Original Article

Effects of omega–3 fatty acids supplementation on serum adiponectin levels and some metabolic risk factors in women with polycystic ovary syndrome

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Objective: Polycystic ovary syndrome (PCOS) is a common female endocrine disorder associated with several risk factors of type 2 diabetes and cardiovascular diseases. The objectives of this study were to investigate the effects of omega–3 fatty acids on serum adiponectin levels and some metabolic risk factors in PCOS patients.

Methods: This double-blind randomized controlled clinical trial was conducted on 64 overweight or obese PCOS patients; aged 20-35 years. Subjects in omega–3 fatty acids (n=32) and placebo (n=32) groups were given 4 omega–3 fatty acids capsules (each one contained 180 mg eicosapentaenoic acid and 120 mg docosahexanoic acid) or placebo daily for 8 weeks. Fasting blood samples, anthropometric measurements and 3-day, 24-hour dietary recalls were collected at the baseline and at the end of the trial. Results: The study was completed by 61 subjects. Omega–3 fatty acids significantly increased serum levels of adiponectin (p=0.003) and decreased glucose (p=0.001), insulin (p=0.002), homeostatic model assessment for insulin resistance (p<0.001), total cholesterol (p=0.002) and low-density lipoprotein cholesterol (p=0.003) compared with placebo. Serum levels of triglyceride significantly decreased (p=0.024) and high-density lipoprotein cholesterol increased (p=0.018) in the omega–3 fatty acids group, in comparison with baseline values. No significant changes were shown in serum high sensitive C-reactive protein (hs-CRP) levels in both groups. Conclusion: Omega–3 fatty acids had some beneficial effects on serum adiponectin levels, insulin resistance and lipid profile in PCOS patients and may contribute to the improvement of metabolic complications in these patients.

Key Words: omega–3 fatty acids, polycystic ovary syndrome, adiponectin, insulin resistance, lipid profile

INTRODUCTION
Polycystic ovary syndrome (PCOS) is the most common female endocrine disorder, presents in 6–10% of women of reproductive age.¹ The disorder is characterized by irregular menstrual cycle, chronic anovulation, and hyperandrogenism. Polycystic ovary syndrome is the main cause of female infertility due to anovulation.² The etiology of PCOS is not completely known but it is now clear that insulin resistance has an important role in enhancing androgen production in ovaries.¹ Hyperinsulinemia and early onset of type 2 diabetes are more frequent in PCOS patients than in the general population.² Polycystic ovary syndrome is also associated with other risk factors of cardiovascular disease such as dyslipidemia and elevated levels of hs-CRP (high sensitive C-reactive protein), an acute-phase reactant that increases during inflammatory response.³

About half of PCOS women are obese.¹ Adipose tissue, especially visceral fat is considered as an active endocrine organ which produces several proteins that called adipocytokines.⁴ Adiponectin is one of the most abundant adipose-derived factors that improves insulin sensitivity

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and has antiatherogenic and anti-inflammatory effect.\textsuperscript{4}

Several studies have showed a reduction in adiponectin levels in PCOS patients.\textsuperscript{5,6} It seems that hypo-adiponectinemia can be associated with the pathogenesis of PCOS and metabolic complications of this syndrome such as hyperinsulinemia and dyslipidemia.\textsuperscript{6}

It was reported that specific dietary unsaturated fatty acids can be associated with improved endocrine and metabolic characteristics in women with PCOS.\textsuperscript{7} Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are n−3 long chain polyunsaturated fatty acids (n−3 LC PUFA) found primarily in fatty fish. In Current diets, n−6 fatty acids are predominant PUFA and imbalance in the n−6/n−3 PUFA ratio may be related to chronic disease.\textsuperscript{8}

Studies have shown increasing evidence for antiatherogenic and anti-inflammatory effects of fish oil and it is conceivable that dietary PUFA might also have benefit effects on glycemic control and lipid profile.\textsuperscript{8–11} It is suggested that positive effects of EPA and DHA on metabolic parameters can be partially due to enhancement of adiponectin production.\textsuperscript{12}

