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Review Article

Omega-3 fatty acids and the treatment of depression: a review of scientific evidence

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ABSTRACT

Depression is a condition in which an individual feels lethargic, irritable, and guilty, has difficulty and trouble, no enjoyment in life, mood swings, sometimes suicidal ideation and thoughts, and loss of pleasure in activities. There are hundreds of millions of individuals suffering from major depression disorder all over the world. This leads to a considerable portion of the economy going for treatment as large amounts of money are spent on drugs every year. Pharmaceutical drugs are not very effective and they also have side effects that compound the problem. There are number of studies which shows that omega-3 fatty acids are proving to be very effective against the treatment of major depression disorder and other psychiatric disorders. However, the data regarding the efficacy of omega-3 fatty acids in depression treatment are conflicted. This article reviews the recent research showing the relation between omega-3 fatty acids and depression. The roles of the omega-3 fatty acids in the treatment of depression are being studied with increased pace in the last decade due to heightened prevalence of depression. It is emphasized that omega-3 fatty acids have no record of associated side effects, which deserves greater attention for further research.

1. Introduction

Globally, depression is considered the most widespread disease.[1] Depression is a complex, polygenic, heterogeneous, multifactorial brain disorder in which the mood of the person is affected, so it is also known as mood disorder. Depression includes symptoms such as anxiety, feelings of lethargy, irritability, or guilt, difficulty in concentrating, no or less enjoyment in life, fatigue, loss of interest in daily activities, and loss of pleasure activities.[2,3] Depression can occur in any individual irrespective of age. Depression disorders are prevalent in the general population, besides it is also found in comorbid with other disorders, which increases its burden.[4,5] Owing to its burden, it is a widely studied disorder with emphasis on its treatment strategy. A number of natural and synthetic antidepressants have been used to treat depression. In the last decade omega-3 fatty acids have gained special attention regarding their efficacy in depression treatment.

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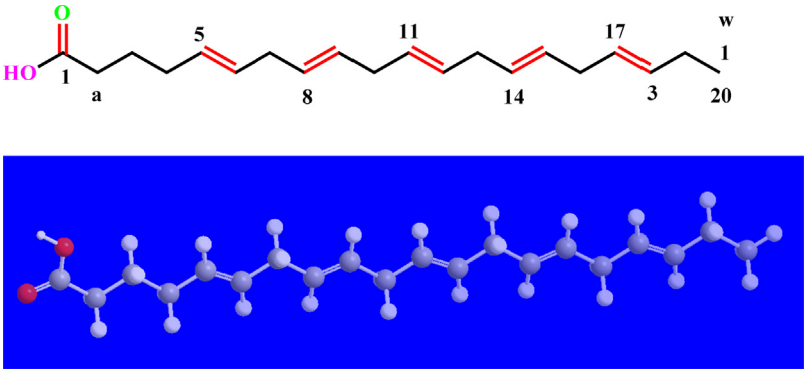

Fig. 1 – Optimized three-dimensional molecular geometry of eicosapentaenoic acid.

Omega-3 fatty acids are polyunsaturated, containing more than one double bond. They are called omega-3 because their first double bond is placed at the third carbon atom when counting from the methyl end of the fatty acid. In the USA, it has been found that, in both children and adults, omega-3-fatty acids are the most frequently used nonvitamin supplement.[6] Basic, translational, and clinical research efforts are taking place to clarify whether this important nutritional factor plays a role in mental illness and health. There are some epidemiological data emphasizing that people who usually consume a diet with rich content of omega-3-fatty acids are at lower risk of developing major depression, prenatal depression, and bipolar depression.[7–9] Omega-3 fatty acids are scarce in the western diet as compared with other countries. The contribution of omega-6-fatty acids, however, has developed very much with an emphasis on soy and genetically modified organisms in food production.[10] It is noteworthy to mention here that factory farming of domesticated animals (including fish) has led to changes in the animal diet composition creating products having lower omega-3 fatty acid contents than those produced earlier. The presence of a rich content of omega-6 fatty acids in western diets is usually associated with proinflammation.[11] The most appropriate amount of omega-3 fatty acid is a difficult target to achieve, because of genetic variations and heterogeneity among individuals.

