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Effect of omega-3 supplementation with lifestyle modification on depression and anxiety in overweight women

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A B S T R A C T

Background: Anxiety, stress and depression are still one of the common chronic diseases among Iranian population especially among women in the age of 15-29 years. Associations between depressed mood and lifestyle are well known. The aim of this study was to investigate the effect of omega-3 PUFAs supplementation with lifestyle modification on depression and anxiety in overweight women.

Methods: 38 women aged between 20-45 years; BMI~25-30; having sedentary lifestyle without any known metabolic, cardiovascular or pulmonary diseases or taking any medication which affect heart rate, blood pressure or exercise capacity were included. Patients randomly divided into two experimental groups. Group 1 received omega-3 capsules + aerobic exercise and took healthy nutrition class. Group 2 received placebo capsules + aerobic exercise and took healthy nutrition class. All of the subjects were asked to take one capsule/day, for 8 weeks. The depression level was measured using the Hospital Anxiety and Depression Scale.

Results: There were no significant differences between anxiety and educational level, depression and educational level in overweight women at baseline, 4 and 8 weeks of the study. In addition, no significant correlation was found between changes observed on anxiety and depression extent and different occupations among volunteer women at baseline, 4 and 8 weeks of the study. According to the data, omega-3 capsules significantly decreased anxiety and depression compared to control group (P=0.032).

Conclusion: Omega-3 fatty acids supplementation may have beneficial effects on anxiety and depression in overweight women that is not related to lifestyle modification. Further randomized controlled trials with large sample size are needed to confirm these results.

Introduction

Anxiety and depression are common psychiatric illnesses influencing people perfor mance and health. There are growing report on prevalence of anxiety and depression worldwide as well as among Iranian population [1]. Stress, affects physiological functions and plays role in the pathogenesis of several disorders [2]. It is reported the rate of anxiety and depression are higher for women than men [3]. The highest risk for developing depression is in the age ranges of

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15-29 years [3]. Based on the evidence, stress could influence health by changing nutritional behavior such as food choice via changes in appetite [1]. Stress and anxiety has been linked with either increased or decreased appetite. Mild stress may lead to hyperphagia whereas severe stress results to hypophagia [4].

The newly, PUFAs hypothesis on depression provides a promising path to discover a new treatment for depression. For instance, in societies with high consumption of fish [as a good source of omega-3 PUFAs), prevalence of depressive disorders is low [5]. Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are the major bioactive components of n-3 PUFAs and are not synthesized in human body [6]. These factors are associated with neuronal membrane stability and the functions of the neurotransmitters which might connect to the etiology of mood and cognitive manifestations of depression [6].

It is reported hostility and anger are related to insufficient fatty acids intake, while anger was reduced in patients received medication following n-3 PUFAs supplementation (2085 mg EPA and 348 mg DHA) compared to patients received just medication [7, 8]. Investigation on effect of omega-3 PUFAs on reducing anxiety has become an interesting field of study [9]. For instance, a recent study revealed that an EPA-rich diet could reduce the development of anxiety like behavior in rats [10].

The direct cellular and molecular mechanism of antidepressant effect of omega-3 is not fully elicited. It is suggested abnormal composition of fatty acids in cell membrane could be important in etiology of depression [11] but, the epidemiological studies on interconnection of dietary fish consumption and depression is not prove causation, yet. However, there were several cultural, economic and social factors which might confound the results [12]. Consistent with the theoretical relevance and findings, our hypothesis in the current study was to investigate the effect of omega-3 capsules plus lifestyle modification on depression and anxiety in overweight women.