Mehendale \textit{et al.} reported that plasma EPA and erythrocyte DHA levels were reduced in infertile women as compared with controls and hypothesized that omega−3 fatty acids probably contribute to the management of female infertility.\textsuperscript{13} Another study by Cussons \textit{et al.} showed that omega−3 fatty acid supplementation had beneficial effects on some cardiometabolic risk factors in PCOS patients.\textsuperscript{14} However, effects of n−3 LC PUFA on adiponectin levels and metabolic status in PCOS women are little known. So the objectives of this study were to determine the effects of omega−3 fatty acids on serum adiponectin levels and some metabolic risk factors including insulin resistance, serum lipids and hs-CRP levels in PCOS patients.

**MATERIALS AND METHODS**

Sixty-four PCOS patients aged 20–35 years old and with BMI ranging from 25 to 40 kg/m\textsuperscript{2} were recruited in this double-blind randomized controlled clinical trial from outpatient department of obstetrics of Alzahra hospital in Tabriz, Iran in 2011. The Ethical Committee of Tabriz University of Medical Sciences approved the study protocol. The registration ID of this study in Iranian Registry of Clinical Trials was: IRCT201011083664N3. Written informed consent obtained from each subjects prior to study.

The diagnosis of PCOS was established according to 2003 Rotterdam criteria, which require at least two of three features for diagnosis: chronic anovulation, clinical or biochemical evidence of hyperandrogenism, and polycystic ovaries in ultrasonography.\textsuperscript{15} Study exclusion criteria included: smoking, pregnancy, using any medications, consumption of fish oil and other dietary supplements with the past 3 months or during the study, his consumption of fish oil and other dietary supplements and it is conceivable that dietary PUFA might also have antiatherogenic and anti-inflammatory effects on glycemic control and lipid profile. Several studies have showed a reduction in adiponectin levels in PCOS patients. EPA and DHA found primarily in fatty fish. In Current diets, n−6 fatty acids are predominant PUFA and imbalance in the n−6/n−3 PUFA ratio may be related to chronic disease.

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Mehendale \textit{et al.} reported that plasma EPA and erythrocyte DHA levels were reduced in infertile women as compared with controls and hypothesized that omega−3 fatty acids probably contribute to the management of female infertility. Another study by Cussons \textit{et al.} showed that omega−3 fatty acid supplementation had beneficial effects on some cardiometabolic risk factors in PCOS patients. However, effects of n−3 LC PUFA on adiponectin levels and metabolic status in PCOS women are little known. So the objectives of this study were to determine the effects of omega−3 fatty acids on serum adiponectin levels and some metabolic risk factors including insulin resistance, serum lipids and hs-CRP levels in PCOS patients.

Serum adiponectin level was measured by ELISA method using BioVendor kit (Germany). Serum glucose was measured using the standard enzymatic methods with commercially available Pars Azmun kit (Karaj, Iran). Serum Insulin level was measured by ELISA method using DiaMetra kit (Italy) and insulin resistance was determined by Homeostasis Model Assessment (HOMA) index with formula: HOMA-IR = fasting insulin (\(\mu\text{U/mL}\)) \times fasting glucose (mg/dl)/405.\textsuperscript{15} Serum total cholesterol (TC), triglyceride (TG), and high-density lipoprotein cholesterol (HDL-C) were measured using the standard enzymatic methods by Pars Azmun kits. Low-density lipoprotein cholesterol (LDL-C) concentration was determined by the Friedewald formula: LDL-C=TC−(HDL-C + TG)/5.\textsuperscript{15} Serum hs-CRP level was measured using immunoturbidometric methodology by Pars Azmun kit at 500 nm and 37°C.

**Statistical analysis**

Data were analyzed using SPSS software (version 11.5; SPSS Inc., Chicago, IL) and the results are expressed as mean±SD. The normality of the distribution of variables was determined by the Kolmogorov-Smirnov test. The baseline measurements and dietary intakes of subjects in two groups were compared using independent samples t-test. ANCOVA was used to identify any differences between the two groups at the end of the study, adjusting for baseline values and covariates. The changes in anthropometric measurements, energy and nutrient intakes, serum
levels of adiponectin, glucose, insulin, HOMA-IR, lipids and hs-CRP between the beginning and end of the study were compared by paired samples \( t \)-test. The percentage of changes in variables after intervention was determined by formula: \([\text{after values} - \text{before values}]/ \text{before values}] \times 100\). A \( p \) value less than 0.05 was considered statistically significant.

