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Use of Omega-3 Supplements for the Amelioration of Glucose Levels and Lipid Profile Parameters in Female University: A Randomized Control Study

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Authors' contributions

This work was carried out in collaboration between all authors. Author MIE designed the study. Authors KAH, NZAD, ARSAE and EMEN performed the samples collection and all laboratory analyses. Authors A/RH and SAA performed the statistical analysis. Authors MIE, MH and AHM wrote the protocol and wrote the first draft of the manuscript and managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Aim: We aimed to evaluate the effect of omega-3 supplementation on the glucose levels and lipid profile parameters in female university students in Southern Gaza.
Materials and Methods: Sixty female university students were divided into two groups. The intervention group (n = 30) received omega-3 fatty acid supplementation (one capsule/day) for three months, while the control group students (n = 30) were allowed to consume standard oils. Blood samples (5 mL) were randomly collected using plain vacutainers before and after the three months of intervention. The blood glucose level and lipid profile parameters were measured using standard methods. Data were analysed using SPSS software.
Results: The present study showed that omega-3 fatty acid supplementation has a significant

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impact on blood glucose levels and lipid profile parameters. The levels of glucose (83.9 ± 8.8 vs. 101.0 ± 11.7 md/dL, P = 0.000), total cholesterol (141.6 ± 15.0 vs. 165.4 ± 31.4 mg/dL, P = 0.001), triglycerides (137.6 ± 4.1 vs. 151.1 ± 12.8 mg/dL, P = 0.000), and low-density lipoprotein cholesterol (67.1 ± 12.3 vs. 97.8 ± 32.8 md/dL, P = 0.000) significantly decreased, while the high density lipoprotein cholesterol significantly increased (47.0 ± 5.0 vs. 37.3 ± 2.1 mg/dL, P = 0.032) in the intervention group after omega-3 supplementation. In addition, BMI was significantly associated with low-density lipoprotein cholesterol (r = 0.319, P = 0.016).

Conclusions: The present work documented a significant improvement in the glucose levels and lipid profile parameters following omega-3 supplementation in female university students. Therefore, we believe that regular consumption of omega-3 fatty acids can have a beneficial impact on dyslipidaemia, thus providing protection against heart diseases.

Keywords: Omega-3 fatty acids; polyunsaturated fatty acids; glucose; lipids profile; Palestine.

1. INTRODUCTION

Fatty acids are an important component of the diet [1]. Omega-3 (ω3) fatty acids represent a class of polyunsaturated fatty acids derived from α-linolenic acid (18:3ω3). The nomenclature for the ω3 fatty acids relates to a double bond present at the third carbon from the methyl terminus of the fatty acid chain benefits [2]. ω3 fatty acids, including eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and α-linolenic acid (ALA) are dietary fats with several health benefits [3,4]. Studies have shown that EPA and DHA are important for appropriate foetal development in terms of neuronal, retinal, and immune function. In addition, EPA and DHA have shown promising results in prevention, weight management, and cognitive function in patients with very mild Alzheimer's disease [5].

ω3 fatty acids are considered essential fatty acids that cannot be synthesized in the human body. Fish oil, flaxseed, as well as some nuts are very rich sources of ω3 fatty acids [1,6]. In addition, ω3 fatty acids are available in the form of prescription drugs; dietary supplements from fish oil, krill oil, algal oil, and plant oil, as well as emerging options, such as free fatty acids [7].

Currently, the dietary patterns of individuals are geared toward fast food that contains higher amounts of saturated fat and smaller amounts of essential ω3 fats than home-cooked foods [5,8]. Moreover, modern agricultural practices emphasize on production, resulting in the reduction of the ω3 fatty acid content of several foods, including green leafy vegetables, animal meats, eggs, and even fish [9].

We hypothesized that supplementation with ω3 fatty acids would ameliorate the lipid profile parameters and glucose levels of female university students. Cardiovascular diseases (CVD) are more prevalent in women than in men (49% vs. 40%) and this prevalence increases with age. While CVD occurs in 10.0% of women aged 20–39 years, the prevalence is 35.5% among women aged 40–59 years [10]. This study aimed to investigate the effect of omega-3 fatty acids supplementation on the glucose levels and lipid profile parameters in female university students.

