

Effects of Prenatal Fish Oil and Folic Acid Supplementation on Infant Psychomotor and Mental Development: Results from NUHEAL Randomized Controlled Trial

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Abstract

Background: Prenatal supply of folic and fatty acids is related to infant's neurodevelopment; however, the potential

Methods: (FO), folic acid (5-MTHF), both, or placebo, and assessed their infant's mental and psychomotor development at 6 and

Results:

Conclusions:

acid composition [27-30]. Recent cohort studies of folate supplemented mothers have shown that their infants have fewer behavioural and emotional problems [31,32], improved neurodevelopment and reduced hyperactivity and peer problems in children [33,34].

Nevertheless, the recent reviews and meta-analyses of randomised clinical trials conclude that there is no clear long-term benefit of folate and n-3 fatty acids supplementation during pregnancy on child's neurodevelopment [35-38]. Despite of the growing interest in the topic, the optimal content of micronutrient supplementation and whether there is a long-term impact on child's neurodevelopment needs to be investigated further. In addition, as folates can influence fatty acid composition in the blood and tissue, the effect of folic acid supplementation together with n-3 fatty acids on child's neurodevelopment has not been investigated in other clinical trials.

In the current study we set out to assess the effects of maternal Fish Oil (FO) and folic acid (5-MTHF) supplementation during the second half of pregnancy on their offspring psychomotor and mental development during the first 20 months of postnatal life.

Materials and Methods

Study design

This study is a part of a European randomized multicentre trial, NUHEAL (Nutraceuticals for a Healthier Life; registration no. NCT01180933). The detailed study design, subject recruitment and characteristics, inclusion criteria, dietary intervention, and collection of data and biological material have been described previously [30,39]. In short, healthy women aged 18 to 40 years with uncomplicated pregnancies were invited to participate in the study before 20 weeks gestation. Babies born within the Spanish cohort (n=154) were assessed for neurodevelopment at 6 and 20 months of postnatal life.

Four mothers were randomly allocated in a double-blind fashion to one of four treatment groups during the second half of pregnancy: (a) fish oil (500 mg DHA+150 mg EPA/day) (FO), (b) folic acid (5-methyltetrahydrofolic acid (5-MTHF), 400 µg /day) (5-MTHF), (c) fish oil + folic acid (FO+5-MTHF), and (d) placebo (see [30] for detailed recruitment description). Women were provided with 180 sachets, each containing 15g of a milk-based supplement (Blemil Plus Matter, Ordesa Laboratorios, Barcelona, Spain). Each sachet was to be consumed as one daily dose, providing 500 mg DHA and 150 mg EPA (provided as modified fish oil (Pronova Biocare, Lysaker, Norway)), or 400 µg 5-MTHF (BASF, Ludwigshafen, Germany), both, or placebo together with vitamins A, C, E, K, B1, B2, B6, B12, Folate, and Omega-3 fatty acids.

	Bayley Scales Scores at 6 months		Bayley Scales Scores at 20 months	
	MDI	PDI	MDI	PDI
FO				
5-MTHF				
FO+5-MTHF				
Placebo				
p-value				
Effect size:				
Cohen-d (C.I.)				
Combined groups	Bayley Scales Scores at 6 months		Bayley Scales Scores at 20 months	
	MDI	PDI	MDI	PDI
p-value				
Effect size:				
Cohen-d (C.I.)				

Table 3:

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	FO supplemented	No FO	p-value
Pregnancy week 20			
Pregnancy week 30			<0.001
			<0.001
			<0.001
At delivery			<0.001
			0.04
			<0.001
			<0.001
Cord blood			0.02
			0.02
			0.003

standard deviation

Table 5:

	Supplementation group			p-value
	FO	5-MTHF	Placebo	

arachidonic acid

Table 6:

arach0052004600520 102 -1227004fCID 155 >>BDC 7b5F74600520056000003-2 1 TfC00000B005A057000000w 0d2B0024>549-000000B00150015001D6 7b5F7460052

Exploratory outcomes: Comparison of BSID scores at 6 and 20 months as a function of LC-PUFAs and folate levels in mothers and neonates at delivery

Although no significant differences in BSID scores at 6 and 20 months were observed among the four/two supplementation groups, PDI scores at 20 months were higher in infants whose mothers had plasma phospholipid DHA concentrations above the median (11.51 mg/dL) at delivery (>P50): 122.80 (9.20) vs. 126.20 (12.50) (P<0.045), and n6/n3 ratio median values (<P50): 127.40 (10.90) vs. 122.0 (11.10) (P<0.045) (Table 7). Mothers with DHA concentrations in plasma phospholipids above the P50, had an average of DHA intake higher than 44, 20 g/daily, and represented the 39.3% of the whole group of the Spanish pregnant women studied.

Furthermore, infants whose mothers had a higher concentrations of DHA in plasma phospholipids at delivery, showed a significant improvements in the standard deviations obtained in the Bayley PDI from 6 to 20 months, which resulted in one or two standard deviations

Findings of the current study of no effect of prenatal FO and/or folic acid supplementation on neurodevelopment outcome assessed by Bayley scores at the age of 6 and 20 months does not preclude a beneficial or non-beneficial effect of prenatally acquired FO and/or folic acid on neurodevelopment outcome at a later age. In fact, longer follow-up studies of FO supplementation during pregnancy do provide positive influence of the supplementation on child's neurodevelopment later in life [14,19,22]. Our study results are in line with previous studies. Tofail et al. demonstrated that FO or soy oil supplementation during the last trimester of pregnancy on psychomotor and mental development of infants at 10 months of age resulted no significant group differences with respect to infant Bayley's MDfapr (de)->>BDC P .224 h (c)-7 EIMCB1hS @au M (c)-16 .0043 (es a (n)8 (s)5 (t)-4.9 (ra)19 2)9

