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Consuming a balanced high fat diet for 16 weeks improves body composition, inflammation and vascular function parameters in obese premenopausal women☆

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ABSTRACT

Objective. Inflammation, insulin resistance and vascular dysfunction characterize obesity and predict development of cardiovascular disease (CVD). Although women experience CVD events at an older age, vascular dysfunction is evident 10 years prior to coronary artery disease. Questions remain whether replacing SFA entirely with MUFA or PUFA is the optimal approach for cardiometabolic benefits. This study tested the hypotheses that: a) body composition, inflammation and vascular function would improve with a high fat diet (HFD) when type of fat is balanced as 1/3 SFA, 1/3 MUFA and 1/3 PUFA; and b) body composition, inflammation and vascular function would improve more when balanced HFD is supplemented with 18C fatty acids, in proportion to the degree of 18C unsaturation.

Methods. Obese premenopausal women were stabilized on balanced HFD and randomized to consume 9 g/d of encapsulated stearate (18:0), oleate (18:1), linoleate (18:2) or placebo.

Results. Significant improvements occurred in fat oxidation rate (↑6%), body composition (%fat: ↓2.5 ± 2.1%; %lean: ↑2.5 ± 2.1%), inflammation (↓ IL-1α, IL-1β, 1 L-12, Il-17, IFNγ, TNFα, TNFβ) and vascular function (↓BP, ↓PAI-1, ↑tPA activity). When compared to HFD + placebo, HFD + stearate had the greatest effect on reducing IFNγ (↓74%) and HFD + linoleate had the greatest effect on reducing PAI-1 (↓31%).

Abbreviations: AR1, autoregressive order one; BP, blood pressure; BMI, body mass index; CVD, cardiovascular disease; DEXA, dual energy x-ray absorptiometry (DEXA); FFA, free fatty acid; FMD, flow mediated dilatation; HDL, high density lipoprotein; HFD, high fat diet; HFD + P, high fat diet + placebo; HFD + S, high fat diet + stearate; HFD + O, high fat diet + oleate; HFD + L, high fat diet + linoleate; HOMA-IR, homeostatic model assessment of insulin resistance; IL, interleukin; PAQ, modified Baecke physical activity questionnaire; LDL, low density lipoprotein; PL, phospholipid; PAI-1, plasminogen activator inhibitor-1; tPA, tissue plasminogen antigen; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid; RQ, respiratory quotient; REE, resting energy expenditure; SAEI/LAEI, small and large artery elasticity index; TG, triglyceride; VCRC, Vanderbilt clinical research center.

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Conclusions. Balancing the type of dietary fat consumed (SFA/MUFA/PUFA) is a feasible strategy to positively affect markers of CVD risk. Moreover, reductions in inflammatory molecules involved in vascular function might be enhanced when intake of certain 18C fatty acids is supplemented. Long term effects need to be determined for this approach.

1. Introduction

Inflammation, insulin resistance and vascular dysfunction are characteristics of obesity that predict development of cardiovascular disease (CVD) [1]. Dietary fatty acids, particularly long chain saturated fatty acids (SFA), promote obesity related inflammation and vascular dysfunction by regulating production of adipocyte derived chemokines and cytokines [2,3] and macrophage accumulation into vascular walls. During weight stability, diets high in SFA can impair endothelial function, a marker of coronary vascular function that predicts atherosclerosis [4]. Conversely, weight loss may improve endothelial function [5,6], whether caloric restriction encompasses low or high fat intake [7,8]. Rather than focusing solely on amount of fat, recent strategies target replacing SFA with monounsaturated (MUFA) or polyunsaturated (PUFA) fat.

Although high MUFA or PUFA intake decreases total and LDL-cholesterol, and apolipoprotein B levels [9,10], a high MUFA diet has not wholly improved vascular function or reduced coronary artery atherosclerosis [11]. Alternatively, high PUFA intake may improve endothelial function [12] and reduce coronary disease risk [9], although the type of PUFA could impact effects [13]. Additionally, not all SFA can be considered unfavorable as metabolic effects differ, partly due to carbon chain length [14]. While the 16-carbon SFA palmitate raises total, LDL- and HDL-cholesterol levels and robustly promotes inflammation and vascular dysfunction [15,16], the 18-carbon SFA stearate has neutral effects [17]. Hence, a high fat diet where the proportion of total fat from SFA, MUFA and PUFA is balanced may potentiate the greatest CVD risk reduction.

