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Editorial

DHA - The new vital molecule on the block

Introduction

Pregnancy is a period characterized by increased nutritional requirements to meet the needs of the growing fetus and placenta, Now that the importance of folic acid, iron and calcium supplementation has been accepted worldwide; focus has shifted to the other micronutrients required for the optimal health of the mother and child. The current focus is on the role of essential fatty acids, especially Docosahexaenoic acid (DHA) in pregnancy. DHA is the new molecule on the block, essential for optimum maternal and perinatal outcome.

DHA

DHA is a long chain omega 3 essential fatty acid that is found throughout the human body. But more specifically, DHA is a major fatty acid found in the sperm and brain phospholipids. It is the predominant fatty acid in the brain, mostly distributed in the cerebral cortex, mitochondria and the photoreceptors of the retina after second trimester of pregnancy and continues to accrue 18 months postpartum[1]. Low levels of DHA result in reduction of brain serotonin levels and have been associated with Alzeimer's disease and depression. Development of the brain and retina begins in fetal life and hence the growing interest in the optimal DHA levels in pregnancy.

Mechanism of Action

DHA is considered to exhibit its important functioning at the level of cell membranes, where it is incorporated into the membrane phospholipid components to mediate its special structure-function effects. It modulates the carrier-mediated transport of choline glycine and taurine, the function of delayed rectifier potassium channels and the receptor response of rhodopsin contained in the synaptic vesicles [2]. It is credited to reduce cellular and vascular inflammation in the brain and ensure integrity of brain cell membranes to keep them soft and pliable.

DHA reduces thromboxane levels and increases prostacyclin levels leading to enhanced tissue perfusion and oxygen delivery due to vasodilatation and increased blood viscosity. DHA is also credited to increase the "feel good" neurotransmitter serotonin and "memory boosting" chemical acetylcholine [3].

DHA is known to significantly alter many basic properties of cell membranes, including their fluidity, elastic compressibility, permeability and interaction with key regulatory proteins. Its action on the nervous system is thought to underlie its role in supporting the functions of the brain such as learning ability and memory [4].

Role of DHA in cell signaling

Scientists have recently discussed the role of DHA in cell signalling, which is an important aspect of all cells for optimal functioning. Cell signaling controls intracellular and extracellular communication as well as communication between cells and genes. With the help of DHA, the cell signalling molecules perform an assortment of functions including [5].

1) Regulating cellular energy via the mitochondria
2) Activating or silencing genes
3) Generating specialized genes
4) Ion regulations
5) Regulating inflammatory mediation. DHA regulates a number of second messengers, which in turn regulates cellular inflammatory mechanism such as nuclear factor kappa B and inflammatory eicosanoid generation. By down regulating glutamate receptor activity, DHA protects against nerve damage.
6) DHA also maintains the activity of the Na+ / K+ ATPase pump which controls intercellular electrical impulses. A diet deficient in DHA lowers activity of Na+ / K+ ATPase by 40%. Na+ / K+ ATPase pump is also linked to 60% of the energy consumed by the brain [7].

7) DHA is also a major regulator of calcium oscillation, which regulates a vast array of cellular functions, including neurotransmitter release, mitochondrial functions, gene activation, oxidative stress and in the developing brain, neuron migration and motivation. Low DHA levels are also known to lower brain and cellular growth factors, such as brain derived growth factor [8].

8) DHA accumulate in phosphatidylserine in the hippocampal region increasing memory consolidation and protecting the neurons via its action on cell-signaling. Its deficiency has been correlated with approximately 30-35% reduction in phosphatidylserine levels in key neuronal cells, during the prenatal and postnatal periods [9].

Dietary Sources

The main dietary sources of omega 3 fatty acids are vegetable oils like linseed oil, canola oil, peanut oil, olive oil, soya oil, walnut oil, green leafy vegetables, fenugreek seeds, kidney beans, dry fruits and fish oil. Most Indians consume omega-6 and omega- 3 fatty acids in the ratio of 30-70% , but the ideal ratio is 5-10% for optimal health benefits [6].

Maternal benefits of DHA

Evidence from the literature suggests a potential role of DHA in the prevention and treatment of maternal depression. An analysis by Hibbeln of the data pooled from several countries showed a negative correlation between the prevalence of postpartum depression and either sea food consumption or breast milk DHA concentration [10]. In a study of approximately 14000 women, self reports of a low sea food intake at 32 weeks gestation was associated with an approximate doubling of the risk of severe depressive symptoms during pregnancy and in the postpartum period [11].

DHA is credited to reduce the levels of thromboxane and increase prostacyclin levels leading to enhanced uteroplacental perfusion and oxygen delivery, vasodilatation and thinning of blood. There is reduced risk of development of toxemia of pregnancy in mothers who received supplements of DHA. There is also a potential application of DHA supplementation in women experiencing recurrent miscarriage associated with persistent anti phospholipid syndrome [12].

Evidence from both observational studies and interventional trials suggested that higher DHA intakes during pregnancy may result in smaller increase in the duration of gestation and also a possible increase in birth weight. Olsen et al showed that the risk of preterm delivery was four times less in mothers who received DHA supplements during pregnancy [13]. The mechanism proposed for the prolongation of gestational length include decreased formation of prostaglandins PGE2, and PGF2 ? due to decreased arachidonic content of cell membrane due to DHA supplementation. This was substantiated by the finding of Facchinetti, that under conditions stimulating inflammation, supplemental omega 3 fatty acids decrease PGE2 and PGF2 ? production in cultured decidual cells, which may reduce the risk of preterm premature rupture of membranes, the leading cause of preterm birth [14].

