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Effect of Omega 3 and Zinc on Glycemic Indices, Serum Zinc, and Blood Pressure in Diabetic Patients

Setareh Alibakhshi[1], Mehdi Khakian[1], Peyvnd Mohammadi[2], Majid Manafi*[1]

[1]MSc in Nutrition Sciences, Urmia University of Medical Sciences, Urmia, Iran,
[2]Endocrinology sub-specialist, Urmia University of Medical Sciences, Urmia, Iran.

***Corresponding Author**

Abstract: *Background: The objective of this study was to investigate and compare the effect of omega 3 and zinc supplementation (both simultaneously and separately) on glycemic indices (fasting blood sugar (FBS), fasting insulin, insulin sensitivity, insulin resistance, HbA1C), serum zinc level, blood pressure, and Body composition in the patients with diabetes type 2. Method: This study is a double-blind randomized controlled clinical trial conducted on 100 patients with diabetes. The patients were divided into four intervention groups: omega 3 group (n=25, a daily 1000 mg of omega-3), zinc group (n=25, 30 mg zinc gluconate), zinc and omega-3 group (n=25), and the placebo group (n=25). Results: There was a significant reduction in the individuals' weight after intervention in omega 3 and zinc groups (p=0.000 and p=0.038, respectively). Zinc supplementation (by itself or with omega 3) significantly changed the patients' BMI (p=0.033). Blood pressure has been significantly reduced after intervention in all three groups of intervention with omega 3 and zinc (p<0.001). FBS was reduced in all three groups after intervention; however, this reduction was significant in the zinc group and the zinc and omega 3 group (p<0.001 and p=0.002, respectively). The values of serum insulin were significantly reduced after intervention in all three groups of intervention with omega 3, intervention with zinc, and intervention with omega 3 and zinc (p=0.001, p=0.000, and p=0.002). HBA1C was also significantly reduced after intervention in all three groups of intervention. Conclusion: Omega 3 and zinc supplementation can be useful for improving weight and controlling glycemic as well as blood pressure. The effects of zinc supplementation on glycemic indices are more useful than omega 3.*

Keywords: *Supplementation, Blood Pressure, Diabetes Mellitus Type 2, Insulin Resistance, Omega 3, Zinc*

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is caused by the insulin resistance and its insufficient secretion; approximately, 90 percent of the patients with diabetes across the world are afflicted with this type of the diabetes (lberti, Zimmet, 1998). According to the report of the world health organization, over 422 million people have been afflicted with diabetes in the world in 2014 (Organization WH, 2016). α-linolenic Acid (ALA) (18:3 (n-3)) makes unsaturated long-chain omega-3 fatty acids eicosapentaenoic acid (EPA) (20:5 (n-3)) and Docosa Hexaenoic Acid (DHA) (22:6(n-3)); it is not synthesized in the body and is regarded as an essential fatty acid (Mahan LK, Escott-Stump, 2008). The effect of omega-3 fatty acids on the improvement of blood glucose may be due to the prevention of decreased phosphatidylinositol 3-kinase activity. Moreover, the long-chain omega-3 fatty acids impede the expression of the hepatic glucose-6-phosphatase activity. This can justify the inhibition of the increased glucose liver transporter by the omega-3 fatty acid (Delarue et al., 2004). The level of the essential fatty acids in patients with diabetes is lower than the ordinary people. The reason for their lowness is

not clear; however, some researchers claim that patients with diabetes have a lower ability to convert ALA to EPA and DHA, Toorang et al. (2009) conducted a study in Iran and indicated that omega-3 fatty acids supplementation were used for 8 weeks that led to the improvement of blood glucose and HbA1C in the people T2DM. However, Sirtoria et al. (1997) conducted a study in Italy and indicated that daily supplementation of omega-3 for 8 weeks did not have a significant effect on HbA1C and FBS. Therefore, the results of the studies are still contradictory. Zinc is an essential element that has been used in the structure of more than 300 metalloenzymes; it plays a role in most of the major metabolic paths such as the metabolism of fat, protein, and carbohydrate (Coleman, 1992). The zinc level is low in the individuals with diabetes type 2. It can be due to the increased diuresis and zinc removal. Besides, the shortage of zinc in the people with diabetes leads to diabetes-related complications (micro and macro vascular); it is caused by decreased enzymes which are dependent on zinc as well as the increased oxidative stress. A recent study showed that the existence of zinc in the beta cells in the pancreas change the insulin monomers into a dimeric form and this form can be either stored or secreted as crystal (Rahimi et al., 2008). Sun et al. (2009) conducted a study in America and showed that zinc can have useful effects on delaying the affliction with diabetes. However, the results of the studies are still contradictory such that Roshanravan (2015) conducted a study in Iran and showed that zinc supplementation does not significantly increase sensitivity to insulin in the patients with diabetes. Clinical studies show that taking omega-3 fatty acids may reduce the blood pressure of people with high blood pressure and patients with other risk factors for cardiovascular diseases such as overweight, hyperlipidemia, diabetes, or hemodialysis patients (Cabo et al., 2012). Blood pressure is defined as systolic blood pressure greater than 140 mmHg and diastolic blood pressure greater than 90 mmHg. Eric et al. In 2002, an Eric et al study conducted with the aim of affecting fish oil on blood pressure showed that daily intake of 3 grams of oil Fish can significantly reduce systolic and diastolic blood pressure in the elderly and people with hypertension (Geleijnse et al., 2002). While in another study aimed at the effect of omega-3 fatty acids on blood pressure, there was no significant relationship between omega-3 and low blood pressure (Sarafrazi et al., 2002). A meta-analysis showed that consumption of omega-3 fatty acids could significantly reduce blood pressure in people with hypertension (Morris et al., 1993). These differences can be due to the amount of fatty acids consumed, the size of the samples, and whether or not they are affected by blood pressure. According to studies, omega-3 fatty acids have low and dose-dependent effects on blood pressure (Howe, 1997). However, due to high doses to lower blood pressure and effectiveness, increasing omega-3 fatty acids has a limited role in managing high blood pressure (Mori et al., 2000). Reducing serum zinc can also play a significant role in increasing blood pressure such that in the study of Afkhami, zinc supplementation in diabetics has been shown to reduce systolic blood pressure (Afkhami-Ardekani et al., 2008). On the other hand, studies have shown that zinc plays a role in regulating blood pressure and pathogenesis of hypertension (Harlan et al., 1985; Frithz, Ronquist, 1979). Another risk factor for increasing insulin resistance and glucose is obesity such that visceral fat decreases insulin release from liver deposits, increases glucose production, and reduces glucose consumption by muscle tissue (DeNino et al., 2001). Human and animal studies have shown that increased consumption of omega-3 fatty acids is associated with reduced body fat, but these studies are relatively low in humans. And in general, during short periods with small sample sizes, it is difficult to conclude. Omega-3 fatty acids, which have an effect on triglyceride levels and blood platelet activity, have been shown to improve body composition (Buckley, Howe, 2009). In the Rosado study in diabetic patients receiving 1.5 g of omega-3 supplementation, weight loss and waist to hip ratio decreased, while 2.5 mg omega-3 doses did not have a significant effect on body composition in diabetic patients (Crochemore et al., 2012). Studies have shown that zinc can play a key role in muscle building and the improvement of protein status in the body, as well as in people with zinc deficiency, the synthesis of protein in the muscle decreases. The Millward (1987) study showed that protein degradation in muscle occurs much faster and faster in mice that are deficient in their diet. But in a study by Kim in obese people, supplementation with zinc did not have a significant effect on the body composition (Kim, Lee, 2012). Zinc is acting as a cofactor in the activity of the desaturase enzyme (short chain fatty acids to DHA and EPA), thus decreasing serum levels of the enzyme and decreasing serum

EPA and DHA levels. However, no study has measured the effect of these two nutrients (omega-3 with fish and zinc) on complementary glycemic parameters in diabetic patients (Maes et al., 1999). Therefore, due to the controversy of the results of the studies, this study aimed to evaluate the effect of supplemental omega-3 and zinc on glycemic indexes, serum zinc level, blood pressure and body composition in patients with type 2 diabetes.