Sex differences have been recognized in vascular function, apparently due to the smaller size and greater stiffness of the female heart and vasculature as well as distinct hormonal milieu [18]. Although women experience cardiovascular events later than men, vascular dysfunction has been detected 10 years prior to actual CVD [19]. The aim of the present study was to test the hypothesis that body composition, inflammation and vascular function in obese premenopausal women would improve with a high fat diet (HFD) when the type of fat is balanced as 1/3 SFA, 1/3 MUFA and 1/3 PUFA. We further hypothesized that, while consuming the balanced HFD, improvements in body composition, inflammation and vascular function would be greater when supplemented with 18C fatty acids — in proportion to degree of 18C fatty acid unsaturation. To test these hypotheses, subjects were stabilized on balanced HFD during a two-week standardization period and then randomized to 9 g/d of encapsulated pure stearate (18:0), oleate (18:1), linoleate (18:2) or placebo while continuing HFD.

2. Methods

2.1. Subjects

Of 731 respondents, 245 met inclusion criteria of being female, age 21–50 years, premenopausal, and Class I/II obesity (BMI 30–39.9 kg/m^2) with weight stability (± 2.2 kg) over three months prior (Fig. 1). Exclusion criteria were tobacco use; alcohol or substance abuse; diabetes, cardiovascular, thyroid, kidney or liver disease; inflammatory condition; hypertension (systolic ≥ 150/diastolic ≥ 95 mmHg); hyperlipidemia (serum triglycerides ≥200 mg/dL or LDL-cholesterol ≥130 mg/dL); pregnancy or lactation. Additional exclusions were evidence of disordered eating by Eating Attitudes Test score ≥20 [20] and/or Three Factor Eating Questionnaire score <14 [21]; appetite reducing medications, daily aspirin, Coumadin or ACE inhibitors, or dietary supplements other than multivitamin/mineral; and consuming >4 cups regular coffee or black tea daily.

Upon consent, demographic information was collected and a fasting venous sample was obtained for complete blood count, basic metabolic panel, liver enzymes and lipid profile to rule out serious illness and hyperlipidemia. Physical measures were obtained in triplicate for seated blood pressure, height (± 0.1 cm), weight (± 0.1 kg), and waist and hip circumferences (± 0.1 cm), and BMI was calculated for eligibility.

Subjects were interviewed for diet, weight and gastrointestinal health history and the Modified Baecke Physical Activity Questionnaire (PAQ) [22]. Three 24-h diet recalls were performed by the Vanderbilt Nutrition and Diet Assessment Core using standardized probes (NDSR 2011, Nutrition Coordinating Center, Minn., MN), portion estimation utensils, and multiple-pass methodology [23]. Of 245 qualifying respondents, 230 were enrolled and scheduled for baseline testing at the Vanderbilt Clinical Research Center (VCRC). The Vanderbilt University Institutional Review Board approved the study protocol which was registered in the U.S. National Institutes of Health ClinicalTrials.gov registry (NCT00696228).

2.2. Diet and supplement protocol

This study was a randomized double-blind placebo controlled trial to compare balanced high fat diet (HFD) to HFD supplemented with stearate (HFD + S), oleate (HDS + O) or linoleate (HFD + L). One hundred and forty-four women began the two-week HFD stabilization period by following daily menus calculated in NDSR to provide a macronutrient composition of 50% fat, 30% carbohydrate and 20% protein. Total fat was balanced as 1/3 SFA, 1/3 MUFA and 1/3 PUFA, and total carbohydrate as ½ simple and ½ complex (Table 1). To further standardize fat intakes, all sources of fats including oils, spreads, nuts and seeds were provided weekly in pre-portioned