THE EFFECTS OF OMEGA-3 FATTY ACIDS ON BLOOD HOMOCYSTEINE LEVEL IN TYPE 2 DIABETIC PATIENTS

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Abstract

INTRODUCTION: Diabetes is regarded as serious condition for both the individual and the society. Its rapidly increasing global prevalence is a significant cause for concern. One of the most important reasons of mortality in diabetic patients is atherosclerosis. Many epidemiologic studies have shown that the total homocysteine concentration is a risk indicator for cardiovascular disease. Studies have shown that its concentration is increased considerably in diabetes mellitus. Epidemiological data indicate that the consumption of omega-3 unsaturated fatty acids (n-3FA) leads to a reduction in cardiovascular disorders and may protect against metabolic diseases. In recent years, many have studied omega-3 fatty acids but still, it cannot be used as an additive. This study aimed to evaluate the effects of ω3 on homocysteine in type 2 diabetic patients.

METHODS: A randomized double blind placebo controlled clinical trial was conducted on 80 type 2 diabetic patients aged 45-85 years with diabetes for at least 2 years. Anthropometric indices including body mass index (BMI) and medical history were obtained. Diabetic patients were randomly assigned to either the case or the control group. Each subject received 3 capsules per day (omega-3 or placebo) for a period of 2 months. A sample of 10 ml blood was collected from each subject at the beginning and at the end of the study. Serum homocysteine was measured by Hitachi autoanalyzer with the Enzymatic Cycling method. Nutrient intake was estimated using 24-hour dietary recall questionnaire at the beginning and at the end of the trial for 2 days and analyzed by FPII. T-test was also used to compare the groups.

RESULTS: Comparison of mean ± SD (standard deviation) of BMI and food intake did not show any difference between the case and control groups. homocysteine levels were 3.10 μmol/lit and 0.126 μmol/lit in the case and control groups, respectively, and the difference was significant.

CONCLUSION: Omega-3 fatty acids supplementation (3 g/per day) in the form of capsules can decrease homocysteine content in diabetic patients.

Keywords: Type 2 diabetes mellitus, omega-3 fatty acid, homocysteine.

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Introduction

Diabetes is a serious condition for both the individual and the society. Its rapidly increasing global prevalence is a significant cause for concern. It is estimated that there will be 366 million people with diabetes in the adult population of the world in 2030, while in 2000, the total was 171 million.[1] One of the most important reasons for mortality in diabetic patients is atherosclerosis.[2] Many epidemiologic studies have shown that the total homocysteine concentration is a risk indicator for cardiovascular disease.[3]

Epidemiological data indicate that consumption of

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Omega-3 unsaturated fatty acids (n-3FA) lead to a reduction in cardiovascular disorders.[4]

In recent years, omega-3 fatty acids have been extensively studied, however, due to conflicting results as regards their effect on fat profile, they cannot be recommended with confidence as additive. The metabolic effect of omega-3 fatty acids in patients with type 2 diabetes is still a matter of debate. This study was carried out in Tehran University of Medical Sciences to evaluate and compare the effects of ω3 homocysteine in diabetic type 2 patients.

Materials and Methods

This is a randomized double blind placebo-controlled clinical trial of 80 type 2 diabetic patients, 45-85 years old. The patients had been diabetic for at least 2 years. Data on anthropometric indices including body mass index (BMI), as well as medical and drug history were obtained via face-to-face interviews. A patient had to meet the following criteria to be included in the study: not taking ω3 supplements, not having renal or hepatic disease, having no history of myocardial infarction and/or cancer, not taking drugs that interact with lipid profile. Written informed consent was obtained from all participants. The research protocol was approved by the Ethics Committee on Human Experimentation of Tehran University of Medical Sciences.

Given the results of previous studies on diabetic patients,[5] a dosage of 3 capsule gels of pure 0mega-3 fatty acids supplement per day for two months was adopted. The supplement was obtained from PBL company, US.

Omega-3 dose was 2714 mg (EPA=1548 mg, DHA=828 mg and 338 mg other omega-3) for 3 capsules gels and placebo consisted of 3 capsules containing 2100 mg sunflower oil (12% SFA, 65% linoleic acid, 23% MUFA). Placebo capsules looked identical and were especially prepared for this study by Zakaria Co.

Diabetic patients were stratified by sex and randomly assigned to either the case or the control group. Each subject received 3 capsules per day for a period of 2 months. After 12-14 h overnight fasting, between 8 and 10 a.m. and before taking oral hypoglycemic agent(s), 10 ml blood was collected from each subject at the beginning and at the end of the 2-month trial. Blood samples were aliquoted of serum then immediately stored at -70 °C for subsequent analyses.

