Can Perinatal Supplementation of Long-Chain Polyunsaturated Fatty Acids Prevent Hypertension in Adult Life?

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Abstract—It is suggested that adequate provision of long-chain polyunsaturated fatty acids during the critical periods of brain growth prevents the development of hypertension in later life. (Hypertension. 2001;38:e6-e8.)

Key Words: fatty acids ■ docosahexaenoic acid ■ breast-feeding ■ tumor necrosis factor ■ insulin resistance ■ hypertension

Stimuli or insults induced during the perinatal period can have lifetime consequences and are called programming. Programming stimuli may be generated endogenously (eg, hormonal signals), or they may be environmental. Early nutrition is an important environmental signal that can induce lifetime effects on metabolism, growth, and neurodevelopment and on major disease processes such as hypertension, diabetes mellitus, and obesity. Barker et al1 reported that small size at birth or in infancy is associated with an increased propensity to abnormal blood lipid values, diabetes mellitus, hypertension, and death from ischemic heart disease. Small body size or body shape at birth has been seen as a marker of poor fetal nutrition, which may result in fetal adaptations that program future propensity to adult disease. However, the data relating birth weight to later outcomes, including blood pressure, has been disputed.2 It was suggested that much of what was claimed to be fetal in origin may, in fact, relate to postnatal nutrition and growth.2 The possibility that early nutrition may have a bearing effect on hypertension and coronary heart disease in later life is an issue of major public-health importance.

Long-Chain Polyunsaturated Fatty Acids and Blood Pressure

Infants preferentially accumulate long-chain polyunsaturated fatty acids (LCPUFAs) in the brain during the last trimester of pregnancy and the first months of life.3,4 Fatty acids longer than C18 are omitted from artificial formulas because it is assumed that infants can synthesize LCPUFAs from the essential fatty acids cis-linoleic acid (18:2 ω-6) and α-linolenic acid (18:3 ω-3) through desaturase enzymes and elongases.5,6 However, studies showed that concentrations of LCPUFAs in plasma, red blood cell membrane, and cerebral cortex are lower in formula-fed infants than they are in infants receiving human milk, suggesting that these enzyme systems may be inefficient or deficient in infants.7,8 Adequate amounts of docosahexaenoic acid (DHA, 22:6 ω-3) and arachidonic acid (AA, 20:4 ω-6) are essential for optimal function and development of central nervous system.9 Vegetable oil–based infant-feed formulas lead to suboptimal neural development and performance because of decrease in brain DHA.8,9 DHA and other LCPUFAs have significant neuroprotective action, protecting neurons from the death signals of tumor necrosis factor-α (TNF-α).10 It is also interesting to note that dietary DHA can enhance hippocampal acetylcholine levels,11 which in turn can enhance NO production, a potent vasodilator. Borovikova et al12 showed that vagus nerve stimulation in vivo inhibits TNF synthesis in the liver and that acetylcholine, the principle vagal neurotransmitter, significantly attenuates the release of proinflammatory cytokines TNF, IL-1β, IL-6, and IL-18 but not antiinflammatory cytokine IL-10 in lipopolysaccharide–stimulated human macrophages in vitro. This suggests that increases in brain acetylcholine levels induced by supplementation with eicosapentaenoic acid (EPA, 20:5 ω-3) and DHA lead to an increase in the parasympathetic tone and, thus, an increase in heart rate variability and protection from ventricular arrhythmias.13

A balance is generally maintained between sympathetic and parasympathetic nervous systems. Hence, when there is an increase in the activity of the parasympathetic nervous system, the tone of the sympathetic nervous system is decreased. Hypertension is believed to be associated with increase in sympathetic tone. This suggests that increase in the tone of the parasympathetic nervous system that is likely to occur because EPA/DHA supplementation can decrease the synthesis and release of TNF-α. EPA and DHA can also inhibit the production of TNF-α, interleukin (IL)-1, and IL-2 both in vitro and in vivo.14,15 This in turn can lead to attenuation of insulin resistance because TNF-α is important...
for inducing insulin resistance,16–18 and insulin resistance and hypertension are interrelated.18,19 Decreased insulin sensitivity was also found to be correlated with decreased concentrations of LCPUFAs in skeletal muscle phospholipids.20,21 Thus, the presence of adequate amounts of DHA/EPA/AA in the membrane phospholipids can decrease insulin resistance and prevent the development of hypertension.

