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Optimization during the First Thousand Days of Child through Dietary Supplement with Lc-Pufas: Systematic Review of the Literature

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Abstract

Objective: To describe data on effects of LC-PUFAS in neuronal formation in the first thousand days of a child.

Methods: A systematic review of 23 articles in the first quarter of 2015 from 2003 to 2015 in Medline, Scielo, Science Direct and Google Scholar. Languages: Portuguese, English and Spanish. Headings (MeSH): fatty acids; arachidonic acid; Omega 3; Omega-6; infant formula; child development; child nutrition; synapses and neurogenesis; child development; child nutrition; synapses and neurogenesis. Inclusion criteria: the LC-PUFAS approach, neuronal training and the first thousand days of children, isolated or associated.

Results: The first thousand days of a child involving rapid growth and physical and mental development. There is no evidence that the foetus has docosahexaenoic acid omega 3 family (DHA) sufficient to meet the demand of its neuronal metabolism. Observational studies indicate that DHA intake during pregnancy promotes a variety of positive results in the development of the newborn. The postnatal supplementation with LC-PUFAs for breastfeeding or formula with LC-PUFAs, if not exclusive breastfeeding is associated with better neurological development indices.

Conclusion: supplementation with LC-PUFAs is essential to improve the neurological development of children. The intake of DHA promotes better cognitive and visual results compared to no feeding of the substance.

Keywords: Fatty acids; Arachidonic acid; Child development; Infant nutrition; Synapses Neurogenesis

Introduction

The moment of conception until the first two years of life of a toddler is an essential period, which involves fast growth and physical and mental development, named the first thousand days. During this time interval, babies and toddlers deserve an appropriate nutrition to their needs, so that they can grow healthy and develop their maximum potential. Therefore, the appropriate nutrition support is crucial during the first years of live, once during this period, the body is developing its metabolism, forming the immune system, the bone density and the cognitive abilities, which consist the base for the future human development.

The long chain polyunsaturated fatty acids (LCPUFAs), as the docosahexaenoic acid omega 3 family (DHA) and the arachidonic acid omega 6 family (ARA) are essential in human diet and they are concentrated in the central nervous system (CNS) being fundamental for the normal brain development. Both, the DHA and the ARA, are present in the membrane lipids of the grey matter and the retina. The eicosapentaenoic acid (EPA) is considered other LCPUFAs dietetic. However, the EPA plays a more important role in the cardiovascular and immune health. The ARA and the DHA participate in the formation of the cerebral cortex grey matter and the myelination of the nerve fibres. The concentrations of these acids accumulate during the third trimester of pregnancy and in the first months of life, being affected by the diet [1].

The DHA concentrations are lower in the cerebral cortex of the premature babies who are fed with the infant formula that does not contain LCPUFAs, if compared with babies who are fed with human milk. It suggests that the DHA synthesis can be inappropriate to meet the need of children during the first months of life. The concentrations of ARA in the breast milk are constant, contrary to EPA and DHA which are variables, according to the mother's diet. Based on this, an international consensus was created in 2008 which recommends pregnant and nursing women should consume at least 200 mg DHA daily [2].

Previous studies show that the DHA deficiency can lead to a variety of neuronal and psychological alterations, such as attention deficit and hyperactivity disorder, depressions, schizophrenia, autism and anxiety. This deficiency can affect the neurotransmission especially in the dopaminergic and serotonergic system, consequently alternating the membrane fluidity and the functions of the related receptors. Furthermore, its presence is important to the regulation of the synaptic plasticity, as well as learning and memory, involving the gene expression regulation and retinoid.

The aim of this systematic literature review is to describe the data about the LCPUFAs effects in the neuronal formation during the first thousand days of a child's life [3].

Methodology

In the second quarter of 2015, this systematic review of the scientific literature was carried out in order to analyse the optimization of the neurodevelopmental during the first thousand days of life through dietetic supplementation with LCPUFAs [4]. The PICOT model was used to formulate the following research question: does the nutrition based on LCPUFAs contribute to neuronal formation during the first

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thousand days of a child's life? To answer this question we preferably searched for studies that have been published during the last twelve years and dealt with these themes or related ones.

