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Does Omega-3 Fatty Acid Supplementation Have Beneficial Effects on Plasma Homocysteine, Insulin Resistance and Lipid Profile of Type 2 Diabetic Patients? A Randomized Clinical Trial

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ABSTRACT

Background: This study was conducted to determine the effects of n-3 PUFAs supplementation on plasma homocysteine (Hcy) level, lipid profile and insulin resistance in patients with type 2 diabetes (T2D). **Methods:** This study is a double-blind controlled trial involving 70 patients with T2D selected from Yazd Diabetes Research Center in 2013. Patients were randomly assigned to receive either 2 g/day omega-3 soft gels (OG) or 2 g/day placebo (PG) for 6 weeks. At the beginning and end of the study, Hcy concentration, fasting plasma glucose (FBG), fasting plasma insulin, total cholesterol (TC), triglycerides (TG), low density lipoprotein cholesterol (LDL-c), high density lipoprotein cholesterol (HDL-c), HDL-c/LDL-c ratio, insulin resistance (HOMA-IR), insulin sensitivity (IS) and beta-cell function were measured and compared. **Results:** Sixty five participants completed the study. The results of this study showed that omega-3 fatty acid supplementation caused significant increase in Hcy (P = 0.007) and LDLc (P = 0.02), while HDLc and HDLc/LDLc ratio were significantly decreased (P = 0.001 and 0.006, respectively). In both groups, insulin and HOMA-IR were increased, while IS decreased significantly. Beta-cell function was increased only in OG (P = 0.005). There was no significant difference in mean change of any factors. **Conclusion:** The present study found no beneficial effects of 2 g/day omega-3 supplement for 6 weeks on biomarkers of Hcy, FBG, insulin and lipid profile in th T2D patients.

Key words: *Type 2 diabetes; Homocysteine; Omega-3; Lipid profiles; HOMA-IR.*

Introduction

Type 2 diabetes (T2D) has been declared "the epidemic of the 21st century" affecting approximately 347 million people worldwide (Danaei *et al.*, 2011). Its rapidly increasing global prevalence is a primary cause of concern (Huang *et al.*, 2012) as it is anticipated to be the 7th leading cause of death in 2030 (WHO, 2011). Diabetes and hyperglycemia cause vascular damage and impaired lipid profile, particularly increased susceptibility to peroxidation. These factors result

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in atherosclerosis, which can lead to decreased blood flow to the heart muscle or brain (Buse *et al.*, 2007).

Homocysteine (Hcy) is a sulfur containing amino acid [COOHCH (CH2CH2SH) NH3] that is produced by the metabolism of methionine in the body and does not participate in the building of proteins (McDowell and Lang, 2000). It is known as an independent risk factor for cardiovascular disease (CVD) (Huang *et al.*, 2012). Recent evidence suggests that high levels of fasting Hcy may be a direct participant of different diseases, including brain atrophy, cognitive impairment and possibly Alzheimer's disease (Sachdev, 2004), diabetic nephropathy (House *et al.*, 2010), stroke and vascular-heart disease (Elias and Eng, 2005, Smulders and Blom, 2011). Hcy has been considered to play an important role in vascular injury, resulting in the development of peripheral and coronary arterial disease (Elias and Eng, 2005). Mild homocysteinemia is an independent risk factor for atherosclerosis, atherothrombosis and may even increase the risk of CVD in people with T2D (Smulders and Blom, 2011, Zeman *et al.*, 2006). On the other hand, in patients with T2D, serum Hcy levels are higher than normal, which is associated with endothelial dysfunction, insulin resistance, diabetic nephropathy and prothrombosis (Huang *et al.*, 2012). High Hcy levels may independently play a direct causative role in the pathogenesis of T2D obesity and metabolic syndrome by promoting oxidative stress, systematic inflammation and endothelial dysfunction (Hofmann *et al.*, 2001, Stamler *et al.*, 1993, Weiss *et al.*, 2003). In human studies, plasma Hcy levels were strongly associated with insulin concentration. As such, this association may also help to explain the discrepancy between plasma Hcy levels in diabetic patients and in healthy ones (Elias and Eng, 2005).

