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Original Article

The Effect of adding Non-saturated fatty acid Omega 3 and Placebo on anti-depressant drugs among patients with depression disorder

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ABSTRACT

Theme: Depression is the most common disorder in psychiatry and nearly 350 million people worldwide suffer from depression while it significantly affects their social and personal functions. Methods: This study was conducted as an internship double blind clinical trial. In the first part, the level and function in patients with depression were measured using the Beck test scores and 60 patients were selected who got scores higher than 13. Then, they were randomly classified into two groups of 30, one of which was received special serotonin reuptake inhibitors (fluvoxine20-80 mg or citalopram 20-40, or sertraline with congestion 50-200 mg) in addition to omega-3 fatty acid while the other group received special serotonin reuptake inhibitors (the same as previous group) in addition to a placebo. The two groups were tested at weeks 0, 2, 4, and 8 in order to evaluate depression and functional status through Beck Test. Results: The results indicated that the mean of depression among patients who received omega- 3 in the first week was 50.3, which reached 9.2 in end of the eighth week. It was significantly different in weeks 2, 4 and 6 from placebo group. Conclusion: The results of this study demonstrated that the use of omega- 3s with optional serotonin-inhibitor drugs can improve the symptoms of patients with major depressive disorder.

Keywords: Major depressive disorder, Omega- 3, Beck test

Introduction

Mood disorders incorporate a wide range of psychological disorders that mood disorder depicts their clinical picture. Depression is a common mental disorder that brings about occupational - social disorder while leading to poor quality of life, which includes key elements such as sadness, depressing mood, indifference and inability to enjoy. [1, 2] The WHO report has revealed that depression disorders are among the top ten causes of disability and malfunction in the world. Lack of proper treatment makes depression cause physical and emotional disability, early death, family issues, and decreased efficacy of the sick person. In addition, in recent years, economic costs and the negative consequences of depression have been taken into account. [2]

Antidepressant drugs are the primary treatment for major depressive disorder. These drugs are classified into four groups of antidepressants including: tri-antidepressants (TCAs), Monoamine oxidase inhibitors (MAOIs), Selective serotonin reuptake inhibitors (SSRIs) And selective inhibitors of serotonin - noradrenaline (SNRIs) Requirements. Omega-3 fatty acid is a polyunsaturated fatty acid, which is impossible to be produced by scientist and it is dependent on receiving nutrition. Omega 3 fatty acids have two biological functions including: the essential elements for membrane cells in neural, especially synapse membranes and dendritic as well as a vital component of cell membranes of organelles including mitochondria and vesicle playing a pivotal role in protecting cell membrane. [3, 4]

Despite the availability of many antidepressants in the market, people still should search for a natural, cheap, safe and effective drug. One of these drugs is possible fatty acids. Some studies have indicated that among Omega 3 fatty acids and mood disorders, the level of depression among the population with food diet including Omega 3 fatty acid was lower than other groups [5].

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It was the first randomized, and the double-blind study was conducted among 70 patients with treatment-resistant major depressive disorder and they found that EPA for 12 weeks could improve the symptoms of depression [6]. In addition, plasma levels of omega-3 fatty acids were reported to be lower in patients with mood disorders in comparison with healthy group of people [7-9] the last meta-analysis confirmed that depression disorders correlated with both omega (EPA) and (DHA). Using the diagnostic and statistical manual of Mentaldisorder (DSM-IV) showed that the difference in the amount of plasma EPA among depressed and non-depressed people for the diagnosis of major depressive disorder, omega- 3 levels have been significantly lower in patients with major depressive disorder [10]. Deacona et.al investigated the effectiveness of omega 3 among depressed patients. Epidemiological, laboratory, and clinical trials have revealed that there is a correlation between omega- 3fatty acid deficiency and mood disorders. Moreover, the use of omega- 3 fatty acids in the treatment of mood may be beneficial [11]. Grosso el. al investigated the effect of omega-3 fatty acids on depression. The findings revealed that use of omega- 3 fatty acid was significantly helpful in patients with major depressive disorder and in patients with depressive symptoms without diagnosis of major depressive disorder. The efficacy of Omega- 3 in combination with other drugs has been higher than mere Omega-3 [12]. Jazayeri et al examined the effectiveness of omega- 3 and fluoxetine alone and in combination in depressed patients. The findings showed that Omega- 3and fluoxetine are effective in treating major depressive disorder, and the combination of omega- 3 and fluoxetine has been more effective than merely omega-3. [13]. Jaryani et al examined adding omega3 to the maintenance treatment of unipolar depression. They found that Omega 3 could be applied as a supplement to antidepressants for patients who are recurrent and resistant to drug therapy [14]. Gertsik Et al. investigated the effectiveness of Omega-3 fatty acids in combination with citalopram in patients with major depressive disorder. The outcomes of the study showed that this treatment was more effective than single-drug therapy in reducing the symptoms of major depressive disorder during the 8th week treatment period. Nevertheless, this merging treatment did not tend to increase the rate of initial anti-depressant response. The last finding of this research was the positive effect of the combining of omega- 3 fatty acids with serotonin absorption inhibitor in the primary treatment of people with major depressive disorder [15].

