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Optimizing the Effect of ω-3 Fatty Acids on the Lipid Profile in Metabolic Syndrome Patients

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Abstract: *Background:* The metabolic syndrome is a clustering of metabolic abnormalities and cardiovascular risk factors. It is vital to start the lifestyle interventions and treatment early in patients with metabolic syndrome to prevent the twin global epidemics of type 2diabetes and CVD. *Objective:* to investigate the overall effects of omega-3 fatty acids supplementation In addition to Dietary Approaches to Stop Hypertension (DASH) nutritional intervention on the lipid profile in patients with metabolic syndrome and to study if the addition of DASH diet will alleviate the rise in LDL- C that occurs with ω-3 fatty acid supplementation. *Research design and methods:* This was a prospective interventional outpatient trial conducted on 42 patients with the metabolic syndrome. They received ω-3 fatty acid supplementation 1 g/d in addition to DASH nutritional education for 12 weeks: the DASH diet with increased consumption of fruit, vegetables, low-fat dairy and whole grains and lower in saturated fat, total fat, and cholesterol. The main outcome measures were the lipid profile of the patients with metabolic syndrome. *Results:* ω-3 fatty acid together with The DASH diet significantly changed the mean of all parameters of lipid profile in metabolic syndrome patients. After 12 weeks, there was a significant increase in HDL-C (14%), significant reductions in TG (37.7%), LDL (29.4%) and a significant reduction in Non HDL-C (24.7%). *Conclusion:* this study demonstrated that the DASH diet optimizes and complements the effect of ω-3 fatty acid on the lipid profile of patients with metabolic syndrome by alleviating the rise in LDL- C that occurs with omega supplementation.

Keywords: Hypertriglyceridemia, Omega-3 Fatty Acids, LDL, Metabolic Syndrome, DASH, LDL

1. Introduction

The metabolic syndrome is a clustering of metabolic abnormalities and cardiovascular risk factors that occur in individuals with impaired insulin sensitivity [1]. Cardiovascular risk in the individual with multiple metabolic abnormalities is significantly higher than the sum of the risk associated with each abnormality [2, 3].

Hyperglycaemia and changes in blood lipids (increase in triglycerides (TG) and decrease high-density lipoprotein cholesterol HDL-C) increase the risk of CVD even before levels of blood glucose are high enough for a person to be diagnosed with diabetes [2].

As the incidence of metabolic syndrome is rising at an alarming rate [4], and it increases the twin global epidemics of CVD and type 2diabetes, it is vital to start the lifestyle interventions and treatment early [5].

Elevated plasma TG levels indicate the presence of pro-atherogenic remnant lipoproteins, and independently associated with increased cardiovascular disease (CVD) risk [6]. Although the primary treatment targets for patients with mild to moderate hypertriglyceridemia is reduction of LDL-C and/or non-high-density lipoprotein cholesterol (non-HDL-C) [7], normal TG levels (<150 mg/dL) is also associated with a reduction in the risk of coronary heart disease [8]. Triglycerides are carried in TG-rich lipoproteins (very low density lipoprotein cholesterol [VLDLs] and chylomicrons) and their remnants [9], studies have shown that remodeled VLDL and chylomicrons can penetrate the arterial intima and retained within the arterial wall, leading to the accumulation of intimal cholesterol leading to plaque formation and progression [10]. Studies demonstrated that a TG-rich lipoprotein remnants lead to impaired vasodilation and increased inflammation which promote the progression of atherosclerosis [9].Therefore, the management of hypertriglyceridemia is important in reducing the risk of CVD in patients with mild to moderate hypertriglyceridemia [11].

ω-3 fatty acid decrease the level of TG in humans; but regarding other lipid parameter, it was found that it increases the LDL –C levels. Therefore concurrent treatment with DASH diet may mitigate the rise in LDL-C in patients treated with hypertriglyceridemia

The purpose of this study was to investigate the overall effects of ω-3 fatty acid supplementation in addition to Dietary Approaches to Stop Hypertension (DASH) nutritional intervention on the lipid profile in patients with metabolic syndrome, and if the addition of DASH diet will improve LDL- C level in the course of omega 3 fatty acid supplementation.

2. Methods

2.1. Study Site and Subjects

This study was a prospective interventional study, conducted in a family medicine unit (FMU) that provides primary health care services in Kasr El-Aini, Egypt. The study site was purposefully selected because it has high rate of outpatient visitors, with different socioeconomic levels, seeking different medical services.

All people in the case area with serum lipid or glucose abnormalities, high blood pressure or obese were invited to complete their labs. Among the patients who accepted, we invited those subjects who were matched with criteria of metabolic syndrome. They were 42 participants.