Methods:

This study was a double-blind randomized controlled trial with the aim of evaluating and comparing the synergistic effects of omega-3 and zinc fatty acids on glycemic measures (fasting blood glucose, fasting insulin, insulin resistance, HbA1C), serum zinc level, and blood pressure and Body composition was performed in people with type 2 diabetes for 8 weeks. Following the necessary measures to implement a research project, such as obtaining a license from Urmia University of Medical Sciences and Health Services, and approval by the Code of Ethics of the University with the code (IR.UMSU.REC.1395.371). Registration of type 2 diabetic patients The Clinic of Endocrine Hospital of Imam Khomeini Hospital in Urmia with the criteria for entering the study was done. Subjects were then interviewed for the subjects eligible for the study, the objectives, importance of the study and the method of studying the study, and it was assured to patients that all the costs of the study were free and at the end of the study, the test results were provided. They were informed by written consenters and noted that if they did not want to cooperate during the study, they could be excluded from the study and any recorded information from the patients remained completely confidential. The willingness to co-operate with diabetic patients who have been at least two years old have been taking metformin or glibenclamide, taking ACE-I or calcium blocker drugs and ages 18 to 65 years old. Exit criteria included insulin injections, pregnancy and lactation, use of omega-3 and zinc supplements in the past three months, and allergies to fish and omega-3 families. The study was registered in the Iranian Center for Clinical Trials with IRCT20170214032571N9 code.

Interventions:

Randomization was assigned to a random assignment list by a research team member as the only non-blind person. Other members of the research team (including team leader and study coordinator) as well as all participants participated in the random allocation of blind groups and remained blind until the end of the study. Finally, 83 patients (omega-3 group n=23, zinc group n=21, omega-3 and zinc group n=21, control group n=18) until the end of 2 months. Taking the supplements was done in the form of receiving omega-3 with lunch and zinc in the afternoon. The capsules used in the control group were similar to the capsule of the intervention groups in terms of shape and color. Supplements were provided to people at the beginning of each month in 30 packs, and they were contacted every two weeks once a week to better remember the use of supplements. In order to ensure the use of supplements by participants, in addition to the weekly phone call, all people were asked. On the 30th and 60th day after the intervention, go to Nourishment Clinic of Imam Khomeini Hospital in Urmia and send blank sheets of supplements.

Study measures:

A personal information questionnaire was used to collect demographic information. Waist circumference was measured by measuring the smallest environment between the chest and the umbilical cord using a non-elastic band measuring meter with a precision of 0.1 cm and the hip circumference of its broadest part with a precision of 0.1 cm. The body mass index was calculated by the formula, by dividing the weight (kg) into the square of the person's height (m^2). Height, Weight, FFM, BFM, Visceral Fat (VFA), Waist to Hip ratio (WHR), Musculoskeletal Muscle (SMM), Soft Muscle Mass (SLM) Mineral Body, Inbody Score, Body Mass Index (PBF), muscle mass and total body water (TBW) were measured in all standard patients using BIA (In Body 770, Made in Korea). Blood pressure measurements were performed after 15 minutes of rest and in sitting position, left-handed with a mercuric pressure gauge and placed under the caudate fittest for adults. The first heard the sound (Coretov's phase 1) was recorded as systolic pressure and the point of discontinuity (Corctov's Phase 5)

as diastolic pressure. The MET (Metabolic Equivalent of Task) questionnaire was used to measure physical activity of individuals.

Collection of dietary information:

To increase the coherence of the study, before the intervention, all subjects were asked not to change their diet and lifestyle during the intervention. Information on dietary changes during the study and the assessment of the amount of omega-3 and zinc in the food during the intervention by recalling 24-hour food in 3 days a week (two open days and one day off) in two steps at the beginning and the end of the evaluation study Became Diet information received through recall using N4 software version 2. 5,3 was evaluated.

Blood collection:

Blood samples were collected from patients in sitting position and after 12 hours of fasting with a 5cc syringe and by a laboratory scientist. Samples of blood samples taken at a centrifuge machine were isolated at a rate of 3000 rpm for 15 minutes. The sera from the specimens were stored in 2 test tubes:

1 test tube containing serum prepared for testing glycemic indexes

2 test tubes containing serum prepared for measuring serum zinc level

Prepared serums were used to measure glycemic indices on the same day. Blood serums were poured into the test tubes to measure serum zinc level and stored with a paraffin of the lid and stored at -70 ° C until measured in a freezer.

Glycemic indexes including fasting blood glucose (kit Pars Test, Iran), fasting insulin concentration (kitspars test, Iran) were measured by ELISA method. To measure glycosylated hemoglobin (kitspars test, Iran), using the BT4500 device made in Italy, was used. HOMA-IR, which expresses the level of insulin resistance and beta-pancreatic cell function indirectly through fasting glucose and insulin levels, was derived from the formula:

HOMA-IR = (fasting serum glucose (mmol/L) × fasting serum insulin (μIU/ml))/22.5

Measuring the QUICKI insulin sensitivity index was calculated from the following formula:

QUICKI = 1/ [log (fasting insulin, μU/ml) + log (fasting glucose, mg/dl)]

Measurement of serum zinc was performed using a colorimetric method, using the Al-Ayazidar apparatus and the German Zalib bio kits.

Sample size and statistical analysis :

A total of 100 type-2 diabetic patients were randomly divided into four intervention and control group. In this study, a single-sample Kolmogorov-Smirnov test was used to check the normal distribution of data. In order to identify confounding variables, the literature review method was used and the four groups with Chi-square and Kruskal-Wallis single-valued tests were compared. The variables that were less than 0.25 were selected as confounding variables. Finally, the confounding variables used in multivariate statistical models were as follows:

Age, level of education, job, change in dietary energy, dietary fat change, dietary SFA changes, dietary PUFA changes, dietary MUFA changes, dietary fiber changes, and insoluble fiber changes. In addition, the ANOVA analysis model was used for multivariate modeling along with regulating the effect of variables. In all cases, the variable "the change over time" is considered. In order to investigate the main effects and mutual effects in the ANOVA analysis model (the main effect of omega-3 supplement, the main effect of Zn supplement and the mutual effect of omega-3 and Zn supplements), two separate models were used as follows:

Model 1: In this raw model, except for the base values of dependent variables, the effect of any of the confounding variables is not regulated.