Subjects and methods

Subjects

Thirty-eight overweight women were participated in this interventional study. They were call up through public advertising and selected by primary interviews and measurements in the multidisciplinary obesity clinic in the Imam Khomeini hospital. The inclusion criteria of the study were women (age between 20 and 45 years) [13]; BMI equals to or more than 25 and less than 30; having sedentary lifestyle (not participating in at least half an hour of moderate intensity exercise 3 days per week in the 3 months prior to the study); neither being pregnant nor menopause; not suffering from any known metabolic, cardiovascular or pulmonary diseases; not taking any medication which have significant affect heart rate, blood pressure or exercise capacity; not experiencing musculoskeletal problems that would limit exercise capacity. Subject who did not accepted participation limitation or showed any indication of exercise test termination during the test; she would be excluded from the study. All protocols for experiments were approved by the institutional of Ethical Committee, Tehran University of Medical Science (TUMS) & health Services (IRCT201504267903N4).

Omega-3 capsules

The omega-3 capsules (NATURALab, Canada) contained 600 mg EPA and 300 mg DHA [14]. Both omega-3 and placebo capsules were taken from Zahravi Co. Tabriz, Iran. The size, color and shape of the placebo capsules matching the omega-3 capsules. Both experimental and placebo subjects used daily orally administration of the capsule for 8 weeks.

Study Protocol

Women randomly divided into 2 experimental groups. Group 1 received omega-3 capsules (600 mg EPA and 300 mg DHA) and aerobic exercise and asked to participate in an educational class about healthy diet (n=19). Group 2 was similar to group 1 in this cases, except receiving placebo capsules (paraffin oil) [15] instead of omega-3 capsules (n=19) (Zahravi Co. Tabriz, Iran). At the first visit, inclusion criteria and study protocol were described. At the second visit limited diet, exercise test and educational session were done. Low calorie diet was prescribed using Harris Benedict Equation with 500-1000 kilocalorie deficit. The main groups of foods, serving sizes and exchange list were described. All of the educations were face to face for each participant. Exercise test on treadmill with Bruce protocol [16] were done for lactate threshold and maximal heart rate determination of each subjects. The participants were asked to performing brisk walking 3 to 5 days per week,

Table 1. Baseline demographics and anthropometric measurements of the study participants

	Placebo group	omega-3 treated group	P value
Age (year)	36.88±5.99	36.34±6.04	0.15
Weight (Kg)	71.63±5.57	71.43±6.88	0.37
BMI (Kg/m^2)	27.57±1.26	27.90±1.45	0.20

Data are expressed as mean±SD unless otherwise stated. Abbreviations: BMI, body mass index. * P<0.05 for statistical difference from baseline to week 6 within the group. SD: standard deviation

Table 2. Comparing results of anxiety at the different educational levels in overweight women

Variables	Education level	Mean ± SD	F-value	P value
Anxiety-1	high school	8.00±3.86	0.626	0.541
	B.A	7.61±2.73		
	M.A	6.40±3.98		
Anxiety-2	high school	6.00±3.16	0.420	0.660
	B.A	7.00±2.95		
	M.A	5.90±4.70		
Anxiety-3	high school	4.90±4.01	0.664	0.521
	B.A	5.22±2.65		
	M.A	3.80±3.08		

Anxiety-1: at the initiation of the study, Anxiety-2: after 4 weeks, Anxiety-3: after 8 weeks of initiation of the study; B.A: bachelor of science, M.A: master of science. SD: standard deviation

30-40 minutes at the lactate threshold heart rate. They were asked to complete physical activity logbook [16]. At the end of week 4 and 8, patients recalled to determine correlation of anxiety and depression with education and occupation levels as well as effects of omega-3 capsules on anxiety and depression.

Measurement of depression

Hospital Anxiety and Depression Scale (HADS) were used to measure the depression and anxiety levels[17]. This scale consists of a 7-item anxiety subscale and a 7-item depression subscale to assess the anxiety and depressive symptoms during the preceding week in medically ill patients. Each item is rated on a scale of 0–7, with higher scores denoting a greater mood disturbance. HADS questionnaire was completed by each subject at baseline, fourth and eighth weeks of the trial. In addition, the correlation of anxiety and depression with different educational and occupational levels was assessed.

Statistical Analysis

Data were analyzed by two-way ANOVA for repeated measurement using SPSS 16.0 for Windows (SPSS Inc. Chicago, IL, USA) and is presented as mean ± SD. For treatments showing a main effect by ANOVA, means were compared using LSD Pairwise Comparisons test. P<0.05 was considered as significant differences between treatments.