The descriptors used in this research, were obtained from the Health Sciences Descriptors (DeCS) and included: fatty acids; arachidonic acid; omega 3; omega 6; infant formula; child development; infant nutrition; synapses and neurogenesis, in English, Portuguese and Spanish [5]. The descriptors were associated to each other and Booleans operators (AND and OR) and the combination with them generated different strategies of search. The bibliographic research was made in the following data basis: Science Direct, Medline (through the Pubmed), Scielo and Academic Google and it was included 23 articles in Portuguese, English and Spanish. It was applied as inclusion criteria the significant approach of LCPUFAs, neuronal development and the first thousand days of children, isolated or associated. It was excluded the articles which were not related to the first thousand days of children and the neuronal development. After the first bibliographic revision had been made, aimed to improve the research, it was added new articles which were given by an expert in neuropediatric.

Results and Discussion

The results were divided into the following categories: physiopathology of LCPUFAs [6], maternal nutrition during pregnancy and its relation to LCPUFAs, the newborn nutrition based on breast milk and infant formula and its link with LCPUFAs, LCPUFAs and its influence in the neuronal development during the first thousand days of a child's life and the consequences of lack of LCPUFAs during the first thousand days (Figure 1).

Physiopathology of LCPUFAs

The LCPUFAs are constituted by twenty or more carbon atoms and three or more double bond, such as arachidonic acid ARA (20: 4 n -6), EPA (20: 5 n -3) and DHA (22:6 n -3), they are considered important biologically active compounds. LCPUFAs are indispensable components in cell neuronal membranes; they are able to modulate its integrity and fluidity. They also act as second messengers in intracellular signalling pathways and used as precursors to the eicosanoids and docosanoids, which are powerful regulators of inflammatory process [7].

The ARA and DHA execute their metabolic functions by forming part of the structure of the phospholipids of the cell membranes, particularly phosphatidylcholine, phosphatidylethanolamine and phosphatidylserine. Due to its outstanding, polyunsaturated these fatty acids will provide high fluidity to the cell membranes from the phospholipids formation. This fluidity is essential to the proteins of the membrane (ion channels, catalytic receptors, junctions, enzymes, vesicles formation) execute the functions of physical mobility important to the metabolism, as well as the membrane surface and inside the lipid bilayer. Thus, during the formation of the neural tissue, especially of the brain, the membrane fluidity is particularly important [8].

