ORIGINAL ARTICLE

Alpha-lipoic acid reduces body weight and regulates triglycerides in obese patients with diabetes mellitus

Azra Okanović[1], Besim Prnjavorac[2,3], Edin Jusufović[4,5], Rifat Sejdinović[2, 6]

[1]Health Centre Tešanj, [2]Department for Internal and Lung Diseases of General Hospital Tešanj, [3]Pharmaceutical Faculty of University in Sarajevo, [4]Polyclinic for Pulmonary Diseases of Health and Educational Institution "Dr. Mustafa Šehović" Tuzla, [5]Medical School of University in Tuzla, [6]Faculty of Health Care, University in Zenica; Bosnia and Herzegovina

ABSTRACT

Aim To determine an influence of alpha-lipoic acid to reduction of body weight and regulation of total cholesterol concentration, triglycerides and glucose serum levels in obese patients with diabetes mellitus type 2.

Methods A prospective study includes two groups of obese patients with diabetes mellitus and signs of peripheral polyneuropathia: examined group (30 patients; 15 females and 15 males), and control group (30 patients; 12 females and 18 males). All were treated with metformin (850-1700 mg/day). Examined patients were additionally treated with alpha-lipoic acid 600 mg/day during 20 weeks. Body mass index and concentrations of total cholesterol, triglycerides and glucose in serum were compared before and after the treatment.

Results The group treated with 600 mg alpha-lipoic acid lost significantly more weight, and had lower triglyceride level than the control group. There were no significant differences in total cholesterol and glucose serum levels between the groups.

Conclusion Alpha-lipoic acid of 600 mg/day treatment have influenced weight and triglycerides loss in obese patients with diabetes mellitus type 2. It should be considered as an important additive therapy in obese patients with diabetes mellitus type 2.

Key words: body mass index, serum glucose, lipid status.

Corresponding author:
Besim Prnjavorac
Department of Internal and Lung disease,
General Hospital Tešanj
Braće Pobrića 17, 74260 Tešanj, Bosnia and Herzegovina
Phone: +387 32 650 662;
Fax: +387 32 650 605;
E-mail: pbesim@bih.net.ba

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INTRODUCTION

Most patients with diabetes mellitus type 2 suffer from disorders of lipoprotein metabolism as well as obesity (1). Diabetic dyslipoproteinemia is characterised with increased levels of total cholesterol, low density lipoproteins (LDL) and triglycerides, as well as decreased level of high density lipoproteins (HDL) (1-3). Lipid metabolic changes and obesity are both strong and intensive risk factors for developing complications, first of all microvascular ones (1,4). Therefore, it is very important to correct properly metabolism disorders of lipoprotein and obesity in diabetes mellitus type 2 patients (1,3).

Alpha lipoic acid is established in many studies as a protector against oxidative damage cells, which is described in diabetes mellitus patients (5) and positively influences the regulation level of glucose (6) and reduces blood lipids (total cholesterol, LDL, and triglycerides (7). It has been shown that that alpha-lipoic acid markedly reduces body weight gain in rodents (8), but also in humans (9-11). Also, alpha-lipoic acid has shown to be effective in reducing symptoms of diabetic polyneuropathy without serious adverse effects (12,13).

The usual daily intake of alpha lipoic acid by foods (muscles, heart, kidney, liver) is quite low in order to achieve a therapeutic effect in conditions of increased needs for this substance. (10). Therefore, the potential health implications of alpha lipoic acid have been investigated in clinical practice in countries such as Germany and Korea (14) with multicentric trials currently ongoing in Europe and North America (15). These studies have included products containing alpha lipoic acid in a very wide range of doses, ranging 50-1800 mg/day (2,6, 9-13, 16-19).

The aim of this study was to examine the effect of alpha lipoic acid in reducing body weight, the regulation of lipid status, as well as the regulation of glucose in blood in obese patients with diabetes mellitus type 2.

PATIENTS AND METHODS

This prospective study has been done in Public Health Centre Tešanj, Bosnia and Herzegovina, in the period from May to September 2013. Sixteen obese patients with diabetes mellitus type 2 and signs of peripheral neuropathy were included. All were treated with metformin (850 to 1700 mg/day) and divided into 2 groups: examined (30; 25 females and 5 males) and control (30; 22 females and 8 males). Control patients were additionally treated with alpha-lipoic acid of 600 mg/day during 20 weeks. Body mass index and serum concentrations of glucose, cholesterol and triglycerides were measured and compared before and after the treatment, as well as between examined and control group. Body mass index was calculated from body weight and height according to the formula:

$$\textbf{BMI (kg/m}^2\textbf{) = Weight (kg) / Height (m)}^2\textbf{.}$$

Referral values of observed parameters were: body mass index 18.50-24.99, concentration of glucose 4.4-6.1 mmol/L, concentration of cholesterol 3.1-5.7 mmol/L and concentration of triglycerides 0.34-2.3 mmol/L.

