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Full Length Research Paper

Evaluation of the effect of omega-3 supplements in the prevention of preeclampsia among high risk women

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Identification of proactive preeclamptic factors in pregnant women, as one of the three maternal and neonatal mortality factors, is of special importance. Omega-3 is a polyunsaturated fatty acid that may reduce blood pressure and brain and heart attacks affecting the production of prostaglandins and reducing unwanted fat, vasodilatation and platelet adhesion. This study was designed and implemented to clinically evaluate the effect of omega-3 supplements in preventing preeclampsia among high risk women of Qazvin city. In a double-blinded clinical trial, 100 high risk preeclamptic women were selected by target-based sampling from among pregnant women referred to health centers in Qazvin city, and voluntarily enrolled into the study. Then, samples were randomly divided into two treatment groups with omega-3 supplementation and placebo, respectively. The population was monitored until termination of pregnancy and childbirth, and post-delivery information was collected and statistically analyzed. Incidence and severity of preeclampsia among the mothers receiving omega-3 supplement 1 g daily during pregnancy was significantly less than that in the control group (p = 0.015). The outcome of pregnancy, including birth time zone and minute 5 Apgar score of neonates in omega-3 group were significantly greater than in the control group. Mean systolic and diastolic blood pressure in omega-3 group was significantly less than that in the control group. Using Omega-3 supplement is effective in reducing incidence of preeclampsia and its severity. It is also effective on improving pregnancy outcome, including birth weight and neonatal minute 5 Apgar score. Therefore, development of nutritional education programs for pregnant women seems to be necessary.

Key words: High-risk pregnancy, preeclampsia, omega-3.

INTRODUCTION

Hypertension disorder during pregnancy, including preeclampsia and gestational hypertension may be accompanied by maternal and neonatal complications and mortality (Lain and Roberts, 2002). Preeclampsia with infection and bleeding is considered as one of the three major causes of pregnant mortality. In developing countries, 25% of all prenatal deaths are related to hypertension disorder during pregnancy (Cunningham and Norman, 2005).

Pathophysiology and etiology of preeclampsia are not completely known and are still under investigation (Cunningham and Norman, 2005). The dominant hypothesis of preeclampsia is decreased placental-uterine perfusion due to defective invasion of cytotrophoblast to uterus spiral arteries. Other hypotheses include intolerance of mother's immunity with fetal-placental tissues, incompatibility of mother with cardiovascular inflammatory changes during normal pregnancy, nutritional deficiencies and hereditary factors

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(Hubel, 1999; Bildeau, 2003). Preeclampsia is known as the disease of theories and there is no cause, treatment, valid and cost-effective preventive and predictive methods for it yet (Bildeau, 2003). However, studies have shown that decidua contains many inflammatory cells which, in case of being activated, can release toxic agents and oxygen free radicals and cause damage to endothelial cells. Antioxidants are a diverse family of compounds which act to prevent excessive production of free radicals and toxic damage by them (Bildeau, 2003; Schiff et al., 1993).

Omega-3 is an unsaturated fatty acid with three twofold bonds which breaks into icosapanthaenoic and decosahexaenoic acids in the body. Omega-3 is a part of the platelet membrane. It prevents adhesion among platelets and so, reduces heart and brain attacks (Qiu et al., 2006). Other functions of omega-3 fatty acid include reduction of the growth of cancer cells, expansion of vessels and decrease of blood pressure, deformation of red globules and improving blood circulation in capillaries and increasing the clotting time of blood (Saldeen and Saldeen, 2004). With increasing of prostacyclin-Thromboxane ratio, omega-3 increases blood flow to uterine and reduces risk of preterm delivery during pregnancy increasing uterine-placental blood flow and causes increase of the birth weight and improved fetal growth (Qiu et al., 2006; Ziaei et al., 2006). Omega-3 also plays a role in increasing expansion of vessels and decrease of blood pressure (Williams et al., 2006). Omega-3 is also effective on decrease of undesirable blood fats and the researches have shown their increase in preeclampsia (Williams et al., 2006; Velzing-Aarts et al., 1999).