In this study, the effect of adding omega-3 unsaturated fatty acid to anti-depressant drugs in patients with major depressive disorder compared to placebo was reviewed. The intensity of depression was determined and compared in one group receiving specific serotonin reuptake inhibitors and omega-3 fatty acids and the other group that received special serotonin and reuptake inhibitors and placebo.

Materials and Methods

The population of the study

This study was a type of a double-blind clinical test, conducted on 60 patients with major depressive disorder who had been to the psychiatric clinic of Golestan. The gender and the age of the patients are presented in Tables 1 and 2, respectively.

Table 1: Gender of the patients studied

Sex	Number	Frequency
male	21	35%
female	39	65%

Table 2: Age category of the patients

Age	Number	Frequency
> 20	5	8%
20-30	19th	6/31%
30-40	23	3/38%
40-50	8	3/13%
50 <	5	8%

Method of implementing the plan and the applied techniques

In this research, patients were randomly classified into two case and control groups of 30 to remove erroneous variables. The criteria for admission in the research were age ranging from 18-65years, major depressive disorder based on DS M -I V Index confirmed by a psychiatrist. The criteria for leaving the study incorporated bipolar disorder and other psychiatric disorders, drug or alcohol consumption during the research, dependence or background of drug or alcohol in recent months, history of allergy to serotonin reuptake inhibitors or omega-3fatty acids , background of seizure, pregnancy, active suicidal thoughts and anxiety, chronic physical disease (blood pressure, diabetes, heart disease, liver and kidney disease), use of anticoagulants and medications that interfere with omega-3 intake (such as anti-platelet drugs such as aspirin and enoxaparin and heparin and warfarin) .Randomization was according to permutation block 4 divided randomly into two equal groups of people. Blindness was according to the fact that which the patients did not know what type of drug they received. The capsule of omega- 3 fatty acids and placebo were exactly in the same shape, color, smell and taste.

Patients were first evaluated by the Beck Test and the depression and functional level of them were measured using Beck Test. Finally, the participants with a score of over 13 were selected. The patients were divided randomly into two groups of 30, one group was given selective serotonin reuptake inhibitors (Fluoxetine 20-80 mg dose or a dose of citalopram or sertraline dose 20-40 50-200 mg) plus omega-3 fatty acids and other group received selective serotonin reuptake inhibitors (Fluoxetine of this dose of 20-80 or citalopram at a dose of 20-40 or sertraline of the dose of the L 50-200 mg) in addition to placebo. The two groups were the same with respect to antidepressant. In the two groups, in addition to specific serotonin reuptake inhibitors, omega- 3s was given at a daily dose of 300-300 mg. In the control group, in addition to

specific inhibitors of serotonin reuptake, a placebo (olive oil) with a single dose of 600-300 mg per day was prescribed. The two groups were analyzed in weeks 0, 2, 4, 6 and 8 so that the researchers could assess the level of depression and Functional testing based on the Beck Test. Moreover, the rate of depression was determined according to the average duration of treatment in the two groups. A checklist was already devised in order to check the side effects of omega- 3s (digestive disorders such as nausea and diarrhea and interference with antiplatelet drugs). In the case of having any serious complication or omega- 3complications, the patient was given the authority to quit the study. In the end, the difference in the parameters of the two groups was investigated. Data collected based on evaluations through Beck Depression Scale were analyzed by statistical software package called SPSS.

