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Effect of Omega-3 Fatty Acıd Supplementation During Pregnancy and Lactation Period on Neuromotor Development of the Children Between the Ages of 0 to 2

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Abstract

The aim of this study is to establish the effect of omega 3 fatty acid supplement to women in pregnancy and lactation on the neuromotor development of children aged 0-2. The study has been carried out with 58 pregnant women-infants. The social-demographic information and anthropometric measurements of pregnant women and infants have been attained via a survey form. The women were given omega fatty acid supplement in the last trimester of pregnancy and first six months of lactation. The neuromotor development of infants was evaluated using the "Denver II Developmental Screening Test". The study data has been processed using the SPSS 24.0 statistical package software. It has been found that the item success scores were higher for omega group ($p>0.05$) in all skills, except fine motor skills at age one and language and personal social development at age two. It has been observed that all skills in both groups developed in time/chronologically and the study group was significantly higher ($p<0.001$) in ages one-two development comparison and six month-one-year age development in personal social development. The general evaluation found that the children with normal development were in the omega group, and a higher rate ($p>0.05$) of children with equivocal and abnormal development in the control group. Consequently, it has been established that omega 3 fatty acid supplement in pregnancy and lactation periods significantly supports the neuromotor development of infants in ages 0-2. It is considered beneficial to carry out more comprehensive studies on the topic.

Key words: Omega 3 Fatty Acids, neuromotor development, early childhood, lactation, pregnancy

Introduction

The first 1000 days of life are critical in terms of development (1). The last trimester of pregnancy is the term with the fastest pace of brain development and highest sensitivity to malnourishment (2,3). Omega fatty acids are among the significant nutritional components for this period (2,4). Omega fatty acids are transferred to the fetus via the placenta and to the infant via breast milk, supporting the

development of brain and central nervous system (3,4). Therefore, the contents of nutrition, particularly the types and quantities of fats consumed are vital in the final terms of prenatal period, first months of postnatal period and the first two years.

Docosahexaenoic Acid (DHA), an omega fatty acid, is known to constitute a significant portion of cerebral cortex and retinal membrane lipids, and 15% of all fatty acids in the frontal cortex and is the fundamental fatty acid in the brain's gray matter. (2,5) In this respect, the effects of omega fatty acids received through daily nutrition or in supplements on infant development have been studied thoroughly (6-10).

It has been demonstrated Docosahexaenoic Acid supports a normal level of intelligence (score/coefficient) and protects visual-spatial learning and memory (11). It has been reported that consumption of fish during pregnancy, rich in DHA, supports visual development in infants (12,13). It has also been asserted that consuming sea food during pregnancy is beneficial to the motor and social development in early childhood and language development in the first 18 month (14,6). Studies by Kannass et al. and Krabbendam et al. revealed that pregnant women with high plasma DHA concentration in the last trimester of pregnancy had babies who, in the first 18 months, displayed lower attention deficit and fewer behavioral disorders at age seven and better development of motor cells overall (15-17).

In Turkey there was no study on the effects of omega-3 fatty acids on the neuromotor development of infants aged 0-2. Therefore, this study has been planned and contacted to investigate the effects of omega-3 fatty acid supplement to women in pregnancy and lactation periods on the neuromotor development of infants aged 0-2.

Material and Methods

The study has been initiated with 74 volunteering pregnant women who applied to a maternity clinic of a private hospital in Istanbul during September 2015 – December 2016 and completed with 58 pregnant women. The study is sectional and descriptive in nature and attained ethical approval from the Non-Invasive Clinical Studies Ethical Approval Board of Istanbul Medipol University with approval number 02 dated 17/10/2012. (B.08.6.YÖK.2.İM.0.05.0.06.02-15).
Healthy women with singleton pregnancy in ≥24.gestation week without chronic ailments and receiving no omega fatty acid supplement have been accepted in the study.

