The Effect of Omega-3 in the Prevention of Preeclampsia in Pregnant Women with Hyperlipidemia

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Abstract--- Introduction: Preeclampsia is one of the most common complications of pregnancy and one of the leading causes of maternal and fetal mortalities. The aim of our study was to evaluate the effect of omega-3 in the prevention of preeclampsia in pregnant women with hyperlipidemia.
Methods: This single-blind randomized clinical trial study was performed on mothers with hyperlipidemia during 2019-2021. The participants of this study were divided into two groups, the placebo receiving group and the omega-3 receiving group, each comprising 36 participants. Mothers in each groups were evaluated for clinical parameters. Obtained findings were analyzed using statistical methods.
Results: The mean age of 72 participants was 32.7 ± 5.1 years. The difference in neonatal weight at birth was statistically significant (P = 0.01). There was a significant relationship between omega 3 consumption and 5-minutes Apgar score of (P <0.05). Complications observed in the omega-3 receiving group were significantly lower than the placebo group (58.3%: placebo and 22.2%: omega 3) (P = 0.02). The frequency of preeclampsia in the omega-3 receiving group was lower than the control group (placebo) and the difference was statistically significant (P <0.05).
Conclusion: Omega-3 has a beneficial effect on preeclampsia and fetal weight during pregnancy, and the prevalence of preeclampsia has decreased significantly in the omega-3 group.

Keywords--- Omega-3, Preeclampsia, Pregnancy, Hyperlipidemia.

I. Introduction

Preeclampsia is one of the most common complications of pregnancy, known as hypertension and symptoms associated with proteinuria, thrombocytopenia, renal failure, liver dysfunction, pulmonary edema, cerebral or visual symptoms after 20 weeks of pregnancy (1, 2). This disorder occurs in 5% to 10% of all pregnancies, 20% of first pregnancies and 40% of women with chronic kidney disease. Preeclampsia is one of the leading causes of maternal, fetal and neonatal mortality. In developed countries, up to 25% of all prenatal deaths are related to gestational

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hypertension. Although about 50,000 women worldwide die each year from eclampsia, and about the same number die without seizures, due to preeclampsia complications, including cerebral hemorrhage and renal failure. (3)

During pregnancy, changes in the levels of triglycerides, fatty acids, cholesterol and phospholipids are associated with preeclampsia, and high levels of triglycerides are associated with an increased risk of preeclampsia, and it is important to adjust these parameters (5, 6, 7). Because most effective drugs for the treatment of hypertriglyceridemia are not approved for use during pregnancy, nutritional interventions are often the only treatment option in these cases (7). However, dietary changes can sometimes make the situation worse. Eating a low-calorie diet can cause the mother to lose weight, which in turn increases perinatal accidents. Attempts to reduce fat intake can paradoxically increase fasting triglyceride levels (8). One solution is to use omega-3 fatty acids which include eicosapentaenoic acid and docosahexaenoic acid. (5). These fatty acids improve hypertriglyceridemia and inhibit the process of atherosclerosis as well as platelet aggregation without any side effects. The mechanism of action of these acids is not fully known, but it is likely that this role is played by inhibiting the liver-activating enzyme responsible for synthesizing lipoproteins. In pregnant women with preeclampsia, omega-3 fatty acids can increase placental circulation (9). Studies have shown that omega-3 levels in pregnant women with preeclampsia decrease compared to healthy pregnant women in the third trimester or postpartum. Also, women with low levels of omega-3s after childbirth are 7.6 times more likely to develop preeclampsia than women with high levels of omega-3s (10). Omega-3 consumption increases the average gestational age and reduces the incidence of preeclampsia (11).

Although various studies have been performed on the association of omega-3 with preeclampsia and hyperlipidemia, there are conflicting findings in this regard and the study population was not among women with hyperlipidemia (10, 11, 12 and 13). Since hypertriglyceridemia can increase the incidence of preeclampsia and the effects of omega-3 on its modulation, in this study we aimed to evaluate the relationship between omega-3 administration in pregnant women with hyperlipidemia and the prevention of preeclampsia.

II. Materials and Methods

This single-blind randomized clinical trial study was performed on pregnant women with hypertriglyceridemia referred to Besat Hospital of Sanandaj, Iran during 2019-2021. The participants of this study were divided into two groups, each comprising 36 participants. All ethical considerations in the clinical trial guideline were observed with the permission of the ethics committee (ethics code: IR.MUK.REC.1398.306). Eligible mothers were selected according to the inclusion and exclusion criteria.