### RESULTS

A total of 3 patients were excluded from the study because of personal reasons. Sixty one patients (30 patients in omega-3 fatty acids group and 31 patients in placebo group) completed the study. Patients demonstrated good compliance with the study design. Age and anthropometric characteristics of the subjects at the beginning and end of the study are shown in Table 1. There were no significant differences between and within groups in weight, BMI, WC and WHR in the beginning of the study and after 8 weeks of intervention.

Daily dietary intakes of participants throughout the study are shown in Table 2. Intake of cholesterol was significantly different between placebo and omega-3 fatty acids group at the beginning of the study \( (p=0.043)\). No significant differences in energy and other dietary intakes were observed between two groups at baseline. Total energy and nutrient intakes also did not change significantly in any of the groups during the study.

Serum levels of adiponectin and metabolic parameters of subjects at baseline and after 8 weeks intervention are shown in Table 3. There were no significant differences between the 2 groups in terms of serum adiponectin, glucose, insulin, HOMA-IR, lipids and hs-CRP levels at baseline. Results of analysis of covariance showed statistically significant differences between two studied groups in serum adiponectin \( (p=0.003)\), glucose \( (p<0.001)\), insulin \( (p=0.002)\), HOMA-IR \( (p<0.001)\), TC \( (p=0.002)\) and LDL-C \( (p=0.003)\) levels at the end of the study, adjusted for energy, PUFA and cholesterol intakes and baseline values, but changes in serum TG, HDL-C and hs-CRP levels were not significant. Supplementation with omega-3 fatty acids increased levels of adiponectin by 19.5% and resulted in 11.4%, 8.4%, 21.8%, 8.1% and 14.9% reduction in serum levels of glucose, insulin, HOMA-IR, TC and LDL-C, respectively, compared with these variables in placebo group.

As shown in Table 3, serum levels of adiponectin and

### Table 1. Characteristics of women with PCOS at baseline and after 8 weeks of either placebo or omega-3 fatty acids intervention

<table>
<thead>
<tr>
<th>variable</th>
<th>Measurement period</th>
<th>Placebo ((n=31))</th>
<th>Omega-3 fatty acids ((n=30))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>Baseline</td>
<td>27.7 ± 4.53</td>
<td>27.3 ± 4.27</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>Baseline</td>
<td>74.9 ± 9.95</td>
<td>73.7 ± 8.87</td>
</tr>
<tr>
<td></td>
<td>After intervention</td>
<td>75.1 ± 9.88</td>
<td>73.4 ± 8.88</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>Baseline</td>
<td>28.8 ± 2.90</td>
<td>28.7 ± 3.21</td>
</tr>
<tr>
<td></td>
<td>After intervention</td>
<td>28.8 ± 2.94</td>
<td>28.6 ± 3.30</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>Baseline</td>
<td>91.2 ± 6.38</td>
<td>91.1 ± 5.99</td>
</tr>
<tr>
<td></td>
<td>After intervention</td>
<td>91.3 ± 6.48</td>
<td>90.9 ± 6.14</td>
</tr>
<tr>
<td>WHR</td>
<td>Baseline</td>
<td>0.82 ± 0.03</td>
<td>0.81 ± 0.03</td>
</tr>
<tr>
<td></td>
<td>After intervention</td>
<td>0.82 ± 0.03</td>
<td>0.82 ± 0.04</td>
</tr>
</tbody>
</table>

BMI: body mass index, WC: waist circumference, WHR: waist to hip ratio.
Data are presented as mean ± SD

### Table 2. Dietary intakes of women with PCOS at baseline and after 8 weeks of either placebo or omega-3 fatty acids intervention