N-3 polyunsaturated fatty acids (n-3 PUFAs), particularly eicosapentaenoic acid (EPA, C 20:5 n-3) and docosahexaenoic acid (DHA, C 20:6 n-3), found in fish oil are known to have potential anti-atherosclerotic effects and anti-inflammatory properties and also reduce deaths due to CVD (D'Alessandro *et al.*, 2002, Grundt *et al.*, 2003). In addition, a high intake of marine n-3 PUFAs is associated with lower risk of CVD (Yokoyama *et al.*, 2007). In non- diabetic people, supplementation with n- 3 PUFAs have potential protective effects on cardiovascular system, such as anti-inflammatory effects, fixing atherosclerotic plaques, increasing fibrinolysis, anti-thrombotic effects and lowering of blood pressure (Hartweg *et al.*, 2007). There is a low prevalence of diabetes in Greenland and Alaskan Eskimos; populations known for a very high intake of n-3 PUFAs (De Caterina *et al.*, 2007). Based on previous researches, supplementation with n-3 PUFAs have been suggested as one of the methods of reducing Hcy levels (Grundt *et al.*, 2003, Huang *et al.*, 2012). In recent years, several studies regarding n-3 fatty acids have been conducted, but none of them have been able to completely show its effects on diabetes patients. However, the results of n-3 PUFAs effects on Hey are still contradictory (De Caterina *et al.*, 2007, Huang *et al.*, 2012). Several clinical trials with small sample size and short duration of the effect of n-3 PUFAs on plasma Hcy have been performed (De Caterina *et al.*, 2007, Selhub, 1999, Zeman *et al.*, 2006). While few studies have been conducted on T2D (De Caterina *et al.*, 2007).

The mechanism of action of n-3 PUFAs on blood Hcy is yet to be well understood. N-3 PUFAs effects on vascular endothelial function can neutralize the effect of Hcy (Grundt *et al.*, 2003). But on the other hand, some studies asserted that supplementation with n-3 PUFAs may lead to increase in oxidative stress (Saedisomeolia *et al.*, 2009). Therefore, the present study was carried out to determine the effect of n-3 PUFAs supplementation on Hcy, lipid and glycemic profile in T2D patients.

Materials and Methods

Patients and study design: This study is a double-blind controlled trial involving 70 patients with T2D selected from Yazd Diabetes Research Center in 2013. Inclusion criteria included: (1) less than 60 years, (2) diagnosed diabetes, (3) a

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minimum of 5 years' experience in diabetes, (4) without any kidney, liver, heart, thyroid or bleeding disorders and malignancies, (5) not taking omega-3 supplementation during recent month, (6) without insulin therapy and (7) not pregnant or lactating. Exclusion criteria included: (1) taking less than 80% of the capsules, (2) changing the type and dose of routine medicines and (3) consumption of B vitamins supplementations during the study. Patients were randomly assigned into 2 groups, and they received either omega-3 soft gels (OG) or placebo (PG).

In previous studies, supplementation dose ranged from 200 to 6 g/day (Huang *et al.*, 2011), but based on similar studies, an effective dose at 2 g/day was intended for this study. The OG received was 2 g/day omega-3 soft gels (Zahravi Pharmaceutical Co, Tabriz, Iran, consists of 240 mg of DHA, 360 mg EPA) and the PG received was 2 g/day placebo (Zahravi Pharmaceutical Co, Tabriz, Iran). The duration of our intervention was 6 weeks. Participants were asked not to change their lifestyle, diet, dietary patterns, physical activity and medication within the intervention. During this study, each person compulsorily took 84 capsules. At the beginning of the study, half of the capsules (42 capsules) were given to participants. After 3 weeks, they were invited to receive the second package of soft gels (another 42 soft gels). During the second session, residual capsules were counted. After completion of intervention, the remaining capsules were counted again.

Measurements: General information questionnaire including age, height, weight, sex, occupation, duration of disease, blood pressure, type and dose of medication etc., was completed. To evaluate anthropometric indices, weight was measured using digital scale (Seca, Germany) with minimal clothing and accuracy of 100 g, and height was measured with a stadiometer with an accuracy of 0.5 cm without shoes. At the beginning and end of the study, 24-h dietary recall questionnaire was used to estimate the intake of energy, macro and micronutrients, and also to check whether the person's eating habits have changed during the study or not.

