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ORIGINAL COMMUNICATION

Role of long-chain polyunsaturated fatty acids in infant nutrition

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Objective: To review briefly the influence of dietary long-chain polyunsaturated fatty acids (LC-PUFA) on tissue composition and functionality in early infancy. Moreover, the influences of LC-PUFA sources on plasma composition as well as the effects of these fatty acids on intestinal repair after malnutrition are discussed.
Results: Human milk not only supplies essential fatty acids but also contains up to 2% of the total fatty acids as LC-PUFA, of which arachidonic acid (AA) and docosahexaenoic acid (DHA) are considered the most important. Plasma and erythrocyte levels of both AA and DHA are decreased in infants fed artificial standard milk formulae. However, the supplementation of formulae with these fatty acids in amounts close to that of human milk leads to tissue LC-PUFA patterns similar to those of breast-fed infants. However, the bioavailability of LC-PUFA depends on the typical LC-PUFA source; egg phospholipids increases both AA and DHA in plasma phospholipids and HDL more than a mixture of tuna and fungal triglycerides.
Conclusions: Dietary LC-PUFA affects positively the growth and development of the infant and ameliorates the visual and cognitive functions, particularly in preterm infants. Likewise, LC-PUFA improves intestinal repair in severe protein-energy malnutrition; therefore, its qualitative and quantitative dietary supply should be considered.
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Introduction

The n-6 and n-3 series of long-chain polyunsaturated fatty acids (LC-PUFA) have an important role during gestation, lactation and infancy since they are constituents of cell membrane phospholipids and precursors of eicosanoids. LC-PUFA are biosynthesised from essential fatty acids (EFA) (linoleic acid, LA, 18: 2n-6, and linolenic acid, LNA, 18:3 n-3) by successive desaturation and elongation steps in the intestine, liver and brain. Both, arachidonic acid (AA, 20:4 n-6) and docosahexaenoic acid (DHA, 22:6 n-3), are found in neural structures and particularly DHA is a component of neurone membranes and external segments of fotoreceptors in the retina (Neuringer *et al*, 2000).

During the last two decades, there has been much attention to ascertain the requirements of LC-PUFA in early life. The ability of human foetus to synthesise LC-PUFA from EFA has been a matter of discussion since both n-6 and n-3 levels of LC-PUFA in plasma and erythrocyte of infants fed with artificial formulas are significantly lower than those found in breast-fed infants (Heird *et al,* 1997). In addition, a number of studies in experimental animals have shown that deficiency of n-3 leads to impairment of brain and visual functions (Neuringer, 2000). Moreover, the level of DHA in the brain cortex and liver of preterm infants who died suddenly and that had been fed with artificial formulas was lower than of those fed with human milk (Farquharson *et al,* 1995). Nonetheless, recent *in vivo* studies using LA and LNA labelled with stable isotopes in at-term newborns, preterm infants and small for date infants have demonstrated that all infants are able to synthesise LC-PUFA (Demmelmair *et al,* 1995; Uauy *et al,* 2000). However, whether the amounts of AA and DHA synthesised are able to meet the daily requirements of infants, particularly in small for date

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infants, who exhibit the lowest rate of synthesis, is currently unknown.

The aim of the present study is to briefly review the importance of LC-PUFA in early life and give some experimental new data to support the role of this fatty acids in the repair of some important organs like the small intestine damaged during protein-energy malnutrition (PEM). In addition, we also focus on the differential absorption and incorporation to tissues of dietary LC-PUFA relying on different biological sources of these fatty acids.

Plasma and tissue levels of AA and DHA in infants fed human milk or formulae

Human milk contains preformed AA and DHA in levels which oscillate between 0.3–1.0 and 0.1–0.9% of the total fatty acids, respectively (Jensen, 1999). Their contents remain almost constant in very different populations regardless of their ethnic origin and food habits (Koletzko *et al,* 1992). When breast feeding is not possible, the supply of dietary LC-PUFA may be given through artificial infant milk formulae. In Europe, since the past few years, and because of the recommendations of some international organisations such as the ESPGHAN Nutrition Committee (1991) and the Commission of the EU (1996), there are a number of infant milk formulae, especially those intended for small weight birth infants, that incorporate LC-PUFA obtained and purified from different sources, namely one single-cell cyanoficeae algae, fungi, fish and eggs.

