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Original article

Effect of omega-3 fatty acids on appetite, energy and macronutrient intake and body weight in obese adults: a randomized clinical trial

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Summary. Obesity as an important health problem can be solved by modulating the appetite, somewhat. Polyunsaturated fatty acids (PUFA) can modulate appetite and by the way be helpful in weight loss. **Method**: We investigated the effect of omega-3 fatty acids on appetite, energy and macronutrient intake and weight in obese adults. 66 participants were randomly allocated in intervention and placebo group, and consumed omega-3 and paraffin soft gels respectively, 1000mg twice a day for four weeks. **Results:** Repeated measure method analysis did not show any significant change in Visual Analogue Scale for appetite and weight in 2 treatments (P=0.46). Dietary intakes of total fat, PUFA, Monounsaturated fatty acids (MUFA) and cholesterol had a significant decrease in treatment group in comparison with placebo (P< 0.05). Energy and protein intakes changed within two groups significantly (P< 0.05). **Conclusion:** This study shows that increasing intake of omega-3 fatty acids would be helpful for weight loss in obese adults.

Key words: omega-3 fatty acids, appetite, energy and macronutrient intake, body weight, obesity

Introduction

Obesity is defined as a condition of body fat accumulation which may impair the individual's health body mass indexes (BMI) .BMI equal to or greater than to 25 is considered as overweight and equal to or greater than 30 as obesity (1). Overweight and obesity prevalence has increased dramatically over the last two to three decades in both developed and developing countries all over the world, a trend that needs to be changed by identifying novel therapeutics methods (2). Approximately 400 million adults in the world were overweight in 2005 and it is predicted it would increase to 2-3 billion overweight and 700 million obese in 2015 (3). A nationwide cross-sectional survey which was conducted in 2005 in Iran, estimated that 11/1% of men and 25.2% of women were obese. Individuals who are overweight are at higher risk for a large variety of disabling and life-threatening chronic conditions, such as high blood pressure, psychosocial dysfunction, cardiovascular disease, diabetes, arthritis, and overall mortality (4).The main reason for this alarming event is positive energy balance which may leads to hypertension, type 2diabetes and high risk of cardiovascular diseases among other physiopathological consequences (2). According to recent researches, obesity was more frequent than expected and

nutrition education can increase nutrition knowledge significantly (5).

Different dietary strategies have been researched with the aim of nutritionally satiety and huger perception after eating (6). One of the dietary strategies which have been reported as appetite modulator is the polyunsaturated fatty acids (PUFA) consumption (7). Previous studies have shown that Eicosapentaenoic acid (EPA) and Docosahexaenoic acid (DHA) supplementation is may be protective against obesity, and may attenuate weight gain in obese animals and humans (8). Parra et al. study showed that long chain n-3 fatty acid intake, modulates satiety in overweight and obese volunteers during weight lost programs (9). DHA and EPA are synthesized by human body only in insignificant amounts, and nutritional intake is essential. Fatty fishes, fish and vegetable oils are the most noticeable sources for omega 3, but also some seaweeds supply too (10) Indeed, it had been reported omega-3-PUFA rich diets consumption can reduce food intake, but increase energy expenditure and finally lower body weight and fat mass in rats and mice. Remarkably, a lower body weight or fat mass was observed in studies with controlled calorie intake (11-13) .Evidence for a similar effect in humans is limited and intervention studies in humans are inconclusive.

As mentioned above, previous studies had restricted the calorie during the intervention, so it isn't clear that weight loss is just related to the intervention. So we conducted a randomized controlled trial to evaluate the omega-3 supplementation effect on appetite, energy and macronutrient intake and body weight in healthy obese adults without calorie restriction.

Materials and Methods

Subjects

A total of 66 subjects consisting 22 men and 44 women with body mass indexes more than 30 kg/m^2 aging between 18 to 45 years old were recruited for this study by the advertisements from a specialty and subspecialty clinic of Tabriz University of Medical Science in Iran.

Exclusion criteria were consisting of smoking, having kidney and liver disease, diabetes, thyroid disorders, immunodeficiency diseases, treatment with anticoagulants, beta blockers, anti-inflammatory drugs and omega-3 supplements within the last 2 months, pregnancy and lactating. Subjects were asked to avoid weight loss drugs and diets during the study.

Study design and measurements

Sixty-six participants were allocated in 2 treatment groups by chance. Randomization was performed by Randomization allocation software (RAS) and so randomization was continued until the two treatments make a proper similarity for many important variables before intervention.

Each Treatment consisted of 33 subjects. Intervention Treatment and placebo consumed omega-3 capsules and paraffin soft gels respectively, containing 1000mg, twice a day for four weeks. Omega 3 soft gels contained 180 mg of EPA and 120 mg of DHA (Figure 1). There has been reported no side effects for consumed doses. The capsules were prepared by Zahravi Pharmacy Company of Tabriz.

