ORIGINAL ARTICLE

Comparative Long-chain Polyunsaturated Fatty Acids Levels in Blood, Placenta and Cord Blood of Pregnant Women with or without Pre-eclampsia

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ABSTRACT

Background and Objective: Long-chain polyunsaturated fatty acids (LCPUFA) play an important role in the regulation of fat metabolism in the placenta and fetus. Changes in placental function in pre-eclampsia affect the transport of fatty acids and affect fetal nutrition. The aim of the study was to compare LCPUFA levels in blood, placenta and cord blood of pregnant women with or without pre-eclampsia.

Methods: The blood, placenta and umbilical cord blood of pregnant women (n = 30 each) who were normotensive and with pre-eclampsia were collected. The levels of fatty acids in maternal blood, placenta and umbilical cord blood were determined by the quartz capillary gas chromatography technique.

Results: The average age of normal pregnant women was 27.0 ± 4.5 years and that of pre-eclampsia pregnant women was 30 ± 4.0 years (P > 0.05). The levels of total fatty acids, arachidonic acid (AA) and docosahexaenoic acid (DHA) were higher in pregnant women with pre-eclampsia than in normal women. The level of linoleic acid in cord blood and placenta was significantly higher in pre-eclampsia group than in the normal pregnant women while linoleic acid content in maternal blood being lower in pre-eclampsia group compared to the normal maternal group.

Conclusion: The changes of LCPUFA in blood, placenta and umbilical blood of pre-eclampsia may be related to the changes of LCPUFA in placenta. These changes may be involved in the pathophysiological process of pre-eclampsia. Maternal supplement of LCPUFA, such as DHA, in early gestation may be helpful in improving morbidity associated with maternal eclampsia.

KEYWORDS: Long chain polyunsaturated fatty acids, Maternal blood, Cord blood, Placenta, Pre-eclampsia.

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INTRODUCTION

Fat is very important to human nutrition. The fatty acids can be divided into saturated and unsaturated fatty acids according to their structure. Unsaturated fatty acids can be further divided into monounsaturated and polyunsaturated fatty acids (polyunsaturated fatty acids, PUFA). PUFA is a bioactive fatty acid, as an important component of

the cell membrane phospholipids, a direct impact on cell membrane function, affecting membrane fluidity and permeability.[1] Long chain polyunsaturated fatty acids (LUPUFA) precursors, linoleic acid and linolenic acid cannot be synthesized in the human body, must be obtained from food. The fetus gains nutrition from the mother through the placenta. The fatty acids that the fetus gains from the mother are affected by the mother's diet and the placenta plays a very important role in the transportation from mother to fetus.[2,3]

LUPUFA plays a potentially important regulatory role for the placenta and fetal lipid environment. Arachidonic acid (AA) may up-regulate the inflammatory response while and docosahexaenoic acid (DHA) down-regulate the inflammatory response.[4] LCPUFA intake change the maternal and placental environment during pregnancy. Also, LCPUFA can improve the oxidative stress by resolving inflammation through increased placental levels of resolvins and protectins.[4]

By analyzing the fatty acid composition of the fetus in vivo, placenta and fetus, the effect of pregnancy induced hypertension on nutritional metabolism of fetal fatty acids can be determined. It may help to find out the potential role of fatty acid metabolism in the pathogenesis of pregnancy induced hypertension that later improve the outcome of pregnancy-induced hypertension.

METHODS

The study was approved by the Medical Ethics Committee of Xinhua Hospital aaffiliated with Shanghai Medical University, China. Pregnant women hospitalized in Xinhua Hospital were divided into normotensive group and pre-eclampsia group. There was n = 30 women in both groups. For normal pregnancy group, women without any complications and any other underlying diseases, full-term newborns with suitable gestational age, having birth weight > 2500g, Apgar scores > 7 points without asphyxia history and singleton pregnancies were included. While pregnancies with complications and infants born with congenital malformations and other diseases were excluded.

Pregnant women without prior history of hypertension and other underlying diseases, hypertension after 20 weeks of pregnancy, proteinuria or terminal organ dysfunction, in addition to high blood pressure were included in pre-eclampsia group. Pregnant women with complications and infants with limb deformities at birth and any other congenital hereditary disease were excluded. Blood samples and placental tissue were taken after informed written consent from mothers.

Venous blood samples of 3 mL were taken from the mother and cord-blood and kept at 4°C for analysis. Tissue from different cotyledons of placenta was taken immediately after maternal delivery and reserved in frozen liquid nitrogen. Blood was centrifuged at the speed of 1500 × g at room temperature for 5 minutes to separate the plasma. Placental tissue was homogenized to get 0.1 ~ 0.5 g tissue for fatty acid extraction.

