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Clinical trial in the treatment of 80 Iranian patients with major depression disorder by the combination of omega 3 fatty acid and a selective serotonin reuptake inhibitor

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Abstract:

Objectives: Bipolar disorder type I is a disturbing psychiatric syndrome, which is treated by mood-stabilizing medications, psychosocial intervention and electroconvulsive therapy. As supplementation with omega 3 has been considered effective in the treatment of many diseases especially mental disorders, this study aimed at evaluating the effect of omega 3 with fluvoxamine compared with fluvoxamine alone in the treatment of the deep depression phase in bipolar patients type I.

Methods: A total of 80 patients in this clinical trial study were selected using a randomized controlled trial in two case and control groups by a psychiatrist. The case group took fluvoxamine and omega 3 tablets and the control group took only fluvoxamine. Patients completed the Hamilton Depression Rating Scale and demographic questionnaire at the beginning of the study and after 2, 4, 8 and 12 weeks.

Results: The mean scores in the Hamilton Depression Rating Scale in both groups under study after 2, 4, 8, 12 weeks decreased. Statistics showed a significant difference in scores in both groups before the treatment and after mentioned weeks.

Conclusions: Since research findings showed the effectiveness of omega 3 and its harmlessness, it is suggested that omega 3 can be prescribed with other antidepressant medications.

Keywords: depression, fatty acids, fluvoxamine, omega 3, selective serotonin reuptake inhibitor

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Objective

Bipolar disorder type I is one of the most disabling conditions in psychiatry [Sadock and Sadock, 2003a]. This disorder is associated with major mood swings between two poles of depression and mania [American Psychiatric Association, 2003]. Treatment is in the most part with mood-stabilizing medications, social psychiatric interventions and, in severe states, with shock treatment [Sadock and Sadock, 2003b]. Recently, there has been interest in herbal medications for controlling some psychiatric syndromes [Weiss, 2000; Lafrance *et al.* 2000; Alderman and Kipfer, 2003; Desari and Grossberge, 2003]. Among new effective treatments there have been reports of omega 3 as monotherapy or combination treatment [Emken *et al.* 1994; Stoll *et al.* 1999; Su *et al.* 2003]. In one double-blind study, it was shown that addition of the omega 3 supplement to the treatment regimen of bipolar disorder has improved clinical outcome and helped with treatment of the patients [Emken *et al.* 1994]. Stoll and colleagues performed a 4-month double-blind clinical trial for bipolar disorder patients. A total of 14 individuals received omega 3 and 16 individuals took olive oil as controls and all patients also took a mood-stabilizing medication at the same time. Results showed that in the omega 3 and mood-stabilizing drug group, the psychiatric condition recurred less and patients stayed in recovery for longer periods. As a result, researchers concluded that omega 3 is not only

effective in decreasing recurrence and improving bipolar disorder, but also the effectiveness of omega 3 should be examined as an antidepressant [Stoll *et al.* 1999]. Another study showed that patients with bipolar mood disorder who have depressive symptoms or decreased function upon taking omega 3 had up to 50% decreased depressive symptoms in the first month [Su *et al.* 2003].

In one study, 66 elderly patients participated for 6 months. Patients were divided into two groups. One group was treated with fish oil capsules containing 300 mg of omega 3 fatty acids and the second group received placebo. Results showed that the severity of depression was different between the treatment and control groups. It was concluded that low-dose omega 3 fatty acids are effective for the treatment of mild to moderate depression in the elderly population [Tajalizadeh Khoub *et al.* 2011].

A large study in Iran showed that adding eicosapentaenoic acid (EPA) to fluoxetine for the treatment of patients with major depression is more effective than fluoxetine or EPA alone [Jazayeri *et al.* 2008].

In addition, studies have shown that the human body uses omega 3 in various ways. This is particularly important in better functioning of the central nervous system and also healthy development of fetal brain and also for the child during milking [Harar, 2012].

Recent years have shown increased attention paid to the use of an omega 3 fortified diet in the treatment of many conditions, particularly psychiatric conditions. As a result, we decided to evaluate the treatment efficacy of omega 3 compared with fluvoxamine in the treatment of the depressive phase of bipolar disorder.

Methods

This study was approved by the University Scientific Committee and the ethics committee and all participants provided written informed consent. This is a randomized controlled trial study. The study population included all patients with bipolar disorder type I who were diagnosed after psychiatric evaluation based on the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision (DSM-IV-TR) criteria [American Psychiatric Association, 2003]. The sample size needed was estimated at 80 individuals and patients were randomly assigned to one of two groups and the study was double blind. Patients were included in the study who had the following criteria: patients were in the major depressive phase for the first time (depression was not psychotic), they had no history of substance abuse or use of psychiatric medication, were not on a diet including omega 3 supplements, did not have history of medical illness or other psychiatric illness. The case group (40 individuals) were treated with fluvoxamine at a dose of 50–300 mg daily and omega 3 fatty acid, one to three capsules a day, and the control group (40 individuals) were treated with daily 50–300 mg fluvoxamine. After assurance about confidentiality of information and consent, all patients completed the Hamilton Depression Rating Scale and demographic information at the beginning of the study and in weeks 2, 4, 8 and 12 in a quiet and stressless environment. They were subsequently evaluated via interview by a psychiatrist. The questionnaires were collected and the information was entered into the computer and analyzed using the SPSS-16 software. Information was presented as distributions and variables were compared using the repeated measures and Freedman tests. The two groups of case and control were compared. The Hamilton Depression Rating Scale is a standard test including 21 questions that evaluate depression. Scoring is by the Likert method and based on total score and severity of depression can be evaluated using the following groupings: score below 9 is normal, 10–13 represents mild depression, 13–17 represents moderate depression, 17–35 represents moderate to severe depression and 35–61 signifies severe depression.