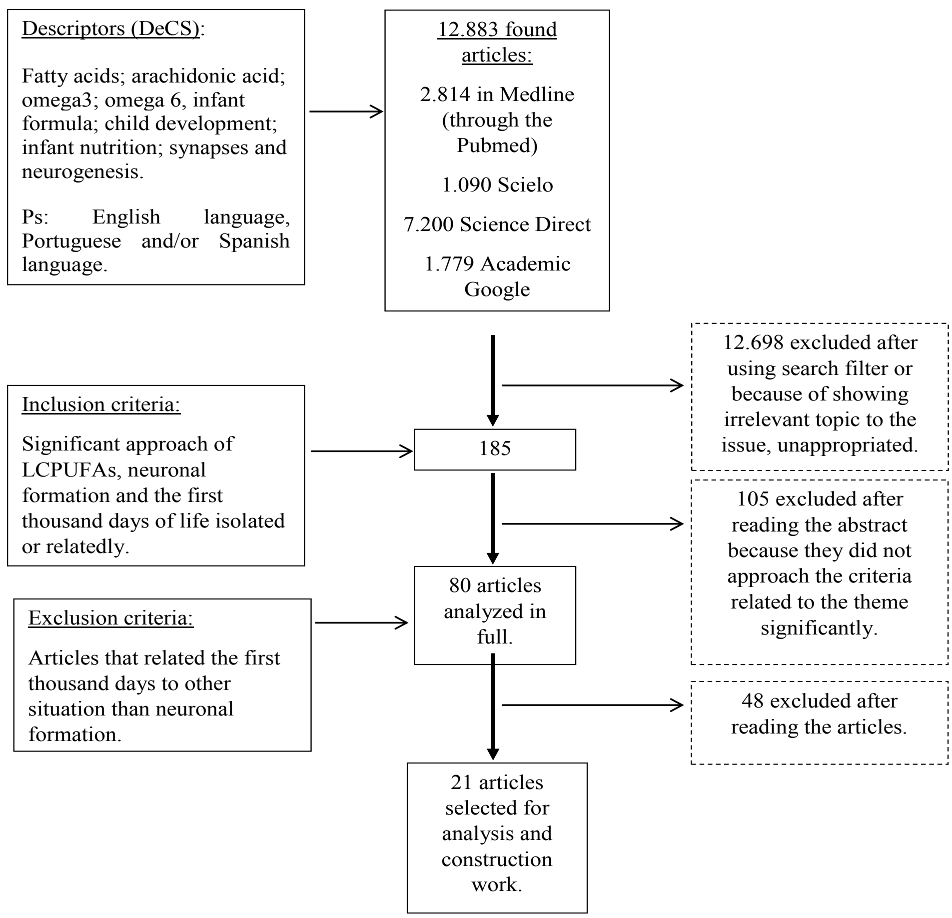

Figure 1: Flowchart on the selection of the articles.

Maternal nutrition during pregnancy and its relation with LCPUFAs

During pregnancy, the transfer of maternal DHA is extremely important to the foetus and its quantity arises according to the maternal nutrition. The researches of Brenna describe successive pregnancies can reduce the value of the maternal DHA and, thus, interfere the ability of transferring the DHA to the foetus during the pregnancy and to the baby through the breast milk.

In addition to the post intake of LCPUFAs, the DHA can also be summarized in an endogenous way from the essential fatty acids, LA and ALA, which come from the vegetable oils. Some researches show that the low quantity of DHA affects both mother and child, arising the probability of postnatal depression; in this case, the omega-3-LCPUFAs supplementation to the nursing could reduce the risk of depression.

Observational studies point that the ingestion of DHA during pregnancy promotes a variety of positive results in the newborn development [9]. The biggest ingestion of maternal DHA was related to the stereoacuity, cognitive function and the immune function, which is responsible for the improvement of the infant immune function. The women, who usually ingest DHA, have a proper storage of it since the beginning of the pregnancy and it shows benefits for both, mothers and babies, when compared to the women who start the DHA supplementation only during the pregnancy.

The average level of DHA in the maternal milk requires an ingestion of about 200 mg per day of this nutrient by the mother in order to ensure that there is no depletion of her body energy stored and possible negative consequences to the baby. The end of the fifth week pregnancy is the most important period to give DHA, with the fast growth of the foetal brain; it justifies the great importance of the fatty acids for the normal development of the brain. The levels of DHA, in the tissues, particularly in the neural ones, which are known for being sensible to the ingestion of this nutrient, when compared to the sensibility related with the LCPUFAs and the arachidonic acids [10].

Newborn and child nutrition based on breast milk and infant formula and its relation with LCPUFAs

The supply of LCPUFAs to the foetus during the pregnancy occurs since the placental transfer from mother to child through the umbilical cord. Considering this context, it is important to emphasise that premature infants show a higher risk for insufficient accumulation of LCPUFAs when compared with the ones who were born in term. This fact is justified by the early interruption of placental supply [11]. The quantities of fatty acid from the umbilical cord are related to the values in the maternal blood and many supplementation studies have shown that the quantities of DHA in the umbilical cord blood are influenced by the mother's nutrition. After that, the LCPUFAs are supplied by breast milk and/or DHA or ARA enriched infant formula.

The breastfeeding consists in an efficient method on nutrition for healthy babies. The infant formula can be used when the breastfeeding is not possible. When they are indicated to in term newborns, these formulas must contain at least 0.2% of the total fatty acids such as DHA and 0.35% ARA. On the other hand, the formulas for premature newborn must include at least 0.35% of DHA and 0.4% ARA.

The meta-analysis of premature babies fed by a supplemented formula with DHA versus formula without DHA showed a significant improvement, which refers to the visual acuity at 2 and 4 months old. Some studies show that dietetic LCPUFAs during the postnatal period have effects on the visual development, problems solving and language. A double-bling clinical trial revealed that premature babies fed with a formula, which contains DHA and ARA during 92 weeks showed an increasing of growth, bigger mental scores and psychomotor development in 118 weeks old, when compared with babies fed with a control formula, which is not supplemented. According to the same study, there is a lack of data about the effects of a rich diet in LCPUFAs about the development of the immune, respiratory and digestive system.

