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CASE STUDY

Effect of omega−3 fatty acid supplementation on reduce body weight and body fat mass in obesity: A case study with an evidence-based approach

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Abstract

Background: Obesity is a public health problem, especially in developing countries. Providing Omega−3 supplementation has benefits to reduce body weight and body fat mass.

Objective: This study aims to determine the effect of omega−3 supplementation on weight loss and body fat mass in obesity.

Methods: This study used a literature search using advanced queries in the databases PubMed, Scopus, ProQuest, Cochrane Library, and combined MeSH terms with Title/Abstract. The collected literature is discarded if there are duplicates, then literature that meets the eligibility criteria is filtered. We used the Oxford Center for Evidence-Based Medicine as a means of critical appraisal and determining the level of evidence of the selected literature.

Results: Four chosen study were selected. The first study involved 39 adults with obesity, there was a weight loss of 6.04 kg in the group given omega−3 supplementation of 6 g/day for 8 weeks compared to the placebo group 5.4 kg and there was a decreased in body fat mass in the intervention group. The second study did not show a significant result. The third study on 65 women showed a weight loss of 3.07 kg in the group given omega−3 consisting of 1.08 g EPA and 0.72 g DHA compared to 1.16 kg in the placebo group for 12 weeks. In the fourth study, a systematic review study, there was no conclusive result.

Conclusion: Omega−3 fatty acid supplementation could be beneficial in reducing weight in obese patients with dietary modification.

Keywords: obesity, omega−3 fatty acids, body weight, body composition, fat mass

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Case report

A 36 year old woman came to the nutrition clinic to lose weight. The patient said that her weight has increased since the Covid-19 pandemic. Weight gain of 20 kg in 3 years. She often eats fried food and also likes sweet cakes. The patient complained that her right leg often hurt, especially if she stood for too long. The patient has tried several diet methods obtained through social media or googling but none of them succeed. The patient works as an employee in a private company. The patient's activity is more often sitting in front of the computer. The patient said she rarely exercises. Her present body mass index is 28 kg/m^2. So far, the patient has never been to a clinical nutrition specialist for a weight loss program. There was no history of diabetes mellitus, hypertension, dyslipidemia, or heart disease. From laboratory examinations, the results were within normal limits. Body composition examination revealed a high fat mass.

Patient is advised to reduce calorie intake and increase physical activity. The patient had read in an online article that supplementation of omega-3 could help weight loss and body fat mass, then the patient asked a clinical nutrition specialist whether omega−3 had that role.

Introduction

Obesity is a global problem with prevalence increasing every year. According to the World Health Organization (WHO) data in 2014, there has been a two-fold increase in prevalence compared to the prevalence figure in 1980. More than 1 billion people worldwide are obese, including 650 million adults, 340 million teenagers, and 39 million children. This number keeps continuing to increase and WHO estimates that by 2025 there will be an additional 167 million people worldwide with obese. [1] According to Riskesdas data in 2018, the prevalence of obesity among adults aged over 18 years was 21.8%. This prevalence has increased compared to Riskesdas in 2013, namely 7%. DKI Jakarta ranks second among all provinces in Indonesia for obesity prevalence, which is 30%.[2]

Obesity is a condition where excess fat accumulates in the body, either generalized or localized in certain parts of the body, and occurs due to an imbalance between energy intake and output. Various etiologies cause obesity including food intake, physical activity, sedentary lifestyle, genetics, environment, neuroendocrine, drugs, other pathological factors, and socio-economics. [3] According to WHO, the definition of obesity is the accumulation of abnormal or excessive fat tissue that impacts health. Obesity can be assessed by body mass index (BMI). In Asia, obese if the BMI value is ≥ 25 kg/m^2.[1]