Model 2: In this model, in addition to the base values of dependent variables, the effect of other confounding variables is also regulated.

The mean, standard deviations, median, inter-quartile domain and frequency distribution tables (abundance and percentage) have been used in order to describe the quantitative data for frequency data.

It should be noted that all stages of statistical analysis were performed using SPSS software version 22, under the significance level of 0.05.

Results:

Of the 100 patients who participated in the study, 83 patients completed the intervention. In Table 1, some demographic variables are compared in four experimental groups. Kruskal-Wallis test showed that there was no significant difference between the four groups in terms of age, duration of disease and BMI (P <0.05); however, the difference between the groups was considerable in terms of age (P=0.089). In addition, the results of Chi-square test showed that there was no significant association between sex, education level, type of occupation of patients and place of residence and type of experimental group. However, the difference between groups was considerable in terms of level of education and the type of job (P=0.126, P=0.147).

Table 1. Comparison of the demographic and background variables of the patients with diabetes type 2 in the groups receiving zinc and omega 3 supplementation

Variable	Category	Experimental group				P-value *
		Omega-3	Zinc	Omega-3 and zinc	Control	
Age (year)	-	58.0 **(13.0)	(8.0) 57.0	(7.0) 53.0	(8.0) 54.5	0.089
Years of affliction with the disease	-	(5.0) 5.0	(2.0) 4.0	(3.0) 4.0	(2.0) 4.5	0.553
BMI (kg/m2)	-	(34.34) 4.56	(31.57) 3.88	(30.25) 4.34	(31.89) 4.27	0.319
Gender	Female	**(52.2%) 12	(57.1%) 12	(57.1%) 12	(61.1%) 11	0.953
	Male	(47.8%) 11	(42.9%) 9	(42.9%) 9	(38.9%) 7	
Educational level	Illiterate	(8.7%) 2	(23.8%) 5	(33.3%) 7	(50.0%) 9	0.126
	Elementary or junior school	(39.1%) 9	(38.1%) 8	(23.8%) 5	(16.7%) 3	
	High school and above	(52.2%) 12	(38.1%) 8	(42.9%) 9	(33.3%) 6	
Job	Housekeeper	(52.2%) 12	(57.1%) 12	(57.1%) 12	(50.0%) 9	0.147
	Retired	(39.1%) 9	(9.5%) 2	(28.6%) 6	(16.7%) 3	
	Other jobs	(8.7%) 2	(33.3%) 7	(14.3%) 3	(33.3%) 6	
Place of living	City	(95.7%) 22	(100.0%) 21	(95.2%) 20	(94.4%) 17	0.778
	Village	(4.3%) 1	(0.0%) 0	(4.8%) 1	(5.6%) 1	

*Kruskal–Wallis test was used to compare quantitative variables in the groups and chi-square test was used to compare qualitative variables.

**Median (interquartile range) was used to describe quantitative variables and frequency (percentage) was used to describe qualitative variables.

Table 2 shows the dietary intake of patients with type 2 diabetes in the four groups under study. The ANOVA analysis showed that there was a statistically significant difference between the four groups in terms of receiving SFA, PUFA, MUFA, dietary fiber and insoluble fiber (P <0.05).

Table 2. Comparison of the received amount of nutrition by the patients with diabetes type 2 in the groups receiving zinc and omega 3 supplementation

Variable	Experimental group												P-value*
	Omega3 (n=23)			Zinc (n=21)			Omega3 and zinc (n=21)			Control (n=18)			
	before	After	change	before	after	change	Before	after	change	Before	after	change	
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	

Dietary fiber (g/d)	Cholesterol (Mg/d)	Glucose (g/d)	MUFA (g/d)	PUFA (g/d)	SFA (g/d)	Fat (g/d)	CHO (g/d)	Protein (g/d)	Energy (Kcal)
14/55±3/3	6.44±136.237	63/48±21/1	6.62±9/25	8.10±6.21	6.72±3.17	7.77±14.74	7.37±40.236	9.36±13.68	3.21±229.1912
14/36±3/4	3.54±131.258	61/77±15/2	8.72±8.25	8.16±10.29	8.51±3.17	2.89±12.67	4.42±43.231	2.33±11.69	53.78±178.1765
-0/19±2/7	2.09±69.21	-1/71±21/3	2.1±7.0	7.05±10.8	2.20±5.-0	8.88±15.-6	6.94±43.-4	3.97±10.0	9.43±235.-146
17/10±5/2	2.99±82.211	60/95±18/2	21/82±5/6	5.74±15.23	1.85±3.16	9.54±16.72	9.86±33.228	5.11±11.68	6.85±427.1990
17/69±5/0	7.34±57.217	63/84±17/5	6.31±5.21	2.35±13.22	8.61±3.17	8.46±9.66	8.58±40.238	6.55±12.67	9.66±286.1890
0/59±6/4	8.34±76.5	2/89±21/3	1.51±3.-0	3.38±5.1	4.76±4.0	1.07±18.6	7.72±34.9	87.56±1.0	6.19±365.100-
15/11±3/9	8.83±96.237	52/19±17/7	71±6.21	4.92±8.23	3.38±3.18	4.67±15.72	7.490±47.240	1.08±11.69	6.52±178.1882
15/73±3/1	6.82±78.227	59/49±16/7	2.77±5.19	3.95±4.20	6.04±3.17	1.83±10.63	5.43±37.244	9.36±10.71	2.95±201.1841
0/62±4/1	4.0±87.-1	7/30±9/9	9.93±4.-1	3.97±6.-2	9.34±5.-1	2.84±14.-8	6.93±40.3	1.28±11.2	5.57±239.-40
14/18±3/9	2.78±111.233	52/61±14/8	6.16±6.21	3.24±13.29	1.67±3.14	8.30±12.74	5.59±29.237	7.60±10.66	6.27±223.1951
13/52±2/7	4.05±109.252	55/40±17/2	7.30±4.18	1.48±9.25	6.09±2.14	2.36±13.71	3.93±17.227	4.14±9.70	4.11±151.1766
-0/65±2/7	3.26±89.18	2/79±7/3	4.86±7.-2	8.76±8.-3	0.57±4.-0	6.93±15.-2	5.66±31.9	7.53±8.3	1.16±237.-185
0/035	405.0	0/676	019.0	001.<0	010.0	248.0	351.0	638.0	156.0

Insoluble fiber (g/d)	6.46±1.3	1.15±1.3	7.31±1.-0	7.39±3.6	2.88±1.2	2.50±4.-3	3.40±1.2	6.13±0.2	4.27±1.0	9.46±0.2	9.44±0.2	3.03±1.-0	008.0
Zinc (Mg/d)	9.33±2.10	9.40±2.10	2.06±1.0	7.67±3.10	5.00±4.11	3.33±3.0	4.54±4.11	5.41±4.11	4.13±6.-0	9.23±2.10	0.39±3.10	3.16±3.0	955.0

*The ANCOVA analysis model with modification of the effects of the basic values was used for comparing the four groups.

Table 3 compares the physical activity level of type II diabetic patients in different groups receiving omega-3 and zinc supplements. The covariance analysis model (by adjusting the effect of base values) showed no significant difference between the four groups in terms of the average change in physical activity (P = 0.546).