2. Omega-3 fatty acids and depression

Omega-3 fatty acids are known to be important for normal metabolism. Most mammals are unable to synthesize omega-3 fatty acids on their own. However, through diet they are able to obtain the shorter chain omega-3 fatty acids such as α-linolenic acid consisting of 18 carbon and three double bonds and later on use them to produce eicosapentaenoic acid (EPA; Fig. 1) which is considered to be a more important fatty acid that consists of 20 carbons and five double bonds. From EPA they further synthesize docosahexanoic acid (DHA; Fig. 2), which is considered more crucial and consists of 22 carbons and six double bonds.

Cell signaling and structure of the cell membrane are changed by omega-3-fatty acids, which demonstrates that an omega-3-fatty acid can act as an antidepressant. An attempt to examine the quantity of omega-3 fatty acids in the brain to investigate its effects on neurogenesis was made by He et al.[12] They generated a transgenic mouse that converts omega-6 fatty acids into omega-3 fatty acids that help in increasing the quantity of DHA in the brain, which is linked with higher neurogenesis in the hippocampus, and show better tests of learning and memory.[12]

Genetic polymorphism that provides a greater risk of developing a depressive episode when treated with proinflammatory cytokines has only begun to be examined in recent times. Inflammatory processes that occur during the course of treatment with α-interferon are linked with a high onset of depression. Genotypes related with elevated levels of EPA and DHA in response to immune activity are known. It is noted that genetic polymorphisms through which omega-3 fatty acid metabolism is influenced, consist of genes FADS1 and FADS2 that code for desaturases, which are widespread and required in omega-3 and omega-6 fatty acid metabolism.[13] Some haplotypes are linked with more inflammation, having

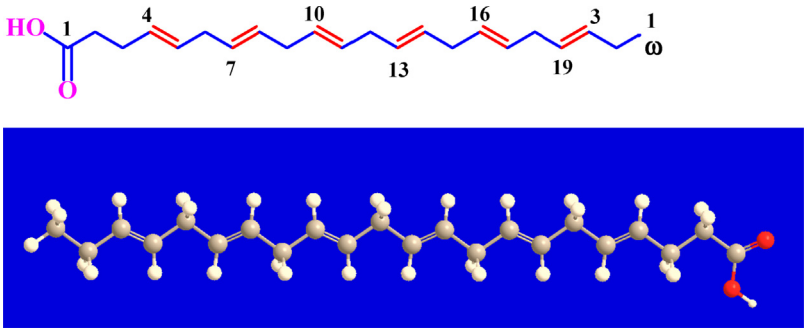

Fig. 2 – Optimized three-dimensional molecular geometry of docosahexaenoic acid.

greater risk of developing cardiovascular disease.[14] Such haplotypes are more likely to add inter-individual differences in more than one trait or features such as variation in intelligence and response to omega-3 fatty acid treatment. Whether these genes are linked with onset of depression or whether they can be used to find an antidepressant treatment response to omega-3 fatty acid are yet to be studied. Possible links exist between the consumption of seafood and the rate of incidence of disorders such as bipolar I disorder, bipolar II disorder, and bipolar spectrum disorder.[9] Through analysis of seafood consumption, DHA content from mother's milk, and the incidence rate of *postpartum* depression, it has been found that consumption of seafood, which is a rich source of omega-3 fatty acids results in a lower prevalence of depression. Depression is almost 50 times more frequent in South Africa with a prevalence of 24.5% than in Singapore (0.5%), compared with a mean global incidence of 12.4%. Increased quantities of DHA in mother's milk and seafood consumption can lead to lower prevalence of *postpartum* depression. It is evident that the higher consumption of seafood by lactating mothers would lead to higher DHA content in the mother's milk. By contrast, the arachidonic acid, EPA, content in a mother's milk or noticeable seafood consumption are not found to be related to occurrence of *postpartum* depression.[7]

