NUTRITION RESEARCH 34 (2014) 17–24

Available online at www.sciencedirect.com

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Long-chain polyunsaturated fatty acid supplementation had no effect on body weight but reduced energy intake in overweight and obese women

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A R T I C L E I N F O

Article history:
Received 13 December 2012
Revised 8 October 2013
Accepted 9 October 2013

Keywords:
DHA
Long-chain polyunsaturated fatty acids
Energy intake
Body mass index
Body composition
Randomized controlled trial

A B S T R A C T

Longer-chain polyunsaturated fatty acids may have greater appetite-suppressing effects than shorter-chain, monosaturated, and saturated fatty acids. Because fish oils are predominantly composed of *n*-3 long-chain polyunsaturated fatty acid and may assist in the treatment of obesity comorbidities, their effect on body weight and body mass index is of interest. We hypothesized that daily supplementation with docosahexaenoic acid (DHA)–rich oil would reduce energy intake and body weight in overweight and obese women compared with supplementation with oleic acid (OA) rich oil. A double-blinded, randomized, parallel intervention was conducted. Body mass index (in kilograms per meter squared), body weight (in kilograms), body fat (in percent), and lean tissue (in kilograms) were measured at baseline and 12 weeks after intervention with DHA or OA. Diet diaries were also completed at these time points for estimation of energy and macronutrient intake. Subjects reported significantly lower energy (P = .020), carbohydrate (g) (P = .037), and fat (g) (P = .045) intake after DHA compared with OA. Body mass or composition was not affected by treatment, although a fall in body weight in the DHA group approached statistical significance (P = .089). Daily ingestion of DHA over a 12-week period may reduce energy intake in overweight and obese females, but longer-term and adequately powered studies using subjects of both sexes are needed. Other factors that should be considered include the following: the choice of control, the body mass index category of subjects, and ways of improving the compliancy and accuracy of dietary assessment.

Abbreviations: %E, percentage total energy intake; BMI, body mass index; DHA, docosahexaenoic acid; LCPUFAs, long-chain polyunsaturated fatty acids; OA, oleic acid.

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0271-5317/$ – see front matter

http://dx.doi.org/10.1016/j.nutres.2013.10.004

1. Introduction

If recent trends continue, it has been predicted that up to 57.8% of the world's adult population could be either overweight or obese by 2030, and if realized, obesity will be the leading cause of death and disability worldwide [1]. The increase in obesity incidence has been primarily attributed to environmental and behavioral changes. Modern diets, which are typically high in fat, saturated fat, and trans-fatty acids, have been shown to attenuate lipid-induced satiety feedback signals, impair energy balance regulation, and favor weight gain. Paradoxically, the presence of fat in the small intestine and its subsequent digestion into free fatty acids slows gastric emptying, stimulates gastrointestinal hormone release, and suppresses appetite and energy intake [2,3]. The notion that lipids are the least satiating macronutrient remains controversial [4,5], and the suggestion that dietary fat intake plays a major role in obesity [6] has been fiercely contended [7,8].

Dietary fats vary substantially in terms of their fatty acid composition, chain length, double-bond position, and stereoisomeric configuration. Research to examine potential effects of the individual physiochemical properties of lipids on body weight and body composition is not comprehensive, but so far suggests that structural differences such as fatty acid chain length and degree of saturation could be influential [4,9-11]. Several mechanisms to explain why dietary intake of *n*-3 long-chain polyunsaturated fatty acids (LCPUFAs) can facilitate weight loss have been proposed but are not well understood. These include the following: increases in body fat oxidation and energy expenditure [12,13], changes in adipocyte apoptosis [14], reduction of adipose tissue mass [12,15-17], alterations in gene expression in adipose tissues that suppress lipid oxidation [14,16,18,19], increases in adiponectin [20], and appetite suppression [14].