Table 3- Comparison of the rate of physical activity in the patients with diabetes type 2 in the groups receiving omega3 and zinc supplementation (MET.h/day)

Omega-3 (n=23)				Zinc (n=21)				Omega-3 and Zinc (n=21)				Control (n=18)				P-value**
before	After	Change		Before	After	Change		before	after	change		before	after	change		
Mean±SD	Mean±SD	Mean±SD	P-value*	Mean±SD	Mean±SD	Mean±SD	P-value*	Mean±SD	Mean±SD	Mean±SD	P-value*	Mean±SD	Mean±SD	Mean±SD	P-value*	
41.1±16.6	43.0±17.7	1.9±6.3	0.581	39.8±18.5	42.2±20	2.4±5.5	0.607	38.3±2.14	39.2±19.5	0.9±5.3	0.866	40.0±15.7	43.6±17.8	2.1±6.7	0.394	0.546

* shows the comparison the before and after values in each group.

** shows the comparison between the four groups in terms of the average value change.

Table 4 compares glycemic indices of diabetic patients in different groups receiving omega-3 and zinc supplements. Fasting blood glucose was decreased in all three intervention groups after study, but this decrease was significant in zinc and zinc groups with omega-3 (P = 0.001, P = 0.002, respectively). Also, the covariance analysis model (by modulating the effect of all confounding variables) showed that the effect of using zinc supplementation alone or with omega-3 supplementation was significant on the mean FBS change (P = 0.005) such that FBS values in zinc supplementation group decreased by an average of 14/857 units, while in other groups an average of 1/423 units was observed. Serum insulin levels in the three intervention groups with omega-3, zinc and omega-3 plus zinc decreased significantly (p = 0.001, p = 0.002, p = 0.002, respectively). On the other hand, the interaction of omega-3 and zinc on the average of insulin-induced non-invasive decreases was significant such that the highest decrease in zinc group with omega-3 was found to be 1/255 unit, while in control group was observed 1/117 unit of the increase. HBA1C also decreased significantly in all three intervention groups with omega-3, zinc and omega-3 with zinc after intervention (P = 0.013, P = 0.001, P <0.001, respectively). The interaction between omega-3 and zinc on the mean change in HOMA-IR index was significant (P = 0.05) such that the highest reduction in HOMA-IR in the zinc group alone was 0/739 units and then in zinc group with omega 3 at a rate of 0/627, while in the control group it was observed at 0/348 of the increase. Finally, the covariance analysis model (by modulating the effect of all confounding variables) showed that the effect of using zinc supplementation (alone or with omega-3 supplementation) on the mean QUICKI change was significant (P = 0/000), such that in zinc Consumer groups QUICKI values showed an increase of 0.016 units. Also, the effect of using omega-3 supplementation (alone or with zinc supplementation) was significant on

QUICKI mean change (P = 0.027) such that in the omega-3 consumer groups QUICKI values in the group Those who consumed omega-3 have shown an increase of 0/012 points.

Table 4. Comparison of the glycemic indices of the patients with diabetes type 2 in the groups receiving omega-3 and zinc supplementation

Variable	Omega-3 (n=23)				Zinc (n=21)				Omega-3 and Zinc (n=21)				Control (n=18)				Model 1(without modifying the effect of the confounding variables			Model 2 (modifying the effect of the confounding variables)		
	Before	after	change		before	After	change		before	after	change		Before	after	change							
	Mean±SD	Mean±SD	Mean±SD	P-value*	Mean±SD	Mean±SD	Mean±SD	P-value*	Mean±SD	Mean±SD	Mean±SD	P-value*	Mean±SD	Mean±SD	Mean±SD	P-value*	P-value 1**	P-value 2+	P-value 3++	P-value 1**	P-value 2+	P-value 3++
FBS	128.95±37.5	34/125.34.5	3.60-±17	0.321	149.19±41.2	131.61 ±36.1	-17.57±18.6	<0.001	150.61±36.8	128.80±22.2	-21.80±27.5	0.002	116.00±31.0	125.11±23.7	9.11±8.5	0.053	0.109	0.001	0.535	0.246	0.005	0.746
Insulin	10.78±5.4	9.97±5	-0.81±1	0.001	6.23±2.9	5.09±2.4	-1.14±0.7	0.000	8.53±4.4	7.37±4	-1.16±1.4	0.002	10.32±5.6	12.38±6.5	2.05±2.3	0.016	0.736	0.766	0.861	0.034	0.000	0.084
HbA1c	6.99±1.1	6.44±0.9	-0.54±0.9	0.013	7.74±1.4	7.17±1.3	-0.57±0.6	0.001	7.45±1.2	6.9±1	-0.54±0.5	<0.001	6.54±1.1	6.56±1.0	0.01±0.3	0.856	0.075	0.582	0.145	0.126	0.681	0.885
HOMA-IR	3.89±2.4	3.56±3	-0.32±0.7	0.061	2.79±1.7	2.10±2.1	-0.69±0.6	0.000	3.28±1.9	2.73±1.7	-0.5510	0.001	3.13±2.3	3.84±2.2	0.70±0.9	0.007	0.666	0.302	0.860	0.197	0.000	0.050
QUICKI	0.32±0.04	0.33±0.03	0.007±0.01	0.058	0.34±0.03	0.35±0.05	0.01±0.01	0.000	0.33±0.04	0.35±0.05	0.01±0.01	0.001	0.33±0.02	0.31±0.02	-0.01±0.02	0.013	0.656	0.167	0.413	0.027	0.000	0.185

* shows the significance of the before and after comparison of the dependent variables in each experimental group using Wilcoxon test.

**shows the significance of the major effect of omega-3 supplementation on the average change of responses (it compares the groups receiving omega-3 supplementation with other groups).

+ shows the significance of the major effect of zinc supplementation on the average change of responses (it compares the groups receiving zinc supplementation with other groups).

++ shows the significance of the mutual effect of omega-3 and zinc supplementation on the average change of responses.

Table 5 compares the blood pressure levels of type II diabetic patients in different groups receiving omega-3 and zinc supplements. Blood pressure decreased in all three intervention groups with omega-3 and zinc significantly after intervention (p <0.001). The covariance analysis model (by modulating the effect of all

confounding variables) showed that the effect of supplementation of omega-3 (alone or with zinc supplementation) was significant on the mean systolic blood pressure changes (P <0.001); thus, systolic blood pressure in the omega-3 supplementation group decreased by an average of 15.732, while in other groups an average of 7/835 was observed.

Similarly, the effect of supplementation of omega-3 (alone or with zinc supplementation) on the mean diastolic blood pressure change was also significant (P = 0.019) such that diastolic blood pressure in the omega-3 supplement group average decreased 8/823 units, while in other groups, the average of 4/358 units has fallen. Meanwhile, the effect of using zinc supplementation alone or with omega-3 supplementation was significant on the mean change in systolic blood pressure (P = 0.013); that is, systolic blood pressure in the zinc supplementation group was On average, 14/269 units have fallen, while in other groups an average of 9/297 units of decline has been observed. It should be noted, however, that the effect of zinc supplementation (alone or with omega-3 supplementation) on the mean diastolic blood pressure change was not significant (P = 0.666).