Fatty acids were extracted by the process of one-step direct esterification by using Japan's Shimadzu company quartz capillary GC-2010 gas chromatograph. The column in chromatograph is 60 m × 0.32 mm, coated with 0.2 m silica; chromatograph injection chamber and the temperature of detection chamber was 250° and 280°. Temperature program method was used for blood and placenta for various fatty acid components. First the absolute content of each fatty acid was determined, then calculated the percentage of total fatty acids.

STATISTICAL ANALYSIS

The data was entered and analyzed using IBM SPSS (Statistical Package for Social Sciences version 16.0). Mean ± standard deviation was determined for quantitative variables while independent samples T test were applied for comparative analysis. P-value < 0.05 for the difference was considered as statistically significant.

RESULTS

The mean age of normal pregnant women was 27.0 ± 4.5 years and that of pre-eclampsia women was 30 ± 4.0 years old (P > 0.05). The birth weights of infants from normal pregnant women and pre-eclampsia women were 3320 ± 127g and 2830 ± 947g (P < 0.05) with gestational age of 38.0 ± 2.0 weeks and 37.0 ± 2.0 weeks (P < 0.05) respectively.

This study measured maternal blood, umbilical cord blood and placenta fatty acids, including saturated, monounsaturated and polyunsaturated fatty acids. Maternal blood total fatty acid content was significantly higher than neonatal cord blood of the total fatty acid content, about five times the total fatty cid content in cord blood ($p < 0.05$) (Table-1).

Table-1: Maternal blood and cord blood total fatty acid content comparison.

	Maternal Blood	*Cord Blood*	*t*	*P*
Normal group	3.56 ± 0.60	0.73 ± 0.19	22.216	**0.000**
Pregnancy-induced hypertension group	4.56 ± 1.99	0.73 ± 0.23	7.911	**0.000**

The levels of total fatty acids, arachidonic acid (AA) and docosahexaenoic acid (DHA) were higher in pregnant women with pre-eclampsia than in normal women (4.56 ± 1.99 g/L and 3.56 ± 0.60 g/L; 0.12 ± 0.02 g/L and 0.09 ± 0.02 g/L; 0.14 ± 0.05 g/L and 0.10 ± 0.05 g/L), with AA and DHA $P < 0.05$ (Table 1-2). The content of linoleic acid in maternal blood was lower in pre-eclampsia group than in normal maternal group (30.18 ± 5.08% and 35.46 ± 3.04%, respectively) ($P < 0.05$) (Table-2).

Table-2: Comparison of fatty acids in maternal blood.

Fatty Acid	*Pre-eclampsia*	*Normal Pregnancy*	*t*	*P*
LA	30.18 ± 5.08	35.46 ± 3.04	3.846	**0.001**
ALA	0.58 ± 0.14	0.58 ± 0.19	0.069	0.945
EPA	0.13 ± 0.09	0.11 ± 0.01	0.834	0.409
AA	0.12 ± 0.05	0.09 ± 0.02	2.259	**0.036**
AA%	2.67 ± 0.41	2.62 ± 0.36	0.386	0.702
DHA	0.14 ± 0.05	0.10 ± 0.02	3.301	**0.004**
DHA%	3.19 ± 0.81	2.81 ± 0.53	1.695	0.102
AA/DHA	0.87 ± 0.20	0.87 ± 0.28	0.868	0.391
Total fatty acids	4.56 ± 1.99	3.56 ± 0,60	2.012	0.059

The ratio of AA/DHA in placenta was higher in pre-eclampsia than in normal women (1.86 ± 0.38 and 1.64 ± 0.27, respectively, $P < 0.05$). The content of linolenic acid (18: 2n3) in the placenta increased significantly in pre-eclampsia group (0.07 ± 0.03%) (Table-3).

Table-3: Comparison of fatty acids in the placenta.

Fatty Acid	*Pre-eclampsia*	*Normal Pregnancy*	*t*	*P*
LA	13.06 ± 1.73	13.90 ± 2.18	1.492	0.142
ALA	0.07 ± 0.03	0.06 ± 0.01	2.517	**0.016**
EPA	0.10 ± 0.03	0.11 ± 0.03	0.513	0.610
AA	14.33 ± 1.59	13.55 ± 1.48	1.752	0.086
DHA	7.96 ± 1.41	8.40 ± 1.27	1.132	0.263
AA/DHA	1.86 ± 0.38	1.64 ± 0.27	2.181	0.034

The content of linoleic acid (18: 2n6) in cord blood of pre-eclampsia group was significantly higher than that in normal maternal group (17.10 ± 4.45% and 14.20 ± 1.92% respectively) ($P < 0.05$) (Table-4).

Table-4: Cord blood fatty acid composition comparison.