Inclusion and Exclusion Criteria

Inclusion criteria included age 20 to 40 years and hyperlipidemia with triglyceride level higher than 150 mg / dL. Exclusion criteria included metabolic diseases, history of preeclampsia in previous pregnancies or in first-degree relatives, twins, body mass index equal to or greater than 29, kidney disease and hypertension, diabetes, hyperthyroidism, aspirin use, calcium, anti-coagulation and insulin had no history of allergy to omega-3.

Description of the Method

After obtaining ethical codes and obtaining informed consent, the studied pregnant women were randomly divided into two groups; one receiving Perl Omega 3 and other receiving placebo. Patients were divided into two groups using double blind random block sampling method and quadruple randomization. (Group A receiving omega 3 and group B receiving placebo).

The first intervention group used an omega-3 jelly capsule (Pearl) containing EPA eicosapentalenoic acid and DHA docosahexaenoic acid (50 Zahravy? omega-3 capsules without mercury) daily until the end of pregnancy. The control group received placebo, which was in the form of pearls containing gelatin, which was used daily until the end of pregnancy. Blood pressure and triglyceride levels were measured during pregnancy

The necessary information for the study was collected and analyzed using a checklist. Finally, the incidence of preeclampsia was studied and compared between the two groups.

Data Analysis

The obtained data were entered into SPSS software version 24 and were analyzed. Quantitative data are described as mean and standard deviation and qualitative data are described as number and percentage and Independent Student T-test and Chi-square test will be used to compare the rate of preterm delivery in the studied groups. All results of statistical tests less than 0.05 were considered significant.

III. Results

Out of 74 female participants, 2 were excluded from the study due to reluctance and 72 were examined. The mean and standard deviation of age of women participating in the study was 32.7 ± 5.1 years. Mean age, body mass index and gestational age were not significantly different between the two groups (P-value > 0.05). Demographic characteristics of the participants are shown in Table 1.

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Table 1: Demographic Characteristics of the Participants

		Control group (Placebo)	Case group (Omega-3)	P-value
Age of mother		28.97 ± 5.23	30.08 ± 4.19	0.32
BMI		28.98 ± 0.82	28.54 ± 0.74	0.74
Gestational age at labor		38.19 ± 4.25	38.61 ± 1.36	0.57
Gender	Female	23	18	0.341
	Male	13	18	0.18

The difference between the mean weight of neonates at birth in the two groups was statistically significant (P value=0.01). The difference in 5-minutes Apgar score among the two groups was statistically significant (P value=0.02). In general, a significant relationship was observed between omega-3 intake and 5-minutes Apgar score (P value<0.05).

Table 2: Comparison between Neonate's Birth Weight and Apgar Score among the Two Groups of the Study

			Control group (Placebo)	Case group (Omega-3)	P-value
Neonates Birth Weight (gr)			3137 ± 211	3231 ± 273	0.011
Apgar Score (Number of participants-Percent)	Min 5	8	8 (22.2)	17 (47.2)	0.026
		9	28 (77.8)	19 (52.8)	
	Min 7	10	36	36	

In the omega-3 receiving group, triglyceride levels after the intervention showed significant reductions compared to before the intervention, but in the placebo group, triglyceride levels before and after the intervention were not significantly different from each other (P value>0.05).

Table 3: Comparison between the Triglyceride Levels of the Two Groups before and after the Intervention

		Control group (Placebo)	Case group (Omega-3)	P-value
Triglyceride level	Before Intervention	233.61 ± 20.52	238.83 ± 17.68	0.25
	After Intervention	229.39 ± 18.68	223.75 ± 15.67	0.17

Complications were lower in the omega-3 receiving group than in the placebo group (58.3% in the placebo group and 22.2% in the omega-3 receiving group). Most of the complications related to diabetes were in the placebo group. The frequency of pregnancy complications in the two groups are significantly different from each other.

Table 4: Complications Observed in the Two Groups of the Study

		Control group (Placebo)	Case group (Omega-3)	P-value
Complications (Number of participants-Percent)	None	15 (41.7)	28 (77.8)	0.043
	Diarrhea	1 (2.8)	1 (2.8)	
	Dyspepsia	1 (2.8)	0	
	Preterm labor	1 (2.8)	1 (2.8)	
	Diabetes Mellitus	4 (11.1)	3 (8.3)	
	Gestational Hypertension	3 (8.3)	1 (2.8)	
	Cholestasis	1 (2.8)	1 (2.8)	

The frequency of preeclampsia at birth in the two groups can be seen in Table 5. The results showed that the incidence of preeclampsia in the omega-3 receiving group was lower than the placebo group and this difference was statistically significant (P <0.05).

