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Supplementation of docosahexaenoic acid (DHA) / Eicosapentaenoic acid (EPA) in a ratio of 1/1.3 during the last trimester of pregnancy results in EPA accumulation in cord blood

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ABSTRACT

Omega-3 fatty acids (n-3 FA), specifically DHA, are associated with fetal growth and development. We aimed to determine the levels of DHA and EPA in cord serum after n-3 FA supplementation during the last trimester of pregnancy. Among 55 women, 23 were administered daily one capsule of n-3 FA supplement, involving DHA/EPA in a ratio of 1/1.3. Twenty nine women were enrolled as control group. Blood samples were collected at 22–24 weeks of gestation and at delivery. Fatty acids were analyzed with the method of GC-MS. Cord DHA level increased and EPA level decreased in both groups between the days of 22–24 and delivery. However, decrease in cord EPA level was significant in control group ($p < 0.001$) but not in supplement group ($p > 0.05$). Supplementation of DHA/EPA in a ratio of 1/1.3 during the last trimester of pregnancy caused higher cord EPA level compared to control group indicating an accumulation in umbilical cord.

1. Introduction

The major members of n-3 polyunsaturated fatty acid (PUFA) family are α-linoleic acid (ALA; C18:3n-3), eicosapentaenoic acid (EPA; C20:5n-3) and docosahexaenoic acid (DHA; C22:6n-3). The n-3 long chain PUFAs have been identified as important structural components of the membrane lipids of the human central nervous system [1–3]. Particularly DHA is important for the primary building block concentrated in the brain and retinal tissue [4,5].

EPA and DHA can be synthesized from ALA which is the parent molecule of omega-3 series long chain PUFAs. Moreover, the conversion efficiency of ALA to DHA and EPA is very limited [6–9]. Therefore, EPA and DHA are accepted as conditionally essential [10] and are recommended to obtain from dietary intake of n-3 FA or intake with oral supplements [11]. Fish, fish oil supplements, fortified foods and plants are main sources of n-3 FA in the diet. The World Health Organization (WHO) and the Food and Agriculture Organization of the United Nations (FAO) advised daily intake of at least 2.6 g of n-3 FA and 100–300 mg of DHA during pregnancy [12,13].

It has been known for several years that n-3 FA involved in fetal development [14,15]. In the fetus and the newborn, synthesis of n-3 FA is insufficient and so they depend on maternal diet and metabolism [16]. Large amounts of DHA are transferred from maternal to fetal blood, resulting in high levels of DHA in both placenta and fetal bloodstream and tissues [17]. Cord DHA concentration at birth is higher than maternal blood levels, implying high fetal DHA demand in the last months of pregnancy and a preferential placental transfer to the fetus [18].

Indeed, the greatest need for n-3 FA is during the third trimester of pregnancy and lactation [19]. It was shown that the fetus accumulates about 50–60 mg DHA per day during the last trimester [20]. The deficiency of n-3 FA in fetus may cause vision and nerve problems [5]. In addition, a recent research indicates that maternal n-3 FA intake lowers the infant's risk of developing allergies and asthma later in his/her life [21]. Omega-3 fatty acids are also important for maternal health and the outcome of pregnancy [22]. They appear to reduce incidence of

Abbreviations: DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; n-3 FA, omega-3 fatty acids; PUFA, polyunsaturated fatty acid; ALA, α-linoleic acid; PGE_2, prostaglandin E_2; $PGF_{2\alpha}$, prostaglandin $F_{2\alpha}$; BMI, body mass index; FATP, fatty acid transport protein

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preeclampsia, preterm labor and the risk for perinatal and postpartum depression [23]. Therefore increasing maternal omega-3 status throughout pregnancy and lactation improves infant's omega-3 status and enriches the maternal stores [24–26].

The health related effects of EPA and DHA have argued in several studies [27–29] however the specific roles of EPA in pregnancy and lactation are largely unknown. The omega-3 fatty acid EPA is synthesized from ALA and the precursor of series-3 prostaglandins and certain eicosanoids. ALA conversion is too low and blocked by high intakes of DHA and EPA [30]. High intake of dietary EPA may lead to a reduction in the production of proinflammatory eicosanoids such as prostaglandin E_2 [PGE_2] and prostaglandin $F_{2\alpha}$ [$PGF_{2\alpha}$] which associated with the initiation of labor and preterm labor [31]. There has been enormous information about that DHA has many functions on fetus growth and development nonetheless EPA seems to have an important role in DHA transplacental transport and intracellular absorption [22].

In present study we aimed to define the levels of DHA and EPA in cord serum after giving the DHA/EPA supplementation in a ratio of 1/1.3 during the last trimester of pregnancy.

