 1999; **27**: 309–314.
26 Ansar H, Mazloom Z, Kazemi F, Hejazi N. Effect of alpha-lipoic acid on blood glucose, insulin resistance and glutathione peroxidase of type 2 diabetic patients. *Saudi Med J* 2011; **32**: 584–588.
27 Hagen TM, Moreau R, Suh JH, Visioli F. Mitochondrial decay in the aging rat heart. *Ann NY Acad Sci* 2002; **959**: 491–507.
28 Vasdev S, Ford CA, Parai S, Longerich L, Gadag V. Dietary alpha-lipoic acid supplementation lowers blood pressure in spontaneously hypertensive rats. *J Hypertens* 2000; **18**: 567–573.
29 Vasdev S, Gill V, Longerich L, Parai S, Gadag V. Salt-induced hypertension in WKY rats: prevention by alpha-lipoic acid supplementation. *Mol Cell Biochem* 2003; **254**: 319–326.
30 Vasdev S, Gill V, Parai S, Gadag V. Dietary lipoic acid supplementation attenuates hypertension in Dahl salt sensitive rats. *Mol Cell Biochem* 2005; **275**: 135–141.
31 Vasdev S, Gill VD, Parai S, Gadag V. Effect of moderately high dietary salt and lipoic acid on blood pressure in Wistar-Kyoto rats. *Exp Clin Cardiol* 2007; **12**: 77–81.
32 El Midaoui A, de Champlain J. Prevention of hypertension, insulin resistance, and oxidative stress by alpha-lipoic acid. *Hypertension* 2002; **39**: 303–307.
33 Mazloom Z, Ansar H. The effect of alpha-lipoic acid on blood pressure in type 2 diabetics. *Iranian J Endocrinol Metab* 2009; **11**: 245–250.
34 Noori N, Tabibi H, Hosseinpanah F, Hedayati M, Nafar M. Effects of combined lipoic acid and pyridoxine on albuminuria, advanced glycation end-products, and blood pressure in diabetic nephropathy. *Int J Vitam Nutr Res* 2013; **83**: 77–85.
35 Rahman ST, Merchant N, Haque T, Wahi J, Bhaheetharan S, Ferdinand KC *et al.* The impact of lipoic acid on endothelial function and proteinuria in quinapril-treated diabetic patients with stage I hypertension: results from the QUALITY study. *J Cardiovasc Pharmacol Ther* 2012; **17**: 139–145.