2. MATERIALS AND METHODS

2.1 Study Design and Population

In this study, we recruited 60 apparently healthy female university students in the third academic year at Al-Aqsa University, Southern Gaza, Palestine. The participants were randomized into the intervention and control groups The intervention group included 30 students who received the ω3 fatty acid supplements (one capsule/day; capsule weight 1400 mg). These capsules were purchased from SupHerb, 12 Hamaayan St., Har-Yona Industrial Zone, Nazareth Illit, 17000. The ω3 fatty acids capsules contained 1000 mg fish oil, 300 mg omega-3 fatty acids (180 mg EPA and 120 mg DHA), 3 IU vitamin E, glycerol, and water. The control group included 30 students who were age-matched; they were not given ω3 fatty acids supplements and were permitted to consume standard oils, such as olive oil and soybean oil.

Female university students who were 20-22 years old and were apparently healthy were included in the study. Students < 20 years old or > 22 years old; those who were pregnant or breastfeeding; and those with hypertension, diabetes mellitus, or any chronic disease were excluded.

Data regarding the participants' demographic characteristics and dietary habits were recorded using a questionnaire designed for the study.

2.2 Determination of Body Mass Index (BMI)

Body weight and height were recorded for each study subject. BMI was used to estimate the nutritional status of the subjects, calculated as the weight (in kilograms) divided by the square of the height (in metres), using the BMI calculator form the website: https://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmi-m.htm

2.3 Sample Collection and Preparation

The duration of the present study was three months. Blood samples were drawn twice, once at the beginning of the study and then at the end of the study period. Blood samples (5 mL) were collected in plain tubes from all the participants in both the groups (intervention and control groups). Blood samples were drawn at the Department of Medical Laboratory Sciences, Al-Aqsa University, Palestine. The collected blood samples were allowed to clot at room temperature to obtain serum aliquots by centrifugation at 3000 rpm for 20 minutes. The sera were stored in the freezer at -20℃ until analyses.

2.4 Laboratory Parameters Analyses

2.4.1 Determination of glucose levels

Blood glucose levels were determined using the glucose oxidase peroxidase (GOD- POD) method with Mindray BA-88A, a semi-automatic chemistry analyser with a large touch screen. Briefly, the glucose in the samples is oxidized by glucose oxidase to produce gluconic acid and hydrogen peroxide. The hydrogen peroxide reacts with 4-aminoantipyrine and p-hydroxybenzoic acid in the presence of peroxidase to produce quinoneimine dye, the colour of which is proportional to the glucose level in the sample.

2.4.2 Determination of serum total cholesterol (TC) Level

TC was determined using the cholesterol oxidase-peroxidase (CHOD-POD) method. Briefly, cholesterol esters in the samples are enzymatically hydrolysed by the cholesterol esterase to produce cholesterol and free fatty acids. The free cholesterol is then oxidized by the cholesterol oxidase to cholest-4-en-3-one and hydrogen peroxidase (H_2O_2). In the presence of peroxidase, the formed hydrogen peroxide effects the oxidative coupling of phenol and 4-aminoantipyrine to form a red-coloured quinoneimine dye that is measured at 546 nm. The intensity of the coloured dye is proportional to the concentration of the cholesterol in the sample.

2.4.3 Determination of serum total triacylglycerol (TG) level

TG was determined based on the glycerol-3-phosphate oxidase-peroxidase (GPO- POD) method. Briefly, triacylglycerol is hydrolysed by lipoprotein lipase to glycerol and free fatty acids. The glycerol phosphorylates to glycerol-3-phosphate by ATP-dependent glycerol kinase catalysed reaction. Then, glycerol-3-phosphate is oxidized to dihydroxyacetone phosphate and hydrogen peroxide by glycerol phosphate oxidase. In the presence of peroxidase, the hydrogen peroxide forms the oxidative coupling of 4-chlorophenol and 4-aminoantipyrine to form a red-coloured quinoneimine dye.

2.4.4 Determination of high-density lipoprotein cholesterol (HDL-C)

High-density lipoprotein-cholesterol (HDL-C) was determined based on the phosphotungstic-precipitation method. Briefly, phosphotungstate binds to the positively charged apoprotein B-containing lipoproteins (very low-density lipoprotein [VLDL] and low-density lipoprotein [LDL]) that are then cross-linked by the use of divalent cation manganese to form a precipitate. After centrifugation, the cholesterol in the supernatant, HDL-C, is measured using the previously described method for TC.