Pediatric Benefits

Pediatric benefits conferred by DHA include:

i) Improved cognitive development in the infant upto the age of 4 years.

ii) Higher intelligence quotient at 4 years of age.

iii) Improved psychomotor development index at 30 months of age.

iv) Improved visual maturation and acuity at 9 and 12 months of age.

v) Lowered diastolic and mean blood pressure at 6 years of age.

vi) Improved attention of the child during the first year and lowered frequency to get distracted during second year of life [15].

DHA deficiency

Deficiency of DHA can have several important negative effects, including change in the biochemistry and function of brain and retina. Deficiency of DHA is associated with reduced visual acuity, impaired vision, abnormal EEG, and stereotypic behavior. DHA deficiencies are also associated with fetal alcohol syndrome, attention deficit hyperactivity disorder, optic fibrosis, phenylketonuria, unipolar depression, aggressive hostility and adrenoleucodystrophy. Decrease in DHA in the brain are associated with cognitive decline and depression. Thus in order that the benefits of DHA are obtained, the mother and child must ensure that their DHA status is well maintained [16].

DHA recommendations

While a recommended daily value is yet to be established by the FDA, the National Institute of Health recommends 300mg per day of DHA in pregnant and nursing women [6].

Conclusion

Before birth, DHA is transported across the placenta to the growing fetus. After birth, breast milk is the major source of DHA for the infant. The critical period for DHA supplementation for promoting neurodevelopment and visual development is during the last trimester of pregnancy and first 2 postnatal years - the period of "brain growth spurt". Thus maternal supplementation of DHA during pregnancy, as well as lactation will ensure that the growing fetus and the breast fed infant receives adequate DHA, as DHA is vital for both the mother and the child.

References

I. Jensen CL. Effects of n-3 fatty acids during pregnancy and lactation. *Am J Clin Nutr 2006;83:1452S-1457S*.

2. Spector AA. Essentiality of fatty acids. *Lipids 1999;34:S1-3*.

3. Singh M. Essential fatty acids, DHA and human brain. *Indian J Pediatr 2005;72:239-42*.

4. Salem N, Litman B, Kim HY et al. Mechanisms of action of docosahexaenoic acid in the nervous system. *Lipids 2001;36:945-59*.

5. Litman BJ, Niu SL, Polozova A et al. Role of docosahexaenoic acid containing phospholipids in modulating G protein coupled regulatory pathways. *J Mol Neurosci 2001;16:237-42; discussion 279-84*.

6. WHO and F AO Joint consultation: fats and oils in human nutrition. *Nutr Rev 995;53:202-05*.

7. Turner N, Else PL, Hulbert AJ. Docosahexaenoic acid (DHA) content of membranes determines molecular activity of the sodium pump: implications for disease states and metabolism. *Naturwissenschaften 2003;90:521-3*.

8. Sergeeva M, Strokin M, Reiser G. Regulation of intracellular calcium levels by polyunsaturated fatty acids, arachidonic acid and docosahexaenoic acid, in astrocytes: possible involvement of phospholipase A2. *Reprod Nutr Dev 2005;45:633-46*.

9. Hamilton L, Greiner R, Salem N Jr. n-3 fatty acid deficiency decreases phosphatidylserine accumulation selectively in neuronal tissues. *Lipids 2000;35:863-*

10. Hibbeln JR. Sea food consumption, the DHA content of mothers' milk and prevalence rates of postpartum depression: a cross-national ecological analysis. *J Affect Disord 2002;69:15-29*.

11. Hibbeln JR, Davis JM, Heron J et al. Low dietary omega-3s and increased depression risk in 14,541 pregnancies. American Psychiatric Association Annual Meeting, 2003, San Francisco, CA, New Research Abstracts [Abstract NR418].http://archive.psych.org/edu/other_res/lib_archives/archives/meetings/AMN/2003nra.cfm (Accessed on November 17, 2008)

12. Rossi E, Costa M. Fish oil derivatives as a prophylaxis of recurrent miscarriage associated with anti phospholipid antibodies (APL): a pilot study. *Lupus 1993;2:319-23*.

13. Olsen SF, Grandjean P, Weing P et al: Frequency of seafood intake in pregnancy as a determinant of birth weight: evidence for a dose dependent relationship. *J Epidemiol Community Health 1993;47:436-40*.

14. Facchinetti F, Fazzio M, Venturini P. Polyunsaturated fatty acids and risk of preterm delivery. *Eur Rev Med Pharmacol Sci 2005:9:41-48*.

15. Helland IB, Smith L, Saarem K et al. Maternal supplementation with very long chain n-3 fatty acids during pregnancy and lactation augments children's IQ at 4 years of age. *Pediatrics 2003;11:e39-44*.

16. Denomme J, Stark KD, Holub BJ. Directly quantitated dietary (n-3) fatty acid intakes of pregnant Canadian women are lower than current dietary recommendations. *J Nutr. 2005 Feb;135:206-11*.

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