Dietary n-3 LC-PUFA during the Perinatal Period as a Strategy to Minimize Childhood Allergic Disease

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The prevalence of allergic diseases in many industrialized countries has increased over the last 30 years and is now estimated to be at least 20%. This increase in allergic disease has occurred too rapidly (within one to two generations) to be a result of population genetic changes, so is likely to be related to environmental changes. In this context, strategies to reduce the burden of disease through prevention are important.

The period of increase in allergic diseases has coincided with a substantial shift in dietary intake of fatty acids to favor n-6 fatty acids over n-3 fatty acids, leading to speculation that the change in dietary fatty acid balance may be linked to the increased prevalence of childhood allergic disease. Diets rich in n-6 fatty acids, via increased consumption of linoleic acid (18:2n-6)-rich vegetable oils as well as increased consumption of arachidonic acid (AA; 20:4n-6) through animal products, lead to a predominance of AA in tissues. AA gives rise to eicosanoids such as prostaglandin E₂ that can enhance the synthesis of T helper type 2 cytokines and immunoglobulin E antibodies – the hallmark of atopic responses to allergens. When diets are high in n-3 long-chain polyunsaturated fatty acids (LC-PUFA; e.g. fish) they are readily incorporated into cellular phospholipids, in the process displacing AA. This leads to a range of biochemical and immunological changes, including reduction of prostaglandin E₂ synthesis, alteration of receptor expression and activity and reduced pro-inflammatory cytokine responses. Thus, there are plausible mechanisms by which diets high in n-3 LC-PUFA may modulate the development of immunoglobulin E-mediated allergic disease and regulate immune responses.

With this rationale, several randomized controlled trials have been conducted to investigate whether n-3 LC-PUFA supplementation will lower the risk of developing childhood allergies. Most studies have included children with higher than normal risk of developing allergic disease because of their family history. These studies may be grouped
according to whether supplementation with n-3 LC-PUFA occurred during the postnatal period or primarily during the prenatal period.

There are two major dietary intervention studies with n-3 LC-PUFA supplementation during the postnatal period. One trial randomly allocated newborn infants to receive a fish oil supplement (approximately 500 mg n-3 LC-PUFA/day) or an olive oil control until 6 months and assessed allergic outcomes including sensitization, eczema, and food allergy at 12 months of age [1]. There were no differences between the groups in the risk of allergic disease at 12 months [1]. The other trial was designed to increase n-3 LC-PUFA status through a combination of docosahexaenoic acid (22:6n-3)-rich tuna oil supplementation and a reduction in dietary linoleic acid intake from 6 to 18 months of age, and showed that dietary intervention lowered the prevalence of early asthma symptoms such as wheeze and cough at 18 months and 3 years, respectively [2, 3]. There was no effect of intervention at 5 years of age [4].

On the other hand, randomized trials that have commenced n-3 LC-PUFA intervention during pregnancy are producing interesting results. One of the earliest prenatal supplementation studies involved high-risk infants and showed changes in neonatal immune responses which were consistent with a less allergic phenotype in the fish oil group compared with the control group [5]. More recently, two studies have demonstrated that n-3 LC-PUFA supplementation with at least 1 g per day during the last half of pregnancy reduced the risk of atopic eczema during the first year of life and reduced the frequency of egg sensitization in infants who are at high hereditary risk of allergies [6, 7]. Of interest are the findings by Olsen et al. [8] who demonstrated that n-3 LC-PUFA supplementation during pregnancy reduced asthma in adolescence in a study including families at normal risk of allergies. However, the allergy outcomes from the trial of Olsen et al. [8] were obtained through linkage to a national registry of doctor visits. The expected event rates in their study are low, and it is not known whether diagnoses were made according to standard definitions.

In summary, supplementation with n-3 LC-PUFA during the perinatal period and before allergic response is established and may be a useful strategy to prevent early childhood allergic disease in children at high hereditary risk.

References