Breast milk consumption has been associated with lower blood pressure in later life.22,23 In a recent study, Singhal et al24 confirmed that breast milk consumption was associated with lower later blood pressure in children born prematurely. But, the exact mechanism responsible for this association is not clear. I suggest that the reason why breast-feeding lowers blood pressure later in life is because of its fatty acid profile. Human milk is rich in LCPUFAs, especially in DHA and AA (DHA > AA). Further support to this concept is derived from the observation that breast-fed infants had a significantly higher percentage of DHA and total percentage of LCPUFAs in their skeletal muscle phospholipid fraction compared with those of the formula-fed group.25

Recently, Weisinger et al26 showed that DHA deficiency in the perinatal period results in raised blood pressure later in life, even when animals were subsequently replete with this fatty acid. They observed that animals raised on LCPUFAs-deficiency diet underdrank water and overingested sodium, suggesting an aberration in central osmo/sodium sensors or angiotensinergic mechanisms. This fits well in the role of DHA in the central nervous system as discussed above. It is possible that decrease in DHA/EPA content in the brain will lead to death of neurons that are concerned with osmo/sodium sensor mechanisms, because LCPUFAs not only protect neurons from insults induced by TNF-α but also can inhibit its production. Hence, availability of adequate amounts of DHA and other LCPUFAs to breast-fed infants or when fed externally during the critical periods of growth prevents development of hypertension in adulthood. In addition, LCPUFAs can interact with many other nutrients and lower blood pressure.18,27

Conclusion

It is proposed that LCPUFAs, when given in adequate amounts during the perinatal period, can protect against the development of insulin resistance and hypertension in later life. Provision of sufficient amounts of LCPUFAs can be achieved by adequately breast-feeding the infant. This does not mean that other nutrients, minerals, trace elements, vitamins, and hormones do not have a major role in programming the fetus and the newborn. In fact, it is likely that LCPUFAs may interact with all such factors to fine tune their beneficial actions by their ability to influence the cell membrane fluidity, expression of receptors on the membrane, and subsequent postreceptor events.18,25 Thus, it is envisaged that a close interaction exists between nutrients, minerals, trace elements, vitamins, hormones, and LCPUFAs as discussed in detail elsewhere.6,18,27 But, for this interaction to be optimum, adequate amounts of LCPUFAs should be available not only in the specified areas of the brain but also in vessel wall including endothelium, kidney, heart, and other tissues. Only then will various tissues be able to counteract the pathological mechanisms that tend to induce hypertension.18 The major criticism of this proposal is that even when many infants have been breast-fed (and as a result are presumed to have received adequate amounts of LCPUFAs), they are not protected from the development of hypertension in adulthood. It may be mentioned here that breast-feeding alone may not be sufficient to ensure that the infants have received adequate amounts of LCPUFAs. This depends on 2 factors: (1) the presence of adequate amounts of LCPUFAs in the mother’s milk, and (2) the duration of the breast-feeding. These 2 critical factors should be taken into consideration to determine whether the infant has received adequate amounts of LCPUFAs or not. It is suggested that adequate amounts of LCPUFAs should be provided from the third trimester of pregnancy to 2 years of age of the child, because this is the critical period of brain growth. In the light of this proposal, it will be interesting to study whether provision of LCPUFAs or infant feed formula containing adequate amounts of various LCPUFAs during this critical period of brain growth can prevent or postpone the development of hypertension in later life when given to infants as opposed to infants who receive the standard feed formula. Obviously, such a study needs careful planning, immense effort and funding. But it is probably worth it.

References


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