A relationship between depression and the ratio of omega-3 and omega-6 fatty acid concentration of erythrocyte phospholipids and plasma was examined by Adams et al[15] in 20 moderate to severe depressed patients. The ratio of erythrocyte arachidonic acid to EPA in a significant correlation with depression severity was observed. In addition, a significant negative correlation was observed between erythrocyte EPA and depression. The authors, however, concluded that these results cannot be explained simply by differences in the dietary intakes of EPA.[15]

A screening of 3,884 individuals for depressive symptoms at an age of 60 years or older was done in Rotterdam. A comparison of 264 individuals with symptoms of depressive symptoms against 461 reference individuals was made.[16] It was observed that the patients who experienced severe symptoms of depression contain a low concentration of omega-3 fatty acids and a considerably higher concentration of omega-6 fatty acids. Such relationships seem to have considerable importance to disorders such as inflammation and atherosclerosis.[15,16]

In a study by Maes et al[17], a comparison was made of 36 patients with major depression, 14 with minor depression, and 24 individuals with no reports of depression.[17] A significantly higher proportion of serum cholesteryl esters and phospholipids such as arachidonic acid to EPA and increased levels of omega-6/omega-3 proportion were found in those with major depression, than in the those having no signs of depression or minor depression. However, a significantly lower level of α-linolenic acid and decreased overall levels of omega-3 in serum cholesteryl esters and reduced EPA in both phospholipid fractions and serum cholesteryl ester were found in the same study. In the Maes et al[17] study, 34 patients with major depression and 14 normal volunteers were examined for their omega-3 and omega-6 levels. A significantly strong association between reduced EPA and overall omega-3 levels and an increased omega-6/omega-3 proportion in phospholipids and cholesteryl esters was found in individuals experiencing major depression. It has been suggested by a number of researchers that major depression is the outcome of the significantly lower concentration of omega-3 fatty acids in the body. However, a considerable degree of boosting of depressive symptoms is also the result of higher levels of monosaturated fatty acids and omega-6 fatty acids in phospholipids. In another study, an estimation of erythrocyte membrane fatty acids in 10 depressed patients and 14 comparison individuals was made, in which researchers had taken into consideration full dietary analysis, in addition to age, sex, stress level, and smoking habits.[18] It was reported that erythrocyte membrane omega-3 quantity was considerably lower in the depressed patients. In another study by Peet et al,[19] similar results were repeated where the researchers studied 15 patients having depression and 15 properly matched healthy individuals as comparison group. It was observed that omega-3 levels of erythrocytes in depressed patients were considerably poorer. The relationship between polyunsaturated fatty acids in mildly depressed individuals was examined by Mamalakis et al.[20] In this study, 247 healthy adults were examined; it was observed that patients with mild depression had lower DHA levels in the adipose tissue than the individuals without depression. An increased amount of EPA and DHA intake is related to increased gray matter in those regions of the brain with an important role in regulating depression and other mood disorders.[21] It has been shown in various controlled clinical studies, that depression patients who receive omega-3 fatty acids have shown a progress in lowering depression as compared with those assigned a placebo.[22,23]

It should be noted that lower levels of membrane related omega-3 fatty acid and enhanced levels of omega-6 fatty acids may boost the rate of depression and alter the functioning of neurons. Analogous proportions of omega-3 and omega-6 fatty acid, considered to be due to dietary intake, may clarify the low prevalence of mood disorders in the east, where large levels of fatty fish are consumed, against rates in the west where elevated levels of saturated fat acts as nutritional support.