Table 5. Comparison of the blood pressure level of the patients with diabetes type 2 in the groups receiving omega-3 and zinc supplementation

Variable	Omega-3 (n=23)				Zinc (n=21)				Omega-3 and Zinc (n=21)				Control (n=18)				Model 1(without modifying the effect of the confounding variables			Model 2 (modifying the effect of the confounding variables)		
	before	after	change		before	after	change		before	after	change		before	after	change							
	Mean	Mean	Mean	P-value*	Mean	Mean	Mean	P-value*	Mean	Mean	Mean	P-value*	Mean	Mean	Mean	P-value*	P-value 1**	P-value 2+	P-value 3++	P-value 1**	P-value 2+	P-value 3++
Systolic blood pressure	138.30±12	123.47±9.8	-14.82±6.5	<0.001	138.09±12.7	126.28±10.0	-11.80±7.9	<0.001	142.28±13.9	123.85±8.2	-18.42±11.3	<0.001	133.61±8.6	131.83±9.0	-1.77±5.9	0.224	<0.001	0.001	0.030	<0.001	0.013	0.331
Diastolic blood pressure	87.86±7.0	76.21±15.8	-11.65±15.9	0.002	88.33±5.1	81.66±5.1	-6.66±4.9	<0.001	87.61±7.1	80.52±4.8	-7.09±5.4	<0.001	81.94±6.6	81.38±6.0	-0.55±5.2	0.660	0.030	0.713	0.075	0.019	0.566	0.165

* shows the significance of the before and after comparison of the dependent variables in each experimental group using Wilcoxon test.

**shows the significance of the major effect of omega-3 supplementation on the average change of responses (it compares the groups receiving omega-3 supplementation with other groups).

+ shows the significance of the major effect of zinc supplementation on the average change of responses (it compares the groups receiving zinc supplementation with other groups).

++ shows the significance of the mutual effect of omega-3 and zinc supplementation on the average change of responses.

Table 6 shows the anthropometric indices of type 2 diabetic patients in four groups receiving omega-3 and zinc supplements. Significant decrease in the weight of subjects after intervention was observed in omega-3 and zinc groups (p = 0.000, p = 0.038). The covariance analysis model (after adjusting the effect of confounding variables)

showed that the effect of omega-3 supplementation alone or with zinc on the weight change was significant (P = 0.032) such that it can be said in consumer groups Omega-3 has the highest weight loss recorded at 1/529 units, which is statistically significant, while in groups that did not consume omega-3, weight loss was 0/06 units. Also, the covariance analysis model (after adjusting the effects of confounding variables) showed that zinc supplementation alone or with omega-3 supplementation could significantly change the weight of patients with type 2 diabetes (P = 0.069) In other words, we can say that the average weight of patients in supportive groups decreased by 1/414 units, while in groups that did not receive this supplement 0.175 units were reduced. The effect of omega-3 supplementation (alone or with zinc supplementation) on the mean BMI changes was considerable (p = 0.095) so that it can be said that the BMI values in the groups receiving omega-3 supplementation have been reduced by an average of 0/933 units, while in groups that did not receive this supplement, about 0/210 units Dropped. Zinc supplements (alone or with Omega-3 supplementation) also significantly altered the BMI of patients (P = 0.033) such that the mean BMI of patients receiving supplements decreased by 1/046 fold while in other groups, an average of 0/097 units of reduction has been observed. The use of omega-3 supplementation alone or with zinc supplementation has a significant effect on the WHR of the diabetic patients, but this effect was not statistically significant (P = 0.087); more precisely After adjusting the effect of the confounding variables, it can be stated that the WHR values in the omega-3 supplementation groups decreased by an average of about 0/011 per unit, while in other groups it was reduced to about 0.001 units. Meanwhile, the use of omega-3 supplementation (alone or in combination with zinc supplementation) significantly altered the body's percentile (PBF) of diabetic patients, but this effect was not statistically significant (P = 0.087) such that after adjusting the effect of the confounding variables, it can be said that the levels of PBF in the groups receiving omega-3 supplementation have been reduced by an average of about 1/058 units while in other groups about 0/075 units have been increased. The covariance analysis model showed that zinc supplementation (alone or with omega-3 supplementation) significantly altered the PBF of the patients (P = 0. 01) such that after adjusting the effect of the confounding variables, Meanwhile, the mean of PBF in supplemented consumer groups decreased by 1/382. The use of Omega-3 supplementation (alone or with zinc supplementation) significantly altered the VFA of diabetic patients, but this effect was not statistically significant (P = 0.085); despite This, after adjusting the effect of the confounding variables, can be said that the mean VFA in the groups receiving the supplement of omega-3 was reduced by about 6/155 units, while in other groups it was reduced to 0/965 units. Zn supplementation also significantly reduced VFA in patients (P = 0.02); in other words, after adjusting the effect of the confounding variables, it can be stated that the mean VFA in the supplementation group was 7/224 units dropped. It should be noted that the total body weight of TBW (total body weight) has changed considerably and, of course, insignificantly (P = 0.092); more precisely, after adjusting the effect of the confounding variables, it can be stated Indicating that the mean TBW in the supplementary consumer groups decreased by 0/346 units. Also, covariance analysis indicated that zinc supplementation (alone or with omega-3 supplementation) could modify the Mineral Body values of the patients However, this effect was not statistically significant (P = 0.057); more precisely, after adjusting the effect of the confounding variables, it can be stated that the average mineral content in the groups Supplemental supplement increased by 0/087 units while other groups increased by 0/018 increment units. Finally, zinc supplementation (alone and in combination) can also significantly change the Inbody Score (P=0.001). In other words, after adjusting the effect of the confounding variables, it can be stated that the average Inbody Score increased by 1/666 in the supplementary drug groups while in other groups, 0/365 units Reduced observation. For details of the comparison before and after the anthropometric indicators within each experimental group, see Table 6.

Table 6. Comparison of the Anthropometric Indices of the patients with diabetes type 2 in the groups receiving omega-3 and zinc supplementation