To be enrolled in the study, patients had to have three or more of the following criteria to be diagnosed as having metabolic syndrome according to The IDF consensus worldwide definition of the metabolic syndrome [5]. The criteria are 1) abdominal adiposity (defined as waist circumference >94 cm [men] or >80 cm [women]), 2) low levels of serum HDL cholesterol (<40 mg/dl [men] or < 50 mg/dl [women]) or receive drug treatment for reduced HDL, 3) hypertriglyceridemia (triacylglycerol level of ≥150 mg/dl) or receive drug treatment for elevated triglycerides, 4) elevated blood pressure (≥130/85 mmHg) or take antihypertensive drug treatment in a patient with a history of hypertension, and5) impaired glucose homeostasis (fasting plasma glucose concentration of ≥100 mg/dl) drug or take treatment for elevated blood glucose. Patients were excluded if they had cardiovascular disease, psychiatric problems, and hypothyroidism or took any medication affecting blood lipids.

2.2. Compliance with Ethical Standards

The study was approved by the Family Health and Public Health Councils. Selected members constituted the internal review board to guarantee the ethical conformity of the study. Informed verbal consents were obtained from all the participants before recruitment in the study, after explaining the objects of the work and procedures. All questionnaire forms and clinical sheets were coded to preserve confidentiality. All participants were informed about the results of their medical examination.

2.3. Study Intervention

All participants asked to complete a personal health and medical history questionnaire; they underwent focused medical examination for initial screening before recruitment.

Twelve-hour fasting blood samples were obtained from the participants to get their baseline lipid profile and to exclude hypothyroidism by assessing TSH level. All participants had mean fasting TG levels ≥200 and <500 mg/dL.

They all received ω-3 fatty acid 1 g/d for 12 weeks. The DASH diet was explained on the first day, and then follow-up continued for the next 12 weeks. The participants were asked to come to the FMU every 4 weeks for counseling and discussions regarding the diet. Greatest emphasis was placed on consuming the fruits, vegetables and low-fat dairy foods, whole grains, poultry, fish, as well as the salt restriction. The importance of reducing saturated fat, red meat and refined carbohydrate and increasing complex carbohydrate intakes was also stressed [12].

Suggestions on how to increase fruit and vegetable consumption were also provided.

Guidance as to how to add flavor without using salt was given. Under participant's request, diets were organized in sheets according to their needs.

To maximize benefit, group discussions were conducted monthly. In these sessions, patients were encouraged to follow their diets.

After 12 weeks, Blood samples were obtained after 12-hr fast to assess the participants' lipid profile.

2.4. Statistical Methods

All collected questionnaires and data were coded and revised for completeness. A database on Excel was developed for data entry and analysis. Pre-coded data was entered on the computer using the statistical package of social science software program, version 15(SPSS) to be statistically analyzed. Data was summarized using Mean, SD, median and inter quartile range for quantitative variables which were not normally distributed while frequency and percent were used for qualitative data. Comparison between pre and post intervention quantitative variables was done using the paired t test for quantitative variables which where normally distributed and Wilcoxon signed-rank test for quantitative variables which were not normally distributed. P value less than 0.05 were considered statistically significant.

3. Results

The participant's mean age was 46.57± 3.9 years. The base line characteristics of the participants are shown in (Table 1).

The intervention resulted in reduction in the mean of TG level from 221.29 to 137.0 mg/dl with average reduction 37.7%, mean of LDL level from 193.26 at base line to 136.29 after 12 weeks of intervention, increase in HDL cholesterol, from 41.10 to 46.86 mg/dl (average increase 14%) and a reduction of Non HDL - C (54.02−mg/dl), (all P < 0.001). (Table 2).

Table 1. *Baseline characteristics of participants.*

		N (42)	%
Gender	Male	9	21.4
	Female	33	78.6
Age(mean ± SD)	46.57 ± 3.9		
Marital status	Married	32	76.2
	Unmarried	10	23.8
Education	Illiterate	3	7.1
	average	18	42.9
	Above average	16	38.1
	High education	5	11.9
Job	working	41	97.6
	Not working	1	2.4
smoking	Smoker	5	11.9
	Non smoker	37	88.1
Diabetes	Diabetics	20	47.6
	Non diabetics	22	52.4
Hypertension	Hypertensive	33	78.6
	Non hypertensive	9	21.4
BMI (mean ± SD)	30.1 ± 3.8		

Table 2. *Means of the lipid profile at baseline and after 3 months of intervention by DASH diet.*

