

Original Article

## The effect of omega-3 on the serum visfatin concentration in patients with type II diabetes

*Hossein Hajianfar<sup>a</sup>, Mohammad Javad Hosseinzadeh<sup>b</sup>, Ahmad Bahonar<sup>\*c</sup>,  
Kazem Mohammad<sup>d</sup>, Golam Reza Askari<sup>e</sup>, Mohammad Hassan Entezari<sup>f</sup>,  
Ali Keshavarz<sup>g</sup>, Nazli Ansari<sup>h</sup>*

**Abstract**

**BACKGROUND:** Visfatin is an adipocytokine which is secreted from adipose tissue and can affect on the diabetes inflammatory reaction and also serum lipids level. On the other hand, Omega-3 can also prevent formation of insulin resistance. In the present study, the effect of Omega-3 on the serum visfatin concentration was evaluated.

**METHODS:** 71 women with type II diabetes were randomly assigned to the group that took Omega-3 capsules or control group with placebo capsules. In the first step, study subjects filled a questionnaire collecting their age, height, weight, waist circumference, and hip circumference. Also their blood samples were taken for blood tests. In the second step, the intervention was done for 8 weeks and in the third step the aforementioned were collected again. In the blood samples visfatin and lipid profiles (low density lipoprotein [LDL], high density lipoprotein [HDL], triglyceride [TG], and cholesterol), glucose and HbA1c were measured.

**RESULTS:** There was no significant difference in serum visfatin level between Omega-3 and placebo groups before the intervention ( $p = 0.14$ ), while after the intervention, the mean serum visfatin level in the Omega-3 group was significantly higher ( $p < 0.001$ ). In addition, the mean difference between the serum visfatin level before and after the intervention in both groups was significant ( $p < 0.001$ ).

**CONCLUSIONS:** This study showed an increase in visfatin level following consuming Omega-3 fats but according to controversial issues on insulin-like function of visfatin, the effects of Omega-3 on diabetes should be studied more in further studies.

**KEYWORDS:** Fatty Acids, Omega-3, Nicotinamide Phosphoribosyltransferase, Diabetes Mellitus, Type 2.

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According to the reports of the World Health Organization, in recent years, 150 million people have suffered from type II diabetes all over the world; it is estimated that this figure would be doubled by 2025.<sup>1</sup> The mortality rate of the patients with diabetes is 1.5-2.5 times more than the total

population after the matching age.<sup>2</sup> In most cases, insulin resistance, and type II diabetes have been associated with obesity; so the obesity and overweight are the main causes of diabetes and insulin resistance.<sup>3</sup>

Adipose tissue, in addition to the important role of energy storage in the form of triglyce-

<sup>a</sup> Department of Nutrition, Tehran University of Medical Sciences, Tehran, Iran

<sup>b</sup> Associate Professor, Department of Nutrition, Tehran University of Medical Science, Tehran, Iran

<sup>c</sup> Isfahan Cardiovascular Research Center, Isfahan University of Medical Sciences, Isfahan, Iran (Corresponding Author)

<sup>d</sup> Department of Statistics, Tehran University of Medical Sciences, Tehran, Iran

<sup>e</sup> PhD Student, Department of Nutrition, Isfahan University of Medical Sciences, Isfahan, Iran

<sup>f</sup> Department of Nutrition, Isfahan University of Medical Sciences, Isfahan, Iran

<sup>g</sup> Department of Nutrition, Tehran University of Medical Sciences, Tehran, Iran

<sup>h</sup> Researcher, Skin Diseases and Leishmaniasis Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

\* Corresponding Author

E-mail: bahonarahmad@gmail.com

ride, has the major impact on the secretion of various hormones such as leptin, adiponectin, and visfatin and cause activation of the insulin signals. In fact, adipose tissue is an endocrine tissue which some of the proteins such as adipokines are secreted from; the impact of some adipokines on lipid and glucose metabolism (directly or indirectly) has been proven and also they can increase insulin resistance; whereas some others (e.g. adiponectin) have protective effect against insulin resistance in type II diabetes.<sup>4</sup>

Visfatin is a new adipokine identified in visceral fat tissue by Fukuhara et al; they described it as "a protein secreted by visceral fat that mimics the effects of insulin. Fat tissue produces a variety of secreted proteins (adipocytokines) with important roles in metabolism."<sup>5</sup> It is mainly secreted by the visceral adipose tissue<sup>6,7</sup> and has an insulin-like function.<sup>6-8</sup> The association between plasma level of visfatin with factors such as type II diabetes, body mass index (BMI) and fat percentage is in controversial.<sup>6,7,9-12</sup> There are several evidences regarding the harmful effects of elevated visfatin level, which should also be considered.<sup>13</sup>

