Effect of Omega-3 on lipid profile in type 2 diabetic patients

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Abstract

Diabetic complication is a major health concern , especially uncontrolled lipid profile, contributing to cardiac, renal and multisystem disorders. To evaluate the effect of 2 months supplementation of Omega-3 on lipid profile in type 2 diabetic patients and in comparison with the control. This non-randomized clinical trial was conducted at Al-Wafa'a Center for Diabetes Management and Research in Mosul City in the period from 1st of February 2012 to the 1st of July 2012. A total number of 84 patients (42 males and 42 females) diagnosed with type 2 diabetes mellitus (T2DM) for 2-5 years and were treated with metformin (dose of 500 mg twice daily) + glibenclamide (dose of 2.5 mg once daily) with no other liver or renal disorders, the patients were divided into two groups: First group included 50 patients with age ranged from 37 to 61 years, the patients were given Omega-3 capsules (1000 mg twice daily) for two months (Omega-3 group). The second group included the remaining 34 diagnosed diabetic patients, matched with the first group by age, sex , and BMI and considered as (control group). Fasting blood samples were taken from the first group at the beginning then after two months of Omega-3 use and from the control group once. The sera obtained from all participants in this study were used to measure lipid profile parameters by using the commercial kits, serum low-density lipoprotein cholesterol (LDL-c) was calculated using Friedewald equation. Atherogenic index (AI) was recognized by simple equation and BMI measured by dividing weight in (kg) by square of height in (meter). There was a significant reduction of serum triglycarides (TG) level and atherogenic index but no significant changes in total cholesterol (TC), high density lipoprotein-cholesterol HDL-c, nor in LDL-c level after 2 months therapy with Omega-3 and in comparison with the control group. The use of Omega-3 supplementation for two months in type 2 diabetic patients resulted in significant reduction in the serum TG level and atherogenic index but there was no effect on the other lipid profile parameters. This may be of therapeutic importance in lowering of the cardiovascular risk factors in patients with T2DM.

Key words: Omega-3, lipid profile, diabetes.

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تأثير اوميغا-3 على دهون الدم لدى مرضى السكري من النوع الثاني

الملخص

إن مضاعفات السكري لها أهمية صحية كبيرة وخصوصا مستوى دهون الدم العالية و التي تساهم في حدوث اضطرابات قلبية وكلوية وأجهزة الجسم المتعددة . لتقييم تأثير تناول اوميغا-3 على مستويات دهون الدم لدى مرضى السكري من النوع الثاني ، لمدة شهرين وبالمقارنة مع مجموعة الضبط . هذه الدراسة سريريه تجريبية غير عشوائية أجريت في مركز الوفاء لأبحاث وعلاج السكري في مدينة الموصل للفترة من الأول من شباط 2012 إلى الأول من تموز 2012 تم أخذ 84 مريضا من كلا الجنسين (42 ذكر و 42 أنثى) المصابين بداء السكري من النوع الثاني منذ   2-5 سنوات ، والمعالجين