<table>
<thead>
<tr>
<th>variable</th>
<th>Measurement period</th>
<th>Placebo ((n=31))</th>
<th>Omega-3 fatty acids ((n=30))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (kcal/day)</td>
<td>Baseline</td>
<td>1735 ± 408</td>
<td>1742 ± 419</td>
</tr>
<tr>
<td></td>
<td>After intervention</td>
<td>1680 ± 368</td>
<td>1668 ± 415</td>
</tr>
<tr>
<td>Carbohydrate (g/day)</td>
<td>Baseline</td>
<td>215 ± 63.5</td>
<td>224 ± 65.9</td>
</tr>
<tr>
<td></td>
<td>After intervention</td>
<td>216 ± 52.8</td>
<td>209 ± 51.5</td>
</tr>
<tr>
<td>Protein (g/day)</td>
<td>Baseline</td>
<td>62.8 ± 19.5</td>
<td>63.6 ± 19.2</td>
</tr>
<tr>
<td></td>
<td>After intervention</td>
<td>62.1 ± 18.7</td>
<td>61.7 ± 21.9</td>
</tr>
<tr>
<td>Total Fat (g/day)</td>
<td>Baseline</td>
<td>67.0 ± 22.0</td>
<td>65.0 ± 21.2</td>
</tr>
<tr>
<td></td>
<td>After intervention</td>
<td>65.8 ± 19.8</td>
<td>64.6 ± 20.1</td>
</tr>
<tr>
<td>SFA (g/day)</td>
<td>Baseline</td>
<td>17.7 ± 6.59</td>
<td>16.8 ± 6.20</td>
</tr>
<tr>
<td></td>
<td>After intervention</td>
<td>17.3 ± 6.30</td>
<td>18.1 ± 6.82</td>
</tr>
<tr>
<td>MUFA (g/day)</td>
<td>Baseline</td>
<td>20.3 ± 6.20</td>
<td>18.3 ± 6.72</td>
</tr>
<tr>
<td></td>
<td>After intervention</td>
<td>21.1 ± 7.11</td>
<td>19.7 ± 6.87</td>
</tr>
<tr>
<td>PUFA† (g/day)</td>
<td>Baseline</td>
<td>20.9 ± 8.65</td>
<td>20.0 ± 9.55</td>
</tr>
<tr>
<td></td>
<td>After intervention</td>
<td>20.9 ± 8.65</td>
<td>20.0 ± 9.55</td>
</tr>
<tr>
<td>Cholesterol (mg/day)</td>
<td>Baseline</td>
<td>203 ± 39.4</td>
<td>183 ± 34.5*</td>
</tr>
<tr>
<td></td>
<td>After intervention</td>
<td>188 ± 45.8</td>
<td>191 ± 38.1</td>
</tr>
</tbody>
</table>

SFA: Saturated fatty acids, MUFA: Monounsaturated fatty acids, PUFA: Polyunsaturated fatty acids
† Excluding the PUFA from the supplement
*Significant difference between two groups at baseline \((p<0.05)\), independent sample \( t \)-test
Data are presented as mean ± SD
HDL-C significantly increased in the omega-3 fatty acids group (by 19.8%, \( p=0.006 \) and by 7.4%, \( p=0.018 \), respectively) at the end of the study. Significant decrease in serum levels of glucose, HOMA-IR, TC and LDL-C (by 10.9%, 16.3%, 8.2% and 12.6% respectively, \( p<0.001 \) for all), TG (by 5.0%, \( p=0.024 \)) and insulin (by 7.5%, \( p=0.002 \)) was obtained in omega-3 fatty acids group over the 8 weeks in comparison to baseline values. Levels of serum hs-CRP remained unchanged in both groups at the end of the study.

**DISCUSSION**

Current evidence from clinical, experimental and epidemiologic investigations indicates that omega-3 fatty acids are protective against cardiovascular disease and inflammatory disorders.16

According to our results, no significant changes were observed in anthropometric measurements, energy and macronutrient intakes within omega-3 fatty acids and placebo groups during the study. These results were similar to the previous studies in PCOS patients.14,15 Cussons et al. reported that omega-3 supplementation by dose of 4 g/day for 8 weeks, had no significant effects on BMI and WHR of PCOS patients with nonalcoholic fatty liver disease.14 Results of another study conducted by Vargas et al. in PCOS patients indicated that 6 weeks supplementation with 3.5 g/day fish oil did not change weight, BMI, and WC significantly.17 No other published data are available about the effects of omega-3 supplementation in PCOS subjects. However, Hajianfar et al. reported that consumption of fish oil reduced BMI, WC and WHR in women by type 2 diabetes compared with the placebo group.18 Findings obtained by Flachs et al.13 and Nakatani et al.20 demonstrated that PUFA of marine origin resulted in lower body weight in mice.