Regardless of the diet, after birth there is a decrease in the percentage of LC-PUFA in both plasma and erythrocytes of newborn infants (Pita *et al,* 1989). However, the absolute amounts of LC-PUFA in plasma are maintained fairly constant (Ramirez *et al,* 1998). Anyhow, it is well established that both at-term infants and preterm infants fed with human milk show significant higher percentages of LC-PUFA in plasma lipids and erythrocyte phospholipids than those fed a standard infant formula (Pita *et al,* 1989). The supply of LC-PUFA by human milk would account for 50% of DHA and 15% AA levels in the erythrocyte of infants (Carlson *et al,* 1993). Moreover, it should be emphasised that infants receiving a formula without LC-PUFA during the first months of life are unable to reach the plasma AA and DHA levels of those breast fed, during the second semester of life (Decsi *et al,* 2000). The supplementation of a formula with 0.35–0.40% DHA mimics the plasma and erythrocyte DHA levels of those breast fed (Carlson *et al,* 1993; Hoffman *et al,* 1993). The supplementation of DHA and AA to formulas, whose content in both fatty acids is similar to that of human milk, leads to similar patterns of LC-PUFA in plasma and erythrocyte phospholipids in breast-fed and formula-fed infants (Decsi & Koletzsko, 1995).

We have observed that the bioavailability of LC-PUFA depends on the biological source used to supplement the milk formula. In piglets, egg phospholipids are more efficient than a mixture of tuna and fungal triglycerides to elevate both AA and DHA in plasma phospholipids as well as in HDL. However, the latter mixture increases both fatty acids more than egg phospholipids in LDL (Figure 1).

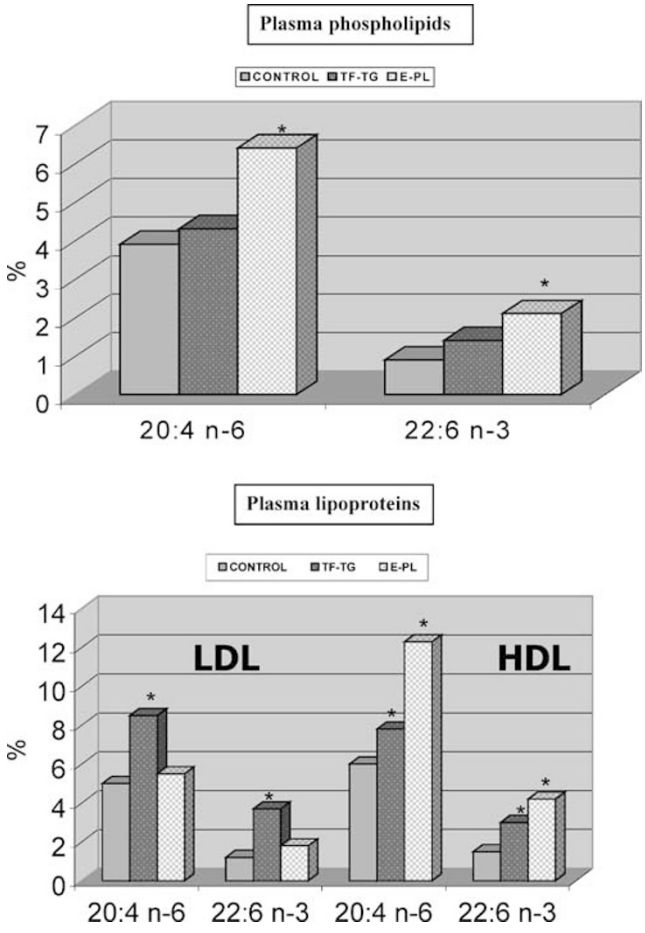

Figure 1 Percentages of arachidonic and docosahexaenoic acids in plasma phospholipids and lipoproteins (LDL and HDL) of lactating piglets fed infant formulas supplemented with long-chain polyunsaturated fatty acids from different sources (tuna and fungal oil triglycerides, TF-TG; egg phospholipids, EP) * $P<0.05$ with respect to control (Amate *et al,* 2001).