Pregnant women were randomly placed in two groups, with one group receiving omega-3 fatty acid supplement and the other receiving no support whatsoever, including placebo. The group receiving omega supplement was designated as the Study Group (SG) and the other as Control Group (CG). The study group received a supplement of 950 mg polyunsaturated omega-3 fatty acid (Martek Biosciences Corporation, Solgar (Leonia, NJ, USA) containing 378 mg DHA and 504 mg EPA starting in the 25th week of

gestation until and throughout the first six months of lactation (a total of nine months).

The infants included in the study are full-term (<38th week of gestation), healthy, solely breastfed in the first six months, supplemented with formula without omega fatty acids where the mother's milk is inadequate or absent and not supplemented with any omega fatty acid. The infants born to mothers receiving omega fatty acid supplement were designated as the Study Group, while the others were designated the Control Group. The general health and physiological development of infants was monitored from birth till the second birthday (at birth, on the sixth month, first year, second year) by a pediatrician.

Data Collection and Evaluation

Demographic information on pregnant women was attained through interviews featuring a survey form. The anthropometric information of pregnant women (body weight, height) were collected by the researcher, while the infants' anthropometric measurements (body weight, height, head diameter) were received by a neonatal nurse. The anthropometric measurements of infants (growth and development) have been observed by calculating the Z-score. To calculate the (18) Z score, WHO ANTRO Plus (19) software was used.

The neuromotor development of infants was determined using the "Denver II Developmental Screening Test". The test was implemented by an experienced "Child Development Specialist" in house visits. Measuring the four skills in children aged 0 to 6, the Denver II Developmental Screening Test is generally a developmental screening test, yet is also used to evaluate neuromotor development by measuring fine-gross motor skills. Indeed, Codina et al. include the Denver II Developmental Screening Test in the methods used to evaluate development in early childhood (20). Similarly, a study carried out in Turkey in 2011 evaluated neuromotor development using the Denver II test (21). Neuromotor Development was evaluated in three parameters, namely: abnormal, normal and equivocal. (Abnormal: has growth deficiency, Normal: developing in line with chronological age group, Equivocal: Has developmental risks). The Denver II test was scored using item success percentage method. Personal-social, fine motor, language and gross motor aspects have been calculated individually for each infant.

Statistical Analysis

The findings of the study have been statistically analyzed using the SPSS 24.0 Statistics package software. Descriptive statistical methods have been utilized to evaluate the study data (Frequency (n), Percentage (%), Average (X), Standard Deviation (SD)). To investigate the differences between the groups, Pearson Chi-Square test and Fisher Exact test was used on categorical data and independent t test in numerical data. To examine the correlations between measurements, Pearson Correlation Analysis was used. The results were attained with 95% reliability range and $p<0.05$ of

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significance. Repeated ANOVA test and its continuation, the Post-HOC Bonferroni test have been used to check any variation in the Denver II parameters of 6-month, 1-year and 2-year age groups. The significance for the repeated ANOVA test was taken as ($f=1955.899$: $p<0.001$).

Since the number of abnormal infants in neuromotor development evaluation was low ($n<5$), it was not considered in statistical analysis. Similarly, the head diameter was not included for the 2-year age group due to low number, which constitute the limitations of the study.

Results

This study examines data on the effects of omega-3 fatty acid supplement on the neuromotor development of infants in 0-2 age group. Table.1 demonstrates demographic information on mothers.

Table 1. Sociodemographic characteristics of mothers

Feature	Study Group		Control Group		Total		p
Age (year)	31.9±4.5		30.2±4.0		31.1±4.3		0.148
Gestation period (day)	272.1±11.3		269.3±10.5		271.0±11.0		0.301
BMI, beginning of pregnancy (kg/m^2)	22.6±2.8		22.9±2.9		22.7±2.8		0.712
BMI, end of pregnancy (kg/m^2)	28.2±2.7		28.7±3.3		28.4±3.0		0.592
Weight gained in Pregnancy (kg)	15.8±5.4		15.5±6.9		15.7±6.0		0.855
	n	%	n	%	n	%	
Education Level							
High School or Below	17	20	10	40	27	46	0.462
Above High School	17	50	15	60	32	54	
Vocation							
Employed	20	61	12	48	32	56	0.262
Unemployed	13	39	13	52	26	44	
Birth Type							
Cesarean	37	88	25	86	62	87	0.544
Normal	5	12	4	14	9	13	