Adipose tissue plays a key role in the pathogenesis of obesity and associated complications. Three types of adipose tissue with different precursor cells, phenotypes, functions, and regulation have been, so far, identified: the energy-storing white adipose tissue (WAT), the energy-consuming brown adipose tissue (BAT), and the recently described/"brite" adipose tissue.[4] White adipose tissue is the main storage organ, accumulating the excess energy in the form of triglycerides, which can be mobilized under energy deprivation conditions. In addition, WAT acts as an important endocrine organ releasing a broad range of molecules called adipokines involved in the regulation of many physiological functions including body weight (leptin), vascular metabolism (PAI-1), glucose metabolism, and insulin sensitivity (adiponectin) and several inflammatory cytokines and chemokines (TNF-α, IL-1, IL-6, RBP-4 or MCP-1).[5,6] WAT is distributed around the body in different depots such as abdominal, subcutaneous, or gonadal regions with different adipokine secretion profiles. The presence of hypertrophy and hyperplasia of adipocytes causes increased secretion of pro-inflammatory cytokines. On the other hand, BAT is known to be specialized in adaptative thermogenesis being uncoupling protein 1 (UCP1) the main responsible. This thermogenic mechanism plays a key role in defending against hypothermia and obesity.[7] Omega-3 fatty acids fatty acids are polyunsaturated fatty acids with multiple double bonds. The three most crucial omega-3 fatty acids fatty acids are alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and

docosahexaenoic acid (DHA), which cannot be endogenously synthesized and must be obtained from dietary sources.[8] The possible mechanisms related to the effect of omega-3 fatty acids on body weight or body fat mass seem to be linked to metabolic changes related to obesity, including the modulation of lipid metabolism, regulation of adipokines (such as adiponectin and leptin), and decreased inflammation of adipose tissue.[9] Several studies omega-3 fatty acids at doses of more than 3 g/day can reduce appetite and increase thermogenesis, increasing plasma concentrations of adiponectin and leptin. In addition, administration of omega-3 fatty acids at a dose of 3 g/day can reduce body weight and body fat through postprandial satiety and changes in gene expression involving the regulation of fat oxidation in adipose tissue.[10]

Research demonstrating the effects of omega-3 fatty acids supplementation in reducing body weight and body fat mass in patients with obesity includes a study by Munro et al.[11]In this study, 39 obese individuals were divided into two groups, placebo, and intervention, with the intervention group receiving 6g/day of omega-3 fatty acids fatty acid capsules for eight weeks with diet modification. Patients receiving omega−3 fatty acids had significant weight loss (- 6.04 kg) compared to the placebo group (- 5.2 kg). A study by Noreen et.[12] with 44 individuals with obese was divided into two groups, placebo, and intervention, with the intervention group receiving omega-3 fatty acids fatty acid capsules 4 g/day containing 1.6 g EPA and 0.8 g DHA for 6 weeks. The omega-3 fatty acids group lost 0.5 kg of fat mass, while the control group gained 0.2 kg. This contrasts with a study by Defina et al.[13] there were no differences between group intervention and placebo in weight loss.

Based on previous research, it is not yet conclusive whether omega-3 fatty acids can reduce body weight and body fat mass in obese patients. This evidence based case report seeks to assess the impact of omega-3 fatty acids supplementation on weight loss and body fat mass in obese patients.

Clinical Question

"Can omega-3 fatty acids reduce body weight and body fat mass in patients with obesity?"
Participants [P]: Adult patients with obesity
Intervention [I]: omega-3 supplementation in conjunction with diet modification
Control [C]: diet modification
Outcome [O]: weight loss and body fat mass

Methods

Searching Strategy

A literature search was managed using an advanced search with a combination of MeSH Terms and Titles/Abstracts in four databases: PubMed, Cochrane Library, Scopus, and Proquest. Keywords included " *obesity", "obese", "omega 3", "omega-3 fatty acids', "placebo", "weight loss", "fat mass", body composition*". The Oxford Centre for Evidence-Based Medicine guidelines were utilized for critical literature assessment and determining the level of evidence**.**

Eligibility Criteria

Inclusion criteria: 1) adult with obesity aged > 18 years; 2) patients receiving omega−3 fatty acids supplementation; 3) research outcome focusing on weight loss and body fat mass; 4) study design being a controlled clinical trial or a systematic review/meta-analysis of randomized controlled trials; 5) articles published in English; 6) subject of study is human. Exclusion criteria: articles not available in full text.