The evaluation of the results of more than 20 randomized controlled trials involving in term babies, who received supplemented formula with DHA and ARA or a control formula, revealed that different levels of DHA in diet had different results. The clinical trials, which showed infant formula with values of DHA close to the level, found in the breast milk, 0.32% of the total fatty acids were more inclined to generate important benefits to the infant neural development. Furthermore, there are significant correlations between the levels of red blood cells (RBC) or DHA plasma with better and cognitive results in newborns fed with formula. The gains of the supplementation postpartum usually manifest with an accelerated function in the development of visual acuity during the first year of life. However, another study did not find relation between the levels of DHA in the blood and the neurodevelopment [12].

After weaning, the child nutrition varies considerably depending on food choices made by parents [13]. In a low-DHA diet, the blood levels of DHA in children at 18-60 months old are lower if compared to children fed with formulas, which do not contain DHA. Based on food consumption data, considering local and national researches, children who do not live near the sea show a diet consisted of low levels of DHA, EPA and probably ARA [14].

Several randomized studies showed benefits in supplementation of formulas with LCPUFAs for the retinal maturation, visual acuity development and cognitive development during childhood. Therefore, low levels of dietetics DHA have a negative effect in the neurological development and in the retina during the infancy. The retina and the brain are embryological ectodermal origin tissues and for this reasons they provide an accessible index for the neurodevelopment milestones. However, other studies did not find any benefits.

According to another study published in 2009, children who received supplementation with enriched LCPUFAs formulas, such as DHA and ARA, showed more intentional solutions, in other words, conclusions of successful tasks and higher scores – behaviours directed to the target – than the controls [15]. The same study also ratified other data discussed previously, which were presented in others literary sources, such as the importance of breast feeding, which is considered a natural source of DHA, generally associated with superior cognitive abilities, when compared with a diet free of DHA. In conclusion, the postnatal supplementation with formula contained LCPUFAs in children who were born at term is associated with a beneficial effect about neurological development in short term. Possibly, this effect is due to the levels of DHA of at least 0.30%, if we compared with the world average of breast milk DHA, which is 0.32%.

The International European Food Safety Authority (EFSA) consensus, recommends 20-50 mg/day of DHA during the period of 0-6 months old and 100 mg/day during the period of 6-24 months old. The dietary intake for children 2-18 years old might be consistent and similar to the adult population (250 mg/day of DHA associated with (EPA) [16].

LCPUFAs and their influence in the neuronal development during the first thousand days of a child

The human babies can synthesize LCPUFAs, DHA and ARA, from their precursors, which are the linoleic acid (LA) (18: 2n-6) and the linolenic acid (18: 3n-3). The results of studies from autopsies showed that there are less DHA in the frontal cortex of in term newborns fed with formulas, which contained α-linolenic acid (ALA) than infants fed with breast milk, which contained both the α-linolenic acid and the DHA [17].

At the end of pregnancy and in the initial postnatal period, the newborn brain has a significant growth in relation to the volume as well as the cell proliferation. This process is called "Ontogenetic Brain Development". The quantity of DHA and ARA in the forebrain increases about 30 times showing an active placental transfer of LCPUFAs in prenatal and a considerable demand for a postnatal supplying of LCPUFAs. Considering the fast growth of the newborn, there is an increasing demand of complex lipids to form the vital structures of the cell membrane. In this way, the availability of preformed substrates, such as DHA and ARA, which are components of the neural membrane, are of great importance.

The development of the nervous system, specially the brain, occurs since the first trimester of pregnancy and continues until two years after the birth. It is during this period that the formation of the neurons and other glial cells starts actively and the demand of DHA increases significantly. This morphogenic process, which starts in the neural crest, is characterized by successive stages of neurogenesis, neuronal migration, selective apoptosis, synaptogenesis and myelination; these are essential stages to the development of the brain tissue. These cell processes require the active participation of glial cells, in special, the astrocytes, which give to the neurons the required metabolites, physical support and mobilisation inside the encephalon. This morphogenesis closely associated with the brain function requires an extraordinary contribution of LCPUFAs, specially DHA and ARA [18].