Biochemical measurements recorded were plasma fasting glucose (FBG), plasma fasting insulin, lipid profile (triglycerides (TG), HDL-c, LDL-c and total cholesterol (TC)) and serum Hcy. At the baseline and after 6-week, 10 ml of blood samples were taken after 12 h of fasting. For serum separation, samples were centrifuged at 3000 rpm for 10 min at room temperature.

Serum Hcy was measured using enzymatic cycling method (REAGENT kit by Axis-shield of England) and Alfa classic autoanalyzer (Iran). The normal range of Hcy based on the kits is 5-15 µm/L. Serum insulin was measured by ELISA method using monobind kits (made by USA) and with autoanalyzer having a sensitivity of 2 µIU per ml. Serum glucose, TG, TC and HDLc were assessed using enzymatic-colorimetric method with autoanalyzer, and the serum LDLc was calculated with FriedWald formula. In order to calculate the insulin resistance (IR), insulin sensitivity (IS) and β-cell function (B%), HOMA Calculator Software (version 2.2.2, Diabetes trials Unit University of oxford) was used.

Data analysis: In this study, to analyze the 24-h dietary recall data, Nutritionist4 was used. Data were analyzed using SPSS software v.16. Descriptive statistics were used to explain the general characteristics of the participants. Student's *t*-test was used to compare the mean of variables before and after the intervention between the groups and paired *t*-test for within group caparison. A P-value < 0.05 was considered to be statistically significant.

Ethical considerations: Written consent was obtained from the participants before beginning the study. Entering and leaving of the study was completely voluntary, and all experiments were performed free of charge. This study was approved by the Shahid Sadoughi University of Medical Sciences Research Ethic Committee. In addition, it was registered with the Iranian Clinical Trial Registration Center (www.irct.ir) under the code of IRCT2013011312122N1.

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Results

Sixty five out of 70 participants completed the study and 5 patients were excluded (**Figure 1**). From the 65 participants, 21 were men (52% in OG and 48% in the PG) and 44 were female (54.5% in the OG and 45.5% in the PG). Before the intervention, 71.4% and 73.3% of subjects received OG and PG, respectively and had normal serum Hcyconcentration (> 15 µm/L). But at the end of the study, it was 41.2% and 57.1% that received OG and PG, respectively.

The baseline characteristics, such as age, height, weight, body mass index (BMI), and sex at the beginning of the study are shown in **Table 1**. There were no significant differences in baseline variables between the two groups. The dietary energy and the other nutrients intakes are shown in **Table 2**. No significant differences were observed in dietary intakes between the two groups.

The mean Hcy level was compared in between and within groups in **Table 3**. Omega-3 supplementation caused a significant increase in Hcy level as compared with placebo (P = 0.007). But there was not any significant difference in mean change between the groups. **Table 4** shows the mean of TC, TG, LDLc, HDLc concentration and HDLc/LDLc. According to these findings, we observed no significant differences in TG and TC before and after the intervention between groups. But LDLc and HDLc/LDLc ratio were significantly increased, while HDLc concentration was significantly decreased in OG (P < 0.05). No significant differences were observed in mean changes of TG, TC, LDLc, HDLc concentration and HDLc/LDLc between groups.

Table 5 shows the changes of insulin, IR, IS, β-cell function and FBG before and after the study. Insulin and IR significantly increased, IS significantly decreased in both groups and β-cell function was significantly increased only in OG, while there were no differences in mean changes of fasting insulin, IR, IS, β-cell function.

