Plasma Fatty Acid Profiles in 37 Pairs of Maternal and Umbilical Cord Blood Samples

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Abstract

Objectives and Methods: In order to study the fatty acid transfer from the mother to fetus, their fatty acid profiles were compared by 37 pairs of maternal and umbilical cord plasma specimens obtained from healthy Japanese women at delivery.

Results: The fetal/maternal fatty acid concentration ratios differed among individual fatty acids. The ratios were low for linoleic acid (LN, 0.12 ± 0.04) and linolenic acid (LnN, 0.07 ± 0.05) but high for arachidonic acid (AA, 0.66 ± 0.17) and docosahexaenoic acid (DHA, 0.44 ± 0.13). Significant correlations were observed between the maternal and fetal EPA ($r=0.74$) and DHA ($r=0.40$) concentrations.

Conclusions: These results suggest that DHA and AA are preferentially transferred to the fetus. Fetal fatty acid profile reflects the maternal intake of EPA and DHA.

Key words: docosahexaenoic acid, arachidonic acid, mother, fetus, plasma fatty acid profile

Introduction

The human body cannot synthesize n-3 and n-6 fatty acids from the n-methyl terminus. Therefore, n-3 and n-6 fatty acids must cross the placenta to control the supply of fatty acids to the fetus during gestation. In recent decades, more attention has been focused not only on essential fatty acids such as linoleic acid (LN, 18:2n-6) and linolenic acid (LnN, 18:n-3) but also on their longer chains of polyunsaturated fatty acid (PUFA) such as arachidonic acid (AA, 20:4n-6), eicosapentaenoic acid (EPA, 20:5n-3) and docosahexaenoic acid (DHA, 22:6n-3), for normal brain development and function (1–4). Rapid brain growth occurs primarily during the third trimester in humans (5), and the brain at this period is known to be at highest risk to toxic pollutants. On the other hand, the amount of DHA and AA in the brain also increases dramatically during this period (6). We wanted to investigate the fatty acids, which may act against some of the pollutants to promote the normal growth and function of the developing brain. The placenta forms a selective filter that allows nutrients to pass through to the fetus (7, 8).

Therefore, we thought that the fatty acids which were essential for brain growth must be preferentially transferred to the fetus through the placenta. The aim of this study was to determine whether fetal/maternal ratios were different among individual n-3 and n-6 fatty acids. Moreover, the contributions of concentrations of maternal fish-originated fatty acids such as EPA and DHA to the fetus were examined. The fatty acid transfer was studied by comparing the maternal-fetal plasma fatty acid concentrations of 37 pairs living in the northern part of Japan's southern islands of Kyushu.

Materials and Methods

Thirty-seven healthy pregnant Japanese women, ranging in age from 22 to 41 yr (average 30.2 ± 4.2), planning to deliver in Munakata Suikokai General Hospital, Munakata City, in Fukuoka, Japan, gave informed consent to take part in the present trial. Venous blood samples were collected from 37 pairs of mothers and umbilical cords. The samples included 13 ml of venous umbilical cord blood at birth and 10 ml of venous maternal blood 1 day after parturition before breakfast. All blood was sampled by venipuncture with a small amount of heparin-Na and centrifuged at 3000 rpm for 10 min for separation into red blood cells (RBCs) and plasma. Samples were stored at -80°C until analysis. This study was approved by the Ethics Committee of the National Institute for Minamata Disease (NIMD).