Therefore, the maternal diet and the genetic play fundamental roles in the sufficiency of reserves of LCPUFAs. The mobilisation of DHA from mother to foetus though the placenta must be sufficient for its concentration in the brain – where falls short of 40% of the level of long chain polyunsaturated fatty acids – be greater than the concentration in the foetal plasma, in the placenta and in the maternal plasma. This process has been identified as biomagnification, which means a demonstration of active transference of maternal placenta foetal DHA. It is also important to highlight the blood-brain barrier is waterproof to saturated fatty acids, monounsaturated and cholesterol, which should be formed by the brain. Conversely, it is permeable to omega-3, fatty acids and omega-6. It is even questionable, if during the pregnancy period, the brain can form DHA from the linoleic acid or it comes from a preformed DHA, due to its inability of desaturation and elongation of ALA. However, it is described that in the final stages of the last pregnancy trimester the astrocytes have the task of supplying with DHA the neurons, which will be formed.

The consequences of lacking of LCPUFAS during the first thousand days of a child

The LCPUFAs are metabolically essential in neuronal and visual development. The DHA, ARA and EPA are derived from the LA and ALA. Both the foetus and the newborn are able to convert ALA and LA to DHA and ARA, respectively, but the efficacy of this transformation is related to genetic and environmental determiners. Thus, this conversion can be insufficient to store deposits to a satisfactory formation of the central nervous system [19].

Several studies showed reduced growth of premature newborns, who were fed with formula containing LCPUFAs and DHA, but without ARA. Other observational and controlled studies of breastfed newborns and also studies randomized and controlled of complemented formulas showed that newborns, who fed with levels of DHA similar to the world average and levels of ARA a little larger than the ones of DHA, had benefits in visual and cognitive development.

Diets deficient in LCPUFAs during the development lead to characteristics alterations in the brain and retina. These alterations interfere with intracellular and intercellular signalling pathways leading to functional deficits. Some studies have shown that the depletion of DHA is associated with the reduction of the visual function, neurological development, in addition to behavioural abnormalities due to the decrease of the membrane protein, activities of the receptor ion channel and changes in the metabolism of neurotransmitters. The deficiency of omega-3 fatty acids in newborns results in lower sensitivity of the retinal rods and abnormal cognitive development. Experimental animal studies indicate that the dopaminergic and serotoninergic suffer influence of deficit of LCPUFAs and can thus join the behaviour already mentioned above. The deficit of DHA in the brain during the perinatal period can represent an avoidable risk factor to the abnormal neurologic development and the later emergence of psychopathology.

According to Morale, there is knowledge about the critical period that food sources containing LCPUFAs can influence the visual function maturation in children born in term. However, some randomized clinical trials suggest that this phase can be around the 52 weeks old. This long period suggest that the brain after the childbirth cannot have enough ad quick source of LCPUFAs to support the visual cortex maturation, corroborating the importance of a rich diet in LCPUFAs and its impact on visual acuity.

Including the contribution of Barbosa and Volp, another illness that have been linked to the insufficient consumption of polyunsaturated fatty acids is the mood disorder, because the lipids are essential to the normal function stabilizer mood areas in the brain. The high ratio between the fatty acids of omega 6 and omega 3 series has been related to the increased incidence of psychiatric disorders. This change in diet is considered as a relevant factor in deficiency of phospholipids. Phospholipids made of fatty acids of omega 3 and omega 6 series have an important function in translation and transmission of nerve impulses and the integrity of the cell membrane and its fluidity. The correct balance of these acids in the phospholipids is essential for normal neuronal function and disruption of this balance can also trigger other psychiatric disorders, such as depression [20].

Both precursors, omega 3 and omega 6 fatty acids, are metabolized by enzymatic pathways and are influenced by factors like diet, oxidative stress, alcohol, smoking, age and genetic factors [21]. These common pathways can be overloaded generating important metabolic implications. In the brain, excessive ingestion of omega 6 fatty acid or insufficient ingestion of omega 3 may increase the risk of depression changing the serotonergic neurotransmission of catecholamine [22].

