ISSN NO. 2320-5407

Journal homepage:http://www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH

RESEARCH ARTICLE

Omega (n- 3) Polyunsaturated Fatty Acids and Diabetic Patients

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Manuscript Info

Manuscript History:

Received: 11 December 2013
Final Accepted: 26 January 2014
Published Online: February 2014

Key words:
Diabetes, lipid profile, Omega-3 polyunsaturated fats (PUFA).

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Abstract

Diabetes mellitus is a metabolic disease associated with dyslipidemia that increase risk of cardiovascular disease to three or four folds compared with normal individual. This study investigates the effect of Omega-3 polyunsaturated fatty acids (PUFAs) on glycemic state, lipid profile of diabetic patients. It is a 3 month observational study of 63 type 2 diabetes mellitus patients of both genders divided in to PUFA group n=31 and Control group n= 32. Fasting blood glucose and lipid profile were assessed pre and post enrolment in the study. Omega-3 PUFA supplementation lowered fasting blood glucose, triglycerides, total cholesterol, and LDL levels with an increase in HDL level. The statistical significant lowering of triglyceride level in diabetic patients consuming omega-3 supplementation contributes significantly to the decrease incidence of cardiovascular diseases in diabetic patients.

Introduction

Diabetes mellitus is considered as a common, growing, serious and potentially preventable public health problem with a worldwide prevalence rate of 8.9% - 12.3% , the number of diabetic patients is estimated to increase from 117 million in 2000 to 366 million in 2030 (Adams et al.,2011 and Zangiabad et al.,2007). Diabetes is a general metabolic disorder of all -the three - energy nutrients (Susan, 2007). The most common problem encountered in diabetes is atherosclerotic cardiovascular disease (Steiner, 2001), seen frequently associated with typical dyslipidaemia (Howard, 1987). Postprandial lipoproteins are thought to be atherogenic (Karpe et al., 1994, Tkac et al., 1997and Sakata 1998). An abnormal metabolism of postprandial lipoproteins is a common finding in type2 diabetes (Curtin et al., 1994). Consequently, the exaggerated postprandial triglyceride responses are responsible for the increased morbidity from CAD in type 2 diabetes. Furthermore, postprandial lipemia determines plasma HDL concentrations (Parekh et al., 1998). The negative correlation between HDL and CAD seems to originate in the highly positive correlation between postprandial triglyceride concentrations and CAD (Oakes et al., 1997). Diabetic patients with moderate hypertriglyderidaemia are considered to be at increased risk for coronary heart disease (CHD) (Castelli, 1986), as it enhanced the atherogenic potential of low density lipoprotein (LDL) (DE Graaf et al., 1993).

Both physical activity and dietary intervention have been recommended to control and prevent diabetes and hypertriglyceridaemia (De Logegeril et al., 1999). If the measures prove unsuccessful, severely elevated triglycerides levels should be treated with lipid-lowering drugs. Such drugs include fibric acid derivatives, nicotinic acid and its analogues which decrease triglycerides and increase HDL cholesterol (Frick et al., 1997).

Epidemiologic evidence showed that populations with high intakes of fish had less risk of cardiovascular disease and diabetes, suggesting that (n-3) fatty acids may play a role in controlling and preventing diabetes (De Logegeril et al., 1999). Also, studies suggest that a high dietary intake of n-3 PUFAs may confer a protective effect against

atherosclerotic disease and reduce serum triglycerides levels; since fatty acids are fundamental components of phospholipids in cell membranes so by altering the fatty acid composition of membrane phospholipids, (n-3) fatty acids modify membrane mediated processes such as insulin transduction signals, activity of lipases, and synthesis of eicosanoids . (n-3) Fatty acids also control the expression of various metabolic genes (e.g. genes involved in lipid and glucose metabolism and adipogenesis) in part through the activation of PPAR (De Logegeril et al., 1999, Frick et al., 1997 and Harris 1997).