Visfatin has a regulator role in fat metabolism,<sup>9</sup> a direct relation with BMI,<sup>10</sup> and a direct relation with waist to hip ratio (WHR).<sup>7</sup> Serum visfatin level has a direct association with HDL-c level and a reverse association with serum triglyceride level. These are positive effects of visfatin on the lipid profile of non-diabetic people.<sup>11</sup> This insulin-like function and increasing of insulin sensitivity by visfatin are improved.<sup>12</sup>

Omega-3 disrupts the fatty constructive genes and reduces hormones associated with obesity such as leptin and also prevents the construction of Omega-6 compounds.<sup>14</sup> The study of Shah et al has indicated that consumption of Omega-3 improves the effect of insulin in type II diabetic patients without reducing the blood glucose and triglyceride level.<sup>15</sup> Friedberg et al revealed that Omega-3 does not affect HbA1c in patients with diabetes and stated that consumption of Omega-3 can reduce 30% of triglyceride level which is ap-

propriate in the treatment of lipid disorders in these patients.<sup>16</sup>

According to controversial issues on insulin-like function of visfatin, this study aimed to investigate the effect of Omega-3 consumption on the serum visfatin level.

## Methods

This was a clinical controlled double-blind randomized study. The study population included the 45 to 65 years old women with type II diabetes who referred to Charity Center of Diabetes in Isfahan. Sample size was determined to be 39, using sample size formula and considering 15% additional samples. The women with type II diabetes, who were at least diagnosed five years ago, entered the study.

Exclusion criteria were injecting insulin, having secondary complications of diabetes such as ophthalmic and renal complication, amputation, etc, and having inflammatory diseases with the CPR level of +++ or more.

This study was approved by the Ethics Committee of Tehran University of Medical Sciences; the aim of the study and its method was explained for the participants and then all of them signed the consent form.

We assessed 2500 profiles of patients with diabetes type II in the center. 150 patients had the criteria to enter the study from which, 39 patients were selected in each group randomly. Some subjects did not end the study and finally, 37 patients set in the Omega-3 group and 34 in the placebo group. All the patients filled in a questionnaire for collecting data including age, height, weight, waist circumference, and hip circumference; besides, their blood samples were taken for blood tests. The hip circumference was measured from the middle and the largest part of it and waist circumference also from the cord at the end of a normal exhalation.

In patients with type II diabetes, the consumption of more than 4 grams EPA (Eicosapentaenoic Acid) or DHA (Docosahexaenoic Acid), Omega-3 derivatives, can increase the serum glucose and reduce TG<sup>17</sup> and some researches mentioned that at least 2,000 mg per

day of Omega-3 could be beneficial to patients with diabetes.<sup>18</sup> So, the Omega-3 group was given two capsules containing Omega-3 with dose of 2000 mg each day for 8 weeks; each capsule contained 1,000 mg Omega-3, 65% EPA (360 mg) and 35% DHA (240 mg). The placebo group was given two placebo capsules containing 1 g of cornstarch for the same period.

Then, height, weight, waist circumference, and hip circumference and also the blood sample were checked again with the same method.

The blood sampling was conducted after 10-12 hours of fasting (10 cc in each time) before taking the antidiabetic tablets. LDL, HDL, TG, cholesterol, glucose, and HbA1c levels were measured using Pars Azmoon Kits (Tehran, Iran). Visfatin level was measured using ELISA method with the sensitivity of 30 pg/ml via Human Visfatin Kit (ADIPOGEN Inc., South Korea). All the tests were conducted automatically by HITACHI 911.

Data were analyzed using SPSS software version 18. The Fisher's exact test was used for qualitative data and student t-test for quantita-

tive data. The weight changes were analyzed by chi-square test and Pearson correlation test was used for the data correlation. Moreover, paired t-test was used for comparing serum visfatin concentration before and after the intervention in both groups and independent t-test was used for comparing mean concentration changes between the two groups.

## Results

The Omega-3 group and placebo group had no significant differences in terms of underlying variables such as age, sex, education, and occupation. Besides, there was no significant difference between the two groups in terms of other variables such as comorbidities and taking medication and the diet type. Hence, probably these variables had no confounding effect.

The obtained data such as BMI, serum visfatin level, weight, waist circumference, hip circumference, WHR, blood glucose, and HbA1c are shown in table 1.