It was observed that the mothers had an average age of 31.1±4.3 years, with 44% being housewives and more than half (54%) having university-level education. Gestation period was 271.0±11.0 days with BMIs at the start and the end of pregnancy as 22.7±2.8 kg/m^2. 28.4±3.0 kg/m^2 respectively. gave birth with cesarean (87.3%). No statistical variation was identified among the groups in terms of demographic Gaining an average of 15.7±6.0 kg during pregnancy. the mothers commonly attributes. Table 2 provides the weight and height measurement of infants. It has been observed that weight and height at birth was similar in both groups, and the

body weights of infants in the study group were higher in all phases compared to the control group (6-month-1-year: $p<0.05$).

Table 2. Anthropometric measurements of infants

Measurement	Study Group	Control Group	Total	P
	X±SS	X±SS	X±SS	
Birth				
Weight (g)	**3.417 ± 618**	**3.401 ± 679**	**3.410 ± 639**	**0.92**
Weight Z Score	**0.07±1.3**	**0.22± 1.3**	**0.1±1.3**	**0.625**
Height (cm)	**50.3 ± 2.3**	**50.5 ± 2.1**	**50.3 ± 2.2**	**0.738**
Height Z Score	**0.06±1.2**	**0.48± 1.1**	**0.2±1.2**	**0.404**
6 months				
Weight (g)	**8.146 ± 1.018**	**7.587 ± 681**	**7.918 ± 929**	**0.048**
Weight Z Score	**0.2±0.9**	**-0.23± 0.8**	**0.06±0.9**	**0.223**
Height (cm)	**67.8±2.7**	**67.3±2.4**	**67.6±2.6**	**0.562**
Height Z Score	**0.07±1.3**	**-0.2±1.1**	**0.03±1.2**	**0.321**
1 year				
Weight (g)	**9.947 ± 990**	**8.862 ± 994**	**9.465 ± 1.117**	**0.009**
Weight Z Score	**0.4±0.7**	**-0.55±1.08**	**-0.02±1.04**	**0.123**
Height (cm)	**75.1 ± 2.4**	**75.9 ± 2.6**	**75.5 ± 2.4**	**0.59**
Height Z Score	**-0.3±1.01**	**0.12±0.88**	**-0.09±0.9**	**0.25**
2 years				
Weight (g)	**13.228 ± 1.125**	**12.795 ± 1.349**	**13.066 ±1.220**	**0.201**
Weight Z Score	**0.9±0.7**	**0.57±1.01**	**0.7±0.8**	**0.595**
Height (cm)	**89.7 ± 3.48**	**90.6 ± 3.7**	**90.1 ± 3.58**	**0.342**
Height Z Score	**0.8±1.05**	**1.1±1.2**	**0.9±1.1**	**0.721**

In the comparison of skill developments by item success scores, provided in Table 3.

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Table 3. Comparison of infants' Denver II test item success scores (%)

Skill	Study Group	Control Group	t	p
	X± SS	X± SS		
6 months				
Personal social development	100	100	-	-
Fine motor	95.45± 12.38	94.64±12.46	0.27	0.788
Language development	96.02 ±13.14	96.42±8.90	-0.144	0.886
Gross motor	90.90 ±22.01	84.50±24.83	1.143	0.257
1 year				
Personal social development	87.10± 22.99	83.30±21.30	0.703	0.485
Fine motor	29.54±40.80	39.28±39.33	-1.001	0.32
Language development	68.75±24.78	68.75±28.56	0	1
Gross motor	44.88±36.79	30.35±31.44	1.726	0.089
2 years				
Personal social development	48.80±24.23	53.85±23.43	-0.888	0.377
Fine motor	45.13±22.25	44.23±16.51	0.188	0.851
Language development	55.38±24.40	60.51±21.75	-0.923	0.359
Gross motor	25.16±17.20	22.19±16.57	0.738	0.463

The language development scores were similar in both groups in the 6th month and age 1, and were low in omega group at age two, and the personal social development score at age two was also low in the omega group, while the item success score in other skills was higher in the omega group. No statistically meaningful difference was found between the groups in item success scores ($p>0.05$).