Results

Comparing results of anxiety and depression at the different educational and occupational levels is presented in Tables 2-5. The Baseline demographics and anthropometric measurements of the study are presented in Table 1. As seen, there was no significant difference for demographics and anthropometric measurements before the study among the experimental groups (P>0.05 for all).

Comparing results of anxiety with the different educational levels is presented in Table 2. According to the results, there was no significant difference between anxiety and educational levels in overweight women at the beginning (anxiety-1), middle (after 4 weeks, anxiety-2) and the end of the study (after 8 weeks, anxiety-3) (P>0.05 for all).

As seen in Table 3, there was no significant difference on comparing results of depression with the different educational levels in overweight women at the start (anxiety-1), middle (after 4 weeks, anxiety-2) and the end of the study (after 8 weeks, anxiety-3) (P>0.05 for all).

The result of anxiety level based on the occupation is shown in Table 4. The participants were divided into three groups of housewife, practitioner or student. As seen in table 4, there was no significant difference between anxiety and different occupations during study (P>0.05 for all).

Table 3. Comparing result of depression at the different educational levels in overweight women

Variables	Education level	Mean ± SD	F-value	P value
Depression-1	high school	5.40±3.13	0.078	0.925
	B.A	5.72±3.04		
	M.A	5.30±2.58		
Depression-2	high school	3.70±2.71	0.792	0.461
	B.A	4.89±3.08		
	M.A	3.70±2.75		
Depression-3	high school	2.40±1.71	0.169	0.054
	B.A	4.17±2.18		
	M.A	2.40±2.50		

Depression -1: at the initiation of the study, Depression -2: after 4 weeks, Depression -3: after 8 weeks of initiation of the study; B.A: bachelor of science, M.A: master of science. SD: standard deviation

Table 4. Comparing result of anxiety at the different occupation in overweight women

Variables	Occupation	Mean ± Std. Deviation	F-value	Pvalue
Anxiety-1	housewife	7.50±1.38	0.006	0.994
	Practitioner	7.39±3.76		
	Student	7.25±2.87		
Anxiety-2	housewife	6.00±2.45	0.166	0.847
	Practitioner	6.64±3.83		
	Student	5.75±2.36		
Anxiety-3	housewife	4.50±3.39	0.045	0.956
	Practitioner	4.86±3.26		
	Student	4.50±2.38		

Anxiety-1: at the initiation of the study, Anxiety-2: after 4 weeks, Anxiety-3: after 8 weeks of initiation of the study.

The result of depression level on occupation is presented in Table 5. There was no significant difference between depression extent and different occupation among volunteer women (P>0.05 for all).

Effect of omega-3 capsules on anxiety in overweight women is presented in Figure 1. Despite the anxiety diminished in control group along the 8 weeks of the trial, the decline was no significant (P>0.05 for all). Additionally, omega-3 supplementation significantly diminished anxiety scores compared to the control group (P=0.04).

According to the results, supplementation of omega-3 significantly diminished depression in overweight women in comparison to control group after 8 weeks (P=0.032) (Figure 2).

Discussion

To the best of our knowledge, this is the first report on effect of omega-3 capsules and lifestyle modification on depression and anxiety in overweight women. The fatty acid composition of the modern society diet changed dramatically the last century, where people consume much more saturated fatty acids, prevalence of depression and other chronic diseases such as cardiovascular disease increased [18]. We found omega-3 supplementation significantly correlated with anxiety and depression control in overweight women. The results of this study were consistent with epidemiologic data and clinical trials. PUFAs play role on decrease depression and anxiety in

Table 5. Comparing result of depression at the different occupation in overweight women

Variables	Occupation	Mean ± Std. Deviation	F-value	P value
Depression-1	housewife	3.83±2.14	1.248	0.300
	Practitioner	5.86±2.98		
	Student	5.75±2.87		
Depression-2	housewife	4.17±2.32	0.024	0.976
	Practitioner	4.32±3.22		
	Student	4.00±0.82		
Depression-3	housewife	3.17±2.14	0.029	0.971
	Practitioner	3.21±2.48		
	Student	3.50±1.00		

Depression -1: at the initiation of the study, Depression -2: after 4 weeks, Depression -3: after 8 weeks of initiation of the study.