Formation of neurotransmitters and prostaglandin is affected by omega-3 and omega-6 fatty acid proportion, which is very important in the maintenance and regulation of normal functioning of the brain.[24] There are other drugs that are used in the treatment of depression; lithium carbonate, for example, is used for the treatment of bipolar disorder. However, it has been observed that arachidonic acid turnover was lowered by 75% within brain phospholipids in rats fed lithium chloride for 6 weeks, whereas there were no changes observed in the production of rat omega-3 fatty acids. Valproic acid when given therapeutically on a long-term basis leads to a decline in arachidonate production in rat brain. The downregulation of gene expression and action of enzyme cytosolic phospholipase A2, an enzyme that particularly releases arachidonic but not omega-3 fatty acid from phospholipids, corresponded to the decline of lithium's arachidonate production.

The quantity of cyclooxygenase-2 and downstream metabolite prostaglandin E2 in the brain is reduced by lithium. This result indicates that lithium and anticonvulsants act by targeting part of the arachidonic acid inflammatory pathway, which may be highly expressed in mania.[25]

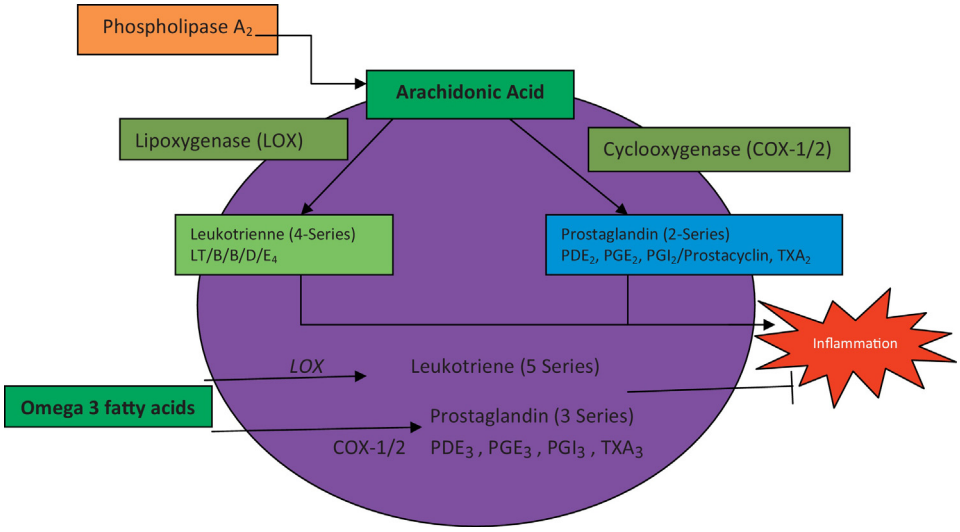

Fig. 3 – Diagrammatic view of omega-3 fatty acid inflammation pathway. Possible molecular mechanism of action of omega-3 fatty acids.

DHA and EPA seem to reduce the synthesis of eicosanoids from their precursor arachidonic acid by two possible pathways. The first is that they combine with arachidonic acid for amalgamation into membrane-based phospholipids, declining both cellular and plasma concentrations of arachidonic acid. The other way may be that for cyclooxygenase enzyme system EPA may compete with arachidonic acid and help block the process of proinflammatory eicosanoid synthesis from arachidonic acid (e.g., prostaglandins, thromboxanes and leukotrienes), prostaglandin E2 and thromboxanes B2. DHA and EPA also hamper release of proinflammatory cytokines, such as interferon-γ, tumor necrosis factor (TNF)-α, interleukin (IL)-1β, IL-2, and IL-6, which is determined by eicosanoid discharge and also linked with depression and its form of bipolar illness (Fig. 3).

EPA is also believed to decrease IL-1 and TNF-α by inhibiting nuclear factor-κB. In addition to this, EPA inhibits the upstream mitogen activated protein kinase (MAPK) pathway, which then results in the reduction in the activity of protein-1 transcription factor. It is proposed that omega-3 fatty acids have a role in transcriptional regulation by phosphorylation inhibition of JNK, ERK, and MAPK proteins, which downregulates protein-1 expression.[26] Furthermore, omega-3 fatty acids are proposed to have a role in restraining nuclear factor-κB nuclear translocation secondary to IκB phosphorylation[27] (Fig. 4).