It has been reported that effects of omega-3 fatty acids on anthropometric measurements might be dependent on sex, age and BMI of subjects at baseline.21,22 It was also proposed that along with different mechanisms, intake of fish oil may decrease fat mass via lowering energy intake.23 The overall energy intakes of our studied subjects in both groups were not significantly different at the end of the study compared to baseline values, so no significant variations in anthropometric measurements of all subjects would be partially expected. As a result, anthropometric measurements would not be considered as confounding factors in the interpretation of studied biochemical variables.

Adiponectin is an adipose tissue-derived protein that exists in the human serum at range of 5-30 µg/mL.4 Our results indicated the mean baseline levels of adiponectin in all studied subjects was near to low range and interpreted on anthropometric measurements might be dependent on sex, age and BMI of subjects at baseline.21,22 It was also proposed that along with different mechanisms, intake of fish oil may decrease fat mass via lowering energy intake.23 The overall energy intakes of our studied subjects in both groups were not significantly different at the end of the study compared to baseline values, so no significant variations in anthropometric measurements of all subjects would be partially expected. As a result, anthropometric measurements would not be considered as confounding factors in the interpretation of studied biochemical variables.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Measurement period</th>
<th>Placebo (n=31)</th>
<th>Omega-3 fatty acids (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adiponectin (µg/mL)</td>
<td>Baseline</td>
<td>12.3 ± 3.62</td>
<td>11.8 ± 3.18</td>
</tr>
<tr>
<td></td>
<td>After intervention</td>
<td>12.0 ± 3.10</td>
<td>13.5 ± 2.41</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>Baseline</td>
<td>91.7 ± 12.3</td>
<td>95.2 ± 10.3</td>
</tr>
<tr>
<td></td>
<td>After intervention</td>
<td>92.4 ± 9.92</td>
<td>85.4 ± 8.95</td>
</tr>
<tr>
<td>Insulin (µIU/mL)</td>
<td>Baseline</td>
<td>16.4 ± 3.54</td>
<td>16.5 ± 2.96</td>
</tr>
<tr>
<td></td>
<td>After intervention</td>
<td>16.4 ± 3.39</td>
<td>15.1 ± 2.68</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>Baseline</td>
<td>3.79 ± 1.28</td>
<td>3.91 ± 1.03</td>
</tr>
<tr>
<td></td>
<td>After intervention</td>
<td>3.80 ± 1.11</td>
<td>3.20 ± 0.80</td>
</tr>
<tr>
<td>TC (mg/dL)</td>
<td>Baseline</td>
<td>188 ± 29.2</td>
<td>187 ± 32.5</td>
</tr>
<tr>
<td></td>
<td>After intervention</td>
<td>187 ± 25.9</td>
<td>170 ± 32.0</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>Baseline</td>
<td>126 ± 28.5</td>
<td>127 ± 29.5</td>
</tr>
<tr>
<td></td>
<td>After intervention</td>
<td>120 ± 28.5</td>
<td>119 ± 26.0</td>
</tr>
<tr>
<td>LDL-C (mg/dL)</td>
<td>Baseline</td>
<td>117 ± 31.5</td>
<td>118 ± 29.4</td>
</tr>
<tr>
<td></td>
<td>After intervention</td>
<td>117 ± 27.4</td>
<td>102 ± 29.6</td>
</tr>
<tr>
<td>HDL-C (mg/dL)</td>
<td>Baseline</td>
<td>44.9 ± 6.11</td>
<td>43.1 ± 6.55</td>
</tr>
<tr>
<td></td>
<td>After intervention</td>
<td>45.3 ± 4.49</td>
<td>45.9 ± 6.53</td>
</tr>
<tr>
<td>hs-CRP (mg/L)</td>
<td>Baseline</td>
<td>2.22 ± 0.83</td>
<td>2.26 ± 0.70</td>
</tr>
<tr>
<td></td>
<td>After intervention</td>
<td>2.08 ± 0.80</td>
<td>2.11 ± 0.80</td>
</tr>
</tbody>
</table>