Beck Test

Beck test includes 21 questions while each question has four options. Each part in the questions shows the status of the person. Each question is rated from 0 to 3. Beck questionnaire is based on five factors including signs and symptoms of depression as which will be explained in the following:

1) Pessimism and the feeling of failure, hating oneself, feeling of committing suicide, having indecision and 2) feeling sinful, expecting punishment and blame 3.) Crying, changing the view of oneself, dissatisfaction and sadness, losing weight, physical complaints and not eating enough. 1-10 normal, 11-16 a little depressed, 17-20 requiring advisory with psychologist and psychiatrists, 21-30 quite depressed, 31-40 severe depression and over 40 extreme depressions.

Method of calculation of sample size and sampling method

It should be noted that 9 units of difference is significant. Given the the standard deviation of 13.28 and 11.59 in the two groups and $\alpha = 0.05$, the volume of the sample would be equal to 30.

$$n = \frac{\left(Z_{1-\alpha/2} + Z_{1-\beta}\right)^2 (s_1^2 - s_2^2)}{(\bar{x}_1 - \bar{x}_2)^2} = 60 \qquad (1)$$

Statistical methods for analyzing the results

After collecting statistical findings statistical software SPSS 20th edition was used to compare the qualitative and frequency variables of the two groups using chi-square test. Independent, dependent, qualitative and quantitative variables are explained in Table 3. First, a Kolmogorov - Smirnov test was performed to check the normality of the data. The results of this test showed that the distribution of data is not normal. Therefore, u Mann-Whitney was used for comparing the mean of two groups.

Table 3: Variables defined in this study

Variable features	Independent	Dependent	Qualitative: Continuous	Qualitative: Discrete	Qualitative: Nominal	Qualitative: Ranking	Practical definition	Scale
Severity of depression		*		*			Based on the Beck Inventory	Relation
treatment duration		*		*			The length of time the patient symptoms improve	Relation (Weekly)
Omega 3	*			*			The amount of omega-3 fatty acid that is given to the patient	Relation (Mg)
Placebo	*			*			The amount of drug-like medicine that is given to the patient	Relation (Mg)
Beck Test	*					*	Depressed and functional depression level questionnaire	Relation

Ethical considerations

Patients were totally aware of the research and they were required to write written consent letter. In the patient data record, their name and personal details were not included. During the research, codes were used to group the data if necessary instead of their names. The way for prescribing the drugs was explained to the patients and their content was obtained before the beginning of the research. All information about the patients was confidential and all the cultural, ethical and medical issues were observed. The main treatment was performed in each group of patients and excluded from the study if there were any possible side effects. The patients also were not charged for anything.

Results

The results demonstrated that among 60 patients with major depressive disorder, 35% were male and 65% were female. The highest range of depression was during 30-40 years for patients who had major depressive disorder in 38.3%. Under the age of 20 years, it was 8%, between 20-30 years, it was 31.6%, between 40-50 years, it was 13.3% and 50, and it was around 8% frequency. The results of the evaluating the severity of depression in both groups were provided for weeks 6, 4, 2 and 8 in Table 4 and Figure 1. The mean depression in the Omega- 3 group was 50.3 in the first week, reaching 2.9 at the end of the eighth week. In the 2nd, 4th and 6th weeks, there was a significant difference the first group and the placebo group (p value <0/05). Further, data analysis indicated that for both groups, time lapse had a significant effect on depression.

