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Review Article

Omega 3 Fatty Acids: An Adjunct for Schizophrenia

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ABSTRACT

***Aim*:** The treatment of schizophrenia is commonly viewed from a pharmacological and social perspective, but issues of broader lifestyle are frequently examined. Effective antipsychotic medicines are available that usually only partially relieve the symptoms. Recently, the omega-3 fatty acid EPA has been shown to be a powerful adjunct. This article focuses on omega 3 fatty acid and its importance as adjunct in schizophrenia treatment.

Background: omega 3 fatty acid is a essential poly unsaturated fatty acid consist of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Various studies depicted that omega 3 Fatty acid in the cell membrane of schizophrenic patient, if it added in diet there will be positive outcome from the effect.

***Methods*:** In this review paper, schizophrenia and significance of omega 3 fatty acid is discussed. The omega 3 fatty acid metabolism, physiology, sources, review on the significance of omega 3 fatty acid as a adjunct for schizophrenia.

***Discussion*:** A food rich in omega acids needs to be given for the schizophrenic patients. The health effects of omega 3 fatty acids come mostly from DHA and EPA. Preliminary evidence suggests that people with schizophrenia may have improvement from symptoms when omega 3 fatty acids are given.

***Conclusion*:** The omega 3 fatty acids play a crucial role in brain function, as well as normal growth and development. There is no doubt that cerebral lipids in particular, have significant direct and indirect actions on cerebral function, hence it has significant effect on schizophrenia.

Key words: Omega 3 fatty acid, Schizophrenia

INTRODUCTION

Fatty acids can be broadly divided into saturated, monounsaturated and polyunsaturated. The polyunsaturated fatty acids (PUFAs) have the most functional significance and are divided into two main types: the n6 and the n3. The distinction between n3 and n6 relates to the position of the first double bond in the carbon chain. The more double bonds, the more unsaturated the fatty acid. Arachidonic acid and docosahexaenoic acid (DHA) are the most abundant fatty acids in the brain. Arachidonic acid, dihomogamma-linolenic acid and eicosapentaenoic acid (EPA) are also important as cell-signalling and enzyme-regulating molecules and as precursors of eicosanoids (prostaglandins, thromboxanes and leukotrienes).[1]

Omega-3 is an anti-inflammatory[2] essential fatty acid play a crucial role in brain function, as well as normal growth and

development.[3,4] Omega 3 fatty acids are highly concentrated in the brain and appears to be important for cognitive (brain memory and performance) and behavioral function. Symptoms of omega 3 fatty acids deficiency include fatigue, poor memory, dry skin, heart problems, mood swings or depression and poor circulation.[5] They are not synthesized by the body but only available through the diet.[6] Neuronal cell membrane structure and metabolism is dependent on blood levels of these fatty acids.[7]

The two omega 3 fatty acids are Eicosapentaenoic acid (EPA) and Docosahaxaenoic acid (DHA). It has important function in central nervous system. The health effects of omega 3 fatty acids are come from EPA and DHA. DHA is a major structural component of neuronal membranes and changing the fatty acids composition of neuronal membrane leads to functional changes in the activity of receptors and other proteins embedded in the membrane phospholipids. EPA has important physiological function that affects neuronal activity.[8]

Metabolism:

The fat found in foods consists largely of a heterogeneous mixture of triacylglycerols (triglycerides)--glycerol molecules that are each combined with three fatty acids. The fatty acids can be divided into two categories, based on chemical properties: saturated fatty acids, which are usually solid at room temperature, and unsaturated fatty acids, which are liquid at room temperature. No fatty acids found in food are considered essential because they can all be synthesized from the shorter chain fatty acids.[9]

Following ingestion, fatty acids undergoes digestion in the small intestine which allows for absorption, transport in the blood, and subsequent assimilation within tissues themselves through the body (including brain, retina, heart, and other tissues). First, the fatty acids converted to alpha-linolenic acid (ALA) and linoleic acid (LA), it can be further converted in the liver to the long chain, more unsaturated n-3 (omega 3 fatty acids ALA) and n-6 (omega 6 fatty acid LA) by a complex set of synthetic pathways that share several enzymes.[10]