Laboratory tests for fatty acid concentration were performed by SRL Inc. (Tokyo, Japan). Total lipids were extracted from

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Table 1 Comparison of plasma fatty acid concentrations for mother and fetus at birth

Fatty acid		Mother		Fetus		Correlation coefficients
		μg/ml	(%)	μg/ml	(%)	
Palmitic	(C16:0)	1133 (278)	29.1	296 (64)	29.9	0.041
Palmitoleic	(C16:1n-7)	117 (44)	3.0	36 (10)	3.7	0.064
Stearic	(C18:0)	199 (39)	5.1	106 (22)	0.7	0.087
Oleic	(C18:1n-9)	924 (204)	23.8	192 (47)	19.4	-0.000
ΣSFA+MUFA		2373 (534)	61.5	631 (138)	64.7	
Linoleic	(C18:2n-6)	1032 (188)	27.0	122 (36)	12.9	0.181
Linolenic	(C18:3n-3)	31 (10)	0.8	2.1 (1.4)	0.2	0.219
Dihomo γ-linoleic	(C20:3n-6)	58 (19)	1.5	35 (7.8)	3.6	0.283
Arachidonic	(C20:4n-6)	183 (40)	4.7	117 (27)	12.0	0.252
Eicosapentaenoic	(C20:5n-3)	36 (22)	0.9	7.0 (3.7)	0.7	0.743**
Docosahexaenoic	(C22:6n-3)	146 (38)	3.8	62 (19)	6.3	0.395*

SFA=saturated fatty acid, MUFA=Mono-unsaturated fatty acid.

Values are means (SD).

The association between maternal and fetal fatty acids were studied by correlation analysis. ** $p < 0.01$ and * $p < 0.05$.

the samples according to the method of Folch et al. (9). The total lipid was saponified with 5% KOH-methanol. Five M HCl was then added to the saponified fatty acid to obtain free fatty acids, and eicosatrienoic acid (23:0) was added as an internal standard. Free fatty acids were extracted with chloroform, and methylated with 0.4 M potassium methoxide-methanol solution and 14 wt% boron tri-fluoride-methanol. Fatty acid-methyl esters were separated by capillary gas chromatography (GC17A, Shimadzu Co., Japan) and identified by comparison with standards (Sigma Chemical Co., Poole, UK). Fatty acid compositions were expressed as a concentration (μg/ml plasma) and percentage by weight of total fatty acids.

The associations between maternal and fetal fatty acid concentrations were studied by correlation analysis. Fetal/mother plasma fatty acid concentration ratios for the n-3 and n-6 series against the sum of saturated and mono-unsaturated fatty acids as a reference value were analyzed by a one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison test.

Results and Discussion

All the fatty acid concentrations presented were lower in the fetal plasma than in that of their mothers (Table 1). However, the difference in the composition percentage of the individual fatty acids for mothers and fetuses suggested some difference in the transfer selectivity of the fatty acids. For example, the composition percentages of DHA (3.8% for mothers and 6.6% for fetuses) and AA (4.8% for mothers and 12.4% for fetuses) were higher in the fetuses than in the mothers. The differences in fetal/maternal fatty ratios among the n-3 and n-6 fatty acid concentration ratios were further calculated and shown in the Figure. The fetal/maternal ratio of saturated and mono-unsaturated fatty acid concentrations was 0.26. The ratios of n-3 and n-6 fatty acid concentrations were compared with the sum of saturated and mono-unsaturated fatty acids assumed as a reference value. The ratios for LN (0.12 ± 0.04) and LnN (0.07 ± 0.05) were significantly lower than the value for the sum of saturated and mono-unsaturated fatty acids, whereas those for AA (0.66 ± 0.17), DHA (0.44 ± 0.13), and dihomogamma-linoleic acid

Fig. 1 Fetal/mother plasma fatty acid concentration ratios for n-3 and n-6 series against the sum of saturated and mono-unsaturated fatty acids as a reference value.

Footnotes: Data represent the mean and SD for 37 fetus and mother pairs. Data from this study were analyzed by a one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison test. * $p < 0.01$, significantly different compared with the sum of saturated and mono-unsaturated fatty acids assumed as a reference value.

(DGLA, 0.66 ± 0.17) were significantly higher than the reference values. There were significant correlations in EPA ($r = 0.74$) and DHA ($r = 0.40$) between maternal and fetal concentrations.