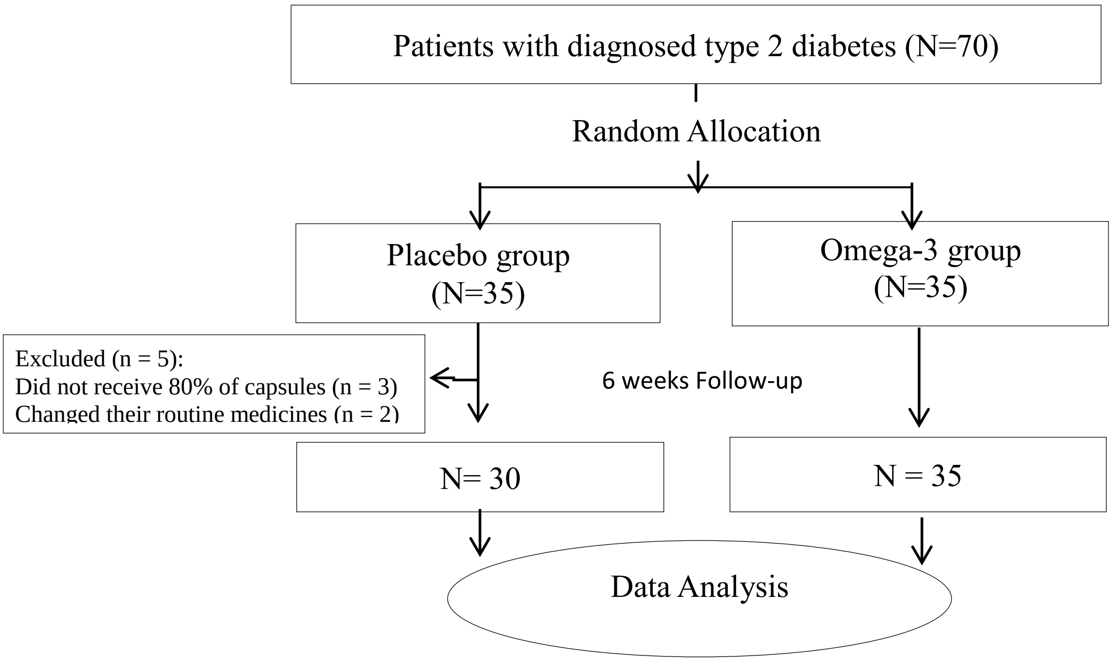

Figure 1. The Intervention framework

Table 1. Baseline characteristics of participants

Characteristics	Omega-3 Group (N = 35)	Placebo Group (N = 30)	P-value
Age (y)	48.51 ± 6.80 [a]	50.66 ± 6.62	0.1 [b]
Height (cm)	162.12 ± 7.75	161.97 ± 8.83	0.4 [b]
Weight (kg)	73.97 ± 13.46	72.27 ± 12.31	0.9 [b]
BMI (kg/m^2)	28.16 ± 4.96	27.50 ± 4.63	0.8 [b]
Sex	N (%)	N (%)	
Male	11 (31.4)	10 (33.3)	0.6 [c]
Female	24 (68.6)	20 (66.7)	

[a]: Mean±SD, [b]: Student *t*-test, [c]: Chi square test

Table 2. Daily dietary energy and nutrients intake

Variables	Before	After	P-value [c]
Energy(Kcal)			
Omega-3 Group	1450.44 ± 400.45 [a]	1450.76 ± 521.11	0.43
Placebo Group	1532.65 ± 634.12	1427.32 ± 534.36	0.72
P-value [b]	0.70	0.83	
Carbohydrate(g/day)			
Omega-3 Group	143.43 ± 48.65	44.65 ± 145.65	0.24
Placebo Group	165.48 ± 85.34	72.54 ± 153.65	0.52
P-value	0.45	0.65	
Protein (g/day)			
Omega-3 Group	53.21 ± 27.43	55.12 ± 37.87	0.33
Placebo Group	53.23 ± 54.23	56.61 ± 26.92	0.76
P-value	0.45	0.92	
Fat (g/day)			
Omega-3 Group	60.42 ± 22.14	61.31 ± 21.34	0.94
Placebo Group	65.15 ± 34.55	26.83 ± 61.76	0.85
P-value	0.28	0.66	
Omega-3 (g/day)			
Omega-3 Group	6.43 ± 6.51	6.72 ± 5.43	0.23
Placebo Group	5.98 ± 5.83	5.13 ± 4.96	0.47
P-value	0.64	0.86	
B6 (mg/day)			
Omega-3 Group	1.21 ± 0.57	1.60 ± 0.43	0.54
Placebo Group	1.36 ± 0.37	1.45 ± 0.76	0.34
P-value	0.12	0.29	
B12 (µg /day)			
Omega-3 Group	2.23 ± 0.98	2.45 ± 0.92	0.54
Placebo Group	3.02 ± 1.45	2.61 ± 1.76	0.34
P-value	0.12	0.29	
Folate (µg/day)			
Omega-3 Group	210.34 ± 54.12	213.54 ± 60.43	0.94
Placebo Group	189.12 ± 43.23	184.28 ± 42.96	0.12
P-value	0.54	0.8	