2.4.5 Determination of low-density lipoprotein cholesterol (LDL-C)

LDL-C concentrations were calculated using the Friedewald formula (LDL-C = TC - [HDL-C + TG/5]), when the TG concentrations were < 400 mg/dL.

2.5 Statistical Analyses

Data were analysed using the Windows based statistical package for social sciences (SPSS) software (version 20, Chicago, Illinois, USA). Categorical variables are expressed as numbers (percentages), and the between-group comparisons were made using Chi-square test. Numerical variables are expressed as means ± standard deviation value (95% confidence

interval [CI]), and the between-group comparisons were made using independent (unpaired) Student's t-test. Pearson's correlation test was applied for evaluating the association of TC and BMI with glucose levels and other lipid profile parameters. *P* values < 0.05 were considered statistically significant.

2.6 Ethical Considerations

The study was conducted after obtaining ethical approval from the first author`s institution where the study was conducted. The protocol of the current study adhered to the principles of the Helsinki Declaration. Participation was voluntary, and verbal consent was obtained from each study subject. The objective of the study was thoroughly explained to all participants. Patient confidentiality was maintained because no patient names were requested.

3. RESULTS

3.1 Socio-Demographic Characteristics and Dietary Habits of the Study Participants

Total sixty female university students were randomized into the following two groups: the intervention group (n = 30, average age 20.07 ± 0.45 years) and the control group (n = 30, average age 20.15 ± 1.1 years). All students lived either in Khanyounis or Rafah city. The mean ± standard deviation (SD) values for body mass index (BMI) were 21.6 ± 2.2 kg/m^2 and 21.9 ± 2.8 kg/m^2 for the intervention and control groups, respectively.

The participants in both groups were matched for their socio-demographic characteristics; no significant difference was recorded in the analysed socio-demographic variables. Moreover, an evaluation of their daily diet showed that most control group subjects ate two meals; however, 50% of the cases ate three meals and the other 50% ate two meals, indicating a considerable difference between the two groups (p = 0.033).

Table 1 shows the socio-demographic characteristics and distribution of the dietary habits and life style of the study population.

3.2 Results of the Lipid Profile Evaluation Before and After the Intervention

The present study showed that ω3 fatty acid supplementation had a significant impact on the blood glucose levels and lipid profile parameters. The levels of glucose (83.9 ± 8.8 vs. 101.0 ± 11.7 md/dL, *P* = 0.000), TC (141.6 ± 15.0 vs. 165.4 ± 31.4 mg/dL, *P* = 0.001), TG (137.6 ± 4.1 vs. 151.1 ± 12.8 mg/dL, *P* = 0.000), and LDL-C (67.1 ± 12.3 vs. 97.8 ± 32.8 md/dL, *P* = 0.000) had significantly decreased, while the HDL-C had significantly increased (47.0 ± 5.0 vs. 37.3 ± 2.1 mg/dL, P = 0.032) in the intervention group following ω3 supplementation.

3.3 Association of Total Cholesterol and BMI with Glucose Levels and Other Lipid Profile Parameters

Pearson correlation analyses of TC and BMI with TG, HDL-C, LDL-S, and glucose levels was conducted. A strong, statistically significant positive association (r = 0.899, P = 0.000) was observed between TC and LDL-C, an intermediate positive association was found between TC and TG (r = 0.0284, P = 0.008), and an intermediate negative association was observed between TC and HDL-C (r = -0.353, P = 0.001). However, no association was found between TC and glucose (r = 0.111, P = 0.306). By contrast, BMI was only positively correlated with LDL-C (r = 0.319, P = 0.016), while no correlations were found between BMI and the other variables (TG, HDL-C, glucose). Table 3 shows the association of TC and BMI with glucose levels as well as the other lipid profile parameters.

4. DISCUSSION

In this study, the female subjects who received ω3 fatty acid supplementation showed a marked decrease in their TG levels after 3 months. Consistent with our findings, Mozaffarian D et al [11] reported that the greatest effect of ω3 fatty acids is on TG, with reductions of 20%–30%. Further, several clinical studies have shown that ω3 supplementation reduces TG levels [12,13,14].