The distribution of values was determined by D'Agostino test. Mean values were shown as mean ± standard deviation. Student's t-test, Mann-Whitney test, Fisher's test and χ^2 test, with double and single orientation, are used for calculating the difference between the groups.

ANOVA test was used to calculate relative differences of variance of the distribution between the variables. Statistical hypotheses were tested at the level of α=0.05, and the difference between the groups was considered significant if $p<0.05$ or less.

RESULTS

Sex distribution was similar in both groups (p=0.6042).

Age distribution was similar among patients between the groups for both genders, as well as after stratification to male and female patients. Also, age distribution was similar among male and female patients in both groups (experimental group: p=0.1691; control group: p=0.4541) (Table 1).

Table 1. Age and sex distribution in experimental and control group

Gender	No (%) of patients		Mean age ± standard deviation		p
	Experimental	Control	Experimental	Control	
Males	15 (50)	18 (60)	64.40±1.887	61.0±1.7	0.0955
Females	15 (50)	12 (40)	61.53±2.255	61.33±2.294	0.4755
Total	30 (100)	30 (100)	62.97±1.469	61.13±1.347	0.1808

Before the treatment, body mass index in both groups was similar (p>0.05).

Body mass index was significantly lower in experimental and control groups after the treatment ($p<0.001$ and $p=0.01$, respectively).

Body mass index was significantly lower in the group treated with metformin and alpha-lipoic than in the group treated with metformin only ($p<0.05$) (Figure 1).

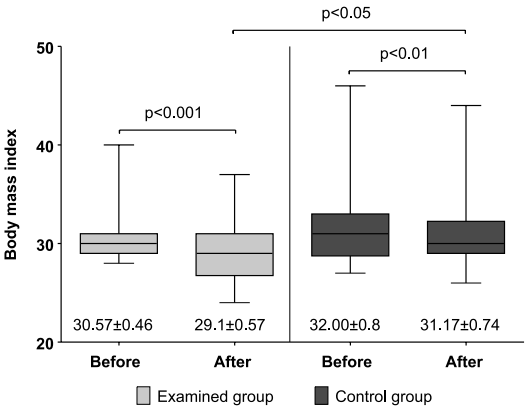

Figure 1. Body mass index in experimental and control group before and after the treatment

Serum concentration of triglycerides was similar in both groups before the treatment ($p>0.05$).

After the serum concentration of triglycerides was significantly lower in both groups (experimental group: $p<0.01$; control group: $p<0.05$).

After the treatment, serum concentration of triglycerides was significantly lower in the group treated with metformin and alpha-lipoic than the group treated with metformin only ($p<0.5$) (Figure 2).

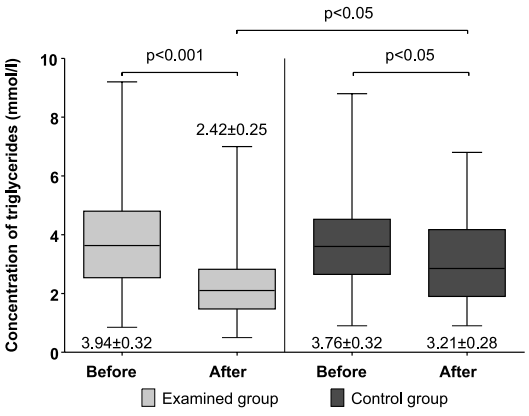

Figure 2. Serum concentration of triglycerides in experimental and control group before and after the observed period

Before and after the treatment, serum concentration of total cholesterol was similar in both groups ($p>0.5$).

Despite lowering of serum concentration of total cholesterol after the treatment, differences were not significant before and after the treatment in any of the two groups ($p>0.5$).

Also, despite lower concentration of total cholesterol after the treatment in the group treated with metformin and alpha-lipoic acid than in the group treated with metformin only, this difference was not significant ($p>0.05$)

Before, as well as after the treatment, serum concentration of glucose was similar in both groups ($p>0.05$).