In a single-blind clinical trial performed on pregnant women referred to health centers in Qazvin city with gestational age of 14 to 18 weeks and with risk of preeclampsia, the effect of use of omega-3 on reduction of preeclampsia risk in women was investigated.

METHODS AND MATERIALS

In a single-blind clinical trial, one hundred pregnant women with risk of preeclampsia and gestational age of 14 to 18 weeks, based on inclusion criteria, were randomly placed in two case or control groups and used for the study. Clinical examinations were performed after obtaining consent from patients. According to previous studies with a confidence level of 99% and test power of 95%, the number of samples for each group was estimated to be 45 and 50 with falling index of 10%. Until the end of pregnancy, the case group got the drug including one gram of omega-3 supplement containing eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), and the control group got the placebo containing starch. The required data were collected and entered in the respective questionnaires. People were visited monthly until the end of pregnancy and their health and possible side effects of drug and placebo were evaluated. At the time of delivery, delivery information and the presence of preeclampsia were investigated. The main variables included omega-3 and placebo and the incidence of preeclampsia.

High risk patients for preeclampsia include primipara women, ages under than 20 and above 40 years, previous history of preeclampsia or a positive family history, twin pregnancy, body mass index (BMI) > 29, history of renal disease and hypertension, those who did not use any anticoagulant or antihypertention drugs at the time of entering the study.

Two groups were homogeneous. All information were entered into the computer and SPSS ver. 11.5 soft ware for Windows was used and independent-samples T test and Chi-square test was used for analysis of data and $p < 0.05$.

RESULTS

Age, gravidity, parity, primary systolic blood pressure (mmHg), primary diastolic blood pressure (mmHg) and body mass index (BMI) of patients are shown in Table 1. Frequency distribution of causes leading to admission at the time of delivery is shown in Table 2 which indicates a significantly greater prevalence of hypertension in patients in the control group than in the case group ($p = 0.03$). Delivery type of patients between two groups is shown in Table 3. The mean systolic blood pressure of mother was 112.8 ± 8.3 mmHg in the case group and 120.4 ± 15.9 mmHg in the control group which was significantly lower in the case group than in the control group ($p = 0.003$). The mean diastolic blood pressure of mother was 71.6 ± 6.8 mmHg in the case group and 76.6 ± 11.1 mmHg in the control group which was significantly lower in the case group than in the control group ($p = 0.008$). Frequency of Apgar score at minute 5 in the two groups is shown in Table 4 and neonatal minute 5 Apgar score in case group was significantly better than that in the control group ($p = 0.002$). The mean birth weight was 3380.2 ± 395.6 g in the case group and 2996 ± 493.9 g in the control group which was significantly greater in the case group than in the control group ($p < 0.001$).

Incidence and severity of preeclampsia in case and control groups is shown in Table 5 indicating that the severity of preeclampsia in mothers in the control group was significantly greater than in those in the case group ($p = 0.015$).

DISCUSSION

In a study by Schiff et al. (1993), they expressed that thromboxane A_2 levels and the risk of preeclampsia is reduced after the daily administration of 1.6 g of omega-3 in the third quarter of pregnancy.

Qiu et al. (2006) showed that the erythrocyte omega-3 level in women with preeclampsia is significantly less than that in the healthy pregnant women. In a study, Williams et al. (2006) reported the relationship between increased consumption of fish twice a week and reduction of incidence of risk of preeclampsia, and believed that DHA, with its vasodilatating effects and effect of reducing undesirable fats, can be effective in the prevention of preeclampsia.

Table 1. Age, gravidity, parity, primary systolic and diastolic blood pressure and BMI of patients in the two groups.