All participants were instructed to follow their usual dietary habits and lifestyle. This study was a double-blind, placebo controlled clinical trial. Neither the subjects nor the investigators were aware of treatment assignments.

Information about appetite, energy and macronutrient intake and weight measurements was collected at the beginning and end of trial in the morning before eating the breakfast.

Appetite was measured using the visual analogue scale (VAS) that contained four questions on separate 100 mm scales to express their fasting sensations of hunger, satiety, desire to eat and prospective food consumption. Participants drew a vertical mark across the horizontal line of each scale. The distances on the VAS were converted into scores by measuring the distance from the left end of each line to the mark in millimeters using a ruler.

Energy and macronutrient intake and weight measurements

Nutrient intakes were estimated using three 24-h dietary recalls at the beginning and at the end of the study. If a participant ate a food that was not in the database, similar nutrient composition food was cho-

sen instead of that. Body weight was measured using a scale (Seca, Hamburg, Germany) with 0.1 kg accuracy without shoes and wearing light clothing. Heights were measured using a wall-mounted meter scales with 0.1 cm accuracy without shoes. Body mass index was calculated by body weight (in kilograms) over height squared (in meters).

This study was approved by the regional Medical Ethics Committee of Tabriz University of Medical Sciences in Tabriz city of Iran. This study also registered in Iranian Registry of Clinical Trials (IRCT138903162017N3). The protocol and aims of the study were fully explained to the subjects and all volunteers gave informed consent at the beginning of the study.

Statistical methods

In this study, class of variables defined some of variables that are similar (eg, Total Fat, Saturated fat, Cholesterol, MUFA, PUFA). The influential variables were adjusted between two treatment groups, Omega-3 and placebo. For quantitative data, normality was evaluated by Q-Q test and then Mauchly's W test was checked for covariance matrix identity. Finally repeated measure with control covariates test was used by Minitab Software version 17. The results include four P-values for comparing multi and univariates. The first was P-value$_{Matching}$ was used for matching dependent variables before the intervention and the second was P-value$_{Treatment}$ for comparing between Omega-3 and Placebo by repeated measure. Third P-value$_{Time}$ was used for comparing variations in two times of intervention by repeated measure and the last was P-value$_{T. time}$ for comparing variations in each class of variables in two times of intervention by MANOVA repeated measured and finaly was P-value$_{.T\ treatment}$ for comparing variations in each class of variables between Omega-3 and Placebo by MANOVA repeated measured. The level of significance was set at 0.05 and all results were expressed as Mean ± SE.

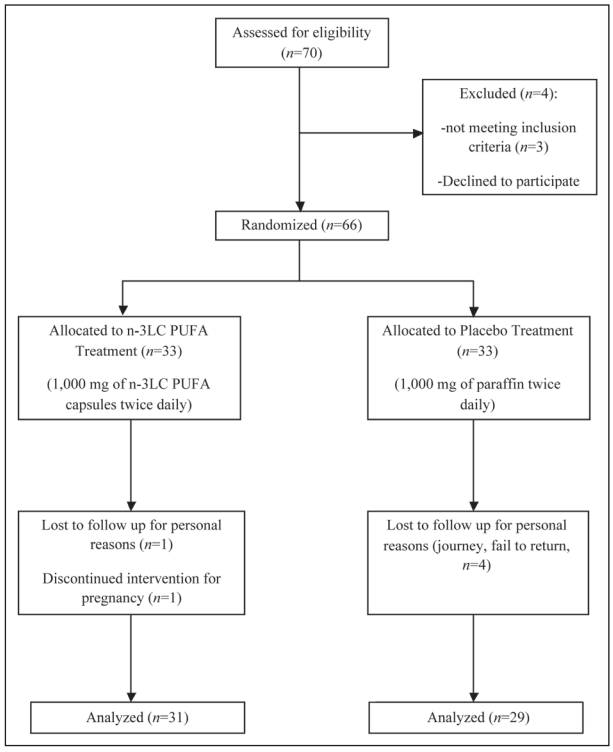

Figure 1. Flowchart of Subject Screening and Enrollment

Result

Study population

Sixty of 66 subjects entered the trial, but 60 completed the four week intervention (n=31 in omega-3 Treatment and n=29 in placebo Treatment). Two of omega-3 receiving subjects and four of placebo receiving subjects dropped out. Withdrawals were due to pregnancy, traveling and refusal to continue the study.

Baseline characteristics of the 2 Treatments were not significantly different (Table 1), which shows that two treatments are well matched.

Weight measurement

There was no significant weight change in 2 treatment groups (Pg=0.46) before and after the study (P_{time}=0.99). Weights at the baseline and end of intervention were 88.15±1.8 kg *vs*. 87.96±1.8 kg in the omega-3 group, and 88.30±3.3 kg *vs*. 88.63±3.33 kg in the placebo group, respectively (Table 1).