In addition to the reduction in TG levels, the current study demonstrated significant reduction in the levels of TC and LDL-C in the female subjects following 3 months of ω3 supplementation. In contrast to our findings, Balk EM et al reported that fish oil consumption caused a net change of +6 (95% CI +3, +8) mg/dL in LDL-C, while it did affect TC levels [15]. However, Rajkumar H et al agreed with our findings and reported that the ω3 group had a decrease not only in their LDL-C, but in also their

Table 1. Demographic and physical characteristics of the study participants

Variable	Total (n=60)	Control group (n=30)	Intervention group (n=30)	*P*-value
Location, City				
Khanyounis	38 (63.3%)	18 (60%)	20 (66.6%)	0.563
Rafah	22 (36.7%)	12 (40%)	10 (33.3%)	
Age, years				
mean ±SD,	20.10±0.8	20.15±1.1	20.07±0.45	0.722
(95% CI)	(19.9-20.3)	(19.7-20.6)	(19.9-20.2)	
Weight, Kg				
mean ±SD,	58.8±7.2	57.8±8.1	55.9±6.2	0.312
(95% CI)	(54.9-58.7)	(54.6-61.0)	(53.5-58.2)	
Height, cm				
mean ±SD,	161.5±4.9	162.1±4.9	160.9±4.9	0.372
(95% CI)	(160.2-162.8)	(160.2-164.1)	(159.1-162.8)	
BMI				
(mean± SD),	21.8±2.4	21.9±2.8	21.6±2.2	0.549
(95% CI)	(21.1-22.4)	(20.9-23.1)	(20.8-22.4)	
Meals/day				
One	08 (13.3%)	06 (20.0%)	02 (06.7%)	0.033*
Two	32 (53.3%)	19 (63.3%)	13 (43.3%)	
Three	20 (33.4%)	5 (16.6%)	15 (50.0%)	
Fast-food/week				
None	09 (15.0%)	04 (13.3%)	05 (16.6%)	
One	15 (25.0%)	10 (33.3%)	05 (16.6%)	0.340
Two	17 (28.3%)	06 (20.0%)	11 (36.7%)	
Three	19 (31.7%)	10 (33.3%)	09 (30.0%)	
Milk				
None	19 (31.7%)	12 (40.0%)	07 (23.3%)	
One	16 (26.7%)	10 (33.3%)	06 (20.0%)	0.077
Two	09 (15.0%)	02 (06.7%)	07 (23.3%)	
Three	16 (26.7%)	06 (20.0%)	10 (33.3%)	
Fruits				
None	11 (18.3%)	08 (26.7%)	03 (10.0%)	
One	25 (41.7%)	11(36.7%)	14 (46.7)	0.212
Two	17 (28.3%)	09 (30.0%)	08(26.7%)	
Three	07(11.7%)	02 (06.7%)	05 (16.6%)	
Meats				
None	14 (23.3%)	04 (13.3%)	10 (33.3%)	
One	22 (36.7%)	13 (43.3%)	09 (16.6%)	0.386
Two	15 (25.0%)	09 (16.6%)	06 (20.0%)	
Three	09 (15.0%)	04 (13.3%)	05 (16.6%)	
Sweets				
None	14 (23.3%)	09 (16.6%)	05 (16.6%)	
One	16 (26.7%)	05 (16.6%)	11(36.7%)	0.425
Two	18 (30.0%)	10 (33.3%)	08 (26.7%)	
Three	12 (20.0%)	06 (20.0%)	06 (20.0%)	
Doing physical activities 30 min per day				
Yes	28 (46.7%)	16 (53.3%)	12 (40.0%)	0.146
No	32 (53.3%)	14 (46.7)	18 (60.0%)	

Values are expressed are mean ± standard deviation (SD) values (95% confidence interval) or number (%). P-values for comparison between the control and intervention groups were determined using chi-square (for categorical data) or unpaired t-tests (for continuous data)

*$P < 0.05$

Table 2. Lipid profile of the intervention and control groups

Variable	Control* group (n=30)	Intervention group (n=30)		*P*-value[a]	*P*-value[b]
		Pre-treatment	post-treatment		
TC, mg/dl	158.3±24.6	165.4±31.4	141.6±15.0	0.001*	0.003*
TG, mg/dl	134.3±15.1	151.1±12.8	137.6±4.1	0.000*	0.081
LDL-C, mg/dl	94.8±26.3	97.8±32.8	67.1±12.3	0.000*	0.000*
HDL-C, mg/dl	36.6±1.7	37.3±2.1	47.0±5.0	0.032*	0.000*
Glucose, mg/dl	82.1±10.3	101.0±11.7	83.9±8.8	0.000*	0.489