There were significant differences between the two groups in BMI, weight, waist circumfe-

**Table 1.** Anthropometric data and visfatin level in two studied groups

|                           |                        | Omega3         | Placebo      | P value |
|---------------------------|------------------------|----------------|--------------|---------|
| Visfatin                  | Before Intervention    | 3.28 ± 1.06    | 3.37 ± 1.11  | 0.14    |
|                           | After Intervention     | 6.36 ± 2.40    | 3.76 ± 1.23  | < 0.001 |
|                           | Change After to Before | 3.08 ± 2.56    | 0.094 ± 1.06 | < 0.001 |
| Body Mass Index (BMI)     | Before Intervention    | 27.7 ± 3.4     | 28 ± 3.8     | 0.76    |
|                           | After Intervention     | 27.4 ± 4.1     | 28.7 ± 4.4   | 0.19    |
|                           | Change After to Before | -0.31 ± 0.7    | 0.73 ± 1.2   | < 0.001 |
| Weight                    | Before Intervention    | 69.6 ± 13.2    | 70.1 ± 11.3  | 0.84    |
|                           | After Intervention     | 68.8 ± 12.4    | 71.7 ± 12.8  | 0.33    |
|                           | Change After to Before | -0.8 ± 1.8     | 1.5 ± 2.5    | < 0.001 |
| Waist Circumference       | Before Intervention    | 89 ± 10        | 88 ± 9.5     | 0.76    |
|                           | After Intervention     | 87.9 ± 9.4     | 90 ± 10.4    | 0.19    |
|                           | Change After to Before | -1.2 ± 2       | 2 ± 2.7      | < 0.001 |
| Hip Circumference         | Before Intervention    | 104.9 ± 7.6    | 104 ± 6.4    | 0.57    |
|                           | After Intervention     | 104.6 ± 7.4    | 104.6 ± 6.5  | 0.57    |
|                           | Change After to Before | -0.3 ± 0.7     | 0.7 ± 1      | < 0.001 |
| Waist to Hip Ratio (WHR)  | Before Intervention    | 0.84 ± 0.05    | 0.84 ± 0.04  | 0.8     |
|                           | After Intervention     | 0.83 ± 0.04    | 0.85 ± 0.05  | 0.09    |
|                           | Change After to Before | -0.009 ± 0.016 | 0.014 ± 0.02 | < 0.001 |
| Fasting Blood Sugar (FBS) | Before Intervention    | 146 ± 51.6     | 142.9 ± 57.6 | 0.81    |
|                           | After Intervention     | 149.6 ± 52.5   | 150.5 ± 55.4 | 0.94    |
|                           | Change After to Before | 3.6 ± 30.3     | 7.7 ± 47.1   | 0.66    |
| HbA1c                     | Before Intervention    | 8.4 ± 1.5      | 8.5 ± 1.7    | 0.8     |
|                           | After Intervention     | 7.8 ± 1.1      | 8.5 ± 1.7    | 0.09    |
|                           | Change After to Before | -0.61 ± 0.7    | -0.02 ± 0.9  | 0.003   |

rence, hip circumference and WHR value after the intervention; but changes after the intervention in each group were not significant compared to the value before the intervention.

Serum visfatin level had no significant difference before the intervention between two groups ( $p = 0.14$ ); the serum visfatin level of the Omega-3 group had a significant difference after the intervention comparing to its before value ( $p < 0.001$ ) while the serum visfatin level of placebo group had no significant difference after the intervention ( $p > 0.05$ ).

FBS level had not significant difference before and after the intervention between two groups ( $p > 0.05$ ). HbA1c level had no significant difference between two groups before the intervention ( $p = 0.8$ ) and after it ( $p = 0.09$ ); whereas there was a significant difference in mean of HbA1c level difference before and after the intervention between two groups ( $p = 0.003$ ).

Based on the findings of the present study, consumption of Omega-3 caused the patients to lose weight while the patients who had not taken it gain weight during the intervention and weight changes in two groups had a significant difference (Figure 1).

## Discussion

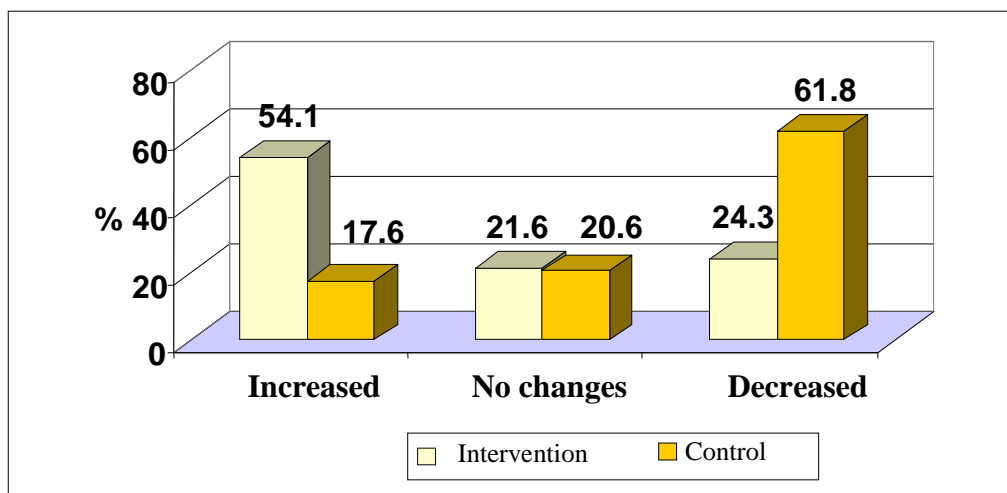
This study aimed to determine the efficacy of Omega-3 on serum visfatin concentration in patients with type II diabetes. According to the

results, consumption of Omega-3 had been effective on preventing weight gain.