[a]: Mean±SD, [b]: Student *t*-test, [c]: Paired *t*-test

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Table 3. Means of Homocysteine concentration (μm/L) before and after the study.

Groups	Before	After	Change	P-value[a]
Omega-3 Group	13.21 ± 4.97	15.24 ± 5.53	2.02 ± 3.80	0.007
Placebo Group	13.19 ± 4.89	14.40 ± 5.68	1.20 ± 4.82	0.21
P-value[b]	0.98	0.57	0.47	

[a]: Paired t-test, [b]: Student *t*-test

Table 4. Means of total cholesterol, TG, LDLc, HDLc, HDLc/LDLc concentration before and after the study.

Variables	Before	After	Change	P-value[a]
Total cholesterol (mg/dL)				
Omega-3 Group	163.8 ± 29.77	163.88 ± 35.45	0.07± 31.68	0.98
Placebo Group	184.07 ± 46.06	177.14 ± 45.29	- 6.92 ± 46.43	0.43
P-value[b]	0.10	0.20	0.48	
Triglyceride (mg/dL)				
Omega-3 Group	168.58 ± 105.37	156.51 ± 105.25	12.07± 72	0.33
Placebo Group	155.16 ± 60.90	165.22 ± 97.66	10.05 ± 70.03	0.46
P-value	0.36	0.75	0.48	
LDLc (mg/dL)				
Omega-3 Group	84.26 ± 22.93	96.40 ± 32.36	12.14 ± 28.09	0.02
Placebo Group	105.27 ± 44.78	96.24 ± 37.39	- 9.02 ± 36.71	0.21
P-value	0.07	0.97	0.16	
HDLc (mg/dL)				
Omega-3 Group	47.63 ± 11.63	40.50 ± 11.45	7.13 ± 10.89	0.001
Placebo Group	47.67 ± 10.49	44.55 ± 8.61	3.12 ± 10.31	0.12
P-value	0.89	0.12	0.14	
HDLc/LDLc				
Omega-3 Group	0.59 ± 0.18	0.48 ± 0.26	- 0.11 ± 0.21	0.006
Placebo Group	0.54 ± 0.27	0.51 ± 0.18	- 0.02 ± 0.25	0.59
P-value	0.36	0.49	0.16	

[a]: Paired t-test, [b]: Student *t*-test

Discussion

In this study, which involved 65 T2D patients, after 6 weeks of n-3 PUFAs supplementation, the overall results showed that a daily intake of 2 g n-3 PUFAs capsules caused a significant decrease in HDLc, HDLc/ LDLc and IS; a significant increase in LDLc, Hcy, fasting insulin, IR and β-cell function; a reduction in TG; and an increase in FBG level. But based on mean changes, n-3 PUFAs supplementation had no positive effects on Hcy, lipid and insulin profile.

The results of the present study on Hcy are in line with some previous studies (Piolot *et al.*, 2003) and inconsistent with some others (Grundt *et al.*, 2003, Zeman *et al.*, 2006). Zeman et al. (Zeman *et al.*, 2006) recommended that 3.6 g PUFA n-3 supplementation for 3 months decreased Hcy levels in diabetic dyslipidemia. But in the present study, omega-3 supplementation was accompanied by statin-fibrate treatment. Several studies have shown that supplementation with omega-3 can reduce Hcy concentration in T2D (Benito *et al.*, 2006, Tayebi-Khosroshahi *et al.*, 2013). Fiedler et al.

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Table 5. Means of insulin, insulin resistance, insulin sensitivity, beta cell function and fasting glucose before and after the study.