Our literature review suggests an overall small, yet useful role of omega-3 PUFAs in improving the glycemic state and lipid profile of type 2 diabetic patients. Due to the presence of contradictory findings and results in previous studies depending on the specific populations' strata, and study design, we could not establish a strong recommendation regarding the role of PUFAs dietary supplement preparations in the treatment plans of diabetic patient regularly seen in GMC hospitalnor could we determine whether such approach is more useful with specific gender, age group or patients with particular co-morbidity such as dyslipidemia and hypertension. We conducted a prospective observational study that has an intervention (PUFA) groupand a control group to investigate the effect of omega-3 polyunsaturated fat (PUFA) regular intake on the glycemic state and lipid profile of the type 2 diabetic patients seen at the outpatient department in GMChospital.

Material and Methods

It is a 3 month observational study of 63 type 2 diabetes mellitus patients of both genders conducted in outpatient clinic (OPD) of internal medicine department at GMCH & RC, Ajman, UAE during the period of June 2011- March 2013. Patients diagnosed with diabetes and on medication were included in the study, excluding patient presented with any complication of diabetes or taking lipid lowering drugs or hormone replacement therapy. The study was performed in accordance with the ethical standards laid down in the 1974 Declaration of Helsinki.

The study included PUFA group n=31 given 1 g fish oil (Omacor 1g/day) as a source of n-3 PUFA and Control group n= 32 , both groups were allowed to take their routine diet and diabetic medication without any alterations . Fasting blood glucose and lipid profile were assessed pre and post enrolment in the study; serum total cholesterol and triglyceride concentrations were determined by enzymatic colorimetric assay (Technicon Instruments, Ltd., N.Y., USA), HDL was determined enzymatically in the supernatant after precipitation of other lipoproteins with dextran sulfate-magnesium. LDL was calculated using Friedewald formula. A pre designed, validated questionnaire was filled to assure explaining the study purpose and procedures to participants, obtaining official consent and to facilitate data collection which included socio-demographic variables, details of the disease-diabetes- and treatment. Anonymity of the participants was maintained throughout the study. Chi-squre test, Paired and unpaired t-test were used. Results were expressed as mean ± SD deviation and a p value < 0.05 was considered to be of statistical significant level.

Result and Discussion

Results:

63 patients (31 PUFA group and 32 Control group) the mean age of the participants was 53.6 year with 73% males and a mean duration of diabetes of 8.6 years. 78% of participants were Arabs, 17 patients had dyslipidemia, 9 patients in PUFA group versus 8 patients in control group. 22 patients were hypertensive, 10 patients in PUFA group versus 12 patients in control group. There were no statistical significant differences detected between the two groups at the start of the study (table 1). 3 month of follow up of both the groups showed a reduction in the blood levels of FBG, Triglyceride ,Cholesterol, LDL levels with an increase in HDL levels yet the detected changes were more in the PUFA group as it showed a reduction by 4.4.mg/dl (3.48%), 31.8 mg/dl (19.8%), 9.98 mg/dl (5.89%), 5.04 mg/dl (5.4%) respectively with an increase in HDL level by 1.71 mg/dl (3.9%), the reduction in triglyceride level was theonly parameter showing statistical significant difference compared to its level at the start of the study (table 2 & 3) .

Table 1: The characteristics of the groups at the start of the study.

Variables	Groups	Control group (32 patients) N (%)	PUFA group (31patients) N (%)	P value
Gender	Male (73%)	24 (75%)	22 (71%)	> 0.05

	Female (27%)	8 (25%)		9 (29%)	> 0.05
Ethnicity	Arabs (78%)	24 (75%)		25 (81%)	> 0.05
	Non Arabs (22%)	8 (25%)		6 (20%)	> 0.05
Patients with dyslipidemia			17 (26.9%)		
		8 (25%)		9 (29%)	> 0.05
Patients with hypertension			22 (34.9%)		
		12 (35%)		10 (32%)	> 0.05

Table 2: Blood glucose level and lipid profiles of the study participants at the start of the study (baseline value).