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Table 4. Chronological comparison of infants' neuromotor skills

Skill	Study Group				Control Group			
	Mean Difference	SE	p	95%CI	Mean Difference	SE	p	95%CI
Personal social development								
6-month-1-year	11.67	3.23	0.002	3.61-19.72	16.69	3.88	0.001	6.8-26.58
6-month-2-year	51.2	3.61	<0.001	42.20-60.19	46.45	4.4	<0.001	35.23-57.67
1-year-2 year	39.52	4.26	<0.001	28.89-50.16	29.76	6.53	<0.001	13.12-46.4
Fine motor								
6-month-1-year	65.13	6.09	<0.001	49.96-80.30	55.35	7.16	<0.001	37.11-73.60
6-month-2-year	50.21	3.88	<0.001	40.53-59.89	50.31	4.22	<0.001	39.55-61.07
1-year-2 year	-14.91	6.09	0.056	-30.38	-5.04	7.86	1	-40.03
Language Development								
6-month-1-year	26.18	4.06	<0.001	16.07-36.30	27.67	5.16	<0.001	14.52-40.83
6-month-2-year	40.54	3.92	<0.001	30.76-50.32	35.56	4.45	<0.001	24.21-46.91
1-year-2 year	14.36	5.02	0.02	1.83-26.88	7.89	6.91	0.791	-35.2
Gross Motor								
6-month-1-year	44.78	6.44	<0.001	28.74-60.83	54.15	6.59	<0.001	37.34-70.95
6-month-2-year	65.53	4.7	<0.001	53.80-77.25	62.5	5.34	<0.001	48.91-76.10
1-year-2 year	20.74	5.92	0.003	5.98-35.50	8.35	6.66	0.662	-33.95

As provided in Table 4, both groups displayed meaningful development in neuromotor skills in line with age, with the exception of personal social development in six-months-one-year, language development in one-year-two year, gross motor skills in one-year-two-year periods for the control group and language development in one-two-year periods for the study group ($p<0.001$). It was established that the study group is significantly in lead with one-two-year period gross motor skills and six-month-one-year period personal social development ($p<0.001$), with no variation between groups in other skills.

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Table 5. Results of general neuromotor development evaluation of infants

	Study Group		Control Group		Total		p
	n	%	n	%	n	%	
6 months							
Normal	34	94.4	23	85.2	57	90.5	
Equivocal	1	2.8	3	11.1	4	6.3	0.392
Abnormal	1	2.8	1	3.7	2	3.2	
1 year							
Normal	29	80.6	20	74.1	49	77.8	
Equivocal	4	11.1	3	11.1	7	11.1	0.717
Abnormal	3	8.3	4	14.8	7	11.1	
2 year							
Normal	29	85.3	20	74.1	49	80.3	
Equivocal	1	2.9	0	0	1	1.6	0.259
Abnormal	4	11.8	7	25.9	11	18	

The neuromotor development evaluation. as shown in Table 5, elicited the ratio of infants with normal development for all groups as higher in the study group. and the ratio of infants with equivocal and abnormal development as higher in the control group. However, the variation between the groups was deemed insignificant ($p>0.05$).

Discussion

It has been established that Omega-3 fatty acids received in mother's womb accumulate in the eyes, brain, testicles and placenta taking a critical role in many vital functions. Commonly found in brain tissue and particularly in grey matter and the cerebral cortex, the omega-3 fatty acids are important for growth-development. gene expression. immune response and cerebral development. Thus, the omega fatty acids are vital for the nerve cell growth. proliferation and development in early life (5,22).

Interest in omega-3 fatty acids soared after Olsen et al. found that the infants in the Faroe Islands in Denmark were 194g heavier. with pregnancies lasting four days longer compared to infants born in mainland Denmark (23). A subsequent study by the said researchers established that the pregnant women living in the Faroe Islands had a meaningfully high level of n-3/n-6 in their nutrition (24). Similar to the study of Olsen et al., the infants in our study group were heavier by 559 g in the sixth month and 1100 g at age one, which are significant. and by 433 g at age two.