The omega-6 fatty acid LA is converted to gamma-linolenic acid (GLA), an omega- 6 fatty acid that is a positional isomer of ALA. GLA, in turn, can be converted to the longer chain omega-6 fatty acid, arachidonic acid.[11]

The omega-3 fatty acid ALA can be converted to the long-chain omega-3 fatty acid, eicosapentaenoic acid (EPA). EPA can be elongated to docosapentaenoic acid (DPA), which is further elongated, desaturated, and beta-oxidized to produce docosahexaenoic acid (DHA). EPA and DHA are also precursors of several classes of eicosanoids and docosanoids, respectively, are known to play several other critical roles.[11]

Evidence that fatty acid metabolism is abnormal in schizophrenia.[12]

- Reduced fatty acid levels in cell membranes
- Reduced skin flush response to topical niacin
- Abnormal electro retinogram
- Increased levels of calcium-independent phospholipase A2 in blood and brain
- Abnormal 31P magnetic resonance spectroscopy of brain phospholipid

Common Physiological Functions:

As stated earlier, fatty acids play a variety of physiological roles. The specific biological functions of a fatty acid are determined by the number and position of double bonds and the length of the acyl-

chain. Both EPA and AA are precursors for the formation of a family of hormone-like agents called eicosanoids.[13]

Eicosanoids are rudimentary hormones or regulatory molecules that appear to occur in most forms of life. However, unlike endocrine hormones, which travel in the blood stream to exert their effects at distant sites, the eicosanoids are autocrine or paracrine factors, which exert their effects locally- in the cells that synthesize them or adjacent cells. Processes affected include the movement of calcium and other substances into and out of cells, relaxation and contraction of muscles, inhibition and promotion of clotting.[11]

Physiological function related to schizophrenia:

About 50 to 60 percent of the dry weight portion of the human brain consists of lipids. Omega -3 fatty acids, particularly EPA and DHA, play important roles in the development and maintenance of normal central nervous system (CNS) structure and function. DHA is a major constituent of neuronal membranes, making up about 20 percent of the brain's dry weight. Synapses contain a high concentration of DHA, which appears to play a role in synaptic signal transduction. DHA is also important for normal cognitive development, may function in the brain to protect against ischemic damage. [12]

Mode of action:

The levels of omega 3 fatty acids were reduced cell membranes of patients with schizophrenia. Abnormal neurotransmission has been found in sufferers of schizophrenia and schizophrenic symptoms may be the result of altered neuronal membrane structure. Hallucinations and delusions are two telltale signs of schizophrenia. Therefore, it was postulated that supplementation of omega 3 fatty acids may be of therapeutic benefit.[14]

Evidence of abnormalities of EFAs has been found in erythrocyte membranes and cultured skin fibroblasts of patients with schizophrenia, and abnormal retinal function and niacin skin flush tests (markers of omega-3 polyunsaturated fatty acid depletion) have also been reported.[14]

A cross-national ecological analysis of international variations in outcome of schizophrenia in relation to national dietary practices showed that high consumption of sugar and of saturated fat is associated with a worse long-term outcome of schizophrenia. It is known that a high sugar, high fat diet leads to reduced brain expression of brain-derived neurotrophic factor (BDNF) which is responsible for maintaining the outgrowth of dendrites. Low brain BDNF levels also lead to insulin resistance which occurs in schizophrenia and is associated with diseases of the metabolic syndrome. It appears that the same dietary factors which are associated with the metabolic syndrome, including high saturated fat, high glycaemic load, and low omega-3 PUFA, may also be detrimental to the symptoms of schizophrenia, possibly through a common mechanism involving BDNF.