Energy and macronutrient intake

There were no significant differences in total energy and macronutrient intakes between the groups at baseline (Table 2). At the end of the intervention, total fat, PUFA, MUFA and cholesterol intakes had decreased significantly in the omega-3 group than

Table 1. Characteristics of subjects at baseline and after 4 week intervention (n =60).

Treatment	Omega-3 (n=31)		Placebo (n=29)		#PMatching	†PTreatment	‡PTime
	Before	After	Before	After			
Age(year)	34.24 ± 1.33	-	33.56 ± 1.60	-	0.74	-	-
Gender(M:F) *	11: 22	10:21	11:22	10:19	0.85	-	-
Weight(kg)	88.15± 1.83	87.96±1.86	88.3± 3.32	88.63±3.33	-	0.46	0.99
BMI(kg/m2)	32.73± 0.42	31.77±0.53	32.25±0.95	31.35±1.06	-	0.45	0.28

*Frequency

#PMatching: independent t-test
†PTreatment: P value for comparing between Omega-3 and Placebo by repeated measure model.
‡PTime: P value for difference between two times before an dafter by repeated measure model.

placebo. Energy and protein intakes did not change between groups but their intakes changed within the groups significantly after four weeks (Ptime=0.02, Ptime=0.03, respectively). No significant differences in carbohydrate and saturated fatty acid intakes were observed between and within the 2 groups (Table 2).

Appetite

Visual analogue scale (VAS) measurements were shown before and after the supplementation for each group in Table 3. Fasting appetite measurement remained statistically unchanged between 2 groups after the intervention. There was a significant difference in satiety within the groups after four weeks. (Ptime =0.03, Pg=0.45). No statistically significant differences were observed in the other appetite parameters within the groups.

Discussion

Appetite control is one of the most important factors which involve in dietary treatment of obesity success (14). Evidence shows that omega-3 fatty acids can suppress the appetite, so this study was conducted as a randomized, placebo-controlled trial in obese adults.

Table 2. Dietary intake of subjects throughout the study.

Treatment	Omega-3 (n=31)		Placebo (n=29)		#PMatching	†PTreatment	‡PTime	!PTreatment	§PTime
	Before	After	Before	After					
Energy(Kcal)	2678.2± 104.4	2137.9± 77.43	2681.3± 98.2	2680.11± 97.5	0.98	0.112	0.021	-	-
Carbohydrate(g)	366.31± 17.61	308.26± 14.81	367.45± 14.6	367.04± 18.51	0.82	0.360	0.270	-	-
Protein(g)	96.22 ± 5.28	74.54 ± 4.47	93.90± 3.27	100.67± 4.04	0.97	0.152	0.031	-	-
Total fat(g)	97.08 ± 3.33	71.02 ± 2.69	96.13± 2.75	108.35± 3.08	0.89	0.000	0.000		
Saturated fat(g)	22.44 ± 1.33	17.66 ± 0.99	23.51± 1.32	23.22± 1.33	0.73	0.110	0.000		
MUFA(g)	26.19 ± 1.15	19.89 ± 1.00	25.77± 0.94	29.66± 1.01	0.82	0.000	0.000	0.000	0.000
PUFA(g)	31.82 ± 1.55	21.76 ± 1.39	29.12± 1.88	36.82± 1.79	0.50	0.000	0.000		
Cholesterol(mg)	272.54± 20.55	199.18± 14.60	270.4± 13.7	410.07± 22.96	0.95	0.000	0.000		

MUFA: mononusaturated fatty acids. PUFA: polyusaturated fatty acids
#PMatching: P value for matching dependent variables before intervention Omega and Placebo
†PTreatment: P value for comparing between Omega-3 and Placeboby repeated measure model.
‡PTime: P value for difference between two times before andafter by repeated measure model.
!PTtreatment: for comparing variations in each class of variables between Omega-3 and Placeboby model.
§PTtime: P value for comparing variations in each class of variables in two times of intervention by model

Table 3. Visual Analogue Scales measurements before and after supplementation in 2 Treatments.