These findings show the role of increase in visfatin level and secretion of cytokine from the adipocytes along with receiving Omega-3. The possible reason might be due to more accumulation of adipocytes and/or quicker differentiation and consequently synthesis and more secretion of visfatin to the patients' serum level.<sup>19</sup> According to the study of Tanaka et al, visfatin is secreted from the 3T3-L1 adipocytes which are dependent to the endoplasmic-Golgi reticulum or micro-vesicles.<sup>20</sup> Also, the role of hyperglycemia on the increase of visfatin synthesis from the cultures adipocytes was observed.<sup>21</sup> The biological mechanisms of visfatin role in pathogenesis of type II diabetes are not well determined.

Unlike Berndt et al,<sup>22</sup> Krzyzanowska et al,<sup>23</sup> Fukuhara et al,<sup>5</sup> and Chen et al,<sup>7</sup> the present study showed a significant and positive association between the abdominal obesity value and serum visfatin level in patients with type II diabetes.

Furthermore, the results of other studies showed a significant correlation between the level of circulating visfatin and BMI value in the participants.<sup>5,6,12,22</sup> Otherwise, the results of Paganano et al on non-diabetic obesity<sup>21</sup> and the study of Samara et al on diabetic patients with different weights<sup>24</sup> reported the reverse association between BMI and circulating visfatin level.



**Figure 1.** Percentage distribution of weight changes in the studied groups

Moreover, Chen et al found no significant correlation between BMI and circulating visfatin level in patients with type II diabetes.<sup>7</sup>

In general, the visceral fat values or abdominal obesity and body obesity which measured by WHR and BMI respectively are in association with synthesis and visfatin secretion rates; based on the study of Berndt et al, there is a correlation between the emergence of abdominal visfatin gene and BMI and the percentage of body fat while it had no association with subcutaneous fat;<sup>22</sup> this is a reason for secretion of cytokine from the visceral adipose tissue cells or adipocytes.<sup>25</sup> According to the present results, the correlation between plasma visfatin concentration and various parameters related to metabolic syndrome such as insulin sensitivity, fasting insulin and fasting plasma glucose can be realized.

Omega-3 consumption causes more burning of body fat and by increased metabolism cause weight loss in the patients.<sup>14</sup> In this study, BMI was also reduced in the Omega-3 group and had been increased in the placebo group.

In this study, WHR also reduced in the Omega-3 group and increased in the placebo group. Therefore, Omega-3 can be effective in weight control of diabetic patients.

The results of this study showed increase of fasting plasma glucose level in both groups of Omega-3 and placebo. This finding was not in accordance with the results of previous stu-

dies.<sup>26,27</sup> This finding showed the role of Omega-3 consumption in controlling the HbA1c level which itself is an index to assess the quality of controlling plasma glucose level in diabetes which was in accordance with some other studies in this regard.<sup>26,27</sup> This finding was in contrast with Fukino et al study.<sup>28</sup> This study, unlike the previous studies, showed a reverse association between circulating visfatin level and fasting blood glucose.<sup>6,7,29</sup> There was a direct relationship between fasting glucose changes and visfatin level in the two groups; because there was no significant relationship between visfatin level and fasting blood glucose. Similar to insulin, visfatin can increase the removal of the glucose by the adipocytes and muscle cells and reduce the fasting hepatic glucose production.

#### **Limitations**

We did not assess the changes in dietary intakes, lifestyle, and variables including diet and physical activity due to lack of budget; another study with more subjects could be done to determine these variables' effects.

At the end, according to controversial issues on insulin-like function of visfatin, this study focused on the effect of Omega-3 on the serum visfatin level; the beneficial effects of Omega-3 on diabetes should be studied more in further studies.

#### **Conflict of Interests**

Authors have no conflict of interests.

#### **Authors' Contributions**

HH has designed the research collected the data and analyzed it and took place in writing article draft and revising it; MJH has designed the research collected the data and analyzed it; AB wrote article draft and the final version of article. KM, GRA, MHE, AK, and NA were consulted in research designing and had role in article draft. All authors have read and approved the final manuscript.

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