Results

The selected articles met eligibility criteria through systematic reviews, meta-analyses, and controlled clinical trials. The literature search was independently conducted across four databases: PubMed, Cochrane Library, Scopus, and ProQuest. The literature search process is depicted in Figure 1. Keywords employed were "obesity", "obese", "omega 3", "omega-3 fatty acids fatty acids", "weight loss", "reduce weight", and "fat mass". Additionally, a review using Mendeley was performed subsequently to exclude duplicate

articles. The research will be critically assessed using the Oxford Centre of Evidence-based Medicine (CEBM) critical appraisal. The review assesses aspects of the validity, importance, and applicability of the research. As we can see in **table 1**, the research results of this study obtained 6 kinds of literature from Pubmed, 12 kinds of literature from the Cochrane Library, 8 kinds of literature from Scopus, and 138 kinds of literature from ProQuest. Duplication filtering was done using Mendeley. Furthermore, filtering was carried out based on method, title-abstract, PICO criteria, and full-text availability. The filtering results can be seen in **figure 1**.

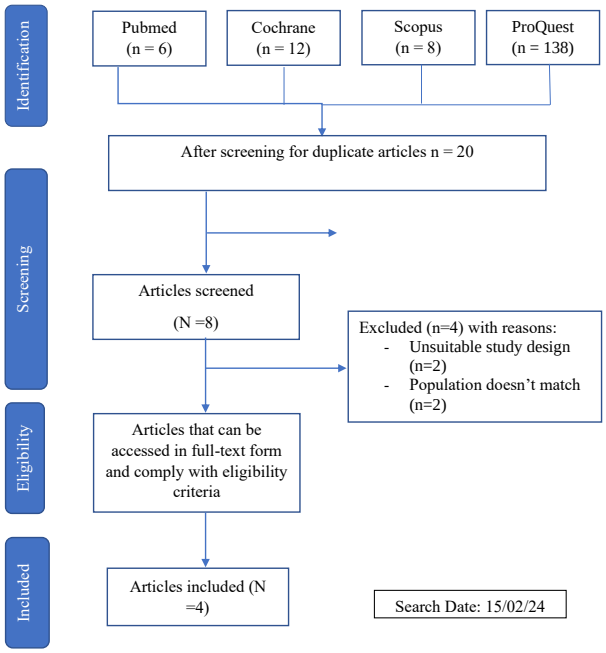

Figure1. Prisma's flow chart

Table 1. Literature searching strategies

Database	Search Strategy	Hits
Pubmed	((((((((((((obesity[Title/Abstract]) OR (obesity[MeSH Terms])) OR (obese[Title/Abstract])) OR (obese[MeSH Terms])) AND (omega 3[Title/Abstract])) OR (omega 3[MeSH Terms])) OR ("omega 3 pufa"[Title/Abstract])) OR (omega 3 pufa[MeSH Terms]))) AND ("weight loss"[Title/Abstract])) OR (weight loss[MeSH Terms])) AND ("body fat mass"[Title/Abstract])) OR (body fat mass[MeSH Terms])) OR ("body composition"[Title/Abstract])) OR (body composition[MeSH Terms])	6
Cochrane	ID Search Hits #1 (obesity):ti,ab,kw (Word variations have been searched) #2 (obese):ti,ab,kw (Word variations have been searched) #3 #1 OR #2 #4 ("omega 3 PUFA"):ti,ab,kw (Word variations have been searched) #5 ("omega 3 fatty acids"):ti,ab,kw (Word variations have been searched) #6 ("omega 3 polyunsaturated fatty acid"):ti,ab,kw #7 #4 OR #5 OR #6 #8 ("weight-loss"):ti,ab,kw (Word variations have been searched) #9 (reduce weight):ti,ab,kw (Word variations have been searched) #10 #8 OR #9 #11 ("body fat mass"):ti,ab,kw (Word variations have been searched) #12 ("body composition"):ti,ab,kw #13 #11 OR #12 #14 #3 AND #7 AND #10 AND 13	12
Scopus	TITLE-ABS-KEY (obesity) OR TITLE-ABS-KEY (obese) AND TITLE-ABS-KEY (omega 3) AND TITLE-ABS-KEY (weight AND loss) AND TITLE-ABS-KEY (Fat AND Mass)	8
ProQuest	obesity AND (omega 3) AND (loss weight) AND (fat mass)	138

