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Postprandial coagulation activation in overweight individuals after weight loss: Acute and long-term effects of a high-monounsaturated fat diet and a low-fat diet

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ABSTRACT

Diet is important in the prevention of cardiovascular disease, and it has been suggested that a high-MUFA diet is more cardioprotective than a low-fat diet. We hypothesised that the postprandial thrombotic risk profile is improved most favourably by a high-MUFA diet compared with a low-fat diet. This was tested in a parallel intervention trial on overweight individuals (aged 28.4 (SD 4.7) years) randomly assigned to a MUFA-diet (35-45% of energy as fat; >20% as MUFA, n = 21) or a low-fat (LF) diet (20-30% of energy as fat, n = 22) for 6 months after a weight loss of ~10%. All foods were provided free of charge from a purpose-built supermarket. Meal tests designed after the same principles were performed before and after the dietary intervention, and blood samples were collected at 8.00 h (fasting), 12.00 h, and 18.00 h and analysed for factor VII coagulant activity (FVII:C), activated FVII, fibrinogen, prothrombin fragment 1 + 2 (F1 + 2), D-dimer, plasminogen activator inhibitor (PAI:Ag), and thrombin activatable fibrinolysis inhibitor. There were significant postprandial increases in F1 + 2 and D-dimer before and after dietary intervention, with significantly lower values after 6 months. No significant differences were observed between the postprandial changes induced by the two diets. The postprandial decrease in FVII:C and PAI:Ag did not differ before and after intervention, irrespective of the diets. Our findings suggest postprandial coagulation activation in overweight subjects with more pronounced acute than long-term effects. We observed similar effects of the MUFA diet and the LF diet on the postprandial prothrombotic risk profile.

Introduction

The type of dietary fat and carbohydrate are important factors in the prevention of cardiovascular disease (CVD) as demonstrated in The Nurses´ Health Study, a large prospective study in 121.700 initially healthy nurses [1]. Based on this study, an alternative dietary pyramid was introduced in the United States [2]. The main difference between Willett's new pyramid and the United States Department of Agriculture (USDA) 2004 Food Pyramid is that the new pyramid has no restrictions on fat as long as it is of vegetable origin, and the carbohydrates should have a high content of whole grains. Such a diet is assumed to have a more cardioprotective effect than a diet following the USDA 2004 Food Pyramid [3].

Although the Nurses´ Health Study is a very large and well-designed study, the study conclusions should not alone be used to change the established dietary recommendations without results from long-term controlled comparisons with existing dietary recommendations. Because a controlled randomised dietary study in healthy individuals with CVD as end point will be practically infeasible CVD risk markers can be studied as an alternative.

In a 6-month strictly controlled dietary intervention study in overweight subjects after weight loss we have recently compared the diet in Willett's new pyramid with the official Nordic dietary recommendations [4]. There was no difference between the two diets with respect to weight loss maintenance [5], but the Nordic diet was superior with respect to changes in fasting concentrations of haemostatic variables [6], which are important markers of CVD risk in prospective studies [7–11]. In the fasting state, only concentrations of fibrinogen differed between the two diets, but because we spend most of our lives in the

Abbreviations: CVD, cardiovascular disease; USDA, United States Department of Agriculture; MUFA, monounsaturated fatty acids; GI, glycaemic index; MUFObes, Mono Unsaturated Fatty acids in Obesity; LF, low-fat; BMI, body mass index; FVII, factor VII; TAFI, thrombin activatable fibrinolysis inhibitor; F1 + 2, prothrombin fragment 1 + 2; PAI, plasminogen activator inhibitor type 1; ELISA, enzyme-linked immunosorbent assay; ANOVA, analysis of variance; ICAM, intracellular adhesion molecule; CRP, C-reactive protein; VLDL, very low density lipoprotein.

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non-fasting state it seems even more relevant to focus on the postprandial effects on haemostatic variables. A number of studies have reported postprandial effects on these CVD risk markers in high-energy/high-fat meal studies [12–17], but no studies have looked at the long-term effects of complex ad libitum dietary changes.

The aim of this study was therefore to investigate the acute and long-term postprandial effects on haemostatic variables of two different diets in healthy overweight subjects. The diets compared were Willett's new Healthy Eating Pyramid (high in monounsaturated fatty acids (MUFA) and low in glycaemic index (GI)) and the Official Nordic Dietary Guidelines (low in fat and medium in GI). Based on the results of the Nurses' Health Study we hypothesise that the acute and long-term postprandial thrombotic risk profiles are improved most favourably by the high-MUFA diet compared with the low-fat (LF) diet.

Materials and Methods

Study population

The dietary intervention, Mono Unsaturated Fatty acids in Obesity (MUFObes), was conducted at the Department of Human Nutrition, Faculty of Life Sciences, University of Copenhagen, (Frederiksberg, Denmark) and described in detail elsewhere [5,18]. Briefly, 131 overweight individuals were randomly assigned to one of three diets (a MUFA diet, a LF diet, and a control diet) as well as to subgroup A or B, which determined the type of clinical examination that subjects should undergo at 0 months and after 6 months of dietary intervention. The inclusion criteria for the study were age 18–35 years, BMI 28–36 kg/m^2, body weight fluctuations of <3 kg over the previous 2 months, and a non-smoking status. Subjects were healthy and took no regular medicine other than contraceptive pills. All subjects gave oral and written informed consent, and the Ethics Committee of the Municipalities of Copenhagen and Frederiksberg approved the study according to the Helsinki Declaration. The trial was registered at clinicaltrials.gov as NCT00274729.