The meta-analysis of 571 studies on the consumption of omega-3 fatty acids during pregnancy highlights

its supportive effect on the neuro-cognitive development of infants. thus it is important for women and infants to receive adequate amount of omega-3 fatty acids (25). To fortify the meta-analysis. the item success scores for all skills. excluding fine motor skills at age one and language and personal social development skills at age two. were found higher for our study group. Furthermore. the difference in the development of gross motor skills for the one-two-year age group and personal social development skill for the six-months-one-year age group significantly favored the study group.

The AVON study carried out in UK's Bristol University in 1991 with 13.761 pregnant women. the first longitudinal cohort study of Europe. is one of the most crucial studies focusing on the health of pregnant women and child development. The AVON study. presenting the strongest evidence on omega-3. points out that receiving omega-3 fatty acids during pregnancy and infancy support the infants' neurocognitive functions and is significant for pregnant women and infants (26). Similar to the AVON study. the infants in our study group showed meaningful normal development at all age groups in terms of general neuromotor development. while infants with signs of abnormal development. falling short of their chronological age-development curve. were mostly in the control group (25.9%). which we consider striking.

The meta-analysis evaluating studies published in the 2000-2010 period on omega-3 supplements and infant growth and development concluded that omega-3 supplements were more effective on the cognitive development of infants with unfavorable social-economic conditions (27). A double-blind. randomized. controlled study carried out in Canada in 2014 found no clear effect of omega-3 supplement on neuromotor development. However, it supported the hypothesis that, as omega-3 supplements increase maternal DHA intake. it would protect babies born to women on typical western diets from the risk of DHA deficiency (28).

It has been reported in the literature that the development phases are not clearly distinguished from others. Development occurs in a regular, constant and intersecting manner. Growth and development rates are not identical in all age groups. It has been reported that increased development in one field may lead to a slow-down in other fields. For instance, it has been reported that motor development speeding up may lead to development of walking skills, while language development concurrently slows down or halts (29.30). In our study, the development rates have shown variance similar to the reported literature. The lagging language development at age two in our study group, while not significant. may stem from the variation of development rates. It is also known in the literature that fine motor skills may accelerate after age two (31.32). This supports the expectation that the study group will fall behind the control group in one-year age fine motor skills. then catch up

and outpace the control group at two-year age period.

A study conducted in Turkey in 2016 studied the mother's sensitivity to the infant's development. measuring neuromotor development using Denver II test, similar to this study. It has been observed that the infants' development was meaningfully proportional to the mothers' sensitivity to the infants' signs. In particular. a meaningful difference was identified in personal-social. fine motor and gross motor fields (33). It is considered that the infants in study group training in year-two period personal social development scores, though with insignificant variance, may be influenced by the lack or environmental stimuli and the mother-infant relationship.

Another study investigating the effect of prenatal omega-3 supplement in the second half of pregnancy on the development of 18-months old infants, examining 730 infants, considered the quality of house environment. a powerful factor in child development. While omega-3 supplement revealed no effect on the development of 18-months old infants, the study concluded that prenatal omega-3 supplement may offer benefits for infants in environments lacking the necessary stimuli for the infant's motor and cognitive development. Since the infants with signs of abnormal development in our study were mainly in the control group and the groups were homogenous in terms of demographic attributes and comprised working mothers, it is believed that omega-3 supplement may compensate for the shortcomings in the mother-infant-stimulus relationship (34).

Consequently. the meta-analysis on omega-3 is substantially limited by heterogeneity. While some studies point to the beneficial effects of omega-3 supplement on visual. motor and cognitive development in early childhood. others reported no meaningfully beneficial effects. There is, however, no evidence of negative effects either (35).

In this study, we've observed positive effects of omega 3 supplement on body weight and neuromotor development. It's been remarked that infants receiving omega-3 supplement in pregnancy and lactation periods displayed significantly better results in neuromotor development. particularly with increasing age. A plethora of nutritional and environmental factors influence healthy neuromotor development. It is considered that comprehensive and long-term studies evaluating neuromotor development by examining various other factors, including house environment variables. are necessary.

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