Fatty Acid Requirements in Preterm Infants and Their Role in Health and Disease

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KEYWORDS

• Long-chain polyunsaturated fatty acids • Docosahexaenoic acid • Arachidonic acid • Eicosapentaenoic acid • Linoleic acid • Lipid emulsions

KEY POINTS

- There is selective uptake and transfer of free long-chain polyunsaturated fatty acids (LCPUFAs) from the maternal circulation to the developing fetus.
- LCPUFAs are critical for many biological processes, principally organogenesis (especially of the brain and retina) and regulating inflammation.
- Current nutritional practices are unable to meet the intrauterine fetal accretion rates of LCPUFAs in the early postnatal period for preterm infants.
- Inadequate postnatal delivery of LCPUFAs results in early, rapid deficits in critical fatty acids, notably docosahexaenoic acid and arachidonic acid.
- Altered postnatal LCPUFA levels and n-6/n-3 fatty acid ratios in the preterm infant are associated with chronic lung disease and late-onset sepsis.
- Current scientific literature, including both animal and human data, support the role of LCPUFA supplementation in preventing disease and optimizing health in the preterm infant.
- The optimal strategy to delivery LCPUFAs to preterm infants to emulate recommended fetal accretion rates, maintain birth levels of fatty acids and their relative ratios, prevent early deficits in fatty acid levels, and achieve clinical benefit without potential harm remains to be defined.

INTRODUCTION

Enhancing somatic growth through our knowledge of macronutrient requirements (carbohydrates, proteins, and fats) is only one aspect of fully extracting the potential of nutrition to optimize health in preterm infants. The composition and balance of

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Clin Perinatol 41 (2014) 363–382
http://dx.doi.org/10.1016/j.clp.2014.02.007 **perinatology.theclinics.com**
0095-5108/14/$ – see front matter

the individual building blocks within the macronutrients (sugars, amino acids, and fatty acids) are equally essential to understand. These building blocks often serve as bioactive molecules regulating many biological processes, such as organ development, metabolic homeostasis, and immune responsiveness.

Provision of fats is part of a balanced nutritional diet that delivers high-energy content, enhances gluconeogenesis, and prevents essential fatty acid deficiency. A large percentage of dietary fats are in the forms of triglycerides: 3 fatty acids on a glycerol backbone. Enzymatic hydrolysis releases the fatty acids from the glycerol backbone, allowing for trafficking and incorporation of the fatty acids into cell membranes, their primary site of action.

There is an extensive and evolving scientific literature showing the pleiotropic effects of fatty acids in health and disease. However, this literature is considerably more expansive for the adult than for the neonate. Despite this situation, strong evidence exists to support the beneficial role of fatty acids in neonatal health, especially in the preterm infant, and the need for ongoing efforts to further understand their mechanisms of action and to identify best nutritional or therapeutic strategies for delivery.

PLACENTAL TRANSFER AND FETAL ACQUISITION OF LONG-CHAIN POLYUNSATURATED FATTY ACIDS

Placental Transfer of Long-Chain Polyunsaturated Fatty Acids

Long-chain polyunsaturated fatty acids (LCPUFAs) are critical for the development of the fetal brain and retina. The importance of fetal acquisition of these critical fatty acids is highlighted by the presence of specific mechanisms allowing for maternal and placental transfer of fatty acids to the developing fetus. Although placental mechanisms for transfer are necessary, the synthesis of LCPUFAs in the placenta is limited, as it is in the developing fetus; thus, the maternal circulation is still considered the major source of LCPUFAs.[1–3]

Two major pathways have been proposed to facilitate the transfer of fatty acids from the maternal circulation, across the placenta, to the developing fetus: passive diffusion and protein-mediated transport (**Fig. 1**).[1,4,5] Maternal lipoproteins, triglycerides and phospholipids, are converted by placental lipoprotein lipase and endothelial lipase to form nonesterified or free fatty acids. Maternally derived free fatty acids are then transported into the placenta by passive diffusion or via protein-mediated transport. Transport proteins essential for the latter pathway include fatty acid transport proteins (FATP) 1– 6, of which FATP-4 seems to be of particular significance, because expression of this protein is directly correlated with docosahexaenoic acid (DHA) content in cord blood phospholipids,[6] placental plasma membrane fatty acid binding protein, and fatty acid translocase/CD36 (FAT/CD36). Once in the placenta, additional fatty acid binding proteins carry the fatty acid to the fetal interface, where FATP and FAT/CD36 deliver the free fatty acid to the fetal circulation.

Unique to this environment is the selective update and accumulation of LCPUFAs in the placenta and the fetal circulation, a phenomenon termed biomagnification. Labeled carbon studies tracking the transfer of fatty acids from the maternal to fetal circulation have shown higher DHA (22:6 n-3) content in cord blood versus maternal plasma, again emphasizing the unique role of the placenta in selectively transferring sufficient quantities of LCPUFAs to support the needs of the developing fetus (**Fig. 2**).[2,7]

Fetal Acquisition of LCPUFAs

The delivery of LCPUFAs substantially increases during the third trimester, coinciding with continued organ development and rapid fetal growth. Fetal accretion is targeted