Long-chain polyunsaturated fatty acid requirements during pregnancy and lactation

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ABSTRACT Much interest has been expressed about the long-chain polyunsaturated fatty acid (LCPUFA) requirements of both preterm and term infants, whereas relatively little attention has been given to the LCPUFA needs of mothers, who may provide the primary source of LCPUFAs for their fetuses and breast-fed infants. Although maternal requirements for LCPUFAs are difficult to estimate because of large body stores and the capacity to synthesize LCPUFAs from precursors, biochemical and clinical intervention studies have provided some clues. From a biochemical viewpoint, there appears to be no detectable reduction in plasma n–3 LCPUFA concentrations during pregnancy, whereas there is a clear decline during the early postpartum period. The postpartum decrease in maternal plasma docosahexaenoic acid (DHA) concentration is not instantaneous, may be long-term, is independent of lactation, and is reversible with dietary DHA supplementation (200–400 mg/d). From a functional standpoint, the results of randomized and is reversible with dietary DHA supplementation (200–400 mg/d). From a functional standpoint, the results of randomized clinical studies suggest that n–3 LCPUFA supplementation during pregnancy does not affect the incidences of pregnancy-induced hypertension and preeclampsia without edema. However, n–3 LCPUFA supplementation may cause modest increases in the duration of gestation, birth weight, or both. To date, there is little evidence of harm as a result of n–3 LCPUFA supplementation during either pregnancy or lactation. However, researchers need to further elucidate any potential benefits of supplementation for mothers and infants. Careful attention should be paid to study design, measurement of appropriate health outcomes, and defining minimum and maximum plasma n–3 LCPUFA concentrations that are optimal for both mothers and infants. Am J Clin Nutr 2000;71(suppl):307S–11S.

KEY WORDS Docosahexaenoic acid (DHA), n–3 long-chain polyunsaturated fatty acids, n–3 LCPUFA, pregnancy, lactation, breast-feeding, breast-fed infants, preterm infants, term infants, fatty acid requirements, fatty acid supplements, n–3 LCPUFA supplementation

INTRODUCTION

Much attention and controversy has surrounded the debate about the long-chain polyunsaturated fatty acid (LCPUFA) requirements of infants. Many authors have argued that preformed LCPUFAs may be required in the diets of infants to meet the high demands of rapidly growing tissues and organs (1–4). Conversely, relatively little consideration has been given to the LCPUFA requirements of mothers, who may be the primary source of LCPUFAs for their fetuses and breast-fed infants. In this review, we discuss issues relating to the maternal requirement for LCPUFAs and whether there is sufficient evidence based on biochemical and functional outcomes to suggest a depleted state during pregnancy, lactation, or both. Particular attention is given to the n–3 LCPUFAs, docosahexaenoic acid (DHA, 22:6n–3) and eicosapentaenoic acid (EPA, 20:5n–3), because these are the fatty acids that have been hypothesized to affect functional outcomes during both pregnancy and lactation.

PREGNANCY

During pregnancy, maternal nutritional requirements are increased by the needs of the growing fetus and placenta. In the case of iron, for example, losses to the fetus and placenta and expansion of the maternal red blood cell mass are estimated to at least double the maternal iron requirement compared with the nonpregnant state (5, 6). Because such intakes are difficult to achieve in the diet and biochemical evidence indicates iron deficiency and depletion during pregnancy, some nutrition committees have recommended routine iron supplementation despite scant information regarding any functional benefit to either the mother or baby (5). In the case of n–3 LCPUFAs, estimating fatty acid balance is more complex because one must account for maternal synthesis as well as stores.

During pregnancy, the maternal demands for n–3 LCPUFAs include normal oxidation for energy and physical requirements of...
the mother and accretion by the fetus. From postmortem studies of fetuses, stillbirths, and preterm infants, it was estimated that the fetus accretes ≈50–60 mg n−3 LCPUFAs/d during the last trimester of pregnancy, most of which is DHA (7–10) and is probably transferred from the placenta (11). To balance these requirements, maternal intake of n−3 LCPUFAs is estimated to be ≈100 mg/d (12, 13). Unlike other nutrients, DHA and EPA can be synthesized from α-linolenic acid (ALA, 18:3n−3) and are also present in maternal stores. Furthermore, pregnancy results in a state of amenorrhea, which is a form of nutrient conservation because there is no loss of LCPUFAs via blood and other cellular material. Finally, the fetus may contribute to its own LCPUFA needs by synthesis. Although there is no direct evidence of fetal synthesis, the finding that preterm infants are capable of synthesizing LCPUFAs make this a viable possibility (14).

Biochemical outcomes

To assess fatty acid balance during pregnancy and to determine whether the mother is at risk of n−3 LCPUFA depletion, studies have either compared the fatty acid profiles of pregnant and nonpregnant women (15) or longitudinally assessed the plasma fatty acid profile throughout gestation (16, 17). Although the study by Holman et al (15) found lower amounts of LCPUFA, including DHA, in plasma of pregnant compared with nonpregnant women, the studies of Al et al (16, 17) have shown that plasma phospholipid DHA and EPA concentrations remain constant throughout pregnancy. Furthermore, plasma phospholipid DHA and EPA values in pregnancy were similar to reference ranges for nonpregnant women in other Western countries with moderate fish consumption (12, 15). Such data do not provide compelling evidence that women’s n−3 LCPUFA status is disturbed significantly during pregnancy.