Homocysteine was measured by Hitachi autoanalyzer with Enzymatic Cycling method. Nutrient intakes were estimated using 24-hour dietary recall questionnaires at the beginning and at the end of the trial for 2 days and analyzed by Food Processor ver.2 software. The subjects were asked not to alter their usual diets and physical activity throughout the study and any changes in their medication were avoided.

Statistical analysis

All values are expressed as mean ± S.D (standard deviation). Differences between the two groups were determined using t-test for group data. P values less than 0.05 were considered to be statistically significant. All data were analyzed using SPSS.

Results

As shown in Table 1, the groups were similar with respect to the sex, age, duration of diabetes and body mass index (BMI) at the beginning of the study. Table 2 shows the energy and nutrient intake before and after intervention; it seems that there were no changes during the study, thus all changes at the end of study would be related to omega-3 consumptionTable 3 shows the serum homocysteine concentration before and after supplementation for subjects who completed the study. Following 2 months of supplementation, serum levels of homocysteine changed significantly in the case group (Table 3).

TABLE 1. Demographic, anthropometric and biological data in case and control groups.

	Case	Control
N	41	40

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Age (years)	56.38±9.24	52.7±10.65
Duration of diabetes (years)	8.72	8.02
BMI (Kg/m^2)	27.78±3.41	28.09±5.03

Data are expressed as means ± SD.

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TABLE 2. 24-hour recall for case and control group.

	Before intervention	after intervention
Total Calorie (kcal)		
Case group	1212.88±270.2	1216.65±407.33
Control group	1203.77±352.91	1311.92±423.12
Total Fat(g/day)		
Case group	35.5± 16.3	37.6±12.6
Control group	36.07±11.8	37.9±13
Polyunsaturated fatty acid (g/day)		
Case group	7.23±5.9	7.19±5.9
Control group	7.50±5.4	7.60±4.7
Cholesterol (g/day)		
Case group	151.23±1.57	144.69± 1.37
Control group	140.97 ±6.5	144.04 ± 6.2
Vitamin B12 (µg)		
Case group	12.13±1.19	11.83±1.08
Control group	13.02±3.6	12.59±2.65
Folate(µg)		
Case group	191.16±86.8	191.16±86
Control group	216±44.2	213±63.02

Independent t-test was used
P values <0.05: significant
Data are expressed as means ± SD

TABLE 3. Levels of homocysteine and malondialdehyde before and after 2 months ω3 supplementation in type 2 diabetic patients

Homocysteine (µmol/lit)	Before	After	Difference	P value
Case group	14.40±4.07	11.29±2.1	3.10±2.7	0.000
Control group	13.39±2.45	13.29±2.44	0.13±1.9	NS

Data are expressed as means ± SD
P value <0.05: Statistically significant
Independent and paired t-test were used

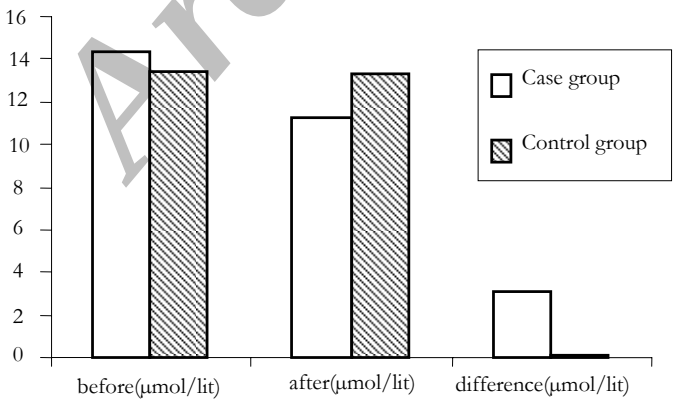

FIGURE 1. Levels of homocysteine before and after 2 months of ω3 supplementation in type 2 diabetic patients.

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Conclusion

Homocysteine levels decreased significantly in the case group at the end of the trial and a significant difference was found between case and control groups, suggesting that using ω3 without any supplements can decrease homocysteine. The changes in total homocysteine and NO(x) plasma concentrations were observed after 8 weeks of supplementation with omega-3 by Piolot et al. ($r=0.78$, $P<0.001$); the latter study reported for the first time the apparent action of n-3 fatty acids and nitric oxide on homocysteine metabolism in healthy individuals.[6]

The observation of Li.D and Zeman showed the same results as our study.[7,8] Zeman showed that n-3 PUFA supplementation together with statin + fibrate combination in diabetic patients can significantly decrease serum homocysteine.[8] Baro found that simultaneous daily intake of n -3 PUFA and oleic acid-supplemented skimmed milk plus folic acid and B-type vitamins would cause a decrease in homocysteine content.[9]

We did not observe any significant change in folate or vitamin B12 content, so we conclude that omega-3 fatty acid supplementation (3 g/per day) in the form of capsules can decrease homocysteine in diabetic patients.

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