Variables	Before	After	Change	P-value[a]
Insulin (mU/L)				
Omega-3 Group	7.04 ± 4.72	10.04 ± 4.53	2.99 ± 3.66	<0.001
Placebo Group	7.73 ± 4.98	11.07 ± 7.49	3.34 ± 4.56	0.001
P-value[b]	0.73	0.50	0.74	
Fasting blood glucose (mg/dL)				
Omega-3 Group	137.01 ± 40.48	142.53 ± 48.34	5.07 ± 27.19	0.28
Placebo Group	150.98 ± 48.57	159.11 ± 48.08	5.09 ± 26.15	0.25
P-value	0.21	0.18	0.9	
Insulin resistance				
Omega-3 Group	1.06 ± 0.66	1.52 ± 0.67	0.45 ± 0.49	<0.001
Placebo Group	1.21 ± 0.66	1.74 ± 0.98	0.52 ± 0.62	<0.001
P-value	0.76	0.28	0.64	
Insulin sensitivity (%)				
Omega-3 Group	124.03 ± 63.47	78.86 ± 37.42	- 45.16 ± 57.59	<0.001
Placebo Group	110.66 ± 73.72	84.05± 60.14	- 26.60 ± 56.13	0.02
P-value	0.99	0.66	0.23	
Beta cell function (%)				
Omega-3 Group	46.89 ± 23.13	62.07± 34.67	15.18 ± 28.40	0.005
Placebo Group	46.01 ± 31.38	51.84± 34.52	15.83 ± 25.92	0.29
P-value	0.86	0.32	0.21	

[a]: Paired t-test, [b]: Student *t*-test

(Fiedler *et al.*, 2005) administered 1.2 g of omega-3 with 11.2 g of pectin for 12 weeks to 11 hemodialysis patients. They conducted a short-term intervention and found no reduction in Hcy level. Piolot et al. (Piolot *et al.*, 2003) observed a progressive and significant increase in Hcy concentration in 16 normolipidemic subjects, which is in line with our study. However, certain effect of omega-3 fatty acids on Hcy is equivocal. This inconsistency may be due to different target groups, supplementation doses, intervention duration, sample size, type of medications and disease progression in different studies. Fiedler (2005) suggested that high doses of omega-3 for a long time may have anti-inflammatory effects (Fiedler *et al.*, 2005). In addition, the initial Hcy concentration in subjects may also be effective in results.

Some proposed mechanisms of the association between omega-3 and Hcy: Omega-3 PUFAs in cell membranes can cause modulation of the expression of enzymes involved in Hcy metabolism (Li *et al.*, 2007), such as Cystathionine beta synthase. Dietary fatty acids may interact with methylene tetrahydrofolate reductase (MTHFR) and methionine adenosyl transferase I, alpha (MAT1A) genetic variants in determining the Hcy level (Huang *et al.*, 2012). Omega-3 fatty acids may counteract the adverse effects of Hcy on endothelial function (Grundt *et al.*, 2003), they may increase nitric oxide (NO) production and subsequently inhibit methionine synthase (Haglund *et al.*, 1993, Zeman *et al.*, 2006). The increased Hcy concentrations during supplementation with n-3 fatty acids may be explained by the last mechanism, but other studies are needed to identify more precise mechanisms.

According to results of the present study, there was unfavorable effect on LDLc and HDLc. Thus there was no change in total cholesterol, and non-significant reduction in TG concentration in OG was observed. As such, n-3 PUFAs did not ameliorate lipid profiles in diabetic patients. N-3 PUFAs have been shown to improve plasma lipid profile in normal and hypertriglyceridemic subjects in some studies (Friday *et al.*, 1989, Haglund *et al.*, 1993) but in contrast, some others did not show the same (García-Alonso *et al.*, 2012). The result obtained in a study by West et al. (West *et al.*, 2005) on diabetic patients is in line with the finding of the present study in terms of LDLc. Piolot (Piolot *et al.*, 2003), Schiano (Schiano *et al.*, 2008) and Garci (García-Alonso *et al.*, 2012) in different studies showed that supplementation with n-3 PUFAs had not significant effects on HDLc and total cholesterol. But another study on patients with hyperlipidemia proved increasing HDLc (Haglund *et al.*, 1993). Crochemore suggested that the reduction effects of omega-3 PUFAs on total cholesterol and TG are dose dependent (Crochemore *et al.*, 2012).