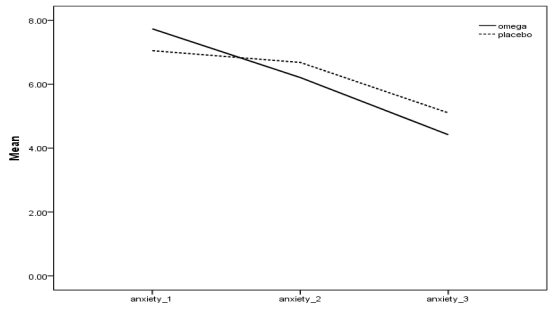

Figure 1. Effect of omega-3 capsules on anxiety in overweight women. Anxiety-1: at the initiation of the study, Anxiety-2: after 4 weeks, Anxiety-3: after 8 weeks of initiation of the study.

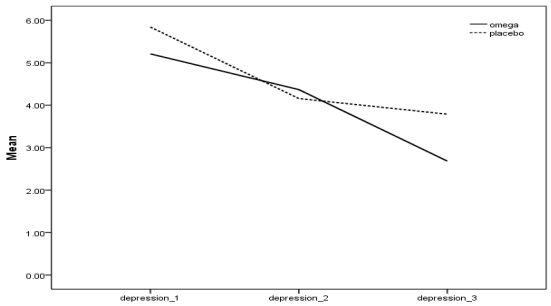

Figure 2. Effect of omega-3 capsules on depression in overweight women. Depression -1: at the initiation of the study, Depression -2: after 4 weeks, Depression -3: after 8 weeks of initiation of the study.

patients [5]. In this regard, inverse relationships reported between fish consumption and depression where clinical depression as well as depressive symptoms is lowered in people fed more fish [14].

Psychologic stress is known as a considerable risk factor for cardiovascular diseases among adults. A progressive decline in anxiety was observed in patients who were given 3 g of EPA and DHA for 3 months [19]. The direct cellular and molecular mechanism of the antidepressant effect of omega-3 is not fully identified. Previous studies indicated clinical depression could be accompanied by low levels of n-3 PUFAs in RBC, plasma as well as in brain tissue. The pathophysiology of depression in the CNS level is an imbalance, mainly in serotonergic and noradrenergic neurotransmission. One of the suggested mechanisms for how omega-3 PUFAs impress their effects is that they influence the depressive status via central serotoninergic and dopaminergic systems. Changes in serotonin and dopamine receptors by PUFA provide the theoretical rationale connecting fatty acids with the current receptor and neurotransmitter theories of depression (Grosso et al. 2014). It is reported omega-3 deficiency lead to an increase of serotonin receptor in the central nervous system [20]. For instance, in animal experimental models of depression, dopamine levels were higher in the nucleus accumbens while omega-3 supplementation increased expression of the dopamine receptors [21]. However, in this study, we were not able to measure direct neurotransmitter levels of patients received omega-3 supplementation.

It is assumed chronic systemic inflammation contributed to the progression of neuro degeneration [22]. This theory is another possible mechanism of the omega-3 effect on anxiety and depression. Depression is accompanied by increased secretion of eicosanoids, such as prostaglandins and secretion of proinflammatory cytokines [23]. Omega-3 fatty acids impress its effect by decreasing secretion of eicosanoids and proinflammatory cytokines via inhibition of phospholipase A_2 enzyme [22].