Results

Results of the study show that the Hamilton score for both groups studied decreased significantly after 2, 4, 8 and 12 weeks and patient functionality improved.

The repeated measures test showed significant change in the depression score for both groups before treatment and at 2, 4, 8 and 12 weeks after treatment ($p < 0.001$). Among 80 patients participating in this study, 47.5% of the treatment group with fluvoxamine and omega 3 and 45% of patients treated with fluvoxamine were male and 52.5% of the case group and 55% of the control group were female. Mean age for the case group was 37.3 years (standard deviation [SD] 11.62)

and for the control group was 40.27 years (SD 14.41). A total of 60% of the case group and 65% of the control group were married. Of the total, 27.5% of the case group and 32.5% of the control group were office workers. Education level for 40% of the case group and 37.5% of the control group was a diploma. A total of 65% of the case group and 60% of the control group were city dwellers (Table 1).

Results showed that mean depression score in the treatment group with fluvoxamine and omega 3 at the second week of treatment was 36.30 (SD 14.87) and decreased to 23.90 (SD 12.50) at the fourth week, to 15.73 (SD 9.87) at the eighth week and to 13.10 (SD 10.82) at the twelfth week of treatment (Table 1).

Mean depression score for the fluvoxamine-only group decreased from 42.07 (SD 7.59) at the second week of treatment to 26.18 (SD 10.21) at the fourth week, to 17.88 (SD 8.97) at the eighth week and 15.18 (SD 8.27) at the twelfth week. The repeated test measures showed a statistically significant difference between depression level and functionality between the case and control group ($p < 0.001$) (Table 2).

Conclusion

This study showed that omega 3 fatty acid supplements accompanied with the antidepressant fluvoxamine in comparison with fluvoxamine alone was able to lead to a significant decrease in mean

Table 1. Total and relative distribution of demographic characteristics of study groups.

Demographic variables		Treatment with fluvoxamine and omega 3		Treatment with fluvoxamine		Demographic variables		Treatment with fluvoxamine and omega 3		Treatment with fluvoxamine	
		No	%	No	%			No	%	No	%
Gender	Female	21	52.5%	22	55%	Job	Unemployed	9	22.5%	6	15%
	Male	19	47.5%	18	45%		Self-employed	12	30%	11	27.5%
Age	<20	4	10%	4	10%		Office worker	11	27/5%	13	32.5%
	20–29	8	20%	6	15%		Labor worker	8	20%	10	25%
	30–39	14	35%	8	20%	Education	illiterate	8	20%	8	20%
	40–49	8	20%	9	22.5%		Under diploma	8	20%	9	22.5%
	≥50	6	15%	13	32.5%		diploma	16	40%	15	37.5%
Marital status	Single	11	27.5%	9	22.5%		Above diploma	8	20%	8	20%
	Married	24	60%	26	65%	Place of living	City	26	65%	24	60%
	Widow	5	12.5%	5	22.5%		Village	14	35%	16	40%

Table 2. Mean depression scores at follow-up sessions.

Follow-up session		Treatment with fluvoxamine and omega 3	Treatment with fluvoxamine
At 2 weeks after treatment	Mean	36.30	42.07
	Standard deviation	14.87	7.59
At 4 weeks after treatment	Mean	23.90	26.18
	Standard deviation	12.50	10.21
At 8 weeks after treatment	Mean	15.73	17.88
	Standard deviation	9.87	8.97
At 12 weeks after treatment	Mean	13.10	15.18
	Standard deviation	10.82	8.27
Significance	$p < 0.001$ (df = 5)		

depression score and improvement of depressive symptoms starting 2 weeks after treatment.

There is significant correlation between irregular fatty acid metabolism and depression and decreased omega 3 unsaturated fatty acid levels can lead to depressed mood [Partifitt, 2007; Kasper *et al.* 2007]. In recent years significant attention has been paid to the use of omega 3 sources in the treatment of medical conditions, particularly psychiatric conditions and depression [Grenyer *et al.* 2007; Lin and Su, 2007; Sanchez-Villegas *et al.* 2007]. Results of a study by Upton showed the effectiveness of ethyl EPA compared with placebo for treatment of the depressive phase of bipolar disorder. Addition of EPA has significantly decreased Hamilton scores in the depressive phase of bipolar disorder [Upton, 2006]. Also, the results of a double-blind study by Stoll and colleagues showed the effectiveness of omega-3 compared with placebo in a 4-month follow up of bipolar patients [Stoll *et al.* 1999].

In addition, the effectiveness of ethyl EPA in treating the depressive phase of bipolar disorder was shown in a case-control study by Frangous and colleagues [Frangous *et al.* 2006].

In a double-blind study including 432 patients with major depression, it was shown that omega 3 has improved depressive symptoms in patients who did not have anxiety [Lespérance *et al.* 2010].

In another study it was shown that the use of omega 3 by patients who are at increased risk of developing psychiatric conditions prevents the development of psychiatric symptoms [North Shore-Long Island Jewish (LIJ) Health System, 2012].

Keck and colleagues, in a double blind case-control study, showed that ethyl EPA is effective for the treatment of the depressive phase of bipolar disorder and rapidly changing mood bipolar disorder [Keck *et al.* 2006].

Considering the above studies and the effectiveness of the treatment of major depression with omega 3 supplements, this medication is recommended for more rapid recovery and satisfaction of patients.

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Conflict of interest statement

The authors declare no conflicts of interest in preparing this article.

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