*Results expressed as Mean ±SD, *P < o.o5*

P-value[a]: pre- and post- intervention comparison in the cases (administration omega-3)

P-value[b]: comparison of the variables of the controls with the post-intervention values of the cases

Between-group comparisons were made using two-tailed (unpaired) Student's t-test

** No differences were recorded in glucose levels and lipid profile parameters of the controls before and after the treatment.*

Table 3. Correlations of TC and BMI with glucose levels and other lipid profile parameters

Variable (n=60)	TC		BMI	
	r	p-value	r	p-value
TG	0.284	0.008*	0.007	0.958
HDL-C	-0.353	0.001*	-0.234	0.080
LDL-C	0.899	0.000*	0.319	0.016*
Glucose	0.111	0.306	0.065	0.632

Abbreviations: TC; Total cholesterol, TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; BMI; body mass index

TC levels [16]. In contrast, data from our current study documented increased HDL-C levels. This finding was supported by Davidson MH et al. who reported that in patients with persistent hypertriglyceridemia, ω3 fatty acid plus simvastatin supplementation with dietary counselling improved the non-HDL-C and other lipid and lipoprotein parameters substantially compared to simvastatin alone [17]. Moreover; in a double blind, placebo-controlled trial with a parallel design, 59 overweight, non-smoking, mildly hyperlipidaemic men, Mori TA el al. [18] reported that DHA improved the serum lipid status; they particularly noted a small increase in the HDL-C level and a significant increase in the HDL2-C sub-fraction.

Regarding blood glucose levels, our study showed a significant decrease in the blood glucose level after three months of ω3 supplementation. In contrast to the latter finding, Akinkuolie AO et al. [19] reported that ω3 fatty acids had no significant effect on the fasting blood glucose level, insulin sensitivity, and glycosylated haemoglobin in patients with Type 2 diabetes.

Elevated TG levels can promote atherogenesis by increasing the TC levels, LDL-C levels, and reducing the HDL-C levels. Such a condition could be explained in part by the increasing conversion of VLDL-C into LDL-C, inducing a pro-coagulant state [12]. Therefore, understanding how fish oil reduces plasma TG levels is important not only because elevated TG levels are a cardiovascular risk factor, but also because such an understanding of basic lipid biology can help in the development of new approaches for treating hypertriglyceridemia [20]. Thus, majority of the evidence suggests that ω3 fatty acids reduce the synthesis and secretion of VLDL particles and increase the removal of TGs from VLDL and chylomicron particles by upregulating enzymes, such as lipoprotein lipase [21]. Moreover, ω3 fatty acids accelerate chylomicron and VLDL elimination from the blood, and the activation of peroxisome proliferator-activated receptor gamma (PPAR-gamma) ω3 ramp up the cellular equipment used to convert fatty acids to energy through β-oxidation [22,23].

In contrast, the reduction of blood glucose levels by ω3 fatty acids consumption, as documented in this study can be attributed to the improved insulin secretion and sensitivity owin to enhanced insulin signalling. ω3 fatty acids (mainly EPA) reportedly increase the G-protein-receptor-

mediated release of glucagon-like peptide 1 (GLP-1) from enteroendocrine L-cells in the intestine, up-regulation of the apelin pathway, and down-regulation of other control pathways to promote insulin secretion by the pancreatic β-cells [24,25].

5. CONCLUSION

Atherogenic dyslipidaemia is characterized by elevated levels of TG land small LDL particles with reduced LDL levels, often accompanied by elevated apolipoprotein B (Apo B) and non-HDL-C [26]. The present findings show a significant positive impact of ω3 supplementation on blood glucose levels and lipid profile parameters. Thus, we believe that regular consumption of ω3 fatty acids (from dietary sources or as supplemental products) may help reduce the cardiovascular disease risk. The recommended daily intake of ω3 fatty acids is debatable. The European Food Safety Authority has approached these requirements scientifically and recommend at least 250 mg EPA + DHA daily for healthy adults [27]. Moreover, since 2008, the World Health Organization has recommends daily intake of 250 mg EPA + DHA for primary prevention of coronary heart disease and 2 g for secondary prevention [28].

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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