Omega 3 fatty acid for schizophrenia:

Schizophrenia is a severe mental illness with a prevalence of 1-2% is characterized hallucinations, delusions, disorganized thought and behaviour, flattened mood, poverty of speech, and deficits in goal directed behaviours. O*mega* 3 fatty acids have membrane-enhancing capabilities in brain cells. It plays a function in the fortification of the myelin sheaths. Omega-3 its name, conclude that "DHA is structure; EPA is function. It is helping the brain to repair damage by promoting neuronal growth. In the prefrontal

cortex (PFC) of the brain, low brain *n*−3 fatty acids are thought to lower the dopaminergic neurotransmission, possibly contributing to the negative and neuro-cognitive symptoms in schizophrenia. This reduction in dopamine system function in the PFC may lead to over activity in dopaminergic function in the limbic system of the brain, which is suppressive controlled by the PFC dopamine system, causing the positive symptoms of schizophrenia. This is called the *n*−3 polyunsaturated fatty acid/dopamine hypothesis of schizophrenia. This mechanism may explain why *n*−3 supplementation shows effects against positive, negative and cognitive symptoms in schizophrenia. [15]

Biochemical studies have shown reduced levels of omega 3 fatty acids in red blood cell membranes in schizophrenic patients. Various studies reported therapeutic benefit from omega 3 fatty acids, particularly when eicosaphentaenoic acid is added on to existing psychotropic medications. The phospholipids in the neuronal membranes of the brain are rich in highly unsaturated essential fatty acids. It has been hypothesized that abnormalities of phospholipid metabolism are present in patient with schizophrenia and the omega 3 fatty acids and eicosapentaenoic acid in particular, may have a role in treating this illness. [15]

The Amminger et al study demonstrates a significant benefit of omega-3 fatty acid supplementation for preventing or delaying transition to psychosis in ultra-high risk adolescents. One important implication of this finding that deserves elaboration is that it provides support for omega-3 fatty acid deficiency as a 'risk factor' for schizophrenia. A risk factor, unlike a risk marker, implies a causal link with the illness, correction of which reduces the risk of developing the illness. [11]

Schizophrenia is a chronic brain disorder; it is structurally and functionally coupled to several cortical and subcortical brain regions participating in cognitive, emotional and motivational behavior. DHA is a major omega-3 polyunsaturated fatty acid in the phospholipid of neuronal cell membranes . EPA, in contrast, is not present in neuronal cell membranes. Because of this, DHA and EPA have different physiological effects on neuronal function. Thus, there is good evidence that changing the DHA content of neuronal cell membranes can alter densities of dopamine, serotonin and muscarinic receptors in brainneurotransmitter and neuromodulatory effects. It has been shown repeatedly that schizophrenic patients have reduced cell membrane levels of polyunsaturated fatty acids, particularly DHA and arachidonic acid (AA). [11]

Use of omega-3 poly-unsaturated fatty acids especially EPA in schizophrenia has shown significant improvement in both schizophrenic symptoms and tardive dyskinesia. Interestingly clozapine, one of the atypical antipsychotics, has been shown to increase the concentration of such fatty acids in red blood cell membranes, thereby suggesting that atypical antipsychotics may contribute to the normalization of neuronal membrane function by increasing their polyunsaturated fatty acid content. Thus omega 3 fatty acids may provide an important and novel approach to the development of antipsychotics in the future. [12]

Dietary Sources and Requirements:

Both ALA and LA are present in a variety of foods. LA is present in high concentrations in many commonly used oils, including safflower, sunflower, soy, and corn oil.

ALA is present in some commonly used oils, including canola and soybean oil, and in some leafy green vegetables.

Humans do not have the enzymatic machinery required to synthesize omega-3 fatty acids, they must be obtained from the diet. The sources are as follows: [11-13]

- Foods rich in omega 3 fatty acids, including whole grains, fresh fruits and vegetables, fish, olive oil, garlic, as well as, moderate wine consumption.
- EPA and DHA are found in cold water fish such as salmon, mackerel, halibut, sardines, tuna and herring.
- ALA is found in flax seeds, flax seed oil, canola oil (rape seed), soy beans, soy bean oil, pumpkin seeds, pumpkin seed oil, purslane, perilla seed oil, walnuts and walnut oil.
- Other sources of omega 3 fatty acids include sea life such as krill and algae.

CONCLUSION

Schizophrenia is a chronic disorder shows delusion and hallucination as primary symptoms. Various studies conclude that omega 3 fatty acid has benefit effect for the schizophrenic patient. Currently no omega 3 fatty acid prescription is licensed. The concept of adjunct of omega 3 fatty acids needs evidence based study and it also a clinically significant so, it is recommended for lot of research evidence.

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