Table 4: Severity of depression in the two groups studied

time	Omega-3 (mean rank)	Placebo (mean rank)	P value
Baseline	50/4± 8/5	53/1± 5/7	0/203
Week2	27/2± 4/1	32/8 ± 4/3	0/000
Week4	19/4± 3/5	23/13± 3/4	0/000
Week6	14/9± 3/4	15/9± 2/2	0/126
Week8	9/2± 3/2	9/4± 2/9	0/941

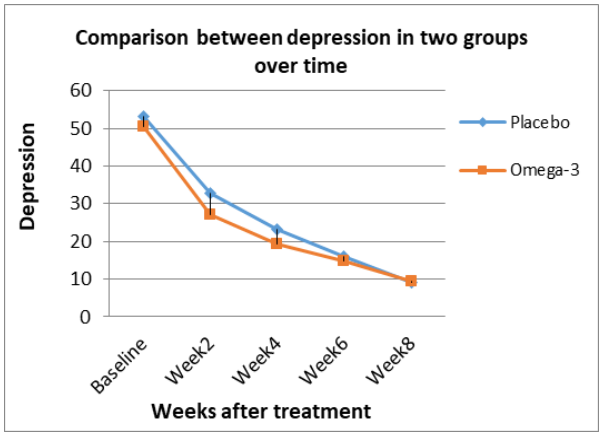

Figure 1. Relationship between severity of depression and weeks of treatment

Discussion

The findings about depression severity in the group that received selective serotonin reuptake inhibitors and the other group receiving omega-3 fatty acid- Serotonin and placebo reuptake inhibitors showed that the mean depression in the omega- 3 group was lower in weeks 2, 4 and 6 than in the placebo group. This was in line with the findings of other researchers. Appleton et al found that the use of omega-3 improves symptoms of depression in adults suffering from depression disorders in comparison with placebo [16]. Hallahan et al also found that EPA combination of strong fatty acids is useful for controlling the symptoms of depression in patients suffering from depression. However, the fatty acid did not cause depression among those who were not suffering from depression [17]. Santos et al also identified that there was a significant correlation between depression and level of omega-3. The concluded that omega-3 has anti-inflammatory properties, thereby improving neurotransmitter estrogenic and dopaminergic system. [18]. Beydoun et al showed that levels of omega-3 and omega-6 were correlated with depressive symptoms while improving the symptoms in the long term [19]. Using Beck test, Ginty et al revealed that omega- 3s have positive effects on mild depression among adult patients. Jariani et al showed that omega-3 can be used as supplements in addition to antidepressants for patients with recurrent depression and resistant to medical therapy [20]. The results of the studies by Gertsik et al showed that the use of a combination of drugs in the treatment of depression was more effective than single-drug therapy. The supplementary application of omega- 3s and selective serotonin inhibitors is an initial choice for treating major depressive disorder, and it improves Hamilton's standard of depression in patients with impaired depression [21]. Su et al also conducted a double blind trial on 21 patients with major depression while the findings showed that the use of omega-3 improved the standard of Hamilton compared to placebo. The use of omega-3 improves the patients' status with major depressive disorder [22]. Freeman et al found that in patients with major depressive disorder, Omega-3 as a supplement to the treatment of depression is effective for perinatal women and can reduce the dose of antidepressant drugs among them [23]. Sublette et al showed that omega-3 deficiency can cause major depression and have effects on dopaminergic systems. The results showed that an enhanced therapeutic strategy is to use antidepressants with fish oil [24]. Hariri et al carried out a study on 60 patients with major depressive disorder within 4 weeks and the results showed that the use of omega-3 and fluoxetine had equal power in treating depression among patients, and the use of these two drugs simultaneously was more effective than each of them alone. [13]. Nemets et al demonstrated that omega- 3 has a very significant effect on the rate of depression among children [25]. Sinn et al showed that DHA and EPA available in fish oil can have significant effects on the depressive symptoms and physical activities including health parameters such as cognition and effective physical activity [26]. SU et al showed the effectiveness of omega-3 during pregnancy and it was accepted because of pathophysiological effects and being healthy [27]. Hariri and et al also found that Omega- 3 could be effective on behavioral disorders. However, the use of high dose of omega- 3s can have reverse effects in the long run [28].

General Conclusion

Evaluating the effect of adding omega- 3 unsaturated fatty acid to anti-depressant drugs in patients with major depressive disorder compared to placebo group demonstrated that the use of omega- 3s with selective serotonin-suppressing drugs can improve the symptoms of patients with major depressive disorder.

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