CYP2C9 and CYP2C19 are two drug metabolic hepatic enzymes. It has been shown that EPA has got a prohibitory effect on both. At high dosage, it may also hamper the activity of CYP2D6 and CYP3A4, which are considered major enzymes in drug metabolism.[28]

3. More recent insights on omega-3 fatty acids and depression

A growing number of reports on omega-3 fatty acids and depression from the past few years have been added to the literature. There is evidence that omega-3 fatty acids are closely linked to mental health.[29] In addition to this there is evidence that they may be useful as a supplement for the treatment of bipolar disorder related depression[30] and evidence that EPA-supplemented food is helpful in patients suffering depression are well documented.[31] By contrast, due to participant recall and diet-related systematic differences there is an important complexity in interpreting the literature to specific conclusions.[32]

For major depressive disorder, omega-3 fatty acids have not, so far, proved significant as a monotherapy.[33,34] An increase in the symptoms of depression is correlated with lower intakes of dietary omega-3 fish oil as revealed by various epidemiological research studies. Individuals experiencing the symptoms of depression also found to have lower serum concentrations of essential fatty acids, which was also revealed by several studies of EPA and DHA.[35]

In order to combat this problem, some foods are usually recommended. Fish with red flesh such as salmon or mackerel are a good source of omega-3 oils. Omega-3 is also present in small amounts in some plant oils such as flaxseed oil. Omega-3 oils are fatty acids in which EPA and DHA are the two most useful components. The more important is EPA, which is usually considered to provide more health benefits. The long chains of unsaturated fatty acids from omega-3 oils are regarded as important for health because they are believed to decrease cholesterol levels and clear fatty deposits in the arteries. The cardiovascular system is also benefitted,[36] and it also helps in exacerbating dysfunctions in insulin receptor signaling in the brain and cognition.[37]

There is also significant evidence which support that omega-3 oils can be used in the treatment for schizophrenia and bipolar depression disorder. Besides treating depression omega-3 fatty oils may also be useful in treating the symptoms of dementia.[38] Omega-3 oils are approved if a depressed person's diet appears to be deficient of it. Omega-3 oil pills are used in combination with selective serotonin reuptake inhibitors (SSRIs) and are considered as more standard

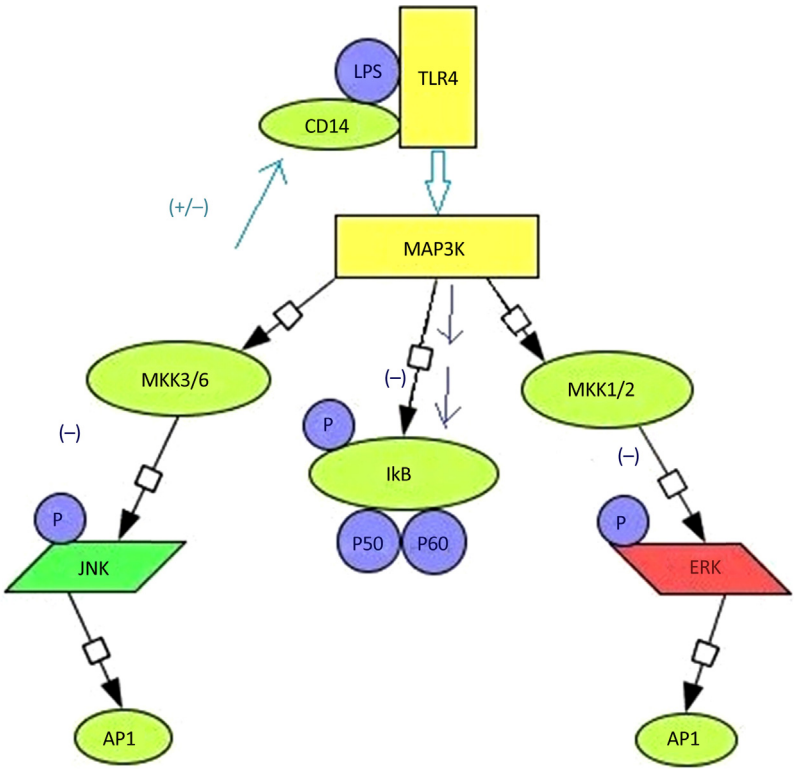

Fig. 4 – Omega-3 fatty acid transcriptional regulation mechanism. ERK, extracellular signal-regulated kinase; JNK, c-Jun N-terminal kinase.

treatment for depression as recommend by some physicians.