Variable																							
			Omega-3 (n=23)				Zinc (n=21)				Omega-3 and Zinc (n=21)				Control (n=18)				Model 1(without modifying the effect of the confounding variables			Model 2 (modifying the effect of the confounding variables)		
			before	after	Change		before	after	change		before	after	change		before	after	change							
SMM	PBF	BFM	WHR	FFM	TBW	BMI	weight	Mean	Mean	Mean	P-value*	Mean	Mean	Mean	P-value*	Mean	Mean	Mean	P-value*	Mean	Mean	Mean	P-value*	P-value 1**	P-value 2+	P-value 3++	P-value 1**	P-value 2+	P-value 3++
27.97±5.4	43.07±7.9	43.10±16.6	1.02±0.0	50.62±9.1	37.35±6.6	34.34±4.5	87.67±12.5	87.67±12.5	86.78±12.4	-0.89±0.9	0.000	82.07±10.5	81.24±10.2	-0.82±1.6	0.038	76.31±11.3	74.56±9.4	-1.75±4.9	0.116	80.32±8.9	80.50±9.3	0.17±1.3	0.595	0.910	0.007	0.057	0.032	0.069	0.574
27.87±5.4	42.95±7.9	38.20±9.0	1.01±0.0	50.53±9.1	37.31±6.6	34.18±4.6	87.67±12.4	87.67±12.4	86.78±12.4	-0.89±0.9	0.000	82.07±10.5	81.24±10.2	-0.82±1.6	0.038	76.31±11.3	74.56±9.4	-1.75±4.9	0.116	80.32±8.9	80.50±9.3	0.17±1.3	0.595	0.910	0.007	0.057	0.032	0.069	0.574
-0.10±0.6	-0.11±1.2	-4.90±15.1	-0.003±0.01	-0.08±1.1	-0.03±0.8	-0.16±0.5	-0.89±0.9	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.910	0.007	0.057	0.032	0.069	0.574
0.464	0.659	0.133	0.215	0.737	0.849	0.200	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.910	0.007	0.057	0.032	0.069	0.574
27.11±4.6	39.50±8.3	32.99±8.5	1.01±0.0	49.08±7.7	36.22±5.6	31.57±3.8	82.07±10.5	82.07±10.5	81.24±10.2	-0.82±1.6	0.038	76.31±11.3	74.56±9.4	-1.75±4.9	0.116	80.32±8.9	80.50±9.3	0.17±1.3	0.595	80.32±8.9	80.50±9.3	0.17±1.3	0.595	0.910	0.007	0.057	0.032	0.069	0.574
28.31±6.6	39.02±8.1	32.02±8.3	1.01±0.0	49.46±7.6	35.80±6.2	31.22±3.7	81.24±10.2	81.24±10.2	81.24±10.2	-0.82±1.6	0.038	76.31±11.3	74.56±9.4	-1.75±4.9	0.116	80.32±8.9	80.50±9.3	0.17±1.3	0.595	80.32±8.9	80.50±9.3	0.17±1.3	0.595	0.910	0.007	0.057	0.032	0.069	0.574
1.20±4.9	-0.48±2.0	-0.96±1.2	0.001±0.0	0.38±1.0	-0.42±3.2	-0.34±0.6	-0.82±1.6	-0.82±1.6	-0.82±1.6	-0.82±1.6	0.038	76.31±11.3	74.56±9.4	-1.75±4.9	0.116	80.32±8.9	80.50±9.3	0.17±1.3	0.595	80.32±8.9	80.50±9.3	0.17±1.3	0.595	0.910	0.007	0.057	0.032	0.069	0.574
0.276	0.290	0.002	0.820	0.106	0.554	0.023	0.038	0.038	0.038	0.038	0.038	0.038	0.038	0.038	0.038	0.038	0.038	0.038	0.038	0.038	0.038	0.038	0.038	0.910	0.007	0.057	0.032	0.069	0.574
24.79±3.7	40.08±8.2	32.57±11.9	1.00±0.07	45.16±6.1	33.41±4.6	30.25±4.3	76.31±11.3	76.31±11.3	74.56±9.4	-1.75±4.9	0.116	76.31±11.3	74.56±9.4	-1.75±4.9	0.116	80.32±8.9	80.50±9.3	0.17±1.3	0.595	80.32±8.9	80.50±9.3	0.17±1.3	0.595	0.910	0.007	0.057	0.032	0.069	0.574
24.80±3.8	39.07±7.5	31.30±13.2	0.99±0.08	45.24±6.4	33.32±4.7	29.16±3.6	74.56±9.4	74.56±9.4	74.56±9.4	-1.75±4.9	0.116	76.31±11.3	74.56±9.4	-1.75±4.9	0.116	80.32±8.9	80.50±9.3	0.17±1.3	0.595	80.32±8.9	80.50±9.3	0.17±1.3	0.595	0.910	0.007	0.057	0.032	0.069	0.574
0.009±0.8	-1.00±3.5	-1.26±12.6	-0.01±0.03	0.08±1.4	-0.09±1.07	-1.09±3.2	-1.75±4.9	-1.75±4.9	-1.75±4.9	-1.75±4.9	0.116	76.31±11.3	74.56±9.4	-1.75±4.9	0.116	80.32±8.9	80.50±9.3	0.17±1.3	0.595	80.32±8.9	80.50±9.3	0.17±1.3	0.595	0.910	0.007	0.057	0.032	0.069	0.574
0.961	0.209	0.651	0.019	0.789	0.703	0.140	0.116	0.116	0.116	0.116	0.116	0.116	0.116	0.116	0.116	0.116	0.116	0.116	0.116	0.116	0.116	0.116	0.116	0.910	0.007	0.057	0.032	0.069	0.574
26.06±5.03	42.03±8.5	36.47±13.08	1.03±0.03	47.45±8.3	35.10±6.1	31.89±4.2	80.32±8.9	80.32±8.9	80.50±9.3	0.17±1.3	0.595	80.32±8.9	80.50±9.3	0.17±1.3	0.595	80.32±8.9	80.50±9.3	0.17±1.3	0.595	80.32±8.9	80.50±9.3	0.17±1.3	0.595	0.910	0.007	0.057	0.032	0.069	0.574
25.88±5.2	43.01±8.3	36.75±13.3	1.02±0.03	47.32±8.6	35.03±6.4	31.70±4.3	80.50±9.3	80.50±9.3	80.50±9.3	0.17±1.3	0.595	80.32±8.9	80.50±9.3	0.17±1.3	0.595	80.32±8.9	80.50±9.3	0.17±1.3	0.595	80.32±8.9	80.50±9.3	0.17±1.3	0.595	0.910	0.007	0.057	0.032	0.069	0.574
-0.17±0.4	0.97±3.3	0.28±1.0	-0.005±0.0	-0.13±0.9	-0.06±0.7	-0.18±0.9	0.17±1.3	0.17±1.3	0.17±1.3	0.17±1.3	0.595	0.17±1.3	0.17±1.3	0.17±1.3	0.595	0.17±1.3	0.17±1.3	0.17±1.3	0.595	0.17±1.3	0.17±1.3	0.17±1.3	0.595	0.910	0.007	0.057	0.032	0.069	0.574
0.143	0.231	0.250	0.360	0.542	0.711	0.402	0.595	0.595	0.595	0.595	0.595	0.595	0.595	0.595	0.595	0.595	0.595	0.595	0.595	0.595	0.595	0.595	0.595	0.910	0.007	0.057	0.032	0.069	0.574
0.325	0.197	0.473	0.088	0.639	0.649	0.432	0.910	0.910	0.910	0.910	0.910	0.910	0.910	0.910	0.910	0.910	0.910	0.910	0.910	0.910	0.910	0.910	0.910	0.910	0.007	0.057	0.032	0.069	0.574
0.193	0.018	0.323	0.455	0.187	0.611	0.039	0.007	0.007	0.007	0.007	0.007	0.007	0.007	0.007	0.007	0.007	0.007	0.007	0.007	0.007	0.007	0.007	0.007	0.910	0.007	0.057	0.032	0.069	0.574
0.283	0.648	0.644	0.054	0.536	0.711	0.115	0.057	0.057	0.057	0.057	0.057	0.057	0.057	0.057	0.057	0.057	0.057	0.057	0.057	0.057	0.057	0.057	0.057	0.910	0.007	0.057	0.032	0.069	0.574
0.302	0.087	0.588	0.087	0.976	0.166	0.095	0.032	0.032	0.032	0.032	0.032	0.032	0.032	0.032	0.032	0.032	0.032	0.032	0.032	0.032	0.032	0.032	0.032	0.910	0.007	0.057	0.032	0.069	0.574
0.533	0.010	0.143	0.463	0.416	0.092	0.033	0.069	0.069	0.069	0.069	0.069	0.069	0.069	0.069	0.069	0.069	0.069	0.069	0.069	0.069	0.069	0.069	0.069	0.910	0.007	0.057	0.032	0.069	0.574
0.240	0.459	0.631	0.878	0.640	0.550	0.491	0.574	0.574	0.574	0.574	0.574	0.574	0.574	0.574	0.574	0.574	0.574	0.574	0.574	0.574	0.574	0.574	0.574	0.910	0.007	0.057	0.032	0.069	0.574