The hypotriglyceridemic effect of n-3 PUFAs have been proven, but this effect is dose dependent (Kris-Etherton *et al.*, 2003). Based on previous studies, n-3 PUFAs reduced TG, mainly by declining the production and secretion of hepatic VLDL and also increasing the catabolism of VLDL (Grimsgaard *et al.*, 1997). After n-3 PUFA supplementation, PPARα increased which resulted in an increase in lipoprotein lipase (LPL), thereby reducing VLDL production (Schmidt *et al.*, 2012). In addition, it has been observed that the lowering effects of omega-3 fatty acids consumption on postprandial TG (PPTG) is significant (Kris-Etherton *et al.*, 2003). That $\leq$ 2 g of omega-3 consumption can significantly reduce PPTG(Roche and Gibney, 1996).

In the present study, fasting insulin level and IR were significantly increased in both groups after the intervention, while IS was significantly reduced. β -cell function and fasting glucose level had increasing trend in both groups, which was statistically significant in the intervention group. Several studies have shown the useful effects of omega-3 fatty acids on insulin function in animals (Chicco *et al.*, 1996, D'Alessandro *et al.*, 2002, Vessby, 2000). However, limited and conflicting results on humans, especially on diabetic patients are available. It has been shown that Greenland Eskimos, with diets rich in fish, have a low prevalence of diabetes. Giacco et al. (Giacco *et al.*, 2007) observed in their study that 3.6 g/day omega-3 PUFAs supplementation on 162 healthy subjects had no effect on IS, insulin secretion, beta-cell function and glucose tolerance. In another study, omega-3 fatty acids supplementation did not cause detrimental glycemic effects (Holness MJ, 2003).

Similar to our study, In overall, n-3 PUFAs may lead to higher glucose concentrations. Possible mechanism may: (1) lower glucose utilization and increase glucagon-stimulated C-peptide (2) increase gluconeogenesis in liver, and (3) increase glucose circulation (Kaushik *et al.*, 2009). Several mechanisms have been suggested for n-3 PUFAs mediated effects on insulin action: (1) the prevention of decrease by phosphatidylinositol 3' kinase (PI3 kinase) activity; (2) prevention of the depletion of glucose transporter protein GLUT4 in muscles; (3) the prevention of decrease in expression of GLUT4 in adipose tissue; and (4) inhibition of both the activity and expression of liver glucose-6-phosphatase (Delarue *et al.*, 2004, Taouis *et al.*, 2002). With regard to the adverse effect of omega-3 supplementation on insulin function, some studies suggested that dioxins or methyl mercury can disrupt insulin signaling pathways (Kaushik *et al.*, 2009, Lee *et al.*, 2006).

Omega-3 fatty acids can cause oxidative stress by increasing the production of reactive oxygen species and intracellular antioxidant defense reduction. Experimental studies have shown that oxidative stress can disrupt insulin signaling and insulin secretion. Endothelial dysfunction, due to Omega-3 fatty acids, lowers insulin delivery to insulin sensitive tissues, which in turn impairs the insulin-dependent glucose metabolism, leading to insulin resistance. Dietary intake of n-3 PUFAs s may have

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favorable effects on T2D prevention, but supplementation in people diagnosed with T2D seems not to be suitable.

The limitations of our study were short duration of intervention and low DHA concentration in omega-3 soft gels. To determine the pure effect and mechanisms of omega-3 fatty acids in T2D, future studies with longer periods are needed.

Conclusions

The present study found no beneficial effects of 2 g/day omega-3 supplement for 6 weeks on biomarkers of Hcy, FBG, insulin and lipid profile in patients with T2D.

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Authors' contribution

Mozaffari-Khosravi H participated to conception and design of study, managing the project and drafting the manuscript. Naghdipour Biregani A and Poursoleiman F participated to acquisition of data, data analysis and drafting the manuscript. All authors read manuscript and they finally verified it.

Conflict of interest

The authors declare that there is no any conflict of interests.

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