One study showed that using omega-3 fatty acids from marine sources results in lowering of inflammation markers such as C reactive proteins, TNF-α and IL-6 in the blood.[39]

Recently, Patrick et al[40] proposed a model whereby insufficient levels of vitamin D, omega-3 fatty acids, and various other genetic factors that play a role during critical periods of development, lead to dysfunction in serotonin activation and function, which may be an important underlying mechanism that may lead to depression and other neuropsychiatric disorders. This model further suggests that optimizing the intake of omega-3 fatty acids from marine sources and vitamin D may help in modulating and preventing the severity of brain functions.[40]

A recent review by Deacon et al[41] formed variable conclusions by systematic review and meta-analysis. Results from the research done on the effects of omega-polyunsaturated fatty acids on the depression related mood disorder have led to variable results.[41] Furthermore as the findings from various research studies about omega-3 fatty acids and the treatment of depression are conflicted. Keeping in view the conflicting results from a number of studies there is a need for more research on omega-3 fatty acids and depression treatment through well-designed experiments.

A number of nutrients was reviewed against pediatric depression.[42] The author was concerned about the lack of high quality study examining the nutrients such as omega-3 fatty acids, S-adenosyl methionine, vitamin C, vitamin D, zinc, iron, and B vitamins as antidepressants.[42] High quality studies involving an in depth analysis about depression treatment based on such nutrients is encouraged.

In a two-site placebo-controlled, randomized, double-blind clinical trial,[43] two omega preparations enriched with EPA versus DHA were examined as monotherapy for major depression disorder. The authors found neither EPA-enriched nor DHA-enriched omega-3 to be superior to placebo for the treatment of major depression disorder.[43]

There is evidence that intake of omega-3 fatty acid is associated with reduction in the depression-like symptoms most often in women.[44] A recent study examined the effect of diet enriched with omega-3 fatty acid in rats has shown that it helps promote behavioral escape changes, which is consistent with enhanced adaptive management of stressful events suggesting that omega-3 fatty acids can help in preventing the onset of stress-related depressive disorders.[45] A study was undertaken to address the question of how maternal diet influences development and puberty. The researchers examined the effect of DHA sufficient and deficient diets on rat gestation, lactation and weaning periods; the findings suggest that increased resilience to emotional stressors and decreased propensity to mood disorders, which are common occurrences during adolescence, can be controlled by maintaining sufficient DHA levels in the diet throughout development.[46] High concentration of omega-3 fatty acids are also suggested to help in rebalancing the essential fatty acid composition of military diet, which can possibly help in reducing the psychiatric disorders such as depression, suicide, and impulsive aggression among military personal.[47] Research was conducted on nurses to manage their stress as

they were considered/reported to be most vulnerable for developing depression; the authors evaluated the additive effect of omega-3 fatty acid and mindfulness-based stress management. It was recommended that omega-3 fatty acids and mindfulness could be maintained for healthy mental state in nurses, for stress management program and reducing depression in nurses.[48]

In a randomized controlled trail, prenatal stress in African American women was examined in association with supplementation of omega-3 fatty acid DHA. It was concluded that DHA can attenuate the effects of late-pregnancy maternal stress.[49]