2. Methods and materials

2.1. Study population and design

This experimental study was planned on healthy, singleton pregnant women between 24 and 41 years of age. The voluntary participants (signed an informed consent) were enrolled after a brief explanation about trial at the beginning of their last trimester (22–24 weeks) during routine prenatal care visits. Demographic data were obtained using a face-to-face questionnaire. They were asked for taking n-3 FA supplement daily during last trimester of pregnancy. Twenty three pregnant women accepted to take supplement and classified as omega positive group and 29 of them involved to the study as control group without accepting to take supplement. The pregnant women who had a history of chronic diseases and/or consumed n-3 FA supplements were excluded. Maternal venous blood samples were collected from each subject in the morning at 22–24 weeks of gestation. Cord blood samples were collected at delivery. All procedures and protocols received prior approval by the Istanbul Medipol University Ethics and Research Committee.

2.2. Supplements

The pregnant volunteers were assigned to receive a softgel capsule as supplement daily from last trimester to delivery. The supplement was a product produced by Martek Biosciences Corporation, Solgar, (Leonia, NJ, USA) each providing 378 mg docosahexaenoic acid (DHA) and 504 mg eicosapentaenoic acid (EPA) in total 950 mg omega-3 polyunsaturates. Control group had no supplement or placebo. No dietary instructions were given for both groups.

2.3. Analysis of fatty acids

The blood samples were centrifuged at 1500 g for 10 min. Plasma were separated and then stored at −80 °C till analysis. After thawing, the total fatty acids from serum were extracted according to Folch method [32]. The esterification of fatty acids to fatty acids methyl ester was performed by an alkylation derivatization reagent [33]. Then the fatty acid composition analyzed by GC-MS chromatography. A standard mixture including 37 fatty acids was used for standardization and their retention times were recorded. Chromatograms were analyzed in terms of % by weight of total fatty acids.

2.4. Statistical analyses

Statistical analyses were performed using the IBM Statistical Package for Social Sciences (SPSS) version 21.0. The results were presented as mean ± SD or median (IQR). The evaluation of significant differences was performed with the use of paired samples t-test and independent samples t-test and its nonparametric equivalent Mann Whitney-U. Differences were considered statistically significant if $p < 0$ 0.001. Considering a 0.05 two-sided significance level and large effect size, the power was 0.80. Cohen's Effect sizes were also calculated. Nonparametric tests were used when the data were not normally distributed.

Table 1
The main baseline characteristics at the 22–24 weeks of the study population.

	Total	Control group	n-3 group	p	r
N	52	29	23	–	–
Age (year)	32.9 ± 3.9	32.1 ± 3.8	33.9 ± 3.9	0.117	0.10
BMI (kg/m^2)	25.7 ± 2.6	25.8 ± 2.6	25.4 ± 2.5	0.621	0.16

BMI, body mass index; r, Cohen's effect size. Values are presented as means ± SD.

3. Results

3.1. The main characteristics of the study population

The main characteristics of the study population are presented in Table 1. The mean age of participants was 32.9 ± 3.9 years. The mean body mass index (BMI) was 25.7 ± 2.6 kg/m^2. There were no statistically significant differences in any of the main baseline characteristics measured between supplement and control groups at the 22–24 weeks of gestation indicating the homogeneity of both groups at the beginning of the study.

3.2. The distribution of fatty acids

The distribution of fatty acids in serum at 22–24 weeks of pregnancy and umbilical cord is presented in Table 2. The analysis of serum samples at the beginning of the study (22–24 weeks of pregnancy) revealed no significant value for total SFA, MUFA and PUFA. Among PUFAs, total n-6 FA values decreased and total n-3 FA values increased over time in both groups. However, after the omega supplementation during last trimester, total n-3 FA increased significantly in supplement group with large effect size ($p < 0.001$; $r > 0.50$). In addition, the changes over time between 22 and 24 weeks and umbilical cord were significant for the levels of total SFA, MUFA and PUFA for each control and supplement groups ($p < 0.001$). In umbilical cord serum, total SFA and MUFA values increased and the total PUFA values decreased in control and supplement groups irregardless of omega supplementation.

3.3. Relationship of omega-3 fatty acid levels between omega-3 supplement and control groups

The DHA and EPA compositions in maternal blood in cord at delivery for control and supplement groups are presented in Table 2. At the beginning of the last trimester, the changes in DHA and EPA levels between the groups were not found significant. However, after omega fatty acids supplementation for 3 months, the differences of DHA and EPA levels were statistically significant ($p < 0.001$).

3.4. The omega-3 fatty acid levels within each omega-3 supplement and control groups

In cord serum at delivery, DHA level increased and EPA level decreased in both control and supplement groups ($p < 0001$). Without consuming any omega supplement, during the last trimester, the level of cord DHA increased from 1.90 to 2.36 with a significancy ($p < 0.001$, effect size 0.69). In case of omega supplementation, the