The present study focuses on effects of the MUFA diet and the LF diet in subgroup B, i.e. in individuals who underwent meal tests at 0 months (n = 21 for the MUFA diet, n = 22 for the LF diet). The control diet was left out of analysis due to a low number of study participants completing the intervention (n = 8). The population characteristics at study entry of subjects randomised to the meal tests are described in Table 1. For various reasons, 10 participants dropped out during the 6-month intervention period, leaving 15 participants in the MUFA group and 18 participants in the LF group for the meal tests at 6 months [5]. The primary reasons for drop-outs were related to personal reasons and diseases, but also related to the demanding nature of the project.

Table 1
Population characteristics at study entry of subjects randomized to the meal tests.

Variable	MUFA meals (n = 21)		LF meals (n = 22)	
	Mean	95%CI	Mean	95%CI
Age	29.5	27.6-31.3	28.0	26.0-30.1
Gender (♂/♀)	10/11		9/13	
BMI (kg/m^2)	29.1*	27.9-30.4	27.0	25.9-28.1
WHR	0.87	0.84-0.90	0.85	0.82-0.88
Triglycerides (mmol/l)†	1.07	0.87-1.30	0.99	0.82-1.20
Cholesterol (mmol/l)	4.29	3.97-4.60	4.38	3.99-4.76
LDL-cholesterol (mmol/l)	2.65	2.35-2.94	2.62	2.29-2.96

LF, low-fat; WHR, waist-hip ratio.
Values were compared with an unpaired t-test. Gender was compared with the chi^2-test.
*$p < 0.05$. †Triglycerides were logarithmically transformed before analysis (geometric mean and 95% CI).

Study design

The study was a parallel intervention trial comparing dietary effects on body weight and cardiovascular risk after 6 months of intervention. The study design is presented in Fig. 1 and described in detail previously [5,18].

The focus of the present study was the meal tests, which were conducted at 0 months (the end of the 3-week standardization period, during which the participants were eating an average Danish diet) and after the 6-months dietary intervention period in order to test the acute and long-term postprandial effects of the MUFA diet and the LF diet (Fig. 1). The test meals (MUFA meals and LF meals) were served to the participants and eaten under observation at the Department of Human Nutrition. On both meal test days (at 0 months and 6 months) breakfast and lunch were served immediately after blood sampling at 8.00 h and 12.00 h, respectively. The evening before, the study participants consumed an average Danish diet (at 0 months) or one of the two experimental diets (at 6 months). They were not allowed to eat anything after 20.00 h. On the two study days the participants were not allowed to leave the Department, and they were not allowed to eat anything except the study meals, drink anything except water, or to perform any heavy physical activity.

The experimental diets

The 6-months dietary intervention was based on an ad libitum design in order to mimic free-living conditions and to test the real appetite regulation of the diets. To provide the subjects with all necessary foods, free of charge, and to accomplish a total recording of the food consumed, a validated supermarket model was established at the department [5,18–20]. The MUFA diet and the LF diet were as follows: (1) the MUFA diet moderate in fat (35-45% of energy), high in MUFA (>20% of energy) and moderate in low-GI carbohydrates (40-50% of energy); (2) the LF diet low in fat (20-30% of energy) and high in mixed-GI carbohydrates (55–65% of energy). Both diets were moderate in protein (10–20% of energy). Foods recommended for the two dietary groups have previously been described [5,19]. The actual dietary composition was in accordance with the prescribed dietary composition, and the biopsy content of fatty acids (assessment of compliance) was in accordance with the prescribed diets [5,19].

The test meals were designed after the same principles, and the energy and nutrient contents of the meals are described in Table 2. The dietary composition has been described in detail elsewhere [21]. The experimental meals were isoenergetic, and the energy content was calculated individually using World Health Organization equations [21,22]. The breakfast and the lunch contained 20% (~2.5 MJ) and 33% (~4.0 MJ) of the daily energy requirement, respectively. All meals were prepared in the metabolic kitchen at the Department of Human Nutrition, and all ingredients were precisely weighed out. A detailed description of the meal test days has been published by Sloth et al. [21].

Blood sampling

Venous blood samples were drawn at 8.00 h (fasting), 12.00 h, and 18.00 h after 10 min of standardized resting in a chair. Blood samples at 8.00 h were drawn after at least 10 h fasting and 24 h abstention from alcohol and strenuous physical activity.

Blood samples were collected with minimal stasis using siliconized vacutainers and 21-gauge needles. For the present study, 4.5 ml blood were collected in 0.5 ml 0.129 mol/l trisodium citrate at room temperature and used for the analysis of blood coagulation factor VII (FVII), fibrinogen, D-dimer, thrombin activatable fibrinolysis inhibitor (TAFI), triglycerides, and total cholesterol, and 4.5 ml blood were collected in 0.5 ml 0.129 mol/l trisodium citrate tubes on ice for the analysis of