Low EPA levels are found to be associated with heightened trait aggression and impetuous patients of major depression with history of substance-use disorder comorbidity.[50] In adolescents with SSRI-resistant major depression disorder, there is robust DHA deficiency that can be improved by supplementation of fish oil, which is well tolerated and helps in increasing long chain omega-3 fatty acids status and boosts SSRI antidepressant effects.[51] In patients of hepatitis C depression is often found to be associated with interferon-α therapy. In examining the effect of omega-3 ECA and DHA, it was observed that ECA but not DHA significantly lowers the incidence of depression in patients receiving interferon-α therapy.[52] Fish oil supplementation during critical prenatal and postnatal periods helps to diminish anxiety, cognitive dysfunction and depression-like behaviors induced in rats by olfactory bulbectomy.[53]

Omega-3 fatty acids were evaluated with and without SSRI fluvoxamine and the findings suggest that the patients treated with a combination of omega-3 fatty acids and fluvoxamine showed a significant difference compared with those treated with fluvoxamine alone in improving depression symptoms.[54] Among women in the USA, depressed symptoms were examined in relation to intake of omega-3 fatty acids and omega-6 fatty acids. Higher intake of omega-3 fatty acids than omega-6 fatty acids was found to be associated with decreased risk of heightened symptoms of depression.[55]

Omega-3 fatty acids—mostly DHA—were also found at increased levels in brain of fat-1 transgenic mice and is suggested to have influence on depression and mood. Further it is suggested that omega-3 fatty acids, particularly DHA helps in the hippocampal neurogenesis and may help to treat and prevent depression.[56] Boosting of standardized antidepressant levels of omega-3 fatty acids results an apparent improvement in symptoms of depression. Improvement of depression symptoms by using fatty acids were found proportional to using potential therapeutic agents such as lithium and lamotrigine.[57] Omega-3 fatty acids such as EPA in comparison to DHA or placebo were observed to be of greater efficacy in adjunctive treatment in mild-to-moderate depression.[58,59]

4. Ethyl-EPA depression treatment

One study[60] conducted a double-blind, placebo-controlled, randomized clinical trial among middle-aged women who were having psychological distress and depressive symptoms and were using ethyl-EPA (E-EPA) and supplementation against placebo. It was observed that psychological distress and depressive symptoms improved significantly more with E-EPA than placebo.[60]

Another randomized double-blind placebo-controlled study examined the efficacy of E-EPA in depression treatment and bipolar depression patients in which the E-EPA was found to be an effective and well-tolerated intervention in bipolar depression.[61]

E-EPA is a synthetic derivative of EPA that has been widely studied for its benefits on health. E-EPA is widely used and is believed to exhibit beneficial antipsychotic and antidepressive effects, so it receives special attention in the field of psychiatry.[62]

In psychiatric disease such as schizophrenia, E-EPA has been examined in a number of trials,[63–69] although the evidence for recommendation of its use is still weak.[22] As omega-3 fatty acids have been investigated to act as inflammatory agents. Clinical depression has been found to have an association with low-grade inflammation.[19,70–73] A number of clinical trials using E-EPA have been done to test this hypothesis. Omega-3 fatty acids were observed to smoothen the rigid cell membrane in participants.[74] Studies also show that E-EPA has antidepressive properties that have demonstrated efficacy against bipolar depression.[60]

5. Conflicts surrounding omega-3 fatty acid and depression

Conflicting results have been reported in some studies, in which depression prevalence and severity after myocardial infarction were evaluated by the supplementation of the omega-3 fatty acids ECA and DHA. No effects on the symptoms of depression were reported.[75,76] Another conflicting result from a study was reported in which the effects of fish oil and omega-3 polyunsaturated fatty acid (PUFA) supplementation were examined on the anhedonic response and body weight in a chronic stress rat model. Neither fish oil nor omega-3 polyunsaturated fatty acid-enriched egg yolk phospholipid supplementation reversed disturbances caused by chronic mild stress in rats.[57]

An examination of whether there is an increase in the influence of serum base-brain derived neurotrophic factor in diabetes mellitus patients with major depression disorder using omega-3 E-EPA was made. No evidence in improvement of brain derived neurotrophic factor was reported with supplementation or E-EPA in depressed patients.[77]