After the treatment serum concentration of glucose was significantly lower compared to concentration before the treatment in both groups ($p<0.001$) (Figure 3).

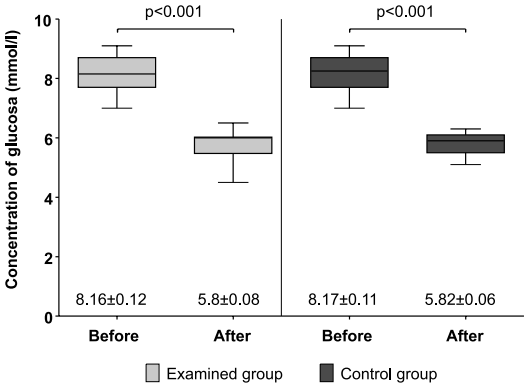

Figure 3. Serum concentration of glucose in experimental and control group before and after the observed period

Achievement referral values of body mass index, concentration of tryglicerides, as well as glucose, before and after the treatment were similar ($p=0.0562$, $p=0.0602$ and $p=0.5$, respectively) (Figure 4).

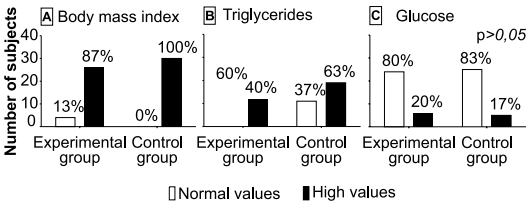

Figure 4. Achievement referral values (Normalisation) of body mass index (A), serum concentration of triglycerides (B) and serum concentration of glucose (C) after the treatment in experimental and control group.

DISCUSSION

There has been little research that would evaluate an effect of oral treatment of humans with diabetes mellitus type 2 with alpha lipoic acid so far

(2,9,10). Limited evidence from human studies suggests that alpha lipoic acid may be an effective body weight or lipid-lowering compound (20). To our knowledge, this is the first study in Bosnia and Herzegovina showing that alpha-lipoic acid treatment could lead to a significant weight reduction and regulate lipid status in obese patients with diabetes mellitus type 2. As a dietary supplement, alpha lipoic acid appears to have broad molecular specificity with an impressive array of metabolic benefits including protection against weight gain (10), diet-induced dyslipidemia (4,7), arterial lesion formation (5,18,19), and insulin resistance (21).

Our research included patients in experimental and control group with similar sex and age distribution, which led to a minimization of impact of these factors on metabolic and oxidative changes that could be possibly linked to sex differences or aging.

Several studies showed body weight loss and reduction of triglycerides serum concentration in obese patients with diabetes mellitus type 2 treated with alpha lipoic acid (4,9, 10-12). But, some of the studies showed that oral dose of 600 mg/day of alpha lipoic acid did not influence weight lost or normalization of lipid status (9). However, the dose of 600 mg/day applied intravenously led to a significant reduction in plasma free fatty acids, triglycerides, total cholesterol, LDL-cholesterol, oxidized LDL-cholesterol, and VLDL-cholesterol in obese patients treated for 2 weeks (21). Therefore, in most studies the patients were treated with 1200 mg/day or higher orally (2,6, 9-12, 16,18). In the randomized double-blind and placebo-controlled study during 20 weeks 360 obese individuals (body mass index 27-30 kg/m2 plus hypertension, diabetes mellitus, or hypercholesterolemia) were randomized to alpha-lipoic acid 1200 or 1800 mg/day or placebo. Reduction in body mass index was significantly greater in the 1800 mg/day alpha-lipoic acid group than in the placebo group, as was the percentage of patients who achieved a 5% reduction in baseline body weight (21.6% vs 10.0%) (9). In our research, patients who completed 20 weeks treatment with 600 mg/day of alpha-lipoic acid orally showed modest but significant reduction in body mass index and serum triglycerides concentration in comparison with the patients that were not treated with alpha lipoic acid. Hence our results are opposite to literature results with regard to orally administrated alpha-lipoic acid dose. However, 20 weeks treatment in our research was longer than in other studies and this might result in regulation of body weight and triglycerides. At the same time, after the observed period there were no differences in frequencies of normalized weight or triglyceride between the group treated with and group not treated with alpha-lipoic acid in our research. Considering literature studies (2,9,12,13,18) and results of our study, doses of alpha-lipoic acid higher than 600 mg/day could have more benefit in obese patients with diabetes mellitus type 2. Although the maximum tolerated dose of alpha-lipoic acid in human patients has not been well defined, some studies have suggested that humans can tolerate several grams per day of oral alpha-lipoic acid (9). Thus, this could be a part of another prospective research based on tolerance of alpha-lipoic acid.