Treatment	Omega-3 (n=31)		Placebo (n=29)		†PTreatment	‡PTime
	Before	After	Before	After		
hunger	3.33 ± .44	3.00± .51	3.46± .65	2.67± .58	0.94	0.47
satiety	4.36± .49	4.72± .57a	5.82 ±.67	3.50± .59a	0.45	0.03
desire to eat	3.93± .45	3.69±.40	4.21± .59	3.03± .57	0.66	0.23
PFC	2.78± .39	2.96± .43	3.25± .66	2.60±.56	0.97	0.63

†PTreatment: P value for comparing between Omega-3 and Placebo by repeated measure model.
‡PTime: P value for difference between two times before and after by repeated measure model.
PFC: prospective food consumption

According to this study results (Table 2), there was no significant difference between the groups in weight at the end of study. Our results aren't parallel to Hajianfar *et al* study that showed 8 weeks omega3 supplementation in type2 diabetes women reduced BMI (15). In another study, twenty severely obese women during a very low calorie diet supplemented with omega-3 long chain PUFA showed higher weight losses than placebo group (16). Our results were similar, however, to the study conducted by Cussons *et al*. which showed omega-3 fatty acids supplementation for 8 weeks had not significant effects on weight and BMI of polycystic ovary syndrome patients (17). Mori *et al*. study showed no significant changes in BMI after 6 weeks supplementation by purified EPA and DHA in hyperlipidemic men (18). Kartz *et al*. also showed that dietary omega-3 PUFA content increasing up to 3.6% of total energy intake did not have any effect on body weight in healthy overweight and moderate obese, men and women (19).

An important aspect of human trial's results is concerning about the levels of dietary n-6 PUFAs and linoleic acid (LA) in particular, in diet background. In the US, estimated consumption of soybean oil, containing about 50% LA, has increased more than 1,000-fold from 1909 to 1999 per capita; today representing 7.21 percent of total diet energy (20). A recent study performed with Alvheim et al demonstrated that increasing the dietary levels of LA from 1 to 8 percent of total energy which reflects the increase during the 20th century, elevated the level of Arachidonic acid phospholipids and results the obesity in mice (21).By adding 1% n-3 PUFA to the 8% of total LA in diet, EPA and DHA replaces by AA in tissue phospholipids and obesity develop attenuated (21).

In our study, total fat, PUFA, MUFA and cholesterol intakes were decreased significantly after four weeks. Omega-3 fatty acid supplementation had not any effect on total energy and macronutrient intake between the groups, but changed the both within the groups significantly. Although, it had a trend to decrease but may be due to short duration of the study, we could not observe a statistically significant decrease in total energy intake that was a limitation for our study. Our findings were consistent with some recent studies. Kartz *et al*. showed that increasing dietary omega-3 PUFA content to 3.6% of total energy intake didn't have any effect on food intake in men and women (19). Ruzickova *et al*. and Huang *et al*. study results also showed no changes in energy intake in their studies (22, 23). In the Mori *et al*. study, dietary fish meal (3.65 g omega-3 fatty acids) decreased total fat, MUFA and total energy intakes (24). Contradictory results that were shown in the rat studies might be due to high doses of omega-3 in rats in comparison with human ones. These doses vary widely and generally are not safe in humans. However, we cannot distribute animal results to humans', because of possible differences in pharmacokinetics for omega-3 fatty acids (EPA and DHA) supplementation between them. This reduction in total fat, PUFA, MUFA and cholesterol intakes in our study, were by satiety modulation mechanism related to omega-3.

As shown in Table 3, significant changes were observed within two groups in satiety after four weeks from baseline but it did not change between two

groups. In agreement with our observations, Kartz *et al*. reported no significant changes in hunger and fullness in well-controlled 16 weeks randomized clinical trial (19). Inconsistently, Parra *et al*. showed that high long chain omega-3 fatty acids (LCFA) diets modulate satiety in overweight and obese volunteers during weight loss programs (9).

One of the satiety mechanisms is mediated by leptin which is secreted from adipose tissue. Leptin orders the hypothalamus to inhibit the orexigenic effects of the neuropeptide Y and agouti-related peptide, but activates the anorexigenic effects of pro opiomelanocortin downstream targets and cocaine amphetamine regulated transcript. Together, this leads to satiety, and stimulates energy expenditure and ultimately results in weight loss (25). Other researchers have shown that dietary supplementation with fish oil increases plasma leptin in rats (26).

On the other hand, circulating lipids, particularly LCFAs, may regulate appetite and glucose production by prompting an increase in intracellular LCFA-CoAs in the hypothalamus, and this homoeostatic mechanism alteration may be related to central obesity. LCFA-CoAs appear to initiate hypothalamic satiety signal by activating neuronal pathways to reduce food intake (27).

Some confounding factors may be responsible for the changes observed in satiety after four weeks or short duration of study did not allow us to observing significant changes between the two groups.

In this study, we could not assess leptin levels and it is one of the limitations in our study. In this study we could not get food records because of low cooperation in some participants and dietary data results would tend to be weak because of dietary assessment limitation. Our suggesting for next studies is to prolong the intervention duration.

Conlusion

We concluded that omega-3 fatty acids supplementation can reduce intakes of total fat, PUFA, MUFA and cholesterol intake in obese adults .Although significant changes were not observed in weight and energy intake. This study suggests that of omega-3 intake increase would be helpful for weight loss, by diet or supplementation.

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