Inbody Score	57.78±6.4	57.95±6.7	0.17±2.5	0.743	62.14±6.6	63.66±6.3	1.52±1.4	<0.001	60.66±7.2	62.09±6.04	1.42±3.3	0.064	58.77±8.07	58.33±7.7	-0.44±1.0	0.088	0.778	<0.001	0.437	0.535	0.001	0.476
Mineral Body	3.33±0.7	3.28±0.7	-0.04±0.1	0.050	3.18±0.5	3.23±0.6	0.05±0.1	0.101	2.85±0.3	2.99±0.4	0.13±0.2	0.007	3.07±0.5	3.09±0.4	0.02±0.1	0.413	0.799	0.002	0.027	0.104	0.057	0.272
Physical Body	30.51±12.0	29.92±11.7	-0.58±2.2	0.221	24.01±6.2	24.00±6.3	-0.01±1.0	0.964	25.66±2.9	25.60±2.9	-0.05±0.4	0.560	23.61±2.2	23.80±2.2	0.19±0.9	0.418	0.393	0.781	0.370	0.633	0.715	0.171
SLM	47.88±8.5	47.83±8.6	-0.04±1.0	0.834	46.46±7.3	46.76±7.1	0.29±0.9	0.187	42.83±5.9	42.83±6.1	0.000±1.3	>0.999	44.97±7.9	45.06±8.8	0.09±1.4	0.792	0.436	0.562	0.962	0.876	0.932	0.616
VFA	192.50±47.1	191.82±46.9	-0.68±7.4	0.666	169.17±51.1	164.84±50.2	-4.32±5.7	0.003	164.39±52.8	155.78±45.7	-8.60±21.6	0.084	185.47±52.03	185.57±50.1	0.10±5.7	0.942	0.345	0.004	0.394	0.085	0.020	0.983

* shows the significance of the before and after comparison of the dependent variables in each experimental group using Wilcoxon test.

**shows the significance of the major effect of omega-3 supplementation on the average change of responses (it compares the groups receiving omega-3 supplementation with other groups).

+ shows the significance of the major effect of zinc supplementation on the average change of responses (it compares the groups receiving zinc supplementation with other groups).

++ shows the significance of the mutual effect of omega-3 and zinc supplementation on the average change of responses.

Table 7 compares serum zinc levels of type II diabetic patients in different groups receiving omega-3 and zinc supplements. Serum zinc levels in zinc and zinc groups with omega-3 significantly increased after intervention (P <0.001, P <0.001, respectively). The covariance analysis model (by adjusting the effect of all confounding variables) showed that the effect of using zinc supplementation alone or with omega-3 supplementation was significant on the mean serum zinclevel (P <0.001). Therefore, after adjusting the effect of the confounding variables, serum zinc levels in zinc supplementation groups increased by an average of about 20/694 units. While in other groups, an average of 9/101 units of decrease was observed.

Table 7. Comparison of the serum zinc level of the patients with diabetes type 2 in the groups receiving omega-3 and zinc supplementation

Omega-3 (n=23)				Zinc (n=21)				Omega-3 and Zinc (n=21)				Control (n=18)			Model 1(without modifying the effect of the confounding variables				Model 2 (modifying the effect of the confounding variables)		
before	after	change		before	after	change		before	after	change		before	after	change							
Mean	Mean	Mean	P-value*	Mean	Mean	Mean	P-value*	Mean	Mean	Mean	P-value*	Mean	Mean	Mean	P-value*	P-value 1**	P-value 2+	P-value 3++	P-value 1**	P-value 2+	P-value 3++

81.83±16.3	67.47±10.9	-14.36±19.0	0.002	77.30±11.2	99.67±17.1	22.37±15.0	<0.001	66.45±11.6	88.66±17.3	22.20±14.4	<0.001	81.98±14.5	69.67±14.5	-12.30±13.1	0.001	0.192	<0.001	0.527	0.224	<0.001	0.952

* shows the significance of the before and after comparison of the dependent variables in each experimental group using Wilcoxon test.

**shows the significance of the major effect of omega-3 supplementation on the average change of responses (it compares the groups receiving omega-3 supplementation with other groups).

+ shows the significance of the major effect of zinc supplementation on the average change of responses (it compares the groups receiving zinc supplementation with other groups).

++ shows the significance of the mutual effect of omega-3 and zinc supplementation on the average change of responses.

Discussion and Conclusion:

This study is a first study of the effects of omega-3 and zinc supplements on glycemic indexes, blood pressure, body composition, and serum zinc levels in people with type 2 diabetes. Due to the role of zinc in the activity of the desaturase enzymes, it seems that the simultaneous intake of omega-3 and zinc will enhance the effects of each other. As such, this study was conducted. Type 2 diabetes is developing significantly throughout the world, according to studies, insulin resistance is the most important factor in the pathogenesis of type 2 diabetes (Katz et al., 2000). Genetic and high-risk factors directly contribute to insulin resistance and diabetes (Crook, 2004). The effects of omega-3 fatty acids on glycemic control, especially in patients with type 2 diabetes, remain controversial. The effects of omega-3 fatty acids on glycemic control, especially in patients with type 2 diabetes, remain controversial. Studies have controversial effects of omega-3 on blood glucose (Malasanos, Stacpoole, 1991; Prince, Deeg, 1997; Kasim, 1993; Heine, 1993; Axelrod, 1989; Friedberg et al., 1998). but have not had adverse effects in people with hypertension and dyslipidemia after omega-3 (Toft et al., 1995; Grundt et al., 1995). These results, compared with reports, indicate that side effects of glycemic control are often seen (Glauber et al., 1988; Schectman et al., 1988) but not always (Connor et al., 1993) after high doses (4-10 g) of omega-3 fatty acids. In the present study, receiving 1000 mg of omega-3 daily resulted in a decrease in blood glucose but this was not significant. In the study of Toorang (2009) and Axenlrodl (1994), omega-3 did not have a significant effect on blood glucose levels. Since the glycated hemoglobin test reflects the average plasma glucose levels in the last two to three months and can be done at any time of the day and in non-positive state, this test is for the evaluation of glycemic control in diabetic patients has become a standard (Kamali et al., 2017). In this study, as with the study of Toorang (2009), there was a significant reduction in HBA1C levels after two months of omega-3 supplementation, Suggesting that omega-3 supplementation can improve blood glucose over the long term. Receiving omega-3 fatty acids with an effect on metabolic pathways can improve insulin function (Mori et al., 1999; Lovejoy, 2002). In our study, like the study of Farahbakhsh (Farsi et al., 2014) and Boden (2005), omega-3 supplementation reduced blood levels of insulin, but in the Koh's study, receiving 2 grams of omega-3 daily did not significantly affect insulin sensitivity (Koh et al., 2012). In the present study, insulin sensitivity increased and insulin resistance decreased due to decreased blood glucose and serum insulin levels. Our study showed that, unlike many other studies, the use of omega-3 doses of 1 gram can contribute to increased insulin sensitivity. Zinc deficiency can play a role in intolerance to glucose, diabetes, insulin resistance, and cardiovascular disease (Rahimi et al., 2008). Zinc supplementation significantly increased serum zinc levels, decreased fasting blood glucose, serum insulin, HBA1C, insulin resistance, and increased insulin sensitivity. For the association of zinc, secretion and insulin resistance, several mechanisms described Zinc elemental antioxidant effects can protect insulin and pancreatic cells from free radicals (Sun et al., 2009; Al-Maroof RA, Al-Sharbatti, 2006). According to studies, Zinc is required for the synthesis of insulin, its storage and secretion from pancreatic beta cells (Wiernsperger, Rapin, 2010). Zinc can regulate insulin function with the effect on the induction of the cascade (PI3K / PKB), Phosphatidylinositol-3-Kinase and Protein Kinase B (an important mediator in the insulin signal) (Foster et al., 2013). Studies have shown that zinc