Nutritional deficiencies during the pregnancy provide a vulnerable mean to damage in the postnatal period. LCPUFAs are critical nutrients in the beginning of that period when most of the brain areas goes through its fast development. It is well established that the nutritional deficiencies (and excesses) can affect the child's brain and change the development and subsequent behaviour permanently. These deficiencies generate effects that begin in childhood but can extend

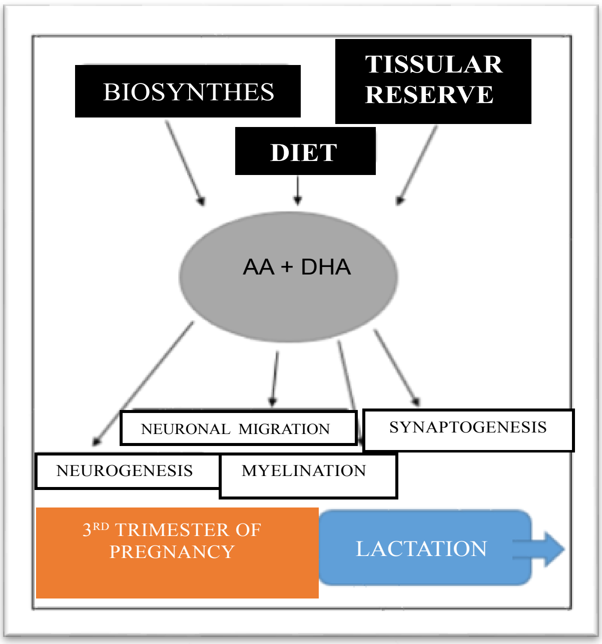

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Figure 2: Synthesis of LCPUFAs and its neuronal repercussions.

to aging with symptoms of immunity impairment, gastrointestinal disorders, circulatory disorders, growth retardation and sterility [23]. In addition to these symptoms, the lack of essential fatty acids in the diet has been implicated in the development or worsening of breast cancer, rheumatoid arthritis, asthma, preeclampsia, schizophrenia and attention deficit hyperactivity disorder (Figure 2).

Conclusion

The study showed that the maternal and infant supplementation with LCPUFAs in the period of a thousand days of life is essential to improve the neurological of children. The intake of DHA during the pregnancy promotes a variety of positive results in the development of the new born. Babies born at term, who could not be breastfed and received DHA and ARA supplementation formula obtained better cognitive and visual results than the ones who did not receive the supplementation. Deficient diets in LCPUFAs during the development leads to characteristic brain and retina alterations. These alterations interfere with intercellular and intracellular signalling pathways leading to functional deficits. Therefore, it is concluded that the appropriate intake of DHA and ARA in pregnant women during the first thousand days of life is essential for proper growth and neuronal maturation, which results in satisfactory psychomotor development.