It is accepted that the environment and lifestyle of the individuals have a strong influence on the health of the body and mind. Also, adequate levels of exercise and healthy dietary practices have the advantage on cognitive disorders. Evidences support the relation between the n-3 fatty acids consumption, exercise and weight loss [24, 25] where omega-3 PUFAs supplementation increased cytoplasmic fatty-acid-binding protein content and fat oxidation in rats [26]. As observed in this study, exercise and omega-3 capsules for 8 weeks significantly diminished anxiety and depression in overweight women compared to the patients received placebo and exercise (control). Thus, we think the observed results might belong to effect of omega-3 capsules. Moreover, depression is associated with excessive production of pro-inflammatory cytokines such as interleukins, interferon-gamma and tumor necrosis factor-α. Omega-3 PUFA inhibits the production of pro-inflammatory cytokines, via reduction in the production of pro-inflammatory prostaglandins and leukotrienes [27-30]. However, the exact mechanism involved in the pathogenesis of depression is not known. The major limitation of this study is we were not able to measure that PUFA levels in blood plasma, erythrocytes, liver, muscle, adipose and etc. The authors suggest merit studies needed to investigate direct mechanism of omega-3 capsules on anxiety and depression in

overweight women.

Conclusion

Omega-3 fatty acids supplementation may have beneficial effects on anxiety and depression in overweight women which is not related to lifestyle modification. Further randomized controlled trials with large sample size are needed to confirm these results.

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Conflict of interest

None of authors have conflict of interests.

References

1. Laviano A, Meguid MM. Nutritional issues in cancer management. Nutrition 1996; 12: 71-358.
2. Bozzetti F. Nutrition and gastrointestinal cancer. Curr Opin Clin Nutr Metab Care 2001; 4: 541.
3. Fearon KC, Voss AC, Hustead DS .Definition of cancer cachexia: effect of weight loss, reduced food intake, and systemic inflammation on functional status and prognosis. Am J Clin Nutr 2006; 83: 1345-50.
4. DeWys W, Begg C, Lavin P, Band P, Bennett J, Bertino J. Tormey, DC. Prognostic effect of weight loss prior to chemotherapy in cancer patients. Eastern Cooperative Oncology Group. Am J Med 1980; 69:491-7.
5. Andreyev H, Norman A, Oates J, Cunningham D. Why do patients with weight loss have a worse outcome when undergoing chemotherapy for gastrointestinal malignancies? Eur J Cancer 1998; 34: 503-9.
6. Rickard KA, Detamore CM, Coates TD, Grosfeld JL, Weetman RM, White NM, et al. Effect of nutrition staging on treatment delays and outcome in stage IV neuroblastoma. Cancer 1983; 52: 587-98.
7. Ovesen L, Hannibal J, Mortensen EL. The interrelationship of weight loss, dietary intake, and quality of life in ambulatory patients with cancer of the lung, breast, and ovary. Nutr Cancer 1993; 19: 159-67.
8. Stephens N, Fearon K. Anorexia, cachexia and nutrition. Medicine 2008; 3: 78-81.
9. MacDonald N. Is there evidence for earlier intervention in cancer-associated weight loss? J Support Oncol 2003; 1: 279-86.
10. Den Broeder E, Lippens R, Van't Hof M, Tolboom J, Van Staveren W, Hofman Z, et al. Effects of naso-gastric tube feeding on the nutritional status of children with cancer. Eur J Clin Nutr 1998; 52: 494-500.Roberge C, Tran M, Massoud C, Poiree B, Duval N, Damecour E, et al. Quality of life and home enteral tube feeding: a French prospective study in patients with head and neck or oesophageal cancer. Br J Cancer 2000; 82: 263-9.
11. Van Bokhorst-de Van der Schuer MA, Langendoen SI, Vondeling H, Kuik DJ, Quak JJ, Van Leeuwen PA. Perioperative enteral nutrition and quality of life of severely malnourished head and neck cancer patients: a randomized clinical trial. Clin Nutr 2000; 19: 437-44.
12. Jho DH, Cole SM, Lee EM, Espat NJ. Role of omega-3 fatty acid supplementation in inflammation and malignancy. Integr Cancer Ther 2004; 3: 98-111.
13. Elia M. Enteral (oral or tube administration) nutritional support and eicosapentaenoic acid in patients with cancer: a systematic review. Int J Oncol 2006; 28: 5-23.
14. Hardman WE. (n-3) fatty acids and cancer therapy. J Nutr 2004; 134: 3427S-3430S.
15. Ajani JA, Moiseyenko VM, Tjulandin S, Majlis A, Constenla M, Boni C, et al. Clinical benefit with docetaxel plus fluorouracil and cisplatin compared with cisplatin and fluorouracil in a phase III trial of advanced gastric or gastroesophageal adenocarcinoma: The V-325 Study Group. J Clin Oncol 2007; 25: 3205-9.
16. Naber TH, Schermer T, de Bree A, Nusteling K, Eggink L, Kruimel JW, et al. Prevalence of malnutrition in nonsurgical hospitalized patients and its association with disease complications. Am J Clin Nutr 1997; 66: 1232-9.
17. Baker JP, Detsky AS, Wesson DE, Wolman SL, Stewart S, Whitewell J, et al. Nutritional assessment. N Engl J Med 1982; 306: 969-72.
18. Segura A, Pardo J, Jara C, Zugazabeitia L, Carulla J, de las Peñas R, et al. An epidemiological evaluation of the prevalence of malnutrition in Spanish patients with locally advanced or metastatic cancer. Clin Nutr 2005; 24: 801-14.
19. Slaviero KA, Read JA, Clarke SJ, Rivory LP. Baseline nutritional assessment in advanced cancer patients receiving palliative chemotherapy. Nutr Cancer 2003; 46: 148-57.
20. Strasser F, Luftner D, Possinger K, Ernst G, Ruhstaller T, Meissner W, et al. Comparison of orally dministered cannabis extract and delta-9-tetrahydrocannabinol in treating patients with cancerrelated anorexia-cachexia syndrome: a multicenter, phase III, randomized, double-blind, placebocontrolled clinical trial from the Cannabis-In-Cachexia-Study-Group. J Clin Oncol 2006; 24: 3394-400.
21. Grimble R. Nutritional therapy for cancer cachexia. Gut 2003; 52: 1391-2.
22. Rose DP, Connolly JM. Omega-3 fatty acids as cancer chemopreventive agents. Pharmacol Ther 1999; 83: 217-44.
23. Argilés JM, Olivan M, Busquets S, López-