	Group*		P
	Case	Control	
Age (year)	30.06 ± 7.59	28.96 ± 6.40	0.436
Gravidity	1.50 ± 0.50	1.44 ± 0.50	0.552
Parity	0.46 ± 0.50	0.40 ± 0.49	0.549
Primary Systolic blood pressure (mmHg)	122. 10 ± 29.45	117.80 ± 21.10	0.403
Primary Diastolic blood pressure (mmHg)	75.10 ± 16.27	74.98 ± 12.30	0.967
BMI	27.22 ± 6.73	28.16 ± 7.36	0.524

Table 2. Causes of hospitalization in the two groups of patients.

Causes of Hospitalization*	Case group	Control group
Labor	45	34
Vaginal bleeding	0	2
Premature Rupture Of Membranes	2	1
Passing the time of delivery	1	3
Hypertension	2	10

*P = 0.03 (between two group).

Table 3. Delivery type of patients in the two groups.

Delivery type*	Case group	Control group
Vaginal delivery	27	28
Caesarean section	23	22

*P = 0.841 (between two group).

Table 4. Apgar of infants at 5 minute in the two groups of patients.

Apgar of infants at 5 minute*	Case group	Control group
0-4	0	0
5-7	1	12
8-10	49	38

*P=0.002 (between two group).

Table 5. Severity of preeclampsia in the two groups of patients.

Severity of preeclampsia*	Case group	Control group
Non preeclampsia	48	40
Mild preeclampsia	2	4
Severe preeclampsia	0	6

*P=0.015 (between two group).

In the present study on 100 patients evaluated in two 50-patients groups, 50 of them used Omega 3 and 50 used placebo during pregnancy (weeks 14 to 18 of pregnancy until the end). It is worth noting that the two groups were equal in terms of age, BMI, number of pregnancies, gestational age and results of blood pressure tests at the time of entering the study. According to the results obtained, regarding the 16% difference in risk of preeclampsia and 12% difference in the severity of preeclampsia between the two groups, using Omega-3 supplements is effective in reducing the incidence of preeclampsia ($p = 0.015$), and also the increase of systolic ($P = 0.008$) and diastolic blood pressure ($P=0.003$) in the case group were significantly lower than those in the control group.

Usable amount of omega-3 oils or fish liver is very important because insufficient or excessive use of it intensifies the risk of preeclampsia; hence, moderate use of it (at least 200 mg/day) is recommended during pregnancy (Olafsdottir et al., 2006; Oken et al., 2007; Kaiser and Allen, 2008). In a study by Olsen et al. (1986) and Olsen and Joensen (1985), a significant relationship was reported between higher fish consumption during pregnancy and increased fetal weight and reduced preeclampsia. Our study was concordant with this research and some other researches (Innis 2007; Makrides et al., 2006) have been reported in line with our findings.

In their study, Dirix et al. (2009) obtained a significant relationship between receiving DHA, especially in early pregnancy, and birth weight and head circumference of newborns and suggested that omega-3, with its vasodilatation effect and improvement of uterine-

placental blood flow, may lead to enhanced fetal growth.

Omega-3 fatty acids through diet or dietary supplementation may reduce the risk of early preterm birth (Mozurkewich and Klemens, 2012). Preeclamptic women showed reduced total omega-3 fatty acids ($P<0.05$), increased omega-6 : omega-3 ratio ($P<0.05$), higher oxidative stress ($P<0.05$) and lower antioxidant ($P<0.05$) levels. Similar trends were also observed in cord samples (Mehendale et al., 2008).

Reduced antioxidants and increased oxidative stress leading to impaired essential polyunsaturated fatty acid levels may be a key factor in the development of preeclampsia (Mehendale et al., 2008).

Conclusion

This study indicated that daily use of one gram of omega-3 supplements from the second trimester of pregnancy is effective in reducing the risk of preeclampsia and its severity. In general, the results of this research confirm the reduction of the effects of preeclampsia and improvement of pregnancy results (neonatal weight and Apgar score) as a result of using Omega-3 in high risk women during pregnancy and could be considered as one of the preventive ways for the incidence of preeclampsia.

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