Discussion

The results of the literature search obtained four studies that met the criteria. Delpino, et al[14]., conducted research with a systematic review design, with details of 20 RCT studies. The study aims to assess the benefits of omega-3 fatty acids supplementation in reducing body weight and fat mass in patients with obesity. The exclusion criteria that the authors applied were studies that were not RCTs, studies conducted by experimental animals, and studies that did not assess body weight or body fat mass as outcomes. The risk of bias was assessed based on the Cochrane risk assessment tool for RCT studies.

Table 2. Characteristic of the study

Researcher	Design	Population	Outcome	Result
Mendes F, et al.[14] (2021)	A systematic review of Randomized Controlled Trials consisting of 20 RCT	RCT: Patients with obesity taking omega−3 fatty acids supplementation	Weight loss and reduced body fat mass	From 20 RCT, 11 studies said there was no effect of supplementation omega-3 fatty acids on weight loss and body fat mass but another 9 studies said there was an effect of supplementation omega−3 on weight loss and body fat mass.
Munro, et al.[11] (2013)	*Randomized Double-Blinded Controlled Trial*.	Thirty-nine (n=39) subjects obesity with IMT 30-40 kg/m2, age 18-60 years, After randomization, divided into intervention and placebo groups. The intervention group received 6x1 g omega−3 supplementation in conjunction with diet modification and the placebo group received sunola oil. The intervention was carried out for 8 weeks	Weight loss and reduced body fat mass	After giving omega-3 for 4 weeks there was a significant reduction in body weight of 6.12 kg and a reduction in body fat mass of 4.36 kg in the intervention group ($p < 0.01$) and after continuing 4 weeks later there was a reduction in body weight of 5 .79 kg and fat mass of 4.46 kg ($p < 0.01$).
Defina, et al.[13] (2011)	*Randomized Double-Blinded Controlled Trial*	A total of 128 obese patients with a BMI of 26-40 kg/m2 aged 30-60 years, the intervention group received [3.0 g eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), ratio 5:1 (EPA:DHA)] with diet modification. The intervention was carried out for 24 weeks	Weight loss and reduced body fat mass	There was no significant in weight loss($P = 0.33$) and body fat mass ($p = 0.37$) between the intervention and placebo groups.
Ali S, et al.[15] (2018)	*Randomized Double-Blinded Controlled Trial*	A total of 65 overweight and obese patients with a BMI ≥25 kg/m^2 were given 6 omega−3 capsules per day containing 180 mg EPA and 120 mg DHA with diet modification. The intervention was carried out for 12 weeks	Weight loss	In the intervention group, there was a significant weight loss of 3.07 ± 3.4 kg, and in the placebo group 1.16 kg ± 2.7 kg with a p value = < 0.05

Table 3. Validity Criteria for Mendes F, et al[14]

Article	Study Design	Question	Find	Appraise	Inclusion	Total Up	Result	Applicability
Mendes F, et al.[14] (2021)	*Systematic Review*	+	+	+	+	+	A	+

A = Research involving 20 RCT studies providing omega−3 supplementation with a dose range of 2.8 g to 6 g with a duration of 3 weeks – 24 weeks showed inconsistent results. Nine studies state that providing omega−3 supplementation provides significant results in reducing body weight and body fat mass.