HOMA-IR: homeostatic model assessment for insulin resistance, TC: total cholesterol, TG: triglyceride, LDL-C: low density lipoprotein, HDL-C: high density lipoprotein, hs-CRP: high sensitive C-reactive protein

*Significant difference within groups after intervention (\( p<0.05 \), paired sample t-test)

†Significant difference between groups after intervention (\( p<0.05 \), analysis of covariance)

Data are presented as mean ± SD

Table 3. Serum adiponectin levels and metabolic parameters of women with PCOS at baseline and after 8 weeks of either placebo or omega-3 fatty acids intervention
ed to metabolic status of subjects or different study designs. Vargas et al. also reported no significant changes in serum adiponectin levels in PCOS patients after 6 weeks supplementation by fish oil.17

According to results, omega−3 fatty acids caused a considerable decrease in insulin resistance. Our results were similar to the findings of other studies which reported decreased fasting glucose serum in healthy female,20 reduction in insulin levels and HOMA-IR in young women16 and decreased fasting insulin levels in non-diabetic, moderately hyperglycaemic patients11 and hemodialysis patients12 after supplementation with omega−3 fatty acids. Lower plasma glucose22 and insulin19 concentrations were reported in studies on mice fed diets rich in EPA and DHA compared to other experimental diets.

Improvement in insulin sensitivity by omega−3 fatty acids in our patients might be resulted from elevated adiponectin level which has anti-diabetic, anti-atherosclerotic and anti-inflammatory effects.23 Adiponectin increases glucose utilization by activation of AMPK (AMP-activated protein kinase).27,33 Moreover, AMPK suppresses gluconeogenesis in the liver and stimulates glucose transport in muscle.31 It has also been suggested that inhibition of the activity and expression of glucose-6-phosphatase by n−3 fatty acids, decreases hepatic glucose output.34

Conversely a number of other studies have failed to show improvement in insulin sensitivity by omega−3 fatty acids in PCOS patients14,17 young healthy subjects31 and type 2 diabetic patients.36 It seems that the dose and fatty acid composition of the n−3 PUFA supplements, duration of intervention, health status of the study subjects, degrees of obesity and insulin resistance, the presence of other conditions that may also affect insulin sensitivity and differences in the sensitivities of the tools used to assess insulin resistance, also contribute to the inconsistencies.35

In our study supplementation with omega−3 fatty acids lead to significant reduction in serum lipids. Cussons et al. and Vargas et al. also showed significant decrease in serum TG levels in PCOS patients after supplementation with fish oil but serum TC, LDL-C and HDL-C concentrations remained unchanged.14,17 In addition, reduction in serum TG levels by fish oil was reported in several other studies.6,35 In a study by Nilsen et al., intake of omega−3 fatty acids, resulted in significant reduction in serum TG and increase in HDL-C levels in patient with acute myocardial infarction.36 The omega−3 fatty acids are natural ligands for 4 metabolic nuclear receptors including PPARs, LXR (liver X receptor), HNF-4α (hepatocyte nuclear factor-4α) and FXR (farnesol X receptor). Activation of these receptors by EPA and DHA down-regulates genes encoding proteins that stimulate lipid synthesis and up-regulates genes that enhance fatty acid oxidation in liver and muscle.37 In addition, some positive effects of n−3 LCPUFA on lipid profile is mediated by enhancement of AMPK, a major sensor of cellular energy status which regulates partitioning between lipid oxidation and lipogenesis.33 It is also proposed that fish oil intake improves LDL receptor activity in the liver, reduces LDL-C synthesis and increases fractional rate of catabolism of LDL-C.28,38,39

Based on obtained results, serum levels of TG significantly decreased and HDL-C increased in the omega−3 fatty acids group only compared to their baseline values. It was shown that effect of fish oil on TG levels is dose-dependent.8 Studies on hypertriglyceridaemic patients demonstrated that high doses of fish oil had remarkable effects in reducing TG levels.8,40 It was possible that in our study, dose of omega−3 fatty acids or duration of intervention period were not sufficient to have considerable impact on serum TG and HDL-C levels in comparison to placebo group.