In the majority of studies alpha-lipoic acid led to significant reduction of serum total cholesterol concentration in obese patients (3,4, 6-9). In our research the cholesterol concentration did not differ after the treatment with alpha-lipoic acid in comparison with baseline level at the beginning of the treatment. Possible reasons for this could be that the patients in our study were treated with 600 mg/day, but in majority of other studies this dose was pretty higher (9,10, 12-14, 18,21). Also considering low dose of alpha-lipoic acid, the treatment period (20 weeks) was relatively short in our study.

Although alpha lipoic acid regulates glucose concentration (2,6,8) in our study there were no differences between groups in glucose concentration after the treatment with alpha-lipoic acid. This could be explained with the fact that metformin, given in both groups, leads to a significant reduction of glucose levels in obese patients (22), as well as relatively low dose (600 mg/day) of alpha-lipoic acid; probable reason is a relatively short treatment period.

This research has several limitations. The duration of observed period (20 weeks) was relatively short. Furthermore, outpatients were not monitored intensively with regard to individual conducting of hypocaloric diet, which was prescribed in a similar way to all patients.

In conclusion, this study showed that 600 mg/day of oral alpha-lipoic acid was effective in achieving significant regulation of weight loss and serum triglycerides in obese patients with diabetes mellitus type 2, but without difference in frequencies of normalization in patients with and without alpha-lipoic acid. Alpha-lipoic acid may be effective as an additional treatment in obese patients with diabetes mellitus type 2, but further studies are required to determine an adequate dosage of alpha-lipoic acid as well as long-term safety and efficacy.

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TRANSPARENCY DECLARATION

Competing interests: None to declare.

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Alfa-lipoična kiselina smanjuje tjelesnu masu i regulira koncentraciju triglicerida u gojaznih pacijenata sa šećernom bolešću

Azra Okanović[1], Besim Prnjavorac[2,3], Edin Jusufović [4,5], Rifat Sejdinović [2,6]

[1]Dom zdravlja Tešanj, [2]Odjeljenje za interne i plućne bolesti Opće bolnice Tešanj, [3]Farmacijski fakultet Univerziteta u Sarajevu, [4]Poliklinika za plućne bolesti Zdravstveno-nastavne ustanove "Dr. Mustafa Šehović" Tuzla, [5]Medicinski fakultet Univerziteta u Tuzli, [6]Univerzitet u Zenici; Bosna i Hercegovina

SAŽETAK

Cilj Utvrditi utjecaj alfa-liponske kiseline na smanjenje tjelesne mase i regulaciju koncentracije ukupnog holesterola, triglicerida i glukoze u gojaznih osoba sa šećernom bolešću tipa 2.

Metode Prospektivno istraživanje uključilo je dvije grupe gojaznih osoba sa šećernom bolešću i znakovima periferne polineuropatije: ispitivana grupa (30 pacijenata, odnosno 15 žena i 15 muškaraca) i kontrolna grupa (30 pacijenata, odnosno 12 žena i 18 muškaraca). Svi su bili tretirani metforminom (850-1700 mg/dan). Ispitanici u ispitivanoj grupi bili su dodatno tretirani alfa-liponskom kiselinom, 600 mg/dan tokom 20 sedmica. Indeks tjelesne mase i koncentracije ukupnog holesterola, triglicerida i glukoze u serumu uspoređivani su prije i poslije tretmana.

Rezultati Ispitanici tretirani alfa-liponskom kiselinom, u dozi od 600 mg/dan, imali su značajniji gubitak indeksa tjelesne mase, kao i triglicerida u poređenju s kontrolnom grupom. Nije bilo značajne razlike u koncentraciji ukupnog holesterola i glukoze u serumu između grupa.

Zaključak Tretman alfa-liponskom kiselinom, u dozi od 600 mg/dan, utječe na gubitak indeksa tjelesne mase i dovodi do snižavanja koncentracije triglicerida u gojaznih osoba sa šećernom bolešću tipa 2. Alfa-liponska kiselina treba biti uzeta u obzir kao važna dodatna terapija u gojaznih bolesnika sa šećernom bolešću tipa 2.

Ključne riječi: indeks tjelesne mase, serumska glukoza, lipidni status