References

1. Victora C (2012) Los mil días de oportunidad para intervenciones nutricionalesArchivos Argentinos de Pediatría 4: 311-317.
2. Ryan AS, Astwood JD, Gautier S, Kuratko CN, Nelson EB, et al.. (2010) Effects of long-chain polyunsaturated fatty acid supplementation on neurodevelopment in childhood. A Review of Human Studies 4: 305-314.
3. Willatts P, Forsyth S, Agostoni C, Casaer P, Riva E, et al. (2013) Effects of long-chain PUFA supplementation in infant formula on cognitive function in later childhood. The American Journal of Clinical Nutrition 2: 536-542.
4. Colombo J, Carlson SE, Cheatham CL, Shaddy DJ, Kerling EH, et al. (2013) Long-term effects of LCPUFAs supplementation on childhood cognitive outcomes. The American Journal of Clinical Nutrition 2: 403-412.
5. Herrera M, Machado L, Villalobos D (2013) Nutrición em recién nacidos a término y em niños de 1 a 6 meses. Arch. venez. pueric. Pediatr 3: 117-125.
6. Janssen CI, Zerbi V, Mutsaers MP, Jong BS, Wiesmann M, et al.(2015) Impact of dietary n-3 polyunsaturated fatty acids on cognition, motor skills and hippocampal neurogenesis in developing C57BL/6J mice. The Journal of Nutritional Biochemistry 1: 24-35.
7. Castillo-Durán C, Balboa P, Torrejón C, Bascuñán K, Uauy R(2013) Alimentación normal del niño menor de 2 años: Recomendaciones de la Rama de Nutrición de la Sociedad Chilena de Pediatría. Revista chilena de Pediatria 5: 565-572.
8. Valenzuela BV, Nieto KS (2003) Ácidos grasos omega-6 y omega-3 em la nutrición perinatal: su importância em el desarrollo del sistema nervioso y visual. Rev, chil. Pediatr 2: 149-157.
9. Brenna JT, Carlson SE (2014) Docosahexaenoic acid and human brain development: Evidence that a dietary supply is needed for optimal development. Journal of Human Evolution 77: 99-106.
10. Lattka E, Koletzko B, Zeilinger S, Hibbeln JR, Klopp N, et al. (2013) Umbilical cord PUFA are determined by maternal and child fatty acid desaturase (FADS) genetic variants in the Avon Longitudinal Study of Parents and Children (ALSPAC). British Journal of Nutrition 7: 1196-1210.
11. Hsieh AT, Brenna JT (2009) Dietary docosahexaenoic acid but not arachidonic acid influences central nervous system fatty acid status in baboon neonates. Prostaglandins, Leukotrienes and Essential Fatty Acids 2: 105-110.
12. Koletzko B, Boey CC, Campoy C, Carlson SE, Chang N, et al. (2014) Current information and Asian perspectives on long-chain polyunsaturated fatty acids in pregnancy, lactation, and infancy systematic review and practice recommendations from an early nutrition academy workshop. Ann Nutr Metab 1:49-80.
13. Colombo J, Carlson SE, Cheatham CL, Fitzgerald-Gustafson KM, Kepler A, et al. (2011) Long-chain polyunsaturated fatty acid supplementation in infancy reduces heart rate and positively affects distribution of attention. Pediatric Research 4: 406-410.
14. Hoffman DR, Boettcher JA, Schade DAD (2009) Visando otimizar a visão e a cognição em recém-nascidos a termo por suplementação de dieta com ácido docosahexaenóico e araquidônico Uma revisão dos estudos randomizados controlados, Rev. J. Plefa, 3.
15. Birch EE, Sharon Garfield S, Yolanda Castañeda Y, Hughbanks-Wheaton D, Uauy R (2007) Visual acuity and cognitive outcomes at 4 years of age in a double blind, randomized trial of long-chain polyunsaturated fatty acid-supplemented infant formula. Early Human Development 83: 279–284.
16. Drover J, Birch EE, Hoffman DR, Castaneda YS, Morale SE(2009) Three randomized controlled trials of early long-chain polyunsaturated fatty acid supplementation on means-end problem solving in 9-month-olds. Child Dev 80:1376–1384
17. Hadders-Algra M (2010) Effect of Long-Chain Polyunsaturated Fatty Acid Supplementation on Neurodevelopmental Outcome in Full-Term Infants. Nutrients 2: 790-804.
18. Cheatman CL, Colombo J, Carlson SE (2006) n− 3 Fatty acids and cognitive and visual acuity development methodologic and conceptual considerations. The American Journal of Clinical Nutrition 6: 1458-1466.
19. Neubronner J, Schuchardt JP, Kressel G, Merkel M, Schacky VC (2011) Enhanced increase of omega-3 index in response to long-term n-3 fatty acid supplementation from triacylglycerides versus ethyl esters. European Journal of Clinical Nutrition 2: 247-254.
20. Morale SE, Hoffman DR, Castañeda YS, Wheaton DH, Burns RA (2005) Duration of long-chain polyunsaturated fatty acids availability in the diet and visual acuity. Early Hum Dev 2:197-203.
21. Barbosa KBF, Volp ACP, Renhe IRT, Stringheta PC(2007) Ácidos graxos das séries ômega 3 e 6 e suas implicações na saúde humana Omega-3 and 6 fatty acids and implications on human health. Omega 2: 129-145.
22. Gow RV, Hibbeln JR (2014) Omega-3 fatty acid and nutrient deficits in adverse neurodevelopment and childhood behaviors. Child and Adolescent Psychiatric Clinics of North America 3: 555-590.
23. Yehuda S, Rabinovitz S, Mostofsky DI (2005) Essential fatty acids and the brain from infancy to aging. Neurobiologyofaging 1: 98-102.