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بالأكلينيكلامايد 2,5ملغ يوميا والميتفورمين 500 ملغ مرتين يوميا ولا يعانون من أمراض الكبد، أو الكلية أو أية أمراض مزمنة أخرى، وقد تم تقسيمهم إلى مجموعتين : المجموعة الأولى تضمنت 50 مريضا وتتراوح أعمارهم بين 37-61 سنة اعطو اوميغا-3 (1000 ملغ مرتين يوميا) بشكل كبسول لمدة شهرين (مجموعة اوميغا-3). المجموعة الثانية تضمنت 34 من مرضى داء السكري من النوع الثاني و المشخصين منذ 2-5 سنوات وقد اعتبرت كمجموعة سيطرة و كانت مماثلة للمجموعة الأولى من ناحية العمر والجنس ومقياس كثافة الجسم 0 تم أخذ عينات من الدم بعد فترة صيام من المجموعة الأولى في البداية ثم بعد شهرين من العلاج بأوميغا- 3 ومن مجموعة الضبط مرة واحدة0 وتم استخدام عينات مصل الدم المأخوذ من نماذج الدم من كل المش اركين في الدراسة لقياس مستويات دهون الدم بواسطة العدد اليدوية ، أما مستوى الكولسترول واطئ الكثافة تم حسابه بمعادلة فريديوالد وتم حساب مؤشر تصلب الشرايين (AI) من خلال معادلة بسيطة وتم حساب مقياس كثافة الجسم من قسمة الوزن   (كغم) على مربع الطول (متر). كان هناك انخفاض معنوي في مستوى الدهون الثلاثية ومؤشر تصلب الشرايين (AI) في المجموعة التي تتناول اوميغا-3 عند مقارنتها مع مجموعة الضبط ولم يكن هناك تغييرات معنوية في مستوى الكولسترول الكلي و الكولسترول عالي الكثافة ولا الكولسترول واطئ الكثافة بعد شهرين من تناول اوميغا-3 وبالمقارنة مع مجموعة الضبط. استنتجت هذه الدراسة أن استخدام اوميغا- 3 لمرضى السكري من النوع الثاني لمدة شهرين أدى إلى انخفاض معنوي في مستوى الدهون الثلاثية ومؤشر تصلب الشرايين (AI) في مصل الدم ولكن ليس له تأثير على مستوى باقي دهون الدم . وهذا قد يكون له أهمية علاجية في خفض عوامل خطورة القلب الوعائية في المرضى المصابين بداء السكري من النوع الثاني.

مفتاح الكلمات: *اوميغا-3 ، دهون الدم، داء البول السكري*

Introduction

Diabetes incurs microvascular and macrovascular complications, resulting in a high degree of morbidity and a 30% decrease in life expectancy[1,2]. Therefore, diabetes and cardiovascular diseases (CVD) are often regarded as the same entity[3-5], forming the basis for the 'common soil' hypothesis, which postulates that T2DM and CVD share common genetic and environmental antecedents, and that the development of these conditions is a consequence of the clustering of risk factors. These risk factors can be divided into traditional (e.g. abdominal obesity, hyperglycemia, dyslipidemia and hypertension) and nontraditional (e.g. low-grade inflammation, hypercoagulation and hypofibrinolysis) factors [6]. It is thought that insulin resistance underpins this clustering of risk and together, the collection of traditional risk factors has been defined, using different criteria, as the metabolic syndrome[3,4,7]. Many studies have confirmed that an abnormal lipid profile is a risk factor for CVD[8,9,10]. Patients with diabetes exhibit an atherogenic lipid profile characterized by elevated triglyceride (TG) and low levels of high-density lipoprotein cholesterol (HDL). LDL levels are not significantly different in subjects with diabetes compared with the general population but there is an increased proportion of small, dense atherogenic LDL particles among patients with diabetes[11]. The lipids essential for health are the omega-3 and omega-6 polyunsaturated fatty acids (PUFA) [12]. Interest in Marine-derived n-3 (also known as omega-3) polyunsaturated fatty acids (PUFA) began in 1972. Studies by Bang and Dyerberg [13] showed that Greenland Inuit who consumed a diet high in protein and fat (mainly from fish) had significantly lower TC, LDL-c, and triglyceride levels than most other people had. Omega-3 fatty acids have antiarrhythmic effects, including preventing atrial fibrillation[14]; antithrombotic action[15]; antiatherogenic effects[16]; anti-inflammatory effects[17]; and the ability to improve endothelial function[18], lower blood pressure[19], lower TG level [20], increase high-density lipoprotein (HDL) level[21], and decrease apolipoprotein B-100[22]. So the aim of this nonrandomized clinical trial was to assess the effect of two months therapy with Omega-3 fatty acids on lipid profile in Type 2 diabetic patients.