Another study tested the efficacy of omega-3 E-EPA added as antidepressant medication as adjuvant, in the treatment of depressive symptom in adults of diabetes mellitus. The authors found no evidence for the efficacy of E-EPA to antidepressants.[78] No significant difference were observed on any outcome measure between omega-3 E-EPA and placebo group in double-blind, placebo-controlled trials.[79]

Many products such as prostaglandins that are involved in omega-3 fatty acids synthesis are found to have a role in regulating information. This has led to an attribution of the link between the omega-3 fatty acids and depression.[80] Involvement of omega-3 fatty acid in the regulation of inflammation has been supported by *in vivo*[81] and *in vitro* studies as well as studies involving meta-analytic approaches.[82] However,

despite many studies supporting the inflammation regulation, the exact nature and mechanism behind omega-3 and inflammation system in still not known, which has led to controversy.[83] Owing to the number of studies supporting claims of anti-inflammatory effects, it is commonly prevailed as a belief and is still lacking evidence. Although the evidence regarding the role of omega-3 fatty acids in the treatment of depression is growing with continuous research, due to the systemic differences in the diet and participant recall, there arises a noteworthy difficulty in the interpretation of the literature.[32] A number of meta-analyses led to the controversy on the effectiveness of omega-3 fatty acids, as the authors of such papers find heterogeneity among results which can be possibly explained by publications bias.[84,85] No significant benefit of omega-3 fatty acids in major depression disorder was suggested by the trials published by Bloch and Hannestad.[85] In the treatment of depression using omea-3 fatty acids, a significant correlation was observed between shorter trials of treatment and increased efficacy of omega-3 fatty acids, which further incriminates publication bias.[85] However, the empirical efficacy for considering the omega-3 fatty acids as an auspicious alternative for the treatment of depression has still many unsettled questions that need to be addressed,[86] Considering the conflicting results surrounding the omega-3 fatty acid efficacy, it is recommended that environmental history be traced before treatment that can help to use the specific approach, because environment can be the foremost factor for any behavioral disorder.[87] Many studies have proven potential benefit of the omega-3 fatty acids for treatment of wide variety of disorders such as neurological, cerebrovascular, cardiovascular, cognitive, and mood disorders, as well as metabolic disease. Considering the evidence from the clinical trial data omega-3 fatty acids deserves extensive deliberation and more comprehensive studies for treatment of depression.

6. Conclusion

The literature on omega-3 fatty acids and depression treatment consists of considerable claims about the efficacy of omega-3 fatty acids. However, there is a substantial number of studies that show no efficacy of omega-3 fatty acids against depression. This can possibly be explained by many factors that may be responsible for the variable results, such as variable experimental designs, differences in sample size, biological and genetic differences among patients, environmental variability, and variability in response to omega-3 fatty acids. Depression is a multifactorial disorder and depression due to insufficient omega-3 fatty acids diets can be of one type. Those patients who may have depression because of insufficient omega-3 fatty acids can respond well to the diet containing high levels of omega-3 fatty acids and can show positive signs regarding treatment of depression. However, for patients who have depression due to factors other than omega-3 fatty acids diet, expecting that type of depression can be treated due to omega-3 fatty acid supplement does not seem reasonable. This could be the possible reason why the literature contains conflicting results on omega-3 fatty acid efficacy. To reach any conclusion regarding efficacy of omega-3 fatty acids on depression treatment, it is necessary to categorize the patients of depression based on their causes. Although it is very difficult in the present scenario to trace the exact cause of depression, it is encouraging that vital research can help us to categorize the patients of depression on the basis of their cause which can possibly help us to narrow down the use of omega-3 fatty acid on depression patients. At present, it could be a premature decision to conclude anything about omega-3 fatty acids and treatment of depression. However, considering the individual variations in the onset of depression and response to certain treatment strategies would help us to reach a clearer conclusion.

Conflicts of interest

The authors declare that no conflict of interest exists in publishing this article.

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