supplements can be effective in improving blood glucose and insulin resistance and controlling diabetes (Roshanravan et al., 2015; Soheilykhah et al., 2012). In our study, such as Roshanravan (2015) and Kim (2012), serum zinc level significantly increased in zinc supplementation groups. Also, in the study of Kim (2012), as in this study, 30 mg zinc for two months was able to significantly reduce blood glucose and insulin resistance. In another randomized study, 30 mg of zinc supplementation for 4 weeks reduced the level of fasting insulin and insulin resistance significantly (Nascimento Marreiro et al., 2006). The present study shows that after two months of intervention with omega-3 and zinc glucose levels in the simultaneous interventional group significantly decreased. This decrease in blood glucose levels was higher than the other two intervention groups. Therefore, it can be concluded that simultaneous use of zinc and omega-3 supplements can enhance the effects of each other in reducing fasting glucose and insulin.

In this study, the intake of omega-3 supplementation significantly reduced systolic blood pressure and diastolic blood pressure. In the Sidika study, omega-3 fatty acids significantly reduced systolic and diastolic blood pressures in diabetic patients for 2 months (Kasim et al., 1988). In the Eric study, it also reduced the daily intake of 3 grams of omega-3 blood pressure in people with hypertension (Geleijnse et al., 2002). Another study also found that the use of omega-3 fatty acids can lower blood pressure in hypertension (Cabo et al., 2012). In a meta-analysis of Appel et al. (1993) A study of 17 clinical trials showed that the intake of more than 3 grams of omega-3 fatty acids reduced systolic blood pressure (SBP) and diastolic blood pressure (DBP) in people with hypertension. The mechanism of the effect of omega-3 fatty acids on blood pressure remains unclear, but in smooth muscle cells, the effect of DHA on calcium-conducting channels and the activation of potassium voltage has vasodilator effects (Hoshi et al., 2013). Therefore, omega-3 fatty acids with the mechanism can reduce blood pressure in patients. In the present study, contrary to previous studies suggesting that high-dose omega-3 were suggested to lower blood pressure (Kris et al., 2002), omega-3 intake of 1 g for 2 months could be associated with a significant decrease in blood pressure in diabetic patients and reduces the blood pressure lowering drugs. Zinc supplements could significantly reduce blood pressure in this study. There is an inverse relationship between serum zinc levels and blood pressure (Bergomi et al., 1997). Seeking to increase the secretion and excretion of zinc that occurs in diabetes (Rahimi et al., 2008), it increases the risk of developing hypertension following internal and external cell changes. In these people, the level of zinc in the serum, lymphocyte, and bone decreases, while in the heart, erythrocytes, kidneys, liver and spleen increase. These changes lead to loss of zinc homeostasis and high blood pressure (Tubek, 2007). Increased zinc in the cells of the heart, kidney, and liver tissues inhibits the activity of the ATP-dependent calcium pump, which pumps the calcium ions out of the cell, and, by inhibiting the activity of this pump, ions accumulate calcium inside the cell and leads to blood pressure (Henrotte et al., 1990; Vezzoli et al., 1985). In Afkhami's (2008) study, it was also shown that zinc supplementation in diabetic patient's leads to a decrease in systolic blood pressure. Also, in this study, reduction of systolic blood pressure in the intervention simultaneous group was more than that of the separate intervention groups with omega-3 and zinc. In fact, it can be said that zinc and omega-3 together can strengthen the effects of reducing systolic blood pressure.

Contrary to maintaining a diet during the intervention, the use of supplementation of omega-3 could affect the body's composition. Weight significantly decreased after the omega-3 intervention such that it can be said that in the omega-3 consumer groups, after adjusting the effects of the confounding variables, the most weight loss was recorded at 1/529 units, which is consistent with the results of the Buckley study (2009) and Rosado (2012). Obesity is commonly found in most people with diabetes and is a risk factor for cardiovascular disease (Castro et al., 2006). A review study aimed at investigating the relationship between BMI and WHR and their association with the prevalence of diabetes found that both of these factors can contribute to diabetes (Qiao, Nyamdorj, 2010). In the present study, the effect of omega-3 supplementation (alone or in combination with zinc supplementation) on the moderate changes in VFA, PBF, and BMI of patients was considerable, such that all of these indices in the omega-3 consumer groups decreased which was a sign of improved body composition after taking omega-3 supplementation. In another study, Kabir and colleagues evaluated the effects of omega-

3 fatty acids on 26 women with type 2 diabetes for 2 months. In this study, changes in body mass were not observed; however, the fat mass in the omega-3 group was dropped (Kabir et al., 2007). The average Inbody Score in the Zinc supplementation group increased by 1/666, indicating improvement in body composition, fat loss, and increased muscle and body mass after taking Zn, all of this is in the interest of using zinc supplementation to improve the health of people with diabetes. Kelishad et al. (2010) showed that receiving 20 mg zinc for eight weeks reduced body mass and weight in obese individuals. Song also showed that receiving 30 mg of zinc supplementation for 15 days' weight decreased significantly in obese subjects. However, in the study of Dilina, 30 mg of zinc supplementation did not affect the weight of subjects (Nascimento Marreiro et al., 2006). It seems that zinc decreases weight with the effect of the metabolism of leptin in the brain and the improvement of insulin sensitivity (Nascimento Marreiro et al., 2006; Ott, Shay, 2001).
Since the use of omega-3 and zinc in Iran is low and these nutrients in people with diabetes are lower than the general population, it seems that the use of these dietary supplements is associated with the improvement of their lives. On the other hand, in our study, we showed that the use of these two complement supplements may also increase beneficial effects

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