Test	Control group (32 patients) Mean ±SD (mg/dl)	PUFA group (31patients) Mean ±SD (mg/dl)	P value
FBG	135.34±46.553	126.31±48.141	> 0.05
TG	141.27±71.172	159.93±113.947	> 0.05
T.Ch	171.79±47.271	166.63±50.809	> 0.05
HDL	43.65±17.080	43.83±17.560	> 0.05
LDL	102.10±46.117	91.70±49.275	> 0.05

Table 3: Blood glucose level and lipid profiles of the study participants at the end of the study (after 3 months interval)

Test	Control group (32 patients)		PUFA group (31patients)		P value
	Mean ±SD (mg/dl)	Mean difference (mg/dl) and % of change compared to it base line value	Mean ±SD (mg/dl)	Mean difference (mg/dl) and % of change compared to its base line value	
FBG	129.03±47.46	-6.31 (- 4.6%)	121.91±49.14	-4.4 (- 3.48%)	> 0.05
TG	130.62±59.77	-10.65 (- 7.53%)	128.13±77.86	-31.8 (-19.8%)	<0.05*
T.Ch	157.03±34.88	-14.76 (- 8.59%)	156.65±42.44	-9.98 (- 5.98%)	> 0.05
HDL	44.39±15.493	0.74 (1.28%)	45.54±15.493	1.71 (3.9%)	> 0.05
LDL	88±37.064	-14.1 (-13.80%)	86.66±31.192	-5.04 (-5.4%)	> 0.05

* statistical significant

Discussion:

Type 2 diabetes is a disease most strongly associated with obesity and arises from insulin resistance rather than the lack of insulin production. Insulin resistance causes cells to take up glucose less efficiently, resulting in elevated blood glucose concentrations. Increased hepatic gluconeogenesis also results from insulin resistance, which further elevates blood glucose overnight. Increased chronic blood glucose causes glucose-protein adducts, which are instrumental in circulatory dysfunction, leading to retinopathy, kidney damage, and inability to fight infections that may result in gangrene in the limbs, requiring amputation. Hemoglobin A1c (HbA1c) is an indicator of the extent of

glucose adducts and therefore of long-term elevated blood glucose. HbA1c and fasting glucose are the most common indicators of the ability of a treatment or regimen to lessen type 2 diabetes (Washington, DC, 2005, Abdel-Aal et al., 2008 and Haddad et al., 2002).

Since (n-3) Fatty acid effects on diabetes, insulin action and cardiovascular disease have been under study and research in the past few years, this study tried to investigate the effects of n-3 omega (PUFAs) on diabetic patients and to weigh the detected effects and/or benefit from the statistical and clinical point of view. This was done by giving 1g daily /3 months of fish oil as a source of PUFAs (Omacor 1g/day) to diabetic patients and studying the effects of this supplement on their lipid profile and glycemic state as well as comparing the effects detected with the lipid profile and glycemic state of diabetic patients who were not consuming PUFAs.

At the beginning of this study the two groups were statistically comparable as there were no statistical significant differences detected between the two groups regarding the age, gender, and ethnicity, duration of the disease and the prevalence of dyslipidemia of 26.9% and the prevalence of hypertension34.9% when these variables were assessed.

3months consumption of 1g/day of n-3 PUFAs (Omacor tablets) by diabetic patients showed reduction in fasting blood glucose level. The reduction was statistically insignificant but was in accordance to (Al Jama and Ibrahim, 2011) who founded that diabetic patients had 16% statistically significant reduction in their fasting blood glucose level after taking 30 ml of olive oil daily/4 weeks. Studies showed that PUFAs increased membrane fluidity, number of insulin receptors and insulin binding, thus decreasing the fasting blood glucose level (DE Graaf 1993 and Frick 1997).

This study showed that the triglyceride level of diabetic patient taking 1g PUFAs daily / 3 months had a statistically significant reduction; this matched both Haddad et al., (2002) and Bang et al., (1976) who found that diabetic patients consuming 30 ml daily/ 4 weeks of olive oil had a 32% reduction of their triglyceride level.

A systematic review pools 10 years of evidence and 18 randomized controlled trials of fish oil supplementation studying >800 subjects with type 2 diabetes reveled that fish oil supplementation had a statistically significant triglyceride-lowering effect. This effect was most marked in studies that recruited hypertriglyceridemic subjects (Montori et al., 2002).Studies found that Omega-3 fatty acids lower triglycerides level by increasing lipoprotein lipase activity and chylomicron clearance (Harris et al., 1990 and Bang et al., 1976).