Table 5: Frequency of the Preeclampsia at Birth in the Two Groups

		Preeclampsia		P-value
		Yes	No	
Groups	Control	12 (33)	24 (66.7)	0.003
	Case	2 (5.6)	34 (94.4)	

IV. Discussion

Our study shows that although triglyceride levels were reduced in the omega-3 receiving group, triglyceride levels were not significantly different between the two groups. However, Apgar score of 5 minutes in the omega-3 receiving group was statistically significant. Also, the mean birth weight of the newborns was different in the two groups and this difference was statistically significant. Previous studies have shown similar results (12,13). A study by Yaquoob et al. showed that there is a significant difference in the development of preeclampsia during pregnancy between the omega-3 and placebo groups. They stated that omega-3 could be considered a suitable drug to prevent preeclampsia in high-risk pregnant women. (14). Herrera et al. reported that administration of low daily doses of linoleic acid in the third trimester of pregnancy may significantly reduce the incidence of preeclampsia in high-risk

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women by modifying prostaglandin levels (15). In a clinical trial, Olsen et al. reported that fish oil reduced the risk of recurrence of preterm labor from 33% to 21% (16).

In our study, the incidence of preeclampsia was significantly reduced in the omega-3 group. Also, the side effects observed in the omega-3 receiving group (nausea, diarrhea, minor gastric disorders, hyperglycemia, poisoning and hypotension) are less than the control group. In addition, the incidence of preeclampsia in the omega-3 receiving group is significantly lower than the placebo group. The difference between the two groups in terms of the incidence of preeclampsia (mild and severe) was about 11 people (31%) that according to the present findings, the NNT rate for preeclampsia was equal to 3.2. That means an average of 3.2 people should receive omega-3 treatment to prevent a case of preeclampsia. In a study, Ranjkesh et al. found a significant relationship between omega-3 intake and improvement in pregnancy outcome, including Apgar score and birth weight. The results of this study showed that omega-3 supplementation during pregnancy reduces the risk of preeclampsia in high-risk pregnant women (17).

During their meta-analysis, Bakui et al reported that taking omega-3 fatty acid supplements was an effective strategy to prevent preeclampsia in women at low-risk pregnancies (18)

However, some studies have not found the use of fish oil to reduce diabetes and the incidence of preeclampsia. Zhou et al. showed that the overall incidence of diabetes and preeclampsia was 8% and 5%, respectively, and there was no significant difference between the groups. Weight, height and head circumference at birth did not differ between groups. In the placebo group, there were 12 deaths during birth and 5 neonatal seizures, whilst in the fish oil receiving group, 3 perinatal deaths and no neonatal seizures were observed (19). Also, in the study of Davoodabadi Farahani et al., the mean arterial pressure in the placebo and intervention groups was not significantly different (20). In another clinical study, Salvig et al. evaluated the effects of fish oil (omega-3) supplementation on blood pressure in late pregnancy. They reported that the n-3 marine fatty acids presented in the third trimester of pregnancy had no effect on blood pressure (21).

Burchakov et al., in a review study, stated that preeclampsia was associated with low intake of omega-3 long-chain unsaturated fatty acids, according to observational studies. In recent decades, they report, researchers have studied omega-3 supplements as a way to prevent preeclampsia. Most of these systematic trials and studies have shown poor results in this regard. Of course, these trials had several important limitations related to heterogeneity and other issues. Recent research suggests that in the study of preeclampsia fetal sex, the effect of smoking on the prevalence of preeclampsia, and the possibility that high doses of omega-3s in the mid-term or after may cause disorders, should be considered (22).

The present study was performed on women with hyperlipidemia. High cholesterol or hyperlipidemia is one of the common diseases in Iran that has affected a large population in Iran. Studies in Iran have shown that about 23.9% of men and 12.4% of women in the general population have hypercholesterolemia. The frequency of hypercholesterolemia and hypertriglyceridemia were ported 33% and 44% respectively (23, 24, 25). In addition to regulating good cholesterol (HDL) levels, omega-3s can help relieve depression, anxiety, restlessness, restlessness, mental fatigue, stress, and other neurological disorders (26, 27) Given the importance of treating preeclampsia in pregnancy and the irreversible effects that this disease can have on the health of mother and fetus; Paying attention to the diet containing omega 3 can be effective in the health of pregnant mothers.

V. Conclusion

Omega-3 possesses a beneficial effect on preeclampsia and fetal weight during pregnancy. The prevalence of preeclampsia has decreased significantly in the omega-3 receiving group, and in general, the omega-3 receiving group shows good results in terms of the incidence of eclampsia. Triglyceride levels, which play an enormous role in preeclampsia, were significantly reduced in the omega-3 receiving group after the intervention. Admittedly, applying healthy diets for mothers during pregnancy along with omega-3 supplements can be most effective in their health.

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