Table 4. Validity Criteria for Munro, et al.,[11] Defina, et al.,[13] and Ali S, et al[15]

Article	Study Design	Randomization	Similarity	Equally treated	Intention to treat analysis	Blinding	Result	Applicability
Munro, et al.[11] (2013)	*Randomized Controlled Trials*	+	+	+	+	Double-blind	B	+
Defina, et al.[13] (2011)	*Randomized Controlled Trials*	+	+	+	+	Double-blind	C	+
Ali S, et al.[15] (2018)	*Randomized Controlled Trials*	+	+	+	+	Double-blind	D	+

B After giving omega−3 for 4 weeks there was a significant reduction in body weight of 6.12 kg and a reduction in body fat mass of 4.36 kg in the intervention group ($p< 0.01$) and after continuing 4 weeks later there was a reduction in body weight of 5 .79 kg and fat mass of 4.46 kg ($p < 0.01$).
C = There was no significant in reduce of body weight ($p = 0.33$) and body fat mass ($p = 0.37$) between the intervention and placebo groups.
D = In the intervention group there was a significant weight loss of 3.07 ± 3.4 kg and in the placebo group 1.16 kg ± 2.7 kg with a p value = < 0.05

Nine RCTs examined the effects of omega−3 fatty acids supplementation on weight loss and body fat mass, having a total of 572 subjects randomized to get PUFA and placebo. In all nine RCT studies, the results were positive regarding the efficacy of omega-3 fatty acids for body weight loss and fat mass. However, 11 other RCT studies did not show any significant changes in reducing body weight and body fat mass when omega-3 fatty acids supplementation was given. The results of these systematic review studies have not obtained conclusive results on the role of omega-3 fatty acids supplementation in reducing body weight and body fat mass.[14]

Salman et al.,[16] conducted research with an RCT design on 40 adults with obesity having a body mass index of 27−35 kg/m2 in Turkey. In this study, calorie restriction was also carried out apart from being given omega-3 fatty acids supplementation. Subjects were divided into two groups; the intervention group received 1020 mg omega-3 fatty acids (580 mg eicosapentaenoic acid (EPA), 390 mg docosahexaenoic acid (DHA), 50 mg omega-3 fatty acids other PUFAs) for 12 weeks. The researcher assessed anthropometric and body composition data as well as cognitive function assessments which were assessed using the Montreal Cognitive Assessment (MoCA). Based on the results of this study, there was a decrease in body weight, body fat mass, and body mass index in the intervention group compared to the control group ($p\leq0.05$), but no significant results were obtained regarding cognitive function.

Omega-3 fatty acids a polyunsaturated fatty acids (PUFAs) which are generally found in fish oil as Eicosapentaenoic Acid (EPA) and Docosahexaenoic Acid (DHA). Fish oil supplementation containing omega−3 fatty acids can reduce body fat mass by increasing lipid oxygenation. In addition, PUFA supplementation can reduce the incidence of obesity by reducing an individual's appetite, increasing fat oxidation, and reducing fat deposition. The role of omega−3 fatty acids in an individual's appetite is by suppressing the appetite mediated by free fatty acid receptor 4 G protein-coupled receptor 120 (FFAR4 (GPR 120)). Omega-3 fatty acids are an

FFAR4 agonist that stimulates the secretion of cholecystokinin, a peptide hormone that is synthesized and released from the small intestine and plays a role in suppressing hunger. [10]

Several studies stated that giving omega-3 fatty acids supplementation has positive results in reducing body weight and body fat mass. According to a study conducted by Ali S et al.,[15] giving omega-3 fatty acids supplementation could reduce body weight in women with obesity. Omega-3 fatty acids also play a role in reducing insulin resistance, TNF-α and leptin, and increasing adiponectin. Other literature stated that supplementation with EPA 1600 mg and DHA 800 mg can reduce fat mass in healthy adults. In experimental animals, giving omega-3 fatty acids plays a role in reducing retroperitoneal and epididymal fat mass.