Physiologic outcomes

Surprisingly, however, some authors have suggested that increased consumption of DHA and EPA from fish or fish oils may increase birth weight and lower the risk of early delivery and preeclampsia. These theories initially arose from epidemiologic observations of birth-weight statistics from the Faeroes Islands (a group of islands between Iceland and the United Kingdom that belong to Denmark), Denmark, and other European countries. Although the populations of the Faeroes Islands and Denmark are genetically similar, the frequency of newborn infants who weighed < 2501 g was 1.7 times greater in Denmark than in the Faeroes (5.9% and 3.5%, respectively) (18). The authors suggested that eating habits during pregnancy might explain these findings.

Credence was added to this hypothesis by a reanalysis of the People’s League of Health Study, conducted in London in the late 1930s (19). The report indicated that there was a 31% decrease in proteinuric hypertension (preeclampsia) in primiparous women allocated to the group that received a multivitamin and mineral supplement compared with the group given no treatment. Women in the treated group were also 20% less likely to deliver a baby before 40 wk gestation than were the women in the untreated group, although there was no difference in birth weight between the 2 groups. The authors of the reanalysis hypothesized that the beneficial effects of supplementation were due to the fish-oil component of the supplement, because studies of other nutrients used as supplements during pregnancy have not shown similar effects (19). However, it is important to note that the People’s League of Health Study was conducted in a population that was nutritionally depleted as a result of the economic depression. In addition, the n−3 LCPUFAs were incidental to the supplement; the fish oil was added as a source of vitamins D and A (19). Because preeclampsia and preterm birth remain major causes of maternal and neonatal morbidity and mortality, randomized clinical trials of fish-oil supplementation during pregnancy have been undertaken to determine whether there is a causal association between n−3 LCPUFAs and these pregnancy outcomes.

A study of outcomes of preeclampsia in Angola tested the efficacy of either low-dose fish oil (200 mg n−3 LCPUFAs) given with evening primrose oil (EPO) or magnesium oxide compared with an olive-oil control (20). This study was only partially blinded and included 150 mothers. Supplementation with n−3 LCPUFA did not result in any benefit with regard to either pregnancy-induced hypertension (PIH) or proteinuric hypertension. There was, however, a lower incidence of edema in the groups treated with either fish oil and EPO or magnesium oxide compared with the olive oil control group. The authors considered their results preliminary and indicated that further research is needed (20).

In the most recent study on this topic, 233 women with pregnancies at high risk for PIH or intrauterine growth retardation were randomly allocated to either air-filled capsules or fish-oil supplements containing a total of 2.7 g n−3 LCPUFAs (21). This study found no effect of supplementation on length of gestation, birth weight, PIH, or proteinuric hypertension, suggesting that there may be no benefit from fish-oil supplementation for women at risk of adverse pregnancy outcomes (21).

Olsen et al (22) conducted a randomized controlled trial to investigate the possible relation between fish-oil supplementation and duration of pregnancy. Women were randomly assigned in their thirtieth week of gestation to receive either no treatment, an olive-oil control, or fish oil. The fish-oil supplement contained 2.7 g n−3 LCPUFAs (=1.5 g EPA and 1 g DHA). All the women were healthy and had no pregnancy complications. Pregnancies in the fish-oil group lasted 4 d longer on average than those in the olive-oil group. After the data were corrected for parity and sex, infants born to mothers in the fish-oil group were ≈100 g heavier than those born to mothers in the olive oil group. However, mothers in the fish-oil group had greater blood loss at delivery compared with those in the olive-oil group. Interestingly, the blood loss of women in the no-treatment group was equivalent to that of women in the fish-oil group. The authors concluded that fish-oil supplementation during the third trimester seems to prolong pregnancy without detrimental effects on fetal growth (22).

On the basis of the 2 randomized clinical trials that assessed hypertensive outcomes, there is no evidence that n−3 LCPUFAs protect against either PIH or preeclampsia without edema (20, 21). The small increase in pregnancy duration, and hence birth weight, in one study has not been substantiated (22). Thus, evidence to support a beneficial effect of n−3 LCPUFAs on pregnancy outcome is inconclusive. However, it appears that n−3 LCPUFAs have functional roles in many other systems including vascular and inflammatory responses. Further studies of n−3 LCPUFAs in pregnancy should pay closer attention to the risks and benefits for the mother and fetus. For example, although supplementation with ≈2.7 g n−3 LCPUFAs during the last trimester of pregnancy has been found to increase cord phospholipid DHA concentrations (23, 24), supplementation also elevates EPA concentrations and suppresses arachidonic acid (AA, 20:4n26) concentrations (23). EPA competitively inhibits AA, which is the precursor to potent eicosanoids that have estab-
lished roles in parturition. Changes in cord-phospholipid fatty acids may therefore have more extensive effects on the fetus and birth process.

