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Randomized Controlled Trial

Omega-3 supplementation effects on body weight and depression among dieter women with co-morbidity of depression and obesity compared with the placebo: A randomized clinical trial

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SUMMARY

Purpose: We aimed to evaluate the effects of the omega-3 supplementation on body weight and depression among women with co-morbidity of depression and obesity seeking weight reduction compared with the placebo.

Methods: Sixty five patients with co-morbidity of depression and overweight/obesity (BMI $\geq$ 25) signed the informed consent form and enrolled into this 12-week double-blind, placebo-controlled randomized clinical Trial. Subsequently, participants randomly assigned into one of the two groups receiving daily 6 capsules of omega-3 (each capsule containing 180 mg EPA, and 120 mg DHA) or 6 capsules of placebo (two with each meal). We performed body composition assessments and Beck depression inventory at the baseline, and weeks 2, 4, 8, and 12 after the start of the study. One month after stopping the capsules at the follow-up visit, weight was measured to compare weight relapse between the two groups.

Results: Forty five patients finished the study. No significant differences were seen between groups regarding demographic and clinical variables at baseline. Using repeated measures ANOVA, omega-3 significantly reduced depression compared with the placebo ($P = 0.05$). Mean $\pm$ SD weight reduction in omega-3 group 3.07 $\pm$ 3.4 kg and in the placebo group was 1.16 $\pm$ 2.7 kg and the difference between groups was significant using independent sample t-test ($p = 0.049$). Patients in the omega-3 group did not show significantly more side effects compared to the placebo but they were not successful in preventing weight regain one month after the end of the study.

Conclusion: Based on our findings omega-3 capsule as a safe over-the-counter supplement might be helpful in reducing the signs of depression and also body weight in patients with co-morbidity of depression and obesity.

1. Introduction

Depression is a very common disorder. It will be the second most important source of burden of disease after ischemic heart disease in 2030 [1]. The current prevalence of major depressive disorder (MDD) among Iran population is 4.1% (95% CI: 3.1–5.1). Women are 1.95 (95% CI: 1.55–2.45) times more probable to have MDD [2–4]. On the other hand, obesity is very common too, and it is one of the most important risk factors for disabilities and mortality. The prevalence of overweight and obesity in national studies in adult was 21.7% (CI 95%: 18.5%–25%) [5].

Depression and obesity mostly coexist and are correlated with each other [6,7]. The level of this correlation is different in different

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levels of body weight. The prevalence of depression was 11%, 12%, and 23% among normal weight, overweight, and obese subjects, respectively [8]. A meta-analysis have reported that obese individuals are 1.18 times more probable to have depressive symptoms with more likely observation in women [9]. Obesity in women increases 37% risk of depression. When depression and obesity happen together health consequences are more serious and treatment of each depression or obesity by itself is complicated [8]. This co-morbidity is the main reason for the failure of weight reduction programs [8,10].

Many studies have ever been done on depression alone and obesity alone. In fact, clinical studies to evaluate interventions targeting both disorders are rare. Actually, in most of the interventions to treat the obesity, patients with depression are usually excluded. Similarly, in most clinical interventions on depression, gathering the information about eating behavior, and weight gain are overlooked. On the other hand, despite being known drug treatments for depression, but less than 50% (and even in some countries less than 10 percent) of patients with depression use these medications [11]. Barriers to the use of psychopharmacotherapy include lack of resources, lack of expertise and stigma as well as the unwillingness of the medication consumption in some people [11]. Therefore, finding a safe dietary supplement with more access that can simultaneously target both obesity and depression is very important.

There are pieces of evidence that show a dose-dependent effect of omega-3 fatty acids in reducing symptoms of postpartum depression and depression in the elderly. Emanuel and colleagues in a 13-year-old cohort study of polyunsaturated fatty acids (PUFA) and depression over 2744 people have observed that the relationship between PUFA intake and depression was significant, indicating a pattern of inappropriate and inadequate intake of dietary sources of PUFA in people with depression [12]. Studies on the effects of omega-3 in reducing body weight are limited.

The aim of this study was to evaluate effects of the omega-3 supplementation on body weight and depression among women with co-morbidity of depression and obesity seeking weight reduction compared with the placebo.

The clinical trial registration number: IRCT2014053016465N3.