Fatty Acid	*Pre-eclampsia*	*Normal Pregnancy*	*t*	*P*
LA	17.10 ± 4.45	14.20 ± 1.92	2.755	0.010
EPA	0.30 ± 0.54	0.21 ± 0.07	0.794	0.432
AA%	8.10 ± 2.82	8.23 ± 1.07	0.198	0.845
DHA	6.08 ± 1.54	6.10 ± 1.56	0.028	0.978
AA/DHA	1.33 ± 0.35	1.42 ± 0.32	0.868	0.391
Total fatty acids	0.73 ± 0.18	0.73 ± 0.23	0.069	0.946
AA/DHA	0.87 ± 0.20	0.87 ± 0.28	0.868	0.391
Total fatty acids	4.56 ± 1.99	3.56 ± 0,60	2.012	0.059

DISCUSSION

Fat nutrition plays an important role in the growth and development of the fetus, and the storage of fat in the fetus reaches 90% of the total energy storage when the fetus is born in full term. Ninety percent of the fetus's body fat increases exponentially in the last 10 weeks of pregnancy, as much as 7 grams of fat per day in the fetus as it reaches full-term.[5] Most of the fetus body fat comes from the mother, partially synthesized by the fetus themselves. The fatty acids supplied to the fetus are mainly determined by the fatty acids in the mother's body. The placenta is the main channel for maternal and fetal nutrition transport. The placenta itself has the synthetic function. The placenta lacks the desaturase and carbon chain elongase related to fatty acid synthesis.[6] So fetal long-chain polyunsaturated fatty acids are mainly obtained through the placenta from mother. During pregnancy-induced hypertension, fatty acid-related placental translocation enzyme expression decreases that disturbs the fetal growth and

development because of lack of acquisition of important fetal fatty acids.[7] The current study determined the effect of pregnancy-induced hypertension on maternal and fetal fatty acid nutrition from the levels of fatty acids in the maternal blood, placenta, and in the fetus (umbilical cord blood). A significant difference in fatty acid content has been found in pregnancy-induced hypertension and normal pregnant women which is consistent with other study.[8] In pregnancy-induced hypertension (pre-eclampsia) group accumulation of fat in fetal body occurs earlier as there is accelerated transfer to the fetus, while in the normal pregnancy fat accumulation in fetus is late because of the decreased maternal blood fatty acid content. The present study reported the increased AA/DHA value in pregnancy-induced hypertension group. DHA or eicosapentaenoic acid (EPA) put anti-oxidative stress and down-regulate the inflammatory reaction, while AA up-regulate the inflammatory response.[4]

This study observed slightly higher levels of AA, DHA in cord blood in normal pregnancy group but no statistical difference. The mothers in the hypertensive pregnancy group showed high levels of AA, DHA but the difference was not statistically significant thus indicating DHA and AA as an important fatty acid in the fetus, with a decline trend in high-risk cases, which is consistent with other studies.[7,9]

It has been found that fatty acid from mother to fetus pass through the placenta that consists trophoblasts called, syncytiotrophoblasts (SCTB), with two polarized membranes. The microvillous membrane facing maternal circulation and basal plasma membrane containing placental fatty acid-binding protein (FABP) and fatty acid transporter protein (FATP), involved in fatty acid transport.[10] The placental plasma membrane fatty acid-binding protein (P-FABP), is a placental-specific protein present on the placental microvilli.[10] It preferentially binds to some important LCPUFA such as AA and DHA, because of higher affinity for them than LA and other fatty acids.[12,13] Decreased fatty acid transport proteins (FATP1 and FATP4) has been reported in pre-eclampsia.[7] LCPUFA enzyme mRNA levels in pre-eclampsia are low than normal that may affect fetal brain and retina development and later learning ability.[11,14-16]

The last three months of the fetus in the mother's body and the first two years after birth are the most rapid periods of human brain development with a large accumulation of LCPUFA in brain and retinal tissues. Thereby, it is important to supplement these LCPUFA during pregnancy and neonatal period. In addition, placental fatty acid composition changes in pre-eclampsia pregnant women, representing the cause of eclampsia or the outcome of eclampsia. LCPUFA supplementation, especially DHA, may improve the pregnancy outcome of preeclamptic pregnant women which may be related to the high sensitivity of DHA to lipid peroxidation.[17] However, pregnant women should take a certain amount of DHA during pregnancy to ensure normal pregnancy. Consensus guidelines have recommended the pregnant women to take at least 200 mg of DHA per day to optimize pregnancy outcomes and fetal health.[18]

CONCLUSION

The changes of LCPUFA in blood, placenta and umbilical blood of pre-eclampsia may be involved in the pathophysiological process ofhypertension. Therefore, maternal supplement of LCPUFA, such as DHA, in early gestation may be helpful in improving maternal eclampsia.

LIMITATIONS OF THE STUDY

This study did not address other confounding factors like weight, smoking and dietary factors. Further studies are required to be conducted on a larger sample size in order to strengthen the conclusions and further determine the potential link between long-chain polyunsaturated fatty acids and maternal hypertension.

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CONFLICT OF INTEREST

None to declare.

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None to disclose.

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Author's Contribution

The author takes full responsibility of drafting and aapproval of the final version of the manuscript to be published, according to ICMJE guidelines.