Patients & Methods

This study was conducted in Al-Wafa'a Clinic for diabetes in Mosul_City. A total number of 84 patients (42 males and 42 females) age ranged from 37 to 61 years diagnosed with T2DM for 2-5 years with no other liver or renal disorders and were treated with metformin (dose of 500 mg twice daily) + glibenclamide (dose of 2.5 mg once daily) , the patients were divided into two groups: First group included 50 patientsdiagnosed with type 2 diabetes were given Omega-3 capsules of Good'n Natural company as (1000mg twice daily) for two months (Omega-3 group). The second group included 34 diagnosed diabetic patients for 2-5 years, matched with the first group by age , sex , and BMI and considered as control group. Fasting Blood samples were collected from the patients of omega-3 group at the first visit before taking omega-3 therapy then after two months of use and from the control group once at the first visit only. The separated serum was kept frozen at -20°C for measurement of lipid profile tests including serum TC, TG, and HDL-c by using commercial kits supplied by Bio Labo, France, while LDL-c was calculated by using Friedewald equation [23] . Atherogenic index (AI) was calculated by the following equation: AI = Log10 (TG /

HDL)[24] , and BMI obtained by dividing weight in (kg) by square of height in (meter). Standard statistical methods were used to determine the mean and standard deviation (SD). Unpaired student t-test was used to compare the results for measured biochemical parameters between Omega-3 group and control group. All values quoted as the mean ± SD and P-value ≤ 0.05 was considered to be statistically significant. The approval of the study protocol by an ethic committee has been obtained from the local health committee of Ministry of Health and College of Medicine - University of Mosul – Iraq.

Results

From the total number of 84 patients with T2DM were included in this study, only 32 of them with mean age (52.52 ± 6.53 years) continued the study using omega-3 therapy for two months (Omega-3 group). Another 34 diagnosed T2DM patients with mean age (51.24 ± 6.22 years) were taken as a control group. Table (1) demonstrates that there was no significant differences between the characteristic of the T2 DM patients of the two groups, enrolled in this study.

Table (1):- General characteristic of the T2DM patients enrolled in this study

Parameter	Mean ± SD		P-Value
	Group of Patients given Omega-3	Control Group (Type 2 DM) patients	
Age(year)	52.52 ± 6.53	51.24 ± 6.22	NS
Sex male	18	20	NS
Female	14	14	
BMI (Kg/m^2)	28.9 ± 2.69	29.019 ± 2.65	NS
SBP (mmHg)	124.7 ± 4.084	122.7 ± 3.97	NS
DBP (mmHg)	80.6 ± 2.521	83.6 ± 3.97	NS

Tables (2) demonstrates that there is a significant decrease in the mean TG level and atherogenic index after 2 months omega-3 therapy in comparison with its mean level before therapy. But there was no significant differences in the other lipid parameters   after 2 months omega-3 therapy in comparison with their mean levels before therapy.

Table (2):- Comparison between mean $\pm$ SD of lipid profile parameters of Omega-3 group before and after two months therapy

Parameters	Mean $\pm$ SD		P-Value
	Omega-3 group (n= 32) before	Omega-3 group (n= 32) after	
T C mmol/l	5.01 $\pm$ 0.635	4.94 $\pm$ 0.69	NS
TG mmol/l	1.608 $\pm$ 0.40017	1.26 $\pm$ 0.313	0.003
HDL-c mmol/l	1.06 $\pm$ 0.254	1.07 $\pm$ 0.245	NS
LDL-c mmol/l	3.6292 $\pm$ 0.600	3.60 $\pm$ 0.636	NS
Atherogenic Index	0.20 $\pm$ 0.16	0.12 $\pm$ 0.14	0.038

Tables (3) demonstrates a significant lower value of the mean TG level and atherogenic index after 2 months omega-3 therapy in Omega-3 group in comparison with the control group. There was no significant differences in the other lipid parameters   after 2 months omega-3 therapy Omega-3 group in comparison with control group.