2. Methods

This was a 12-week parallel, double-blind, placebo-controlled Randomized clinical Trial with no important changes to methods after trial commencement. We acquired all necessary ethical permissions from ethics committee review board of Tehran University of Medical Sciences, before patients' enrolment. We performed the study in a weight reduction clinic. Sixty five patients with co-morbidity of depression and overweight or obesity (Body Mass Index; BMI $\geq$ 25) signed the informed consent form and then they randomly assigned to one of the two groups receiving daily 6 capsules of omega-3; each capsule containing 180 mg Eicosapentaenoic acid (EPA), and 120 mg decosa-hexaene acids (DHA); Zahravi pharm. Co. or 6 capsules of placebo (two with each meal). A third party was used the computerized simple random allocation method to generate the random allocation sequence. The groups were blinded by placebo to participants and were blinded to the researcher by coding (allocation concealment). Random allocation sequence and subject enrollment were performed by a third party. A psychiatrist enrolled to help in the diagnosis of depression by a semi-structured clinical interview performed based on DSM-5 criteria.

Inclusion criteria were: 18–50 years old women, BMI $\geq$ 25, Identification of depression by semi-Structured Clinical Interview for DSM-5 criteria for depression based on SADS(Schedule for Affective Disorders and Schizophrenia), signing the consent form.

Exclusion criteria: severe mental disorders, bipolar disorder and schizophrenia, as well as severe depression, psychotic depression or have suicidal thoughts, and those who were taking antidepressants, consuming glucocorticoids, anti-inflammatory steroid, those who take medication to reduce appetite or weight, those with diabetes who take medication or insulin, those with heart disease or hypercholesterolemia that take the medications, those who take oral anti-inflammatory drugs, corticosteroids, or any medicine that decrease or increase body weight, hormonal contraceptives, pregnancy and lactation, menopause, hypothyroidism, sport professionals, those on special diets, allergy to fish or fish oil.

The sample size was determined to recognize the difference of 4 kg ($\mu1-\mu2 = 4$) between the omega-3 and placebo groups in the Type I error $\alpha = 0.05$ and the power of 1-$\beta = 0.80$. According to a study by Hill AM and colleagues [13], the standard deviation for weight was determined to be 4.8. Based on above information the sample size of 21 was calculated to be sufficient.

The sample size was determined once again for secondary outcome of depression so that we could able to detect a 5 point difference of depression score between groups ($\mu1-\mu2 = 5$) in type I error $\alpha = 0.05$ and with a power of 1-$\beta = 0.80$. According to the study of Su KP and colleagues [14], the standard deviation of depression score was 3.7 and put into the formula for calculating sample size Based on above information the sample size of 9 was calculated to be sufficient.

Finally, we chose the larger sample size to cover all aims of the study, to compensate for loss to follow up which is common in clinical trials and also to raise the power of the study. So sampling was continued to 32 patients in Omega-3 group and 33 patients in the placebo group.

To eliminate the effect of diet, all the participants in the study received a weight loss diet −500 to −1000 kcal of usual dietary intake and we controlled that by using intermittent three-day food records during the study. Furthermore, to coordinate and control for the physical activity we recommended to all participants to keep 20 min of moderate physical activity that is available to everyone and we inquired it in every visit. Sampling site was a weight loss clinic. Anthropometric, and body composition assessments (including body weight), Beck depression inventory, food craving questionnaire, appetite and food abstinence visual Analogue scales were performed at the baseline visit, and repeated two weeks, 4 weeks, 8 weeks and 12 weeks after the start of the study. One month after stopping the capsules at the follow-up visit, weight was measured to compare weight regain between the two groups.

A clinical dietitian preformed anthropometric assessments including body weight, height, BMI, waist and hip circumferences. Total body fat and muscle percentage, were estimated with body composition analyzer all in standard situations. We used InBody270 BIA (InBody Co., Ltd) device which involves eight electrodes, a tetrapolar electrodes in footpads and another 4 set of electrodes in the handle. The subjects stood on the metal footpads in bare feet and grasped a pair of electrodes fixed to a handle with arms extended in front of the chest. This instrument assesses total body fat, visceral fat, lean body mass, and basal metabolic rate as well as body weight and BMI. The clinical validity of this instrument in measuring body composition is already approved in comparison with Magnetic Resonance Imaging (MRI) and Dual-Energy X-Ray Absorptiometry [15].

Furthermore, subjects were asked to fill a three-day food record. Three-day food records were to be completed at home over two non-sequential weekdays, and one day on a weekend, with the days being assigned randomly. Subjects were instructed to record everything that they eat or drink (including liquids, sweets, and snacks). The portion sizes and scales were also delivered to them. They were required to deliver the three-day food records in the consequent visit.

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