Physiological and clinical effects of LC-PUFA in infancy

LC-PUFA, particularly AA, affects positively growth and development in early infancy (Carlson *et al,* 1993). Moreover, LC-PUFA of n-3 series influences positively the neurological development of preterm infants, including mental development (Agostoni, 1997; Willatts *et al,* 1998). It is known that LC-PUFA affects perception and cognitive functions in infancy, although the potential long-term effects in childhood have not been determined. A number of studies have shown a positive effect of the early consumption of dietary LC-PUFA on the capacity of at-term and small for date infants to solve problems later in life

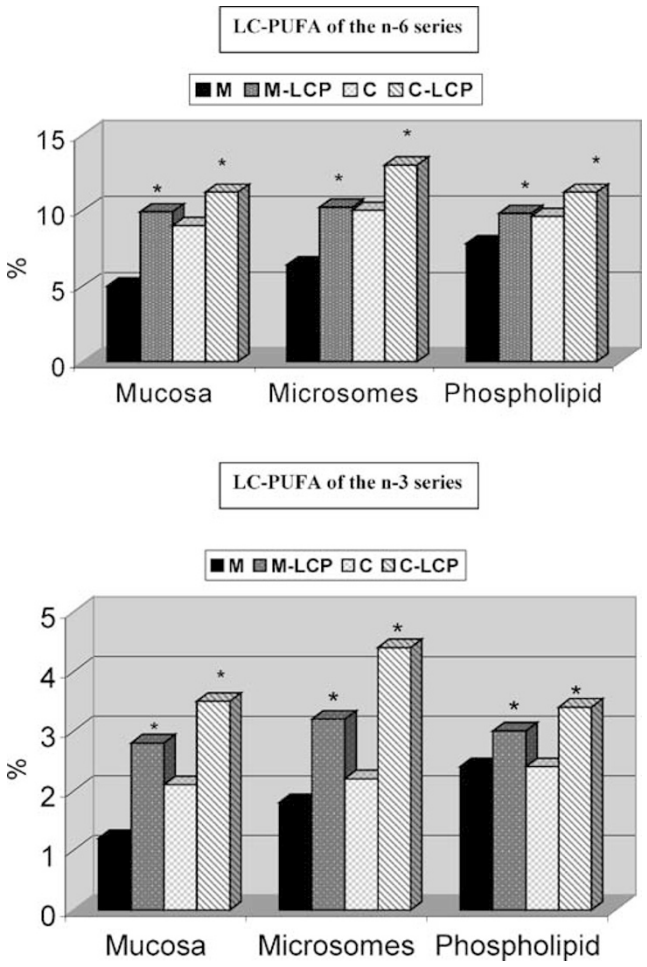

Figure 2 n-6 and n-3 long-chain polyunsaturated fatty acids (LCP) in jejunum mucosa of protein-energy malnourished piglets recovered with an LCP supplemented formula (malnourished, M; malnourished recovered with an LCP formula, M-LCP; Control, C; control fed with an LCP formula, C-LCP) * $P<0.05$ with respect to their corresponding control groups (López-Pedrosa *et al,* 1999).

(Forsyth *et al,* 1966). Likewise, some studies have documented an increased degree of psychomotor development in infants fed with LC-PUFA supplemented formulas (Birch *et al,* 2000). Visual acuity in animals and infants fed with LC-PUFA-deficient diets is lower than in those having LC-PUFA due to immaturity of their fotoreceptors (Neuringer, 2000). Visual acuity increases with the content of ALA in the diet, but DHA leads to better results (Mayer, 1997). However, it is not clear whether these differences in visual acuity remain later on in childhood.

PEM leads to severe alterations of the intestinal mucosal with associated changes in the pattern of LC-PUFA of enterocyte membranes. We have reported that dietary LC-PUFA may be important in the recovery of intestinal lesions in PEM piglets (López-Pedrosa *et al,* 1999). In Figure 2 significant higher levels of LC-PUFA in total intestinal mucosa, enterocyte microsomes and enterocyte phospholipids can be observed in PEM piglets recovered with a milk formula supplemented with LC-PUFA of the n-6 and n-3 series.

In conclusion, LC-PUFA seems to have an important role not only in the development of visual and cognitive functions in early infancy, but also in the intestinal repair after malnutrition.

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