Table (3):- Comparison between mean $\pm$ SD of lipid profile parameters of Omega-3 group after two months therapy and the control group

Parameters	Mean $\pm$ SD		P-Value
	Omega-3 group after 2 months(n= 32)	Control Group (n=34)	
T C mmol/l	4.94 $\pm$ 0.69	4.88 $\pm$ 0.68	NS
TG mmol/l	1.26 $\pm$ 0.313	1.67 $\pm$ 0.40	0.001
HDL-c mmol/l	1.07 $\pm$ 0.245	1.08 $\pm$ 0.266	NS
LDL-c mmol/l	3.60 $\pm$ 0.636	3.46 $\pm$ 0.490	NS
Atherogenic Index	0.12 $\pm$ 0.14	0.21 $\pm$ 0.15	0.013

Discussion

Omega-3 PUFA have been reported to lower the risk of cardiovascular mortality in high-risk and general populations [25], although trials in recent metaanalysis [26] have cast doubt on the strength of this evidence. But two prospective cohort studies[27,28] among women showed that the risk of CVD is much lower among women with type 2 diabetes who consume n-3 PUFA. Three previous systematic reviews[29,30,31] evaluated the effect of n-3 PUFA on cardiovascular events, lipid and glycaemic markers in type 2 diabetes. A fourth systematic review[32] considered additional lipid, lipoprotein and apolipoprotein cardiovascular risk markers, and used changes in the mean from baseline to the end of the trial in the pooled analysis , so this study was conducted to show the effects of 2 months omega-3 PUFA therapy in Type 2 diabetic patients on lipid profile as cardiovascular risk factor. The result of this study are consistent with previous systematic reviews in patients with type 2 diabetes[29-32] and in the general population[25,33,34] , showing that TG levels fall significantly after n-3 PUFA supplementation. After adjusting for HDL, increasing levels of TG have been shown to be an independent risk factor for CVD in epidemiological studies [35], so lowering of TG levels may be an important therapeutic value of n-3 PUFA supplementation in patients with T2DM especially in women because an increase in triglycerides of 1 mmol/l is associated with a 76% increased risk of CVD in women versus 32% in men [35]. This study demonstrated that TC level was non-significantly lowered after 2 months omega-3 PUFA therapy , which is similar to results of previous systematic reviews in type 2 diabetes [29-32] and in the general population [25], but a systematic review study [36] which considered the effects of n-3 PUFA on TG, HDL, VLDL and LDL-c in ten trials including 606 patients with hypertriacylglycerolaemia, but not type 2

diabetes found reduced TC level . This study found that there was no significant difference in serum HDL-c concentration after 2 months omega-3 PUFA therapy which is in agreement with the previous systematic reviews of type 2 diabetes[29-32] and in the general population [25,33]. Also LDL-c concentration was not significantly different after 2 months Omega-3 PUFA therapy in T2 diabetic patients in this study, in contrast to this the meta-analysis study of Hartweg *et al.,* [32] found that sixteen trials reported changes in LDL-cholesterol among 565 subjects and that n-3 PUFA supplementation increased plasma LDL-cholesterol by 5.7%, a mean of 0.11 mmol/l (95% CI 0.00 to 0.22; p= 0.05) and three of these trials reported an increase in LDL cholesterol but was lower than previously reported [30, 31]. Although it remains a potential adverse effect of n-3 PUFA , this increase of LDL-c was not observed in pooled randomized controlled trials of hypertriacylglycerolemic [36] or normolipidaemic patients[25,33]. The extent to which the HDL and LDL lipid sub-fractions may explain the action of n-3 PUFA in reducing cardiovascular risk and how these differ among people with type 2 diabetes to those in other populations remains uncertain[32]. The results of this study are in agreement with the meta-analysis study done by Newberry[36] , who searched on- line databases to identify potentially relevant studies and contacted industry experts for unpublished data and screened 4,212 titles, reviewed 1,097 articles, and included 83 articles, restricting to randomized controlled trials (RCTs). Newberry found that Among 18 studies of type II diabetes or the metabolic syndrome, omega-3 fatty acids had a favorable effect on TG levels relative to placebo (pooled random effects estimate: -31.61; 95% CI, -49.58, - 13.64) but had no effect on TC, HDL-c, LDL- c, fasting blood sugar, or glycosylated hemoglobin.

In conclusion: Two months Omega-3 PUFA supplementation in T2DM causes

significant lowering of serum TG concentration and atherogenic index which may be an important therapeutic importance in lowering of the cardiovascular risk factors in patients with Type 2 DM.

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