We observed that omega−3 fatty acids had no significant effect on serum hs-CRP in studied patients. This finding is in accordance with the results of previous studies in PCOS women.14,17 However, Tsitouras et al. and Rasic-Milutinovic et al. reported significant decrease in HS-CRP levels after diet intervention high in EPA and DHA in healthy older adults and fish oil supplementation in hemodialysis patients.28,32 The effect of n−3 PUFA on markers of chronic inflammation such as hs-CRP is largely unknown.41 When the intake of n−3 PUFA is high, EPA and DHA replace arachidonic acid in the cell membranes and produce eicosanoids which have less inflammatory actions.41 Non significant effect of omega−3 fatty acids on serum hs-CRP levels in our study might be due to low baseline serum levels of hs-CRP in the studied patients. Other studies are needed to evaluate effects of omega−3 fatty acids on serum hs-CRP in PCOS patients with higher baseline serum hs-CRP values or on other inflammatory markers.

Our study had some limitations. This research included only overweight and obese PCOS patients. In addition, effects of omega−3 fatty acids on metabolic parameters are dose-related.5,42 Therefore, the results of our study may not be applicable to underweight or normal weight PCOS patients and also to other doses of omega−3 fatty acids supplements or different intervention period durations.

As a conclusion the present trial showed that supplementation with omega−3 fatty acids had some beneficial effects on serum adiponectin, insulin resistance and lipid profile in PCOS patients. Omega−3 fatty acids may be useful in the control and prevention of metabolic complications of PCOS patients such as type 2 diabetes and cardiovascular diseases.

ACKNOWLEDGMENTS
We thank The Research Vice-Chancellor and Nutrition Research Center of Tabriz University of Medical Sciences, Tabriz, Iran for the financial support; and women who participated in the study.

AUTHOR DISCLOSURES
The investigators did not have any conflict of interest.

REFERENCES


Original Article

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Omega-3脂肪酸的補充對於多囊性卵巢症婦女血清中脂聯素與其他代謝危險因子的影響

多囊性卵巢症是常見的女性內分泌失調疾病，且與第 2 型糖尿病及心血管疾病之某些危險因子相關。此研究的目的在探討 omega-3 脂肪酸，對於多囊性卵巢患者血清中脂聯素和數項代謝危險因子的影響。研究方法採雙盲隨機臨床試驗，研究對象為 64 位過重或肥胖，年齡介於 20-35 歲的多囊性卵巢患者。8 週試驗期內，試驗組(32 位)每天接受 4 顆各含 180 毫克的 EPA 與 120 毫克 DHA 的膠囊；而對照組(32 位)則每天給予 4 顆安慰劑。在試驗前及結束時，皆收集空腹血液樣本、體位測量及 3 天的 24 小時飲食回憶記錄。最後共 61 位參與者完成試驗。研究結果顯示，與對照組相比，omega-3 脂肪酸顯著地增加試驗組的血清脂聯素濃度(p=0.003)，並降低血糖(p<0.001)、胰島素(p=0.002)、胰島素阻抗(p<0.001)、總膽固醇(p=0.002)以及低密度脂蛋白膽固醇(p=0.003)。與試驗前的數值相比，omega-3 脂肪酸的補充顯著地減低血清中三酸甘油酯，且增加高密度脂蛋白膽固醇的濃度。兩組試驗前後的血清高敏性 C 反應蛋白，皆不具顯著的改變。結論：omega-3 脂肪酸有助於多囊性卵巢症患者，維持較佳的血清脂聯素濃度、胰島素阻抗性及血脂狀態，而這可能改善患者的代謝性併發症。

關鍵字：omega-3脂肪酸、多囊性卵巢症、脂聯素、胰島素阻抗、血脂全套指數