	Baseline	After 3 months	Mean difference	% change	P value
Total cholesterol	259.26 ± 60.99	211.0 ± 41.65	48.26± 63.10	18.61	<0.001*
TG	221.29 ± 106.72	137.0 ± 54.99	83.61 ± 110.89	37.77	<0.001**
HDL-C	41.10 ± 6.38	46.86 ± 7.58	-5.76 ± 2.73	14	<0.001*
LDL-C	193.26 ± 65.11	136.29 ± 42.08	56.97 ± 9.20	29.44	<0.001*
Non HDL - C	218.16 ± 62.17	164.14 ±42.19	54.02±63.71	24.76	<0.001*

Data is presented as mean ± standard deviation.
*Baseline and final values were compared using paired t-test.
** Baseline and final values were compared using Wilcoxon signed-rank test.
A p-value < 0.05 was considered to be significant.

4. Discussion

The purpose of this study was to investigate if the DASH diet optimizes the effect of ω-3 fatty acid supplementation on the lipid profile in patients with metabolic syndrome by mitigating the rise in LDL- C.

After 12 weeks of intervention, We found a significant reduction in the mean of the TG (37.7%), LDL levels had significantly decreased with average reduction 29.44%, a 24.76% reduction in the mean of non – HDL - C and a 14% increase in the mean of HDL-C.

Confirming our study's positive effect of adding DASH diet to ω-3 fatty acid supplementation was what (Kelley et al, 2007) have reached after their study; they have found that 2 g ω -3 fatty acid supplementation for 90 days decreased concentrations of fasting triacylglycerol (24%), It elevated concentrations of LDL cholesterol (12.6%) and did not alter plasma concentrations of HDL cholesterol [13].

These changes may have been due to multiple factors. First, ω-3 fatty acid supplementation may have improved the blood lipid profile by decreasing hepatic secretion of TG containing lipoproteins (very low density lipoprotein) and enhancing clearance of TG from circulating TG containing lipoprotein (VLDL and chylomicrons) from the blood[14].

Second, The DASH diet has several common aspects that may lead to some health benefits and improves the component of metabolic syndrome. Calcium in dairy food plays an important role as the dietary calcium appears to modulate the efficiency of energy utilization, with low calcium diets favoring increased efficiency of energy storage and higher calcium diets reducing energy efficiency and instead favoring increased thermogenesis [15]. Fecal bile acids increased significantly with increased dietary calcium, this denotes that increased dietary calcium levels leads to greater fat excretion and decreases fat absorption [16].

Reduced antioxidant capacity and oxidative stress represent a potential mechanism linking obesity to insulin resistance and cardiovascular diseases [17]. Phytochemicals in the DASH diet raises antioxidant capacity, and reduces oxidative stress induced by acute hyperlipidemia [18].

The DASH eating pattern includes eating large number of low–glycemic index foods (i.e., vegetables, whole grains, dairies) which might be another responsible mechanism for its benefits. Brand-Miller et alreported high–glycemic index foods adversely affect markers of the metabolic syndrome (triglycerides and HDL cholesterol) [19].

In addition, the replacement of dietary saturated fat by mono- or polyunsaturated fatty acids significantly lowers the plasma-cholesterol and low density lipoprotein cholesterol (LDL-C) levels [20].

Thisstudy represents the first attempt to investigate the

complementary effects of the DASH diet and ω-3 fatty acid supplementation on lipid profile of metabolic syndrome. However, our study has several limitations. First, we cannot determine whether the improvement of TG, HDL-C, non HDL-C due to the effects of the ω-3 fatty acid supplementation or the DASH diet. It may have been due to the augmented action of DASH diet and ω-3 fatty acid supplementation. Secondly, small sample size as the study subjects were recruited on a voluntary basis and after fulfillment of the inclusion criteria.

Findings of our research were in agreement with other studies that have been demonstrated that a multifactorial approach should be preferred in order to obtain the maximum efficacy in the treatment of the metabolic syndrome [21].

Further researches should focus on the long-term effect of DASH diet education program and ω-3 fatty acid supplementation on the component of metabolic syndrome, also future studies should investigate the beneficial effect of ω-3 fatty acid supplementation in addition to DASH diet in the overweight or obese patients with mild or moderate hypertriglyceridemia as a first step for primary prevention of metabolic syndrome.

5. Conclusion

This study demonstrated that the DASH diet optimizes and complements the effect of ω-3 fatty acid on the lipid profile of patients with metabolic syndrome by alleviating the rise in LDL- C that occurs with ω-3 fatty acid supplementation.

Disclosure of potential conflicts of interest: The authors declare that they have no conflict of interest relevant to this article.

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