LACTATION

Lactation has been described as the greatest physiologic stress of the life cycle, largely because of the increased protein and energy needed to produce breast milk. However, among nutrition researchers, it is generally well accepted that the energy stored as fat during pregnancy can provide one-third of the energy cost of lactation during the first 3 mo (25). As in pregnancy, determining maternal fatty acid balance during lactation, as well as the risk of n–3 LCPUFA depletion, are complicated by the ability of the mother to provide n–3 LCPUFAs from body stores and endogenous synthesis. During lactation, the mother’s body loses ≈70–80 mg DHA/d to breast milk in addition to the amount lost to oxidation or used to fulfill the mother’s own requirement. In women who have resumed menstruation, DHA may also be lost in menstrual blood. On the positive side of DHA balance, one needs to consider dietary intake (which averages 60–70 mg DHA/d in Australian women), synthesis by the mother, DHA that may be available from maternal stores, and DHA saved as a result of lactational amenorrhea.

Biochemical outcomes

In an attempt to determine whether the mother’s body is able to maintain DHA balance during lactation, we assessed the plasma phospholipid profiles of women during late pregnancy and exclusive breast-feeding. Values for maternal DHA concentration at 34 wk gestation and day 5 postpartum were similar to those reported by Al et al (16, 17) at 34 and 40 wk gestation. Between day 5 and week 6 postpartum, we observed a 30% decrease in plasma phospholipid DHA concentrations in breastfeeding mothers (Figure 1). The reduction in plasma DHA concentration was not due simply to parturition because the concentrations 5 d after birth were still the same as the pregnancy and references values (Figure 1). Thus, some process that occurs between day 5 and week 6 postpartum is responsible for this perturbation in the concentration of plasma DHA. Data from a separate group of lactating mothers at 6 and 12 wk postpartum indicated that the decline observed in the first 6 wk postpartum is maintained at 12 wk (27), and additional data indicated that this decline may still be evident 6 mo after birth (16; Figure 1).

To determine whether the postpartum decrease in maternal DHA concentration was due to lactation, we compared maternal plasma phospholipid DHA concentrations between mothers who were fully breast-feeding their infants and those who had chosen to formula-feed from birth. Surprisingly, the difference in maternal plasma DHA concentrations between the mothers who breastfed and those who formula-fed was significant (P < 0.01) but small (Figure 1). Furthermore, both values were similar to previously reported plasma DHA concentrations at 6 wk postpartum and were lower than reference or pregnant values, suggesting only a small difference in DHA status due to breast-feeding.

Maternal plasma DHA concentration decreases by ≈30% during the postpartum period; this effect does not occur immediately after parturition and may be long lasting. However,
the decrease is largely independent of whether the mother chooses to breast- or formula-feed, suggesting that there is little evidence of maternal DHA depletion as a direct result of lactation. The postpartum decrease in maternal DHA concentration may be related to a hormonal effect or increased utilization of maternal DHA reserves, independent of lactation.

Physiologic outcomes

It has been suggested that n−3 LCPUFAs are associated with maternal physiologic function during the postpartum period. Hibbeln and Salem (26) postulated that n−3 LCPUFAs may be one of the complex factors leading to increased risk of depression during the postpartum period. However, we could not find any studies directly relating postpartum mood or depression to maternal fatty acid status.

Another hypothesis is that neural indexes of breast-fed infants may be further enhanced if the DHA concentration in breast milk is increased. Our maternal-supplementation studies with DHA during lactation have shown that supplementation results in dose-dependent increases in both maternal plasma and breast-milk DHA concentrations (27). For example, increasing dietary DHA from ≈100 to 1000 mg/d resulted in an ≈2.5-fold increase in maternal plasma phospholipid DHA concentrations and an ≈5-fold increase in breast-milk DHA concentrations (27). In this study, we also assessed infant growth and some indexes of neural development, including visual evoked potential acuity and Bayley’s mental and psychomotor developmental indexes (28). Although the power of the study was limited, there was no evidence of a consistent effect of dietary DHA on growth or visual evoked potential acuity development of infants who were fully breast-fed for ≥3 mo (28). A small association was found between infant DHA status at 3 mo and Bayley’s mental development score at 1 y of age, but not at 2 y of age (28). It may be naive to think that altering the status of a single LCPUFA has the potential to shift a complex and multifactorial outcome such as neurodevelopment, especially in infants fed breast milk, which is often used as a nutritional gold standard. However, n−3 LCPUFAs have known roles in the regulation of eicosanoid- and cytokine-mediated events. Maternal consumption of diets rich in n−3 LCPUFAs during lactation may have less subtle benefits to both the mother and infant that are independent of putative neurologic effects.

Finally, there is little evidence to suggest that n−3 LCPUFAs provide any functional benefit to lactating mothers or breast-fed infants. In contrast, there is no evidence that supplementation is harmful. Further studies should better characterize maternal postpartum biochemistry before attempting to associate n−3 LCPUFAs with physiologic effects during the postpartum period.

REFERENCES