The study showed that 1g daily of n-3 PUFAs/3months decreased the cholesterol level of the diabetic patients, similar to Puiggros et al, (2002) who reported 8.4% significant decrease in total cholesterol level with the olive oil-enriched diet and Harris et al., (2002) who found 26 % decrease in the cholesterol level of diabetic patient consuming 30 ml daily /4 weeks of olive oil.

Consumption of 1g of PUFAs daily /3 months in diabetic patients in this study showed an increase in HDL level and a decrease in LDL. This in accordance with Al Jamal and Ibrahim, (2011) who found that30 ml daily/4 weeks supplementation of olive oil in the diet of diabetic patients increased HDL level by 27% and decreased LDL level by 22% , also Rodríguez-Villar et al ., (2004) showed that a diet high in olive oil was a good alternative to high carbohydrate diets for nutrition therapy of type 2 diabetics as it lowered VLDL-cholesterol by 35% and VLDL-triglyceride by 16% and had superior patient acceptance . Lopez-Miranda (2000) pointed out two positive consequences of the consumption of a Mediterranean diet, as it increased HDL-cholesterol plasma levels, and it decreased the susceptibility of LDL to oxidation and lipid peroxidation.

The effects of n-3 fatty acids on HDL cholesterol and its subfractions are unclear. However, one of the hypothesis is that HDL- cholesterol subfractions change in composition and absolute size upon n-3 fatty acid treatment: the level of HDL2 tends to rise compared with the level of HDL3. Studies have demonstrated that the increase in HDL2/HDL3 ratio may reduce cardiovascular risk (Rodríguez-Villar et al., 2004, López-Miranda et al., 2000 and GottoJr 1983).

It has been proposed that n-3 fatty acids decrease LDL cholesterol by promoting production of triglycerides poor VLDL cholesterol and accelerating conversion of VLDL cholesterol to LDL cholesterol. However, this mechanism remains unclear (Harris, 1997). It was found also that n-3 PUFAs decrease the level of LDL and its susceptibility to oxidation (Cullinen, 2006).

This study shows that 1 g daily /3 months n-3 PUFA supplement (Omacor 1g /day) improved lipid profile in type 2 diabetic patients ; manifested by decreasing the levels of triglyceride, cholesterol, LDL with an increase in HDL level . Participants also experienced reductions in fasting blood glucose level although the only statistical significant findings was the reduction in the triglyceride level yet the findings were in accordance to Al Jamal and Ibrahim, 2011 who that found the positive effect of daily consumption of 30 ml of olive oil as a source of n-3 PUFAS was much more profound in the diabetic group as levels of FBG, TG, Ch and LDL decreased by 16-32% compared to normal individuals.

Caterina et al. (2007) reviewed clinical studies of the effect of (n-3) fatty acids on the treatment of diabetics with type 1 and 2 ; 28 people with T2D in 2 noncontrolled studies and 671 patients in 13 double-blinded studies were

provided low-dose (>3 g/d) (n-3) fatty acids for 2–24 wk. No effect was found on fasting plasma glucose in most cases. Triglycerides were decreased in most cases. Total cholesterol was decreased in 6 cases and increased in only 1 case. HDL increased in 4 cases and decreased in 1 case. LDL increased in 5 cases and decreased in 4 cases. A total of 112 type 2 diabetic patients participated in 7 high-dose (>3 g/d) studies (4 double-blinded, 1 single blind, and 2 noncontrolled studies) for 3–24 wk. Fasting plasma glucose decreased in 3 studies and was not modified in 4 studies. Total cholesterol was not modified. Triglycerides decreased in 6 cases and LDL increased in 6 cases. HDL increased in 2 cases and decreased in 1 case.

Conclusion:

This study shows that 1 g daily /3 months Omega-3 PUFA supplement (Omacor 1g /day) improved lipid profile in type 2 diabetic patients ; manifested by decrease in triglyceride, cholesterol, LDL blood levels with an increase in HDL level . Participants also experienced reduction in fasting blood glucose level.The statistical significant lowering of triglyceride level may contribute significantly to the decrease incidence of cardiovascular diseases in diabetic patients.

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