The fetal/maternal fatty acid concentration ratios indicated that not all n-3 and n-6 fatty acids were preferentially transferred to the fetus, but DHA, AA and DGLA were (Fig. 1). Interestingly, DHA and AA are abundant in the brain (1–4) and the DGLA concentration is higher than those of LN, EPA and LnN (1). During rapid brain growth, large amounts of AA and DHA from the maternal circulation must reach the fetus or infant to meet its needs for development through the placenta or breast milk, respectively (1, 2, 6, 10). The rapid quantitative accretion of both DHA and AA during the third trimester of pregnancy has been noticed in the human brain (4, 6). Campbell et al. (11) have suggested that preferential incorporation of DHA into triacylglycerols may play an important role in the placental transport of DHA to the fetal circulation. The present study also demonstrated that the fetal/maternal fatty acid

concentration ratios of DHA, AA and DGLA, which are important fatty acids for the brain and its growth, were high at the end of gestation.

The primary sources of DHA and EPA are fish and fish oil, and intake of these fatty acids is reflected in both the maternal and fetal plasma fatty acid composition (12). The present study also demonstrated that the DHA and EPA in the maternal circulation were correlated with those in the fetus, suggesting that the fetal fatty acid profile reflects the maternal intake of these fatty acids.

In conclusion, the fetal/maternal ratios were relatively high not in all the n-3 and n-6 fatty acids but in specific fatty acids such as DHA and AA. Further, the DHA and EPA in the fetal circulation reflected those in the maternal circulation.

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References

- (1) Farquharson J, Cockburn F, Patrick WA, Jamieson EC, Logan RW. Infant cerebral cortex phospholipid fatty-acid composition and diet. *Lancet* 1992; 340: 810–813.
- (2) Yavin E, Glozman S, Green P. Docosahexaenoic acid sources for the developing brain during intrauterine life. *Nutr Health* 2001; 15: 219–224.
- (3) Makrides M, Neumann M, Simmer K, Pater J, Gibson R. Are long-chain polyunsaturated fatty acids essential nutrients in infancy? *Lancet* 1995; 345: 1463–1468.
- (4) Clandinin MT, Chappell JE, Leong S, Heim T, Swyer PR, Chance GW. Intrauterine fatty acid accretion rates in human brain: implications for fatty acid requirements. *Early Hum. Dev.* 1980; 4: 121–129.
- (5) Dobbing J, Sands J. Comparative aspects of the brain spurts, *Early Hum. Dev.* 1979; 3: 79–83.
- (6) Carlson SE. Docosahexaenoic acid and arachidonic acid in infant development, *Semin. Neonatol.* 2001; 6: 437–449.
- (7) Haggarty P. Placental regulation of fatty acid delivery and its effect on fetal growth—a review, *Placenta* 2002; 23: Suppl. A: 28–38.
- (8) Valenzuela A, Nieto MS. Docosahexaenoic acid (DHA) in fetal development and in infant nutrition, *Rev. Med. Chil.* 2001; 129: 1203–1211.
- (9) Folch J, Lees M, Sloane-Stanley G.H., A simple method for the isolation and purification of total lipids from animal tissues, *J. Biol. Chem.* 1957; 226: 497–509.
- (10) Martinez M. Dietary polyunsaturated fatty acids in relation to neural development in human, in: Galli C, Simopoulos AP (Ed.), *Dietary ω3 and ω6 Fatty Acids. Biological Effects and Nutritional Essentiality*. New York: Plenum Press, 1989; 123–133.
- (11) Campbell FM, Clohessy AM, Gordon MJ, Page KR, Dutta-Roy AK. Uptake of long chain fatty acids by human placental choriocarcinoma (BeWo) cells: role of plasma membrane fatty acid-binding protein, *J. Lipid Res.* 1997; 38: 2558–2568.
- (12) De Vriese SR, Matthys C, De Henauw S, De Backer G, Dhont M, Christophe AB. Maternal and umbilical fatty acid status in relation to maternal diet, *Prostaglandins Leukot. Essent. Fatty Acids* 2002; 67: 389–396.