Research conducted by Munro et al.,[11] on 39 adults with obesity showed that giving 6x1 g omega-3 fatty acids supplementation (70 mg EPA and 270 mg DHA) for 8 weeks had a significant reduction in body weight and fat mass in the intervention group compared to the placebo group ($p< 0.01$). The mechanism by which omega-3 fatty acids are associated with reduced body weight and body fat mass is not fully understood. Evidence suggests that omega-3 fatty acids modulate fat metabolism by stimulating lipolysis and increasing hepatic fatty acid oxidation, inhibiting fatty acid synthesis and VLDL secretion. Based on research by Jump et al.,[17] DHA had a key role in hepatic lipid synthesis, having a major impact on fat metabolism. The duration and dose of omega-3 fatty acids supplementation can affect weight loss.

Omega-3 fatty acids PUFAs can partition dietary fuel away from storage and toward oxidation by suppressing lipogenic genes and activating genes that encode mitochondrial and peroxisomal fatty acid oxidation in both the liver and muscle. Omega-3 fatty acids have a cardioprotective role which can improve endothelial function by increasing nitric oxide production.[18] Furthermore, during exercise, fish oil has been shown to increase arterial dilation and blood flow to skeletal muscle. Increased blood flow can improve the distribution of fat which can be used as an energy source in skeletal muscles. EPA plays a role in β-oxidation, while DHA plays a role in catabolism and storage in tissues. [19] Gene expression of fatty acid synthase, hormone-sensitive lipase, lipoprotein lipase, and phosphoenolpyruvate carboxykinase in retroperitoneal fat can be decreased with DHA and EPA/DHA, not just by giving EPA.[20]

In another research by Defina et al.,[13] on 128 subjects with overweight and obesity, intervention in the form of 3.0 g eicosapentaenoic acid (EPA) plus docosahexaenoic acid (DHA) with a ratio of 5:1 (EPA:DHA) for 24 weeks stated that there was no weight loss and significant fat mass. In this study, the intervention and placebo groups received lifestyle interventions and physical activity. The weight loss between the two groups was insignificant due to the lifestyle intervention.

The last research conducted by Ali S et al.,[15] on 45 patients with obesity given 180 mg EPA and 120 mg DHA for 12 weeks showed a significant body weight loss in the intervention group compared to the placebo group (3.07 ± 3.4 kg vs 1.16 ± 2.7 kg, $p = < 0, 05$). This study stated that the mechanism of omega−3 fatty acids for weight loss was still rarely found. Giving Omega-3 fatty acids along with dietary regulation and physical activity had more than 5% effect on weight loss.

The patient in the case is a 36 year old woman with grade 1 obesity. The patient's identity and diagnosis are similar to the identity and diagnosis of the research subjects discussed. Patients can be given omega-3 fatty acids supplementation for weight loss combined with dietary restriction and physical activity. Also, the patient can be advised to consume foods that are very high in omega-3 fatty acids, such as salmon, tuna, nuts, and flaxseed.

Conclusion

Reducing body weight and body fat mass in patients with obesity can be done by giving additional therapy which is omega-3 fatty acids supplementation. Based on a critical review that has been carried out in one systematic review and

three RCTs, omega-3 fatty acids supplementation can provide benefits on fat metabolism so that it can reduce fat mass and weight loss with diet modification in patients with obesity. Although omega-3 fatty acid supplementation is beneficial in reducing weight in obese patients alongside dietary modifications, further research is needed regarding its effective dosage.

Conflict of interest

The authors declare that they have no competing interests.

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