Appetite is partly controlled by multiple integrated physiological mechanisms; short-term signals regulate meal initiation and termination, whereas humoral, long-term signals play a central role in body weight regulation [21]. There are 3 main phases (cephalic, postingestive, and postabsorptive) involved in the control of feeding. These phases initiate a cascade of behavioral, physiological, and metabolic events as well as neurotransmitter and metabolic interactions in the brain that serve to subdue or eliminate hunger and inhibit eating [22]. A number of hormones, neurotransmitters, and peptides that stimulate orexigenic or anorexigenic responses have been identified. The release of gut hormones such as cholecystokinin and glucagon-like peptide-1, for example, has been shown to slow gastric emptying, modulate glycemia, and suppress energy intake [23]. It appears that the composition of dietary fat influences the secretory response of some appetite-regulating hormones. In vitro and human studies have shown, for example, that LCPUFAs are more effective at stimulating cholecystokinin release than shorter-chain, saturated fatty acids [24-27]. Dietary intake of *n*-3 LCPUFA appears to affect other pathways involved in appetite regulation and metabolism. Eicosapentaenoic acid and docosahexaenoic acid (DHA), for example, act on the human mesocorticolimbic and endocannabinoid pathways to decrease the reward associated with food intake, thereby reducing appetite and energy intake and, subsequently, reducing body weight [28].

Studies examining medium-term (4-31 weeks) effects of fish or fish oil (containing high levels of *n*-3 LCPUFA) on body weight and body composition do not present consistent findings. The majority report no statistically significant effect on body weight [29-38]. Some studies found no effect on body weight or lean body mass, but observed significantly reduced body fat mass [39-42]. Conversely, 2 studies found that supplementation with fish oil reduced body weight in females. Kunesova et al [43] documented reduced body mass index (BMI) and hip circumference, but no change in body fat, in severely obese hospital in-patients after a very low-energy diet and exercise regime with 2.8 g/d *n*-3 LCPUFA supplement, as compared with those following the same diet and exercise regime with a saline control. Munro and Garg [44] found that obese women (but not men) had significantly reduced body weight and BMI after 4 weeks of supplementation with 6 g/d fish oil (2040 mg/d *n*-3 LCPUFA) followed by another 4 weeks of the same supplementation regime and a very low calorie diet.

Most researchers that have attempted to isolate the effects of *n*-3 LCPUFA fish oils on body weight have fed subjects oil-filled capsules [31-34,36,39,41,42,45]. There are obvious benefits to this protocol because it allows double-blinding and placebo-controlled conditions. In addition, the orosensory properties of fish oil, which are easily recognizable and commonly regarded as highly unpalatable, are masked. The problem with using capsules for fish oil delivery is that some people do not like taking these or struggle to swallow them and so do not comply with the prescribed regimen. This problem is exacerbated when the dose is high; some *n*-3 LCPUFA fish oil feeding studies have intervened with six 1 g capsules per day [35,40,41].

There is evidence suggesting that emulsification of fish oils improves the digestion and absorption of *n*-3 LCPUFA because of solubility modification; the emulsified and water soluble state increases exposure to lipase and delays gastric clearance rate [46,47]. When investigating the effects of different lipids, it is particularly important to facilitate the digestive process and maximize free fatty acid absorption. The effect of lipids on gastrointestinal motility and anorectic hormone release have been shown to be highly dependent on lipolysis of triglycerides into free fatty acids [24,48].

The objective of the following study was to compare the effects of 45% oil-in-water emulsions, containing predominantly DHA or oleic acid (OA), on body weight, BMI, and food intake in 40 overweight and obese women using a randomized, double-blinded, 2-way, parallel study design. We hypothesized that body weight, BMI, and energy intake would be reduced in those who took a daily supplementation of DHA, compared with a daily supplementation of OA.

2. Methods and materials

2.1. *Subjects*

Women aged 23 to 60 years were recruited via e-mail at the University of Sheffield and Sheffield Hallam University. Subjects were excluded if they had the following: BMI of 24.9 kg/m^2 or 40 kg/m^2; were unable to eat fish; had been diagnosed as having