Soriano FJ. Optimal management of cancer anorexia– cachexia syndrome. Cancer Manag Res 2010; 2: 27-38.
24. Fearon K, Von Meyenfeldt M, Moses A, Van Geenen R, Roy A, Gouma D, et al. Effect of a protein and energy dense N- ٣fatty acid enriched oral supplement on loss of weight and lean tissue in cancer cachexia: a randomised double blind trial. Gut 2003; 52: 1479-86.
25. Moses A, Slater C, Preston T, Barber M, Fearon K. Reduced totals energy expenditure and physical activity in cachectic patients with pancreatic cancer can be modulated by an energy and protein dense oral supplement enriched with n-3 fatty acids. Br J Cancer 2004; 90: 996-1002.
26. Giacosa A, Rondanelli M. Fish oil and treatment of cancer cachexia. Genes Nutr 2008; 3: 25-8.
27. Kratz M, Callahan HS, Yang PY, Matthys CC, Weigle DS. Dietary n-3-polyunsaturated fatty acids and energy balance in overweight or moderately obese men and women: a randomized controlled trial. Nutr Metab (Lond) 2009; 6: 24.
28. Kapoor S. Immunomodulatory properties of omega-3 fatty acids: a possible explanation for their systemic, anti-carcinogenic effects. J Leukoc Biol 2009; 85: 2-3.
29. Goncalves CG, Ramos EJB, Romanova IV, Suzuki S, Chen C, Meguid MM. Omega-3 fatty acids improve appetite in cancer anorexia, but tumor resecting restores it. Surgery 2006; 139: 202-8.
30. Barber MD. Cancer cachexia and its treatment with fish-oil-enriched nutritional supplement-ation. Nutrition 2001; 17: 751-5.